Reviewer's report

Title: Multilevel analysis of systolic blood pressure and ACE gene I/D polymorphism in 438 Swedish families - a public health perspective

Version: 2  Date: 20 January 2006

Reviewer: Cathryn M Lewis

Reviewer's report:

General
My apologies for the length of time it has taken to review this paper. The authors have applied multilevel regression analysis to Swedish families in three studies of hypertension (specifically, SBP). They estimate the familial clustering of SBP, particularly in individuals on ACE-inhibitors, and include the ACE I/D polymorphism in the analysis. They conclude that substantial familial clustering of SBP exists, particularly at later ages, and independent of the ACE I/D polymorphism.

This paper applies a complex statistical tool to a detailed data set, and the description of the methods, results and interpretation are clear throughout. Multilevel modelling is widely used in other fields, and this paper is one of the few applications in genetics, and shows that this may be a valuable tool in family-based genetic studies.

I have only minor comments to improve the clarity of the paper.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
None

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
None

Discretionary Revisions (which the author can choose to ignore)

Statistical analysis, p6. Make clear that model III includes the ACE gene ID polymorphism *in addition* to the variables in model II.

P7/Figure 1. At what level are the random slopes estimated? Does each family produce one slope? This should be made clear in the text.

Table 1: Was there any difference in I/D frequency between the three populations?

P8/9 Could a p-value for the difference in SBP for II and ID individuals be given?

Figure 1: Could the authors explain clearly why familial differences in SBP ‘were higher in users of ACE inhibitors’? (presumably because of the greater spread of points in ‘YES’?)

Typos:
P8 Markov is mis-spelled as Marcov
P10 Believes should be beliefs.
Table1: Absolute values of Change in VF should be 8.3, not 8,3 etc.

What next?: Accept after discretionary revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests