Reviewer's report

Title: The impact of population heterogeneity on risk estimation in genetic counseling

Version: 1 Date: 18 December 2003

Reviewer: Christine Fischer

Reviewer's report:

General
The authors investigated an example of the wellknown biometrical problem of misspecification of a logistic model resulting in biased estimates of outcome variable. They chose the example of population heterogeneity with different disease probabilities and the effect of ignoring part of the structure. The amount of bias was demonstrated using simulated data. The problem is not new although it is valuable to have an example for the application in genetic counseling. Unfortunately the authors ignored the biometrical literature completely (e.g. Begg MD, Lagakos S: On the consequences of model misspecification in logistic regression. Environ Health Perspect. 1990 Jul;87:69-75). Existing knowledge should be reviewed and included in the respective parts of the manuscript.

Discretionary Revisions (which the author can choose to ignore)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
None