Reviewer's report

Title: Notes on causality and susceptibility to disease

Version: 1 Date: 7 February 2006

Reviewer: Jonathan Samet

Reviewer's report:

General
This well-written essay addresses a number of facets of causality in the genomic era. The authors consider concepts of causation and models that consider interactions among multiple factors. While I enjoyed reading the essay and found it to be well-written, I did not find any major advance in the formulation of causation under various scenarios of gene-environment interaction. Much of the manuscript is given over to a review and stage-setting and the examples cited are not adequate. The authors also might better acknowledge more recent literature on causation in epidemiology, biostatistics, ecology and other areas. How could the manuscript be improved?

• A deepening of the discussion of causal inference in epidemiology, perhaps extending beyond the work of Rothman, now many decades in the past.

• A deeper consideration of assessment of interactions and their interpretation in the face of often inadequate data.

• Further consideration of attributable risk estimation under the various scenarios that they propose.

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

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

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Discretionary Revisions (which the author can choose to ignore)

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