Reviewer's report

Title: Validation of a model to investigate the impact of modifying cardiovascular disease (CVD) risk factors on the burden of CVD: the Rotterdam Ischemic heart disease and Stroke Computer simulation model (RISC) model.

Version: 1 Date: 21 June 2012

Reviewer: Simon Capewell

Reviewer's report:

Major Compulsory Revisions
Van Kemperen et al Review.

An interesting paper.
Could be made even better

1. It is not clear how the model, which seems to be a closed cohort simulation comprising age groups >50, could be used for exploring the effects of interventions on CVD burden in the general population. Please clarify.

2. I think that the authors need to discuss more the limits that the age range imposes in their model usefulness. Although they included most of the relevant age groups for the CVD problem, underestimation of premature mortality, particularly among men could be a concern.

3. Interesting difference in performance appear when applied to the EPIC data. Although differences in baseline risk and the calibration procedure itself may explain the discrepancies, could a possible alternative explanation be differences in censoring in the observed data? Please clarify

4. It will be VERY helpful to see the performance of the model presented by gender and age.

5. The authors appropriately addressed the lack of some variables in the EPIC cohort to fully reproduce the model. They suggest that the incremental value of these items is probably limited, and I agree with this. Could the model then be specified with the more limited set of risk factors and still perform well? This certainly will increase its potential for use in different populations and settings. It would be helpful to see this simpler analysis.

6. The authors discuss model validation using a framework that only explores part of the concept. There is a more comprehensive framework published by Kopec et al (see BMC Public Health 2010, 10:710 doi:10.1186/1471-2458-10-710) that covers many of the validation exercises the authors conducted. It will be really useful if the authors can address or discuss some of the other validation aspects that are important and suggested by Kopec.
et al in their paper.

Minor Essential revisions
7. The penultimate sentence in the 3rd paragraph of the discussion citing references 22 and 31 seems to be incomplete.

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**
None