Reviewer's report

**Title:** Life style and longevity among initially healthy middle-aged men: prospective cohort study

**Version:** 3  **Date:** 21 May 2013

**Reviewer:** Giorgio Bedogni

Reviewer's report:

**GENERAL COMMENT**

I was asked to review this paper as BMC statistical referee.

I read version 3 of the MS (05 Feb 2013) and the replies of the Authors to the Reviewers.

I was specifically asked:

1) whether the employed analytic strategy is appropriate;
2) whether sample size is enough to test the study hypothesis.

I will start by answering the two questions that I was specifically asked:

1. The choice of the analytic strategy, i.e. logistic regression, is reasonable in the context of the aim of the study, that is to establish whether selected midlife variables can predict that a person reaches 85 years of age. Of course, the price to pay is a loss of power compared to survival analysis where more subjects would be counted for power, not only those experiencing the outcome. However, the choice of the method should be dictated first of all by the study question.

2. If the Authors have calculated sample size BEFORE performing the study they should tell so and how they did it. I expect that a sample size was calculated for the original aim of the study but this may have not be done for the present analysis. A post-hoc calculation of sample size should be avoided because it is meaningless, eg. http://ndt.oxfordjournals.org/content/early/2010/01/12/ndt.gfp732.full. 95% confidence intervals will tell about the precision of the estimates in every case. Whether the (possible) lack of calculation of sample size is a limitation should also be judged in the context of the available literature, something which I have not the necessary knowledge to do.

I have also the following comments:

**MAJOR COMMENTS**

Please report 95% confidence intervals (CI) for all effect sizes, including frequencies. For instance, 37% of non-smokers vs. 23% of non-smokers survived up to 85 years. What are the corresponding 95% CI? They are important to
MINOR COMMENTS

Please, describe in greater detail the univariable and multivariable regression models under Statistical Analysis. All predictors and their codification for analysis should be reported here. For instance, from Table 4, I infer that cholesterol and systolic blood pressure were modeled as continuous as their effect is coded as 1 SD increase. This should be mentioned under statistical analysis. Speaking of continuous predictors, did you check whether their uni- and multi-variable logits were linear? Or did you transform them appropriately when needed? How?

Smoking is modeled in 3 different ways: yes vs no (table 1), 0 vs. 1-9 vs. >=10 cigarettes (table 2) and >=10 vs <10 (table 4). Table 1 is probably for descriptive purposes of the two groups and there is no reasonable alternative. Why did you switch from [0 vs. 1-9 vs. >=10 cigarettes] to [>=10 vs <10]? Was this because there was no statistically significant difference between the 0 and 1-9 groups in Table 2? Which test was used to assess this difference? I wonder what would happen by modeling the number of cigarettes as continuous. This will make the analysis more difficult but will increase power and make the estimate of the effect of the increasing number of cigarettes more solid. However, the most important point to me is that there is no way to tell in advance whether an n-tomization suggested by univariable analysis will hold at multivariable analysis.

Why was age split at 55 years? Was this the median age of the sample at baseline? Wouldn't it be better to model age as continuous, at least in a preliminary analysis? This may give a better insight into the relations of interest even if one has no reason to suspect that the difference of 8 years between those age 59 and 51 years could impact on the probability of reaching 85 years.

Fitness was operationally defined as work divided per unit of weight and corrected for age by linear regression. Is this the standard practice in the field? Again, I would not risk imposing structures to the data with n-tomization (tertiles) UNLESS they are biologically or clinically sound.

From this perspective, BMI has no problem in being treated as discrete (besides the obvious loss of power as compared to when it is modeled as continuous). How many underweight (e.g. BMI < 18.5 kg/m2) there were among smokers and not smokers?

You performed a separate analysis for smokers and non-smokers. A way to (potentially) increase power is using smoke as predictor (in your case would be <10 vs >=10 cigarettes) in the same logistic regression model. This has added benefit of making possible to test X*smoke interactions (within the power allowed by sample size, of course). Have you considered this possibility? Even more power could be gained by testing continuous X*smoke interactions. I do not think that this way of approaching the problem is at odds with the suggestion you give in the Discussion to model separately smokers and non-smokers. This way one could compare the estimates presently made separately for smokers and
non-smokers.

Please, note that the effect attributable to fitness (high vs low) in non-smokers is highly variable: from very small (1.11) to very high (3.08). I believe that this has to be discussed in the MS by saying that further studies with larger number of subjects reaching 85 years (from were power comes from) are needed to provide more precise estimates of this effect. Although not statistically significant, the effect size attributable to fitness in smokers is not very different (0.95 to 3.39). One wonders whether the uneven distribution of outcomes/subjects in the two groups may be partly responsible for this difference and whether the strategy of using smoke as covariate (see above) could give better insight into this finding.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests