Reviewer's report

Title: A review of the reporting and handling of missing data in cohort studies with repeated assessment of exposure measures

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Reviewer: Volkert Siersma

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This paper contains a review of the methods of reporting and handling missing data in cohort studies with repeated assessment of exposure methods. The message is supposedly that a lot can be improved – and I suspect that a lot has improved over the time span of the review, but I cannot read that from the tables in the paper – but I miss an argument why missing exposure data in just these particular type of studies is especially troublesome. In the meantime, the authors provide a list of methods to deal with missing data and their merits which would be quite useful if provided with some practical guidance.

Major compulsory revisions

1) At first reading I couldn’t believe that there were just 82 papers published where exposure was measured several times in the course of the study. My own experience says that indeed many of such cohorts exist, but not often something intelligent is done to incorporate the repeated exposure measurements. My guess is then that the authors specifically aimed at studies that do incorporate the repeated exposure measurements in the analysis. It would then be interesting to have some stats on which analyses were used in the papers and a discussion what is won by measuring exposure repeatedly. I come to think of two analyses that fit the bill (but correct me if there are others that I have forgotten): survival analyses with time-varying confounders (exposure) and multivariable (outcome + exposure) longitudinal analyses. It is to be noted that both these methods are not without problems: the former often implicitly assumes that a measured exposure is indicative for the exposure over the whole period until the next exposure measurement and thereby using some LOCF principle that supposedly is faulty, and the latter has complicated causal properties and one has to be careful in constructing the model not to estimate the wrong effects. However, there are a lot of fancy and complicated analyses that can be done on observational data, and they may not be in need of the same reporting of missing exposure data as the “usual” methods. I suggest that the authors are more clear in what analyses are assumed in the papers they review.

2) The second thing that lacks is a discussion on what is so peculiar with the missing exposure data; in comparison with missing outcome data for example. Here a data example (simulated data?) could be very helpful to show how missing exposure data and the naïve handling of it results in wrong results. The
same data example could be used to illustrate proper reporting practice and the practicalities of the methods of handling missing data (and how they sometimes fail).

3) I am not familiar with STROBE or Jonathan Sterne’s guidelines, but the short description given in the present paper sounds lofty enough. However, I am not convinced that these reporting guidelines are enough, or feasible (often you just don’t know why a person did not return your questionnaire). Moreover, I suppose that these guidelines assume a particular type of analyses which should be stated in the paper. As these guidelines were published only in 2007, we would not expect papers before this date to adhere to them; can we see this in the data? The authors conclude that journals should provide room for online supplements on missing data; I would add to that “missing data handling” as many techniques for handling missing data use elaborate modeling in itself for which there often is no place in the paper.

Minor essential revisions

4) There is a strong focus on multiple imputation which may not be so appropriate. Weighting methods are often fine and they are in some places classified under complete-case analysis which would make some readers think that they are somehow inferior.

5) The authors should rethink the structure of the manuscript, but this will be necessary anyway if my comments above are to be addressed.

Discretionary revisions

6) Among the reasons why exposure information may be missing I miss death. Maybe this is done on purpose since exposure (and outcome) may not be very well defined for dead people. In the literature on longitudinal studies with attrition, there is discussion on whether it gives meaning to impute the missing values for dead people, and there is a strong argument for not imputing these as this answers the only research question that is clearly relevant in some settings (the average outcome in the survivors). See for example: Kurland, Johnson, Egleston, Diehr (2009) Longitudinal data with follow-up truncated by death: Match the analysis method to research aims. Statistical Science 24, 211-222. Maybe it is good to at least mention this issue somewhere in the paper.

In conclusion, the paper hides over a valuable review, but it needs work to get the message out in a way that will be useful for the readers of BMC Medical Research Methodology.

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