Reviewer’s report

Title: Psychosocial risk factors for hospital readmission in COPD patients on early discharge schemes: a cohort study

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Reviewer: Kim Lavoie

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Biomed Central Pulmonary Medicine
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Psychosocial risk factors for hospital readmission in COPD patients…
Resubmission 1

The authors have addressed many of the questions and concerns raised by myself and the other reviewers, and I thank the authors for taking the time to consider our questions and suggestions. However, there are some responses that either require additional clarification or are not satisfactory. I have detailed these below.

Major compulsory revisions.

1. Authors’s response to Dr. Gruffydd-Jone’s comment: Please justify the use of a questionnaire (ESSI) which has not been validated in the disease area under study.

“We have added more detail in the Methods about why we used the ESSI which includes validated questions about perceived emotional support – this type of support is known to be predictive of people’s ability to cope with stress from mental and physical health problems. The disease group under study should not affect response to generic questions about perceived emotional support which are premised on the buffering hypothesis that has salience across populations (Brown and Harris 1978).”

The additional information about the ESSI is appreciated. However, the 2nd part of the authors’ response suggests they may not have understood Dr. Gruffydd-Jones’s comment. In the absence of a validation study of the psychometric properties of the ESSI in the population under study (ie, COPD patients), we could expect a different factorial structure of the ESSI in the disease area under study. In others words, it is possible that higher scores on the
ESSI observed here would be not due to higher levels on the construct of interest (i.e., perceived social support) but rather (i) to the instrument measuring a different construct, or (ii) measuring it differently in the current sample. In sum, the authors should indicate it in the limitation section.

2. Both Dr. Gruffydd-Jones and myself requested justification for powering the study based on a secondary endpoint (SGRQ). The authors’ response: “We have edited the paragraph in the methods on sample size so that it relates to our primary outcome” and edits made to the paper: “Logistic and survival models produce stable estimates if the limiting sample size allows for a ratio of 10–15 observations per predictor variable [38]. Based on previous data [2] it was estimated that a sample of 150 would yield 100 events for a regression model” on page 7 unfortunately, do not directly address our question and raise additional concerns. Did the authors make a mistake when writing this section the 1st time? Their response does not clarify why they had originally powered the study based on a secondary outcome, nor does it clearly state that the study was ACTUALLY AND ORIGINALLY powered based on their primary outcome (admission/death), which is what the paper edits suggest (but again, it is not clear). The concern here is that there was no acknowledgement of making a mistake (if indeed that was the case in the original version), and I wonder about whether the study was originally powered appropriately. The consequences are that this undermines confidence in the results.

3. I had originally requested information about how many patients were excluded for each of the exclusion criteria, and the authors’ response: “We do not have access to data related to patients excluded from enrolment on an EDS service – this is data used to determine eligibility for EDS at each of the hospital sites. However we have stated in the first paragraph of the results that one patient was excluded from the cohort study because of newly diagnosed lung cancer” was a bit confusing. Study exclusion versus EDS exclusion are not necessarily the same, but this response would suggest there were no specific study exclusion, and that the authors excluded patients who were not eligible for EDS at each hospital site. Is this the case? If so, could the authors clarify? Also, if data on the number of patients excluded for each reason is not available, could they at least provide the total number of patients excluded for these reasons? Ideally, the authors would present the total number of COPD admitted for acute exacerbation across the three study hospitals (if 43 refused + 1 cancer patient, and the final sample size was 79, were only 123 patients refereed to EDS over the study period? This seems low?), and then the total number of patients referred for EDS (across the three sites) that ended up in the study (which appears to be 79). In sum, please clarify the patient flow through the study, which is important to determine generalizability of results.

4. Regarding the modest participation rate of 65%, I suggested that one possible explanation might have been that patients felt the home visits were intrusive. The authors’ response that: “most patients in our study anecdotally reported that they valued the EDS nurses and were comforted by their presence. Furthermore, again, anecdotally, patients that were enrolled in this cohort study were very
enthusiastic about being involved in the study” suggests another possibility, that there was some self-selection bias towards inclusion (or participation) of the most positive and enthusiastic patients, which also potentially limits generalizability of results. Could the authors comment on this?

5. Regarding who collected the data at baseline and follow-up, the authors clarified that indeed it was the study PI and primary author (PC) who undertook both baseline and follow-up assessments, who was not blind to patients’ baseline psychosocial status (see page 5 of paper). While the clarification is appreciated, it does raise some important methodological concerns. How can you exclude the possibility of bias in assessment and recording outcome data when it was not only the same person who conducted baseline and f-up assessments, but the study PI (and first author) who has the greatest stake in the study findings? This is problematic and a major source of potential bias that may be difficult (if not impossible) to exclude, and is a major study limitation that at least be noted in the limitations section. What, if any measures were taken to ensure impartiality? Nothing in the authors’ response to reviews suggests that any measures were taken, or that they understand the potential seriousness of this potential source of bias. Could they comment?

5. Regarding the statistical analysis approach, there are two remaining concerns. First, there is some confusion (perhaps only related to ensuring consistency and clarity across the different sections of the paper) regarding the primary outcomes(s). The authors wrote in the abstract introduction and methods (see page 2) and paper introduction (see page 4) that the primary outcome was “readmission for AECOPD” and that “This study aimed to identify psychosocial risk factors for readmission,” respectively, which is fine. Yet in the methods/outcomes section (see page 5), the authors write: “The primary outcomes were readmission to hospital for AECOPD or death within 365 days of index admission”, which is inconsistent with both the abstract and introduction, and which adds confusion. Was the primary outcome readmissions only or readmissions and death? The sample size estimate section, which does not actually refer to any primary outcome(s) specifically (see page 7), did not help clarify these inconsistencies. This is important to clarify as this affects the sample size estimate and power calculation.

Second, I disagree with the author’s position on the appropriate way to determine covariates. They write in their response: “We do not agree with the reviewers suggestion that ‘a number of a-priori determined covariates should have been selected, based on known of theoretical links with the primary outcome and/or predictors (e.g., age, some measure of COPD severity such as lung function or number of previous exacerbations’. We believe that the methodology of assessing each individual covariate in a univariate model and then entering those covariates that were statistically associated with the outcome into a multivariate model is the correct method of conducting statistical analyses. It would be very difficult to defend the selection of variables into the model if we had just used a-priori determined covariates; in fact we do not believe that this would constitute a valid research protocol for this study.” In fact, one of (if not the most) highly
respected journal in the field of behavioural medicine and psychosocial research, Psychosomatic Medicine (as well as the CONSORT guidelines for clinical trial reporting) has clear and published guidelines on several aspects of statistical practice, including covariate selection and adjustment that been available for several years. The authors are encouraged to consult this link for details: http://www.psychosomaticmedicine.org/site/misc/stat.xhtml#number5, but here is the except regarding covariate selection that is supported by several noteworthy references:

5. Covariables and Covariate Adjustment

The traditional practice of pre-screening covariates by choosing ones with significant univariate p values is well known to bias the results of multiple regression models. The choice of covariates should be based as much as possible on external information such as previous research and clinical knowledge. For example, it is often necessary to control for the severity of medical illness when modeling the effects of psychological variables on medical outcomes. The decision to include a particular index of medical illness severity as a covariate should be based primarily on such a priori considerations as whether previous research suggests that it is a potential confounder of the relationship of interest. It should not be based on whether the index was significantly associated with the psychological variable and/or the medical outcome in preliminary univariate analyses.

In addition, exceeding the recommended ratio of observations to predictors (or of events per predictor in the case of logistic or survival models) yields unreliable estimates. When confronted with too many predictors for the data at hand, we strongly recommend eliminating redundant predictors or combining ones that are highly correlated. This applies not only to the predictor variables that are of primary interest to the investigator, but also to a) covariates that are included to control for potential confounders and b) covariates that are included because they are well-established predictors and the investigators are trying to determine whether the variable of interest has independent predictive value.

More generally, we recommend consulting the NIH guidelines for prognostic modeling (Steyerberg and Harrell, 2003).

References

So the authors are encouraged to re-consider this aspect of their statistical approach, and to re-consider their choice of covariates, which should include smoking for example, as current smoking is theoretically likely to influence the primary outcome, even though it did not emerge as significant in univariate
analyses. As the authors correctly point out, “It is not unusual for variables to be found not significant at p<0.05 in a univariate analysis but then to be found to be significant in a multivariate model”, which is an additional reason for determining covariates a-priori.

Minor revisions:

As no measure of gender was used, all references to gender (a complex psychosocial construct related to sex-role identity, masculinity/femininity, among others) should be replaced with sex (which refers to one being male or female).

Decision:

Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.

Interest:

An article whose findings are important to those with closely related research interests.

Quality of English:

Acceptable

Statistical Review:

No, the manuscript does not need to be seen by a statistician.

Competing Interests:

'I declare that I have no competing interests'

**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'