Reviewer's report

Title: Association between Anemia and Quality of Life in a Population Sample of Individuals with Chronic Obstructive Pulmonary Disease

Version: Date: 25 April 2006
Reviewer: Roger Goldstein

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Reviewed by Dr Roger Goldstein and Mr Tom Dolmage

General

The aim of this study was to determine the association between anemia and health related quality of life in individuals with COPD. This is original research reporting a retrospective analysis of a population sample in which the data was collected between 1996 and 2001. The study was not originally designed to test the hypothesis stated in this report.

After multiple regression analysis the authors conclude that anemia may be associated with HRQL in individuals with COPD; the study is hypothesis generating. This is an admirable population sample which is rare and therefore quite valuable to the literature. This is a major strength and includes an estimate of the prevalence of people with anemia and COPD in the general population.

The methods are well designed and sufficient detail is provided to replicate the study. The data sound and well controlled. The manuscript adheres to the relevant standards for reporting and data deposition. The discussion and conclusions well balanced and adequately supported by the data. The title and abstract correctly identify the nature of the study. The writing is clear and concise with appropriate focus on the topic. There are a few redundancies in the text (see minor comments below).

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

Is the question posed important? While quality of life is an important outcome in treatment studies, how relevant is its importance in regards to anaemia in this scenario? Regardless of its short term or acute effects on quality of life, should it be treated regardless of comorbidity and effects on quality of life measure?

This is a retrospective analysis of data from a previous study with a different hypothesis governing the design. They appropriately identify the study as "explorative post-hoc analyses" but this distinction should be made clear in the abstract and the introduction.

Study Population p5: It is misleading at this point to use the term "This study enrolled...". The phrase implies that the data collection and test of the stated hypothesis was prospective. It should be stated early in the Methods that this is a retrospective analysis of data collected between 1996 and 2001.

The authors have analyzed the association between anemia and HRQL in patients with COPD. Why not include COPD, or the factors used to define the severity of COPD, as an independent variable in the multiple regression analysis of the entire sample population? The first inclination of a non-statistician would be to use multiple regression to find a model or some form of multiple stepwise or best subsets regression to identify the important independent variables from the selected possible independent variables. They have evaluated the need to use a variable transformation.

Why were covariates limited to liver cirrhosis, diabetes, myocardial infarction and renal diseases? Would the results be influenced if other co-morbidities that effect fatigue and quality of life such as CHF, cardiovascular and neuromuscular disease were included? Were medications included as dependent variables? For example ACE inhibitors and AT1 receptor blockers have been shown to reduce hemoglobin concentrations such that the use of ACE inhibitors and AT1 receptor blockers might have been a covariate in this study.

The authors use their own data to establish predictive equations for FEV1 and FVC excluding smokers. Are these equations similar to those used to guide the GOLD standards? Could the percent-predicted values
underestimated lung function increasing the number of patients labelled as COPD. For example, the authors€™ predicted FEV1 for a 40 y, 1.8 m Caucasian male is 4.3 L, whereas the predicted used in many laboratories would give 3.8 L resulting in a difference of the %predicted.

In the abstract the authors conclude 'that anemia may be associated with HRQL in individuals with COPD but comorbidity may explain part or all of the association' and in the Discussion state "our analyses provide evidence for a negative association between HRQL and hemoglobin levels". Clarify that the latter statement is in individuals with COPD. Please ensure the statements in the Abstract and Discussion are consistent.

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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)

Background p4: "This outcome measures helps differentiate between individuals" should be measure.

Background p4: "For example, in patients with end-stage renal diseases investigators showed a strong association between improvements in HRQL, reduction in hospitalizations, and survival in those with higher hemoglobin levels". The strong association was among HRQL, hospitalizations, survival with haemoglobin levels not improvements and reductions of these variables as there were no treatment in the cited study. In fact the reference supporting this statement is a review article and case study.

Background p4: "Mortality is increased in patients with lower hematocrit, and increasing hemoglobin levels could result in a lower risk of death not only in patients with cancer, but also in renal failure, congestive heart failure and ischemic heart disease". This is a hypothesis not specific to the topic of anaemia and quality of life in COPD.

There is some redundancy. For example, a description of the SF-36 occurs in the "Interview" section and similar statements are made in the section of HRQL indicators. On page 9: "We considered the following covariates in the analyses: education (years of education used as a continuous variable... We used education as a continuous variable calculating"

Page 9: A reference should be provided for the WHO criteria for anaemia.

Discussion: study participants should not be referred to as "patients".

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests