Title: Protocol for a systematic review and economic evaluation of the clinical and cost-effectiveness of non-hospital based non-invasive ventilation (NIV) in patients with stable end stage COPD with hypercapnic respiratory failure

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Author's response to reviews: see over
Protocol for a systematic review and economic evaluation of the clinical and cost-effectiveness of non-hospital based non-invasive ventilation (NIV) in patients with stable end stage COPD with hypercapnic respiratory failure.

Version: 2 Date: 17 January 2014
Reviewer: Kerry Dwan
Reviewer's report with response:

1. Survival is now mentioned in the abstract but mortality in the main text.
   This has now been changed in the main text.

2. The analysis section needs further work. It needs to be made clear whether there will be a narrative synthesis or quantitative synthesis. 95% confidence intervals should be presented with the pooled treatment effect estimate. More Information on the analysis of a network meta-analysis/multiple treatment comparison needs to be included i.e. Bayesian using Winbugs or frequentist using STATA? If a Bayesian approach is used, what prior will be used?
   Details on this have now been added to the end of the section labelled “Analysis”. It indicates a Bayesian approach will be taken and considers the prior.

3. Although the authors state that different timepoints are likely to be reported, it would be useful to note what are the clinically relevant timepoints.
   Important time points can be defined in a number of ways and involve consideration of underlying risk of the outcome in question for the population in question. For example, patients discharged from hospital after intensive emergency treatment for an exacerbation of their COPD are at higher risk of a recurrent exacerbation in the immediate aftermath (e.g. 3 months) than patients who have been stable without a severe exacerbation for many months. In the first population one could envisage it is important some outcomes are measured in the shorter term initially and/or with higher frequency than the latter. In both cases longer-term outcomes are important. As the benefits of NIV are currently unclear, and there is variation in population severity/risk in studies likely to be included in the review, for most outcomes short-term (3-6 months) to longer-term (up to life time) outcome assessment is required. The majority of studies are likely to have follow-up periods of 6 to 12 months (or possibly two years). We have already alluded to this issue in part in paragraph two of the background when considering the definition of “end stage” COPD. Additionally we have added a sentence in to the analysis section on this point.