Author's response to reviews

Title: The effectiveness and cost-effectiveness of treatments for Idiopathic Pulmonary Fibrosis: systematic review, network meta-analysis and health economic evaluation.

Authors:

Emma Loveman (emma.loveman@soton.ac.uk)
Vicky R Copley (V.R.Copley@soton.ac.uk)
Jill L Colquitt (J.Colquitt@soton.ac.uk)
David A Scott (david.scott@oxfordoutcomes.com)
Andy J Clegg (A.Cegg@soton.ac.uk)
Jeremy Jones (Jeremy.Jones@soton.ac.uk)
Kate MA O'Reilly (koreilly@mater.ie)
Sally Singh (sally.singh@uhl-tr.nhs.uk)
Claudia Bausewein (Claudia.Bausewein@med.uni-muenchen.de)
Athol Wells (Athol.Wells@rbht.nhs.uk)

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Author's response to reviews: see over
Dear Dr Cornacchia,

Re: The effectiveness and cost-effectiveness of treatments for Idiopathic Pulmonary Fibrosis: systematic review, network meta-analysis and health economic evaluation

Thank you for forwarding the comments of the statistical peer reviewer for the above entitled article and for allowing us the opportunity to respond to these in a revised document. I have re-submitted an updated document and have outlined here the changes that we have made in response to the comments (table below).

I hope that these changes are acceptable and look forward to hearing from you again soon.

Yours sincerely,

Emma Loveman

<table>
<thead>
<tr>
<th>Statistical review comments</th>
<th>Authors response</th>
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<td>Major Compulsory Revisions</td>
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| p 5 l 170-173: I found some of these assumptions to be contradictory-one could enter the study with FVC < 70% predicted and one could have a >10% decline in FVC% predicted but still have FVC% predicted >70%. This probably just needs some clarification. | There seems to be a typo here where the < should be a >, so the reviewer’s comment should read “one could enter the study with FVC > 70% predicted and one could have a >10% decline in FVC% predicted but still have FVC% predicted >70%”. P5 lines 170-173 say ‘Key assumptions are that all patients enter the model in the
unprogressed state; those experiencing a ≥10% absolute decline in FVC % predicted are considered to be in the progressed health state; treatment has a constant effect on relative rate of FVC % decline; and FVC % predicted of ≥70% indicates unprogressed IPF."

We used an FVC % predicted of ≥70% to indicate unprogressed IPF from the point of view of QoL only. It's an arbitrary distinction that was necessary to find a HRQoL value for the two health states, progressed and unprogressed (using the mean FVC% predicted that was reported in these studies). This is an assumption but we don’t believe it is contradictory.

<table>
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<tr>
<th>p 4 l 156: More detail should be provided regarding prior distributions for the variances of the random effects and model fit criteria (was DIC used?)</th>
<th>DIC was used to determine relative model fit between the fixed and random effect models; there was no evidence the RE was a better fit, and considerable uncertainty around the RE standard deviation, hence the FE was favoured and the RE used in a sensitivity analysis. This has been added to the text. Further detail has also been provided on the vague priors used and the model code is now provided as an Appendix.</th>
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<td>p 4 l 157: I think the authors have the conversion backwards-they report SMDs and appear to have converted to them from odds ratios.</td>
<td>Data on the FEV endpoint obtained from the RCTs was converted to the SMD scale, which was then used as inputs into the meta-analysis. The SMDs output from the meta-analysis were then converted to log odds ratios using the formulae from Chinn (ref 15). This was done for ease of interpretation and use in the economic model. We have clarified this in the text and Table 2.</td>
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<td>p 8 l 280 and 285: More detail should be provided regarding the estimation techniques to fit the parametric survival models, for example, was a Bayesian approach used here too?</td>
<td>The parametric survival models were fitted in Stata using the method of maximum likelihood. Alternative parametric models to Weibull were also examined e.g. exponential, lognormal. Goodness of fit was assessed using the Akaike Information Criterion (AIC). The Weibull model was selected because of the balance of good fit and face validity. The text has been updated to reflect this.</td>
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<td>p 9 l 319: &quot;is&quot; should be &quot;are&quot;</td>
<td>P9 line 319 says ‘Azathioprine and prednisolone is dominated by BSC’. It is the label of one treatment and so should be ‘is’.</td>
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