Author's response to reviews

Title: Clinical effectiveness and cost-effectiveness of pegvisomant for the treatment of acromegaly: a systematic review and economic evaluation

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Referee 1 comments

'1. I am still concerned that Fig 4 is misleading as it does not compare other effective treatments. The absolute number of patients who have failed surgery and are non-responsive to somatostatin analogs is miniscule--far too small to garner such elegant curves!
2. I could not find ref 64 enumerating side effects in the ms. These must be cited.'

RESPONSES TO REFEREE1 COMMENTS

1. Fig 4.
[a] Comparing effective treatments:
In Europe, PEG is licensed for patients who have had an inadequate response to surgery and/or radiation and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-1 concentrations or was not tolerated. Essentially this means that for economic modelling the comparator for PEG as licensed is best supportive care. Hence, Fig 4 does not compare PEG to other effective treatments.

[b] The elegant curves are not based on absolute numbers of patients but are modelled. The PEG curves are based on National Statistics data for mortality (population in tens of millions, hence the smooth curves; for convenience the graphs have ordinate in terms of “alive per 100,000”). The “no-PEG” curves (i.e. comparator) are also smooth because likewise they are modelled on National Statistics data by applying a SMR to the PEG curves. To apply a plausible range of SMR values for the comparator arm we examined studies reporting SMR rates for acromegaly patients (see Fig 5).

We have modified the caption to Fig 4 so as to clarify the origin of the curves depicted. We have removed the sentence “Figure partly compiled from published
data [26] and data provided in MM” and have inserted the following sentence into the caption:

“The curves shown are modelled using mortality data from the Office of National Statistics for England (population about 50 million) or for Wales (population about 5 million) as appropriate.”

2.

[a] Ref 64.
We are unclear as to the point the referee is making. The references extend to number 42 only, so there is not a reference 64.

[b] Side effects
In response to the same referee’s previous comments about adverse events we previously incorporated the points made and the supporting reference supplied by the referee into the manuscript. This is reference 42 in the manuscript (Bonert et al JCEM 2008). The wider consideration of adverse/side events was covered in the discussion section and in the results sections of our paper.