Conceptual modelling for cost-effectiveness analysis of intravitreal therapy with ranibizumab (Lucentis), aflibercept (Eylea) or bevacizumab (Avastin) for macular oedema due to central retinal vein occlusion

Dr M. Goodall (m.elindagoodall@nice.org.uk), Dr J. Tosh, Mr A. Alshereef, Dr P. Tappenden
Health Economics and Decision Science, School of Health and Related Research, University of Sheffield, UK
October 2016

Introduction and objective

Macular oedema (MO) is an eye condition that can result in severe visual impairment. The objective of this study was to develop a conceptual model comparing bevacizumab, aflibercept and ranibizumab treatment for MO caused by central retinal vein occlusion (CRVO). These are high-cost treatments that are given as monthly intravitreal injections, until maximum visual acuity is achieved or there are no signs of disease activity. The conceptual model would be used to inform a lifetime costs and quality-adjusted life years (QALYs) decision model.

This study had three parts: a targeted literature review, critique of published cost-effectiveness modelling and conceptual modelling.

1. Literature review

Methods: In August 2015, Medline was searched using OVID and the National Institute for Health and Care Excellence website and Google Scholar were searched using free text searches. Search terms included: “Cost” OR “Costs and Cost Analysis” OR “Cost effectiveness” OR “Cost-Benefit Analysis” AND “Retinal Vein Occlusion”

Results: 11 records were identified, of which 5 met the search criteria. The cost-effectiveness analyses identified were:

- Taylor 2014 (journal article): Ranibizumab vs. best supportive care
- Eriksson 2014 (Abstract): Aflibercept vs. ranibizumab
- TA305 (NICE Technology appraisal): Aflibercept vs. ranibizumab
- TA283 (NICE Technology appraisal): Ranibizumab vs. best supportive care
- TA229 (NICE Technology appraisal): Dexamethasone vs. sham injection

2. Existing models and critical appraisal

Methods: The studies identified in the literature review were critiqued using the Phillips 2004 checklist as a guide. The model type, health states, fellow eye involvement, direction and extent of movement between health states, time horizon, cycle length, data identification, baseline patient data, mortality, changes in visual acuity over time, modelling the fellow eye, treatment protocols, treatment effects, post-trial extrapolation, adverse events, costs, monitoring, and health-related quality of life

Results: In the published models, all health states were based around best corrected visual acuity (BCVA) (Figure 1). The following limitations of the structures in the existing models were identified:

- BCVA health state boundaries were arbitrary
- Treatments are given once maximum visual acuity is achieved or there is no sign of disease activity, but the models assume that all patients receive the same number of injections; response to treatment did not influence whether another injection was given.
- Response to prior injections did not influence the response to the next one
- Injections were not linked to adverse events or costs
- Only one eye was generally modelled (fellow eye involvement was often not included), so a judgement was needed as to whether this was the better or worse eye seeing
- Health-related quality of life was determined by only one eye, but is influenced by both eyes
- After the first 3 monthly injections, treatment intervals are determined by clinical judgement. In the models, differences across the population in treatment duration and overall treatment time were not accounted for.

Figure 1. Health states of published models

3. Conceptual modelling

Methods: Problem-orientated conceptual models were developed to outline disease progression and clinical management. A range of modelling approaches were considered in the conceptual modelling: decision tree, state transition or discrete event simulation. A decision tree approach soon became too complex and so was not fully explored.

Results: Potential structures for state transition model and a discrete event model are shown in figures 2 and 3. The state transition approach continues to base the model on BCVA, whereas the discrete event simulation approach structures the model based on injections. Table 1 summarises how these approaches could address the key limitations of the models identified in the literature. The key challenge to both of the approaches would be whether there is sufficient data available to populate the model in a way to address the limitations identified.

Figure 2. Conceptual model – State transition model

Figure 3. Conceptual model – Discrete event simulation

Table 1. How the conceptual models can address modelling limitations

<table>
<thead>
<tr>
<th>Limitation</th>
<th>State transition model</th>
<th>Discrete event simulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arbitrary best corrected visual acuity boundaries</td>
<td>Not addressed by structure</td>
<td>Addressed through model structure</td>
</tr>
<tr>
<td>Relationship between response to treatment and the need for an additional injection (different number of injections per patient)</td>
<td>Can be addressed through the way data is inputted to the model (different % of patients receiving injections each cycle)</td>
<td>Addressed through model structure</td>
</tr>
<tr>
<td>Association between injection and adverse events and costs</td>
<td>Can be addressed through the way data is inputted to the model (effectiveness weighted differently each cycle)</td>
<td>Addressed through model structure</td>
</tr>
<tr>
<td>Modelling both eyes</td>
<td>Addressed through model structure</td>
<td>Addressed through model structure</td>
</tr>
<tr>
<td>Health-related quality of life linked to both eyes</td>
<td>Addressed through model structure</td>
<td>Can be addressed through the way data is inputted to the model</td>
</tr>
<tr>
<td>Account for different treatment interval lengths</td>
<td>Not addressed as set cycle lengths required</td>
<td>Addressed through model structure</td>
</tr>
</tbody>
</table>

Conclusion

Several important limitations were identified in the published models. In particular, the second eye is often clinical condition that does not tend to be a relationship between having an injection and adverse events and costs, and reaction to one injection does not influence whether another injection is modelled or the treatment interval length. These limitations restrict how generalisable the models are to clinical practice, and do not reflect the continuation rules specified within the marketing authorisations for these technologies. Many of these limitations could be addressed using a different state transition model and inputting data to allow these issues. All of the limitations could be addressed through a discrete event simulation approach, if sufficient data are available to populate it.

References


