

# Social Values and Health Priority Setting Case Study

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| <b>Title of Case Study</b>   | <b>Lucentis for the treatment of Age-Related Macular Degeneration in the UK</b>   |
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| <b>Date of Submission</b>  | <b>20 June 2012</b>   |
| <b>Case Summary (approx. 350 words)</b><br><br>Please include information here about why the case is of particular interest  | The case of Lucentis for the treatment of age-related macular degeneration proved to be controversial for the UK National Institute of Health and Clinical Excellence (NICE). It raises questions of social values around the significance of particular health states, the way in which those health states might be balanced in relation to other values such as cost-effectiveness, and the role of adaptive preferences as they relate to the utility values used in cost-effectiveness modeling. The case also highlights the impact that pressure from patient groups can have on the policy process, and the extent to which exceptions to institutional decision rules might be justifiable, even desirable, in light of the social values features of particular cases and the pressures brought to bear on decision-makers by interested parties.   |
| <b>1. Facts of the case</b>  | <b>Facts of the case</b>  |
| Please include information on as many of the following as are relevant to the case: <ul style="list-style-type: none"> <li>• At what condition is the intervention, program or service aimed?</li> <li>• What are its effects? Eg. Is it curative, preventative, palliative, life-prolonging, rehabilitative?</li> <li>• Is there a relevant comparator? If so how does this intervention, service or program compare to the alternative? Include ICER estimates/QALY costs if relevant.</li> <li>• What are the significant features about the condition and/or about the patient population in this case? Eg. patient population is very young, very old, condition is rare, life-threatening, life-limiting etc.</li> <li>• How are the benefits of the intervention distributed across the patient population and/or across time?</li> <li>• What is the cost or budget impact of the intervention/service/programme?</li> </ul> | <ul style="list-style-type: none"> <li>• <b>Background</b><br/>Lucentis is a treatment for Age-Related Macular Degeneration (AMD), a disease which affects the macula, an area in the centre of the retina of the eye. It produces progressive loss of central vision, whilst retaining peripheral vision.<br/><br/>The disease affects the elderly and comes in two varieties, wet and dry. AMD is the commonest cause of visual impairment in the UK with around 26,000 new cases of wet AMD annually, with the wet form of the disease being a progression from the dry form. Dry AMD is the more common form of the disease, and involves a gradual deterioration of the light receptor cells in the retina as they fail to take in vital nutrients and to clear by-products of cell functioning. Dry AMD is characterized by a slower and more gradual progression in worsening of vision compared to wet AMD. Wet AMD accounts for 10-15% of cases and involves the abnormal growth of new blood vessels beneath the retina which results in distortion of vision and scarring that causes rapid visual loss. Wet AMD is always a progression from dry AMD, but it can develop very quickly.<br/><br/>Smoking is thought to aggravate the AMD disease process and to contribute to damage to the cells in the macula. The risk of developing AMD is 3.6 times greater for current and former smokers than for people who have never smoked (NICE, 2008a).<br/><br/>The macula plays a vital role in central visual functions needed for performing details tasks such as reading, writing, and driving. It also enables us to recognise faces and see color. Hence all of these functions suffer as the macula degenerates in either dry or wet AMD.</li> </ul> |

- What is the nature and strength of the evidence about the outcomes of the intervention, service or programme? Eg. randomized clinical trials, evidence on patient-related outcomes.
- How did the issue about this case arise - for example, from clinical practice, from a policy setting, from a topic selection process?

Evidence suggests that patients with AMD suffer; ‘increased risks of mortality and reduced life expectancy, increased morbidity, particularly in relation to accidents and psychological ill-health, ...have longer hospitalisations, make greater use of health and community care services and are more likely to be admitted to nursing homes (Colquitt et al, 2008; 8).

Patients’ ability to adapt may also play an important role in quality of life with visual loss ‘Central field loss impairs the ability of patients to conduct a wide range of daily activities. Visual disability is associated with an increased risk of emotional distress and clinical depression. However, some patients may adapt and cope with visual disability so that the quality of life impact may vary according to duration of vision loss (Colquitt et al, 2008; 48).

Two drugs were considered for use in this disease: Ranibizumab (Lucentis) and Pegaptanib in TA155. This study focuses on the case of Lucentis.

Lucentis is a treatment for the wet form of AMD. It is an antibody that interferes with the process by which the new blood vessels behind the retina form and which cause fluid leakage and lesions, leading to deterioration of the macula. Lucentis targets a protein involved in this process called vascular endothelial growth factor (VEGF). Lucentis is a VEGF inhibitor, and is administered by injection into the eye, under the macula.

- Clinical evidence

Clinical evidence was comprised of the results of four Randomised Clinical Trials (RCTs) of Lucentis, looking at different types of neovascular lesion and the combined results of two concurrent RCTs comparing three doses of pegaptanib with a placebo in all types of lesion. Three Phase 3 clinical trials (MARINA, ANCHOR, and PIER) had been carried out.

The manufacturer’s model for ranibizumab used a different dosing schedule to that used in the clinical trials. The MARINA4 and ANCHOR trials involved 24 injections over 2 years and 12 injections over 1 year respectively, but in the base case analysis for the model, 8 injections in the first year and 6 injections in the second year were used with the assumption that the same clinical efficacy would be achieved with this lower dosing frequency.

Patient data was primarily from a sample of wet AMD.

- Cost-effectiveness

Cost-effectiveness of Lucentis in cases where there were classic lesions was estimated at £15,638/QALY compared with the current practice of Photodynamic Therapy (PDT); and 11,412/QALY compared with the best supportive care for non-classic lesions and £25,098/QALY compared with best supportive care for classic lesions. In this instance ‘best supportive care’ is defined as “social support, visual rehabilitation and the provision of aids to help with low vision” (NICE, TA155).

For patients with predominantly classic lesions compared with PDT, Lucentis had a probability of being cost effective of 72% at £20,000/QALY and 97% at £30,000/QALY. For patients with predominantly classic lesions compared with best supportive care, Lucentis had a probability of being cost effective of 95%

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|  | <p>at £20,000/QALY and 99% £30,000/QALY. For patients with minimally classic and occult no classic lesions, for the base-case analysis ranibizumab had a probability of being cost effective (compared with best supportive care) of 15% at £20,000/QALY gained and 81% at 30,000/QALY.</p> <p>There is a problem in relation to the Markov modeling used in the cost-effectiveness assessments because Markov modelling assumes independence of the condition being assessed from other conditions (and hence cannot account for co-morbidities associated with age and smoking).</p> <ul style="list-style-type: none"> <li>• Cost and budget impact</li> </ul> <p>In cost and budget impact terms, Lucentis is a very expensive intervention. Each injection of the drug costs £761.20. The 2-year cost of the drug is about £10,700 assuming 8 injections in the first year and 6 injections in the second year, and about £18,300 assuming 12 injections in the first year and another 12 in the second year as per the clinical trial regimen (NICE, TA155).</p> <p>It has been estimated that a typical Primary Care Trust (PCT) in the UK which serves a population of 250,000, could expect around 107 new cases of wet AMD a year. The cost of Lucentis treatment for these patients would amount to over £1.1 million per annum. Some commentators have suggested that overall costs including outpatient review over 10 years could add up to 1% of the total NHS budget (Lee, 2008).</p> |
| <p><b>2. Policy decision: process</b></p> <p>Please include information on as many of the following as are relevant to this case:</p> <ul style="list-style-type: none"> <li>• What stages/institutions were involved in the decision making process?</li> <li>• Is legal context important in this case? If so, in what way?</li> <li>• Who was involved? Eg. key stakeholders, the public, professionals, industry, patients, governmental or non-government policy actors.</li> <li>• How were they involved, and at what stages of the process?</li> <li>• Was there disagreement between any of the parties involved in the decision process?</li> <li>• Do any rules or frameworks exist to guide decision making? If so, were they followed in this instance?</li> <li>• Do mechanisms exist for challenging the decision at any stage of the process?</li> <li>• How, if at all, is the decision process or the decision itself publicized?</li> </ul> | <p><b>Policy decision: process</b></p> <p>The case of Lucentis for age-related macular degeneration was considered by the UK National Institute for Health and Clinical Excellence (NICE), according to the rules of its Single Technology Appraisal process. The process was as follows in this case:</p> <ul style="list-style-type: none"> <li>• Evidence was obtained by NICE from the manufacturer of Lucentis (Novartis) and Pegaptanib (Pfizer)</li> <li>• This evidence was critically reviewed by an independent Evidence Review Group (ERG)</li> <li>• NICE invited clinical specialists, NHS commissioning experts and patient experts to attend Appraisal Committee meetings to consider the intervention, and to provide their views in writing. Details of all stakeholders invited to attend meetings were made available on the NICE website.</li> </ul> <p>The following were those involved in the consultation process:</p> <p>- Professional/specialist and patient/carer groups:</p> <ul style="list-style-type: none"> <li>• Age Concern England</li> <li>• College of Optometrists</li> <li>• Counsel and Care for the Elderly</li> <li>• Department of Health</li> <li>• Macular Disease Society</li> <li>• Royal College of Nursing</li> <li>• Royal College of Ophthalmologists</li> <li>• Royal National Institute of Blind People</li> <li>• Welsh Assembly Government</li> </ul>   |

- Commentator organisations (without the right of appeal):

- Medicines and Healthcare Products Regulatory Agency (MHRA)
- NHS Quality Improvement Scotland
- Novartis
- Institute of Ophthalmology, University College London
- NCCHTA Southampton Health Technology Assessment Centre (SHTAC) National Collaborating Centre Acute Care

The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer/sponsor consultees and commentators. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on ranibizumab and pegaptanib by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD.

- Professor Simon Harding, Consultant Ophthalmologist, nominated by the Royal College of Ophthalmologists – clinical specialist.
  - Professor Andrew Lotery, Professor of Ophthalmology, nominated by the Royal National Institute of Blind People – clinical specialist.
  - Barbara McLaughlan, Eye Health Campaigns Manager, nominated by the Royal Institute of Blind People – patient expert.
  - Mrs Lydia Willie, nominated by the Royal Institute of Blind People – patient expert.
- The Appraisal Committee met to consider the evidence for the intervention - the meeting was open to the public and the press (NICE publishes a notice of the meeting and a draft agenda on its website 20 days before the meeting date).
  - An appraisal consultation document summarising the evidence and views that were considered by the Appraisal Committee and its provisional recommendations were published for public consultation.
  - After considering the evidence on clinical and cost-effectiveness, the Appraisal Committee issued draft guidance recommending that ranibizumab (Lucentis) was only cost-effective if it was prescribed only to people with wet AMD, only where both eyes were affected, and that treatment should only be given to the better seeing eye (NICE, 2008b).
  - These conclusions led to a wave of protest from patients and healthcare professionals that continued after the statutory consultation period closed, with a campaign led by the Royal National Institute for the Blind (RNIB). This campaign was over not only the substance of the decision in the draft guidance issued by NICE, but also over the length of the appraisal period, with RNIB stressing that patients could be losing their sight whilst the process was ongoing.
  - NICE decided to postpone its final appraisal until after it had re-considered the evidence on cost-effectiveness and the models used, and until after a second consultation period (during which time the campaign led by RNIB continued).
  - After the second consultation period, NICE concluded that treatment with ranibizumab of the *first* eye to come to clinical attention would be cost

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|  | <p>effective if the manufacturer pays for the costs of the drug beyond 14 injections in the treated eye (NICE, 2008a). This was the conclusion issued in the final appraisal document.</p> <ul style="list-style-type: none"> <li>• An appeal was launched by the manufacturer of the other drug considered in this appraisal - pegaptinib - by its manufacturer, Pfizer, and by Derbyshire Primary Care Trust on the consideration of Lucentis, but both no legal grounds were found for either challenge, and the appeals were rejected by the independent Appeal Committee (see NICE, 2008c).</li> </ul>  |
| <p><b>3. Policy decision: content</b></p>  | <p><b>Policy decision: content</b></p>   |
| <p>Please include information on as many of the following as are relevant to this case:</p> <ul style="list-style-type: none"> <li>• What decision was made about the intervention, service or program, if any?</li> <li>• What values were relevant in the case or in the decision itself? For example, values of cost-effectiveness, clinical effectiveness, justice/equity, solidarity or autonomy. How did they affect the decision itself?</li> <li>• Was the way in which these values were balanced affected by any specific features of the case? For example, end of life considerations, age of patients, impact on carers, disease severity, innovative nature of the intervention, social stigma or cultural sensitivity?</li> <li>• Did the case challenge established guidance or 'decision rules'? Eg. on cost-effectiveness, cost thresholds, age discrimination etc. If so, in what way?</li> <li>• Were any health system-wide considerations influential in the decision? For example, displacement of old technologies, professional practice issues, or infrastructure/feasibility considerations.</li> </ul> | <p>NICE approved Lucentis for use in the wet form of age related macular degeneration. Since its original decision, a scheme has been developed whereby costs to the NHS are capped, such that after treatment for any one patient reaches a certain level of cost, the manufacturer must then cover all future injections of the drug (the exact amount of discount/saving to the NHS is a matter of commercial confidence).</p> <p>One of the crucial issues in this case was whether to approve treatment with Lucentis only in cases where both eyes were affected with wet AMD and even then only to treat the better seeing of the two affected eyes. This was the initial decision issued in draft guidance by NICE after the appraisal process, before it re-considered the evidence and reversed its decision to say, in its final appraisal document, that Lucentis should be made available to treat the first eye that came to clinical attention with AMD - ie. that clinicians should <i>not</i> wait until the disease had progressed to the both eyes.</p> <p>The final guidance issued by NICE details the Appraisal Committee's discussions on this point, as follows:</p> <p>“The Committee discussed whether it would be appropriate to consider recommending treatment in the better-seeing eye only: that is, not to treat where patients present with only one eye affected. It noted the concerns raised by consultees and understood that most consultees felt that it would be unacceptable, and clinically inappropriate, not to treat the first eye that comes to clinical attention. It was persuaded that any other scenario could result in losing the opportunity to preserve vision because the untreated better-seeing eye could subsequently be affected by an untreatable cause of vision loss, or might not respond to treatment with anti VEGFs. With all these issues in mind the Committee concluded that its considerations of cost effectiveness should relate to starting treatment with the first eye to present clinically” (NICE, 2008a: 27)</p> |
|  | <p>There were, however, cost-effectiveness implications from moving from the position of only treating the better seeing eye of two affected eyes, to treating the first eye that comes to clinical attention:</p> <p>“The Committee noted that economic modelling was carried out assuming that the better seeing eye was treated. A policy of treating the first eye to come to clinical attention would result in substantially higher costs but fewer savings and lower utility gains than a policy of only treating the better seeing affected eye. In addition there would be reduced savings on costs of blindness. Based on this the Committee agreed that an expected cost per</p>  |

QALY for a first eye strategy would be about 50% higher than that for treating the better seeing affected eye. It concluded that the ICERs for ranibizumab (or pegaptanib) would not fall within a range considered to be a cost effective use of NHS resources assuming a strategy of treating the first affected eye.” (NICE, 2008a: 28)

The judgement that the cost-effectiveness ratios for Lucentis for treating the first eye that came to clinical attention would not be within those thought to indicate a good use of NHS resources, led to consideration of a proposal from the manufacturer of a patient access scheme. With this patient access scheme, drug costs to be paid by the NHS are capped and any injections needed by the patient which take costs beyond that cap, are paid by the manufacturer. It was estimated by NICE that “ranibizumab was likely to be cost effective if cost was limited to the NHS such that the manufacturer pays for the drug cost of ranibizumab beyond 14 injections in the treated eye.” (NICE, 2008a: 29).

In its considerations, the committee noted the impact on quality of life of losing one’s vision, noting that loss of binocular (two-eyed) vision even where there is good vision in the remaining better-seeing eye, can result in a reduction in quality of life. It noted that considerable anxiety and depression is associated with allowing an eye affected by AMD to deteriorate without treatment (NICE, 2008a)

#### 4. Discussion

Please use this space to reflect on, for example:

- The reasons or values explicitly used in making the decision. Do these reflect any institutional decision rules or statements of value, for example commitments to equality, non-discrimination or fairness? Do they reflect wider social, moral, cultural, religious values, and if so how?
- Considerations not explicitly taken into account in the decision, but which may nonetheless have been important ‘background’ factors. These might include, for example, public opinion, political sensitivity, moral sensitivity, and international reputation, as well as cultural, social, moral, religious or institutional norms.
- The impact of the decision making process on the decision itself, if any.
- Any issues relating to implementation. For example, whether access may be restricted by capacity issues, even if the intervention, service or

#### Discussion

There are a number of issues of social values that arise from the process and content of the decision made by NICE on Lucentis:

- The distress caused for patients if a disease is allowed to progress without treatment appears to have been a significant issue in the decision process. The appraisal draws attention to the anxiety and depression that can be caused as a consequence of allowing sight to deteriorate without treatment. There is a sense here of the importance to patients of ‘something being done’ about ill-health, even if it would be possible for them to continue, as in this case, with a reasonable quality of life until the other eye became affected with AMD. Recall that the policy of treating the first eye to come to clinical attention was found to result not only in substantially higher costs but also in *lower utility gains* for patients than a policy of only treating the better seeing affected eye (NICE, 2008a). It is possible that adaptive preferences may be significant in accounting for those lower utility gains however (see below).

This sense of importance around ‘something being done’, perhaps combined with the anxiety and distress that were shown to be associated with losing vision in one eye, even when the other one is working well, seems to have been significant. However, it is difficult to know what influence this ‘must do something’ value had in its own right on the members of the Appraisal Committee, and to what extent the decision to re-consider the draft guidance was simply the result of lobbying by powerful and vocal patient lobby groups.

programme is provided on a 'universal' basis.

- Anything else you think significant or interesting about the decision.

- Additionally, the loss of sight is arguably an event which carries some amount of 'dread' amongst many people, even those who are not old and not immediately threatened with it - the concept itself is enough to provoke strong feelings in many (perhaps most) people. Whilst it is difficult to determine exactly to what extent this kind of 'feeling' affects decisions or decision-makers, it might nonetheless be a background factor which could have some influence on why considerations of cost-effectiveness were ultimately over-ridden (or, as it turned out eventually, got around via cost-capping) in this case when they may not be so negotiated in a different case. It could also be argued, however, that if this social 'dread' is a factor, it is already accounted for in the power of the patient groups representing visually impaired people, which may thus benefit from the psychological importance which is accorded to sight, leading to greater support and power for organizations representing visually impaired people than, say, those suffering with mental illness.
- The influence of patient groups in the policy-making process was significant in this case. The campaign led by the Royal National Institute for the Blind appears to have been instrumental in NICE extending the consultation period and reviewing its initial decision. NICE's actions could be interpreted as their being highly responsive to patient groups and willing to re-consider recommendations in the light of strong stakeholder views. Or they could be interpreted as NICE being unwilling, in this case, to hold to a rules-based decision in the face of such strong opposition. The latter is not necessarily a cause for criticism, however, since it may in fact indicate a recognition that some (social) values - in this case perhaps the value of sight, the value of the fear of loss of sight, and the value of treatment, as opposed to allowing a disease to progress untreated - are so strongly held that NICE should make exceptions to its rules and that the balance of values should be altered accordingly.
- There is an issue around adaptive preferences in the estimates of utility gains which were used in the modeling for cost-effectiveness of this intervention. Adaptive preferences are the preferences that people can develop in response to a set of deprived circumstances or restricted options. In short, people adapt their preferences to their circumstances and, as such, their 'adaptive preferences' may be quite different to the preferences of people who do not find themselves in the relevant circumstances (there is some controversy over the validity of adaptive preferences and whether or how they should be taken into account in resource allocation decisions, however - see for example, Nussbaum, 2001).

One consideration here is the use of 'Brazier' utility values in the cost-effectiveness evaluations carried out in the assessment of Lucentis. The relevant section of the appraisal guidance reads as follows:

"The utility values used in the model were based on a study in which outcomes were assessed in members of the general UK population (n = 108) who experienced simulated AMD vision states using custom-made lenses. The study included a preference-

based measure (HUI-3), selected questions from a visual function questionnaire and time-trade-off (TTO) by direct elicitation (Brazier study). The utility values derived using TTO by direct elicitation were stated to have a strong relationship with visual acuity and these were the utility values used in the model. The difference in mean values between the lowest and highest visual acuity groups was 0.367 (0.497 in the group with a visual acuity of less than 3/60 and 0.864 in the group with a visual acuity of 6/15 or better)." (NICE, 2008a; 12).

So, utility values were based on the preferences of individuals *without* genuine visual impairment, rather than those *with* visual impairment: this is significant in terms of adaptive preferences, given that people with visual impairment may have developed adaptive preferences and ceased to value visual acuity quite so highly as those who still have perfect vision, giving different utility values.

Related to this is the wider question of how to use an informed public in these kinds of values assessments. Recent work by Butt, Gallagher, Morris, Orr and Rubin, compares labeling, informed public, and adaptation information conditions. Butt et al found that: "There was a trend (not significant) towards lower utility in groups 2 (labeling) and 3 (disease information) and higher utility in group 4 (adaptation) with respect to group 1 (no information). This may suggest that informing the public about the condition through labeling and patient description leads them to value the health state more seriously, but informing them that one can adapt to the condition leads to less serious valuations. Although it should be noted that the provision of information suggesting one can adapt over time may be confounded by the certainty of health condition over time required for the time-trade-off (TTO) task." (Butt et al, in publication)

Since NICE took the decision to approve Lucentis, an additional issue has arisen as a result of its cost. A number of Primary Care Trusts in the UK have been advising clinicians to prescribe an alternative drug - Avastin (bevacizumab) - for age-related macular degeneration. This is off-label prescribing, as Avastin is only licensed for the treatment of bowel cancer, not of macular degeneration. Avastin is, however, much cheaper than Lucentis: some estimates suggest it is 10 times cheaper, but with comparable effectiveness, such that switching to Avastin instead of Lucentis could save the NHS an estimated £556m over three years (Jackson et al, 2012).

The company which markets Lucentis in the UK (Roche) has raised a high court challenge to the Primary Care Trusts that have recommended the use of Avastin over Lucentis - this is currently ongoing. Significantly, both Lucentis and Avastin were developed by the US firm Genentech, so there is clearly little financial incentive for it to apply for a licence for Avastin as a cheaper treatment for AMD than Lucentis.

NICE is unable to assess Avastin as a treatment for AMD because it can only assess drugs for the indications for which they have been licensed. Therefore until Genentech takes the unlikely step of applying for a license for Avastin to treat AMD, NICE cannot make an assessment of its clinical or cost



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|  | effectiveness.   |
| <b>5. References/Links to relevant documents</b> |  |
|  | <p>Colquitt J, Jones J, Tan SC, Takeda A, Clegg AJ, and Price A. (2008) Ranibizumab and pegaptanib for the treatment of age-related macular degeneration: a systematic review and economic evaluation <i>Health Technology Assessment</i> 12:16. Available at: <a href="http://eprints.soton.ac.uk/72762/1/mon1216.pdf">http://eprints.soton.ac.uk/72762/1/mon1216.pdf</a></p> <p>Lee, A. (2008) The Lucentis Saga: NHS 0 Pharma 1 BMJ Rapid Response to NICE is accused of “jockeying for position” in new drug pricing scheme, <i>British Medical Journal</i> 2008;337:a1422 <a href="http://www.bmj.com/rapid-response/2011/11/02/lucentis-saga-nhs-0-pharma-1">http://www.bmj.com/rapid-response/2011/11/02/lucentis-saga-nhs-0-pharma-1</a></p> <p>NICE (2008) <i>Macular degeneration (age-related) – pegaptanib and ranibizumab: Appraisal consultation</i>. (London: NICE).</p> <p>NICE (2008a) <i>Macular degeneration (age-related) ranibizumab and pegaptanib (TA155)</i> Available at: <a href="http://www.nice.org.uk/TA155">http://www.nice.org.uk/TA155</a></p> <p>NICE (2008b) <i>Press release: 2008/052 NICE issues final guidance on the use of ranibizumab and pegaptanib for the treatment of age-related macular degeneration (AMD)</i>. Available at: <a href="http://www.nice.org.uk/media/FF8/DF/2008052LaunchOfLucentisForAMD.pdf">http://www.nice.org.uk/media/FF8/DF/2008052LaunchOfLucentisForAMD.pdf</a></p> <p>NICE (2008c) <i>Health Technology Appraisal, Appeal Hearing: Advice on ranibizumab and pegaptinib for the treatment of age-related macular degeneration</i>. Available at: <a href="http://www.nice.org.uk/nicemedia/live/11700/41675/41675.pdf">http://www.nice.org.uk/nicemedia/live/11700/41675/41675.pdf</a></p> <p>Nussbaum, M. (2001). Adaptive Preferences and Women's Options. <i>Economics and Philosophy</i>, 17, 67-88.</p> <p>Jackson, T.L, Kirkpatrick, L, Tang, G and Prasad, G (2012) Cost analysis comparing adjuvant epimacular brachytherapy with anti-VEGF monotherapy for the management of neovascular age-related macular degeneration, <i>Eye</i> 26, 557-563</p> |