National Institute for Health and Care Excellence
External Assessment Centre correspondence

GreenLight XPS 180W for prostate vaporisation in benign prostatic hyperplasia

The purpose of this table is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the sponsors’ original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the sponsor
b) need to check “real world” assumptions with NICE’s expert advisers, or
c) need to ask the sponsor for additional information or data not included in the original submission, or
d) need to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is made available to MTAC. The table is presented to MTAC in the Assessment Report Overview, and is made available at public consultation.
<table>
<thead>
<tr>
<th>Submission Document Section/Sub-section number</th>
<th>Question / Request</th>
<th>Response</th>
<th>Action / Impact / Other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>17/09/2015 Teleconference between EAC and manufacturer</td>
<td>Dear Catherine, et al.,</td>
<td>Noted by the EAC.</td>
</tr>
</tbody>
</table>
|                                               | Asked for additional materials.                                                    | As requested, we are sending along several documents in support of MT265, GreenLight XPS.  
  1. We have included a folder containing clinical studies comparing GreenLight HPS 120W to GreenLight XPS 180W. There is also a marketing brochure highlighting technical features of the GreenLight XPS 180W system. Dr. Kevin Zorn, a Urologist from Montreal Canada, has published an excellent article on how he uses GreenLight. This article shows photographs and provides clinical descriptions that are very detailed.  
  2. We also agreed to send a table showing where AMS has laser consoles, both 180W and 120W, across the UK. We respectfully request that this console placement table be treated as Commercial in Confidence.  
  3. We have included a recent RCT out of China comparing HoLEP to TURP. Please let us know if you need any additional information.  
    Best Regards, Kathy Kathy Sherwood,                                                                                                                                                                                                                     |                                  |
|                                               |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                       |                                  |
From: Catherine Meads  
Sent: Tuesday, September 29, 2015 10:07 AM  
To: Sherwood, Kathy;  
Subject: RE: Deliverables from AMS per TCon on Sept. 17  

Hi Kathy  
Many thanks for sending these through. Could you possibly send us the Greenlight operator's manual (the one with a complete list of possible risks and complications)?  
Kind regards Catherine

From: Ho, Ta-Yuan  
Sent: 29 September 2015 16:53  
To: Sherwood, Kathy; Catherine Meads;  
Subject: RE: Deliverables from AMS per TCon on Sept. 17  

Catherine,  
Attached is the GreenLight XPS Operator’s Manual. I want to point out that the XPS console is approved for multiple soft tissue surgery indications. The complications and risks are grouped by surgical specialty, so even within Urology, there are more indications than just BPH in there.  
Best regards,  
Ta  
Ta-Yuan Ho

From: Subhash Pokhrel  
Sent: Friday, October 16, 2015 9:07 AM  
To: Sherwood, Kathy  
Cc: Abigail Stevenson; 'Paul Dimmock'; Olu Onyimadu; Catherine Meads  
Subject: RE: MT265 Greenlight Section C Submission  
Importance: High  

Dear Kathy,  
As we are going through the model, we have identified a few issues (attached). Please can you get back to us at your earliest?  

From: Sherwood, Kathy  
Sent: 19 October 2015 22:02  
To: Subhash Pokhrel  
Cc: Abigail Stevenson; 'Paul Dimmock'; Olu Onyimadu; Catherine Meads; Ho, Ta-Yuan  
Subject: RE: MT265 Greenlight Section C Submission  

Dear Subhash,  
I wanted to let you know that our consultant economist is finalizing responses, and we should be able to get all your questions answered and returned  

Noted by the EAC.
| Many thanks,  
| Olu and Subhash.  
| Brunel Team  
| | to you sometime today (Tuesday, Oct. 20). We apologize for the delay, but needed to validate a few things with the team who pulled the HES data for us.  
| From: Sherwood, Kathy  
| Sent: 20 October 2015 16:17  
| To: Subhash Pokhrel  
| Subject: RE: MT265 Greenlight Section C Submission  
| Dear Subhash,  
| Attached, you will find two documents in response to your questions. The first is a Word document providing our (and our economist’s) answers, and the second is a slightly revised model incorporating the tweaks that are described in the Word document. Please let me know if you need anything else.  
| Best Regards,  
| Kathy  
| | arrived safely. Many thanks Kathy.  
| From: Subhash Pokhrel  
| Sent: Wednesday, October 21, 2015 4:34 AM  
| To: Sherwood, Kathy  
| Cc: Abigail Stevenson; ’Paul Dimmock’; Olu Onyimadu; Catherine Meads; Ho, Ta-Yuan  
| Subject: RE: MT265 Greenlight Section C Submission  
| Importance: High  
| Should there be any further questions, we will get back shortly.  
| From: Sherwood, Kathy  
| Sent: 21 October 2015 14:53  
| To: Subhash Pokhrel  
| Cc: Abigail Stevenson; ’Paul Dimmock’; Olu Onyimadu; Catherine Meads; Ho, Ta-Yuan  
| Subject: RE: MT265 Greenlight Section C Submission  
| Dear Subhash,  
| Thank you. Our economist wanted to add one more  
| Noted by the EAC.
Hope that’s OK.
Best wishes,
Subhash.

| Hope that’s OK. | minor clarification to our responses. For the 5 day trim point response, the reference costs are from 2013/14. |
| Best wishes, | Best Regards, |
| Subhash. | Kathy |

| General |  
| Wed 21/10/2015 16:51 |  
| Mr Andrew Thomas, consultant urologist |  
| Mr Andrew Thorpe, consultant urologist |  
| Mr Gordon Muir, consultant urologist |  
| Hi all |  
| I am contacting you because we are the EAC doing the evaluation for NICE on GreenLight. I wonder if any of you could help us with a couple of questions? |  
| Firstly, what proportion of urologists would you think are using bipolar TURP as opposed to monopolar TURP in the UK? |  
| Secondly, we have a number of urology-specific outcomes that are being reported in the clinical evidence. There seems to be a numerical difference between GreenLight and TURP but we are not clear about how much of a numerical difference would be seen as a clinically noticeable or meaningful improvement. For example in the table below from the GOLIATH trial, how many of the results would result in a noticeable difference between the two groups? If these numbers below wouldn’t result in seeing a noticeable difference, what would be the magnitude of numbers that would? |  

| Wed 21/10/2015 16:51 |  
| Mr Andrew Thomas, consultant urologist |  
| Mr Andrew Thorpe, consultant urologist |  
| Mr Gordon Muir, consultant urologist |  
| Hi all |  
| I am contacting you because we are the EAC doing the evaluation for NICE on GreenLight. I wonder if any of you could help us with a couple of questions? |  
| Firstly, what proportion of urologists would you think are using bipolar TURP as opposed to monopolar TURP in the UK? |  
| Secondly, we have a number of urology-specific outcomes that are being reported in the clinical evidence. There seems to be a numerical difference between GreenLight and TURP but we are not clear about how much of a numerical difference would be seen as a clinically noticeable or meaningful improvement. For example in the table below from the GOLIATH trial, how many of the results would result in a noticeable difference between the two groups? If these numbers below wouldn’t result in seeing a noticeable difference, what would be the magnitude of numbers that would? |  

<p>| General information useful but no specific actions taken. |<br />
| 22/10/2015 12:53 |<br />
| From Gordon Muir |<br />
| I would hope all surgeons now use bipolar but know this is not the case. Don’t have the numbers though Generally speaking patients are not aware of symptom score differences of less than about three points on the ipss and SHIM scores except perhaps at the extreme lower ends of both ranges (perfect erectile function and no urinary symptoms) I think when looking at the post op scores the pre-amp need to be considered since the perception of change is important to men. Clearly when there is a binary issue (eg severe bleeding vs no bleeding) that is very noticeable for the patient |<br />
| BW Gordon Muir Sent |<br />
| 22/10/2015 08:13 |<br />
| From Andrew Thorpe |<br />
| Dear Catherine, |<br />
| Off the top of my head its probably about 50:50 monopolar to bipolar, but that’s just an educated desk |</p>
<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Arm</th>
<th>6 month (mean (SD))</th>
<th>1 year (mean (SD))</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS (mean (SD))</td>
<td>GreenLight 180W</td>
<td>6.8 (5.2) (n=136)</td>
<td>7.0 (6.0)</td>
</tr>
<tr>
<td></td>
<td>TURP</td>
<td>5.6 (4.9) (n=133)</td>
<td>5.7 (5.3)</td>
</tr>
<tr>
<td>Qmax (mean (SD))</td>
<td>GreenLight 180W</td>
<td>23.3 (10.1) (n=136)</td>
<td>23.0 (10.7)</td>
</tr>
<tr>
<td></td>
<td>TURP</td>
<td>24.2 (11.4) (n=133)</td>
<td>24.7 (10.1)</td>
</tr>
<tr>
<td>PVR (mean (SD))</td>
<td>GreenLight 180W</td>
<td>38.4 (50.0) (n=132)</td>
<td>42.8 (56.9) # (n=129)</td>
</tr>
<tr>
<td></td>
<td>TURP</td>
<td>34.6 (50.6) (n=129)</td>
<td>33.4 (43.7) # (n=125)</td>
</tr>
<tr>
<td>Prostate volume (mean (SD))</td>
<td>GreenLight 180W</td>
<td>23.0 (11.7) (n=132)</td>
<td>21.9 (11.0) (n=100)</td>
</tr>
<tr>
<td></td>
<td>TURP</td>
<td>20.5 (11.7) (n=127)</td>
<td>21.0 (12.7) (n=102)</td>
</tr>
<tr>
<td>PSA (mean (SD))</td>
<td>GreenLight 180W</td>
<td>1.4 (1.5) (n=130)</td>
<td>1.3 (1.3)</td>
</tr>
<tr>
<td></td>
<td>TURP</td>
<td>1.0 (0.9) (n=127)</td>
<td>1.1 (1.0)</td>
</tr>
</tbody>
</table>

As far as the table below goes the only measures that might make a clinical noticeable difference, if there was a significant difference in them would be the quality of life scores, complication free rates and re-operation rates. However in Goliath there are no real significant differences. Goliath was only ever powered for equivalence and not superiority (I participated in it and co-wrote some of the papers), to show superiority it would require about perhaps 500-1,000 patients per group.

Another paper which we have just published on the health economics side is referenced below – hope it helps.

The Continuing Story of the Cost-Effectiveness of Photoselective Vaporisation of the Prostate versus Transurethral Resection of the Prostate for the Treatment of Symptomatic Benign Prostatic Obstruction


Best wishes

Andrew C Thorpe
<table>
<thead>
<tr>
<th></th>
<th>GreenLight 180W</th>
<th>TURP</th>
<th>GreenLight 180W</th>
<th>TURP</th>
<th>GreenLight 180W</th>
<th>TURP</th>
</tr>
</thead>
<tbody>
<tr>
<td>QoL (mean (SD))</td>
<td>1.5 (1.4) (n=134)</td>
<td>1.2 (1.2) (n=130)</td>
<td>1.3 (1.4) (n=129)</td>
<td>1.2 (1.3) (n=126)</td>
<td>1.3 (1.2) (n=127)</td>
<td>1.2 (1.3) (n=120)</td>
</tr>
<tr>
<td>ICIQ-UI SF (mean (SD))</td>
<td>3.0 (4.1) (n=132)</td>
<td>1.7 (2.8) (n=128)</td>
<td>3.3 (4.5) (n=128)</td>
<td>2.1 (3.3) (n=122)</td>
<td>2.8 (4.1) (n=122)</td>
<td>2.0 (3.3) (n=188)</td>
</tr>
<tr>
<td>IIEF-5 (mean (SD))</td>
<td>Nr (n=129)</td>
<td>14.2 (8.2) (n=121)</td>
<td>12.9 (7.5) (n=129)</td>
<td>14.2 (8.2) (n=121)</td>
<td>12.9 (7.5) (n=124)</td>
<td>13.9 (8.2) (n=119)</td>
</tr>
<tr>
<td>Complication-free (percentage)</td>
<td>87.3% (117/134)</td>
<td>83.2% (109/131)</td>
<td>84.7% (111*131)</td>
<td>80.5% (102*127)</td>
<td>83.6% (107*128)</td>
<td>78.9% (95*121)</td>
</tr>
<tr>
<td>Surgical retreatments for obstruction (numbers)</td>
<td>4 (n=131) ~</td>
<td>7 (n=125) ~</td>
<td>6 (n=124) ~</td>
<td>2 (n=120) ~</td>
<td>4 (n=58) ~</td>
<td>1 (n=60) ~</td>
</tr>
</tbody>
</table>

* calculated from percentages. # p<0.05,
~ number of patients at risk from Kaplan Meier graph
so calculation of percentages would be misleading.
Nr – not reported

Many thanks Catherine

Dr Catherine Meads

| General | Visit to Frimley Park Hospital by Subhash Pokhrel and Olu Onyimadu on 23/10/2015 to watch GreenLight 180W treatment being used, organised by Justin Hartlen  
(See email below) | General information, no specific actions taken |

4.5 Additional work undertaken by the External Assessment Centre in relation to economic evidence

**From:** Subhash Pokhrel  
**Sent:** Friday, October 23, 2015 7:28 AM  
**To:** Sherwood, Kathy  
**Subject:** RE: MT265 Greenlight Section C Submission

Dear Kathy,

Just to say a big thank you for organising our “GreenLight in Action” this morning. It was indeed very helpful. Please convey our thanks to Justine for looking after us and Mr Barber for showing and explaining the technology so clearly.

One more follow-up question: we thought that having access to GOALIATH dataset (raw data) would be very helpful for us to understand some of the uncertainties raised by published aggregated data. In particular, as it became apparent this

**From:** Sherwood, Kathy  
**Sent:** 23 October 2015 15:06  
**Subject:** RE: MT265 Greenlight Section C Submission

Dear Subhash,

Your welcome! I am indeed pleased that you enjoyed your experience with Mr. Barber.

Regarding the raw data, I will immediately make a request to the clinical organization and our Chief Medical Officer to release the raw data. I know that they will ask for verification that the data will be secure, not made public or shared outside of your organization and that no publications will be
morning in the conversation with Mr Barber, the average values in the published GOLIATH papers which is one over multiple countries where practices vary significantly may not be directly applicable to the UK context. Likewise, it is hard to estimate the likelihood of multiple adverse events in both groups just based on published aggregated data.

Would it be possible by any chance to have the GOLIATH raw dataset (preferable) or at least a detailed trial analysis report in academic confidence?

Best wishes,
Subhash.

| From: | Subhash Pokhrel |
| Sent: | Friday, October 23, 2015 9:25 AM |
| To: | Sherwood, Kathy |
| Subject: | RE: MT265 Greenlight Section C Submission |
| Importance: | High |

Many thanks Kathy.

Yes, the data will be used exclusively for the purpose of current assessment only and will not be shared outside the Assessment Team. Data will be kept secure.

No publications will be developed. However, I am sure that you are aware of the fact that the EAC Report will be in the public domain eventually and we may want to do an academic publication of the assessment once signed off. Depending on it. I am sure it goes without saying, but having a formal response will help me expedite your request.

Best Regards,
Kathy

Dear Subhash,

I am working with the Clinical leaders within Boston Scientific to see if we are able to share raw data. Unfortunately, there is a policy within Boston that we are unable to do so. However, I asked whether we could share a subset of the data for UK specific patients, and was granted permission to do so. The data will be presented in a series of tables summarizing primary endpoint achievement (International Prostate Symptom Scores (IPSS) and Qmax (measure of urinary flow rates), adverse event rates, Time to Stable Health Status (the time when a patient no longer has a catheter and is able to void successfully with no evidence of blood in the urine), which is a surrogate measure of fitness for
what we find from GOLIATH raw dataset and how it will be used in the Assessment Report, both publications may contain some figures from GOLIATH which are unpublished to date.

Hope that is clear and OK.

Best wishes,

Subhash.

discharge, and the length of stay data.

Our bio-stats team is compiling the UK tables, and should have them complete tomorrow or Wednesday at the latest.

Additionally, I thought you might be interested a recently published abstract by Mr. Neil Barber from the World Congress of EndoUrology in London, October, 2015:

**MP26-14** A comparison of the costs of different surgical techniques for transurethral prostate surgery
T Mahesan, SV Segaran, NJ Barber Frimley Park Hospital United Kingdom

**Introduction:** Greenlight photoselective vaporisation of prostate (PVP) is increasingly used in bladder outflow surgery. It has the advantage of being a day case procedure, however costs are thought to be higher than traditional alternatives. At our district general hospital, we perform over 200 cases annually for management of benign prostate hyperplasia. Largely these operations are composed of bipolar transurethral resection of prostate (TURP) and PVP. We compared the overall costs of the different surgical techniques with a view to determining which was more cost effective.

**Method:** All bladder outflow procedures in 2013 were retrospectively identified and case notes reviewed. Demographic data, as well as length of stay and information on any complications...
that occurred were collected. With assistance from the hospital financial department, we calculated costings including staff wages, equipment costs and hospital overhead, accounting for length of stay and operative time. Financial implications of any subsequent readmission were also included.

**Result:** In 2013, our district general hospital performed 214 bladder outflow operations, 144 of which were bipolar TURP and 70 PVP. Average length of stay for TURP was 2.64 days (range 1–16) with 21 patients subsequently developing persistent haematuria and two developing acute urinary retention. 12 (8.3%) were later readmitted, with an average length of stay of 4.18 days (0–16) Average length of stay for PVP patients was 0.46 days (0.5–3), with two subsequent complications (haematuria and acute retention). 9 patients (11.43%) were readmitted, staying an average of 3.13 days (1–7). TURP cost was £2198 and, when factoring in readmission rates increased to £2293. PVP cost was £1763 and allowing for readmission, £1859.

**Conclusion:** Our DGH has a complication rate that is consistent with published data, although our readmission rate was slightly higher than expected. Even allowing for this, our data supports PVP as an excellent day case alternative to TURP with comparable cost and complication rates.

Best Regards,

Kathy
<table>
<thead>
<tr>
<th>Date</th>
<th>From: Sherwood, Kathy</th>
<th>Sent: 28 October 2015 20:05</th>
<th>To: Subhash Pokhrel</th>
<th>Subject: RE: MT265 Greenlight Section C Submission</th>
</tr>
</thead>
<tbody>
<tr>
<td>28/10/2015</td>
<td>Dear Subhash and Team,</td>
<td></td>
<td></td>
<td>I am attaching data from the GOLIATH trial broken</td>
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<td></td>
<td></td>
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<td>out by country, as well as the GOLIATH protocol.</td>
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<td>There are a few definitions that are important:</td>
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<td></td>
<td>1. Time to Stable Health Status is measured as</td>
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<td></td>
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<td></td>
<td></td>
<td>the time from entry into the theater recovery</td>
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<td>room until the time when all of the following</td>
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<td></td>
<td>are met: Absence of clinically significant</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>hematuria, Successful urinary voiding trial,</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>and Pain managed with oral non-narcotic</td>
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<td></td>
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<td>medication (See Table 1 of the Protocol)</td>
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<td>2. Definition of ‘Day Case’: any patient who</td>
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<td>was discharged on the same calendar day as the</td>
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<td></td>
<td></td>
<td>procedure was performed.</td>
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<td></td>
<td></td>
<td>I hope you find this helpful. Please treat this</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>as academic in confidence.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Best Regards,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Kathy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>General</th>
<th>Tuesday 17/11/2015 09:25</th>
<th>17/11/2015 09:42</th>
<th>No action required</th>
</tr>
</thead>
</table>

Noted.

One of the data from the summary tables was used in the AR as academic in confidence.
Hi All

The NICE team has asked if we can confirm with you that in the context of BPH, adenoma is sometimes used as a synonym for BPH, given adenoma is the main tissue involved. Please could you confirm if this is correct.

Thank you.

Carole

Dr Carole Cummins

From Andrew Thorpe

Correct

Thu 19/11/2015 18:47

From Gordon Muir

Terminology is important here and while some urologists still say “adenoma,” this really is based on older surgical techniques rather than anatomical studies

BPH or BPE is better but that is what most people mean when they say “adenoma” unless specifically talking about laser enucleation of the prostate

From: Carole Cummins

Sent: 25 November 2015 18:12

Dear Gordon

NICE has asked if you could clarify what “adenoma” means in the context of laser enucleation of the prostate? Does it still mean BPH or does it for example refer to the lobes/tissue causing obstruction.

Thank you.

Carole

From: Gordon Muir

Sent: 30 November 2015 21:17

Its not an anatomical term really and means different things to different people. Best described as the tissue removed during an expert prostate enucleation or open prostatectomy (which is pretty well obsolete)

But used by TURP surgeons to mean something fairly variable

Gordon
Appendix
Attached to email from Cathy Sherwood 18.9.2015:

Published peer review papers (pdfs not included for reasons of copyright):


Campbell NA et al. "Early experience photoselective vaporisation of the prostate using the 180W lithium triborate and comparison with the 120W lithium triborate laser". Prostate Int 2013;1(1):42-45.


Greenlight – XPS Brochure (pdf file)

Word document with List of sites with Greenlight-XPS laser systems in the UK – text below (commercial in confidence).
Attached to email from Cathy Sherwood 18.10.2015:
Word document with answers to questions on the model – text below:
1) We reconstructed a decision tree using TreeAge based on the Sponsor’s model structure and assumptions, so as to reproduce the expected costs and difference in cost between Greenlight and TURP (as reported in the Results sheet, cell I42). This reconstruction is necessary for us to be explicit about all assumptions involved and also independently evaluate uncertainty in results.
   a. Please can you review and let us know whether if it is accurate depiction of your model structure?
   b. If you think any aspect is not accurately represented, please can you indicate so?

For the most part the tree is represented accurately, with the following exceptions:
- For simplification, the cost of the excess day charge was applied directly to the inpatient stay rather than applying an additional node. As the proportion of patients exceeding a 5-day stay was obtained from aggregate data this was divided by the proportion of patients in the inpatient stay arm to derive to calculate the cost in the decision-tree. In the model results sheet, for simplification this was applied directly to the total procedure cost.
- Similarly, the proportion of patients that were symptom free after 5 months was applied to all branches and assumed to be constant irrespective of whether patients had an extended stay or suffered an adverse event. This was a simplification as this data was only reported at aggregate level. This assumption was not expected to impact on costs as no costs were attributed to this outcome. This was included in the model to demonstrate equivalent effect
- The probability of a grade 2 or a grade 3 events were considered separately in the decision tree and assumed to be independent of each other. As grade 2 events were assumed to be independent of grade 3 events the probability of a grade 3 event was applied to both patients who did and did not have a grade 2 event and this likelihood was assumed to be constant
- All the transition probabilities applied are reported in a new sheet titled ‘DECISION TREE’, added to the sponsor’s revised submission, addressing the issue raised below. The total costs for each arm are the same as the total costs broken down by cost types reported in the results sheet.

2) The estimation of the expected cost of excess bed days for patients who stay less than 5 days and similarly for 5 days or more is unclear in the Sponsor’s model.
   a. Please can you explain why you thought subtracting 5 from mean excess bed days will give you that answer? [Results sheet: cell G36]
   b. What is the justification for setting a 5 day cut-off? Where does the evidence come from?
   c. Can you explain exactly how you estimated/obtained HES data on lengths of stay, e.g. any specific code you used?
The National tariff trim point for BPH surgeries is 5 days. It was therefore assumed that the cost of treating patients that stayed more than 5 days was equivalent to the standard reference cost for an inpatient stay plus the number of days they stayed beyond 5 days multiplied by the excess bed day cost. The cost of the excess bed days was therefore calculated by obtaining the mean length of stay amongst those that stay more than 5 days and subtracting this by 5 as the excess bed day charge was assumed to only apply from day 6 onwards. The value for the mean length of stay amongst those that stayed more than 5 days was obtained from Device Access, who have access to the HES dataset captured by the HSCIC. This analysis was based on the episodes of care which met the criteria M56X and M67.1 for the year of April 2014 and 2015. These data were extracted for all relevant codes and stratified by provider, OPCS description and by proportion of patients with an inpatient stay exceeding 5 days.

3) Please can you provide the following percentages/proportions or probabilities that are currently missing from the model:
   a. Probability/proportion of those who have or don’t have post-surgery complications (adverse events)
   b. Probability or proportion of those who have symptoms or do not have symptoms in the ‘No post-surgery complications’ group.

The original model assumed that all grade 2 and grade 3 events were mutually exclusive and did not account for any overlap between events. This assumption was a simplification and may have overestimated the cost of adverse events as it did not take into account any synergies in treating patients that may have had two or more different types of events. As we agree with the point raised by the NICE review team, that these events are not mutually exclusive, the model structure and assumptions have been revised from the original assumptions as follows:

- Instead of considering the percentage of non-acute events and the percentage of 30-day and 90-day re-admission we applied the total proportion of patients that experience a grade 2, grade 3a and 3b reported in the GOLIATH RCT at 6 months. These were similar but slightly different from the original value applied.
- This change was made as total values were reported by the percentage of patients that had one or more grade 2, 3a or 3b event as well as the proportion of patients that had each type of event, thus the overlap between events could be calculated.
- To account for the proportion of patients that had multiple events a weighted cost was calculated for each comparator. This was calculated as the weighted average cost multiplied by one plus the proportion of patients expected to have more than one event.
- The probability of a grade 2 or a grade 3 events were considered separately in decision and assumed to be independent of each other.
- To validate the results and illustrate the probabilities the total costs are calculated on the model results tab and on an additional sheet titled ‘DECISION TREE’.
• Applying this slightly modified set of assumptions changed the total cost of both comparators slightly but the results and conclusion were very similar. This is because the proportion of patients that experienced more than one grade 2 or grade 3 event was very low and the risk of adverse event was not the main driver of the model.
• The new inputs for the total percentage of patients that had a grade 2, 3a or 3b were added to the sensitivity analysis and the conclusions were similar to the original analysis.

4) Since the adverse events are not mutually exclusive, we are not sure how probabilities of their occurrence are computed in the Sponsor’s model. Our reconstruction of the model makes provision for the proportion of patients (from the total number of patients who have post-surgery complications) who either have a re-admission from Grade 3 adverse events or have no admission from Grade 2 adverse event.
   a. Please can you provide this data along with the sources?
   b. If you think, this data is not needed as the model has already incorporated that in some ways, please explain that.

This has been addressed above. All probabilities for the proportion of patients experiencing grade 2 or grade 3 events were obtained from Bachmann et al. 2014
The probabilities applied for the average risk population were as follows:
• Prob of Grade 2 event for GreenLight= 22.06%
• Prob of grade 3a event for GreenLight = 6.62%
• Prob of grade 3b event for GreenLight = 7.35%
• Prob of Grade 2 event for TURP= 14.29%
• Prob of grade 3a event for TURP = 10.53%
• Prob of grade 3b event for TURP = 9.77%

The probabilities in the high risk patients were the same as the GreenLight probabilities but adjusted for a higher risk of bleeding and the probabilities are assumed to be the same for both GreenLight and HoLEP.

5) We have identified some issues with specific cells as described below. Please can you address those?
<table>
<thead>
<tr>
<th>Sheet</th>
<th>Cell</th>
<th>Issue</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost inputs</td>
<td>Q110</td>
<td>Inflation formula not transparent and result is counterintuitive; unit costs inflated from 2010 are 2013/14 are lower than original unit costs</td>
<td>According to the NHS inflation index sourced from the Office of National Statistics there was deflation in the year 2010/11 as the inflation rate was 0.97. This offsets the very low inflation rate in the subsequent years 2011-2014 of 1.008, 10.1 and 1.007 respectively</td>
</tr>
<tr>
<td>Cost inputs</td>
<td>Q120</td>
<td>Inflation formula not transparent and result is counterintuitive; unit costs inflated from 2010 are 2013/14 are lower than original unit costs</td>
<td>As above</td>
</tr>
<tr>
<td>Results</td>
<td>G38</td>
<td>Formula refers to a cell, M106 on the Cost inputs sheet, which is empty</td>
<td>Originally mild incontinence was considered in the model but this was removed when further investigation found that this incurred no treatment</td>
</tr>
</tbody>
</table>
cost and thus the cost was reduced to zero. The formula error is thus typographical. As this input has been removed this is no longer relevant. Removing this from the equation does not change the result.

<table>
<thead>
<tr>
<th>Results</th>
<th>G38</th>
<th>While model assumption states that mild urinary incontinence would not be used as a cost, it has been included in the formula in cell G38</th>
<th>As Above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical inputs</td>
<td>F29 and J29</td>
<td>Do you mean less than or greater than 5 day stay? Currently it appears as &lt;, whereas the formula suggests otherwise</td>
<td>This was a typographical error and has been amended to be &gt;</td>
</tr>
<tr>
<td>Clinical inputs</td>
<td>G58</td>
<td>Not clear whether definition of excess bed day counts from stay beyond midnight on day of operation or does it count from those</td>
<td>The National tariff trim point is assumed to apply when patients exceed 5 days admission, starting at midnight on day 5. This assumption is</td>
</tr>
</tbody>
</table>
who stay beyond 4 days? explained in more detail above

Attached to email from Cathy Sherwood 28.10.2015:
Commercial in confidence
GOLIATH trial protocol
Academic in confidence