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Dear Reetan,

**Response to Assessment Report:
Stapled Haemorrhoidopexy for the Treatment of Haemorrhoids**

Thank you for the opportunity to respond to the above Assessment Report (AR). The report is extensive and summarises the available evidence in a balanced manner. There are just a few issues that we wish to draw to the Committee's attention, in the hope of informing the discussion to the value of the Stapled Haemorrhoidopexy procedure.

The York Group conclude that there is little from their model to separate the relative costs and benefits of the two procedures, and that on the basis of this, the decision on which is the most appropriate intervention is best left to discussion between patient and surgeon, discussing the risks and benefits of each. Whilst we recognise this is a suitable outcome and appropriate way forward for patients and surgeons, we do believe that the York group have undertaken a very conservative evaluation of Stapled Haemorrhoidopexy. If a more realistic scenario is modelled, using quality of life impacts more representative of the impact of CH, and recognising that Stapled Haemorrhoidopexy can and is already assisting a proactive switch in the delivery of patient care to the day-case setting, the stapled procedure becomes an even more beneficial option for both the patient and the provider.

Our response starts with a few comments on the background, however the key issue we wish to draw to the Committee's attention relates to the different assumptions used to estimate utility values.

If you have any questions on our response prior to the Committee meeting please do not hesitate to contact me.

Yours sincerely,



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Specific Responses to York Assessment Report

Section 3: Background

Section 3.3 Description of technology under assessment: The description in this section is not generic; it is the description of the PPH01 & PPH03 device. It does **not** describe nor apply to the procedure involved in using the STRAM kit.

Section 3.3.3 Costs: This again is the current cost of the PPH03 kit, and not applicable to the STRAM kit.

Section 5.1.2.2: The report indicates that it includes evidence on the STRAM kit, however we note that no evidence is reported or available.

Development from PPH01 to PPH03

The report comments that there is little data related to PPH03. The difference (apart from colour) between PPH01 and PPH03 is that the closed staple height (which is adjustable in both) can be reduced down to 0.75 mm with the PPH03 gun rather than 1mm with the PPH01 gun. As reported in our submission, page 11, the RCT study by Arroyo et al (2006) demonstrated that this modification reduced intra-operative bleeding, all other outcomes being unchanged. The staple materials, device diameter, and firing mechanisms are all unchanged.

Section 5: Assessment of Clinical Effectiveness

Comment on differences between EES & York Meta-Analyses

We recognise that there are differences in the studies included in the two meta-analyses (EES and York), however we are pleased to see the results are broadly in line.

To clarify, the differences in study inclusion are driven by the following:

- EES included all circular stapler studies; this resulted in the inclusion of early studies that used the CDH33, the original circular stapler developed by EES for general colorectal surgery. For information, this was the device used by Longo to develop the Haemorrhoidopexy procedure. As a result of Longo's work, EES then developed the PPH01. York only included PPH01.
- EES restricted studies to only include Milligan Morgan or Ferguson as a comparator, in line with the Final Scope. York included other alternative techniques as comparators, such as Parks, Fransler & Anderson.
- EES restricted its review to English publications. York included non-English language studies.
- EES restricted its review to full published texts. York also included studies published as abstracts.

Despite the differences, the outcomes of the meta-analysis are in agreement.

Section 6: Assessment of Cost Effectiveness Evidence

Economic Evaluation

Whilst there are differences between the structures of the two models, we are reassured that the different models tend to reach similar conclusions, and that the key drivers are the same in each.

We recognise the short-comings in our model, as detailed in page 107 of the York report.

- Our model was restricted to 12 months, yet we feel this is acceptable as the York model demonstrates that activity in yrs 2 & 3 are not drivers of cost.
- We recognise that time to re-do surgery was short in our model, however again sensitivity analysis demonstrated this not to be a significant driver.

We also agree with the general overview from York (6.2.5, p151) that the drivers of cost effectiveness are:

- utility estimates
- length of recovery period
- hospital resources

We address each in turn below:

Driver 1: Utility estimates

As stated in the York report, "*The parameter that most affects the results, and which is most uncertain, is how differences in pain during the early post-operative period should be valued in terms of utility. No evidence has been found to support this, and consequently the base-case uses a series of modelling assumptions*", page 152. Estimating utilities for this review is difficult, and none of the methods followed are perfect. However, we consider that the York estimates significantly underestimate the patient benefits, and therefore the value of the stapled procedure.

Use of HODaR

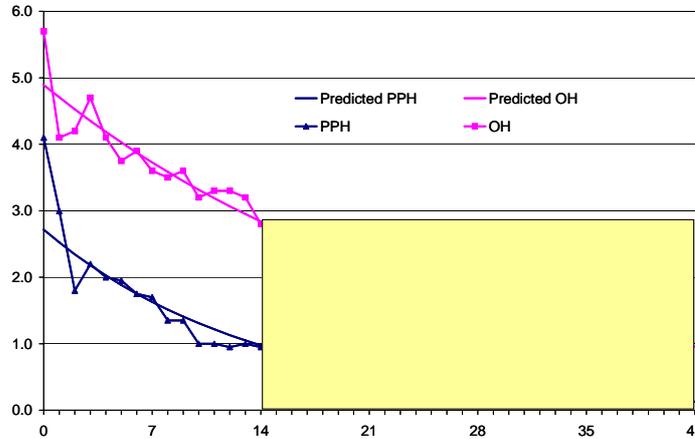
When building our own model for this submission, we considered using HODaR, however rejected it because the recall period used in its QoL assessments is inappropriate to assess the short term benefits of the stapled procedure. The SF-36 used in HODaR is completed at 6 weeks post discharge, and has a 4 week recall period (York report p105). This data source, of 53 patients at one time point, therefore fails to capture the most significant benefit of the stapled procedure, as the report confirms that the most severe pain is reported 2 to 4 days post operatively (York report p36).

Therefore, the HODaR data misses the 1st two weeks which report the biggest impact in terms of pain. For example **Figure 1** below depicts the daily reported VAS pain scores from the Van de Stadt study (2005) used in the EES calculations, and the extrapolated data to 6 weeks. The shaded area represents the recall period covered by the SF-36 survey in HODaR, and therefore used to inform the utilities estimated by York.

Accepting that pain is the key short term driver of Quality of Life, an assumption made by both EES and York, means that the mean SF-36 values used from HODaR will significantly underestimate the dis-utility caused by pain. The detriment in Quality of Life estimated by the York methodology will not be as great as it would have been, had it included the initial follow up

period. In comparison, the relevant data from the Van de Stadt study included 35 patients with 21 time points, including the initial post operative where the largest benefits are observed, giving a basis for modelling as reliable if not better than that offered by the HODaR database.

Figure 1: EES model - Change in daily VAS pain scores over time

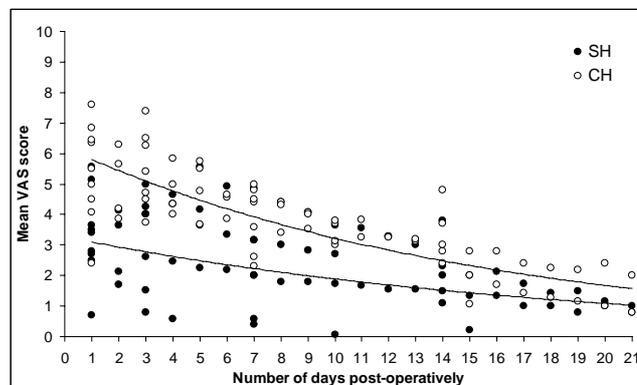


York Modelling

York model the benefit of the Stapled Haemorrhoidopexy procedure as a 35% ‘benefit’ or reduction in the impact of pain compared with CH, calculated using odds. There are two issues with this approach:

- First, using odds applies a relative reduction to pain from the ‘starting position’. As discussed above, the starting position assumed in the York model is too conservative; therefore any percentage benefit applied from that position is likewise under-estimated, as it is relative. The absolute benefit of Stapled Haemorrhoidopexy used in the QALYs calculation is therefore under-estimated.
- Second, **Figure 1** demonstrates that the relative reduction in pain is greater than the 35% modelled by York. This is also confirmed by the York graph (page 54) reproduced below as **Figure 2**, which suggests a reduction closer to 50% in the early phase.

Figure 2: York Report - Mean VAS pain scores reported in the included RCTs over 21 days post-operative period



The 35% benefit is obtained from a Bayesian meta-regression of pain scores (appendix 10.4, p196) that also predicts VAS pain has decreased to less than 0.5 in both groups by day 21. EES

would suggest that the observed data collected directly from clinical trials, presented in Figures 1 & 2, refute both of these conclusions.

Daily pain scores have also been published in another study included in both meta-analyses, Gravie (2005). This supports the argument above that pain is greatest in the first week, and the reduction in pain from SH is greater than 35%, **Figure 3**.

Figure 3: Daily VAS Pain scores, Gravie, 2005

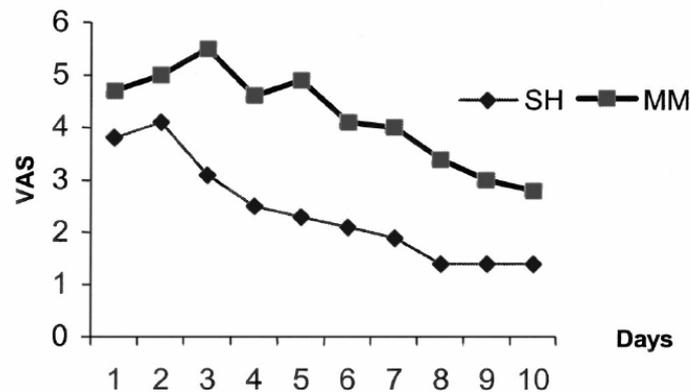


FIGURE 1. Mean pain (visual analog scale [VAS]) during bowel movement.

These findings are aligned with Van De Stadt study. We selected Van De Stadt in preference because of the longer follow up period.

Utility Summary

The York model underestimates utility, and hence the benefits of Stapled Haemorrhoidopexy, on two accounts:

- First, by using an average of SF-36 scores as a baseline from a time period when the most acute pain has passed, over-estimates the utility of the CH procedure, as it is based on a reduced impact of pain.
- Second, the use of a fixed relative benefit for pain reduction from Stapled Haemorrhoidopexy underestimates the procedure's benefit. As the level of 'baseline' pain is already underestimated, any relative reduction from that lower starting point must underestimate the absolute benefit of the procedure.

The York group acknowledge their estimates may be conservative (page 132), but do not adjust for it in their base case. When using our estimates in their model, York reports a cost effective outcome. We propose that the base case is not a fair base case, but an overly conservative one.

Driver 2: Length of recovery period

The York model concludes that all patients (without complications or recurrent prolapse) have returned to normal in 43 days, and state that a flaw in our model is that benefits continue to accrue to day 120.

We consider the York assumption to again be highly conservative, as their own report states that between 6.7% and 52.5% of patients undergoing CH still have unhealed wounds at 6 weeks (42 days), and between 6.3% and 20% of patients undergoing CH have unhealed wounds at 12

weeks. The utility gain accumulated at these later stages is very small in the EES model, but given that some individuals will still have wounds and experiencing pain, this does not appear to be an unjustified inclusion. We assume the York assumption that normality is achieved in 43 days appears to have been driven by their Bayesian meta-regression, discussed above.

Driver 3: Hospital Resources

Unit costs – Discrepancies in report

- Please note, the list price for the PPH03 kit is £420. Whilst this is quoted correctly in the York report (page 28), it appears to be incorrectly used in the York model; the base-case uses a unit cost of £437, (Table 6.15, P117, and excel model {parameters sheet, AZ216}).
- The base case cost of Rubber band ligation & Sclerotherapy is quoted in table 6.10 (Page 112) as £140, and in the text (Page 128) as £149. The model however appears to use figures of £381 & £224, for reasons we do not understand ('Parameters' sheet, cells C223:CI226). Whilst we recognise this is not a driver of cost effectiveness, this discrepancy was found by chance; we have not had an opportunity to validate other entries.

RCTs v Policy: Use as Day Case and Length of Stay

The York report suggests that only RCT data should be used to estimate the relative differences in length of stay, or the ability to deliver as a day case option. We disagree with this. Haemorrhoidectomy has been a DH focus for day-case surgery and identified by the Audit Commission as far back as 2000 as an opportunity to improve efficiency. Only local policy decisions in delivery will trigger that change. Clinical practice has resisted, primarily due to issues around post operative pain management. The Stapled Haemorrhoidopexy procedure now offers an alternative, by delivering less pain, and we are aware of numerous centres who already use PPH to facilitate a policy change of care delivery to a default day case setting. One centre, Mr Pawan Mather, Barnet and Chase Farm NHS Trust, has just submitted a paper on day case surgery using Stapled Haemorrhoidopexy to Colorectal Disease ("Short Term Results of Day Case Stapled Haemorrhoidopexy"). A manuscript can be provided on request.

Our use of HES data and the review by Beattie to inform the day case / length of stay durations in our model are therefore considered to be conservative, for the reasons detailed in our original submission.

Conclusion

We reiterate the conservative nature of the assessment group's valuation of utility benefit and of the ability for Stapled Haemorrhoidopexy to facilitate the move to a greater day-case setting.

Furthermore, we believe that the 29 RCTs included in our systematic review (27 in the York review on the PPH guns) underline the significant body of evidence that supports the value of the Stapled Haemorrhoidopexy procedure. We therefore conclude that on the balance of current evidence, Stapled Haemorrhoidopexy is a cost effective option for the surgical management of haemorrhoids.