Responses to comments on the Stapled Haemorrhoidopexy for the Treatment of Haemorrhoids Assessment Report.

Clinical section

Comment	Response
P2: The description of the technology under assessment 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. The section on costs is the current cost of the PPH03 kit, and not applicable to the STRAM kit.	We found no evidence to include in the review regarding to Autosuture with the STRAM kit, therefore the only technology being assessed in the review was the PPH guns.
P2: The report indicates that it includes evidence on the STRAM kit, however we note that no evidence is reported or available	We state in this section that studies evaluating Autosuture with the STRAM kit were eligible to be included, however, we found no data to include.
P2: 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	The reason we highlighted this issue, is that the modifications to the PPH03 gun could improve outcomes with SH, therefore readers should be aware that we may have under-estimated the effectiveness of the currently available gun.
P2: 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	We acknowledge that Longo used the general GI staple gun, however, as guns specially designed for SH have now been developed, and NICE are unlikely to recommend the use of any other type of gun, it seemed more relevant to the current research question to only evaluate those that are designed for the surgery. It is possible that trials evaluating guns not specially designed for SH would report poorer outcomes than the later developed guns, therefore including them may have underestimated the effectiveness and safety of SH.

P2: 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	Given that there is the use of a wide range of conventional excisional techniques, we deemed it appropriate to include them all, and investigate any heterogeneity this caused. This would allow surgeons that used an alternative technique to Milligan Morgan or Ferguson to assess the comparative efficacy of SH to the technique they used
P2: EES restricted its review to English publications. York included non-English language studies	By avoiding language bias, we maximised the available data
P2: EES restricted its review to full published texts. York also included studies published as abstracts	Of the 27 RCTs, 2 were published only as abstracts, one of which had two associated abstracts; they had to pass the same inclusion criteria as full manuscripts and provide outcome data One RCT informed four outcomes (post-operative pain, bleeding, urinary retention and reintervention rate), and the other two outcomes (post-operative pain and time to normal activity).

Economic section

Comment	**Response**
P3 Use of HODaR data and the reliability of the Van de Stadt data	EE-S and York note that pain is the key short term driver of Health Related Quality of Life (HRQoL). The York model used HODaR data to represent the average SF-36 score during the 0 to 6 week post-operative recovery period in patients who underwent conventional haemorrhoidectomy (CH). These data were adjusted to estimate the values that might have been reported if patients had undergone stapled haemorroidopexy (SH). Based on a meta-regression to predict VAS pain scores for each treatment group (described in Section 5.2.2.2) it was estimated that SH was associated with 35% less pain than CH during this period. The York model combined data from VAS pain scores and SF-36 to estimate utility values that might have been reported if patients had undergone SH. As QALYs are made of utility values and time spent in particular health states, the duration of time over which differences in pain persist across treatments is relevant and this was included in the York model. EE-S argues that the Van de Stadt data is more reliable than other forms of data for assessing pain over the initial 21 day follow-up period. York did include the Van de Stadt data. However, evidence was synthesised across a broader range of

	evidence, incorporating data from nine other RCTs as well. The relative difference in pain scores was applied to the "baseline" data of HRQoL after CH from HoDAR. Therefore the approach assumes that this baseline represents the average HRQoL for the entire 6 week period. The shaded area in EE-S' Figure 1 does not accurately represent the York model results. The baseline is not "zero" for the first two weeks, rather it is the same as in the later period. No other, more relevant data were found in order to estimate utilities over this period. Indeed, it was found that the HODaR data was the best available source of SF-36 data during this early post-operative period for patients undergoing CH. The only RCT (Wilson) reporting SF-36 data suffered methodological flaws (e.g. patient characteristics differed across the arms of the trial, poor reporting and included irrelevant alternatives). However, it may be the case that baseline pain and/or HRQoL could be underestimated in the first few days, based on the HoDAR data. To test the findings of the York model to this assumption, a one-way sensitivity analysis was conducted in which the difference in QALYs across treatments was increased for the first two weeks post-operatively (scenario 2.8). This did increase QALY differences but not sufficiently to reduce the ICER below £40,000 per QALY.
P4 Relative reduction in pain over post-operative period	EE-S suggests that the relative reduction in pain due to SH is greater than the 35% modelled by York using Figure 5.3 in the York report. York chose to present a line of good fit for a constant relative treatment effect of 35%. It was not intended to represent the predicted results of the meta-analysis. York agrees that this graph could be misleading and therefore, to enhance clarity, York will adjust this in subsequent publications.
P5 Duration of the recovery period	EE-S suggests that a Bayesian meta-regression was used by York to assume that patients achieve normality at 43 days post-operatively. York should have made it clear that this time period was estimated based on expert clinical opinion. Added to this, it seems that none of the RCT trialists believed that there would be a difference that merited being recorded after 21 days. It may be the case that there are patients with unhealed wounds which persist beyond 6 weeks. York assumed that it would be complex to appropriately incorporate the healing process for these patients into the analysis, in addition to the symptoms and persistent complications that were already included within the analysis.
P6 Unit costs	EE-S points out that the list price for the PPH03 kit is £420. York reports that the cost is £437 (Table 6.15, P117, and Excel model {parameters sheet, AZ216}) once the 2004/5 cost is uprated to 2005/6. York accepts that if a cost of £420 were used, this would reduce the difference in total cost to only £1 or £2.

	EE-S note that in the York analysis, the base-case cost of rubber band ligation and sclerotheraphy is quoted as £140 (Table 6.10, Page 112) and as £149 in the text (Page 128). York affirms that the value for the base-case in the model is £140. Other values were tried in sensitivity analyses. York agrees that the text is inconsistent and this will be amended in the update version of the report. York notes that the values do not affect the results.
P6 RCTs vs. Policy: Use as Day Case and Length of Stay	EE-S suggests that the non-RCT based data should be considered to estimate the relative differences in length of stay, or the ability to deliver as a day case option across surgery options. York suggests that the RCT evidence is historic and context-specific and that the estimates that they used may overestimate the average resource savings that can be expected to arise in NHS clinical practice. York suggests that whether the procedure is "cost-effective" depends on local conditions, and the degree to which local managers are able to implement the necessary service delivery changes.