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Transperineal biopsy in people with suspected prostate cancer - a systematic review and economic evaluation Addendum

Produced by Southampton Health Technology Assessments Centre (SHTAC)

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Introduction

This document is an addendum to a Diagnostic Assessment Report (DAR) for the NICE Diagnostics programme assessment of 'Transperineal biopsy in people with suspected prostate cancer - a systematic review and economic evaluation'. The DAR was submitted to NICE on 23rd November 2021 and this addendum reports additional analyses of clinical effectiveness and cost-effectiveness requested by the NICE technical team following submission of the DAR. The addendum should be read in conjunction with the DAR.

1 Meta-analysis scenarios

The systematic review of diagnostic test evaluation and clinical effectiveness reported in the DAR included a total of 23 studies evaluating transperineal prostate biopsy, of which all but five were included in quantitative pairwise meta-analyses. In addition, indirect comparisons were performed using network meta-analysis (NMA) to inform an incremental cost effectiveness analyses of the various prostate biopsy modalities within the decision problem. The NMA included randomised controlled trials (RCTs) only (n=6). Following submission of the DAR to NICE, the EAG was asked to explore the impact of adding and/or removing specific studies from the meta-analysis on the cost-effectiveness analysis. Below we report sets revisions made in respect of the following:

1. Removal of three studies from the meta-analysis which used spinal anaesthesia for transperineal prostate biopsy.[1-3])
2. Including cancer detection data previously unavailable to the EAG to permit inclusion in the meta-analysis of a study of local anaesthetic transperineal prostate biopsy (LATP) versus general anaesthetic transperineal prostate biopsy (GATP).[4]
3. Removal of an unpublished study supplied as academic in confidence to NICE and the EAG by one of the transperineal prostate biopsy freehand device manufacturers.[5])

In the following sub-sections, 1.1 to 1.3, we provide the rationale for, and results of, revised meta-analyses (NMA and pairwise). The results inform an updated EAG cost effectiveness base case and alternative cost-effectiveness scenario analyses presented later in this addendum.

1.1 Exclusion of studies using spinal anaesthesia for transperineal prostate biopsy

When screening studies for inclusion in the systematic review there were occasions when . we had to make informed judgements about whether potentially relevant studies should be classified as having used local anaesthetic or general anaesthetic. This judgement determined which of the five biopsy comparisons in the decision problem a study would be included in (Table 1). Following submission of the DAR to NICE, some Specialist Committee Members commented that spinal anaesthesia for transperineal biopsy (as used in three included studies (Table 1) is, in their clinical opinion, more appropriately aligned with general anaesthetic practices rather than (as we had assumed) local anaesthetic. This prompted us to re-examine our interpretation and classification of the anaesthesia used in these three studies.

Table 1 Number of included studies by comparison and decision question

Comparison (Intervention vs comparator)	Number of studies	DQ1	DQ2	Spinal anaesthesia studies
1. LATP-any vs LATRUS	15	✓		Hara 2008 [1] Watanabe 2005 [3]
2. LATP-any vs GATP grid and stepping device	4	✓		Takuma 2012 (AB) 39
3. LATP-freehand vs LATRUS	7		✓	N/A
4. LATP-freehand vs GATP grid and stepping device	1		✓	N/A
5. LATP-freehand vs LATP grid and stepping device	0		✓	N/A
DQ Decision question; ✓ the comparison is primarily relevant to this decision question; AB conference abstract; N/A Not applicable.				

As Table 2 shows, whilst spinal anaesthesia is used for transperineal biopsy in all three studies, in two of the studies the transrectal biopsy comparators use a different form of anaesthesia: “caudal block” in Hara et al (2008) and “general anaesthesia” in Takuma et al (2012). In the case of Hara et al, a clinically informed judgement is needed to classify both the intervention and comparator group in terms of anaesthesia.

Table 2 Details of spinal anaesthesia studies

Study	Transperineal biopsy arm anaesthesia	Transrectal biopsy arm anaesthesia
Hara et al 2008[1]	Spinal anaesthesia:0.5% bupivacaine	Caudal block: 1% lidocaine
Takuma et al 2012;[2]	Lumbar spinal anaesthesia (drug/dose not reported)	General anaesthesia (drug/ dose not reported)

Watanabe et al 2005;[3])	Spinal anaesthesia (drug/dose not reported)	Spinal anaesthesia (drug/dose not reported)

Expert clinical advisors to the EAG commented that, spinal anaesthesia is technically classed as regional anaesthesia, though they could appreciate how spinal (regional) anaesthesia could be aligned with general anaesthetic, based on similarities in factors such as adverse effects, recovery times, settings, anaesthetist involvement and costs. The extent to which anaesthetic modality influences prostate biopsy outcomes (in particular, cancer detection rates) is less clear. In relation to Hara et al (2008) there was suggestion from some clinical experts that caudal block can be regarded as similar to local anaesthetic; however, some suggested caudal block has alignment with spinal/epidural anaesthesia.

Having considered the above clinical opinions we are uncertain which anaesthesia modality (local or general) is most appropriately applied to the arms of these studies for our analysis. This is particularly the case for Hara et al (2008) where the caudal block used in the transrectal biopsy comparator group could conceivably be classed as local anaesthesia or general anaesthesia. We therefore consider three options for analysis:

(i) Remove the three spinal anaesthesia studies from the meta-analysis;

(ii) Re-label the spinal anaesthesia studies as general anaesthesia for the purposes of our analysis (i.e. GATP);

(iii) Retain the studies in the analyses with the current classification, LATP.

Each option has potential limitations:

- Removal of the studies reduces the participant sample size available for meta-analysis, which in turn limits its statistical power and precision of effects estimation. It would mean loss of randomised trial data (i.e. Hara et al) and would consequently increase uncertainty in the NMA results.
- Re-classifying Hara from as a comparison of LATP vs LATRUS to GATP vs LATRUS potentially creates publication bias in the NMA because any other studies comparing GATP vs LATRUS were not sought for inclusion in the systematic review.
- Retaining Hara in the meta-analysis as a comparison of LATP vs LATRUS is fraught with uncertainty, particularly for the caudal block anaesthesia TRUS comparator group which could be conceived as LA or GA.

In section 1.1.1 below we show the results of NMA scenario analyses exploring the exclusion, retention and re-labelling of the arms Hara et al (2008) trial. In section 1.1.2 we

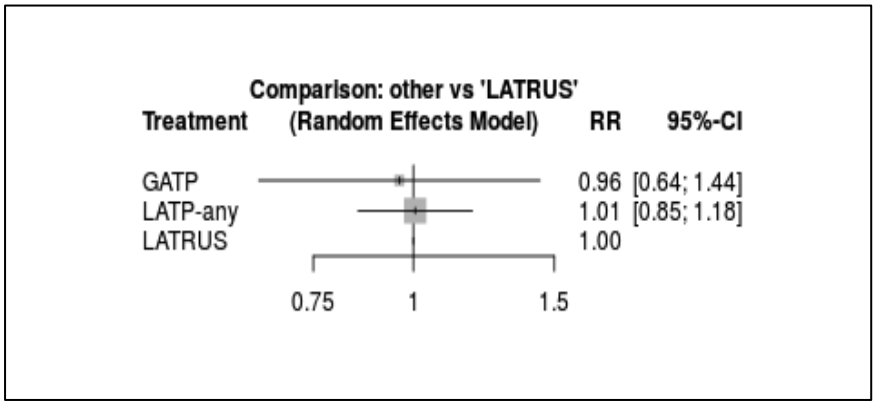
then show results of pairwise meta-analysis scenarios exploring the exclusion and retention of all three studies, plus re-labelling of the arms of the Hara et al (2008) trial.

1.1.1 Revised NMA scenarios

Decision question 1

The forest plots below show the NMA results for the outcome of cancer detection rates according to whether Hara et al (2008) is retained in the analysis as per the DAR (LATP-any vs LATRUS) (Figure 1), is excluded from the analysis (Figure 2), or retained and re-labelled as GATP vs LATRUS (Figure 3). These analyses apply to decision question 1 - the cost effectiveness of any LATP prostate biopsy modality (LATP-any).

Exclusion of Hara et al (2008) reverses the direction of effect for GATP vs LATRUS by a small degree (the relative risk (RR) increases from 0.96 to 1.01), and slightly increases the magnitude of the effect for LATP-any vs LATRUS (Figure 1). Re-labelling of the Hara et al (2008) trial arms as GATP vs LATRUS (Figure 3) has little impact on the relative risks.



NB. Reproduction of DAR Figure 8

Figure 1 Network meta-analysis forest plot of cancer detection rates for LATP-any vs LATRUS vs GATP grid and stepping device, Hara et al 2008 labelled as LATP vs LATRUS (decision question 1)

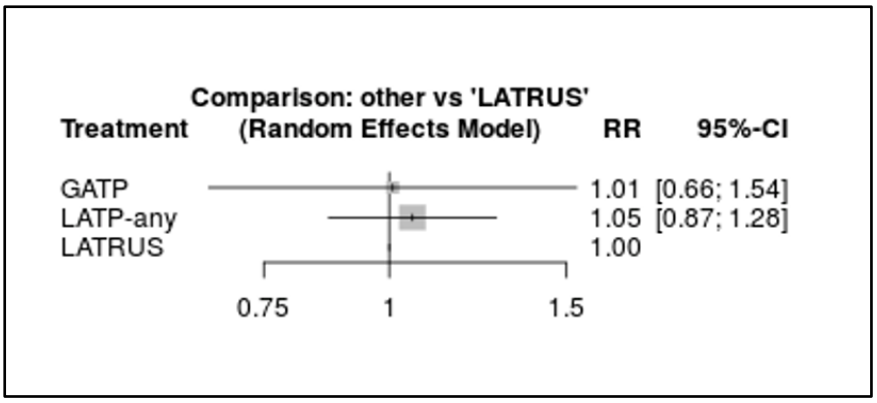


Figure 2 Network meta-analysis forest plot of cancer detection rates for LATP-any vs LATRUS vs GATP grid and stepping device, excluding Hara et al 2008 (decision question 1)

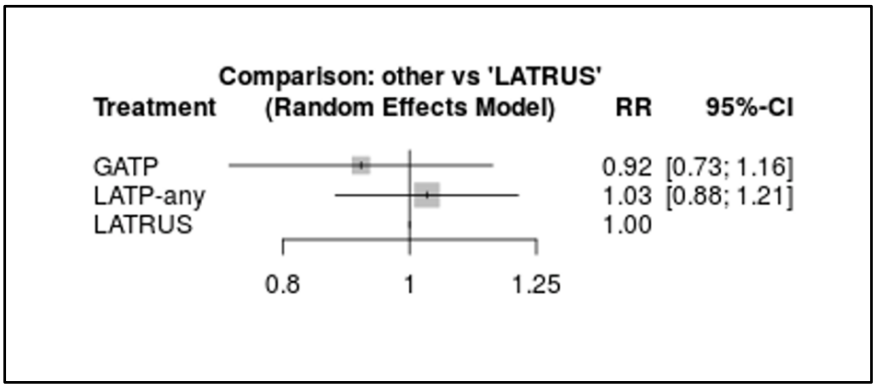
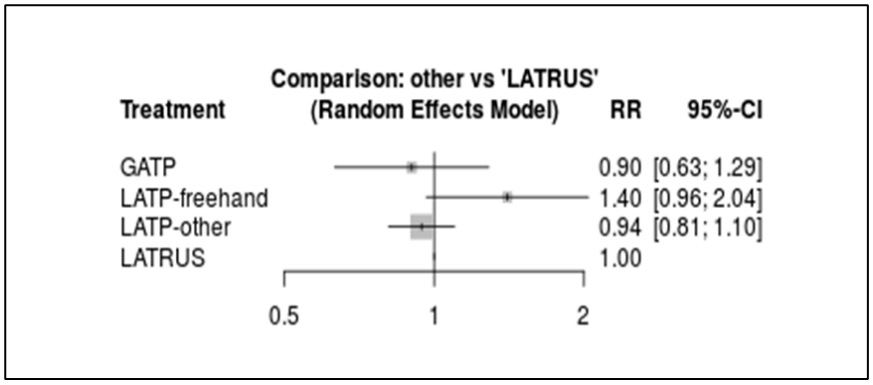


Figure 3 Network meta-analysis forest plot of cancer detection rates for LATP-any vs LATRUS vs GATP grid and stepping device, relabelling Hara et al 2008 as GATP vs LATRUS (decision question 1)

Decision question 2

Following the format above, the forest plots below illustrate the NMA results if Hara is retained (LATP vs LATRUS, as in the DAR) (Figure 4), excluded (Figure 5) or re-labelled (Figure 6); this time for decision question 2 - the cost effectiveness of LATP prostate biopsy using a freehand device (LATP-freehand). As the figures show, excluding or relabelling Hara et al 2008 has little impact on the relative risk estimates.



NB. Reproduction of DAR Figure 13

Figure 4 Network meta-analysis forest plot of cancer detection rates for LATP-freehand vs LATP-other vs LATRUS vs GATP, Hara et al 2008 labelled as LATP vs LATRUS (decision question 2)

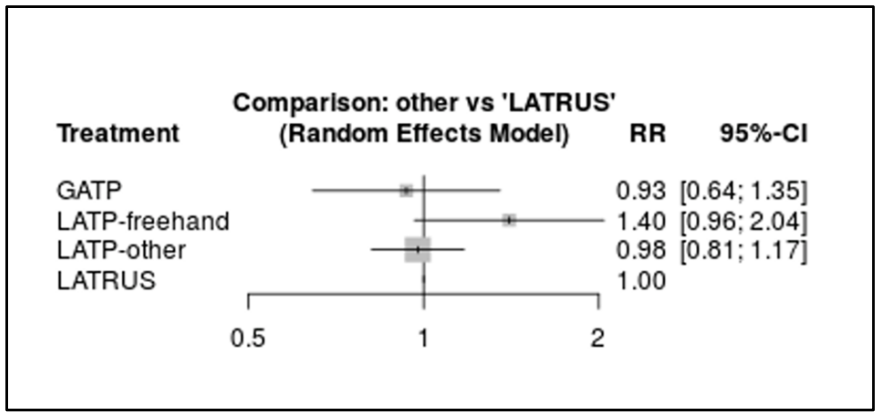


Figure 5 Network meta-analysis forest plot of cancer detection rates for LATP-freehand vs LATP-other vs LATRUS vs GATP, excluding Hara et al 2008 (decision question 2)

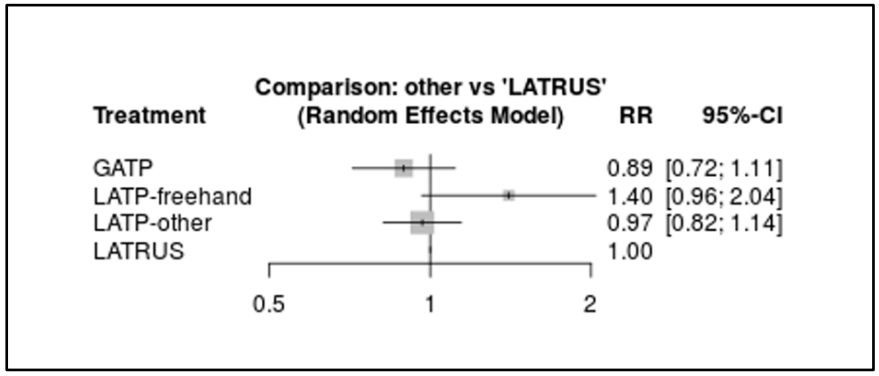


Figure 6 Network meta-analysis forest plot of cancer detection rates for LATP-freehand vs LATP-other vs LATRUS vs GATP, relabelling Hara et al 2008 as GATP vs LATRUS (decision question 2)

As will be discussed in the subsequent sections of this addendum, we use the NMA excluding the Hara et al 2008trial in the revised EAG economic base case.

1.1.2 Revised pairwise meta-analyses scenarios

In the DAR, the pairwise meta-analysis comparison of LATP-other versus LATRUS includes two of the three spinal anaesthesia studies (the RCT by Hara et al 2008 and the prospective cohort study by Watanabe et al 2005). Exclusion of these studies from the analysis has little impact on effect estimates (Figure 7): the overall RR remained at 0.99, whilst the observational studies combined RR decreased from 1.01 to 1.00 and the RCTs combined RR increased from 0.94 to 0.98. Likewise, confidence intervals changed only slightly and all included a RR of 1 (for comparison see DAR figure 10 for the original meta-analysis including Hara et al 2008 and Watanabe et al 2005).

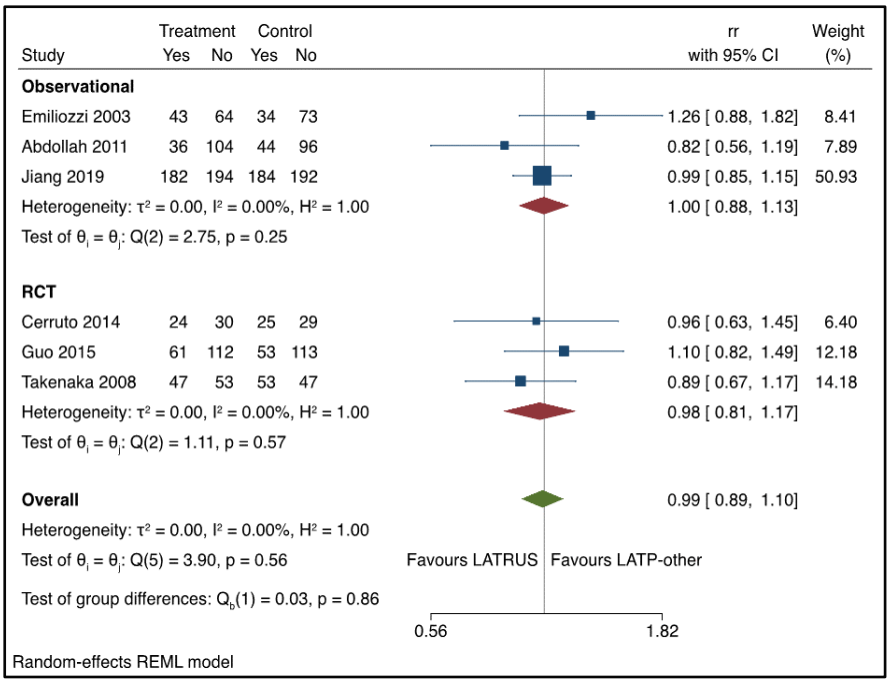


Figure 7 Meta-analysis forest plot of cancer detection rates for LATP-other versus LATRUS, excluding spinal anaesthesia studies Hara et al 2008 and Watanabe et al 2005 (decision question 2)
See DAR Figure 10 for comparison

1.2 Inclusion of the study by Walters et al, 2021

Available clinical effectiveness evidence for the comparison between LATP versus GATP is sparse, with just four relevant studies included in the systematic review. Three of the four studies were included in the pairwise meta-analysis. The fourth study, by Walters et al 2021, was initially available to the EAG only as a conference abstract, but it did not report quantitative cancer detection rates and therefore could not be meta-analysed. After

submission of the DAR the EAG received further conference abstract data from the study investigators, reporting cancer detection rates. These additional data therefore enabled us to include this study in the meta-analysis.

For ease of comparison Figure 8 below shows the results of the meta-analysis prior to the inclusion of Walters et al (2021), i.e. the same analysis as presented in DAR Figure 6. However, please note that Figure 8 supersedes DAR Figure 6 following correction of an error in the latter.

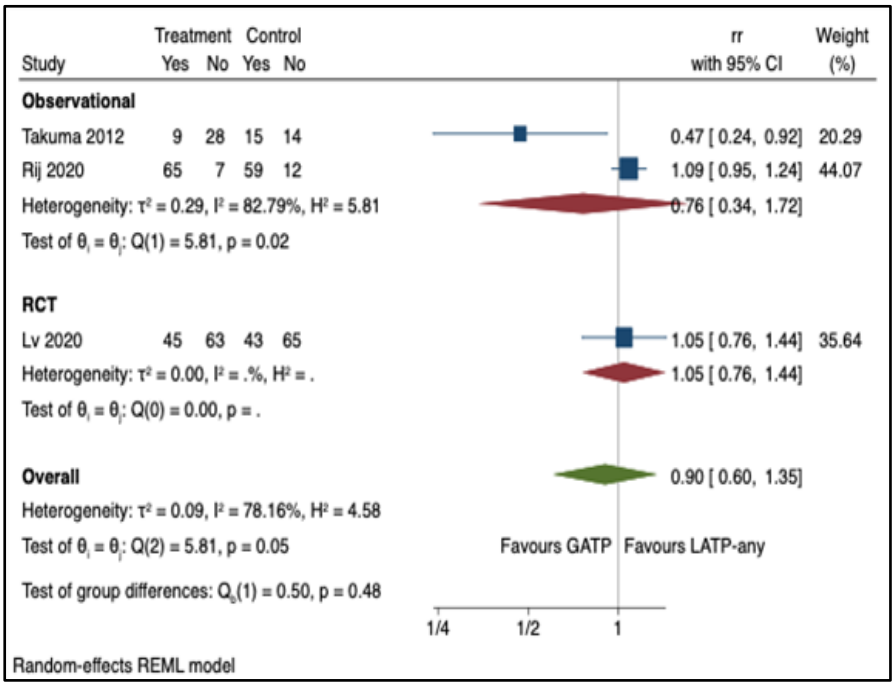


Figure 8 Meta-analysis forest plot of cancer detection rates for LATP-any vs GATP grid and stepping device prior to adding Walters et al (2021) (decision question 1)
NB. This is a corrected version of Figure 6 in the DAR

Adding Walters et al to the meta-analysis changes the overall direction of effects from a RR of 0.90 favouring GATP (Figure 8) to an RR of 1.09 favouring LATP-any (Figure 9), though confidence intervals continue to cross 1.

We repeated the above scenario this time excluding the spinal anaesthesia study by Takuma et al (2012). The change in the direction of effects is maintained with a slight increase in effect estimates favouring LATP-any (Figure 10). The lower bound of the confidence interval decreases to give a RR of exactly 1. Statistical heterogeneity, measured by I^2, is markedly reduced.

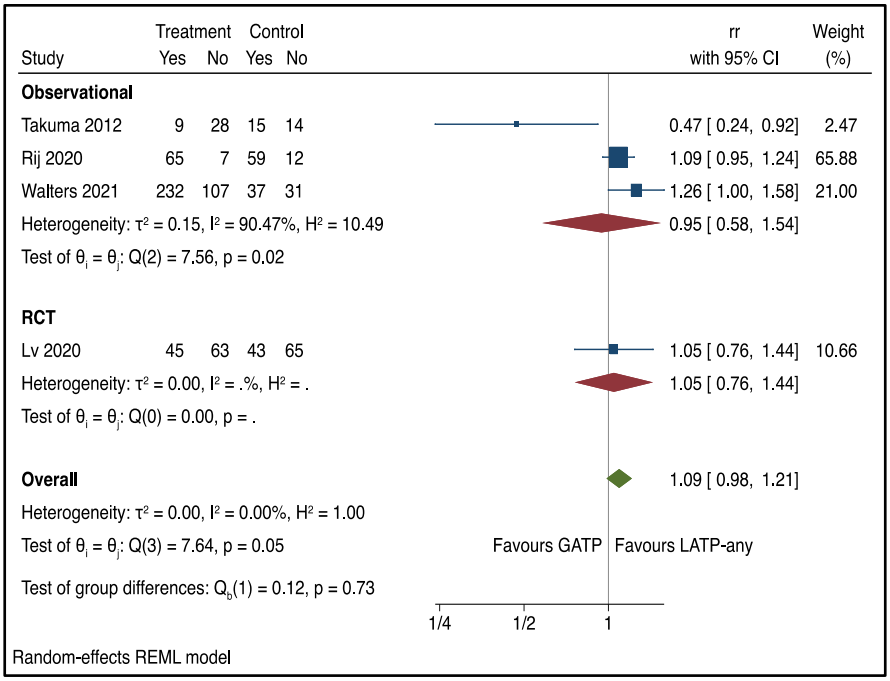


Figure 9 Pairwise meta-analysis forest plot of cancer detection rates for LATP-any versus GATP, updated to include Walters et al (2021) (decision question 1)

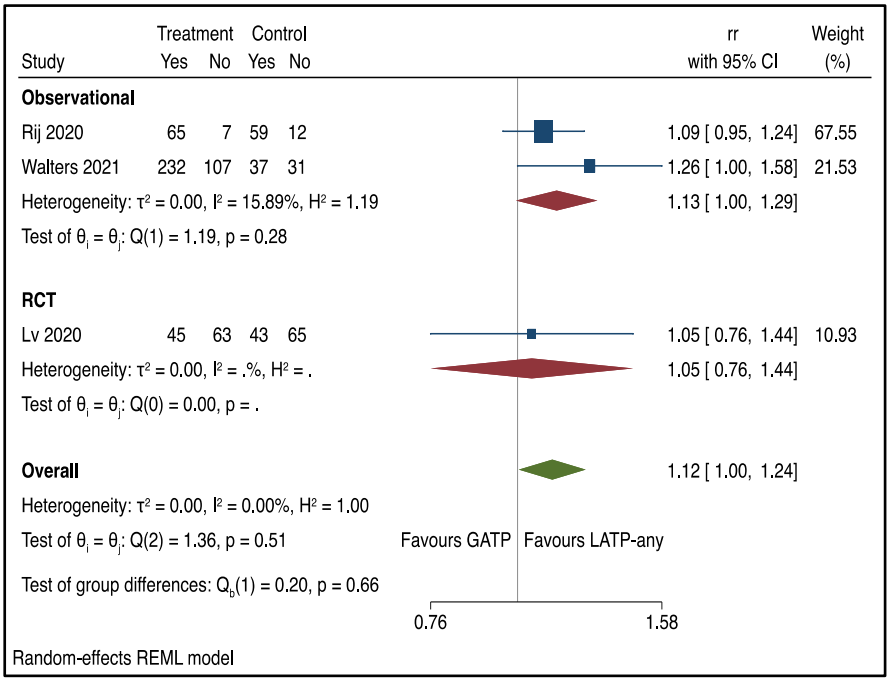


Figure 10 Pairwise meta-analysis forest plot of cancer detection rates for LATP-any versus GATP, including Walters et al (2021) and excluding Takuma et al (2012) (decision question 1)

1.3 Removal of the study by Bojin 2019

The EAG was asked by NICE to consider exploring the impact on clinical effectiveness and cost effectiveness of removing from the meta-analysis the study by Bojin, 2019;[5]). The justification being the study (at the time of writing) is unpublished, available only as a presentation slide-set with no apparent peer-review. The slide-set was supplied to NICE as academic in confidence by the manufacturer of the PrecisionPoint freehand device (BXTAccelyon Ltd) in response to the Institute's request for information from manufacturers at the start of the assessment. The EAG systematically screened the evidence supplied by the manufacturer and determined that the study meets the inclusion criteria for the systematic review. The slide-set appears to have been used in a presentation by a Urology nurse specialist at United Lincoln Hospitals Trust, based on an in-service evaluation of LATP biopsy using historical standard TRUS biopsy practice as a comparison. The slide-set contains no declaration of study sponsorship or competing interests, or details of available or planned study publications. The lack of detail of the study's provenance, its unpublished status and apparent absence of independent peer review (notwithstanding the EAG's critical appraisal of the study) means that the reliability and validity of the data are uncertain.

As Bojin 2019 is not an RCT it was ineligible for inclusion in the NMA; thus we explored the impact of its exclusion from the pairwise meta-analysis only, for decision questions 1 and 2. Figure 11 shows the forest plot for LATP-any versus LATRUS for decision question 1, excluding Bojin 2019 (for comparison with the forest plot in which Bojin is included please see DAR Figure 4). Excluding the study had negligible impact on the combined effect estimate: the RR for the observational studies combined decreases slightly from 1.10 (95% CI 1.01, 1.21) to 1.08 (95% CI 0.97, 1.20); the respective marginal reduction in the confidence intervals means that there is no longer a statistically significant difference favouring LATP-only. The overall RR (i.e. for observational studies and RCTs combined) is reduced marginally from 1.07 to 1.06 (confidence intervals include 1 in both sets of analyses).

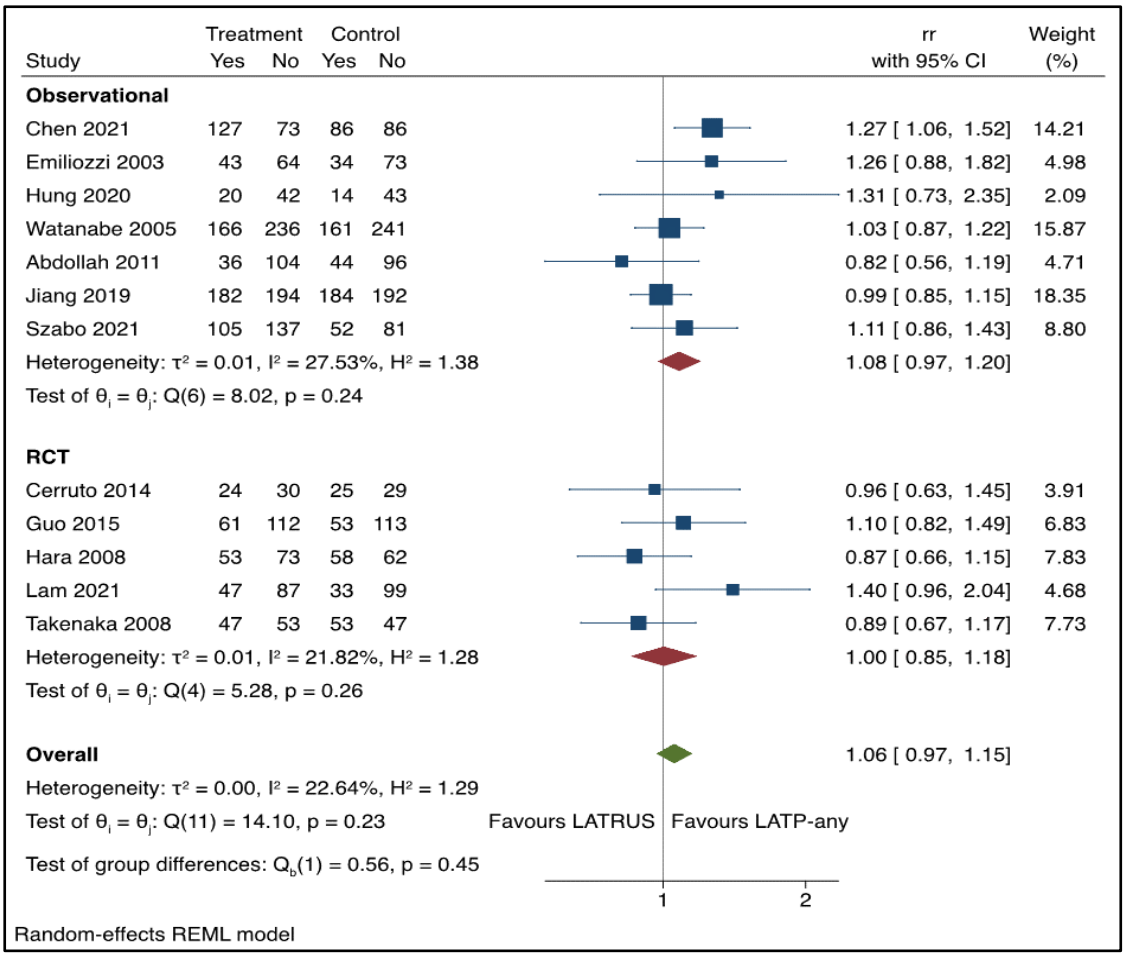


Figure 11 Pairwise meta-analysis forest plot of cancer detection rates for LATP-any versus LATRUS excluding Bojin et al 2019 (decision question 1)

See DAR Figure 4 for comparison

Figure 12 shows the forest plot for LATP-freehand versus LATRUS for decision question 2 excluding Bojin 2019 (for comparison with the forest plot in which Bojin is included please see DAR Figure 9). As was the case for decision question 1 (Figure 11 above), exclusion had negligible impact on the effect estimate: for observational studies combined the RR increased slightly from 1.21 (95% CI 1.08, 1.34) (see DAR Figure 9) to 1.22 (95% CI 1.06, 1.41) (Figure 12).

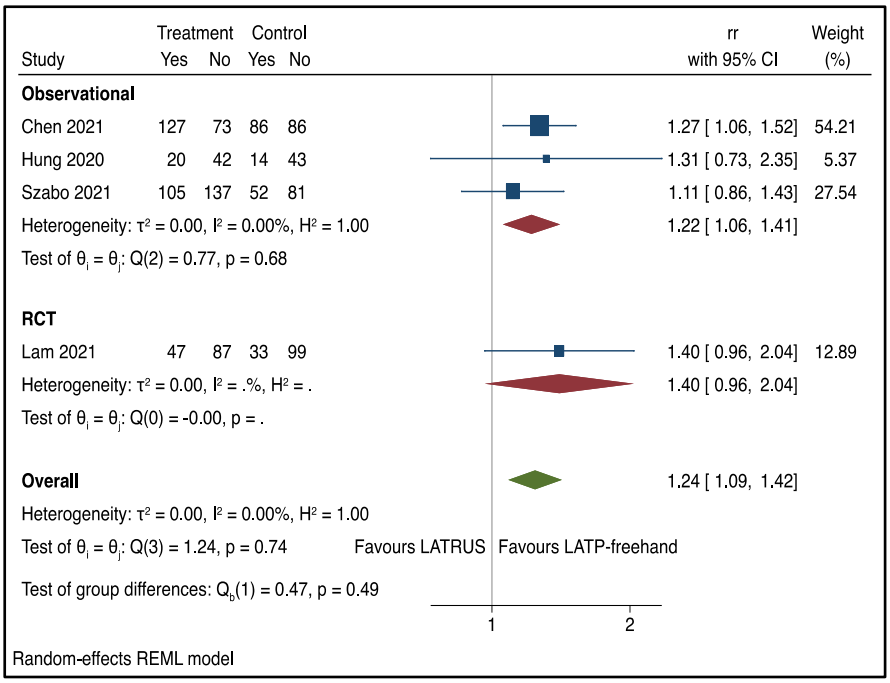


Figure 12 Pairwise meta-analysis forest plot of cancer detection rates for LATP-freehand versus LATRUS excluding Bojin et al 2019 (decision question 2)

2 Additional economic analysis

We conducted additional scenario analyses to test the sensitivity of cost-effectiveness to issues raised by NICE, specialist committee members and stakeholders:

- Cancer detection rates based on the NMA and observational meta-analyses scenarios discussed above
- Removal of Berry et al.[6] estimates of overnight stays after biopsy
- Correction of adverse event rates from the Rosario et al.[7] used in the model
- Different rates of repeat biopsy for different GATP, LATP and LATRUS
- Histopathology costs
- Mean numbers of core samples for LATRUS, LATP and GATP
- Other costs of biopsy procedures: the price of the SureFire device and assumptions about the use of consumables and equipment in the micro-costing

In this section we present results for individual changes applied to our original base case (DAR Tables 68 and 73). We also present a revised EAG base case in section 3 below, and scenario analyses applied to the revised EAG base case in section 4. All of the results below are deterministic, unless stated otherwise. We focus on results for patient subgroup A (first biopsy, MRI Likert score 3+), with discussion for other subgroups where they differ.

2.1 Cancer detection rates

2.1.1 NMA scenarios

Our original base case used relative risks of cancer detection estimated from NMAs of 6 RCTs, including the Hara 2008 trial[1] classified as a comparison between LATP (without freehand device) and LATRUS (Figure 1 and Figure 4 above). As discussed in section 1.1 above, there are uncertainties given the types of anaesthesia in the Hara trial (spinal injection in the transperineal arm and caudal block in the transrectal arm), possible omission of other studies that compared GATP with LATRUS and over the relative costs of biopsy procedures under the different types of anaesthesia.

The effects of the alternative NMA scenarios excluding the Hara trial (Figure 2 and Figure 5) or relabelling it as a comparison between GATP and LATRUS (Figure 3 and Figure 6) on the original EAG base case are shown below.

- **Decision question 1**: In subgroup A (*Table 3*), the ICER for LATP versus LATRUS is lower when Hara is excluded or relabelled than in our original base case, but it remains greater than £30,000 per QALY, and GATP is dominated in all NMA scenarios. The effects of the NMA scenarios are similar in other subgroups.
- **Decision question 2**: See *Table 4* for the results in subgroup A. In this and other subgroups, the ICER for LATP with freehand device compared with LATRUS does not change in the NMA scenarios, because the relative risk does not change. Other comparators are dominated in all NMA scenarios and subgroups.

Given the various uncertainties over the Hara trial, we use the NMA excluding this trial in the revised EAG economic base case (section 3 below) and alternative NMAs in scenario analysis (section 4.1.1).

Table 3 NMA scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	RR [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Original EAG base case NMA (Hara classified as LATP versus LATRUS)						
LATRUS	1.00	£19,472	9.2991			
LATP-any	1.01	£19,620	9.3011	£148	0.0020	£72,503
GATP	0.96	£20,089	9.2993	£469	-0.0018	Dominated
NMA scenario 1: excluding Hara						
LATRUS	1.00	£19,472	9.2991			
LATP-any	1.05	£19,614	9.3025	£142	0.0034	£41,369
GATP	1.01	£20,081	9.3011	£467	-0.0014	Dominated
NMA scenario 2: with Hara reclassified as GATP versus LATRUS						
LATRUS	1.00	£19,472	9.2991			
LATP-any	1.03	£19,617	9.3018	£145	0.0027	£52,807
GATP	0.92	£20,096	9.2977	£479	-0.0041	Dominated
[a] Relative risk for cancer detection compared with LATRUS						

Table 4 NMA scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	RR [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Original EAG base case NMA (Hara classified as LATP versus LATRUS)						
LATRUS	1.00	£19,472	9.2991			
LATP-freehand	1.40	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	0.94	£19,632	9.2985	£50	-0.0135	Dominated
GATP	0.90	£20,100	9.2969	£468	-0.0016	Dominated
NMA scenario 1: excluding Hara						
LATRUS	1.00	£19,472	9.2991			
LATP-freehand	1.40	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	0.98	£19,625	9.3000	£43	-0.0120	Dominated
GATP	0.93	£20,094	9.2981	£469	-0.0019	Dominated
NMA scenario 2: with Hara reclassified as GATP versus LATRUS						
LATRUS	1.00	£19,472	9.2991			
LATP-freehand	1.40	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	0.97	£19,627	9.2997	£45	-0.0124	Dominated
GATP	0.89	£20,102	9.2965	£475	-0.0032	Dominated
[a] Relative risk for cancer detection compared with LATRUS						

2.1.2 Observational scenarios

We previously reported cost-effectiveness scenarios based on pairwise meta-analyses of observational studies (see DAR Tables 79 and 80). Following questions raised by NICE specialist committee members for this assessment, we present additional scenarios to investigate the impact of uncertainty over the included observational data. These use the pairwise meta-analysis scenarios presented above, including data from the Walters study (LATP versus GATP) (Figure 9) excluding the Bojin study (which is currently unpublished)

(Figure 11 and Figure 12), or excluding the Watanabe or Takuma studies in which the TRUS control was performed under general or spinal anaesthetic Figure 7 and Figure 10).[2-5]

- **Decision question 1**: The ICERs for LATP compared with LATRUS are more favourable when based on observational studies than with the trial-based NMAs, reflecting the higher relative risks for cancer detection. In subgroup A, the observational ICERs for LATP (*Table 5*) are all lower than in the NMA scenarios (*Table 3*). Although the estimated relative risks for cancer detection with GATP versus LATRUS are more favourable in most observational scenarios than in the NMA scenarios, GATP is still dominated or has a high ICER.

Table 5 Observational scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	RR [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Observational base case applied to the original EAG base case						
LATRUS	1.00	£19,472	9.2991			
LATP-any	1.10	£19,607	9.3041	£134	0.0051	£26,550
GATP	1.45	£20,032	9.3120	£425	0.0078	£54,223
Observational scenario 1: excluding Bojin						
LATRUS	1.00	£19,472	9.2991			
LATP-any	1.08	£19,610	9.3035	£137	0.0044	£31,058
GATP	1.42	£20,032	9.3121	£422	0.0086	£49,182
Observational scenario 2: excluding Watanabe						
LATRUS	1.00	£19,472	9.2991			
LATP-any	1.12	£19,604	9.3048	£132	0.0057	£23,135
GATP	1.47	£20,033	9.3119	£429	0.0071	£60,161
Observational scenario 3: including Walters						
LATRUS	1.00	£19,472	9.2991			
LATP-any	1.10	£19,607	9.3041	£134	0.0051	£26,550
GATP	1.16	£20,059	9.3059	£452	0.0018	£255,747
Observational scenario 4: including Walters and excluding Takuma						
LATRUS	1.00	£19,472	9.2991			
LATP-any	1.10	£19,607	9.3041	£134	0.0051	£26,550
GATP	0.97	£20,087	9.2998	£480	-0.0044	Dominated

[a] Relative risk for cancer detection

- **Decision question 2**: By contrast, the ICERs for LATP-freehand versus LATRUS are less favourable when based on observational studies than with the trial-based NMAs, as the relative risks for cancer detection are lower. This would not change the interpretation of the cost-effectiveness results for subgroup A, as the observational ICERs for LATP-freehand are still less than £20,000 per QALY (*Table 6* below), and the other comparators have very high ICERS or are dominated.

Table 6 Observational scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	RR [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Observational base case applied to the original EAG base case						
LATRUS	1.00	£19,472	9.2991			
LATP-freehand	1.21	£19,603	9.3074	£130	0.0083	£15,687
LATP-other	1.01	£19,620	9.3011	£17	-0.0063	Dominated
GATP	1.33	£20,039	9.3104	£419	0.0093	£143,129
Observational scenario 1: excluding Bojin						
LATRUS	1.00	£19,472	9.2991			
LATP-freehand	1.22	£19,602	9.3077	£129	0.0086	£15,044
LATP-other	1.01	£19,620	9.3011	£19	-0.0066	Dominated
GATP	1.33	£20,039	9.3104	£419	0.0093	£157,717
Observational scenario 2: excluding Watanabe						
LATRUS	1.00	£19,472	9.2991			
LATP-freehand	1.21	£19,603	9.3074	£130	0.0083	£15,687
LATP-other	1.00	£19,622	9.3008	£19	-0.0066	Dominated
GATP	1.32	£20,040	9.3101	£419	0.0094	£160,157
Observational scenario 3: including Walters						
LATRUS	1.00	£19,472	9.2991			
LATP-freehand	1.21	£19,603	9.3074	£130	0.0083	£15,687
LATP-other	1.01	£19,620	9.3011	£17	-0.0063	Dominated
GATP	1.06	£20,073	9.3030	£452	0.0018	Dominated
Observational scenario 4: including Walters and excluding Takuma						
LATRUS	1.00	£19,472	9.2991			
LATP-freehand	1.21	£19,603	9.3074	£130	0.0083	£15,687
LATP-other	1.01	£19,620	9.3011	£17	-0.0063	Dominated
GATP	0.89	£20,101	9.2967	£481	-0.0045	Dominated

[a] Relative risk for cancer detection

Note that for the purpose of the observational scenarios, we assumed that the studies that compared LATP with GATP (Takuma, Rij and Walters) had not used a named freehand transperineal device. Hence data from these studies was assigned to the comparison between LATP-other versus GATP.

We report results with the observational scenarios applied to the revised EAG base case in section 4.1.2 below.

2.2 Overnight stays after biopsy

The rate of admissions affects costs and QALY loss associated with the biopsy. For the EAG base case, we estimated hospital admission rates from 28-day readmission rates reported by Tamhankar and colleagues together with rates of overnight stay immediately following the biopsy, as reported by Berry and colleagues (see DAR section 5.7.4).[6 8] In this analysis, we assumed the same rate of overnight stay after LATP and GATP biopsy. However, NICE specialist committee members for this assessment and a stakeholder (comment number 23) have argued that the high rate of overnight stay after transperineal biopsy (12.25%) compared with that after transrectal biopsy (2.36%) in the Berry study is not reflective of current practice with LATP, as this study used data from a period prior to March 2017 when transperineal biopsy was conducted under general anaesthetic.

Table 7 and Table 8 below show the effect of two admission scenarios for subgroup A:

1. Assuming that the high rate of overnight stay for transperineal biopsy from the Berry study applies to GATP but not LATP. This reduces the ICER for LATP-any compared with LATRUS in decision question 1, and similarly for LATP-freehand in decision question 2.
2. Excluding the data on overnight stays causes a small reduction in costs and very small increase in QALYs for all biopsy methods. The impact on the ICERs for LATP versus LATRUS is the same as in the previous scenario.

Table 7 Admission scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	Overnight stay [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case: excess overnight stay from Berry applied to LATP and GATP						
LATRUS	2.36%	£19,472	9.2991			
LATP-any	12.06%	£19,620	9.3011	£148	0.0020	£72,503
GATP	12.06%	£20,089	9.2993	£469	-0.0018	Dominated
Admission scenario 1: excess overnight stay from Berry applied to GATP only						
LATRUS	2.36%	£19,472	9.2991			
LATP-any	2.36%	£19,562	9.3012	£90	0.0021	£42,318
GATP	12.06%	£20,089	9.2993	£527	-0.0019	Dominated
Admission scenario 2: overnight stays excluded from analysis						
LATRUS	0.00%	£19,458	9.2991			
LATP-any	0.00%	£19,547	9.3012	£90	0.0021	£42,318
GATP	0.00%	£20,016	9.2994	£469	-0.0018	Dominated

[a] Risk difference for overnight stay after transperineal versus transrectal biopsy from Berry et al. adjusted for biopsy year, age, ethnicity, RCS Charlson score and socio-economic deprivation status

Table 8 Admission scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	Overnight stay [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case: excess overnight stay applied to LATP and GATP						
LATRUS	2.36%	£19,472	9.2991			
LATP-freehand	12.06%	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	12.06%	£19,632	9.2985	£50	-0.0135	Dominated
GATP	12.06%	£20,100	9.2969	£468	-0.0016	Dominated
Admission scenario 1: excess overnight stay from Berry applied to GATP only						
LATRUS	2.36%	£19,472	9.2991			
LATP-freehand	2.36%	£19,524	9.3121	£51	0.0131	£3,926
LATP-other	2.36%	£19,574	9.2986	£50	-0.0135	Dominated
GATP	12.06%	£20,100	9.2969	£526	-0.0017	Dominated
Admission scenario 2: overnight stays excluded from analysis						
LATRUS	0.00%	£19,458	9.2991			
LATP-freehand	0.00%	£19,509	9.3122	£51	0.0131	£3,926
LATP-other	0.00%	£19,559	9.2986	£50	-0.0135	Dominated
GATP	0.00%	£20,027	9.2970	£468	-0.0016	Dominated

[a] Risk difference for overnight stay after transperineal versus transrectal biopsy from Berry et al. adjusted for biopsy year, age, ethnicity, RCS Charlson score and socio-economic deprivation status

2.3 Adverse event rates

In section 5.7.4 of the DAR, we presented estimates of biopsy complications reported by Rosario and colleagues.[7] We had intended to use their rate for non-hospital treatment (10.37%, 119/1147) to estimate the incidence of 'mild' adverse events associated with LATRUS in our base case analysis, and their rate of hospital admissions (1.31%, 15/1147) for serious complications of LATRUS in a scenario analysis. However, we mistakenly entered these figures into the model the wrong way round (1.31% for mild adverse events and 10.37% for hospital admissions). We correct these parameters in the revised EAG base case and scenarios in sections 3 and 4 below.

- The correction to the Rosario non-hospital treatment rate reduces the base case ICERs for LATP-any compared with LATRUS in decision question 1, and for LATP-freehand compared with LATRUS in decision question 2 (Table 9).
- Conversely, the correction to the Rosario admission rate increases the scenario ICERs for LATP and LATP-freehand analysis (Table 10). We note that the high admission rate for transperineal biopsies in the corrected scenario (15.61%) includes overnight stays estimated from Berry et al. Excluding overnight stays (as discussed in section 2.2 above) reduces the transperineal admission rate to 3.54%, much closer to the rate estimated from Rosario et al for LATRUS.

Table 9 Corrected rate of mild adverse events, subgroup A (deterministic)

Biopsy method	Rate of mild AEs	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Decision question 1: base case in DAR Table 68						
LATRUS	1.31%	£19,472	9.2991			
LATP-any	9.13%	£19,620	9.3011	£148	0.0020	£72,503
GATP	9.13%	£20,089	9.2993	£469	-0.0018	Dominated
Decision question 1: corrected rate for LATRUS from Rosario et al.						
LATRUS	10.37%	£19,477	9.2989			
LATP-any	9.13%	£19,621	9.3011	£144	0.0023	£63,668
GATP	9.13%	£20,089	9.2993	£469	-0.0018	Dominated
Decision question 2: base case in DAR Table 73						
LATRUS	1.31%	£19,472	9.2991			
LATP-freehand	9.13%	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	9.13%	£19,632	9.2985	£50	-0.0135	Dominated
GATP	9.13%	£20,100	9.2969	£468	-0.0016	Dominated
Decision question 2: corrected rate for LATRUS from Rosario et al.						
LATRUS	10.37%	£19,477	9.2989			
LATP-freehand	9.13%	£19,582	9.3121	£105	0.0132	£7,983
LATP-other	9.13%	£19,632	9.2985	£50	-0.0135	Dominated
GATP	9.13%	£20,100	9.2669	£468	-0.0016	Dominated

Table 10 Corrected rate of admissions, subgroup A (deterministic)

Biopsy method	Rate of admissions	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Decision question 1: scenario in DAR Table 83						
LATRUS	10.37%	£19,550	9.2980			
LATP-any	15.61%	£19,623	9.3011	£73	0.0031	£23,321
GATP	15.61%	£20,092	9.2993	£469	-0.0018	Dominated
Decision question 1: scenario with corrected rate for LATRUS from Rosario et al.						
LATRUS	1.31%	£19,385	9.3003			
LATP-any	15.61%	£19,618	9.3012	£233	0.0008	£275,505
GATP	15.61%	£20,086	9.2993	£469	-0.0018	Dominated
Decision question 2: scenario in DAR Table 84						
LATRUS	10.37%	£19,550	9.2980			
LATP-freehand	15.61%	£19,585	9.3120	£34	0.0140	£2,430
LATP-other	15.61%	£19,635	9.2985	£50	-0.0135	Dominated
GATP	15.61%	£20,102	9.2969	£468	-0.0016	Dominated
Decision question 2: scenario with corrected rate for LATRUS from Rosario et al.						
LATRUS	1.31%	£19,385	9.3003			
LATP-freehand	15.61%	£19,579	9.3121	£194	0.0118	£16,491
LATP-other	15.61%	£19,629	9.2986	£50	-0.0135	Dominated
GATP	15.61%	£20,097	9.2970	£468	-0.0016	Dominated

2.4 Repeat biopsy rates

For the EAG base case, we assumed a repeat biopsy rate of 15.45% after a first biopsy finding of clinically non-significant (CNS) prostate cancer in patient subgroup A. This figure was based on the reported rate after a first LATRUS biopsy (95/615) reported by Jimenez and colleagues (see DAR *section 5.7.3*).[9] This study reported a lower rate of 5.36% (3/56) repeat biopsies after transperineal (GATP) biopsy. Given the small sample size for the GATP rate and lack of evidence for LATP, we assumed the same rate (15.45%) for all biopsy methods in our base case. However, we presented a scenario analysis with a lower rate of 5.26% for LATP and GATP, retaining the rate of 15.45% for LATRUS (DAR Table 78). Note that the 5.26% rate in this scenario was an error, as we had intended to use the GATP rate from the Jimenez study of 5.36% (see scenario 1 in Table 11 and Table 12 below for the corrected analyses).

Experts advising NICE have stated that they would expect rates of repeat biopsy to be lower for GATP than for LATP and LATRUS. They stated a preference for an analysis with the rate for LATP assumed equal to that for LATRUS (15.45%), but with a lower rate for GATP (5.36%). We show results with these assumptions in repeat biopsy scenario 2 below.

The view that the likelihood of repeat biopsy is similar for LATRUS and LATP is supported by stakeholder comment 51. This attributes the lower rate of repeat biopsy for GATP compared with LATRUS in the Jimenez study to the greater number of biopsy core samples taken for GATP (reported as 12-18 for LATRUS and 30 for GATP). See section 2.5 below for discussion of whether and how the number of core samples taken differ between the biopsy methods in clinical practice.

Table 11 and Table 12 below report results for two repeat biopsy scenarios:

1. In the first scenario we use the lower repeat biopsy rate from Jimenez (5.36%) for LATP and GATP. Note that the results differ from those in DAR Table 78, because we used an incorrect figure for the GATP repeat biopsy rate (5.26%). This causes a large increase in the decision question 1 ICER for LATP-any and a small increase in the decision question 2 ICER for LATP-freehand. Results for other comparators are unchanged as they are still dominated.
2. In the second scenario, we retain the high repeat biopsy rate for LATP (assumed equal to LATRUS) but use the lower rate for GATP. This has no impact on the base case cost-effectiveness results, as GATP remains dominated.

Table 11 Repeat biopsy scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	Repeat biopsy rate [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case: same rate for all biopsy methods						
LATRUS	15.45%	£19,472	9.2991			
LATP-any	15.45%	£19,620	9.3011	£148	0.0020	£72,503
GATP	15.45%	£20,089	9.2993	£469	-0.0018	Dominated
Repeat biopsy scenario 1: lower rate for LATP and GATP						
LATRUS	15.45%	£19,472	9.2991			
LATP-any	5.36%	£19,616	9.3000	£144	0.0009	£164,271
GATP	5.36%	£20,085	9.2981	£469	-0.0019	Dominated
Repeat biopsy scenario 2: lower rate for GATP only						
LATRUS	15.45%	£19,472	9.2991			
LATP-any	15.45%	£19,620	9.3011	£148	0.0020	£72,503
GATP	5.36%	£20,085	9.2981	£465	-0.0030	Dominated

[a] Proportion of patients who have a repeat biopsy after a first biopsy finding of clinically non-significant prostate cancer. Model assumes 5% repeat biopsy after a first biopsy finding of no prostate cancer.

Table 12 Repeat biopsy scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	Repeat biopsy rate [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case: same rate for all biopsy methods						
LATRUS	15.45%	£19,472	9.2991			
LATP-freehand	15.45%	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	15.45%	£19,632	9.2985	£50	-0.0135	Dominated
GATP	15.45%	£20,100	9.2969	£468	-0.0016	Dominated
Repeat biopsy scenario 1: lower rate for LATP and GATP						
LATRUS	15.45%	£19,472	9.2991			
LATP-freehand	5.36%	£19,577	9.3110	£105	0.0119	£8,806
LATP-other	5.36%	£19,628	9.2973	£51	-0.0137	Dominated
GATP	5.36%	£20,096	9.2957	£468	-0.0016	Dominated
Repeat biopsy scenario 2: lower rate for GATP only						
LATRUS	15.45%	£19,472	9.2991			
LATP-freehand	15.45%	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	15.45%	£19,632	9.2985	£50	-0.0135	Dominated
GATP	5.36%	£20,096	9.2957	£464	-0.0028	Dominated

[a] Proportion of patients who have a repeat biopsy after a first biopsy finding of clinically non-significant prostate cancer. Model assumes 5% repeat biopsy after a first biopsy finding of no prostate cancer.

In the EAG base case and above scenarios, we assumed a repeat biopsy rate of 5% after a 'no prostate cancer' result at first biopsy for subgroup A. For subgroup B (MRI Likert score of 1 or 2, no prior biopsy), we assumed a repeat biopsy rate of 5% after a finding of clinically non-significant disease and 1.25% after a no prostate cancer result. For subgroups C and D (previous negative biopsy), we assumed no repeat biopsy after a second negative result.

2.5 Histopathology costs

Experts advising NICE commented that histopathology costs in the model are too low. For the DAR, we used online reported costs from the University of Surrey: £37.50 for 1 or 2 samples and an incremental cost of £7 per additional sample.[10] As an alternative, we use the cost of £36.58 per sample from NHS Cost Data 2019/20 diagnostic code DAPSO2[11] which increases the cost of 12 core samples (as assumed for all biopsy methods in the EAG base case) from £107.50 to £438.96. This has little impact on the ICERs for our base case, as the histopathology costs largely cancel out (see Table 13 and Table 14 below). Note that the ICERs still differ with histopathology costs despite the assumption of equal numbers of cores, because methods have different rates of repeat biopsy.

Table 13 Histopathology costs for decision question 1, subgroup A (deterministic)

Biopsy method	Biopsy samples	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case: £107.50 for 12 cores (University of Surrey)						
LATRUS	12	£19,472	9.2991			
LATP-any	12	£19,620	9.3011	£148	0.0020	£72,503
GATP	12	£20,089	9.2993	£469	-0.0018	Dominated
Histopathology cost scenario: £438.96 for 12 cores (NHS Costs 2019/20)						
LATRUS	12	£19,884	9.2991			
LATP-any	12	£20,032	9.3011	£148	0.0020	£72,314
GATP	12	£20,502	9.2993	£471	-0.0018	Dominated

Table 14 Histopathology costs for decision question 2, subgroup A (deterministic)

Biopsy method	Biopsy samples	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case: £107.50 for 12 cores (University of Surrey)						
LATRUS	12	£19,472	9.2991			
LATP-freehand	12	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	12	£19,632	9.2985	£50	-0.0135	Dominated
GATP	12	£20,100	9.2969	£468	-0.0016	Dominated
Histopathology cost scenario: £438.96 for 12 cores (NHS Costs 2019/20)						
LATRUS	12	£19,884	9.2991			
LATP-freehand	12	£19,981	9.3121	£97	0.0130	£7,445
LATP-other	12	£20,046	9.2985	£66	-0.0135	Dominated
GATP	12	£20,516	9.2969	£470	-0.0016	Dominated

2.6 Number of core samples

The base case assumption of equal numbers of core samples (12) per patient for all biopsy methods was based on a lack of data on the mean number of core samples taken in the clinical trials that contributed to the effectiveness (cancer detection) estimates in the model. Five of the six RCTs in the NMA analyses reported protocols with the same number of cores for intervention and comparator arms. The exception was the Lam 2021 study [12] which used a 'modified Ginsburg' protocol for the LATP arm (with the PrecisionPoint freehand device), but a standard 12-core protocol for LATRUS. The mean number of cores taken for patients in the LATP arm in the Lam study was not reported. The other RCT protocols included between 8 and 14 core samples,[1 13-16] although two of these trials included additional targeted sampling as needed.[14 15]

Experts advising NICE reported that in practice the number of cores is likely to differ between biopsy methods. We understand that LATRUS biopsy is 'almost always' 10-12 cores, and that transperineal biopsy usually follows one of two protocols: the RAPID protocol (12-16 biopsies), mostly used for grid and stepper LATP or GATP; and the Ginsburg protocol (24-34 biopsies), mostly used for freehand LATP or GATP. In a recent study, Lopez and colleagues (2021) report a median of 24 cores (range 1 to 47) in a multi-centre prospective cohort of 1,218 patients who underwent LATP biopsy with the PrecisionPoint device according to the Ginsburg protocol (7 out of 10 centres from the UK).[17]

We consider three alternative scenarios to explore the effect of differences in the numbers of core samples taken for the different biopsy procedures:

1. 24 cores for LATP and GATP, 12 for LATRUS.
2. 24 cores for LATP-freehand and 12 for the LATP-other, GATP and LATRUS.
3. 24 cores for LATP-freehand, 16 for LATP-other and GATP and 12 for LATRUS.

Results for subgroup A are reported in Table 15 and Table 16 below. As might be expected, the ICERs for LATP-any (in decision question 1) and LATP-freehand (in decision question 2) increase in the scenarios with a higher number of core samples for these interventions than for the comparators. This does not change the overall base case results for this subgroup, as the ICER for LATP-freehand remains below £20,000 per QALY gained and LATP-other and GATP are still dominated. The effect of the alternative core scenarios is amplified when combined with the higher cost for histopathology, see Table 17 and Table 18 below. The ICER for LATP-freehand rises to £41,261 per QALY gained in the combined scenarios with a higher histopathology cost and more core samples for transperineal biopsy procedures.

Note that these scenarios give an imperfect illustration of the impact of changing the number of cores taken, as they only affect the modelled estimates of the cost of histopathology. They do not change other costs or QALYs, as the scenarios have no impact on the modelled intermediate outcomes which drive the other costs and QALYs (cancer detection rates, probabilities of repeat biopsy and rates of adverse events).

Table 15 Core scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	Biopsy samples	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case						
LATRUS	12	£19,472	9.2991			
LATP-any	12	£19,620	9.3011	£148	0.0020	£72,503
GATP	12	£20,089	9.2993	£469	-0.0018	Dominated
Core scenario 1: 24 core samples for all transperineal methods						
LATRUS	12	£19,472	9.2991			
LATP-any	24	£19,704	9.3011	£232	0.0020	£113,632
GATP	24	£20,173	9.2993	£469	-0.0018	Dominated

Table 16 Core scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	Biopsy samples [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case						
LATRUS	12	£19,472	9.2991			
LATP-freehand	12	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	12	£19,632	9.2985	£50	-0.0135	Dominated
GATP	12	£20,100	9.2969	£468	-0.0016	Dominated
Core scenario 1: 24 cores for all transperineal methods						
LATRUS	12	£19,472	9.2991			
LATP-freehand	24	£19,666	9.3121	£194	0.0130	£14,918
LATP-other	24	£19,716	9.2985	£50	-0.0135	Dominated
GATP	24	£20,184	9.2969	£468	-0.0016	Dominated
Core scenario 2: 24 cores for LATP-freehand only						
LATRUS	12	£19,472	9.2991			
LATP-other	12	£19,632	9.2985	£160	-0.0006	Dominated
LATP-freehand	24	£19,666	9.3121	£34	0.0135	£14,918
GATP	12	£20,100	9.2969	£434	-0.0151	Dominated
Core scenario 3: 24 cores for LATP-freehand and 16 for LATP-other and GATP						
LATRUS	12	£19,472	9.2991			
LATP-other	16	£19,660	9.2985	£188	-0.0006	Dominated
LATP-freehand	24	£19,666	9.3121	£6	0.0135	£14,918
GATP	16	£20,128	9.2969	£462	-0.0151	Dominated

Table 17 Core scenarios for decision question 1 with higher histopathology costs, subgroup A (deterministic)

Biopsy method	Biopsy samples [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case with histopathology cost £438.96 for 12 cores						
LATRUS	12	£19,884	9.2991			
LATP-any	12	£20,032	9.3011	£148	0.0020	£72,314
GATP	12	£20,502	9.2993	£471	-0.0018	Dominated
Core scenario 1: 24 core samples for all transperineal methods						
LATRUS	12	£19,884	9.2991			
LATP-any	24	£20,471	9.3011	£587	0.0020	£287,243
GATP	24	£20,941	9.2993	£471	-0.0018	Dominated

Table 18 Core scenarios for decision question 2 with higher histopathology costs, subgroup A (deterministic)

Biopsy method	Biopsy samples [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
EAG base case with histopathology cost £438.96 for 12 cores						
LATRUS	12	£19,884	9.2991			
LATP-freehand	12	£19,981	9.3121	£97	0.0130	£7,445
LATP-other	12	£20,046	9.2985	£66	-0.0135	Dominated
GATP	12	£20,516	9.2969	£470	-0.0016	Dominated
Core scenario 1: 24 cores for all transperineal methods						
LATRUS	12	£19,884	9.2991			
LATP-freehand	24	£20,420	9.3121	£536	0.0130	£41,261
LATP-other	24	£20,485	9.2985	£66	-0.0135	Dominated
GATP	24	£20,955	9.2969	£470	-0.0016	Dominated
Core scenario 2: 24 cores for LATP-freehand only						
LATRUS	12	£19,884	9.2991			
LATP-other	12	£20,046	9.2985	£162	-0.0006	Dominated
LATP-freehand	24	£20,420	9.3121	£373	0.0135	£41,261
GATP	12	£20,516	9.2969	£96	-0.0151	Dominated
Core scenario 3: 24 cores for LATP-freehand and 16 for LATP-other and GATP						
LATRUS	12	£19,884	9.2991			
LATP-other	16	£20,193	9.2985	£308	-0.0006	Dominated
LATP-freehand	24	£20,420	9.3121	£227	0.0135	£41,261
GATP	16	£20,662	9.2969	£242	-0.0151	Dominated

2.7 Other costs of biopsy procedures

We include a number of changes to the estimated costs of biopsy in our revised base case:

1. **Price of SureFire device**: In the absence of a price for the SureFire device at the time of the original EAG analysis, we used the mean price of the other disposable freehand devices, PrecisionPoint and CamProbe (£135). After submission of our report, a company submission was received reporting a price of £120 for the SureFire device. This reduces the mean price of freehand devices from £74.28 to £71.78, and the total mean cost per biopsy for LATP-freehand (as used in the EAG base case analysis) from £470.00 to £467.50.
2. **Cost of coaxial needle**: For the DAR analysis, we had included the cost of a coaxial needle (£21.40) for all LATP biopsy procedures with a freehand device. This was questioned in stakeholder comment 26, and we understand that a coaxial needle is only needed with the EZU-PA3U device and the double freehand approach. Removing this cost for other methods reduces EAG base case ICERs for LATP.
3. **Cost of balloon or probe cover**: We mistakenly omitted the cost of a balloon or probe cover (£4.60) for the LATRUS procedure. Adding this cost to the EAG base case reduces the ICERs for LATP versus LATRUS.
4. **Use of lithotomy bed**: An expert has commented that a lithotomy bed (estimated cost £10,000) would be required for all types of transperineal biopsy but not for LATRUS. Apportioning this cost over an estimated lifetime for the bed of 10 years and an assumed 1,000 biopsies per year, this adds about £1 per transperineal biopsy with small increases in the ICERs for LATP.
5. **Cost of ultrasound machine**: we mistakenly apportioned the cost of an ultrasound machine by the estimated number of biopsies for the stepper device. Apportioning by the same estimated number of biopsies per year (1000) as for other capital equipment has little impact on the model results.

The combined effect of these cost corrections is to reduce the ICERs for LATP, see Table 19 and Table 20 below for subgroup A, decision question 1 and 2 respectively.

Table 19 Cost corrections for decision question 1, subgroup A (deterministic)

Biopsy method	Total		Incremental		ICERs
	Cost	QALYs	Cost	QALYs	£/QALY
EAG base case					
LATRUS	£19,472	9.2991			
LATP-any	£19,620	9.3011	£148	0.0020	£72,503
GATP	£20,089	9.2993	£469	-0.0018	Dominated
Correction 1: Price for SureFire Transperineal Needle Guide (£120)					
LATRUS	£19,472	9.2991			
LATP-any	£19,619	9.3011	£146	0.0020	£71,585
GATP	£20,089	9.2993	£471	-0.0018	Dominated
Correction 2: Coaxial needle cost (£21.40) for EZU-PA3U and double freehand only					
LATRUS	£19,472	9.2991			
LATP-any	£19,607	9.3011	£135	0.0020	£65,954
GATP	£20,089	9.2993	£482	-0.0018	Dominated
Correction 3: Cost of balloon/probe cover (£4.60) for all biopsy methods					
LATRUS	£19,478	9.2991			
LATP-any	£19,622	9.3011	£143	0.0020	£70,248
GATP	£20,090	9.2993	£469	-0.0018	Dominated
Correction 4: Use of lithotomy bed (£2.86) for all transperineal biopsies					
LATRUS	£19,472	9.2991			
LATP-any	£19,621	9.3011	£149	0.0020	£72,992
GATP	£20,090	9.2993	£469	-0.0018	Dominated
Correction 5: Capital cost of ultrasound machine based on 1000 biopsies per year					
LATRUS	£19,471	9.2991			
LATP-any	£19,619	9.3011	£148	0.0020	£72,503
GATP	£20,088	9.2993	£469	-0.0018	Dominated
All of the above changes					
LATRUS	£19,477	9.2991			
LATP-any	£19,606	9.3011	£129	0.0020	£63,271
GATP	£20,090	9.2993	£484	-0.0018	Dominated

Table 20 Cost corrections for decision question 2, subgroup A (deterministic)

Biopsy method	Total		Incremental		ICERs
	Cost	QALYs	Cost	QALYs	£/QALY
EAG base case					
LATRUS	£19,472	9.2991			
LATP-freehand	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	£19,632	9.2985	£50	-0.0135	Dominated
GATP	£20,100	9.2969	£468	-0.0016	Dominated
Correction 1: Price for SureFire Transperineal Needle Guide (£120)					
LATRUS	£19,472	9.2991			
LATP-freehand	£19,579	9.3121	£107	0.0130	£8,255
LATP-other	£19,632	9.2985	£52	-0.0135	Dominated
GATP	£20,100	9.2969	£468	-0.0016	Dominated
Correction 2: Coaxial needle cost (£21.40) for EZU-PA3U and double freehand only					
LATRUS	£19,472	9.2991			
LATP-freehand	£19,564	9.3121	£92	0.0130	£7,074
LATP-other	£19,632	9.2985	£68	-0.0135	Dominated
GATP	£20,100	9.2969	£468	-0.0016	Dominated
Correction 3: Cost of balloon/probe cover (£4.60) for all biopsy methods					
LATRUS	£19,478	9.2991			
LATP-freehand	£19,583	9.3121	£105	0.0130	£8,079
LATP-other	£19,633	9.2985	£50	-0.0135	Dominated
GATP	£20,101	9.2969	£468	-0.0016	Dominated
Correction 4: Use of lithotomy bed (£2.86) for all transperineal biopsies					
LATRUS	£19,472	9.2991			
LATP-freehand	£19,583	9.3121	£111	0.0130	£8,524
LATP-other	£19,633	9.2985	£50	-0.0135	Dominated
GATP	£20,101	9.2969	£468	-0.0016	Dominated
Correction 5: Capital cost of ultrasound machine based on 1000 biopsies per year					
LATRUS	£19,471	9.2991			
LATP-freehand	£19,581	9.3121	£110	0.0130	£8,450
LATP-other	£19,631	9.2985	£50	-0.0135	Dominated
GATP	£20,099	9.2969	£468	-0.0016	Dominated
All of the above changes					
LATRUS	£19,477	9.2991			
LATP-freehand	£19,562	9.3121	£86	0.0130	£6,593
LATP-other	£19,633	9.2985	£70	-0.0135	Dominated
GATP	£20,101	9.2969	£468	-0.0016	Dominated

3 Revised EAG base case

In this section we present results for a revised base case analysis, which includes the following changes to the base case that we presented in the DAR:

1. **NMA excluding the Hara et al. study**.[1] This decision is based on uncertainty over how to classify the Hara trial comparison; possible omission of studies that compared GATP with LATRUS (not specified in the scope); and relative costs of regional anaesthesia. We present scenarios including the Hara study in the NMA, classified as either GATP versus LATRUS or LATP versus LATRUS (the latter as it was originally classified in this way in the NMA presented in the DAR).
2. **Exclude overnight stay from Berry et al.[6]** This study was based on 2014-17 data, when transperineal biopsy was mostly done under general anaesthetic. The revised analysis is based only on non-elective admissions within 28 days of a biopsy estimated from Hospital Episode Statistics (HES) for the period 2017-19 by Tamhankar et al: 3.54% for LATP and 3.74% for LATRUS.[8] As in the original EAG base case, we assume the same admission rate for LATP and GATP.
3. **Correction to LATRUS adverse events from Rosario et al.**[7] This correction increases the rate of mild adverse events (non-hospital treatment after biopsy) in the base case from 1.31% to 10.37%. The correction also reduces the modelled rate for severe adverse events (hospital treatment) in a scenario from 10.37% to 1.31%.
4. **Cost of histopathology from NHS cost data 2018/19**[11] Based on expert feedback, this increases the cost for 12 core samples from £107.50 to £438.96. We keep the assumption of 12 core samples per biopsy for all biopsy methods in the revised base case, but we test the impact of using more cores for transperineal methods in scenario analysis.
5. **Price of the SureFire device** as reported in recent company submission
6. **Coaxial needle cost** for EZU-PA3U device and double freehand only
7. **Cost of balloon/probe cover** added for LATRUS
8. **Cost for lithotomy bed** for transperineal biopsies
9. **Cost of ultrasound machine** assuming 1,000 biopsies per year

The effect of these changes applied cumulatively to the original EAG base case are shown in *Table 21* and *Table 22* below for subgroup A decision question 1 and 2, respectively. The net effect is to reduce the ICERs in both sets of analysis

Table 21 Cumulative changes to EAG base case decision question 1, subgroup A

Biopsy method	Total		Incremental		ICERs
	Cost	QALYs	Cost	QALYs	£/QALY
Original EAG base case					
LATRUS	£19,472	9.2991			
LATP-any	£19,620	9.3011	£148	0.0020	£72,503
GATP	£20,089	9.2993	£469	-0.0018	Dominated
+ NMA excluding Hara et al.					
LATRUS	£19,472	9.2991			
LATP-any	£19,614	9.3025	£142	0.0034	£41,369
GATP	£20,081	9.3011	£467	-0.0014	Dominated
+ Exclude overnight stay from Berry et al.					
LATRUS	£19,458	9.2991			
LATP-any	£19,541	9.3026	£83	0.0035	£23,803
GATP	£20,008	9.3012	£467	-0.0014	Dominated
+ Correction to Rosario et al. data.					
LATRUS	£19,462	9.2989			
LATP-any	£19,541	9.3026	£79	0.0037	£21,264
GATP	£20,008	9.3012	£467	-0.0014	Dominated
+ Cost of histopathology from NHS cost data					
LATRUS	£19,874	9.2989			
LATP-any	£19,951	9.3026	£77	0.0037	£20,741
GATP	£20,419	9.3012	£468	-0.0014	Dominated
+ Price for SureFire device					
LATRUS	£19,874	9.2989			
LATP-any	£19,949	9.3026	£75	0.0037	£20,237
GATP	£20,419	9.3012	£470	-0.0014	Dominated
+ Coaxial needle cost only for EZU-PA3U device and double freehand					
LATRUS	£19,874	9.2989			
LATP-any	£19,936	9.3026	£62	0.0037	£16,643
GATP	£20,419	9.3012	£483	-0.0014	Dominated
+ Add cost of balloon/probe cover for LATRUS					
LATRUS	£19,880	9.2989			
LATP-any	£19,937	9.3026	£57	0.0037	£15,399
GATP	£20,420	9.3012	£483	-0.0014	Dominated
+ Cost for lithotomy bed for transperineal biopsies					
LATRUS	£19,880	9.2989			
LATP-any	£19,938	9.3026	£58	0.0037	£15,668
GATP	£20,421	9.3012	£483	-0.0014	Dominated
+ Cost of ultrasound machine (1,000 per year) – Revised EAG base case					
LATRUS	£19,878	9.2989			
LATP-any	£19,937	9.3026	£58	0.0037	£15,669
GATP	£20,420	9.3012	£483	-0.0014	Dominated

Table 22 Cumulative changes to EAG base case decision question 2, subgroup A

Biopsy method	Total		Incremental		ICERs
	Cost	QALYs	Cost	QALYs	£/QALY
Original EAG base case					
LATRUS	£19,472	9.2991			
LATP-freehand	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	£19,632	9.2985	£50	-0.0135	Dominated
GATP	£20,100	9.2969	£468	-0.0016	Dominated
+ NMA excluding Hara et al.					
LATRUS	£19,472	9.2991			
LATP-freehand	£19,582	9.3121	£110	0.0130	£8,447
LATP-other	£19,625	9.3000	£43	-0.0120	Dominated
GATP	£20,094	9.2981	£469	-0.0019	Dominated
+ Exclude overnight stay from Berry et al.					
LATRUS	£19,458	9.2991			
LATP-freehand	£19,509	9.3122	£51	0.0131	£3,926
LATP-other	£19,552	9.3001	£43	-0.0120	Dominated
GATP	£20,021	9.2982	£469	-0.0019	Dominated
+ Correction to Rosario et al. data.					
LATRUS	£19,462	9.2989			
LATP-freehand	£19,509	9.3122	£47	0.0133	£3,537
LATP-other	£19,552	9.3001	£43	-0.0120	Dominated
GATP	£20,021	9.2982	£469	-0.0019	Dominated
+ Cost of histopathology from NHS cost data					
LATRUS	£19,874	9.2989			
LATP-freehand	£19,908	9.3122	£34	0.0133	£2,557
LATP-other	£19,965	9.3001	£57	-0.0120	Dominated
GATP	£20,436	9.2982	£471	-0.0019	Dominated
+ Price for SureFire device					
LATRUS	£19,874	9.2989			
LATP-freehand	£19,905	9.3122	£31	0.0133	£2,369
LATP-other	£19,965	9.3001	£59	-0.0120	Dominated
GATP	£20,436	9.2982	£471	-0.0019	Dominated
+ Coaxial needle cost only for EZU-PA3U device and double freehand					
LATRUS	£19,874	9.2989			
LATP-freehand	£19,887	9.3122	£14	0.0133	£1,025
LATP-other	£19,965	9.3001	£77	-0.0120	Dominated
GATP	£20,436	9.2982	£471	-0.0019	Dominated
+ Add cost of balloon/probe cover for LATRUS					
LATRUS	£19,880	9.2989			
LATP-freehand	£19,888	9.3122	£9	0.0133	£665
LATP-other	£19,966	9.3001	£78	-0.0120	Dominated
GATP	£20,437	9.2982	£471	-0.0019	Dominated
+ Cost for lithotomy bed for transperineal biopsies					
LATRUS	£19,880	9.2989			
LATP-freehand	£19,889	9.3122	£10	0.0133	£740
LATP-other	£19,967	9.3001	£78	-0.0120	Dominated
GATP	£20,438	9.2982	£471	-0.0019	Dominated
+ Cost of ultrasound machine (1,000 per year) – Revised EAG base case					
LATRUS	£19,878	9.2989			
LATP-freehand	£19,888	9.3122	£10	0.0133	£743
LATP-other	£19,966	9.3001	£77	-0.0120	Dominated
GATP	£20,437	9.2982	£471	-0.0019	Dominated

3.1 Revised base case: decision question 1

3.1.1 Deterministic results

Table 23 Revised base case cost effectiveness (deterministic): decision question 1

Biopsy method	Total		Incremental		INHB (QALYs)		ICERs
	Cost	QALYs	Cost	QALYs	£20k	£30k	£/QALY
Subgroup A: MRI Likert 3+ first biopsy							
LATRUS	£19,878	9.2989					
LATP-all	£19,937	9.3026	£58	0.0037	0.001	0.002	£15,669
GATP	£20,420	9.3012	£483	-0.0014	-0.025	-0.016	Dominated
Subgroup B: MRI Likert 1 or 2 first biopsy							
LATRUS	£15,753	9.4781					
LATP-all	£15,815	9.4810	£62	0.0029	0.000	0.001	£21,551
GATP	£16,295	9.4803	£480	-0.0007	-0.025	-0.016	Dominated
Subgroup C: MRI Likert 3+ previous negative biopsy							
LATRUS	£16,653	9.4563					
LATP-all	£16,714	9.4592	£61	0.0029	0.000	0.001	£21,095
GATP	£17,195	9.4585	£481	-0.0007	-0.025	-0.016	Dominated
Subgroup D: MRI Likert 1 or 2 previous negative biopsy							
LATRUS	£14,066	9.5472					
LATP-all	£14,129	9.5497	£63	0.0025	-0.001	0.000	£25,514
GATP	£14,608	9.5493	£479	-0.0003	-0.025	-0.016	Dominated

ICER incremental cost effectiveness ratio (fully incremental)
INHB incremental net health benefit versus LATRUS, at thresholds £20,000-£30,000/QALY gained

3.1.2 Probabilistic results

Table 24 Revised base case cost effectiveness (probabilistic): decision question 1

Biopsy method	Total		Incremental		INHB (QALYs)		ICERs
	Cost	QALYs	Cost	QALYs	£20k	£30k	£/QALY
Subgroup A: MRI Likert 3+ first biopsy							
LATRUS	19,855	9.3027					
LATP-all	19,917	9.3063	62	0.0035	0.000	0.001	17,482
GATP	20,412	9.3036	557	0.0009	-0.027	-0.018	Dominated
Subgroup B: MRI Likert 1 or 2 first biopsy							
LATRUS	15,821	9.4768					
LATP-all	15,884	9.4795	62	0.0027	0.000	0.001	22,833
GATP	16,372	9.4785	550	0.0016	-0.026	-0.017	Dominated
Subgroup C: MRI Likert 3+ previous negative biopsy							
LATRUS	16,571	9.4528					
LATP-all	16,632	9.4554	62	0.003	0.000	0.001	23,468
GATP	17,126	9.4537	555	0.001	-0.027	-0.018	Dominated
Subgroup D: MRI Likert 1 or 2 previous negative biopsy							
LATRUS	13,991	9.5410					
LATP-all	14,052	9.5434	61	0.002	-0.001	0.000	25,453
GATP	14,521	9.5428	530	0.002	-0.025	-0.016	304,804

ICER incremental cost effectiveness ratio (fully incremental)
INHB incremental net health benefit versus LATRUS, at thresholds £20,000-£30,000/QALY gained

Figure 13 Revised base case scatterplot: subgroup A (decision question 1)

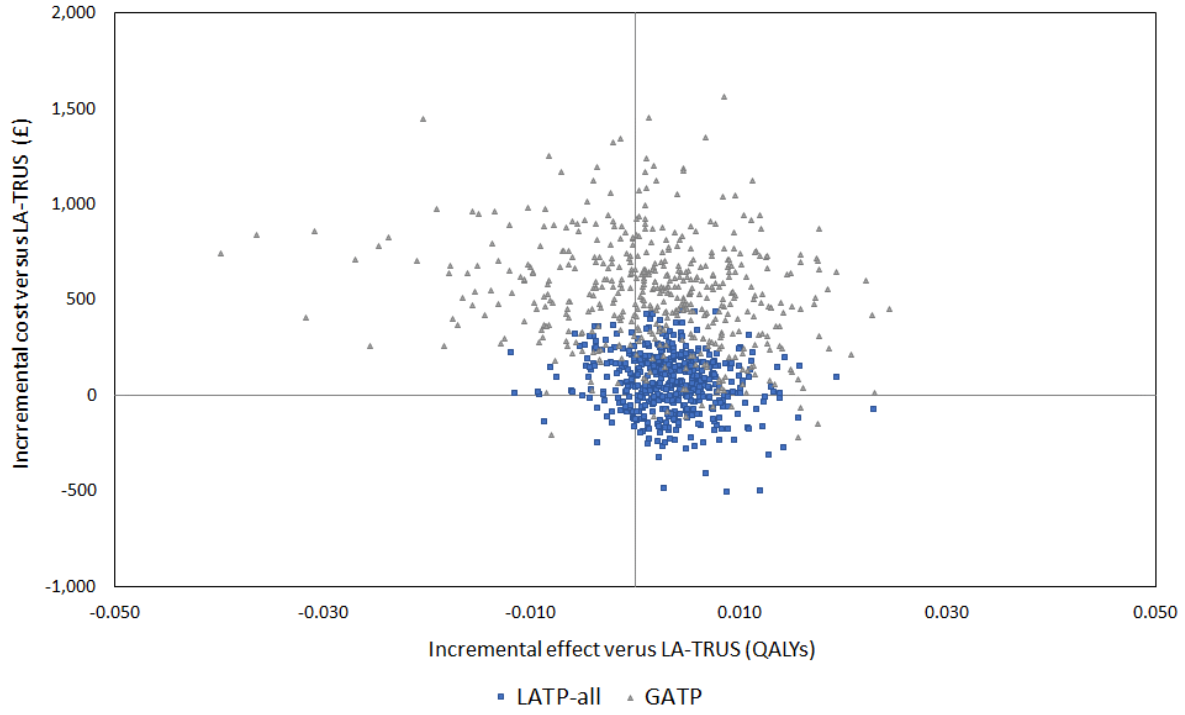
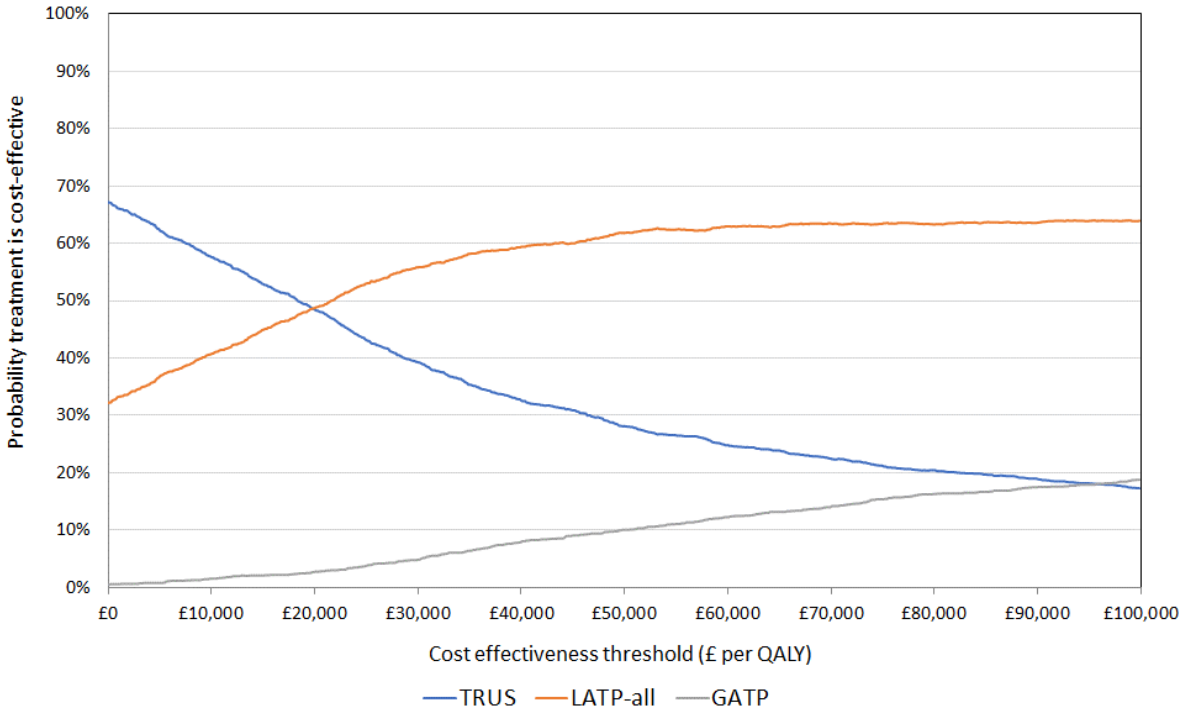


Figure 14 Revised base case CEAC: subgroup A (decision question 1)



3.1.3 Intermediate outcomes

Table 25 Revised base case decision tree intermediate outcomes (deterministic): decision question 1

Biopsy method	Mean biopsies	Undiagnosed		Biopsy related adverse events (AE)			AE QALY loss
		CNS	CS	Mild	Admissions	Deaths	
Subgroup A: MRI Likert 3+ first biopsy							
LATRUS	1.034	9.92%	15.22%	10.7%	3.9%	0.07%	-0.0018
LATP-all	1.034	9.82%	14.16%	9.5%	3.7%	0.05%	-0.0017
GATP	1.034	9.90%	15.01%	9.5%	3.7%	0.05%	-0.0017
Subgroup B: MRI Likert 1 or 2 first biopsy							
LATRUS	1.013	20.40%	6.73%	10.5%	3.8%	0.07%	-0.0018
LATP-all	1.013	20.17%	6.29%	9.3%	3.6%	0.05%	-0.0017
GATP	1.013	20.35%	6.64%	9.3%	3.6%	0.05%	-0.0017
Subgroup C: MRI Likert 3+ previous negative biopsy							
LATRUS	1.000	17.44%	4.45%	10.4%	3.7%	0.07%	-0.0018
LATP-all	1.000	17.11%	4.02%	9.1%	3.5%	0.05%	-0.0017
GATP	1.000	17.38%	4.37%	9.1%	3.5%	0.05%	-0.0017
Subgroup D: MRI Likert 1 or 2 previous negative biopsy							
LATRUS	1.000	21.74%	1.12%	10.4%	3.7%	0.07%	-0.0018
LATP-all	1.000	21.33%	1.01%	9.1%	3.5%	0.05%	-0.0017
GATP	1.000	21.66%	1.09%	9.1%	3.5%	0.05%	-0.0017

CNS clinically non-significant prostate cancer (low-risk localised); CS clinically significant prostate cancer (intermediate or high-risk localised disease)

Table 26 Revised base case health outcomes from Markov model (deterministic): decision question 1

Biopsy method	Deaths (% of whole cohort)			Undiscounted		Discounted	
	Prostate cancer	Other cause	All	LYs	QALYs	LY	QALY
Subgroup A: MRI Likert 3+ first biopsy							
LATRUS	19.60%	80.31%	99.90%	16.010	12.578	11.717	9.301
LATP-all	19.57%	80.35%	99.92%	16.017	12.584	11.722	9.304
GATP	19.59%	80.33%	99.92%	16.014	12.581	11.720	9.303
Subgroup B: MRI Likert 1 or 2 first biopsy							
LATRUS	10.86%	89.03%	99.89%	16.780	12.960	12.138	9.480
LATP-all	10.85%	89.06%	99.91%	16.785	12.964	12.141	9.483
GATP	10.86%	89.05%	99.91%	16.784	12.963	12.140	9.482
Subgroup C: MRI Likert 3+ previous negative biopsy							
LATRUS	12.64%	87.26%	99.90%	16.638	12.903	12.063	9.458
LATP-all	12.62%	87.29%	99.92%	16.643	12.907	12.067	9.461
GATP	12.64%	87.28%	99.92%	16.642	12.906	12.066	9.460
Subgroup D: MRI Likert 1 or 2 previous negative biopsy							
LATRUS	7.32%	92.57%	99.89%	17.087	13.111	12.304	9.549
LATP-all	7.32%	92.60%	99.91%	17.092	13.114	12.307	9.551
GATP	7.32%	92.59%	99.91%	17.091	13.113	12.307	9.551
LY life years; QALY quality adjusted life years							

Table 27 Revised base case intermediate costs from decision tree and Markov model (deterministic): decision question 1

Biopsy method	Decision tree costs			Markov model, undiscounted costs					Discounted Total costs
	Biopsies	AEs	Total cost	Treatment	AE	Follow up	End of life	Total	
Subgroup A: MRI Likert 3+ first biopsy									
LATRUS	£704	£109	£813	£8,965	£2,709	£662	£16,042	£28,378	£19,065
LATP-all	£799	£80	£879	£8,958	£2,711	£658	£16,043	£28,371	£19,058
GATP	£1,275	£80	£1,355	£8,965	£2,710	£661	£16,043	£28,380	£19,066
Subgroup B: MRI Likert 1 or 2 first biopsy									
LATRUS	£690	£107	£796	£5,118	£1,715	£639	£16,040	£23,513	£14,957
LATP-all	£785	£78	£862	£5,115	£1,717	£636	£16,042	£23,510	£14,952
GATP	£1,260	£78	£1,338	£5,119	£1,716	£638	£16,042	£23,515	£14,957
Subgroup C: MRI Likert 3+ previous negative biopsy									
LATRUS	£681	£105	£786	£5,953	£1,987	£654	£16,041	£24,634	£15,867
LATP-all	£776	£76	£852	£5,950	£1,988	£650	£16,042	£24,630	£15,862
GATP	£1,251	£76	£1,328	£5,953	£1,987	£653	£16,042	£24,636	£15,867
Subgroup D: MRI Likert 1 or 2 previous negative biopsy									
LATRUS	£681	£105	£786	£3,568	£1,303	£607	£16,039	£21,516	£13,280
LATP-all	£776	£76	£852	£3,566	£1,303	£603	£16,041	£21,514	£13,277
GATP	£1,251	£76	£1,328	£3,568	£1,303	£606	£16,041	£21,518	£13,280
AE biopsy related adverse events									

3.2 Revised base case: decision question 2

3.2.1 Deterministic results

Table 28 Revised base case cost effectiveness (deterministic): decision question 2

Biopsy method	Total		Incremental		INHB (QALYs)		ICERs
	Cost	QALYs	Cost	QALYs	£20k	£30k	£/QALY
Subgroup A: MRI Likert 3+ first biopsy							
LATRUS	£19,878	9.2989					
LATP-freehand	£19,888	9.3122	£10	0.0133	0.013	0.013	£743
LATP-other	£19,966	9.3001	£77	-0.0120	-0.003	-0.002	Dominated
GATP	£20,437	9.2982	£471	-0.0019	-0.029	-0.019	Dominated
Subgroup B: MRI Likert 1 or 2 first biopsy							
LATRUS	£15,753	9.4781					
LATP-freehand	£15,788	9.4858	£35	0.0077	0.006	0.006	£4,595
LATP-other	£15,838	9.4798	£49	-0.0060	-0.003	-0.001	Dominated
GATP	£16,304	9.4788	£467	-0.0009	-0.027	-0.018	Dominated
Subgroup C: MRI Likert 3+ previous negative biopsy							
LATRUS	£16,653	9.4563					
LATP-freehand	£16,699	9.4612	£46	0.0050	0.003	0.003	£9,284
LATP-other	£16,738	9.4579	£39	-0.0033	-0.003	-0.001	Dominated
GATP	£17,206	9.4569	£468	-0.0010	-0.027	-0.018	Dominated
Subgroup D: MRI Likert 1 or 2 previous negative biopsy							
LATRUS	£14,066	9.5472					
LATP-freehand	£14,112	9.5516	£46	0.0043	0.002	0.003	£10,640
LATP-other	£14,150	9.5491	£38	-0.0025	-0.002	-0.001	Dominated
GATP	£14,615	9.5486	£465	-0.0005	-0.026	-0.017	Dominated

ICER incremental cost effectiveness ratio (fully incremental)
INHB incremental net health benefit versus LATRUS, at thresholds £20,000-£30,000/QALY gained
For abbreviations see *List of Abbreviations*

3.2.2 Probabilistic results

Table 29 Revised base case cost effectiveness (deterministic): decision question 2

Biopsy method	Total		Incremental		INHB (QALYs)		ICERs
	Cost	QALYs	Cost	QALYs	£20k	£30k	£/QALY
Subgroup A: MRI Likert 3+ first biopsy							
LATRUS	19,855	9.3027					
LATP-freehand	19,885	9.3130	30	0.010	0.009	0.009	2,894
LATP-other	19,944	9.3036	88	0.001	-0.004	-0.002	Dominated
GATP	20,427	9.3010	572	-0.002	-0.030	-0.021	Dominated
Subgroup B: MRI Likert 1 or 2 first biopsy							
LATRUS	15,821	9.4768					
LATP-freehand	15,863	9.4833	42	0.006	0.004	0.005	6,473
LATP-other	15,904	9.4784	83	0.002	-0.003	-0.001	Dominated
GATP	16,381	9.4770	560	0.000	-0.028	-0.018	Dominated
Subgroup C: MRI Likert 3+ previous negative biopsy							
LATRUS	16,571	9.4528					
LATP-freehand	16,621	9.4572	51	0.004	0.002	0.003	11,464
LATP-other	16,654	9.4542	83	0.001	-0.003	-0.001	Dominated
GATP	17,133	9.4527	562	-0.000	-0.028	-0.019	Dominated
Subgroup D: MRI Likert 1 or 2 previous negative biopsy							
LATRUS	13,991	9.5410					
LATP-freehand	14,039	9.5451	48	0.004	0.002	0.002	11,757
LATP-other	14,072	9.5429	81	0.002	-0.002	-0.001	Dominated
GATP	14,526	9.5423	535	0.001	-0.025	-0.017	Dominated

ICER incremental cost effectiveness ratio (fully incremental)
INHB incremental net health benefit versus LATRUS, at thresholds £20,000-£30,000/QALY gained
For abbreviations see *List of Abbreviations*

Figure 15 Revised base case scatterplot: subgroup A (decision question 2)

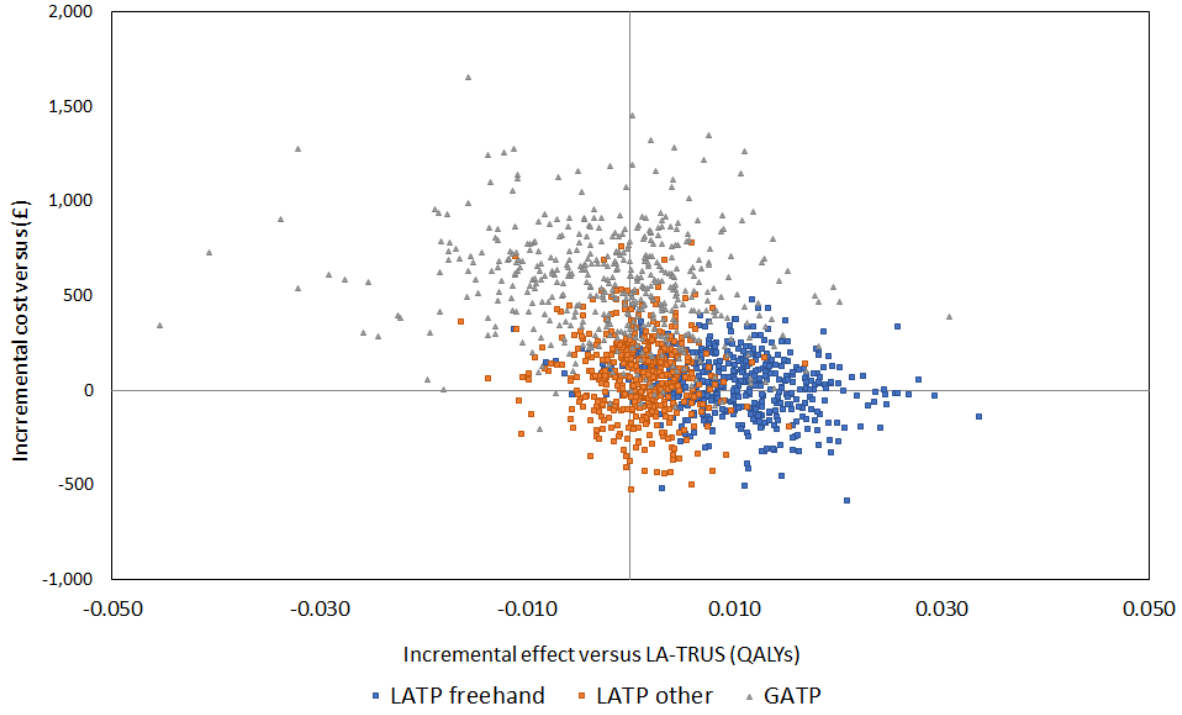
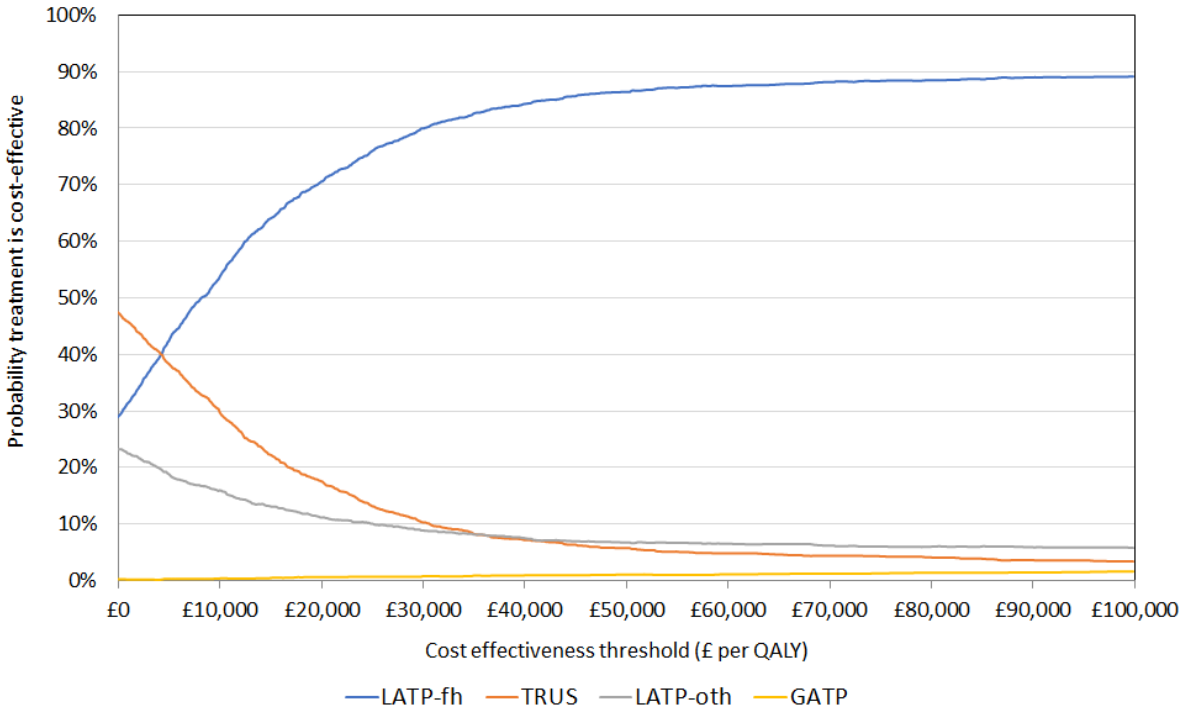


Figure 16 Revised base case CEAC: subgroup A (decision question 2)



3.2.3 Intermediate outcomes

Table 30 Revised base case decision tree intermediate outcomes (deterministic): decision question 2

Biopsy method	Mean biopsies	Undiagnosed		Biopsy related adverse events (AE)			AE QALY loss
		CNS	CS	Mild	Admissions	Deaths	
Subgroup A: MRI Likert 3+ first biopsy							
LATRUS	1.0342	9.92%	15.22%	10.7%	3.9%	0.07%	-0.0018
LATP-freehand	1.0344	9.15%	8.38%	9.5%	3.7%	0.05%	-0.0017
LATP-other	1.0343	9.96%	15.67%	9.5%	3.7%	0.05%	-0.0017
GATP	1.0344	10.07%	16.84%	9.5%	3.7%	0.05%	-0.0017
Subgroup B: MRI Likert 1 or 2 first biopsy							
LATRUS	1.0132	20.40%	6.73%	10.5%	3.8%	0.07%	-0.0018
LATP-freehand	1.0139	18.64%	3.85%	9.3%	3.6%	0.05%	-0.0017
LATP-other	1.0131	20.49%	6.92%	9.3%	3.6%	0.05%	-0.0017
GATP	1.0130	20.72%	7.42%	9.3%	3.6%	0.05%	-0.0017
Subgroup C: MRI Likert 3+ previous negative biopsy							
LATRUS	1.0000	17.44%	4.45%	10.4%	3.7%	0.07%	-0.0018
LATP-freehand	1.0000	14.95%	3.59%	9.1%	3.5%	0.05%	-0.0017
LATP-other	1.0000	17.58%	4.64%	9.1%	3.5%	0.05%	-0.0017
GATP	1.0000	17.92%	5.14%	9.1%	3.5%	0.05%	-0.0017
Subgroup D: MRI Likert 1 or 2 previous negative biopsy							
LATRUS	1.0000	21.74%	1.12%	10.4%	3.7%	0.07%	-0.0018
LATP-freehand	1.0000	18.64%	0.90%	9.1%	3.5%	0.05%	-0.0017
LATP-other	1.0000	21.92%	1.16%	9.1%	3.5%	0.05%	-0.0017
GATP	1.0000	22.34%	1.29%	9.1%	3.5%	0.05%	-0.0017

Table 31 Revised base case health outcomes from Markov model (deterministic): decision question 2

Biopsy method	Deaths (% of whole cohort)			Undiscounted		Discounted	
	Prostate cancer	Other cause	All	LYs	QALYs	LY	QALY
Subgroup A: MRI Likert 3+ first biopsy							
LATRUS	19.60%	80.31%	99.90%	16.010	12.578	11.717	9.301
LATP-freehand	19.41%	80.51%	99.92%	16.037	12.599	11.734	9.314
LATP-other	19.61%	80.31%	99.92%	16.012	12.580	11.719	9.302
GATP	19.64%	80.28%	99.92%	16.008	12.576	11.716	9.300
Subgroup B: MRI Likert 1 or 2 first biopsy							
LATRUS	10.86%	89.03%	99.89%	16.780	12.960	12.138	9.480
LATP-freehand	10.77%	89.15%	99.91%	16.795	12.972	12.147	9.487
LATP-other	10.87%	89.04%	99.91%	16.783	12.962	12.140	9.481
GATP	10.89%	89.03%	99.91%	16.781	12.961	12.138	9.481
Subgroup C: MRI Likert 3+ previous negative biopsy							
LATRUS	12.64%	87.26%	99.90%	16.638	12.903	12.063	9.458
LATP-freehand	12.58%	87.33%	99.92%	16.648	12.911	12.069	9.463
LATP-other	12.65%	87.27%	99.92%	16.641	12.905	12.065	9.460
GATP	12.66%	87.25%	99.92%	16.639	12.903	12.064	9.459
Subgroup D: MRI Likert 1 or 2 previous negative biopsy							
LATRUS	7.32%	92.57%	99.89%	17.087	13.111	12.304	9.549
LATP-freehand	7.28%	92.63%	99.91%	17.096	13.117	12.310	9.553
LATP-other	7.33%	92.58%	99.91%	17.090	13.113	12.307	9.551
GATP	7.34%	92.57%	99.91%	17.089	13.112	12.306	9.550

LY life years; QALY quality adjusted life years

Table 32 Revised base case intermediate costs from decision tree and Markov model (deterministic): decision question 2

Biopsy method	Decision tree costs			Markov model, undiscounted costs					Discounted Total costs
	Biopsies	AEs	Total	Treatment	AE	Follow up	End of life	Total	
Subgroup A: MRI Likert 3+ first biopsy									
LATRUS	£704	£109	£813	£8,965	£2,709	£662	£16,042	£28,378	£19,065
LATP-freehand	£805	£80	£885	£8,909	£2,721	£637	£16,043	£28,309	£19,004
LATP-other	£814	£80	£894	£8,971	£2,709	£664	£16,043	£28,387	£19,072
GATP	£1,275	£80	£1,355	£8,981	£2,707	£668	£16,043	£28,399	£19,082
Subgroup B: MRI Likert 1 or 2 first biopsy									
LATRUS	£690	£107	£796	£5,118	£1,715	£639	£16,040	£23,513	£14,957
LATP-freehand	£791	£78	£868	£5,092	£1,721	£618	£16,042	£23,472	£14,920
LATP-other	£800	£78	£877	£5,121	£1,715	£640	£16,042	£23,519	£14,960
GATP	£1,260	£78	£1,338	£5,126	£1,715	£643	£16,042	£23,525	£14,966
Subgroup C: MRI Likert 3+ previous negative biopsy									
LATRUS	£681	£105	£786	£5,953	£1,987	£654	£16,041	£24,634	£15,867
LATP-freehand	£781	£76	£858	£5,942	£1,990	£633	£16,042	£24,607	£15,841
LATP-other	£791	£76	£867	£5,956	£1,987	£656	£16,042	£24,641	£15,871
GATP	£1,251	£76	£1,328	£5,961	£1,986	£660	£16,042	£24,648	£15,878
Subgroup D: MRI Likert 1 or 2 previous negative biopsy									
LATRUS	£681	£105	£786	£3,568	£1,303	£607	£16,039	£21,516	£13,280
LATP-freehand	£781	£76	£858	£3,560	£1,305	£583	£16,041	£21,489	£13,254
LATP-other	£791	£76	£867	£3,569	£1,303	£608	£16,041	£21,521	£13,283
GATP	£1,251	£76	£1,328	£3,571	£1,302	£612	£16,041	£21,526	£13,287
For abbreviations see *List of Abbreviations*									

4 Scenario analysis on revised base case

4.1 Cancer detection rates

4.1.1 NMA scenarios

Decision question 1: With the revised base case, the ICER for LATP is less than £20,000 per QALY in subgroup A and less than £30,000 per QALY in subgroups B- D. This ICER remains below £30,000 per QALY in all subgroups in NMA scenario 2, but is greater than £30,000 per QALY in subgroups B-D if the Hara trial in NMA scenario 1 (as in the DAR base case). GATP is dominated in all scenarios.

Table 33 NMA scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	RR [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case: NMA excluding Hara						
LATRUS	1.00	£19,878	9.2989			
LATP-any	1.05	£19,937	9.3026	£58	0.0037	£15,669
GATP	1.01	£20,420	9.3012	£483	-0.0014	Dominated
NMA scenario 1: Hara classified as LATP-any versus LATRUS						
LATRUS	1.00	£19,878	9.2989			
LATP-any	1.01	£19,944	9.3012	£66	0.0023	£28,322
GATP	0.96	£20,430	9.2994	£486	-0.0018	Dominated
NMA scenario 2: Hara classified as GATP versus LATRUS						
LATRUS	1.00	£19,878	9.2989			
LATP-any	1.03	£19,941	9.3019	£62	0.0030	£20,472
GATP	0.92	£20,439	9.2978	£499	-0.0041	Dominated

[a] Relative risk for cancer detection compared with LATRUS

Table 34 NMA scenarios for decision question 1, subgroup comparison (deterministic)

Biopsy method	RR [a]	ICERs (£ per QALY gained)			
		Subgroup A	Subgroup B	Subgroup C	Subgroup D
Revised EAG base case: NMA excluding Hara					
LATRUS	1.00				
LATP-any	1.05	£15,669	£21,551	£21,095	£25,514
GATP	1.01	Dominated	Dominated	Dominated	Dominated
NMA scenario 1: Hara classified as LATP versus LATRUS					
LATRUS	1.00				
LATP-any	1.01	£28,322	£30,256	£30,188	£31,261
GATP	0.96	Dominated	Dominated	Dominated	Dominated
NMA scenario 2: Hara classified as GATP versus LATRUS					
LATRUS	1.00				
LATP-any	1.03	£20,472	£25,271	£24,939	£28,143
GATP	0.92	Dominated	Dominated	Dominated	Dominated

[a] Relative risk for cancer detection compared with LATRUS

Decision question 2: Results are not sensitive to the NMA scenarios in decision question 2 because the relative risk for cancer detection with LATP-freehand versus LATRUS does not change and other comparators are dominated in all scenarios and subgroups. ICERs for LATP-freehand vs TRUS are less than £20,000 per QALY in all subgroups.

Table 35 NMA scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	RR [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case: NMA excluding Hara						
LATRUS	1.00	£19,878	9.2989			
LATP-freehand	1.40	£19,888	9.3122	£10	0.0133	£743
LATP-other	0.98	£19,966	9.3001	£77	-0.0120	Dominated
GATP	0.93	£20,437	9.2982	£471	-0.0019	Dominated
NMA scenario 1: Hara classified as LATP-other versus LATRUS						
LATRUS	1.00	£19,878	9.2989			
LATP-freehand	1.40	£19,888	9.3122	£10	0.0133	£743
LATP-other	0.94	£19,974	9.2986	£86	-0.0135	Dominated
GATP	0.90	£20,444	9.2970	£470	-0.0016	Dominated
NMA scenario 2: Hara classified as GATP versus LATRUS						
LATRUS	1.00	£19,878	9.2989			
LATP-freehand	1.40	£19,888	9.3122	£10	0.0133	£743
LATP-other	0.97	£19,968	9.2998	£80	-0.0124	Dominated
GATP	0.89	£20,446	9.2966	£478	-0.0032	Dominated
[a] Relative risk for cancer detection compared with LATRUS						

Table 36 NMA scenarios for decision question 2, subgroup comparison (deterministic)

Biopsy method	RR [a]	ICERs (£ per QALY gained)			
		Subgroup A	Subgroup B	Subgroup C	Subgroup D
Revised EAG base case: NMA excluding Hara					
LATRUS	1.00				
LATP-freehand	1.40	£743	£4,595	£9,284	£10,640
LATP-other	0.98	Dominated	Dominated	Dominated	Dominated
GATP	0.93	Dominated	Dominated	Dominated	Dominated
NMA scenario 1: Hara classified as LATP versus LATRUS					
LATRUS	1.00				
LATP-freehand	1.40	£743	£4,595	£9,284	£10,640
LATP-other	0.94	Dominated	Dominated	Dominated	Dominated
GATP	0.90	Dominated	Dominated	Dominated	Dominated
NMA scenario 2: Hara reclassified as GATP versus LATRUS					
LATRUS	1.00				
LATP-freehand	1.40	£743	£4,595	£9,284	£10,640
LATP-other	0.97	Dominated	Dominated	Dominated	Dominated
GATP	0.89	Dominated	Dominated	Dominated	Dominated
[a] Relative risk for cancer detection compared with LATRUS					

4.1.2 Observational scenarios

Decision question 1: ICERs for LATP vs. LATRUS are lower when cancer detection rates are based on observational data rather than RCT data as in the base case. The ICERs for LATP are similar for alternative observational scenarios, below (or very close to) the £20,000 per QALY threshold for all observational scenarios and subgroups, with the exception of scenario 1 in subgroup D, for which the ICER is £22,260 per QALY. GATP has a high ICERs or is dominated in all observational scenarios and subgroups

Decision question 2: ICERs for LATP-freehand vs. LATRUS are higher when based on observational data than in the revised base case, but they remain below £20,000 per QALY in all observational scenarios and subgroups. LATP-other and GATP are dominated or have high ICERs in all observational scenarios and subgroups.

Table 37 Observational scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	RR [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Observational scenario applied to revised EAG base case						
LATRUS	1.00	£19,878	9.2989			
LATP-any	1.10	£19,927	9.3042	£49	0.0054	£9,159
GATP	1.45	£20,359	9.3121	£431	0.0078	£54,953
Observational scenario 1: excluding Bojin						
LATRUS	1.00	£19,878	9.2989			
LATP-any	1.08	£19,931	9.3036	£53	0.0047	£11,175
GATP	1.42	£20,358	9.3122	£427	0.0086	£49,771
Observational scenario 2: excluding Watanabe						
LATRUS	1.00	£19,878	9.2989			
LATP-any	1.12	£19,924	9.3049	£46	0.0060	£7,609
GATP	1.47	£20,359	9.3120	£435	0.0071	£61,058
Observational scenario 3: including Walters						
LATRUS	1.00	£19,878	9.2989			
LATP-any	1.10	£19,927	9.3042	£49	0.0054	£9,159
GATP	1.16	£20,393	9.3060	£466	0.0018	£263,212
Observational scenario 4: including Walters and excluding Takuma						
LATRUS	1.00	£19,878	9.2989			
LATP-any	1.10	£19,927	9.3042	£49	0.0054	£9,159
GATP	0.97	£20,428	9.2999	£500	-0.0044	Dominated

[a] Relative risk for cancer detection

Table 38 Observational scenarios for decision question 1, subgroup comparison (deterministic)

Biopsy method	RR [a]	ICERs (£ per QALY gained)			
		Subgroup A	Subgroup B	Subgroup C	Subgroup D
Revised EAG base case with observational data					
LATRUS	1.00				
LATP-any	1.10	£9,159	£15,385	£14,855	£20,444
GATP	1.45	£54,953	£110,304	£360,856	£276,471
Observational scenario 1: excluding Bojin					
LATRUS	1.00				
LATP-any	1.08	£11,175	£17,457	£16,935	£22,260
GATP	1.42	£49,771	£102,245	£291,120	£266,195
Observational scenario 2: excluding Watanabe					
LATRUS	1.00				
LATP-any	1.12	£7,609	£13,677	£13,154	£18,850
GATP	1.47	£61,058	£119,446	£469,037	£287,193
Observational scenario 3: including Walters					
LATRUS	1.00				
LATP-any	1.10	£9,159	£15,385	£14,855	£20,444
GATP	1.16	£263,212	£535,092	£537,050	£1,040,627
Observational scenario 4: including Walters and excluding Takuma					
LATRUS	1.00				
LATP-any	1.10	£9,159	£15,385	£14,855	£20,444
GATP	0.97	Dominated	Dominated	Dominated	Dominated

[a] Relative risk for cancer detection

Table 39 Observational scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	RR [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Observational scenario applied to revised EAG base case						
LATRUS	1.00	£19,878	9.2989			
LATP-freehand	1.21	£19,915	9.3075	£36	0.0086	£4,209
LATP-other	1.01	£19,960	9.3012	£45	-0.0063	Dominated
GATP	1.33	£20,367	9.3105	£408	0.0093	£148,623
Observational scenario 1: excluding Bojin						
LATRUS	1.00	£19,878	9.2989			
LATP-freehand	1.22	£19,913	9.3078	£35	0.0089	£3,904
LATP-other	1.01	£19,960	9.3012	£46	-0.0066	Dominated
GATP	1.33	£20,367	9.3105	£408	0.0093	£163,869
Observational scenario 2: excluding Watanabe						
LATRUS	1.00	£19,878	9.2989			
LATP-freehand	1.21	£19,915	9.3075	£36	0.0086	£4,209
LATP-other	1.00	£19,962	9.3009	£47	-0.0066	Dominated
GATP	1.32	£20,369	9.3102	£408	0.0094	£166,422
Observational scenario 3: including Walters						
LATRUS	1.00	£19,878	9.2989			

LATP-freehand	1.21	£19,915	9.3075	£36	0.0086	£4,209
LATP-other	1.01	£19,960	9.3012	£45	-0.0063	Dominated
GATP	1.06	£20,410	9.3030	£450	0.0018	Dominated
Observational scenario 4: including Walters and excluding Takuma						
LATRUS	1.00	£19,878	9.2989			
LATP-freehand	1.21	£19,915	9.3075	£36	0.0086	£4,209
LATP-other	1.01	£19,960	9.3012	£45	-0.0063	Dominated
GATP	0.89	£20,445	9.2968	£486	-0.0045	Dominated
[a] Relative risk for cancer detection						

Table 40 Observational scenarios for decision question 2, subgroup comparison (deterministic)

Biopsy method	RR [a]	ICERs (£ per QALY gained)			
		Subgroup A	Subgroup B	Subgroup C	Subgroup D
Revised EAG base case with observational data					
LATRUS	1.00				
LATP-freehand	1.21	£4,209	£9,699	£10,946	£15,848
LATP-other	1.01	Dominated	Dominated	Dominated	Dominated
GATP	1.33	£148,623	£297,872	£3,702,246	£953,031
Observational scenario 1: excluding Bojin					
LATRUS	1.00				
LATP-freehand	1.22	£3,904	£9,284	£10,848	£15,506
LATP-other	1.01	Dominated	Dominated	Dominated	Dominated
GATP	1.33	£163,869	£327,708	£4,075,476	£1,044,194
Observational scenario 2: excluding Watanabe					
LATRUS	1.00				
LATP-freehand	1.21	£4,209	£9,699	£10,946	£15,848
LATP-other	1.00	Dominated	Dominated	Dominated	Dominated
GATP	1.32	£166,422	£333,352	£4,126,973	£1,070,045
Observational scenario 3: including Walters					
LATRUS	1.00				
LATP-freehand	1.21	£4,209	£9,699	£10,946	£15,848
LATP-other	1.01	Dominated	Dominated	Dominated	Dominated
GATP	1.06	Dominated	Dominated	Dominated	Dominated
Observational scenario 4: including Walters and excluding Takuma					
LATRUS	1.00				
LATP-freehand	1.21	£4,209	£9,699	£10,946	£15,848
LATP-other	1.01	Dominated	Dominated	Dominated	Dominated
GATP	0.89	Dominated	Dominated	Dominated	Dominated
[a] Relative risk for cancer detection					

4.2 Probability of admission

Decision question 1: Results are sensitive to the difference in admission rates between LATP and LATRUS. For scenarios 1 and 3, which include the probability of overnight stay from Berry et al. for LATP, the ICER for LATP is greater than £30,000 per QALY gained. GATP is dominated in all scenarios.

Decision question 2: ICERs for LATP-freehand are higher in scenarios with the Berry et al. probability of overnight stay included, but still well below £20K threshold. LATP other and GATP dominated in all scenarios.

Table 41 Admission scenarios, subgroup A (deterministic) – decision question 1

Biopsy method	Admission rate	Total		Incremental		ICERs £/QALY
		Cost	QALYs	Cost	QALYs	
Revised base case: Tamhankar all arms						
LATRUS	3.74%	£19,878	9.2989			
LATP all	3.54%	£19,937	9.3026	£58	0.0037	£15,669
GATP	3.54%	£20,420	9.3012	£483	-0.0014	Dominated
Scenario 1: include overnight stay from Berry et al for LATRUS, LATP and GATP						
LATRUS	6.10%	£19,893	9.2989			
LATP all	15.61%	£20,010	9.3025	£117	0.0036	£32,025
GATP	15.61%	£20,493	9.3011	£483	-0.0014	Dominated
Scenario 2: include overnight stay from Berry et al. for GATP only						
LATRUS	3.74%	£19,878	9.2989			
LATP all	3.54%	£19,937	9.3026	£58	0.0037	£15,669
GATP	15.61%	£20,493	9.3011	£556	-0.0015	Dominated
Scenario 3: Rosario et al. admission rate for LATRUS						
LATRUS	1.31%	£19,815	9.2999			
LATP all	3.54%	£19,935	9.3026	£119	0.0027	£43,452
GATP	3.54%	£20,418	9.3012	£483	-0.0014	Dominated
Scenario 4: Pepe and Aragona admission rate for LATP and GATP						
LATRUS	3.74%	£19,878	9.2989			
LATP all	1.23%	£19,893	9.3035	£15	0.0047	£3,123
GATP	1.23%	£20,376	9.3021	£483	-0.0014	Dominated
Scenario 5: Rosario et al. for LATRUS and Pepe and Aragona for LATP and GATP						
LATRUS	1.31%	£19,815	9.2999			
LATP all	1.23%	£19,891	9.3036	£75	0.0037	£20,522
GATP	1.23%	£20,374	9.3022	£483	-0.0014	Dominated

Table 42 Admission scenarios, subgroup A (deterministic) – decision question 2

Biopsy method	Admission rate	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised base case: Tamhankar all arms						
LATRUS	3.74%	£19,878	9.2989			
LATP freehand	3.54%	£19,888	9.3122	£10	0.0133	£743
LATP all	3.54%	£19,966	9.3001	£77	-0.0120	Dominated
GATP	3.54%	£20,437	9.2982	£471	-0.0019	Dominated
Scenario 1: include overnight stay from Berry et al for LATRUS, LATP and GATP						
LATRUS	6.10%	£19,893	9.2989			
LATP freehand	15.61%	£19,961	9.3121	£68	0.0132	£5,173
LATP all	15.61%	£20,039	9.3000	£77	-0.0120	Dominated
GATP	15.61%	£20,510	9.2981	£471	-0.0019	Dominated
Scenario 2: include overnight stay from Berry et al. for GATP only						
LATRUS	3.74%	£19,878	9.2989			
LATP freehand	3.54%	£19,888	9.3122	£10	0.0133	£743
LATP all	3.54%	£19,966	9.3001	£77	-0.0120	Dominated
GATP	15.61%	£20,510	9.2981	£544	-0.0020	Dominated
Scenario 3: Rosario et al. admission rate for LATRUS						
LATRUS	1.31%	£19,815	9.2999			
LATP freehand	3.54%	£19,886	9.3122	£71	0.0123	£5,750
LATP all	3.54%	£19,964	9.3002	£77	-0.0120	Dominated
GATP	3.54%	£20,435	9.2983	£471	-0.0019	Dominated
Scenario 4: Pepe and Aragona admission rate for LATP and GATP						
LATP freehand	1.23%	£19,844	9.3131			
LATRUS	3.74%	£19,878	9.2989	£34	-0.0142	Dominated
LATP all	1.23%	£19,922	9.3011	£44	0.0022	Dominated
GATP	1.23%	£20,393	9.2992	£471	-0.0019	Dominated
Scenario 5: Rosario et al. for LATRUS and Pepe and Aragona for LATP and GATP						
LA-TRUS	1.31%	£19,815	9.2999			
LATP-freehand	1.23%	£19,842	9.3131	£27	0.0132	£2,035
LATP-other	1.23%	£19,920	9.3011	£77	-0.0120	Dominated
GATP	1.23%	£20,391	9.2992	£471	-0.0019	Dominated

4.3 Probability of repeat biopsy

Decision question 1: The ICER for LATP-any vs. LATRUS is higher when the lower rate of repeat biopsy (5.36%) observed after transperineal biopsy in the Jimenez et al. study[9] is used for LATP (rather 15.45% as observed after LATRUS). However, the ICER in this scenario remains below £20,000 per QALY gained in subgroup A. Note that these scenarios are not relevant for the other subgroups because we assume lower rates of repeat biopsy for patients with an MRI Likert score of 1, and no repeat biopsy after a second biopsy.

Table 43 Repeat biopsy scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	Repeat biopsy rate [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case: same rate for all biopsy methods						
LATRUS	15.45%	£19,878	9.2989			
LATP-any	15.45%	£19,937	9.3026	£58	0.0037	£15,669
GATP	15.45%	£20,420	9.3012	£483	-0.0014	Dominated
Repeat biopsy scenario 1: lower rate for LATP and GATP						
LATRUS	15.45%	£19,878	9.2989			
LATP-any	5.36%	£19,926	9.3015	£48	0.0026	£18,487
GATP	5.36%	£20,410	9.3001	£484	-0.0014	Dominated
Repeat biopsy scenario 2: lower rate for GATP only						
LATRUS	15.45%	£19,878	9.2989			
LATP-any	15.45%	£19,937	9.3026	£58	0.0037	£15,669
GATP	5.36%	£20,410	9.3001	£473	-0.0025	Dominated

[a] Proportion of patients who have a repeat biopsy after a first biopsy finding of clinically non-significant prostate cancer. Model assumes 5% repeat biopsy after a first biopsy finding of no prostate cancer.

Decision question 2: LATP-freehand dominates all other comparators when the lower rate of repeat biopsy is assumed.

Table 44 Repeat biopsy scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	Repeat biopsy rate [a]	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case: same rate for all biopsy methods						
LATRUS	15.45%	£19,878	9.2989			
LATP-freehand	15.45%	£19,888	9.3122	£10	0.0133	£743
LATP-other	15.45%	£19,966	9.3001	£77	-0.0120	Dominated
GATP	15.45%	£20,437	9.2982	£471	-0.0019	Dominated
Repeat biopsy scenario 1: lower rate for LATP and GATP						
LATP-freehand	5.36%	£19,877	9.3111			
LA-TRUS	15.45%	£19,878	9.2989	£2	-0.0122	Dominated
LATP-other	5.36%	£19,955	9.2990	£77	0.0001	Dominated
GATP	5.36%	£20,427	9.2970	£471	-0.0019	Dominated
Repeat biopsy scenario 2: lower rate for GATP only						
LATRUS	15.45%	£19,878	9.2989			
LATP-freehand	15.45%	£19,888	9.3122	£10	0.0133	£743
LATP-other	15.45%	£19,966	9.3001	£77	-0.0120	Dominated
GATP	5.36%	£20,427	9.2970	£461	-0.0031	Dominated

[a] Proportion of patients who have a repeat biopsy after a first biopsy finding of clinically non-significant prostate cancer. Model assumes 5% repeat biopsy after a first biopsy finding of no prostate cancer.

4.4 Number of core samples

Results are highly sensitive to the scenarios with 24 cores for transperineal biopsies and 12 for LATRUS. For decision question 1, the ICER for LATP versus LATRUS in subgroup A is over £100,000 per QALY; and in decision question 2, the ICER for LATP-freehand is £33,813 per QALY. These ICERs are higher for other subgroups.

Table 45 Core scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	Biopsy samples	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case						
LATRUS	12	£19,878	9.2989			
LATP-any	12	£19,937	9.3026	£58	0.0037	£15,669
GATP	12	£20,420	9.3012	£483	-0.0014	Dominated
Core scenario 1: 24 core samples for all transperineal methods						
LATRUS	12	£19,878	9.2989			
LATP-any	24	£20,376	9.3026	£497	0.0037	£133,641
GATP	24	£20,859	9.3012	£483	-0.0014	Dominated

Table 46 Core scenarios for decision question 2, subgroup A (deterministic)

Biopsy method	Biopsy samples	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case						
LATRUS	12	£19,878	9.2989			
LATP-freehand	12	£19,888	9.3122	£10	0.0133	£743
LATP-other	12	£19,966	9.3001	£77	-0.0120	Dominated
GATP	12	£20,437	9.2982	£471	-0.0019	Dominated
Core scenario 1: 24 cores for all transperineal methods						
LATRUS	12	£19,878	9.2989			
LATP-freehand	24	£20,327	9.3122	£449	0.0133	£33,813
LATP-other	24	£20,405	9.3001	£77	-0.0120	Dominated
GATP	24	£20,876	9.2982	£471	-0.0019	Dominated
Core scenario 2: 24 cores for LATP-freehand only						
LATRUS	12	£19,878	9.2989			
LATP-other	12	£19,966	9.3001	£87	0.0012	Dominated [b]
LATP-freehand	24	£20,327	9.3122	£361	0.0120	£33,813
GATP	12	£20,437	9.2982	£110	-0.0139	Dominated
Core scenario 3: 24 cores for LATP-freehand and 16 for LATP-other and GATP						
LATRUS	12	£19,878	9.2989			
LATP-other	16	£20,112	9.3001	£234	0.0012	Dominated [b]
LATP-freehand	24	£20,327	9.3122	£215	0.0120	£33,813
GATP	16	£20,583	9.2982	£256	-0.0139	Dominated

[b] Extendedly dominated by LATRUS and LATP-freehand

Note that the above scenarios only model changes to histopathology costs related to the number of core samples: the QALYs in Table 45 and Table 46 do not differ between scenarios. One would expect clinical parameters, including rates of repeat biopsy and adverse events as well as cancer detection rates, to be affected by the number of cores sampled in addition to the accuracy of targeting enabled by the different biopsy procedures and methods of anaesthesia. One may argue that the above scenarios with costs for 24 cores for LATP-freehand are more consistent with the RCT evidence from the Lam et al. trial,[12] which used a modified Ginsburg protocol for LATP-freehand and a 12-core protocol for the LATRUS control arm.

4.5 Biopsy costs

Decision question 1

The cost of LATP in the base case for decision question 1 assumes an equal mix of methods, including grid and stepper, double freehand and the six named freehand devices included in the scope. We reported two scenarios for the overall cost of the biopsy procedure for decision question 1 in DAR Tables 85 and 86. We apply these scenarios to the revised base case in Table 47 below.

- Cost scenario 1 uses biopsy costs from the National Schedule of NHS costs 2019/20: £332 for LATRUS (outpatient procedure LB76Z 101, urology), £329 for LATP (outpatient procedure B77Z, 101, urology) and £1,512 for GATP (day case procedure LB77Z). In this scenario, the cost for LATRUS is slightly higher than the cost for LATP, so LATP is dominant in all subgroups.
- Cost scenario 2 is based on the EAG micro-costing, but with different assumptions about the proportion of LATP methods used: 10% conducted with a grid and stepping device and 30% with each of the three freehand devices that we understand are currently most common in the UK (CamPROBE, PrecisionPoint and UA1232). This increases the mean cost of LATP estimated from the micro-costing analysis by £23 per biopsy, which increases the ICER for LATP in subgroup A from £15,669 per QALY in the revised base case to £21,940. The ICER for LATP in this scenario remains below £30,000 per QALY for subgroups B and C but increases to £34,996 in subgroup D.

Table 47 Biopsy cost scenarios for decision question 1, subgroup A (deterministic)

Biopsy method	Cost per biopsy	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case: micro-costing						
LATRUS	£681	£19,878	9.2989			
LATP-any	£776	£19,937	9.3026	£58	0.0037	£15,669
GATP	£1,251	£20,420	9.3012	£483	-0.0014	Dominated
Cost scenario 1: NHS cost data 2019/20						
LATP-any	£329	£19,478	9.3026			
LATRUS	£332	£19,518	9.2989	£40	-0.0037	Dominated
GATP	£1,512	£20,669	9.3012	£1,151	0.0023	Dominated
Cost scenario 2: LATP mix (30% each for CamPROBE, PrecisionPoint and UA1232; and 10% grid and stepping device)						
LATRUS	£681	£19,878	9.2989			
LATP-any	£799	£19,960	9.3026	£82	0.0037	£21,940
GATP	£1,251	£20,420	9.3012	£460	-0.0014	Dominated

Decision question 2

The RCT evidence on which cancer detection rates for the LATP-freehand intervention are based relates to the PrecisionPoint device.[12] This is the most costly of the included freehand transperineal devices: £200 for the device and total cost of the procedure estimated at £894. Table 48 below shows the cost-effectiveness results for decision question 2 with estimated costs for LATP-freehand based on PrecisionPoint, to align with the clinical data. This increases the ICER for LATP-freehand versus LATRUS in subgroup A from £743 per QALY in the revised EAG base case to £9,230 per QALY. In this scenario, the ICER for LATP-freehand is below £20,000 per QALY for subgroups A and B, but more than £30,000 per QALY for subgroups C and D.

Table 48 Freehand device cost £200, decision question 1 subgroup A (deterministic)

Biopsy method	Cost per biopsy	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Subgroup A: MRI Likert 3+ first biopsy						
LATRUS	£681	£19,878	9.2989			
LATP-other	£791	£19,966	9.3001	£87	0.0012	Dominated [a]
LATP-freehand	£894	£20,001	9.3122	£35	0.0120	£9,230
GATP	£1,251	£20,437	9.2982	£436	-0.0139	Dominated
Subgroup B: MRI Likert 1 or 2 first biopsy						
LATRUS	£681	£15,753	9.4781			
LATP-other	£791	£15,838	9.4798	£85	0.0017	Dominated [a]
LATP-freehand	£894	£15,901	9.4858	£63	0.0060	£19,286
GATP	£1,251	£16,304	9.4788	£403	-0.0069	Dominated
Subgroup C: MRI Likert 3+ previous negative biopsy						
LATRUS	£681	£16,653	9.4563			

LATP-other	£791	£16,738	9.4579	£85	0.0016	Dominated [a]
LATP-freehand	£894	£16,812	9.4612	£73	0.0033	£32,002
GATP	£1,251	£17,206	9.4569	£394	-0.0043	Dominated
Subgroup D: MRI Likert 1 or 2 previous negative biopsy						
LATRUS	£681	£14,066	9.5472			
LATP-other	£791	£14,150	9.5491	£84	0.0018	Dominated [a]
LATP-freehand	£894	£14,225	9.5516	£75	0.0025	£36,604
GATP	£1,251	£14,615	9.5486	£390	-0.0030	Dominated

ICER incremental cost effectiveness ratio (fully incremental)

[a] Extendedly dominated by LATRUS and LATP-freehand

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