# Evidence overview: Transperineal biopsy in people with suspected prostate cancer

This overview summarises the main issues the diagnostics advisory committee needs to consider. It should be read together with the final scope and the diagnostics assessment report.

## 1 Aims and scope

The purpose of this assessment is to evaluate the clinical and cost effectiveness of local anaesthetic transperineal (LATP) prostate biopsy, with or without the use of one of the following freehand transperineal biopsy devices: PrecisionPoint (BXTAccelyon), UA1232 (BK Medical), CamPROBE (JEB Technologies), Trinity Perine (KeboMed), SureFire Guide (LeapMed) and the EZU-PA3U (Hitachi).

Targeted prostate biopsies use MRI to identify lesions, which then have a small number of tissue samples or cores taken from them. Systematic biopsies take multiple samples from different regions of the left and right side of the prostate.

They can use one of 2 routes: transrectal and transperineal. Both routes use a transrectal ultrasound probe inserted into the anus to image the prostate.

In a transrectal ultrasound (TRUS) prostate biopsy, samples of prostate tissue are collected using a biopsy needle inserted through the rectal wall via the anus. This is usually done using local anaesthetic. The disadvantage of this method is some people can get serious infections, requiring hospital admission and antibiotics.

In transperineal biopsy the biopsy needle enters the body through the perineum, the skin area between the anus and the scrotum. This could greatly reduce the risk of biopsy-related sepsis compared with a TRUS biopsy, and

therefore may reduce hospital admissions and the need for preventative antibiotics.

Traditionally, transperineal biopsies were done under general anaesthetic using a template or grid and a stepping device. This template or grid based biopsy approach requires the needle to pass through the perineum multiple times as the needle is passed through different holes in the grid to access different regions of the prostate. The grid is mounted on the stepping device, which is also used to hold and position the ultrasound probe.

LATP prostate biopsy can be done during an outpatient appointment. This could reduce the need for theatre time for biopsy procedures and therefore reduce waiting times compared with general anaesthetic transperineal (GATP) approaches. Another potential benefit of LATP compared with GATP is that it requires fewer access points and so may reduce pain during and after the biopsy. GATP biopsy procedures might also tend to oversample the prostate compared with LATP, leading to increased risk of urinary retention and infection.

LATP biopsies can be done using: a grid and stepping device; a freehand transperineal biopsy device; or a double freehand approach (that is, using a coaxial needle only).

## Decision questions

1. Do LATP prostate biopsies in patients with suspected prostate cancer represent a clinical and cost-effective use of NHS resources?
2. Do freehand transperineal biopsy devices for LATP prostate biopsies in patients with suspected prostate cancer represent a clinically and cost-effective use of NHS resources?

Decision question 2 therefore, is a sub-question of decision question 1.

## Populations

People with suspected prostate cancer for whom a prostate biopsy is indicated. If data permits, the following subgroups may be considered:

- People with anterior, posterior, apical or basal lesions.
- People with a Likert or PI-RADS score of 2 or less, or a score of 3, 4 or 5.
- People with an enlarged prostate.
- People who have never had a prostate biopsy.
- People who have had a previous negative prostate biopsy and are referred back.

## Interventions

1. LATP prostate biopsy (for example, using a grid and stepping device, a coaxial needle, or a freehand transperineal biopsy device). In the assessment this was referred to as LATP-any.

2. LATP prostate biopsy done using one of the following freehand transperineal biopsy devices (LATP-freehand):

    - PrecisionPoint transperineal access device (BXTAccelyon)
    - UA1232 puncture attachment (BK Medical)
    - Trinity Perine Grid (KOELIS/Kebomed)
    - CamPROBE (JEB Technologies Ltd)
    - SureFire (Delta Surgical Ltd)
    - EZU-PA3U device (Hitachi Medical Systems).

## Comparators

1. For local anaesthetic transperineal (LATP-any) prostate biopsies:

    - local anaesthetic TRUS (LA-TRUS) prostate biopsy
    - GATP prostate biopsy using a grid and stepping device.

2. For LATP prostate biopsies using a freehand transperineal biopsy device:

- Local anaesthetic TRUS prostate biopsy
- LATP prostate biopsy using a grid and stepping device
- GATP prostate biopsy using a grid and stepping device.

### Healthcare setting

The healthcare setting for this intervention is secondary care.

Further details, including descriptions of the interventions, comparator, care pathway and outcomes, are in the final scope for transperineal biopsy in people with suspected prostate cancer.

## 2 Clinical effectiveness evidence

The external assessment group (EAG) did a systematic review to identify evidence on the diagnostic test performance and clinical effectiveness of LATP prostate biopsies. Find the full systematic review results on pages 55 to 112 of the diagnostics assessment report.

### Overview of included studies

There were 23 unique studies (27 publications) that met the selection criteria for inclusion in the review (see pages 48 to 50 of the diagnostics assessment report for details of the selection criteria). Of the included studies, 19 addressed decision question 1, 8 of which also addressed decision question 2 (8 comparative studies of PrecisionPoint: Lam et al. 2021, Bojin 2019, Chen et al. 2021, Hung et al. 2020, Kum et al. 2018, Starmer et al. 2021, Szabo et al. 2021 and Rij et al. 2020). Six of these studies were reported as conference abstracts only (Lam et al. 2021, Hung et al. 2020, Kum et al. 2018, Rij et al. 2020, Takuma 2012 and Walters 2021). The study by Bojin 2019 is an unpublished slide set provided by one of the companies. One prospective single arm study of CamPROBE and 3 prospective single arm studies (reported as abstracts) of the UA1232 device addressed decision question 2 only. Table 3 on page 58 of the diagnostics assessment report shows the number of included studies for each comparison grouped by study design.

## Studies addressing decision question 1

The 19 studies that addressed decision question 1 were separated into 2 categories based on the type of biopsy being compared:

- LATP-any compared with LA-TRUS biopsy (15 studies)
- LATP-any compared with GATP biopsy (4 studies).

### Studies comparing LATP-any with LA-TRUS biopsy

Of the 15 studies that compared LATP-any with LA-TRUS biopsies, 5 were single centre randomised controlled trials (RCTs) based in Japan (2 studies), China, Hong Kong and Italy. None of the studies reported any pre-biopsy MRI. One of the studies used a coaxial needle (double freehand), 1 used an unnamed needle attachment, 1 used PrecisionPoint and 2 studies did not report what device was used. All 5 RCTs used a systematic biopsy approach.

There were 7 prospective cohort studies set in England (3 studies), Hong Kong, Japan and Italy. The 3 English studies and the Hong Kong study used the PrecisionPoint device, 1 study used an unnamed transperineal access device and 2 studies did not report using a device. One of these studies used a systematic biopsy approach, 5 used a combination of systematic and targeted biopsies and 1 of these studies also used targeted biopsy alone. One study did not report what biopsy approach was used.

There were 3 retrospective cohort studies set in Italy, China and the US. One study used a coaxial needle for LATP, 1 used the PrecisionPoint device, and 1 did not report using any device. One study used a saturation biopsy approach, 1 used a systematic approach only and 1 used a combination of systematic and targeted biopsies.

When reported, the number of biopsy cores taken from participants ranged from 6 to 24. The EAG said that the studies and biopsy procedures used were heterogeneous.

The study populations of the RCTs and some of the prospective and retrospective studies only included participants with suspected prostate cancer who had not had a previous biopsy. However, some of the prospective and retrospective studies included mixed study populations (that is, participants with suspected prostate cancer who had not had a previous biopsy, participants who had repeat biopsy and participants on active surveillance). For 1 of the retrospective studies, only repeat biopsy participants were included. Further details of the studies comparing LATP-any with LA-TRUS biopsies are in table 4 of the diagnostics assessment report. Details of the biopsy procedures used in these studies are in table 5 of the diagnostics assessment report.

An overview of the characteristics of the participants in the included studies is in table 6 of the diagnostics assessment report. Only 2 studies reported a PI-RADS score, based on pre-biopsy imaging. Neither correspond exactly with the NICE subgroups of interest (people with a Likert or PI-RADS score of 2 or less, or a score of 3, 4 or 5).

### Studies comparing LATP-any with GATP biopsy

Of the 4 studies that compared LATP-any with GATP biopsy, 1 was a single centre RCT based in China, 2 were prospective non-randomised studies (1 based in Japan and 1 based in England) and 1 was a single centre retrospective cohort study in New Zealand. The prospective and retrospective studies were reported as conference abstracts only. An overview of these studies, details of the biopsy procedures and participant characteristics are in tables 7, 8 and 9 of the diagnostics assessment report, respectively. The Chinese RCT used a grid and stepper device to do the LATP biopsy and the retrospective New Zealand study used the PrecisionPoint device. The 2 prospective studies from Japan and England did not report using a specific device.

## Studies addressing decision question 2

Of the 8 studies that addressed decision question 2, 7 compared LATP biopsy using a freehand device with LA-TRUS biopsy and 1 study compared LATP using a freehand device to GATP biopsy. The freehand device reported in all these studies was PrecisionPoint.

### Studies of LATP-freehand using PrecisionPoint

An overview of these studies and participant characteristics are in tables 10, 11 and 12 of the diagnostics assessment report. All 8 studies were also used to address decision question 1 and so overlap both decision questions. Of the 7 studies comparing LATP-PrecisionPoint with LA-TRUS, 1 was an RCT based in Hong Kong (Lam et al. 2021), 5 were prospective cohorts from single centres in England (3 studies: Bojin 2019, Kum et al. 2018, Starmer et al. 2021), Hong Kong (Hung et al. 2020) and Singapore (Chen et al. 2021). One study was a single centre retrospective case series based in the US (Szabo et al. 2021). The number of cores taken during the biopsies was only reported in the Chen et al. (12 cores) and Bojin 2019 (24 cores) studies. The study comparing LATP-PrecisionPoint with GATP was a single centre retrospective cohort study done in New Zealand (Rij et al. 2020). This study did not report the indications for the biopsies or the number of cores taken.

### Single arm studies

No comparative evidence was identified for the LATP-freehand devices CamPROBE, UA1232, SureFire, EZU-PA3U and Trinity Perine Grid. Therefore, the EAG included any single arm studies that were identified. One prospective single cohort study (that is, with no comparative biopsy group) evaluated the CamPROBE device (see table 13 of the diagnostics assessment report). This study was done in 6 centres in England. The indications for prostate biopsy were not reported and 2 devices were used per patient per biopsy; one for the right and one for the left side of the prostate. Three single centre prospective single cohort studies done in England

evaluated the UA1232 device. All 3 were conference abstracts only (see table 13 in the diagnostics assessment report for more information).

## Study quality

### Quality assessment of studies addressing decision question 1

#### Quality assessment of RCTs

The EAG used the Cochrane risk of bias tool (version 1) to critically appraise the 6 RCTs. The EAG said that it was unable to fully judge the studies' overall risk of bias because study methodological details were not fully reported. Therefore it recorded an 'unclear' risk of bias for studies across some risk of bias domains, notably for those concerning: reporting bias (because of selective outcome reporting), detection bias (because outcome assessors were not blinded to the type of prostate biopsy done) and selection bias (because participants were not properly randomised to trial arms, the randomisation sequence was not properly concealed, or both). However, there was enough detail for the EAG to assess other risk of bias domains including attrition bias.

All 6 RCTs were at a high risk of performance bias. The EAG noted that this was unavoidable for this type of intervention because the clinician doing the biopsy cannot be blinded to the type of biopsy procedure being done. It is also unlikely that the study participant would not be told what kind of surgical procedure they were having. It was not clear if protocols were in place to reduce the risk of participants and healthcare providers behaving differently because they knew the type of biopsy being done. All 6 trials were judged to be at a low risk of attrition bias, because no or few participants were reported to have been lost to follow up or withdrawn from the study.

Overall, the EAG said the study findings should be interpreted with caution because of uncertainty about potential risks to their internal validity. Full details of the quality assessment are in appendix 5 of the diagnostics assessment report.

### Quality assessment of observational studies

Of the 13 observational studies, 11 were assessed as cohort studies and 2 were assessed as case series. The EAG said that limited reporting of study inclusion criteria and participants' demographic and clinical information meant that it was unclear how comparable the biopsy groups in the studies were. All the studies were judged to have an unclear risk of selection bias. The risk of attrition bias was low for cancer detection rate and pain or tolerability outcomes, but unclear for other outcomes. Similarly, the risk of detection bias was either low or unclear, depending on the outcome in question. Finally, for studies that were only available as conference abstracts, the EAG said that there is a high risk of reporting bias (and several other bias domains), because of the limited information that can be included in an abstract. Further details on the critical appraisal of these studies are in tables 15 and 16 of the diagnostics assessment report. Quality assessments for individual studies are in appendix 5 of the diagnostics assessment report.

## Intermediate outcomes

### Prostate cancer detection: LATP-any compared with LA-TRUS, decision question 1

Prostate cancer detection was the most commonly reported of all the outcome measures relevant to this assessment (14 out of 15 studies). The detection rates reported in each study, including clinically significant cancer rates, are in table 17 on page 84 of the diagnostics assessment report.

The EAG did a pairwise meta-analysis of cancer detection rates. RCT and observational studies were pooled separately in the meta-analysis. Overall, there was no statistically significant difference between LATP-any biopsy and LA-TRUS biopsy in detecting prostate cancer. There was no statistically significant heterogeneity, as reflected by relatively narrow confidence intervals for the pooled effect estimates. There was little difference in pooled effect estimates between the RCT evidence and the observational evidence, indicating consistency between these 2 levels of evidence. The distribution of

individual study effect estimates and the pooled effect estimate, expressed as relative risks for detecting prostate cancer, is shown in figure 1.

**Figure 1 Meta-analysis forest plot comparing cancer detection rates for LATP-any compared with LA-TRUS (decision question 1)**

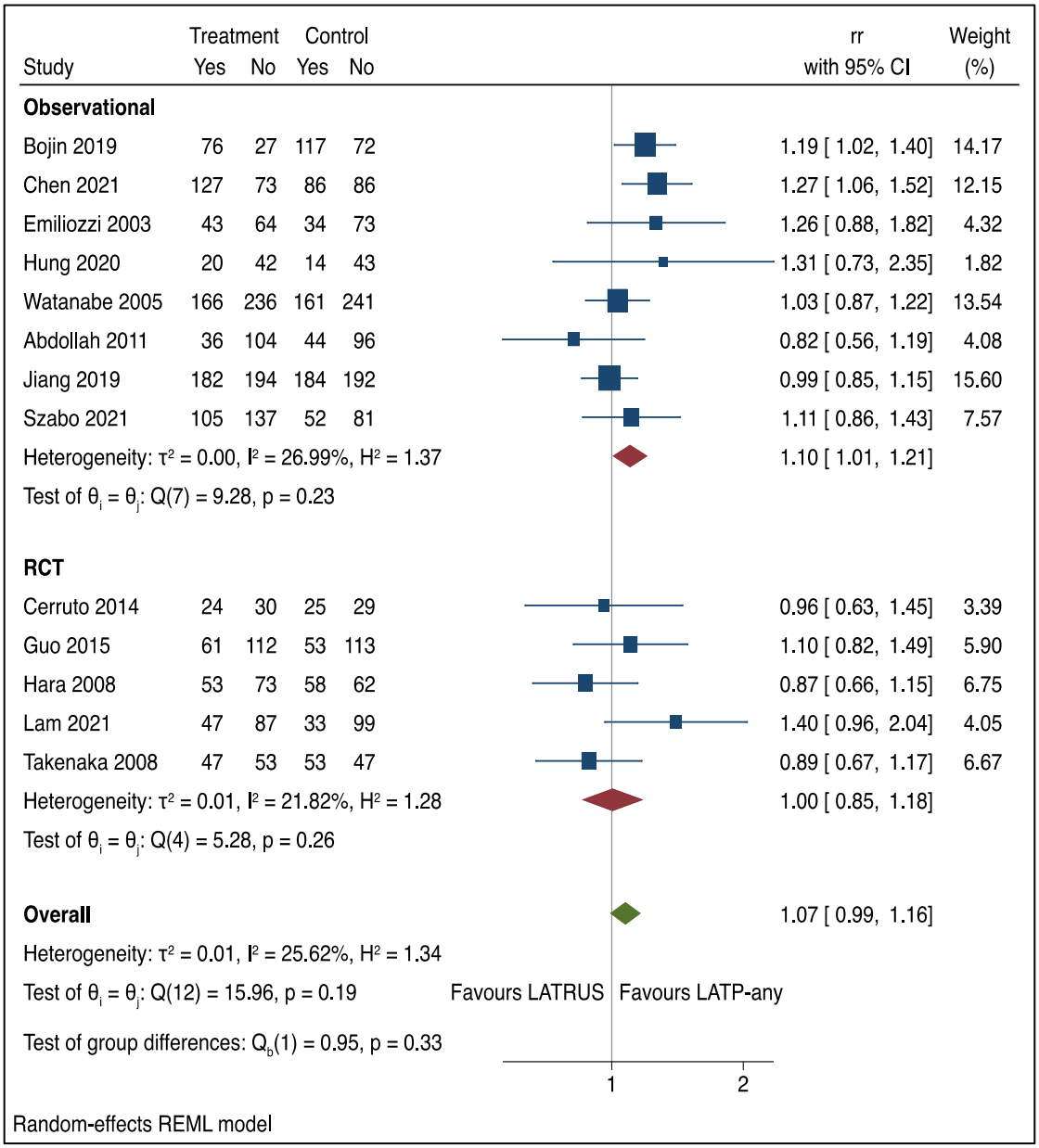


Figure abbreviations: CI, confidence interval; rr, relative risk; LA-TRUS, local anaesthetic transrectal ultrasound; LATP, local anaesthetic transperineal

biopsy; RCT, randomised controlled trial; REML, random effects maximum likelihood.

Similarly, there was no statistically significant difference between LATP-any biopsy and LA-TRUS biopsy in detecting clinically significant prostate cancer as shown in figure 2.

**Figure 2 Meta-analysis forest plot of clinically significant cancer detection rates for LATP-any compared with LA-TRUS**

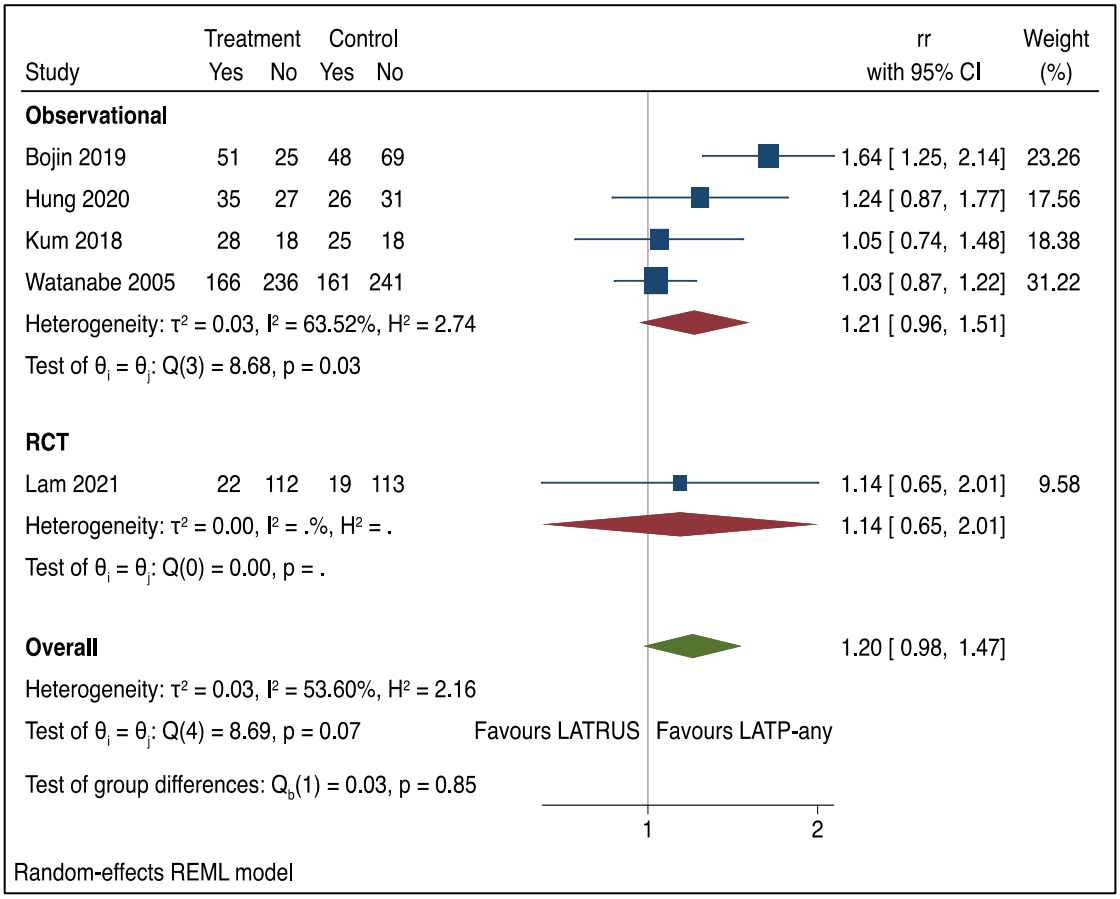


Figure abbreviations: CI, confidence interval; rr, relative risk; LATRUS, local anaesthetic transrectal ultrasound; LATP, local anaesthetic transperineal biopsy; RCT, randomised controlled trial; REML, random effects maximum likelihood.

## Prostate cancer detection: LATP-any compared with GATP grid and stepping device, decision question 1

Cancer detection rates from the 4 studies that compared LATP-any biopsy with GATP biopsy using a grid and stepping device are in table 18 on page 89 of the diagnostics assessment report. Figure 3 shows a meta-analysis forest plot of 3 of the studies. One study (Walters et al. 2021) was not included as it did not provide numerical cancer detection rates. The EAG said that overall there was no statistically significant difference between the 2 biopsy approaches in detecting prostate cancer.

**Figure 3 Meta-analysis forest plot of cancer detection rates for LATP-any compared with GATP grid and stepping device (decision question 1)**

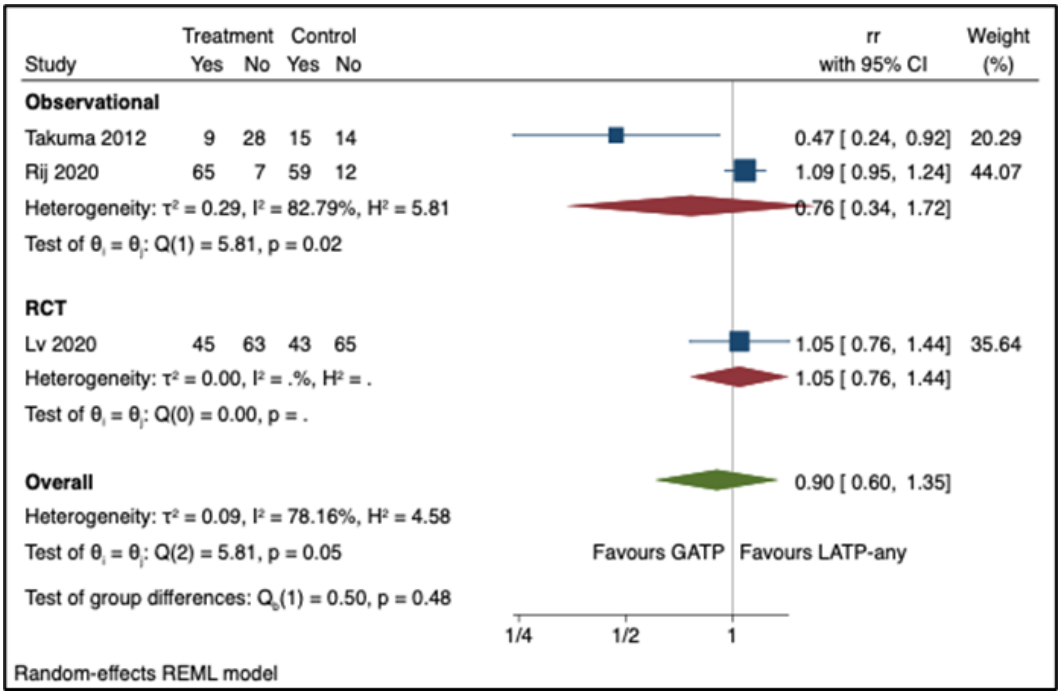


Figure abbreviations: CI, confidence interval; rr, relative risk; GATP, general anaesthetic transperineal; LATP, local anaesthetic transperineal biopsy; RCT, randomised controlled trial; REML, random effects maximum likelihood.

## Prostate cancer detection: network meta-analysis of LATP-any compared with LA-TRUS compared with GATP grid and stepping device, decision question 1

The EAG did a frequentist random effects network meta-analysis (NMA) of the cancer detection rates from the 6 RCTs, for the biopsy approaches relevant to decision question 1. The NMA indirectly compared LATP, LA-TRUS, and GATP grid and stepping device, and the EAG used it to inform clinical effect estimates in its economic analysis. Consistent with the pairwise meta-analyses, there were no statistically significant differences in cancer detection rates between the 3 biopsy approaches (see figure 4).

**Figure 4 NMA forest plot of cancer detection rates for LATP-any compared with LA-TRUS compared with GATP grid and stepping device (decision question 1)**

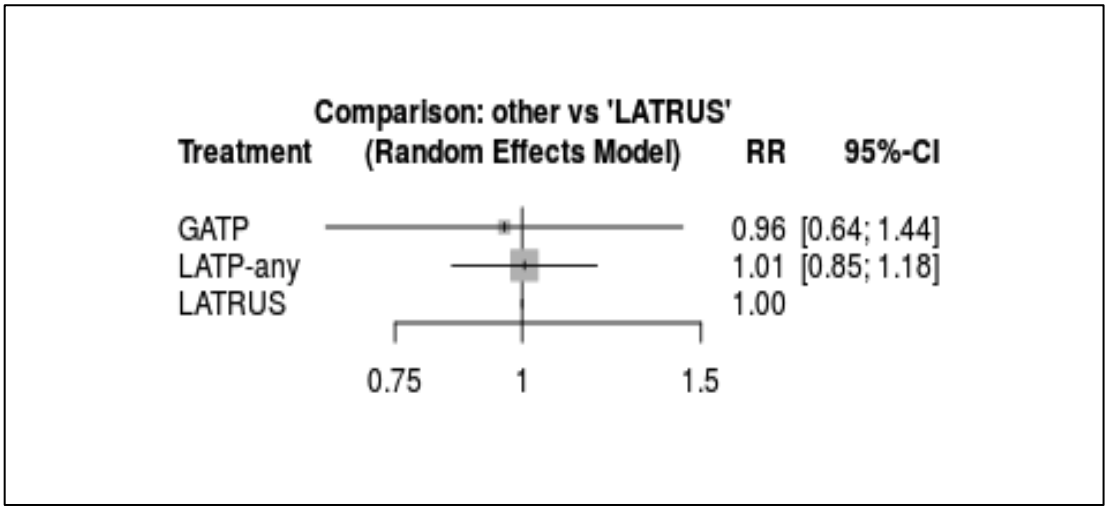


Figure abbreviations: CI, confidence interval; RR, relative risk; GATP, general anaesthetic transperineal; LATP, local anaesthetic transperineal biopsy; LATRUS, local anaesthetic transrectal ultrasound.

## Prostate cancer detection: LATP biopsy using a freehand device compared with LA-TRUS, decision question 2

Cancer detection rates, including clinically significant cancer rates, were reported for 6 of the 7 studies comparing LATP using a freehand device with

LA-TRUS biopsy. These studies are a subset of those used for decision question 1. All studies used PrecisionPoint. The EAG did a pairwise meta-analyses of cancer detection rates for LATP-freehand compared with LA-TRUS. The study by Kum et al. was excluded from this analysis because it did not report cancer detection rates for the LA-TRUS group. Because decision question 2 focuses on LATP-freehand device biopsy, the EAG split the 'LATP-any' study category into biopsy subtypes (that is, LATP-freehand, LATP grid and stepping device and LATP coaxial needle). However, it was unclear from some of the LATP-any studies if they could be reliably classified as LATP grid and stepping device or LATP coaxial needle (double freehand). Therefore the EAG combined these as 'LATP-other'. To do this the EAG assumed LATP with a grid and stepper and LATP with a coaxial needle are equivalent in effects. In the pooled analysis there was a statistically significant benefit in favour of LATP-freehand compared with LA-TRUS (see figure 5). There was no statistically significant difference between LATP-other and LA-TRUS (see figure 6).

**Figure 5 Meta-analysis forest plot of cancer detection rates for LATP-freehand compared with LA-TRUS (decision question 2)**

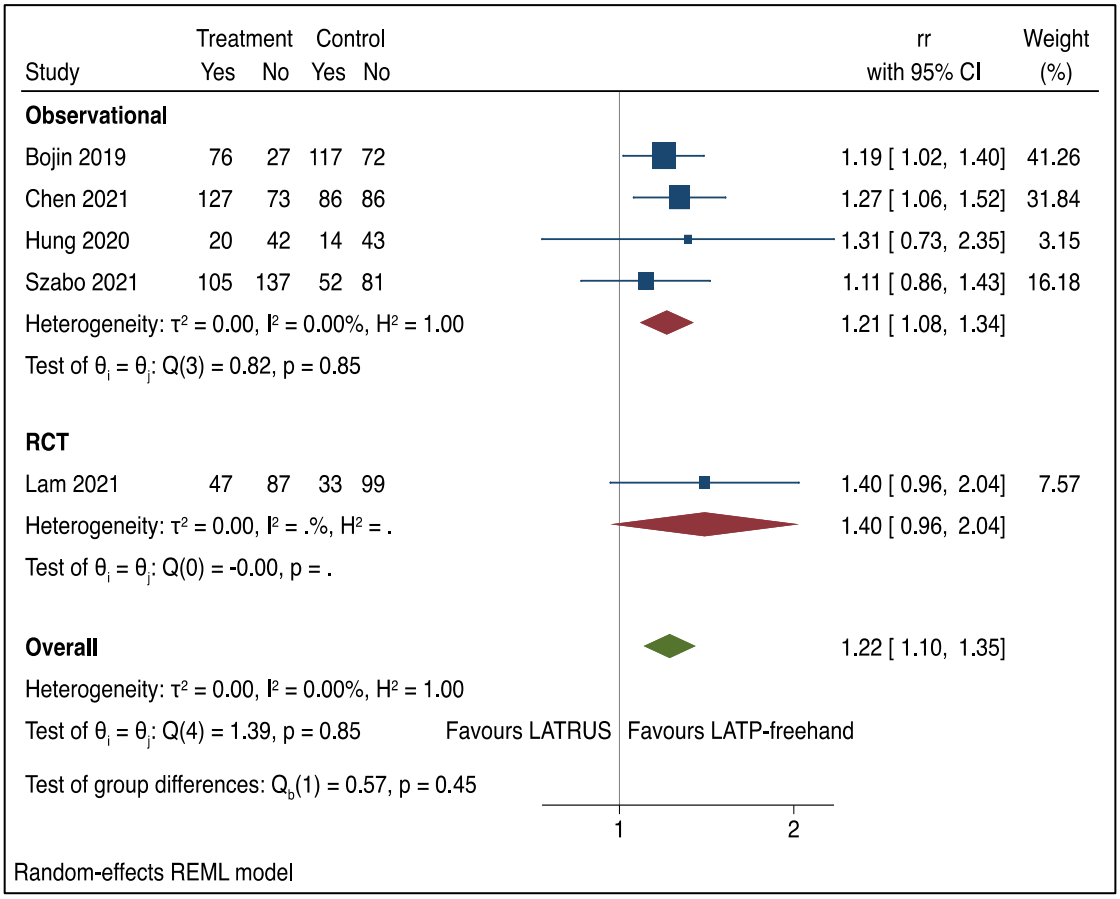


Figure abbreviations: CI, confidence interval; rr, relative risk; LA-TRUS, local anaesthetic transrectal ultrasound; LATP, local anaesthetic transperineal biopsy; RCT, randomised controlled trial; REML, random effects maximum likelihood.

**Figure 6 Meta-analysis forest plot of cancer detection rates for LATP-other compared with LA-TRUS (decision question 2)**

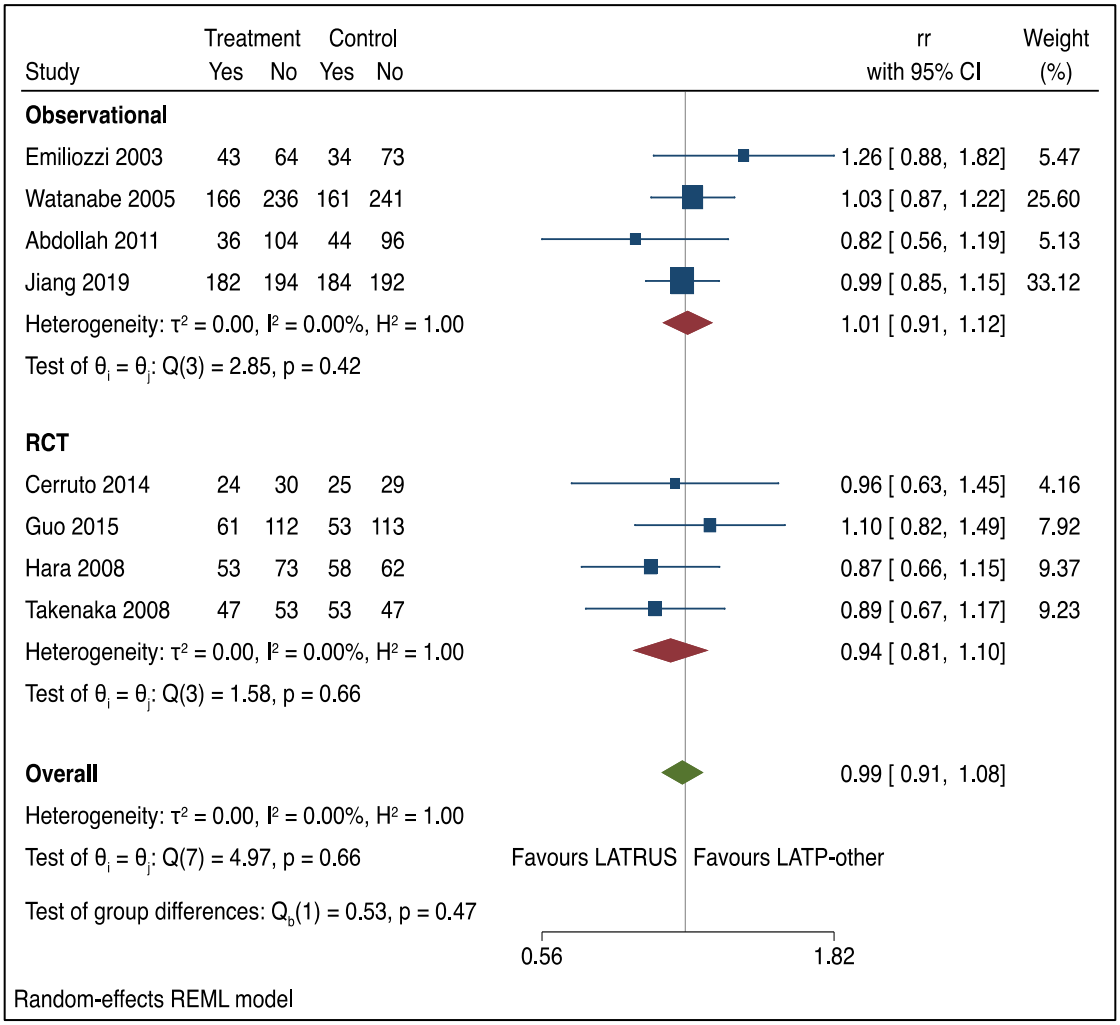


Figure abbreviations: CI, confidence interval; rr, relative risk; LA-TRUS, local anaesthetic transrectal ultrasound; LATP, local anaesthetic transperineal biopsy; RCT, randomised controlled trial; REML, random effects maximum likelihood.

In terms of clinically significant prostate cancer detection, there was a statistically significant difference in favour of LATP-freehand over LA-TRUS in the observational evidence but not in the RCT evidence. When all the studies were pooled in the exploratory analysis, statistical significance was retained (see figure 7).

**Figure 7 Meta-analysis forest plot of clinically significant cancer detection rates for LATP-freehand compared with LA-TRUS (decision question 2)**

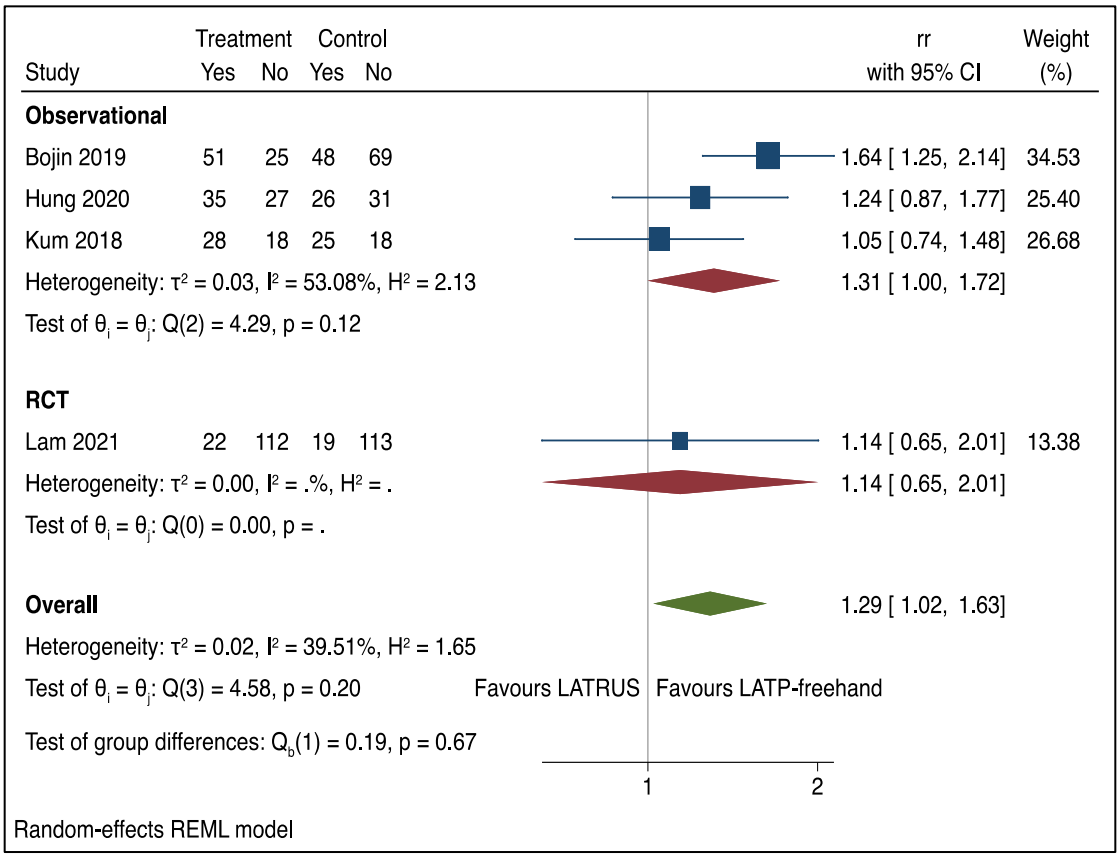


Figure abbreviations: CI, confidence interval; rr, relative risk; LA-TRUS, local anaesthetic transrectal ultrasound; LATP, local anaesthetic transperineal biopsy; RCT, randomised controlled trial; REML, random effects maximum likelihood.

## Prostate cancer detection: LATP-freehand compared with GATP grid and stepping device decision question 2

Only 1 study (reported as a conference abstract) of LATP-freehand (PrecisionPoint) compared with GATP reported cancer detection rates (Rij et al. 2020). This was a retrospective review of people who had a transperineal prostate biopsy under local or general anaesthetic. For the LATP-freehand group the cancer detection rate was 90% compared with 83% for GATP (see table 20 in the diagnostics assessment report).

### Prostate cancer detection: NMA of LATP-freehand compared with LATP-other compared with LA-TRUS compared with GATP grid and stepping device, decision question 2

The EAG did a frequentist random effects NMA of cancer detection rates for decision question 2. This indirectly compared LATP-freehand, LATP-other, LA-TRUS and GATP grid and stepping device, to inform the economic analysis. Consistent with the pairwise meta-analyses, the NMA showed no statistically significant differences in cancer detection rates between biopsy approaches. However, when the observational evidence was combined with RCT evidence the results were statistically significant.

**Figure 8 Forest plot of NMA results comparing cancer detection rates for LATP-freehand, LATP-other, GATP grid and stepping device and LA-TRUS**

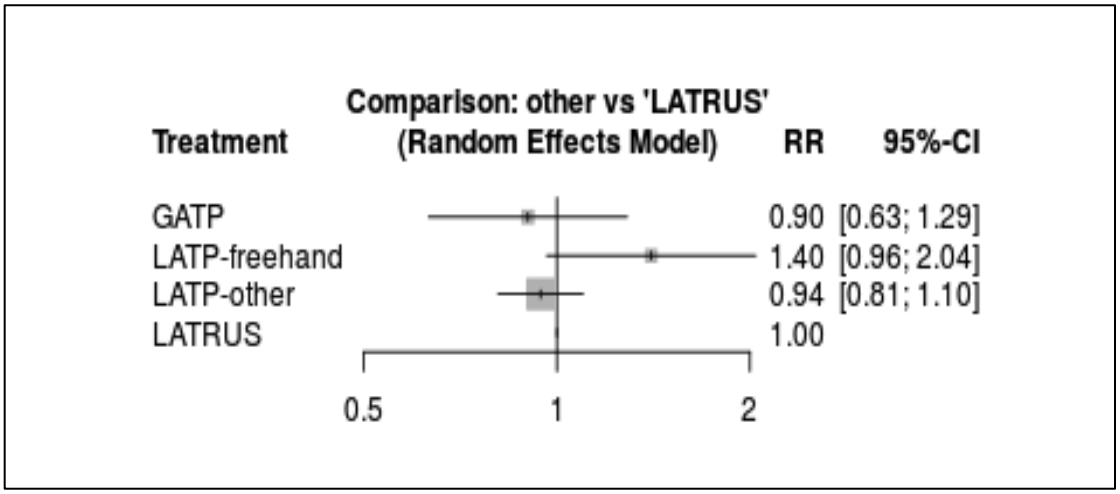


Figure abbreviations: CI, confidence interval; GATP, general anaesthetic transperineal; RR, relative risk; LA-TRUS, local anaesthetic transrectal ultrasound; LATP, local anaesthetic transperineal biopsy; NMA, network meta-analysis.

## Clinical outcomes

### Hospitalisation events after biopsy

Ten studies reported rates of hospitalisation after prostate biopsy. For both decision questions 1 and 2, overall, rates were higher for the comparator biopsy approaches compared with LATP-any biopsy and LATP-freehand, however hospitalisation rates in general were very low so it was difficult to make definitive conclusions. A summary of these studies is in tables 23 to 26 of the diagnostics assessment report.

### Overall biopsy-related complications

Six studies reported overall rates of complications after prostate biopsy. All 6 studies were relevant to decision question 1. Two of the 6 studies were also relevant to decision question 2. Most studies did not report a statistically significant difference between LATP-any and LA-TRUS in terms of complications. An overview of these studies is in table 27 of the diagnostics assessment report.

### Specific biopsy-related complications

#### Bleeding and haematuria

For the comparison of LATP-any and LA-TRUS (decision question 1), 9 studies reported a relevant outcome of bleeding, haematuria or both. Generally, bleeding and haematuria rates were low and in relative terms were higher with LA-TRUS than LATP. However, 1 study reported that urethral bleeding was more common with LATP-any (Cerruto et al. 2014). Further details are in table 28 of the diagnostics assessment report.

For the comparison between LATP-any and GATP biopsy with grid and stepping device, 2 studies reported bleeding-related outcomes. There were no statistically significant differences in bleeding-related outcomes between the 2 biopsy approaches. Further details are in table 29 of the diagnostics assessment report.

### Sepsis

For both decision questions, relatively few studies reported post-biopsy sepsis as an outcome measure. When reported, rates of sepsis were generally less than 10%, and sepsis only occurred in LA-TRUS biopsy participants. No LATP biopsy participants were recorded as having post-biopsy sepsis (see tables 32 and 33 in the diagnostics assessment report). No studies comparing LATP with GATP (for either decision question) included sepsis as an outcome measure.

### Fever

Four studies that compared LATP-any with LA-TRUS (decision question 1) reported post-biopsy fever as an outcome. None of these studies was relevant to decision question 2. Rates of high fever were higher for LA-TRUS, however the number of events was low overall and none of the results were statistically significant. Further details are in table 34 of the diagnostics assessment report.

### Rates of urinary retention

Post-biopsy urinary retention was reported in 9 studies. Eight were studies that compared LATP-any with LA-TRUS biopsy and 4 of these were also relevant to decision question 2. Only 1 study that compared LATP with GATP biopsy reported urinary retention rates. When comparative evidence was available, retention rates were similar between biopsy approaches. Details of these studies are in tables 35 to 37 of the diagnostics assessment report.

### Rates of erectile dysfunction

Only 2 studies, available as conference abstracts, reported assessing post-biopsy erectile dysfunction. Both studies reported that erectile dysfunction was worse after LATP than LA-TRUS biopsy.

### Survival and progression free survival

None of the included studies reported survival outcomes for participants having a biopsy, or progression free survival for participants treated for prostate cancer detected on biopsy.

## Patient reported outcomes

### Patient reported tolerability

Twelve studies reported data on the degree of pain and discomfort during prostate biopsy as rated by patients. All were related to decision question 1, however, 8 of these used PrecisionPoint and so were also relevant to decision question 2. Two of the studies compared LATP with GATP grid and stepping device. Tolerability was measured in a variety of ways across the studies, but often data was only presented for the LATP biopsy group. The studies that reported patient tolerability outcomes are summarised in tables 38 and 39 of the diagnostic assessment report.

# Ongoing studies

The EAG identified 5 ongoing RCTs relevant to this assessment. Four studies will provide further data on LATP compared with LA-TRUS biopsy and 1 study will provide data on LATP compared with GATP biopsy. The multicentre UK study (TRANSLATE) aims to recruit 1,042 participants and provide evidence for freehand LATP using any ultrasound probe-mounted needle guidance device, including the PrecisionPoint and UA1232 devices. This study is expected to complete in October 2023. ProBE-PC is a US based single centre study with a target recruitment of 568 and is expected to complete in December 2022. Two unnamed US based multicentre studies, run by the same institution but with different populations, aim to recruit 400 and 1,302 participants. They are due to complete in June 2025 and April 2025, respectively. LATProBE is an Australian based multicentre study that will provide evidence on freehand LATP compared with GATP using a grid template. This study has not yet started recruiting but aims to recruit 620

participants. Further details of these studies are in table 40 of the diagnostics assessment report.

# 3 Cost effectiveness evidence

The EAG did a systematic review to identify any published economic evaluations of LATP prostate biopsies in people with suspected prostate cancer. It also reviewed a cost minimisation study submitted by one of the companies. Find the full systematic review results and review of the company submission on pages 113 to 128 of the diagnostics assessment report. The EAG also constructed a de novo economic model to assess the cost effectiveness of LATP prostate biopsies.

## Systematic review of cost effectiveness evidence

The EAG identified 1 economic evaluation relevant to the scope of the assessment (Wilson et al. 2021). This reported the cost effectiveness of LATP (using the CamPROBE device) compared with LA-TRUS for diagnosing prostate cancer in men with suspected localised prostate cancer from the perspective of the UK NHS. They used a lifetime model comprising a decision tree with a Markov model. The model was informed by a prospective case series on the safety and acceptability of the CamPROBE device and published studies. It included an economic analysis of diagnostic strategies including mpMRI and TRUS biopsy based on data from the PROMIS study. In the base case Wilson et al. assumed that there was no risk of infection with LATP. The analysis assumed equal diagnostic accuracy for LATP with the CamPROBE device and LA-TRUS. The price of the CamPROBE device was set to zero for the base case analysis, with sensitivity analysis used to estimate the maximum price for the device at which it would be cost neutral, or cost saving compared with LA-TRUS. The EAG said that Wilson et al.'s results are highly uncertain and that the study excluded other relevant comparators. Details and base case results of the Wilson et al. study are in table 41 of the diagnostics assessment report and full details are in appendix 8 (table 108).

## Overview of other published economic studies of interest

The EAG also considered 13 other studies that did not meet the inclusion criteria of the systematic review but were used to inform its model structure and inputs. Details of these further studies are in table 42 of the diagnostics assessment report. The EAG said that 2 economic studies were very influential in developing its model. Firstly, the cost effectiveness analysis done alongside the PROMIS study reported in the Brown et al. (2018) HTA report and in the Faria et al. (2018) publication. This assessed the cost effectiveness of a range of diagnostic strategies using mpMRI, TRUS biopsy, a template prostate mapping biopsy, or any combination of the 3, for men referred to secondary care in the UK NHS with suspected prostate cancer.

The second analysis that informed the EAG's model structure and parameters was that developed for the update of the NICE guideline on prostate cancer. The model was designed to estimate the cost effectiveness of follow up protocols for people with a raised prostate-specific antigen (PSA) level, negative mpMRI, negative biopsy or any combination of the 3. It includes a Markov model that predicts progression and diagnosis of prostate cancer for people with an initial 'true negative' (no or clinically non-significant disease) or 'false negative' diagnosis (intermediate or high risk localised or metastatic disease) and also for those with correctly diagnosed prostate cancer.

## Overview of cost minimisation company submission

The manufacturer of the PrecisionPoint device, BXTAccelyon, submitted a cost minimisation study developed in 2020 by the York Health Economics Consortium (YHEC). This study used an economic model that compared the costs of LATP (with the PrecisionPoint device) with different combinations of TRUS and GATP for UK NHS trusts. It assumed that LATP and GATP had the same rate of successful biopsy (with no need to repeat the procedure) and had fewer complications than LA-TRUS biopsies. The results of this study suggest that LATP using the PrecisionPoint device is cost saving, yielding higher savings as the proportion of biopsies that were previously done as

GATP increases. Further details of this study including model input costs are available from page 126 in the diagnostics assessment report.

## Economic analysis

The EAG developed a health economic model to compare the cost effectiveness of alternative biopsy methods for people with suspected prostate cancer.

### Population

The population in the model is people with suspected prostate cancer who need a prostate biopsy. The EAG assumed that the cohort had multiparametric MRI (mpMRI) as a first-line investigation for suspected clinically localised prostate cancer, with results summarised using a 5-point Likert scale. The model starts with a cohort of interest, 1 of 4 subgroups defined by mpMRI Likert score and history of previous biopsy:

- subgroup A: people referred for a first biopsy with a Likert score of 3 or more (base case)
- subgroup B: people referred for a first biopsy with a Likert score of 1 or 2
- subgroup C: people referred after a previous negative biopsy with a Likert score of 3 or more
- subgroup D: people referred after a previous negative biopsy with a Likert score of 1 or 2.

The mean age of the initial cohort is 66 years.

### Model structure

The model consisted of a decision tree that estimates short term diagnostic outcomes and a cohort health state transition (Markov) model that predicts long term disease progression and associated costs and patient outcomes. The design and parameter sources for the decision tree are largely based on the economic analysis of the PROMIS trial reported by Faria et al. (2018), and the adapted version of this analysis by Wilson et al. (2021).

**Decision tree**

The cohort entering the decision tree is first stratified by true prostate cancer status:

- no cancer (NC)
- low risk (LR; Gleason of 6 or less, PSA of 10 ng/ml or less and clinical stage T1 to T2a)
- intermediate risk (IR; Gleason 7, PSA ng/ml 10 to 20 ng/ml and clinical stage T2b)
- high risk (HR; Gleason 8 to 10, PSA greater than 20 ng/ml and clinical stage T2c or higher) localised or metastatic disease.

The prevalence of LR, IR and HR localised prostate cancer in the 4 subgroups referred for TRUS biopsy was estimated using the true disease status in the PROMIS cohort, diagnostic performance characteristics of mpMRI and TRUS biopsy reported by Faria et al. Intermediate and high risk localised disease are grouped together as clinically significant (CS) disease. Low risk disease is classed as clinically non-significant (CNS).

The decision tree estimates diagnostic outcomes (the proportions of correct and false negative biopsy results) for LA-TRUS biopsy using cancer detection rates from the PROMIS study. Diagnostic outcomes for the other biopsy methods are calculated using relative risks from the network meta-analyses in the base case and pairwise meta-analyses in scenario analyses (see section 2.3). The tree includes a second biopsy for a proportion of patients with a negative first biopsy, with the assumption that this second biopsy would be a LA-TRUS biopsy. The decision tree also estimates incidence of biopsy-related adverse events, including a small proportion of fatal events. The endpoints of the decision tree, comprising correct diagnoses (Dx) or false negatives (FN), represent the health states in the Markov model.

The tree divides the cohort according to the expected incidence of biopsy-related complications, categorised as:

- No AE (adverse event): no or minor adverse events for which the patient does not seek treatment.
- Mild AE: mild or moderate adverse events treated outside hospital.
- Admission: overnight stay immediately after the biopsy or readmission within 28 days.
- Mortality within 28 days of the biopsy.

The structure of the decision tree differs between the different true prostate cancer status groups. For the no cancer group, the EAG assumed that all biopsy methods are perfectly specific, that is, there cannot be false positive results for people who truly do not have prostate cancer. In this group complications may occur after the first or second biopsy. Endpoints for the people without prostate cancer are correct diagnosis (NC Dx) and death from biopsy-related complications (see figure 9).

**Figure 9 Decision tree for people without prostate cancer**

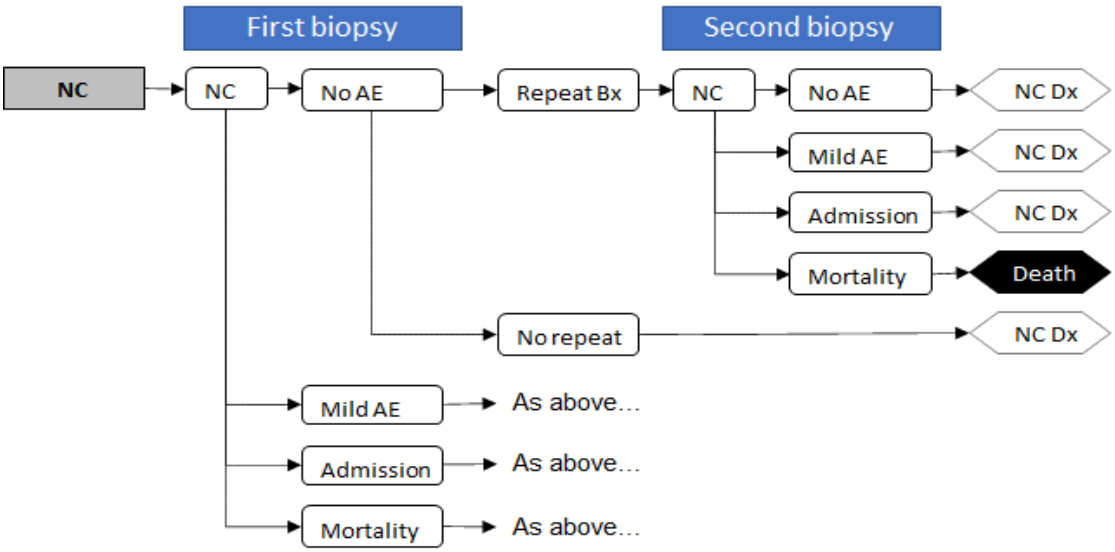


Figure abbreviations: Bx, biopsy; NC, no cancer; LR, true low risk; NC Dx, no cancer correctly diagnosed; AE, adverse events.

For the low risk cancer group (that is CNS disease), the biopsy may give a:

- correct diagnosis of CNS disease

- false positive result of CS disease (the probability of this event in the model is zero)
- false negative result of no cancer.

If the biopsy result is negative (CNS or NC), there may be a repeat biopsy. A second biopsy can report a CS, CNS or NC result, however, the estimated probability of a CS result for a second TRUS biopsy with LR cancer is zero. Complications may occur after the first or second biopsy. Endpoints for this group are correct diagnosis (LR Dx), false positive (LR FP), false negative (LR FN) and death (see figure 10).

For the intermediate and high risk groups (that is CS disease), the tree structure is the same as for low risk, however, the cancer detection and repeat biopsy probabilities differ for these groups. Endpoints for these groups are correct diagnosis (IR Dx; HR Dx), false negative (IR FN; HR FN) and death (see figures 19 and 20 in the diagnostics assessment report).

For all groups, complications can occur after the first or second biopsy and are classified as no AE, mild AE, admission or mortality. The EAG assumed that that the incidence of complications does not differ by cancer risk group.

The trees are replicated for each intervention and comparator in decision question 1 and 2.

**Figure 10 Decision tree for people with low risk prostate cancer**

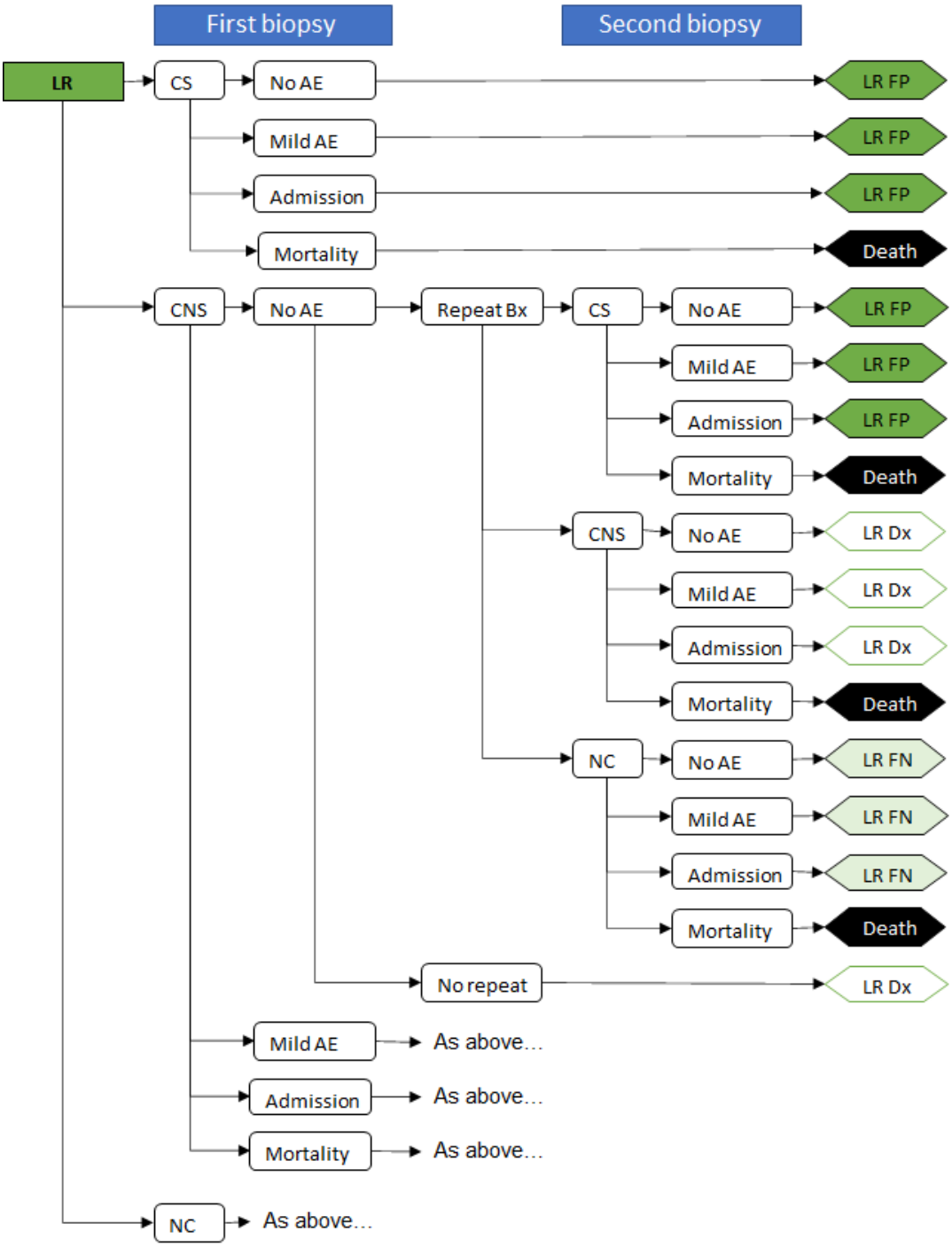


Figure abbreviations: CS, clinically significant; CNS, clinically non-significant; NC, no cancer; LR, true low risk; LR Dx, low risk correctly diagnosed (classified as clinically non-significant); LR FP, low risk false positive (classified as clinically significant); LR FN, low risk false negative (classified as no cancer); AE, adverse event; Bx, biopsy.

### Markov model: long term outcomes

For the Markov model the EAG replicated the model developed for the NICE prostate cancer guideline to estimate long term costs and quality-adjusted life years (QALYs) from the diagnostic outcomes from the decision tree. The Markov model includes 11 health states grouped in 4 categories: 'true negatives' (no prostate cancer); 'false negatives' (undiagnosed disease from low risk to metastatic); 'true positives' (diagnosed disease from low risk to metastatic); and death related to prostate cancer or from other causes. Figure 11 shows the transition between these health states. The Markov model is replicated for each intervention and comparator in decision question 1 and 2. Each version is identical, including input parameters, apart from the initial distribution of the cohort between the health states in the first model cycle, which is taken from the endpoints of the respective decision tree.

**Figure 11 Illustration of guideline Markov model**

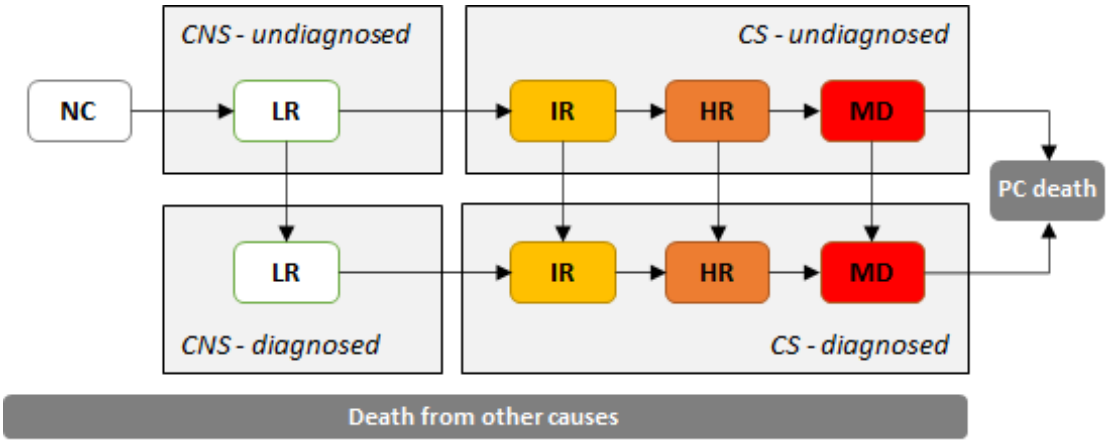


Figure abbreviations: CNS, clinically non-significant; CS, clinically significant; HR, high risk; IR, intermediate risk; LR, low risk; MD, metastatic disease; NC, no cancer; PC, prostate cancer.

## Interventions and comparators

### Table 1 Interventions and comparators

| Decision question | Interventions | Comparators |
|---|---|---|
| Decision question 1 | LATP-any (that is, LATP prostate biopsy including use of grid and stepper unit, a coaxial needle or a freehand transperineal device) | • Local anaesthetic transrectal ultrasound (LA-TRUS) biopsy<br>• GATP biopsy using a grid and stepping device |
| Decision question 2 | LATP-freehand (that is, LATP prostate biopsy with one of the following freehand transperineal biopsy devices: PrecisionPoint, UA1232, Trinity Perine Grid, CamPROBE, SureFire or EZU-PA3U) | • LA-TRUS biopsy<br>• LATP prostate biopsy not using a transperineal biopsy device, that is, coaxial needle or a grid and stepping device (referred to as LATP-other)<br>• GATP biopsy using a grid and stepping device |

Table abbreviations: GATP, general anaesthetic transperineal; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound.

## Model inputs

### Baseline prevalence

The PROMIS economic evaluation (Faria et al. 2018) results were used to estimate the true prevalence of cancer (LR, IR and HR) for the subgroups with mpMRI Likert score 2 or less and Likert 3 or greater, for first biopsy and previous negative biopsy. This provided the starting proportions of the cohort allocated to the different decision trees (see table 2).

**Table 2 True disease status at referral for mpMRI**

| Group | N | % |
|---|---|---|
| No cancer | 159 | 27.9 |
| Low risk cancer | 91 | 16.0 |
| Intermediate risk cancer | 301 | 52.9 |
| High risk cancer | 18 | 3.2 |
| Total | 596 | 100 |

Faria et al. calculated the probability of mpMRI results (NC, CS and CNS) conditional on true disease status from individual patient data (see table 51 on page 147 of the diagnostics assessment report).

The EAG combined the information from PROMIS with Bayes formula to estimate the probability of prostate cancer by level of risk conditional on previous mpMRI Likert score (1 or 2; and 3 or more) and history of previous biopsy. This provided prevalence estimates for the 4 subgroups (see table 3).

**Table 3 Prevalence of prostate cancer for included subgroups**

| True cancer status | Subgroup A (MRI Likert 3 or more first biopsy) | Subgroup B (MRI Likert 1 or 2 first biopsy) | Subgroup C (MRI Likert 3 or more previous negative biopsy) | Subgroup D (MRI Likert 1 or 2 previous negative biopsy) |
|---|---|---|---|---|
| No cancer | 19.4% | 47.7% | 40.0% | 59.4% |
| Low risk cancer | 12.4% | 25.7% | 25.7% | 32.0% |
| Intermediate risk cancer | 63.8% | 26.6% | 34.3% | 8.6% |
| High risk cancer | 4.4% | 0.0% | 0.0% | 0.0% |

### Cancer detection rates

Estimates of diagnostic performance for LA-TRUS biopsy were from the PROMIS economic evaluation (see tables 4 and 5).

**Table 4 Cancer detection rates and 95% confidence intervals for LA-TRUS biopsy - first biopsy after a suspicious mpMRI result**

| True cancer status | Probability of no cancer result | Probability of clinically non-significant result | Probability of clinically significant cancer result |
|---|---|---|---|
| Low risk cancer | 0.79 (0.66 to 0.89) | 0.21 (0.11 to 0.34) | - |
| Intermediate risk cancer | 0.15 (0.09 to 0.21) | 0.11 (0.06 to 0.16) | 0.74 (0.65 to 0.84) |
| High risk cancer | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 0.00) | 1.00 (1.00 to 1.00) |

Table abbreviation: LA-TRUS, local anaesthetic transrectal ultrasound.

**Table 5 Cancer detection rates and 95% confidence intervals for LA-TRUS biopsy – second biopsy after a negative first biopsy and suspicious mpMRI result**

| True cancer status | Probability of no cancer result | Probability of clinically non-significant result | Probability of clinically significant cancer result |
|---|---|---|---|
| Low risk cancer | 0.68 (0.02 to 1.00) | 0.32 (0.02 to 0.91) | - |
| Intermediate risk cancer | 0.05 (0.02 to 0.11) | 0.08 (0.03 to 0.18) | 0.87 (0.71 to 0.95) |
| High risk cancer | 0.05 (0.02 to 0.11) | 0.08 (0.03 to 0.18) | 0.87 (0.71 to 0.95) |

Table abbreviation: LA-TRUS, local anaesthetic transrectal ultrasound.

Cancer detection rates for the other biopsy methods are estimated from the LA-TRUS rates adjusted using relative risks from EAG evidence synthesis (see section 2.3). For the base case, results from the decision question 1 and 2 network meta-analyses were used. The EAG also did a scenario analysis using results from the pairwise meta-analyses of observational data for comparison (see tables 6 and 7). The value for GATP is based on a single RCT that compared against LATP. This value was adjusted using the risk ratio of LA-TRUS compared with LATP to give an indirect comparison between LA-TRUS and GATP.

**Table 6 Relative risks and 95% confidence intervals for cancer detection compared with LA-TRUS used in economic model – decision question 1**

| Biopsy method | Base case (NMA RCT) | Scenario (observational MA) |
|---|---|---|
| LATP-any | 1.01 (0.85 to 1.18) | 1.10 (1.01 to 1.21) |
| GATP | 0.96 (0.64 to 1.44) | 1.44 = 1.31 (0.58 to 2.94) x 1.10 |

Table abbreviations: GATP, general anaesthetic transperineal; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound. MA, meta-analysis; NMA, network meta-analysis; RCT, randomised controlled trial.

**Table 7 Relative risks and 95% confidence intervals for cancer detection compared with LA-TRUS used in economic model; decision question 2**

| Biopsy method | Base case (NMA RCT) | Scenario (observational MA) |
|---|---|---|
| LATP-freehand | 1.40 (0.96 to 2.04) | 1.21 (1.08 to 1.34) |
| LATP-other | 0.94 (0.81 to 1.10) | 1.01 (0.91 to 1.12) |
| GATP | 0.90 (0.63 to 1.29) | 1.32 = 1.31 (0.58 to 2.94) x 1.01 |

Table abbreviations: GATP, general anaesthetic transperineal; LATP, local anaesthetic transperineal; MA, meta-analysis; NMA, network meta-analysis; RCT, randomised controlled trial.

### Probability of a repeat biopsy

The probability of patients having a second biopsy after a negative first biopsy in the model is based on a prospective cohort study reported by Jimenez et al. 2021. For patients with an MRI Likert score of 3 or more, the base case assumed that 5% of patients with a biopsy result NC and 15.45% of patients with CNS repeat the biopsy. For patients with an MRI Likert score of 1 or 2, the base case assumed that 1.25% of patients with biopsy result NC and 5% of patients with CNS repeat the biopsy.

### Biopsy-related complications

The base case analysis used comparative rates of admission based on an analysis of Hospital Episode Statistics (HES) to identify patients coded as M702 (transperineal needle biopsy of prostate) or M703 (TRUS needle biopsy

of prostate) who were readmitted or attended accident and emergency within 28 days after the biopsy. Patients were included if they had undergone either a TP or TRUS biopsy (under general or local anaesthetic) between April 2008 and March 2019. The EAG also separately evaluated data from between April 2017 and March 2019 (see table 8).

**Table 8 Outcomes within 28 days of biopsy for the analysis 2017 to 2019 (Tamhankar et al. 2020)**

| Outcome | TRUS biopsy, n (%) | TP biopsy, n (%) |
|---|---|---|
| Total biopsies evaluated | 76,106 | 37,077 |
| Non-elective admission | 2,845 (3.74) | 1,314 (3.54) |
| Sepsis | 850 (1.12) | 155 (0.42) |
| Urinary retention (non-elective admission) | 236 (0.31) | 354 (0.95) |
| Haematuria (non-elective admission) | 166 (0.22) | 137 (0.37) |
| Mortality | 53 (0.07) | 19 (0.05) |
| Infection | 1,139 (1.50) | 248 (0.67) |
| UTI | 848 (1.11) | 266 (0.72) |
| Cost per patient of non-elective admission | £2,503.14 | £1,894.63 |

Table abbreviations: TP, transperineal; TRUS, transrectal ultrasound; UTI, urinary tract infection.

The National Prostate Cancer Audit (NPCA) comprises comparative rates of admission within 30 days of a transperineal or transrectal biopsy (anaesthesia type not reported). Berry et al. (2020) analysed data from the NPCA linked to HES. The audit data included all people newly diagnosed with prostate cancer between 1 April 2014 and 31 March 2017 identified from the English cancer registry (n=118,526). Of these, HES records for the most recent biopsy done between 1 January 2014 and the date of diagnosis were available for 75,464 patients, and data were available for analysis for 75,630 patients (62.1%; see tables 9 and 10). Differences between outcomes with TRUS and TP biopsies were adjusted for biopsy year, age, ethnicity, Charlson score and socio-economic status, except for mortality, which was only adjusted for age. The EAG noted that the authors of this study suggest that the higher risk of urinary retention with TP rather than TRUS biopsy may be due to more common use

of general anaesthetic and the larger number of cores taken. Therefore, the results may overestimate the risk of admission for urinary retention with LATP.

**Table 9 Overnight stay and readmissions within 30 days of biopsy (Berry et al. 2020)**

| Outcome | TRUS biopsy, n (%) | TP biopsy, n (%) | Adjusted risk difference (% points) Mean % | 95% CI | p |
|---|---|---|---|---|---|
| N | 59,907 | 13,723 | - | - | - |
| Overnight stay | 1,415 (2.36) | 1,681 (12.25) | 9.70 | 7.12 to 12.27 | <0.001 |
| Sepsis | 806 (1.35) | 142 (1.03) | -0.36 | -0.56 to -0.15 | 0.001 |
| Urinary retention | 571 (0.95) | 265 (1.93) | 1.06 | 0.71 to 1.41 | <0.001 |
| Urinary bleed | 396 (0.66) | 97 (0.71) | 0.07 | -0.15 to 0.28 | 0.546 |
| Mortality | 59 (0.10) | 9 (0.07) | -0.03 | -0.07 to 0.01 | 0.197 |

Table abbreviations: CI, confidence interval; TP, transperineal; TRUS, transrectal ultrasound.

**Table 10 Length of stay for readmissions within 30 days of biopsy (Berry et al. 2020)**

| Outcome | TRUS biopsy N (mean) | TP biopsy N (mean) | Adjusted mean difference (days) | 95% CI | p |
|---|---|---|---|---|---|
| Sepsis | 806 (6.53) | 142 (5.08) | -1.10 | -1.84 to -0.36 | 0.004 |
| Urinary retention | 571 (3.87) | 265 (2.58) | -1.32 | -1.97 to -0.66 | <0.001 |
| Urinary bleed | 396 (3.88) | 97 (3.12) | -0.70 | -2.03 to 0.63 | 0.304 |

Table abbreviations: CI, confidence interval; TP, transperineal; TRUS, transrectal ultrasound.

The EAG also used other sources of data on complication rates for TRUS or TP biopsies. These are summarised in tables 11 to 13.

**Table 11 TRUS biopsy complication rates: Cochrane review, low risk with antibiotic prophylaxis (Zani et al. 2011)**

| Outcome | n | Mean | 95% CI |
|---|---|---|---|
| Bacteriuria | 870 | 3.7% | 2.2% to 6.2% |
| Bacteraemia | 494 | 12.7% | 9.3% to 17.5% |
| Fever | 820 | 4.2% | 2.5% to 6.9% |
| Urinary tract infection | 1,077 | 3.3% | 2.0% to 5.6% |
| Hospitalisation | 650 | 0.4% | 0.1% to 1.8% |

Table abbreviations: CI, confidence interval, TRUS, transrectal ultrasound.

**Table 12 TRUS biopsy complication rates: Rosario et al. 2012, prospective cohort study, ProBE**

| Outcome | n | Mean | 95% CI |
|---|---|---|---|
| Consultation with GP, nurse | 1,147 | 10.4% | 8.7% to 12.3% |
| Hospital admission | 1,147 | 1.3% | 0.8% to 2.1% |

Table abbreviations: CI, confidence interval, TRUS, transrectal ultrasound.

**Table 13 TP biopsy complication rates: Pepe and Aregona 2013, Italian cohort study**

| Outcome | n | Mean | 95% CI |
|---|---|---|---|
| One or more complication | 3,000 | 40.2% | 38.5% to 42.0% |
| Emergency department visit | 3,000 | 9.1% | 8.1% to 10.2% |
| Hospital admission | 3,000 | 1.2% | 0.9% to 1.7% |

Table abbreviations: CI, confidence interval; TP, transperineal.

The EAG used rates of non-elective admission and mortality from Tamhankar et al. (2020) in the base case, and rates of admission from NPCA (Berry et al. 2020) as a scenario analysis. Overnight stay rates were also from the NPCA analysis. Biopsy adverse events were categorised into mild (requiring a GP visit), requiring hospital admission (including haematuria, urinary retention, sepsis), and death. The proportion of patients with mild adverse events were from Rosario et al. (2012) for LA-TRUS biopsy and from Pepe and Aragona (2013) for TP biopsies.

### Long term transition probabilities

Transition probabilities for the Markov model were based on values used in NICE's guideline on prostate cancer. The natural history parameters used to calculate transition probabilities are in table 61, page 156 of the diagnostics assessment report. The base case transition probabilities (per 3-month model cycle) are in table 62 of the diagnostics assessment report.

## Costs and resource use

The full list of costs used in the model is on pages 158 to 160 and 173 to 176 of the diagnostics assessment report. Full details of the resource use inputs are in table 64 of the diagnostics assessment report.

### Costs of devices for prostate cancer biopsy

The EAG used a micro-costing approach to estimate biopsy costs. For decision question 1 (LATP-any compared with LA-TRUS and GATP), the cost of LATP-any is the average of the cost of each LATP device (CamPROBE, PrecisionPoint, EZY-PA3, UA1232, Trinity Perine and SureFire Guide, LATP using grid and stepper unit and LATP using double freehand device), giving a cost of £460.83. For decision question 2, (LATP-freehand compared with LA-TRUS, GATP and LATP-other using a grid and stepper unit), the cost of LATP using a freehand device is the average cost of each freehand LATP device (CamPROBE, PrecisionPoint, EZY-PA3, UA1232, Trinity Perine and SureFire Guide), giving a cost of £470.48.

The cost components and the total cost of the biopsy methods are in table 14. A full cost breakdown of biopsy methods is in appendix 12 of the diagnostics assessment report.

**Table 14 Micro-costing analysis: cost components and total cost of biopsy methods**

| Cost component | CamPROBE | PrecisionPoint | EZU-PA3U | UA1232 | Trinity Perine | SureFire Guide | Grid and stepper | Double freehand | GATP | LA-TRUS |
|---|---|---|---|---|---|---|---|---|---|---|
| Device | £70.00 | £200.00 | £19.13 | £14.00 | £7.54 | £135 | £79.95 | - | £79.95 | - |
| Consumables | £108.62 | £108.62 | £107.66 | £107.84 | £110.37 | £108.62 | £87.22 | £108.62 | £169.53 | £81.07 |
| Training | £2.38 | £4.76 | £0.60 | £1.19 | £0.60 | £4.76 | £4.76 | £4.76 | £4.76 | £0.60 |
| Staff: urologist | £48.79 | £39.67 | £44.23 | £44.23 | £44.23 | £44.23 | £44.23 | £44.23 | £119 | £37.21 |
| Staff: nurse | £25.42 | £20.67 | £23.04 | £23.04 | £23.04 | £23.04 | £23.04 | £23.04 | £62 | £19.38 |
| Staff: anaesthetist | - | - | - | - | - | - | - | - | £119 | - |
| Place of biopsy | £52.89 | £43.00 | £47.95 | £47.95 | £47.95 | £47.95 | £47.95 | £47.95 | £193.50 | £40.33 |
| Reprocessing | - | - | £5 | £5 | £5 | - | £5 | - | £5 | - |
| Histopathology | £107.50 | £107.50 | £107.50 | £107.50 | £107.50 | £107.50 | £107.50 | £107.50 | £107.50 | £107.50 |
| Urologist consultation | £59.5 | £59.5 | £59.5 | £59.5 | £59.5 | £59.5 | £59.5 | £59.5 | £59.5 | £59.5 |
| Total | £475.10 | £583.72 | £414.60 | £410.25 | £405.72 | £530.60 | £459.15 | £395.60 | £919.75 | £345.59 |

Table abbreviations: GATP, general anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound.

### Monitoring of suspected and diagnosed prostate cancer

Assumptions about monitoring suspected and diagnosed prostate cancer were based on the recommendations in NICE's guideline on prostate cancer and the assumptions in its decision model. These included:

- Patients without cancer, first biopsy result NC and no repeat biopsy, and patients without cancer and a second biopsy result NC were discharged and no additional costs were incurred.
- Patients with true disease (LR, IR, HR or metastatic) and a first biopsy result NC or CNS who have not repeated the biopsy and patients with true disease and a second biopsy result NC or CNS were assumed to be followed up in primary care:
  - PSA velocity test measurement at 6 months after biopsy and yearly thereafter
  - patients with positive PSA (threshold 0.75 mg/ml/year) have a TRUS biopsy for disease confirmation.
- Patients with metastatic disease and a biopsy result CS take drugs for metastatic disease.
- Active surveillance was assumed to include:
  - year 1: PSA measurement every 3 months, digital rectal examination (DRE) and mpMRI at 12 months
  - subsequent years: PSA measurement every 6 months and DRE every 12 months.
- Patients diagnosed with prostate cancer having radical treatment had PSA every 6 months for 2 years and once a year thereafter.
- Patients diagnosed with prostate cancer on watchful waiting required a PSA measurement once a year.
- Half of the patients diagnosed with IR, 70% diagnosed with HR and 100% diagnosed with metastatic prostate cancer have a CT and a bone scan to monitor for metastases once.

Full details of costs related to follow up are in table 65 of the diagnostics assessment report.

### Treatment for diagnosed prostate cancer

Patients with low or intermediate risk localised prostate cancer will have one of the following treatments: active surveillance, radical prostatectomy or radical radiotherapy, while patients with high risk localised prostate cancer will have radical prostatectomy or radical radiotherapy. Patients with no intent of curative treatment in the intermediate or high risk groups can have watchful waiting. Around 5% of patients with low risk and 79% of patients with high risk localised disease are assumed to have radical treatment. The distribution across radical treatments (radical prostatectomy and radical radiotherapy) are in table 64 of the diagnostics assessment report.

The costs for radical treatment were taken from NHS National Cost Collection Data Publication 2019/20, while the costs for androgen deprivation therapy (ADT) and drugs for metastatic disease were taken from the BNF 2020 and electronic market information tool (eMIT) 2020. Further details on the resource use for treatment of diagnosed prostate cancer are on pages 162 and 163 of the diagnostics assessment report. Further details on treatment costs used in the model are in table 65 on page 174 of the diagnostics assessment report.

### Managing adverse events of prostate biopsy, radical and metastatic treatment

See table 64 in the diagnostics assessment report for a full list of adverse events model inputs and data sources. The costs of adverse events from biopsy are in table 65 of the diagnostics assessment report.

### End of life costs

End of life costs were applied to the number of new deaths per cycle. The end of life costs estimated by Round et al. in 2015 (£14,859) were inflated to the cost year 2019/2020 to give a cost of £16,052.

## Utilities

The EAG did a systematic review to identify data on health-related quality of life. From the 6 studies retrieved by the systematic searches for health-related quality of life in people with suspected or diagnosed prostate cancer, 2 were used to inform the model (Torvinen et al. and Watson et al.). The EAG also considered the utility inputs used by Faria et al. (2018), Wilson et al. (2021) and the decision model that informed NICE's guideline on prostate cancer. The biopsy complication utilities used in the base case are in table 15.

### Table 15 Base case biopsy complication utilities

| Health states | Input | Duration | Source | Notes |
|---|---|---|---|---|
| Mild AEs/ overnight stay | -0.29 | 3 days | Wilson et al. 2021<br>Lee et al. 2018 | Assumed as the decrement for UTI |
| AEs requiring admission | -0.49 | 30 days | Wilson et al. 2021<br>Lee et al. 2018 | Assumed the same decrement as for sepsis |
| Death from complications | -0.49 | 30 days | Assumption | - |

Table abbreviations: AE, adverse event; UTI, urinary tract infection.

## Model assumptions

In addition to the model assumptions described above, table 16 lists the other key assumptions in the de novo economic model.

### Table 16 Model assumptions

| **Natural history** |
|---|
| True negative patients are at continuous risk of developing the disease, but in the base case model the probability is zero. True negative patients who develop the disease must pass through false negative states before moving to true positive states. People with true disease are at continuous risk of progression from LR to IR to HR and then to metastatic. Prostate cancer specific death occurs only among metastatic patients. |
| **Utilities** |
| Utility for localised disease is assumed equal to that of the general population plus disutilities from radical treatment adverse events. |
| False negative patients (LR, IR, HR and metastatic) have the same disutility as patients on active surveillance. |

| **Prostate cancer treatment** |
|---|
| The proportion of patients taking ADT alone for metastatic hormone sensitive prostate cancer was assumed to be 50% and the proportion of patients taking apalutamide plus ADT and enzalutamide plus ADT was assumed to be 7% each. |
| ADT alone, apalutamide plus ADT and enzalutamide plus ADT were taken until disease progression, which was assumed to occur after 2 years of having metastatic hormone sensitive disease. |
| Once patients progress to metastatic hormone relapsed prostate cancer, they can only have abiraterone or enzalutamide if they have not had apalutamide or enzalutamide before. |
| All patients receiving radical radiotherapy have ADT. |
| **Micro-costing analysis** |
| The cost of SureFire Guide is an average of the CamPROBE and PrecisionPoint. |
| Coaxial needle was assumed to be used for biopsies using both freehand and double freehand devices. |
| Antibiotic prophylaxis for TP biopsies is one prophylactic dose of ciprofloxacin (500 mg), while for LA-TRUS biopsies is a course of ciprofloxacin 500 mg twice a day for 3 days. |
| The average cost of the ultrasound machine costs of EZU-PA3U, UA1232 and Trinity Perine was assumed to be the cost of the ultrasound machine and transducer of the remaining biopsy methods and devices. The same lifetime, number of procedures and proportion of biopsies was assumed as for a stepper. |
| An average of 5 urologists have a given amount of training each year regardless of the biopsy method. A whole day (8 hours) of training would be required per person for SureFire Guide, LATP using grid and stepper unit, LATP using double freehand devices and GATP. LA-TRUS, would only require 1 hour of training. |
| All biopsies are carried out by 1 urologist with 2 nurses in the room for assistance. |
| The average procedure time between CamPROBE and PrecisionPoint of 0.37h was assumed for the remaining LATP devices and 1h for GATP. |
| 12 samples were taken from a prostate biopsy regardless of the biopsy method. |
| 1,000 biopsies are carried out per year on average per hospital. This informed estimates of the cost per patient for capital equipment. |

Table abbreviations: ADT, androgen deprivation therapy; GATP, general anaesthetic transperineal; HR, high risk; IR, intermediate risk; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; LR, low risk.

## Base case results

### Base case cost effectiveness (deterministic): decision question 1

LATP-any is more costly but yields more QALYs than LA-TRUS for all subgroups. The incremental cost effectiveness ratio (ICER) for LATP-any

compared with LA-TRUS increases from £72,503 per QALY gained in subgroup A, up to £81,246 per QALY gained for subgroup D. LATP-any dominates GATP in all subgroups (see table 68 in the diagnostics assessment report).

### Base case cost effectiveness (probabilistic): decision question 1

The results are similar to the deterministic results, with slightly higher ICERs for LATP-any compared with LA-TRUS. The ICERs for LATP-any are well above the upper £30,000 per QALY gained threshold and GATP is dominated in all subgroups (see tables 17 to 20).

**Table 17 Base case cost effectiveness (probabilistic) subgroup A (MRI Likert 3 or more first biopsy); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,517 | 9.2974 | - | - | - | - | - |
| LATP-any | £19,667 | 9.2994 | £149 | 0.0020 | -0.006 | -0.003 | £76,288 |
| GATP | £20,140 | 9.2966 | £623 | -0.0008 | -0.032 | -0.022 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; ICER, incremental cost-effectiveness ratio (fully incremental); INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 18 Base case cost effectiveness (probabilistic) subgroup B (MRI Likert 1 or 2 first biopsy); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £15,283 | 9.4787 | - | - | - | - | - |
| LATP-any | £15,431 | 9.4806 | £148 | 0.0019 | -0.006 | -0.003 | £79,575 |
| GATP | £15,900 | 9.4792 | £617 | 0.0005 | -0.030 | -0.020 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; ICER, incremental cost-effectiveness ratio (fully incremental); INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 19 Base case cost effectiveness (probabilistic) subgroup C (MRI Likert 3 or more previous negative biopsy); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £16,188 | 9.4539 | - | - | - | - | - |
| LATP-any | £16,335 | 9.4557 | £147 | 0.0018 | -0.006 | -0.003 | £82,326 |
| GATP | £16,803 | 9.4539 | £615 | 0.0000 | -0.031 | -0.021 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; ICER, incremental cost-effectiveness ratio (fully incremental); INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 20 Base case cost effectiveness (probabilistic) subgroup D (MRI Likert 1 or 2 previous negative biopsy); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £13,625 | 9.5426 | - | - | - | - | - |
| LATP-any | £13,775 | 9.5444 | £150 | 0.0018 | -0.006 | -0.003 | £82,940 |
| GATP | £14,238 | 9.5437 | £613 | 0.0011 | -0.030 | -0.019 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; ICER, incremental cost-effectiveness ratio (fully incremental); INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

Figure 23 on page 186 in the diagnostics assessment report shows the distribution of incremental costs and QALYs (compared with LA-TRUS) from the probabilistic sensitivity analysis for people referred for a first biopsy with a Likert score of 3 or more (decision question 1). LATP-any is associated with a higher expected cost and high uncertainty over the QALY gain compared with LA-TRUS or GATP.

Figure 24 on page 186 in the diagnostics assessment report shows the cost effectiveness acceptability curve for this group. LA-TRUS is predicted to be the most cost-effective option at cost effectiveness thresholds below around £75,000 per QALY gained. Above this threshold, LATP-any is predicted to be more cost-effective than the other comparators.

**Intermediate outcomes: decision question 1**

A full description of the intermediate outcomes is in the diagnostics assessment report from page 187 to 190. Table 21 shows the adverse event rates and QALY loss for the different biopsy approaches in people in subgroup A. Base case estimates of biopsy-related adverse events resulted in a higher proportion of people with mild AEs (not requiring hospital admission) with the transperineal methods (LATP-any and GATP) than with LA-TRUS. The estimated rate of admissions was over 15% for the transperineal methods, although rates are much lower if overnight stays immediately after the biopsy are excluded (approximately 3.5%). The EAG said that there was high uncertainty over differences in adverse event rates and also the impact on patient's health-related quality of life between the biopsy methods.

**Table 21 Base case adverse event intermediate outcomes (deterministic); decision question 1**

| Biopsy method | Mild AE | AE admissions | AE deaths | AE QALY loss |
|---|---|---|---|---|
| LA-TRUS | 1.4% | 6.3% | 0.07% | -0.0016 |
| LATP-any | 9.2% | 15.8% | 0.05% | -0.0018 |
| GATP | 9.2% | 15.8% | 0.05% | -0.0018 |

Table abbreviations: AE, adverse event; GATP, general anaesthetic transperineal; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

### Base case cost effectiveness (deterministic): decision question 2

For decision question 2, LATP-freehand dominates both LATP-other and GATP, giving lower costs and more QALYs (see table 73 in the diagnostics assessment report). The ICER for LATP-freehand compared with LA-TRUS is below £20,000 per QALY gained for subgroups A and B, but above £30,000 per QALY gained for subgroups C and D. The QALY advantage for LATP-freehand in this analysis is driven by the favourable relative risk of cancer detection estimated from the NMA (see section 2.3).

### Base case cost effectiveness (probabilistic): decision question 2

As for decision question 1, the probabilistic results were similar to the deterministic results with slightly higher ICERs for LATP-freehand compared with LA-TRUS in all subgroups (see tables 22 to 25). The ICER for LATP-freehand in people referred for a first biopsy with a Likert score of 3 or more remains under £20,000 per QALY gained. The ICERs for subgroups with a previous negative biopsy are above the £30,000 per QALY threshold. LATP-other and GATP are dominated in all subgroups.

**Table 22 Base case cost effectiveness (probabilistic) subgroup A (MRI Likert 3 or more first biopsy); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,517 | 9.2974 | - | - | - | - | - |
| LATP-freehand | £19,641 | 9.3074 | £124 | 0.0100 | 0.004 | 0.006 | £12,456 |
| LATP-other | £19,680 | 9.2966 | £163 | -0.0008 | -0.009 | -0.006 | Dominated |
| GATP | £20,150 | 9.2944 | £633 | -0.0030 | -0.035 | -0.024 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 23 Base case cost effectiveness (probabilistic) subgroup B (MRI Likert 1 or 2 first biopsy); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £15,283 | 9.4787 | - | - | - | - | - |
| LATP-freehand | £15,422 | 9.4849 | £139 | 0.0062 | -0.001 | 0.002 | £22,320 |
| LATP-other | £15,441 | 9.4792 | £157 | 0.0005 | -0.007 | -0.005 | Dominated |
| GATP | £15,904 | 9.4782 | £621 | -0.0005 | -0.032 | -0.021 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 24 Base case cost effectiveness (probabilistic) subgroup C (MRI Likert 3 or more previous negative biopsy); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £16,188 | 9.4539 | - | - | - | - | - |
| LATP-freehand | £16,335 | 9.4580 | £147 | 0.0041 | -0.003 | -0.001 | £35,674 |
| LATP-other | £16,342 | 9.4544 | £154 | 0.0005 | -0.007 | -0.005 | Dominated |
| GATP | £16,807 | 9.4530 | £619 | -0.0009 | -0.032 | -0.022 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 25 Base case cost effectiveness (probabilistic) subgroup D (MRI Likert 1 or 2 previous negative biopsy); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £13,625 | 9.5426 | - | - | - | - | - |
| LATP-freehand | £13,777 | 9.5464 | £152 | 0.0038 | -0.004 | -0.001 | £39,966 |
| LATP-other | £13,777 | 9.5438 | £152 | 0.0012 | -0.006 | -0.004 | Dominated |
| GATP | £14,240 | 9.5433 | £615 | 0.0007 | -0.030 | -0.020 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

Figure 25 on page 193 in the diagnostics assessment report shows the distribution of incremental costs and QALYs (compared with LA-TRUS) from the probabilistic sensitivity analysis for people referred for a first biopsy with a Likert score of 3 or more (decision question 2). Figure 26 in the diagnostics

assessment report shows the cost effectiveness acceptability curve for this group.

### Intermediate outcomes: decision question 2

Intermediate outcomes and costs for decision question 2 are in tables 75, 76 and 77 of the diagnostics assessment report. Cancer detection estimates for LATP-freehand (8.38% undiagnosed CS prostate cancer) are more favourable than for LATP-any in decision question 1 (15.01% undiagnosed CS prostate cancer) and LATP-other in decision question 2 (16.60% undiagnosed CS prostate cancer). This is driven by the more favourable relative risk estimates from the NMA.

## Analysis of alternative scenarios

The full details of the EAG's scenario analyses are on pages 198 to 214 of the diagnostics assessment report.

### Probability of repeat biopsy

For people referred for a first biopsy with a Likert score of 3 or more, the effect of using a re-biopsy probability of 5.26% for LATP and GATP was tested, retaining the base case probability of 15.45% for LA-TRUS. The results showed an increase in the ICERs for LATP compared with LA-TRUS. For both decision questions, LATP dominated GATP. The full results for this scenario are in tables 26 to 27.

**Table 26 Scenario: probability of repeat biopsy 5.26% for LATP-any and GATP, and 15.45% for LA-TRUS (deterministic); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,472 | 9.2991 | - | - | - | - | - |
| LATP-any | £19,620 | 9.3003 | £148 | 0.0012 | -0.006 | -0.004 | £118,333 |
| GATP | £20,089 | 9.2985 | £469 | -0.0018 | -0.031 | -0.021 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000

to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 27 Scenario: probability of repeat biopsy 5.26% for LATP and GATP, and 15.45% for LA-TRUS (deterministic); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,472 | 9.2991 | - | - | - | - | - |
| LATP-freehand | £19,581 | 9.3110 | £109 | 0.0119 | 0.006 | 0.008 | £9,155 |
| LATP-other | £19,631 | 9.2978 | £50 | -0.0132 | -0.009 | -0.007 | Dominated |
| GATP | £20,099 | 9.2962 | £468 | -0.0016 | -0.034 | -0.024 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

### Cancer detection rates

This scenario tested the effect of using estimates from observational studies, as summarised in EAG's pairwise meta-analyses (see tables 6 and 7 for the relative risk values used in the base case and scenario analyses). Observational data for GATP was only available in comparison with LATP. Therefore, the estimated relative risk for GATP compared with LA-TRUS was adjusted by the relative risk for LATP compared with LA-TRUS for use in the model. Table 28 shows the results for decision question 1 in subgroup A. This analysis reduced the ICERs for LATP-any in all subgroups and improved cost effectiveness for GATP. Full results are in table 79 on page 200 of the diagnostics assessment report.

**Table 28 Scenario: relative risk of cancer detection from observational studies (subgroup A: MRI Likert 3 or more first biopsy); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,472 | 9.2991 | - | - | - | - | - |
| LATP-any | £19,607 | 9.3041 | £134 | 0.0051 | -0.002 | 0.001 | £26,550 |
| GATP | £20,032 | 9.3120 | £425 | 0.0079 | -0.015 | -0.006 | £54,052 |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

For decision question 2 this scenario was less favourable for LATP-freehand than the base case, increasing the ICERs compared with LA-TRUS. Table 29 shows the results for decision question 2 in subgroup A. Full results are in table 80 on page 201 of the diagnostics assessment report.

**Table 29 Scenario: relative risk of cancer detection from observational studies (subgroup A: MRI Likert 3 or more first biopsy); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,472 | 9.2991 | - | - | - | - | - |
| LATP-freehand | £19,603 | 9.3074 | £130 | 0.0083 | 0.002 | 0.004 | £15,687 |
| LATP-other | £19,620 | 9.3011 | £17 | -0.0063 | -0.005 | -0.003 | Dominated |
| GATP | £20,040 | 9.3103 | £419 | 0.0092 | -0.017 | -0.008 | £150,206 |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

### Probability of biopsy complications

A range of scenario analyses was done to test the effect of using different sources to inform estimates of the probability of complications associated with an overnight stay after the biopsy, admissions and death. These were as follows:

- Rosario et al. (2012) as a source of admission for LA-TRUS (increasing the number of admissions for LA-TRUS)
- Pepe and Aragona (2013) as a source of admission for TP biopsies (reducing the number of admissions for TP biopsies)
- Tamhankar et al. (2020) as a source of admission for LA-TRUS and TP biopsies, without including overnight stay from Berry et al. (2020; reducing admissions for TP biopsies)
- Berry et al. (2020) as a source of admission for LA-TRUS and TP biopsies (includes overnight stay; reducing admissions for LA-TRUS).

For decision question 1, using estimates from Berry et al. is the only scenario that benefits LA-TRUS compared with LATP. For decision question 2, LATP using freehand devices either dominates the other options or has an ICER lower than £12,733 per QALY gained compared with LA-TRUS. The results of these different scenarios for decision questions 1 and 2 are in tables 30 to 33 and 34 to 37, respectively.

**Table 30 Scenario: serious biopsy complications from Rosario et al. (2012) subgroup A (deterministic); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,550 | 9.2980 | - | - | - | - | - |
| LATP-any | £19,623 | 9.3011 | £73 | 0.0031 | -0.001 | 0.001 | £23,321 |
| GATP | £20,092 | 9.2993 | £469 | -0.0018 | -0.026 | -0.017 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000

to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 31 Scenario: serious biopsy complications from Pepe and Aragona (2013) subgroup A (deterministic); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,472 | 9.2991 | - | - | - | - | - |
| LATP-any | £19,492 | 9.3025 | £19 | 0.0034 | 0.002 | 0.003 | £5,621 |
| GATP | £19,960 | 9.3007 | £469 | -0.0018 | -0.023 | -0.015 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 32 Scenario: serious biopsy complications from Tamhankar et al. (2020) subgroup A (deterministic); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,429 | 9.2997 | - | - | - | - | - |
| LATP-any | £19,511 | 9.3023 | £82 | 0.0026 | -0.001 | 0.000 | £31,109 |
| GATP | £19,980 | 9.3005 | £469 | -0.0018 | -0.027 | -0.018 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 33 Scenario: serious biopsy complications from Berry et al. (2020) subgroup A (deterministic); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,415 | 9.2971 | - | - | - | - | - |
| LATP-any | £19,620 | 9.2993 | £205 | 0.0022 | -0.008 | -0.005 | £94,454 |
| GATP | £20,089 | 9.2975 | £469 | -0.0018 | -0.033 | -0.022 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 34 Scenario: serious biopsy complications from Rosario et al. (2012) subgroup A (deterministic); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,550 | 9.2980 | - | - | - | - | - |
| LATP-freehand | £19,585 | 9.3120 | £34 | 0.0140 | 0.012 | 0.013 | £2,430 |
| LATP-other | £19,635 | 9.2985 | £50 | -0.0135 | -0.004 | -0.002 | Dominated |
| GATP | £20,102 | 9.2969 | £468 | -0.0016 | -0.029 | -0.019 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 35 Scenario: serious biopsy complications from Pepe and Aragona (2013) subgroup A (deterministic); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LATP-freehand | £19,453 | 9.3135 | - | - | - | - | - |
| LA-TRUS | £19,472 | 9.2991 | £19 | -0.0144 | -0.015 | -0.015 | Dominated |
| LATP-other | £19,503 | 9.2999 | £31 | 0.0008 | -0.016 | -0.015 | Dominated |
| GATP | £19,971 | 9.2983 | £468 | -0.0016 | -0.041 | -0.032 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 36 Scenario: serious biopsy complications from Tamhankar et al. (2020) subgroup A (deterministic); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,429 | 9.2997 | - | - | - | - | - |
| LATP-freehand | £19,473 | 9.3133 | £43 | 0.0136 | 0.011 | 0.012 | £3,196 |
| LATP-other | £19,523 | 9.2997 | £50 | -0.0135 | -0.005 | -0.003 | Dominated |
| GATP | £19,990 | 9.2981 | £468 | -0.0016 | -0.030 | -0.020 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 37 Scenario: serious biopsy complications from Berry et al. (2020) subgroup A (deterministic); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,415 | 9.2971 | - | - | - | - | - |
| LATP-freehand | £19,582 | 9.3103 | £167 | 0.0131 | 0.005 | 0.008 | £12,733 |
| LATP-other | £19,632 | 9.2967 | £50 | -0.0135 | -0.011 | -0.008 | Dominated |
| GATP | £20,099 | 9.2951 | £468 | -0.0016 | -0.036 | -0.025 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Biopsy costs: Source of biopsy costs (decision question 1)**

For decision question 1, costs from the micro-costing analysis were used as the base case and the costs reported in the NHS cost collection data 2019/20 as a scenario analysis. The NHS source costs of £332 for LA-TRUS, £329 for LATP and £1,512 for GATP. Compared with the base case, this reduced the cost of LATP by around £100, resulting in a low incremental cost of £31 compared with LA-TRUS and therefore a large reduction in the ICER. This means that the cost of LATP drives the model results. Results for subgroup A are in table 38. Full results are in table 85 on page 207 of the diagnostics assessment report.

**Table 38 Scenario: biopsy costs from NHS costs (deterministic) subgroup A (MRI Likert 3 or more first biopsy); decision question 1**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,458 | 9.2991 | - | - | - | - | - |
| LATP-any | £19,489 | 9.3011 | £31 | 0.0020 | 0.000 | 0.001 | £15,196 |
| GATP | £20,681 | 9.2993 | £1,192 | -0.0018 | -0.061 | -0.042 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

### Biopsy costs: Cost of transperineal biopsy freehand devices (decision question 2)

This scenario used the cost of the individual PrecisionPoint device, increasing the cost of LATP-freehand (£584) and making it more expensive than LATP with a grid and stepper unit (£459). This leads to the ICER for LATP-freehand compared with LA-TRUS in people referred for a first biopsy with a Likert score of 1 or 2, rising above £30,000 per QALY (see tables 39 to 42).

### Table 39 Scenario: cost of PrecisionPoint device (deterministic) subgroup A (MRI Likert 3 or more first biopsy); decision question 2

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £19,472 | 9.2991 | - | - | - | - | - |
| LATP-other | £19,632 | 9.2985 | £160 | -0.0006 | -0.009 | -0.006 | Dominated |
| LATP-freehand | £19,696 | 9.3121 | £64 | 0.0135 | 0.002 | 0.006 | £17,208 |
| GATP | £20,100 | 9.2969 | £404 | -0.0151 | -0.034 | -0.023 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 40 Scenario: cost of PrecisionPoint device (deterministic) subgroup B (MRI Likert 1 or 2 first biopsy); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £15,314 | 9.4783 | - | - | - | - | - |
| LATP-other | £15,468 | 9.4789 | £154 | 0.0006 | -0.007 | -0.004 | Dominated |
| LATP-freehand | £15,562 | 9.4857 | £94 | 0.0067 | -0.005 | -0.001 | £33,615 |
| GATP | £15,932 | 9.4782 | £370 | -0.0075 | -0.031 | -0.021 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 41 Scenario: cost of PrecisionPoint device (deterministic) subgroup C (MRI Likert 3 or more negative biopsy); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £16,236 | 9.4565 | - | - | - | - | - |
| LATP-other | £16,390 | 9.4570 | £154 | 0.0005 | -0.007 | -0.005 | Dominated |
| LATP-freehand | £16,496 | 9.4611 | £106 | 0.0041 | -0.008 | -0.004 | £55,683 |
| GATP | £16,854 | 9.4562 | £359 | -0.0050 | -0.031 | -0.021 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

**Table 42 Scenario: cost of PrecisionPoint device (deterministic) subgroup D (MRI Likert 1 or 2 negative biopsy); decision question 2**

| Biopsy method | Total cost | Total QALYs | Incremental cost | Incremental QALYs | INHB (QALYs) £20k | INHB (QALYs) £30k | £/QALY |
|---|---|---|---|---|---|---|---|
| LA-TRUS | £13,632 | 9.5474 | - | - | - | - | - |
| LATP-other | £13,783 | 9.5486 | £151 | 0.0012 | -0.006 | -0.004 | Dominated |
| LATP-freehand | £13,894 | 9.5515 | £111 | 0.0029 | -0.009 | -0.005 | £64,771 |
| GATP | £14,246 | 9.5482 | £351 | -0.0033 | -0.030 | -0.020 | Dominated |

Table abbreviations: GATP, general anaesthetic transperineal; INHB, incremental net health benefit compared with LA-TRUS, at thresholds £20,000 to £30,000 per QALY gained; LATP, local anaesthetic transperineal; LA-TRUS, local anaesthetic transrectal ultrasound; QALY, quality adjusted life year.

### Disutility from the biopsy procedure

The effect of increasing the mild adverse events disutility duration from 3 days to 5 days was tested. This further increased the ICERs for LATP-any compared with LA-TRUS in decision question 1 (ICER of £91,937 per QALY gained for people referred for a first biopsy with a Likert score of 3 or more), because the incidence of mild adverse events was higher for LATP. This scenario had little effect on the results for decision question 2 (ICER of £8,738 per QALY gained for LATP-freehand compared with LA-TRUS).

### Other scenarios

Other scenario analyses done for decision questions 1 and 2 in people referred for a first biopsy with a Likert score of 3 or more, are listed in table 88 of the diagnostics assessment report. These scenario analyses had a small impact on the model results.

## Three-way sensitivity analyses

The EAG did an analysis to test the effect of different combinations of the 3 factors that drive the model conclusions: the cost of LATP, the probability of

biopsy-related serious adverse events and the relative risk of cancer detection rates for LATP compared with LA-TRUS. Full details of this analysis are on pages 215 and 216 of the diagnostics assessment report.

### Decision question 1

Table 89 in the diagnostics assessment report shows the results for the base case relative risk of cancer detection. Full details of these results are described on page 216 in the diagnostics assessment report.

Table 90 in the diagnostics assessment report shows the results for the relative risks based on the pairwise meta-analysis including observational studies only. LATP-any is generally below £30,000 per QALY gained but it is above this threshold for every scenario using the cost of PrecisionPoint.

Table 91 in the diagnostics assessment report shows the results with a 20% increase in the relative risks. LATP-any is below £30,000 per QALY gained in all scenarios except for the combination of the cost of PrecisionPoint and the probability of biopsy-related serious adverse events from Berry et al. (2020).

Table 92 in the diagnostics assessment report shows the results with a 10% decrease in the relative risks. LATP-any is dominated or above £30,000 per QALY gained with the only exception being the combination of the cost of EZU-PA3U and the probability of biopsy-related serious adverse events from Pepe and Aragona.

### Decision question 2

LATP-freehand remained below £30,000 per QALY in almost all combinations of LATP costs, probability of biopsy-related serious adverse events and relative risk of cancer detection rates. The exceptions were combinations of:

- Cost of PrecisionPoint plus adverse events from Berry plus relative risk from pairwise meta-analysis including observational studies only

- Cost of PrecisionPoint or SureFire Guide plus adverse events from Tamhankar et al. (both including and excluding overnight stay) plus relative risk reduced by 20%
- Cost of CamProbeCamPROBE, PrecisionPoint or SureFire Guide plus adverse events from Berry et al. plus relative risk reduced by 20%.

# 4 Summary

## Clinical effectiveness

The EAG identified 23 studies that matched the inclusion criteria for the review, which were grouped into 5 pairwise comparisons. Two of these comparisons addressed decision question 1 (LATP-any compared with LA-TRUS, LATP-any compared with GATP with grid and stepping device) and 3 addressed decision question 2 (LATP-freehand compared with LA-TRUS, GATP using a grid and stepping device, and LATP-other). Nineteen studies addressed decision question 1, 15 of which compared LATP-any with LA-TRUS biopsy and 4 studies compared LATP-any with GATP biopsy. Eight of the studies specified using the PrecisionPoint device and so were also relevant to decision question 2. Most compared LATP-freehand with LA-TRUS biopsy and 1 study compared LATP-freehand with GATP biopsy. The strength of the evidence was mixed with 5 RCTs, but most were observational studies. Some of these studies were only available as conference abstracts.

Meta-analyses and network meta-analyses of cancer detection rates and clinically significant cancer detection rates for decision question 1, showed relative risks of around 1. This indicated no statistically significant difference between LATP-any biopsy approaches and LA-TRUS biopsy and GATP in detecting prostate cancer. For decision question 2, in the pooled analysis there was a statistically significant benefit in favour of LATP-freehand compared with LA-TRUS for detecting prostate cancer. However, there was no statistically significant difference between LATP-other and LA-TRUS. In terms of clinically significant prostate cancer detection, there was a

statistically significant difference in favour of LATP-freehand over LA-TRUS in the observational evidence but not in the RCT evidence. However, statistical significance was retained in the pooled analysis.

The evidence available on clinical outcomes from the studies was limited. Hospitalisation rates in general were very low, so it was difficult to make any definitive conclusions. Only 6 studies reported overall rates of complications after prostate biopsy and most did not report a statistically significant difference between LATP and LA-TRUS.

Some of the studies reported specific biopsy-related complication rates (bleeding and haematuria, sepsis, fever, urinary retention and erectile dysfunction). Reported rates of bleeding and haematuria were low and were higher with LA-TRUS than LATP (mainly because of the rates of rectal bleeding), although 1 study reported that urethral bleeding was more common with LATP-any. Relatively few studies reported post-biopsy sepsis. In the studies that did report it, it only occurred in LA-TRUS biopsy participants. Rates of high fever were also higher for LA-TRUS, however the number of events were low overall and none of the results were statistically significant. In the available comparative evidence, urinary retention rates were similar between biopsy approaches. In the model, complication rates were not taken from the systematic review. Admissions for sepsis and urinary retention were taken from Berry et al. In this study the authors highlight the trade-off between admissions for sepsis and for urinary retention, with estimates suggesting that using TP rather than TRUS biopsies would prevent 1 admission for sepsis at the cost of 3 additional admissions for urinary retention. Two conference abstracts reported worse post-biopsy erectile dysfunction after LATP than LA-TRUS.

## Cost effectiveness

The EAG identified 1 economic evaluation relevant to the scope of the assessment and used 13 other studies to inform its model structure and inputs. The EAG developed an economic model consisting of a decision tree

to evaluate short term diagnostic outcomes, biopsy-related costs and adverse effects, and a Markov model that estimates the long term costs and health consequences.

Cost effectiveness was estimated for 4 subgroups of patients with suspected prostate cancer:

- people referred for a first biopsy with a Likert score of 3 or more (subgroup A, base case)
- people referred for a first biopsy with a Likert score of 1 or 2 (subgroup B)
- people referred after a previous negative biopsy with a Likert score of 3 or more (subgroup C)
- people referred after a previous negative biopsy with a Likert score of 1 or 2 (subgroup D).

The subgroups varied by prior likelihood of having clinically significant prostate cancer: from the highest risk in subgroup A to lowest in subgroup D.

For decision question 1, the base case analysis indicated that GATP was more expensive and less effective (yielding fewer QALYs) than LATP-any in all 4 subgroups. This result was based on sparse comparative evidence, with a single randomised controlled trial reporting on the diagnostic performance of GATP compared with LATP. The ICER for LATP using any method compared with LA-TRUS was above £70,000 per QALY gained, in all subgroups. However, scenario analyses using different assumptions and data sources showed that the results were very sensitive to changes in the cost inputs, rates of hospital admissions and cancer detection rates.

For decision question 2, the base case analysis indicated that LATP with a freehand device was the most cost-effective strategy, with an ICER of £8,447 per QALY compared with LA-TRUS for the highest risk subgroup with MRI Likert score of 3 or more at first biopsy, and £18,196 per QALY gained for the subgroup with an MRI Likert score 1 or 2 at first biopsy. For the subgroups with a previous negative biopsy, the ICER was higher than £30,000 per QALY

gained. The more favourable ICER estimates for LATP with a freehand device, compared with the pooled LATP analysis in decision question 1, is mostly driven by the cancer detection rates. When observational evidence on cancer detection rates was used, the ICERs for LATP with a freehand device although less favourable, were still below £20,000 per QALY gained for the highest risk subgroup but higher than £20,000 per QALY gained in the other subgroups. Similarly, when the cost of LATP with a freehand device was increased in a scenario analysis the ICER remained below £20,000 per QALY gained for the highest risk subgroup, but higher than £20,000 per QALY gained in the other subgroups.

LA-TRUS was less clinically effective and cheaper than LATP with a freehand device. The LATP-other comparator (pooled evidence from studies that did not specify a freehand device) and GATP were not cost-effective in any situation, being either dominated or with high ICERs.

The main drivers of the model results were:

- the cost of LATP devices
- the probability of biopsy-related serious adverse events
- relative risk of cancer detection rates.

# 5 Issues for consideration

## Clinical effectiveness

Six of the studies included in the clinical effectiveness systematic review were only available as conference abstracts and 1 study (Bojin 2019) was an unpublished slide set submitted by the company. There is a risk of reporting bias in these studies because of the limited information that they include. Some of these studies are included in the pairwise meta-analyses of cancer detection rates and 1 (Lam et al. 2021) was an RCT that was included in the network meta-analyses used in the model for base case cancer detection rates.

Most of the available evidence addressed decision question 1, because this incorporates all LATP methods. Fewer studies addressed decision question 2, and all those that were included reported comparative evidence for PrecisionPoint. One of these studies was the unpublished slide set submitted by the company (Bojin 2019). Only non-comparative data was available for the CamPROBE and UA1232 devices. No evidence at all was available for the EZU-PA3U, SureFire or the Trinity Perine Grid devices. The ongoing multicentre UK study (TRANSLATE) will provide further evidence for freehand LATP using any ultrasound probe-mounted needle guidance device, including the PrecisionPoint and UA1232 devices. Because the study uses freehand devices to perform the biopsies it is expected to inform both decision question 1 and 2.

The devices used in the studies were often not clearly reported. Therefore, in decision question 2 the LATP studies that used a coaxial needle (that is, a double freehand technique) and those that were assumed to use a grid and stepping device, were grouped together as LATP-other. This was based on an assumption that LATP with a grid and stepper and LATP with a coaxial needle are equivalent in effects, which may not be appropriate. One of the comparisons defined in the scope for decision question 2 was LATP-freehand devices compared with LATP grid and stepper. However, a true comparison was not possible because of a lack of data.

In the clinical effectiveness review, spinal anaesthesia studies were included in the LATP analyses, but this anaesthetic procedure needs to be done in an operating theatre, and therefore these studies are more aligned with GATP.

There was not enough evidence to review the clinical effectiveness of the biopsy procedures for the subgroups listed in the scope: people with anterior, posterior, apical or basal lesions; people with a Likert or PI-RADS score of 2 or less; and people with a Likert or PI-RADS score of 3, 4, or 5.

## Cost effectiveness

The model assumed that 12 cores were taken for every biopsy method. However, this may be too simplistic because different biopsy approaches take different numbers of cores and this may also vary between centres. For example, many of the studies in decision question 2 that used PrecisionPoint took more cores than the other studies. This is an important consideration because the number of cores taken may affect cancer detection rates, with more cores potentially leading to a higher cancer detection rate. However, over-sampling can make the procedure more difficult for the patient to tolerate, and cost more because of the duration of the procedure and pathology costs.

Cancer detection rates may also be influenced by whether or not pre-biopsy mpMRI has been used to inform the biopsy sampling. Most studies did not report whether mpMRI had been done before biopsy. Also, for studies based outside the UK the use of mpMRI in those countries may not reflect UK practice.

The more favourable ICER estimates for LATP with a freehand device (PrecisionPoint) in question 2, compared with the pooled LATP analysis in decision question 1, is mostly driven by the cancer detection rates. For question 2 this relies on data from a single RCT by Lam et al. (2021) reported only as a conference abstract.

The model base case includes overnight hospitalisation data from Berry et al. (2020). This study uses older data from when TP biopsy was frequently done under general anaesthetic and more cores were taken, therefore an overnight stay after biopsy was more common than it is in current practice. The EAG said that sources of evidence for biopsy complications were difficult to interpret, because results were not reported for LATP and GATP separately and therefore it is unclear how many complications (and which ones) correspond to LATP or GATP. These rates are a key driver of the model results.

The base case analysis also used estimates for mild adverse events from 2 different studies. For LA-TRUS biopsy, these data were from Rosario et al. (2012) and for TP biopsies they were from Pepe and Aragona (2013).

# 6 Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination, and fostering good relations between people with particular protected characteristics and others.

- All people with cancer are covered under the disability provision of the Equality Act (2010) from the point of diagnosis.
- Radical treatment for prostate cancer can affect fertility.
- Prostate cancer is more common in older people, people of African family background and people with a family history of prostate cancer.
- People with learning disabilities are often disproportionally affected by cancer.
- Transperineal prostate biopsies may be more suitable than transrectal biopsies for people with inflammatory bowel disease.
- Trans women should have access to prostate biopsy if needed.
- Some people are at a greater risk of complications during general anaesthetic. This includes people with diabetes, older people, people who are overweight, people with heart disease and people with high blood pressure.

# 7 Implementation

The use of transperineal access devices may have a resource impact including the set up and ongoing costs of the single use or reusable components needed to undertake the procedure. There are also clinician concerns about prostate biopsy tolerability using local anaesthetic. With greater anterior prostate access there could be an increase in the numbers of samples taken at biopsy and sent to pathology departments. As the transperineal approach to prostate biopsy is very different to TRUS there is

also a need for training, which will vary depending on previous clinical experience.

# 8 Authors

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# Glossary

## Active surveillance

This is part of a 'curative' strategy and is aimed at people with localised prostate cancer for whom radical treatments are suitable, keeping them within a 'window of curability' whereby only those whose tumours are showing signs of progressing, or those with a preference for intervention are considered for radical treatment. Active surveillance may thus avoid or delay the need for radiotherapy or surgery.

## LATP-any

Refers to local anaesthetic transperineal prostate biopsy done by any method in the NICE scope (that is, prostate biopsy using a grid and stepping device, a coaxial needle (‘double freehand’), or a freehand device).

## LATP-freehand

Refers to local anaesthetic transperineal prostate biopsy done using one of the 6 freehand devices in the NICE scope. This is a sub-category of the LATP-any grouping of biopsy methods.

## Local anaesthetic transperineal (LATP) biopsy

This is either targeted or systematic sampling of sites from the prostate using a transperineal route under local anaesthetic.

## Localised prostate cancer

Cancer that has been staged as T1 or T2 (confined to the prostate gland).

## Multiparametric MRI-influenced prostate biopsy

The information from the mpMRI scan taken before prostate biopsy is used to determine the best needle placement. In rare cases, the biopsy may be MRI-guided (the needle is inserted within the MRI machine). In most cases, the biopsy that follows the mpMRI will be ultrasound guided, but the specific area(s) targeted will be predetermined by the mpMRI data.

## Prostatectomy

Surgery to remove part, or all of the prostate gland. Radical prostatectomy aims at the removal of the entire prostate gland and lymph nodes. This can be

done by an open approach or by keyhole technique (laparoscopic or robotically assisted laparoscopic prostatectomy).

## PSA velocity

The rate of change of PSA in nanograms per ml per year.

## Transrectal ultrasound guided biopsy (TRUS)

This is where core biopsies of the prostate are taken via the rectum under local anaesthetic.

## Template biopsy and mapping template biopsy

A template biopsy is normally done under a general anaesthetic, and involves taking transperineal core biopsies using a grid system. This might involve taking multiple cores from multiple sites, but usually 2 to 3 cores from 8 sites. A mapping template biopsy is where 20 sites are systematically sampled, with 2 or 3 cores per site, sometimes meaning over 50 core biopsies are taken.

## Watchful waiting

This is part of a strategy for 'controlling' rather than 'curing' prostate cancer and is aimed at people with localised prostate cancer who do not ever wish to have curative treatment, or it is not suitable for them. Instead, it involves the deferred use of hormone therapy. Watchful waiting avoids the use of surgery or radiation, but implies that curative treatment will not be attempted.