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Diagnostics Assessment Programme

Transperineal biopsy for diagnosing prostate cancer

The following documents are made available to stakeholders:

1. **Stakeholder comments on the Diagnostics Consultation Document (DCD) and responses**

2. **Addendum to Diagnostics Assessment Report - additional analysis** prepared by Southampton Health Technology Assessments Centre (SHTAC)

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DIAGNOSTICS ASSESSMENT PROGRAMME

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Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 22 March 2022
Theme: Generalisability of the evidence

Comment number	Name and organisation	Section number	Comment	NICE response
1	Royal Surrey NHS Foundation Trust	3.3	1.The diagnostics consultation document has been sent to stakeholders requesting comments on the following questions: • Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? • Are the recommendations sound, and a suitable basis for guidance to the NHS? 2. The document states that "*all the clinical evidence for freehand needle positioning devices is on the PrecisionPoint device. There is no comparative evidence for the EZU-PA3U, UA1232, or Trinity Perine Grid devices but experts suggest that cancer detection rates and adverse events should be similar between the different freehand devices.*" *"All the comparative clinical evidence for freehand needle positioning devices was on the PrecisionPoint device. However, a clinical expert explained that the different freehand devices were all used in a similar way, with a needle positioning guide that attaches to the ultrasound probe. This keeps the needle and ultrasound probe in phase during the procedure. The clinical experts said they would not expect significant differences in cancer detection rates and adverse event rates between the devices. No studies directly compare the individual devices so there was no evidence that one performs better than any other. The committee concluded that the clinical effectiveness in terms of cancer detection and adverse events was likely to be similar for all the freehand needle positioning devices, although this was uncertain."*	Thank you for your comment which the committee considered. The committee discussed the similarities and differences between the different freehand needle positioning devices. Clinical experts said that the EZU-PA3U, PrecisionPoint, Trinity Perine Grid and UA1232 freehand needle positioning devices are all mechanical devices that,despite some technical differences, all work in a similar way for the user. This consideration has been added to the diagnostics guidance document in section 3.3. The committee was aware that there was no comparative evidence on the EZU-PA3U, UA1232, or Trinity Perine Grid devices. But it noted that the different freehand devices all work in a similar way with the same biopsy technique. It concluded that the clinical effectiveness in terms of cancer detection and adverse events was likely to be similar for all the freehand needle positioning devices. See

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			3. We do not believe that these statements are reasonable, evidence-based, assertions when the only evidence comes from one device i.e., the Precision Point device. How can "experts" know/suggest that the cancer detection rates with other devices are similar if this has not been studied and validated in clinical trials? This goes against the whole concept of recommendations driven by evidence-based medicine which NICE has championed since its inception. It also contrary to the NICE's stated aim of "Improving health and wellbeing by putting science and evidence at the heart of health and care decision making." If the committee concluded it was **uncertain** that all freehand devices were likely to be similar regarding clinical effectiveness, then only Precision Point should be recommended until such time the evidence for other devices becomes available.	section 3.4 of the diagnostics guidance document. The committee exercises its scientific and clinical judgement when deciding whether particular forms of evidence are suitable for answering specific questions
2	Web comment	3.3	Cancer detection rates and adverse events are likely to be similar between the different freehand needle positioning devices If the committee did not have data on other devices than Precision , how can the data be generalisable to the other devices. This goes against the whole concept of NICE evidence review prior to issuing guidance to the public.	Thank you for your comment which the committee considered. The committee discussed the similarities and differences between the different freehand needle positioning devices. Clinical experts said that the EZU-PA3U, PrecisionPoint, Trinity Perine Grid and UA1232 freehand needle positioning devices are all mechanical devices that, despite some technical differences, all work in a similar way for the user. This consideration has been added to the

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				diagnostics guidance document in section 3.3. The committee was aware that there was no comparative evidence on the EZU-PA3U, UA1232, or Trinity Perine Grid devices. But it noted that the different freehand devices all work in a similar way with the same biopsy technique. It concluded that the clinical effectiveness in terms of cancer detection and adverse events was likely to be similar for all the freehand needle positioning devices. See section 3.4 of the diagnostics guidance document. The committee exercises its scientific and clinical judgement when deciding whether particular forms of evidence are suitable for answering specific questions
3	BXTAccelyon Ltd	1.2	We do not accept that there is any meaningful evidence to demonstrate that the EZU-PA3U, Trinity Perine Grid and the UA1232 puncture attachment have demonstrated similar cancer detection rates and low incidence of adverse events as PrecisionPoint. Nor do we accept that these devices are technically similar to PrecisionPoint. -The EZU-PA3U, Trinity Perine Grid and the UA1232 puncture attachment devices were designed and are intended to be used in a completely different way to PrecisionPoint which is made clear by their respective 'Instructions for Use'. We would also add that guidance to	Thank you for your comment which the committee considered. The committee considered again the similarities and differences between the freehand needle positioning devices and their considerations have been added into section 3.3 in the diagnostics guidance document. It states that although the

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			use these devices outside of the controlled labelling and "Instructions for Use" means that such use is "off label" and, as such, any liability if there is an adverse event falls on the operating clinician. We have included a comparison table reflecting the respective 'Instructions for Use' of all 4 devices (ie also including PrecisionPoint) to demonstrate that the modus operandi of the EZU-PA3U, Trinity Perine Grid and UA1232 puncture attachment devices are very different to PrecisionPoint. -We consider the implication of the report that these other devices in some way 'approximate to' PrecisionPoint to be completely speculative and given there is limited data to support the claims and recommendations in this clause, we would respectfully suggest that the recommendations are removed until meaningful evidence is obtained	PrecisionPoint device comes with a specific access needle as part of the kit, companies for EZU-PA3U, Trinity Perine Grid and UA1232 said that their devices could be used with needles bought separately provided they are compatible with the guide channel diameter. Use of an access needle or a coaxial needle means that generally 4 or fewer punctures of the skin are needed. The committee concluded that the EZU-PA3U, PrecisionPoint, Trinity Perine Grid and UA1232 freehand needle positioning devices are all mechanical devices that, despite some technical differences, all work in a similar way for the user.
4	BXTAccelyon Ltd	1.2	'Although there is considerably less evidence for them, the following freehand needle positioning devices are also recommended as an option:' We note that the Committee found "there was no comparative evidence on the CamPROBE, EZU-PA3U, UA1232, SureFire or Trinity Perine Grid devices." Accordingly, we would respectfully request that NICE wait until other device manufacturers are able to demonstrate an acceptable level of comparative data as is already available for PrecisionPoint before issuing recommendations on their use.	Thank you for your comment which the committee considered. The committee exercises its scientific and clinical judgement when deciding whether particular forms of evidence are suitable for answering specific questions.

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5	BXTAccelyon Ltd	1.2	'They are expected to have similar cancer detection rates and adverse events to PrecisionPoint because they are technically similar.' We note that the Committee acknowledges all of the clinical evidence for LATP procedures in the report derives from use of the PrecisionPoint device. We do not accept the experts' opinion that cancer detection rates and adverse events should be similar between the different freehand devices. We are not aware that any expert on the panel has personal experience of all the devices. Accordingly, we believe it is not acceptable for NICE to make recommendations on devices for which – by NICE's own assessment – there is, at best, very limited supporting data. Again, we respectfully draw your attention to the "Intended Uses" of the devices (other than PrecisionPoint) which runs wholly counter to any contention that they "should have similar" outcomes	Thank you for your comment which the committee considered. The committee noted that a single RCT available as a conference abstract was the only study used in the network meta-analysis of cancer detection rates for LATP using a freehand needle positioning device. The committee said that there was limited evidence on cancer detection rates and that caution should be used when interpreting the results. These considerations are in section 3.2 of the diagnostics guidance document. The committee considered again the similarities and differences between the freehand needle positioning devices and their considerations have been added into section 3.3 in the diagnostics guidance document. It states that although the PrecisionPoint device comes with a specific access needle as part of the kit, companies for EZU-PA3U, Trinity Perine Grid and UA1232 said that their devices could be used with needles bought separately provided they are compatible with the guide channel diameter.

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				Use of an access needle or a coaxial needle means that generally 4 or fewer punctures of the skin are needed. The committee concluded that the EZU-PA3U, PrecisionPoint, Trinity Perine Grid and UA1232 freehand needle positioning devices are all mechanical devices that, despite some technical differences, all work in a similar way for the user. The committee exercises its scientific and clinical judgement when deciding whether particular forms of evidence are suitable for answering specific questions.
6	BXTAccelyon Ltd	1.4	We note that the Committee found “there was no comparative evidence on the CamPROBE, EZU-PA3U, UA1232, SureFire or Trinity Perine Grid devices.” Accordingly, we would respectfully request that NICE wait until other device manufacturers are able to demonstrate an acceptable level of comparative data as is already available for PrecisionPoint before issuing recommendations on their use.	Thank you for your comment which the committee considered. The committee exercises its scientific and clinical judgement when deciding whether particular forms of evidence are suitable for answering specific questions.
7	BXTAccelyon Ltd	1.4	‘All the clinical evidence for freehand needle positioning devices is on the PrecisionPoint device. There is no comparative evidence for the EZU-PA3U, UA1232, or Trinity Perine Grid devices but experts	Thank you for your comment which the committee considered.

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			suggest that cancer detection rates and adverse events should be similar between the different freehand devices.' All the comparative clinical evidence for freehand needle positioning devices was on the PrecisionPoint device. However, a clinical expert explained that the different freehand devices were all used in a similar way, with a needle positioning guide that attaches to the ultrasound probe." ***For the reasons stated above we strongly disagree with this assertion by a clinical expert on the different freehand devices. The devices are not used in a similar way and anything that suggests they should be used in a similar way is in direct conflict with the controlled labelling of the devices.***	
8	BXTAccelyon Ltd	3.3	'Cancer detection rates and adverse events are likely to be similar between the different freehand needle positioning devices' The committee concluded that the clinical effectiveness in terms of cancer detection and adverse events was likely to be similar for all the freehand needle positioning devices, although this was uncertain." -We note that the Committee concluded that the devices were likely to be similar but that this was uncertain. Therefore, we believe strongly that the recommendations on other devices should be delayed until more certainty was established on their use and outcomes.	Thank you for your comment which the committee considered. The committee exercises its scientific and clinical judgement when deciding whether particular forms of evidence are suitable for answering specific questions.

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Theme: PrecisionPoint comparison with other needle positioning devices

Comment number	Name and organisation	Section number	Comment	NICE response
9	BXTAccelyon Ltd	NA	***Tissue Sampling*** **PrecisionPoint:** • Only two (max 4) access holes required • Easy to manoeuvre access needle and direct biopsy needle precisely • Easy to align with linear array and maintain visualisation • Accurate and precise • Easy to biopsy along planes of peripheral zone **Single column reusable or disposable Grids, the BK UA1232, Fujifilm Hitachi EZU-PA3U and Koelis Trinity Perine Grid:** • Multiple perineal access holes required. Instructions for Use (Controlled Labelling) all indicate to be used directly with Biopsy Needle and no other puncture attachment. • Patients not able to tolerate multiple punctures so GA potentially is required or LA & sedation • Anterior prostate more difficult to access with these guides • Difficult to leverage and direct biopsy needle and may be less well tolerated by patients • Inflexible - not designed for transperineal systematic biopsy ***Targeted and Systematic Biopsies*** **PrecisionPoint:**	Thank you for your comment which the committee considered. NICE has had confirmation from the companies that their devices can be used with needles bought separately according to the needle gauge range specified in their instructions for use. The technology descriptions in the diagnostics guidance document for EZU-PA3U, Trinity Perine Grid and UA1232 devices have been updated with this information. See sections 2.8, 2.11 and 2.12 of the diagnostics guidance document. Clinical experts commented that the needles used with the devices are indicated for taking biopsy samples through the skin. Although the PrecisionPoint device comes with a specific access needle as part of the kit, companies for the EZU-PA3U, Trinity Perine Grid and UA1232 stated that their devices could be used with needles bought separately provided they are compatible with the guide channel diameter. Use of an access

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Theme: PrecisionPoint comparison with other needle positioning devices

Comment number	Name and organisation	Section number	Comment	NICE response
			• Significant data to show accurate and precise in picking up clinically significant cancers and capability of being used for targeted and systematic biopsies • Easy to manoeuvre so target tissue precisely hit • Device designed for all sizes of prostate • Specifically designed access needle that is non-coring so will not traumatise perineal tissues • Access needles precisely fits grid holes in PrecisionPoint to provide security, safety and accuracy of tissue sampling **Single column reusable or disposable Grids, the BK UA1232, Fujifilm Hitachi EZU-PA3U and Koelis Trinity Perine Grid:** • Very little data and unclear methodology. If used as with additional accessories (other than biopsy needle) the devices are potentially being used off label and require appropriate testing and validation and clinical data to support such use and registration • Requires multiple punctures to hit target tissue. Prostate tissue more difficult to manipulate to correct positions if used as per IFU and significant puncture sites required for systematic biopsy • Unclear if can be used with all prostate sizes (very limited data) • If used with coaxial needle (off label use) - cumbersome to use and close fit of coaxial needle with holes not guaranteed or designed. Operator needs to hold coaxial needle in position to conduct biopsy. Coaxial needle is a cutting needle that will tear	needle or a coaxial needle means that generally 4 or fewer punctures of the skin are needed. See section 3.3 of the diagnostics guidance document.

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Comment number	Name and organisation	Section number	Comment	NICE response
			tissue and cause trauma so less likely to be tolerated and will potentially be longer tissue recovery period. • Play of coaxial needle will affect accuracy, alignment, safety and accuracy of tissue sampling ***Training and Teaching Staff*** **PrecisionPoint:** • Has been shown to be reproducible with staff of all skill levels and experience • Can be trained in 10-15 cases • Can be trained to Junior Doctors and Nursing Staff • Tried, tested and established teaching courses with track record of centre training and adoption • Can be used with wide range of u/s equipment and probes so easy to adopt within centres existing equipment **Single column reusable or disposable Grids, the BK UA1232, Fujifilm Hitachi EZU-PA3U and Koelis Trinity Perine Grid:** • Limited use and training network. Very few centres using and experienced in training teams • Training case numbers undisclosed but could be > 50 • Junior Doctor and Nursing staff training unproven • No evidence of proven tested training capability	

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Comment number	Name and organisation	Section number	Comment	NICE response
			• Designed for one model of ultrasound so would need to learn new u/sound system to use device ***Cost and Sterilisation*** **PrecisionPoint:** • £200 per single use PP kit • No sterilisation costs • 1 device per procedure • Can be used with wide range of u/s equipment and probes so limited capital investment required **Single column reusable or disposable Grids, the BK UA1232, Fujifilm Hitachi EZU-PA3U and Koelis Trinity Perine Grid:** • Up to £2000 per reusable grid • Sterilisation Costs and Time to be evaluated • 5 or more devices required per half day list, up to 10 for full day list • Sterilisation Validation required • Limited to U/S manufacturers device so investment required to acquire compatible u/s equipment and probe	The EAG confirmed that costs associated with sterilisation were included in the economic modelling. See section 3.3 of the diagnostics assessment report.

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Theme: Costings

Comment number	Name and organisation	Section number	Comment	NICE response
10	BXTAccelyon Ltd	3.10	'Using the cost of the PrecisionPoint device in a scenario analysis increases the ICERs' 'The EAG did not model alternative scenarios using the costs of the other freehand devices but the committee noted that the PrecisionPoint device was the most expensive device.' Cost of coaxial needle: For the DAR analysis, we had included the cost of a coaxial needle (£21.40) for all LATP biopsy procedures with a freehand device. This was questioned in stakeholder comment 26, and we understand that a coaxial needle is only needed with the EZU-PA3U device and the double freehand approach. Removing this cost for other methods reduces EAG base case ICERs for LATP. -The above comments appear to confirm that the Freehand TP devices are not all used in a similar manner and so cannot be expected to have similar outcomes and adverse events. The other Freehand devices would require multiple punctures of the perineum like grid-guided approaches and it could be challenged whether this is tolerable for the patient with Local Anaesthetic alone rather than additionally requiring, for example, sedation at least. We would respectfully challenge the statement that the cost of reprocessing and autoclaving the reusable devices is only £5 per procedure given the time, materials cost and resources involved. It should also be noted and fully allowed for in any costing exercise for a multiple number of these devices to be required in order to carry out a	Thank you for your comment which the committee considered. The external assessment group (EAG) commented that the costing exercise was based on published data, data from the manufacturers as well as data from clinical experts. Some assumptions were made as no better data was available. The EAG believe that these assumptions did not impact the model conclusions to a great extent. The cost of reprocessing and autoclaving was estimated based on information from a specialist committee member. The EAG

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Theme: Costings

Comment number	Name and organisation	Section number	Comment	NICE response
			full day theatre list, taking due account of the processing requirements within hospitals which are likely to be scheduling several biopsy lists during a week.	do not expect the cost of reprocessing to be high enough to overcome the cost of PrecisionPoint.

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Theme: Cancer detection rates - general

Comment number	Name and organisation	Section number	Comment	NICE response
11	University of Cambridge	Diagnostics consultation document Section 1 Page 2 conclusion on recommendations on double freehand-expert opinion	We also point out that cancer detection rates are also highly dependent on the underlying population selected for biopsy - For example, if only MRI positive men are selected for biopsy then the cancer detection rates are higher – whereas if a biopsy is done regardless of MRI then this may be lower. The impact of cohort selection on reported LATP device efficiency needs to be clarified i.e. what is due tot eh device and what is due to the MRI telling you where to biopsy Please see these citations– O'Connor LP, Lebastchi AH, Horuz R, Rastinehad AR, Siddiqui MM, Grummet J, Kastner C, Ahmed HU, Pinto PA, Turkbey B. Role of multiparametric prostate MRI in the management of prostate cancer. World J Urol. 2021 Mar;39(3):651-659. Hansen NL, Barrett T, Kesch C, Pepdjonovic L, Bonekamp D, O'Sullivan R, Distler F, Warren A, Samel C, Hadaschik B, Grummet J, Kastner C. Multicentre evaluation of magnetic resonance imaging supported transperineal prostate biopsy in biopsy-naïve men with suspicion of prostate cancer. BJU Int. 2018 Jul;122(1):40-49. doi: 10.1111/bju.14049. Hence there is no good way to compare unless it is done in a formal RCT and balanced for use of MRI and MRI targeting. As a result, unless there is such a trial i.e. double free hand versus single freehand – there can be no firm conclusions made about inferiority of biopsy	Thank you for your comment which the committee considered. The studies by O'Connor et al. and Hansen et al. were not identified in the external assessment group's search, but they would not have been included in the systematic review: O'Connor is a review article about mpMRI; and Hansen is a single arm study of TP biopsy, including fusion biopsies. The impact of pre-biopsy MRI on cancer detection rates was discussed by the committee and its consideration is described in section 3.2 of the diagnostics guidance document. The external assessment group said that most studies did not report whether a prebiopsy multiparametric MRI (mpMRI) had been done and some did not report the number of biopsy cores taken. The committee noted that studies that used an mpMRI image to take targeted biopsy samples and those that took more cores may result in higher cancer detection rates regardless of

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Theme: Cancer detection rates - general

Comment number	Name and organisation	Section number	Comment	NICE response
			methods over each other. We ask that this be mentioned for clarity and as uncertainty in all these analyses.	the biopsy technique used. It noted that caution should be used when interpreting the cancer detection rates from the studies. The committee concluded that, because there was generally no significant difference between LATP using any method, LATP using a freehand needle positioning device, local anaesthetic transrectal ultrasound (LA-TRUS) or GATP, it could not say if one technique was better than the others.

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Theme: Cancer detection rates – LATP compared with TRUS

Comment number	Name and organisation	Section number	Comment	NICE response
12	Web comment	3.6	There are some differences between LATP and TRUS biopsy approaches Ongoing research compares the cancer detection rates of TRUS vs LATP. However the move towards using LATP nationally is based on the lower infection rates as well as the ease of access to the anterior prostate lesions.	Thank you for your comment which the committee considered. In section 3.8 of the diagnostics guidance document, the committee noted that the ongoing TRANSLATE RCT will provide further comparative evidence on LA-TRUS biopsy and LATP biopsy using a freehand needle positioning device. It concluded that centres should be encouraged to participate in the TRANSLATE RCT. The committee also concluded that LATP biopsies may reduce the risk of infection and sepsis compared with TRUS biopsies. These considerations are in section 3.6 of the diagnostics guidance document.
13	BXTAccelyon Ltd	1.3	'The evidence on cancer detection rates is limited and suggests no significant difference between different biopsy methods' We have already presented several clinical papers that have confirmed that transperineal prostate biopsies demonstrate a higher rate of cancer detection than TRUS biopsy including: "Initial outcomes of local anaesthetic freehand transperineal prostate biopsies in the outpatient setting; Kum et al, BJUI 2019"	Thank you for your comment which the committee considered. The external assessment group commented that Kum et al. 2019 was included in the systematic review as a

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Theme: Cancer detection rates – LATP compared with TRUS

Comment number	Name and organisation	Section number	Comment	NICE response
			"Xiang, J., Yan, H., Li, J. et al. Transperineal versus transrectal prostate biopsy in the diagnosis of prostate cancer: a systematic review and meta-analysis. World J Surg Onc 17, 31 (2019). https://doi.org/10.1186/s12957-019-1573-0" In the latter paper the authors state: "On the other hand, the TP approach was confirmed to be superior in detecting tumors in the transitional zone and apex of the prostate [16, 22, 23]." -It should also be noted that many of the papers to demonstrate cancer detection rates would have used template grid-guided TP approaches and not freehand approaches with PrecisionPoint which we believe offers demonstrable benefits over the grid-guided approach. -However, we do accept that randomised controlled evidence is limited and that the TRANSLATE Study (currently in recruitment) should provide additional level 1 data on the comparative cancer detection rates of the two methods. We note and agree that TP biopsy approaches show less risk of infective complications.	linked paper with Kum et al. 2018 (reporting on the same study). Xiang et al. 2019 is a systematic review. The external assessment group used systematic reviews, including this one, as a source of potentially relevant evidence by checking their reference lists. They did not formally include the results of these systematic reviews in the report.
14	BXTAccelyon Ltd	3.2	'The evidence on cancer detection rates is limited and suggests no significant difference between different biopsy methods' We note and accept that mpMRi may identify anterior lesions which may be difficult to reach by TRUS biopsy. However we believe there is some date to support that LATP biopsy is able to better access and detect cancer in the anterior regions of the prostate:	Thank you for your comment which the committee considered. The committee heard that there was no evidence to assess the clinical effectiveness of the different biopsy approaches in people with anterior lesions.

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			"Xiang, J., Yan, H., Li, J. et al. Transperineal versus transrectal prostate biopsy in the diagnosis of prostate cancer: a systematic review and meta-analysis. World J Surg Onc 17, 31 (2019). https://doi.org/10.1186/s12957-019-1573-0" In the this paper the authors state "On the other hand, the TP approach was confirmed to be superior in detecting tumors in the transitional zone and apex of the prostate [16, 22, 23]."	Xiang et al. 2019 is a systematic review. The external assessment group used systematic reviews, including this one, as a source of potentially relevant evidence by checking their reference lists. They did not formally include the results of these systematic reviews in the report.
15	BXTAccelyon Ltd	3.6	'There are some differences between LATP and TRUS biopsy approaches' We note and accept that mpMRi may identify anterior lesions which may be difficult to reach by TRUS biopsy. However we believe there is some date to support that LATP biopsy is able to better access and detect cancer in the anterior regions of the prostate: "Xiang, J., Yan, H., Li, J. et al. Transperineal versus transrectal prostate biopsy in the diagnosis of prostate cancer: a systematic review and meta-analysis. World J Surg Onc 17, 31 (2019). https://doi.org/10.1186/s12957-019-1573-0" In the this paper the authors state "On the other hand, the TP approach was confirmed to be superior in detecting tumors in the transitional zone and apex of the prostate [16, 22, 23]."	Thank you for your comment which the committee considered. The committee heard that there was no evidence to assess the clinical effectiveness of the different biopsy approaches in people with anterior lesions. Xiang et al. 2019 is a systematic review. The external assessment group used systematic reviews, including this one, as a source of potentially relevant evidence by checking their reference lists. They did not formally include the results of these systematic reviews in the report.

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Theme: Cancer detection rates – double freehand

Comment number	Name and organisation	Section number	Comment	NICE response
16	JEB	Section 1 - Why the committee made these recommendations	The last paragraph makes statements that experts are suggesting that double free hand may not have the same cancer detection rates and may not be cost effective when compared to LA-TRUS biopsies. In our opinion, this is a non-factual opinion that potentially miss-represents Camprobe. The published Camprobe clinical investigation reported through a sub set of data that cancer detection rates are comparable to current state of the art. We do accept that the clinical investigation outcomes are from a very limited data set so would therefore request a change to this paragraph to remove the current nonfactual statements with the following wording. We suggest the inclusion of:- "there is insufficient evidence available to determine if cancer detection rates and the cost effectiveness of Camprobe (or indeed any other double freehand biopsy method) when compared to LA-TRUS or any other freehand LA-TP methods".	Thank you for your comment which the committee considered. The committee decided to revise section 1 (Why the committee made these recommendations) of the diagnostics guidance document which now reads: There is no comparative evidence on the CamPROBE device, which uses a double freehand technique. Experts said that, because the double freehand technique is different to using the freehand needle positioning devices, more research is needed to understand the cancer detection rates, adverse events and cost effectiveness.
17	University of Cambridge	Diagnostics consultation document Section 1 Page 2 conclusion on recommendations on double	The conclusion to the recommendations about double free hand "potentially" having lower cancer diagnosis rates appears to be based only on opinion - it does not include a formal review of the available literature. Publications to date (although not RCT vs other LATP) have shown reported cancer detection rates comparable to those for other biopsy methods (e.g. Multicentre clinical evaluation of the safety and performance of a simple transperineal access system for prostate biopsies for suspected prostate cancer: The CAMbridge PROstate	Thank you for your comment which the committee considered. The committee decided to revise section 1 (Why the committee made these recommendations) of the diagnostics guidance document which now reads: There is no comparative evidence on the CamPROBE device, which uses a double

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Theme: Cancer detection rates – double freehand

Comment number	Name and organisation	Section number	Comment	NICE response
		freehand-expert opinion	Biopsy DevicE (CamPROBE) study. J Clin Urol. 2020 Sep;13(5):364-370. doi: 10.1177/2051415820932773 - see Table 3) In addition, past papers using the double freehand technique have also reported excellent cancer detection rates with and without using MRI assistance - These don't seem to have been considered in this conclusion and discussions? or considered in the economic review? Please see these citations amongst others: (1) Marra G, Marquis A, Tappero S, D'Agate D, Oderda M, Calleris G, Falcone M, Faletti R, Molinaro L, Zitella A, Bergamasco L, Gontero P. Transperineal Free-hand mpMRI Fusion-targeted Biopsies Under Local Anesthesia: Technique and Feasibility From a Single-center Prospective Study. Urology. 2020 Jun;140:122-131. (2) Wetterauer C, Shahin O, Federer-Gsponer JR, Keller N, Wyler S, Seifert HH, Kwiatkowski M. Feasibility of freehand MRI/US cognitive fusion transperineal biopsy of the prostate in local anesthesia as in-office procedure-experience with 400 patients. Prostate Cancer Prostatic Dis. 2020 Sep;23(3):429-434. doi: 10.1038/s41391-019-0201-y. While we accept the lack of RCT evidence (indeed for any comparison of LATP) and that different clinicians will have different views we please ask that NICE to re-consider this concluding recommendation to make it more balanced.	freehand technique. Experts said that, because the double freehand technique is different to using the freehand needle positioning devices, more research is needed to understand the cancer detection rates, adverse events and cost effectiveness. The external assessment group commented that the CamPROBE study (Gnanapragasam 2020) is referred to in the Diagnostics assessment report. The external assessment group also said that Marra et al. was excluded from the systematic review because it used mpMRI fusion-targeted biopsy (i.e. use of software to overlay the MRI scan image onto a live ultrasound image), which was not in the NICE scope. Wetterauer et al. was excluded from the systematic review because it was non-comparative (single arm study with LATP).

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Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 22 March 2022
Theme: Cancer detection rates – double freehand

Comment number	Name and organisation	Section number	Comment	NICE response
			We ask that NICE in fairness also say that there is literature showing good detection rates from double freehand but this needs more research. We ask therefore that not just opinion is used in this conclusion. We note that despite the above literature on double free hand being available, the document opined that it might be inferior - whereas when it came to different sorts of freehand LATP, the document opined there was no difference in detection despite there not being any evidence to support this at all. This does not seem balanced or equitable.	

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Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 22 March 2022
Theme: Cost effectiveness – double freehand

Comment number	Name and organisation	Section number	Comment	NICE response
18	JEB	3.9 - LATP using a double freehand coaxial needle technique does not appear to be a cost effective use of NHS resources	The finishing wording in this paragraph states that the "committee concluded that LATP using a double freehand coaxial needle technique did not appear to be cost effective, but this was very uncertain and more evidence was needed". We agree with the very uncertain principle of this statement, but the cost effective statement and the supposed lower cancer detection rates is very much based on opinion and not evidence based on trials or publications. .We suggest that this statement is changed to the following: "committee concluded that there is a lack of data to understand the cost effectiveness of LATP using a double freehand coaxial needle technique, and more evidence was needed"	Thank you for your comment which the committee considered. The committee decided to revise section 3.10 of the diagnostics guidance document The clinical experts noted that the relative risks for cancer detection used in the revised base case model were lower for LATP-other (coaxial needle studies) than for PrecisionPoint and for LA-TRUS. However, confidence intervals were wide and overlapped, therefore it is uncertain whether one technique is better than another. The committee concluded that it was uncertain whether LATP prostate biopsy using a double freehand coaxial needle approach is cost effective. It also recalled that there was no comparative evidence on the CamPROBE double freehand device (section 3.5) and therefore concluded that there was not enough evidence to understand the cost effectiveness of LATP using CamPROBE, and more evidence was needed.

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Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 22 March 2022
Theme: Cost effectiveness – double freehand

Comment number	Name and organisation	Section number	Comment	NICE response
19	University of Cambridge	Diagnostics consultation document Section 1 Page 2 conclusion on recommendations on double freehand-economic assessment And Diagnostic assessment report Page 65	We did not understand how the cost modelling can say that double freehand (as a method) may not be cost-effective when the device costs for double freehand are much lower, whereas consumable costs and reported complications rates are identical across any LATP method. Furthermore, there is an actual Health Economic model on this which is published and cited whereas this is not available for any other devices Therefore, we looked closely at the economic evaluation documents: (i) we cannot see that any recent double freehand method papers have been included in the assessment? (See for example the references in our first comment above) (ii) Furthermore, on page 65 of the health economic assessment – it says "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.: Crucially we therefore we note that Double freehand appears to have been grouped together with grid and stepper (LA TO other) *but they are 2 very different techniques and with vastly different costs.* But when it came to the final report it appears that *the cost effectiveness model ONLY mentions double freehand and not that grid and stepper were included in this (the word LATP other is missing)*	Thank you for your comment which the committee considered. In line with the NICE scope, the external assessment group (EAG) sought to include LATP with a grid and stepping device as a comparator in the economic analysis for decision question 2, but it did not include LATP with a coaxial needle ('double freehand'). In the diagnostics assessment report (DAR) and addenda, the EAG used the estimated cost for LATP using a grid and stepper device (£790.67) for the LATP-other arm. At this cost, LATP-other was dominated in the revised EAG base case and all scenarios presented in the DAR addenda of 10 and 17 January 2022. The EAG conducted additional scenario analyses using the estimated cost of LATP double freehand (£727) for LATP-other (DAR addendum 3, 18 March 2022). The cost-effectiveness results are not sensitive to this change. Despite the lower biopsy

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Diagnostics Advisory Committee date: 22 March 2022
Theme: Cost effectiveness – double freehand

Comment number	Name and organisation	Section number	Comment	NICE response
			Using a grid and stepper (which is similar in cost to GATP apparatus) is considerably more expensive and much more so than double freehand. Therefore, if these are combined then it makes double free hand look much more expensive that it really is. We therefore please ask that this is corrected in this report and economic evaluation for accuracy and fairness. We also please ask to NICE alter this statement on cost effectiveness to at least say that there is no comparative evidence to evaluate cost-effectiveness of double versus freehand and this needs further research - rather than a statement of fact suggesting non-cost effectiveness. OR at least be clear that LATP other (which include GA stepper and grid) is not likely to be cost-effective and not simply say “double freehand” when there does not appear to have been a true comparison of costs. The current statement is in our view, inaccurate.	cost of LATP-other, LATP-freehand is still cost-effective in all subgroups. LATP-other is dominated in all subgroups when costed at the estimated biopsy cost for CamProbe (£785). These results are still subject to uncertainty, due to limitations in the clinical evidence base. The committee decided to revise section 3.10 of the diagnostics guidance document. It concluded that it was uncertain if LATP prostate biopsy using a double freehand coaxial needle approach is cost effective. It also recalled that there was no comparative evidence on the CamPROBE double freehand device. The committee therefore concluded that there was not enough evidence to understand the cost effectiveness of LATP using CamPROBE, and more evidence was needed.

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Theme: Cost effectiveness – double freehand

Comment number	Name and organisation	Section number	Comment	NICE response
20	University of Cambridge	Section 3.9	As discussed above "LA-TP other" in the economic assessment include grid and stepper which is NOT the same as the double freehand. Using step and gird significantly increases costs considerably and in fact by definition is NOT freehand at all as you are using the grid and stepper to fix the probe and the biopsy needle direction They are in fact totally different methods This is not made clear in this section and double free hand is then concluded to be not cost effective We ask NICE to please amend and for fairness state clearly that it is "LATP other "that is not likely to be cost effective not simply double freehand" Once again, the opinion about lower cancer detection rates are not borne out by the published data as detailed in comment 1 above – we ask again for fairness that these statements and conclusions be balanced. i.e. opinion is balanced by the data that is available for double freehand and less firm statements made.	Thank you for your comment which the committee considered In line with the NICE scope, the external assessment group (EAG) sought to include LATP with a grid and stepping device as a comparator in the economic analysis for decision question 2, but it did not include LATP with a coaxial needle ('double freehand'). In the diagnostics assessment report (DAR) and addenda, the EAG used the estimated cost for LATP using a grid and stepper device (£790.67) for the LATP-other arm. At this cost, LATP-other was dominated in the revised EAG base case and all scenarios presented in the DAR Addenda of 10 and 17 January 2022. The EAG conducted additional scenario analyses using the estimated cost of LATP double freehand (£727) for LATP-other (DAR Addendum 3, 18 March 2022). The cost-effectiveness results are not sensitive to this change. Despite the lower biopsy

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Diagnostics Advisory Committee date: 22 March 2022
Theme: Cost effectiveness – double freehand

Comment number	Name and organisation	Section number	Comment	NICE response
				cost of LATP-other, LATP-freehand is still cost-effective in all subgroups. LATP-other is dominated in all subgroups when costed at the estimated biopsy cost for CamProbe (£785). These results are still subject to uncertainty, due to limitations in the clinical evidence base.

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Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 22 March 2022
Theme: Double freehand usability and training

Comment number	Name and organisation	Section number	Comment	NICE response
21	JEB	3.4 - The evidence is not generalisable to double freehand prostate biopsy	The phrasing of this paragraph currently states when referring to Camprobe double free hand techniques as “a more difficult technique because one hand guides the ultrasound probe while the other guides the needle”. Although we accept this statement is based on some expert opinion on the panel, we strongly believe it is also a misleading statement due to none of the experts having used Camprobe to perform a Prostate Biopsy. We would therefore request that this statement is changed to point to the differences between the free hand and double free hand techniques and not include the statements that are based solely on opinions. For example the clinicians we have engaged with in our multicentre (6 separate trusts) CamProbe study all found it a straightforward method to use after only a few cases. They too are clinical experts in biopsy. We suggest the following wording :- “Clinical experts on the panel pointed out the differences of this technique when compared to other LA-Trus procedures in that one hand guides the ultrasound probe while the other guides the needle, and they need to be kept in phase manually”.	Thank you for your comment which the committee considered. The committee decided to remove the description of double freehand being a more difficult technique from section 3.5 and the wording of this paragraph has been revised to highlight the differences between the techniques. Clinical experts noted that for double freehand, one hand guides the ultrasound probe while the other guides the needle, and they need to be kept in phase manually.
22	University of Cambridge	Diagnostics consultation document Section 3.4	While we understand that some clinicians may feel it is harder to use and train for double freehand, there is no actual objective evidence that this is the case. We are concerned that all this section of a very important national recommendation is therefore purely based on opinion and does not cite papers which actually reported on its use. for e.g. The NIHR CamPROBE multicentre study was conducted in 6 centre and recruited 5 centres new to the device and all were trained and used the method	Thank you for your comment which the committee considered. The committee decided to remove the description of double freehand being a more difficult technique from section 3.5 and the wording of this paragraph has been revised to highlight the differences between the techniques. Clinical experts

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Theme: Double freehand usability and training

Comment number	Name and organisation	Section number	Comment	NICE response
			successfully – none of these users were asked about their experience in using the device for this appraisal as far as we are aware. In addition, the double freehand method has been used for decades in Italy, Japan and other countries as a routine prostate biopsy method and disseminated and used in thousands of cases routinely - see these papers as examples from the last 20 years: Emiliozzi P, Longhi S, Scarpone P, Pansadoro A, DePaula F, Pansadoro V. The value of a single biopsy with 12 transperineal cores for detecting prostate cancer in patients with elevated prostate specific antigen. J Urol. 2001 Sep;166(3):845-50. (using LATP double freehand method) Ficarra V, Novella G, Novara G, Galfano A, Pea M, Martignoni G, Artibani W. The potential impact of prostate volume in the planning of optimal number of cores in the systematic transperineal prostate biopsy. Eur Urol. 2005 Dec;48(6):932-7. Kojima M, Hayakawa T, Saito T, Mitsuya H, Hayase Y. Transperineal 12-core systematic biopsy in the detection of prostate cancer. Int J Urol. 2001 Jun;8(6):301-7. In fact the double freehand methods is the original method of LATP biopsies and long predates GA, Grid and stepper and current freehand techniques. We appreciate there is different views and thoughts on this, so we only ask that for fairness we ask that opinion is balanced by highlighting the	noted that for double freehand, one hand guides the ultrasound probe while the other guides the needle, and they need to be kept in phase manually. The external assessment group (EAG) commented that the CamPROBE study (Gnanapragasam et al. 2020) is referred to in the diagnostics assessment report. Emiliozzi et al., Ficarra et al. and Kojima et al. were not identified in the EAG literature searches. However, they would not have been included in the systematic review as they were non-comparative single arm studies.

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Theme: Double freehand usability and training

Comment number	Name and organisation	Section number	Comment	NICE response
			large published evidence and widespread decades long use of the double freehand method for prostate biopsies. Opinion and anecdote is hard to rebut and there is no evidence or data to compare if the “freehand methods” are easier or harder to learn than “double freehand”. So for fairness we ask this statement is balanced that there is also no studies or evidence comparing ease of uptake and dissemination between methods. In the same way the statement that smaller lesions are harder to target is also pure opinion -the key is whether MRI is used to guide biopsies or not and whether fusion technology is used – all biopsy methods are harder for small lesions and - Is there evidence that freehand is better than double freehand or even TRUS for smaller lesion? Again for fairness we ask that this lack of objective evidence is mentioned and no statement made only using opinion.	The committee agreed with removing the statement about smaller lesions being harder to target from section 3.5 in the diagnostics guidance document. The external assessment group commented that fusion technology biopsy was not within the NICE scope of the assessment; and there were relatively few studies reporting use of mpMRI in prostate biopsy.

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Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 22 March 2022
Theme: General comments

Comment number	Name and organisation	Section number	Comment	NICE Response/EAG considerations
23	JEB	1.1 Recommendations	We consider the wording that states Precision point is "an option for diagnosing prostate cancer" to be factually incorrect. None of the devices assessed diagnoses prostate cancer, but they do "facilitate" in the diagnosing of prostate cancer by helping to acquire tissue samples in the form of biopsy cores. We therefore suggest the inclusion of the word "facilitate biopsy acquisition" or "obtaining biopsy cores" in this statement which would be in line with the intended use of Precision Point	Thank you for your comment which the committee considered. This wording is a NICE editorial preference based on the view that the biopsy is part of the diagnostic process.
24	Prostate Cancer UK	General	We are happy that all the relevant evidence has been taken into account. We recognise that the evidence base is not extensive and may have been generated prior to the mpMRI-led diagnostic pathway being introduced, but the best possible synthesis of it has been made.	Thank you for your comment which the committee considered.
25	Prostate Cancer UK	General	We are satisfied with the summary of clinical effectiveness. We will not comment on cost-effectiveness analyses.	Thank you for your comment which the committee considered.
26	Prostate Cancer UK	General	We consider the recommendation for NHS practise sound.	Thank you for your comment which the committee considered.
27	Prostate Cancer UK	1 - Recommendations	We are pleased at the recommendation to engage with the TRANSLATE study and hope this will fill in gaps in the evidence base in future.	Thank you for your comment which the committee considered.
28	BXTAccelyon Ltd	1.1	We are pleased to note that PrecisionPoint has been recommended as an option for diagnosing Prostate Cancer	Thank you for your comment which the committee considered.

Diagnostic Assessment Report commissioned by the NIHR on behalf of the National Institute for Health and Care Excellence

Transperineal biopsy in people with suspected prostate cancer - a systematic review and economic evaluation Addendum 3

Produced by Southampton Health Technology Assessments Centre (SHTAC)

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1 Introduction

The NICE scope for decision question 2 included LATP using a grid and stepping device (in addition to GATP and LA-TRUS) as comparators for LATP with the named freehand devices. For the DAR analysis, we grouped evidence relating to LATP biopsy without a named freehand device together as 'LATP-other', see Figure 1 below for the evidence network. Cancer detection rates for LATP-other compared with LA-TRUS in our network meta-analysis (NMA) were based on four RCTs: Cerruto et al.[1] reported using a coaxial needle (double freehand); Takenaka et al.[2] reported using a grid and stepping device; and the other two studies (Guo et al.[3] and Hara et al.[4]) did not report what LATP technique they had used (although it has been suggested to us that Guo et al. used double freehand). Evidence for GATP compared with LATP-other (grid and stepper) came from a trial by Lv et al.[5]

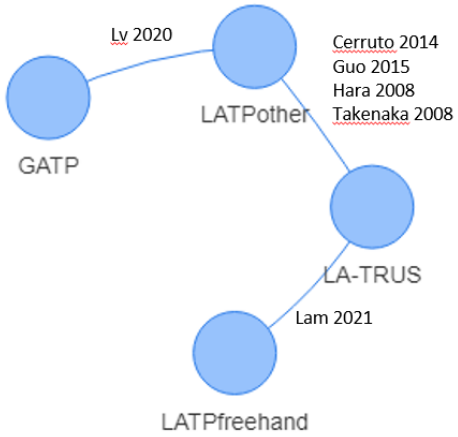

Figure 1 Evidence network for indirect comparison of LATP-freehand, LATP-other, LATRUS and GATP grid and stepping device cancer detection (decision question 2)

We presented a revised EAG base case analysis in the DAR Addendum of 10 January 2022. This included a number of changes to our original base case, including exclusion of the Hara trial from the NMA on the basis that it had used a regional method of anaesthesia (caudal block) rather than local anaesthesia. In a second DAR addendum on 17 January 2022, we presented another scenario also excluding the Takenaka study, which had also used caudal block anaesthesia. The cost-effectiveness results were not sensitive to exclusion of the Hara and Takenaka studies (Addendum 1 Table 22 and Addendum 2 Table 4).

A response to the NICE Diagnostics Consultation Document (comment 12) questioned the conclusion that cost-effectiveness modelling suggests that double freehand LATP techniques may not be cost effective compared with LA-TRUS biopsy. It noted that evidence

for the EAG analyses pooled evidence for LATP with grid and stepping device and double freehand, and that the cost of the cost of LATP-other was based on the estimated cost for LATP biopsy using grid and stepper device (£791). To explore this issue further, we report additional scenarios below, using the cost of LATP biopsy with a double freehand technique (£727) or LATP biopsy with the CamPROBE double freehand device (£785) for the LATP-other comparator.

2 EAG revised base case excluding Hara et al.

In this section we report additional scenarios changing the cost of LATP-other applied to our revised base case, with the Hara trial excluded from the NMA (Table 28 DAR Addendum 1, 10 Jan 2022). The two new scenarios do not affect the cost-effectiveness results for decision question 2 (Table 1 and Table 2 below). The ICER for LATP-freehand compared with LATRUS is constant across the scenarios because the cost of LATP-other does not affect this comparison. Although the total costs of LATP-other are reduced in both scenarios, LATP-other and GATP are dominated for all subgroups and scenarios.

Table 1 Additional economic scenarios on the cost of LATP-other for decision question 2, subgroup A (deterministic)

Biopsy method	Cost	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case (excluding Hara): Cost of grid and stepper						
LATRUS	£681	£19,878	9.2989			
LATP-freehand	£781	£19,888	9.3122	£10	0.0133	£743
LATP-other	£791	£19,966	9.3001	£77	-0.0120	Dominated
GATP	£1,251	£20,437	9.2982	£471	-0.0019	Dominated
Cost of LATP-other scenario 1: Cost of double freehand						
LATRUS	£681	£19,878	9.2989			
LATP-freehand	£781	£19,888	9.3122	£10	0.0133	£743
LATP-other	£727	£19,902	9.3001	£14	-0.0120	Dominated
GATP	£1,251	£20,437	9.2982	£535	-0.0019	Dominated
Cost of LATP-other scenario 2: Cost of CamPROBE						
LATRUS	£681	£19,878	9.2989			
LATP-freehand[a]	£780	£19,887	9.3122	£9	0.0133	£682
LATP-other	£785	£19,960	9.3001	£73	-0.0120	Dominated
GATP	£1,251	£20,437	9.2982	£477	-0.0019	Dominated
[a] Cost of LATP-freehand does not include the cost of CamPROBE						

Table 2 Additional economic scenarios on the cost of LATP-other for decision question 2, subgroup comparison (deterministic)

Biopsy method	Cost	ICERs (£ per QALY gained)			
		Subgroup A	Subgroup B	Subgroup C	Subgroup D
Revised EAG base case (excluding Hara): Cost of grid and stepper					
LATRUS	£681				
LATP-freehand	£781	£743	£4,595	£9,284	£10,640
LATP-other	£791	Dominated	Dominated	Dominated	Dominated
GATP	£1,251	Dominated	Dominated	Dominated	Dominated
Cost of LATP-other scenario 1: Cost of double freehand					
LATRUS	£681				
LATP-freehand	£781	£743	£4,595	£9,284	£10,640
LATP-other	£727	Dominated	Ext. dom.	Ext. dom.	Ext. dom.
GATP	£1,251	Dominated	Dominated	Dominated	Dominated
Cost of LATP-other scenario 2: Cost of CamPROBE					
LATRUS	£681				
LATP-freehand[a]	£780	£682	£4,489	£9,121	£10,453
LATP-other	£785	Dominated	Dominated	Dominated	Dominated
GATP	£1,251	Dominated	Dominated	Dominated	Dominated

[a] Cost of LATP-freehand does not include the cost of CamPROBE
Ext. Dom. Extendedly dominated by LATP-freehand and LATRUS

3 EAG revised base case excluding Hara and Takenaka

In this section we report the additional cost scenarios for LATP-other applied to our revised base case with both Hara and Takenaka trials excluded from the NMA (Table 3 and 4 of the DAR Addendum 2 of 17 Jan 2022). In this case, the interpretation of the results is a little more complicated, but the conclusions do not change at conventional cost-effectiveness thresholds (see Table 3 and Table 4 below).

With the biopsy cost of LATP-other based on the double freehand technique (£727), the total cost for LATP-other is below that of LATP-freehand. In subgroup A, the ICER for LATP-freehand is the same as in the base case and LATP-other is extendedly dominated (the ICER for LATP-freehand compared with LA-TRUS is lower than that for LATP-other). This is also true with this scenario in subgroup B. For subgroups C and D, although LATP-other is not dominated, LATP-freehand remains the most cost-effective option with fully incremental ICERs below £20,000 per QALY gained.

At the biopsy cost of CamPROBE, LATP-other is dominated in all subgroups.

Table 3 Additional economic scenarios on the cost of LATP-other for decision question 2, subgroup A (deterministic)

Biopsy method	Cost	Total		Incremental		ICERs
		Cost	QALYs	Cost	QALYs	£/QALY
Revised EAG base case (excluding Hara and Takenaka): Cost of grid and stepper						
LATRUS	£681	£19,878	9.2989			
LATP-freehand	£781	£19,888	9.3122	£10	0.0133	£743
LATP-other	£791	£19,952	9.3026	£63	-0.0096	Dominated
GATP	£1,251	£20,420	9.3012	£468	-0.0014	Dominated
Cost of LATP-other scenario 1: Cost of double freehand						
LATRUS	£681	£19,878	9.2989			
LATP-other	£727	£19,888	9.3026	£10	0.0037	Ext. Dom.
LATP-freehand	£781	£19,888	9.3122	£0	0.0096	£743
GATP	£1,251	£20,420	9.3012	£532	-0.0109	Dominated
Cost of LATP-other scenario 2: Cost of CamPROBE						
LATRUS	£681	£19,878	9.2989			
LATP-freehand [a]	£780	£19,887	9.3122	£9	0.0133	£682
LATP-other	£785	£19,946	9.3026	£59	-0.0096	Dominated
GATP	£1,251	£20,420	9.3012	£474	-0.0014	Dominated

[a] Cost of LATP-freehand does not include the cost of CamPROBE
Ext. Dom. Extendedly dominated by LATP-freehand and LATRUS

Table 4 Additional economic scenarios on the cost of LATP-other for decision question 2, subgroup comparison (deterministic)

Biopsy method	Cost	ICERs (£ per QALY gained)			
		Subgroup A	Subgroup B	Subgroup C	Subgroup D
Revised EAG base case (excluding Hara & Takenaka: grid and stepper					
LATRUS	£681				
LATP-freehand	£781	£743	£4,595	£9,284	£10,640
LATP-other	£791	Dominated	Dominated	Dominated	Dominated
GATP	£1,251	Dominated	Dominated	Dominated	Dominated
Cost of LATP-other scenario 1: Cost of double freehand					
LATRUS	£681				
LATP-other	£727	Ext. Dom.	Ext. Dom.	£4,385	£5,810
LATP-freehand	£781	£743	£4,595	£16,196	£16,970
GATP	£1,251	Dominated	Dominated	Dominated	Dominated
Cost of LATP-other scenario 2: Cost of CamPROBE					
LATRUS	£681				
LATP-freehand [a]	£780	£682	£4,489	£9,121	£10,453
LATP-other	£785	Dominated	Dominated	Dominated	Dominated
GATP	£1,251	Dominated	Dominated	Dominated	Dominated

[a] Cost of LATP-freehand does not include the cost of CamPROBE
Ext. Dom.: Extendedly dominated by LATP-freehand and LATRUS

1. Cerruto MA, Vianello F, D'Elia C, et al. Transrectal versus transperineal 14-core prostate biopsy in detection of prostate cancer: a comparative evaluation at the same institution. *Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica* 2014;86(4):284-7. doi: 10.4081/aiua.2014.4.284
2. Takenaka A, Hara R, Ishimura T, et al. A prospective randomized comparison of diagnostic efficacy between transperineal and transrectal 12-core prostate biopsy. *Prostate Cancer and Prostatic Diseases* 2008;11(2):134-38. doi: 10.1038/sj.pcan.4500985
3. Guo L-H, Wu R, Xu H-X, et al. Comparison between Ultrasound Guided Transperineal and Transrectal Prostate Biopsy: A Prospective, Randomized and Controlled Trial. *Scientific Reports* 2015;5(1):16089. doi: 10.1038/srep16089
4. Hara R, Jo Y, Fujii T, et al. Optimal approach for prostate cancer detection as initial biopsy: prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. *Urology* 2008;71(2):191-5. doi: 10.1016/j.urology.2007.09.029
5. Lv Z, Jiang H, Hu X, et al. Efficacy and safety of periprostatic nerve block combined with perineal subcutaneous anaesthesia and intrarectal lidocaine gel in transrectal ultrasound guided transperineal prostate biopsy: A Prospective Randomised Controlled Trial. Prostate Cancer and Prostatic Diseases, 2020:74-80.