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

Inês Souto-Ribeiro, Lois Woods, Emma Maund, David Alexander Scott, Joanne Lord, Joanna Picot and Jonathan Shepherd*

Southampton Health Technology Assessments Centre (SHTAC), University of Southampton, Southampton, UK

*Corresponding author jps@soton.ac.uk

Published October 2024
DOI: 10.3310/ZKTW8214

Scientific summary

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

Health Technology Assessment 2024; Vol. 28: No. 60
DOI: 10.3310/ZKTW8214

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Background

Prostate cancer accounts for 30% of all cancers diagnosed in men in the UK and the incidence is rising. It is more common in men over 45 years of age. Symptoms that cannot be attributed to other health conditions include lower back or bone pain, lethargy, erectile dysfunction, haematuria, weight loss and lower urinary tract symptoms.

National Institute for Health and Care Excellence (NICE) guideline NG12 advises on recognition and referral of people presenting with possible prostate cancer. A prostate-specific antigen (PSA) test and digital rectal examination should be performed. If PSA levels are raised above normal or if the prostate feels malignant, then the person should be referred for suspected cancer. NICE guideline NG131 advises on diagnosis and management. It recommends a multiparametric magnetic resonance imaging (mpMRI) test with the results reported using a five-point Likert scale to indicate how likely the presence of prostate cancer is.

The Likert scale score, or alternatively the Prostate Imaging Reporting and Data System (PI-RADS score, not mentioned in the NICE guideline), is used to assess whether the person is offered a prostate biopsy. People with a score of 3 or above should be offered a multiparametric magnetic resonance imaging (mpMRI)-influenced prostate biopsy. People with a score of 1 or 2 will discuss risks and benefits with a clinician and if a prostate biopsy goes ahead, it should be a systematic biopsy.

Two main options for biopsy are transrectal ultrasound prostate biopsy under local anaesthetic (LATRUS) and transperineal prostate biopsy under general anaesthetic (GATP). Biopsies can be either targeted (based on mpMRI findings) or systematic (samples are taken according to a predefined scheme) or both. Recent studies suggest that performing transperineal prostate biopsy under local anaesthetic (LATP) could better identify cancer in particular regions of the prostate and could have lower infection rates than transrectal biopsies while also being able to be carried out in an outpatient setting. Transperineal prostate biopsy is usually carried out under general anaesthetic due to pain caused by the procedure and tolerability is a key issue.

Various freehand devices to assist with LATP prostate biopsy are being introduced to the market. The six specific freehand devices specified in the NICE scope for this review are: Cambridge Prostate Biopsy Device (CamPROBE) (JEB Technologies Ltd, Suffolk, UK); EZU-PA3U (Hitachi Ltd, Tokyo, Japan); PrecisionPoint™ Transperineal Access System (BXTAccelyon Ltd, Burnham, UK); SureFire Guide (LeapMed, Jiangsu, China); Trinity® Perine Grid (KOELIS®, NJ, USA); UA1232 puncture attachment (BK Medical, MA, USA).

Objectives

The aim of this review is to evaluate the diagnostic yield, clinical effectiveness and cost-effectiveness of LATP prostate biopsies performed with or without available specialist devices and equipment, in people with suspected prostate cancer.

Two decision questions were prioritised by NICE for this assessment, with input from relevant stakeholders:

Decision question 1. Do LATP prostate biopsies in patients with suspected prostate cancer represent a clinically and cost-effective use of National Health Service (NHS) resources?

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

There are five comparisons required to address the two decision questions in the NICE scope:

1. LATP-any (using coaxial needle or grid and stepping device or freehand device) versus LATRUS
2. LATP-any (using coaxial needle or grid and stepping device or freehand device) versus GATP
3. LATP-freehand (freehand device only) versus LATRUS
4. LATP-freehand (freehand device only) versus GATP
5. LATP-freehand (freehand device only) versus LATP-grid and stepping device.

Methods

Systematic review of diagnostic test evaluation and clinical effectiveness

A systematic review of diagnostic and clinical effectiveness evidence was conducted following a peer-reviewed protocol. Searches were based on a comprehensive search strategy. Bibliographic databases, including MEDLINE, EMBASE, Web of Science, The Cochrane Library and the International HTA database, were searched for English-language references in July 2021, and these searches were updated at the end of October 2021. Urology conferences and freehand-device company submissions were hand-searched, and reference lists of identified systematic reviews and meta-analyses were checked. Relevant studies were sought through contact with study authors and NICE Specialist Committee members.

Studies were eligible if they included people with suspected prostate cancer with an indication for prostate biopsy and reported diagnostic yield, for example, cancer detection rates, or other clinical or patient-reported outcomes. The eligible interventions were any LATP biopsy (of which LATP-freehand biopsy is a subset) and the eligible comparators were LATRUS and GATP; the LATP-grid and stepping device was an eligible comparator when compared with the LATP-freehand intervention.

The Cochrane risk of bias tool (version 1) was used to assess risk of bias for the included randomised controlled trials (RCTs) and The Joanna Briggs Institute critical appraisal checklists were used to assess the included observational studies. Two reviewers carried out study selection, data extraction and critical appraisal, with any disagreements resolved through discussion and referred to a third reviewer for resolution as necessary.

We conducted meta-analysis of the cancer detection rate outcomes for which sufficient comparative data were available. Pairwise meta-analysis was conducted for the above comparisons, with randomised and non-randomised studies analysed separately. Network meta-analysis was conducted for the two decision questions specified in the NICE scope. We synthesised the data for other outcomes narratively, as evidence was too sparse for meta-analysis.

Review of economic evaluations

We conducted a systematic review of the cost-effectiveness of the prostate biopsy methods in scope. The search strategies were based on an early version of the clinical effectiveness searches with the addition of an economics search filter. Included studies were full economic evaluations that assessed both costs and consequences for the different prostate biopsy methods. Outcomes included measures of resource use and costs and health outcomes: life-years or quality-adjusted life-years (QALYs) gained. Economic evaluations not meeting the inclusion criteria and studies that reported on resource use and costs, and health-related quality of life (utilities) were assessed as potential sources of information for the economic model.

External Assessment Group independent economic assessment

We developed a decision model to estimate the cost-effectiveness of alternative biopsy methods for people referred for biopsy with suspected prostate cancer. The model includes a decision tree to estimate diagnostic outcomes and biopsy-related complications, and a Markov model that predicts the long-term costs and consequences of false-negative biopsy results. We assessed cost-effectiveness for four subgroups at different prior levels of risk, based on previous mpMRI results (Likert 1 or 2; or Likert 3 or more) and history of prostate biopsy (none; previous negative biopsy).

The decision tree used published results from the economic evaluation of the Prostate MR imaging study (PROMIS) to estimate baseline prevalence in the subgroups of interest, and diagnostic yield of LATRUS biopsy. Cancer detection rates were adjusted for the other biopsy methods using relative risks (RRs) from our network meta-analyses, and evidence from the literature on biopsy complication rates and the probability of repeat biopsy. Costs of the biopsy methods were estimated in a microcosting analysis, as well as from submitted evidence and published sources. The Markov model was a replicated version of a model developed for the 2019 update of the NICE guideline (NG131). Model parameters were based on those in the NG131 model, with some adjustments to costs and utilities from more recent published sources.

Results

Systematic review of diagnostic test evaluation and clinical effectiveness

The literature searches identified a total of 1969 references of which 111 references were subjected to full-text screening. Twenty-seven publications reported 23 studies meeting the inclusion criteria for this review: 19 comparative studies of which 6 were RCTs and 13 were observational studies (1 of which is unpublished); and 4 single-arm studies for LATP-freehand devices where no comparative evidence was identified.

There were no statistically significant differences in cancer detection rates for LATP (any method) compared to LATRUS with RR = 1.00 [95% confidence interval (CI) 0.85 to 1.18] (*n* = 5 RCTs). A single randomised trial estimated a non-significant difference in cancer detection rates in favour of LATP using a freehand device (PrecisionPoint) compared to LATRUS RR = 1.40, 95% CI 0.96 to 2.04. This finding was supported by meta-analysis of observational comparative studies RR = 1.21 (95% CI 1.08 to 1.34) (*n* = 4 studies). There were no statistically significant differences in cancer detection rates in meta-analyses comparing other biopsy methods. Evidence from the systematic review for other clinical outcomes, biopsy-related complications and patient-reported outcomes was sparse.

Review of economic evaluations

One economic evaluation was eligible for inclusion in the economic review out of 725 results from the original and update searches. This study evaluated the CamPROBE (LATP-freehand) device versus LATRUS for use in diagnosing prostate cancer from the perspective of the UK NHS. It used a decision-tree model with a Markov model at the terminal nodes and was informed by a prospective case series for the CamPROBE device and data from the PROMIS study. The study suggested that compared with LATRUS, LATP using the CamPROBE freehand device would be cost saving at a device price below £41 per procedure, or more cost-effective at the £20,000 per QALY threshold with a price below £81 per procedure. These calculations assume a zero rate of infection for LATP and equal diagnostic accuracy for LATP using CamPROBE and LATRUS. We considered 13 excluded economic studies as sources to inform our model structure and inputs, including the cost-effectiveness analysis for the PROMIS study and the analysis for the update of the NICE guideline on prostate cancer published in May 2019 (NG131).

Evidence from the BXTAccelyon company submission included a cost minimisation study developed in 2020 by the York Health Consortium that compared the costs of LATP (with the PrecisionPoint freehand device) with different combinations of LATRUS and GATP for UK NHS Trusts. The study suggests that

LATP using the PrecisionPoint freehand device is cost saving, assuming equal diagnostic yield of the different biopsy methods.

Independent economic assessment

The base-case economic analysis comparing LATP (all methods) with LATRUS and GATP indicated that LATP is likely to be the most cost-effective option in all four subgroups, with incremental cost-effectiveness ratio (ICER) estimates for LATP compared with LATRUS below £20,000 per QALY gained, and GATP estimated as more expensive and less effective than LATP. These conclusions were supported by probabilistic sensitivity analysis and a wide range of scenario analyses, although the results for LATP compared with LATRUS were sensitive to some alternative sources of cancer detection rates, rates of biopsy-related hospital admissions, numbers of core samples and histopathology costs.

The economic analysis including LATP-freehand compared with other LATP methods, as well as LATRUS and GATP, indicated that LATP with a freehand device was the most cost-effective strategy, with an ICER of £743 per QALY for the highest-risk subgroup with MRI Likert score of 3 or more at first biopsy, and £4595 per QALY for the subgroup with a MRI Likert score 1 or 2 at first biopsy. For the subgroups with a previous negative biopsy, the ICER remained below £20,000 per QALY. Again, probabilistic sensitivity analysis supported these results, but scenario analysis highlighted uncertainty related to the cost of the devices, the number of core samples and costs of processing them, and the use of other sources of evidence for cancer detection and biopsy-related complication rates.

The more favourable cost-effectiveness estimates for LATP with a freehand device are mostly driven by the cancer detection rates, which rest on a single RCT for LATP with a freehand device (PrecisionPoint). In the scenario based on observational evidence of cancer detection rates, the ICERs for LATP with a freehand device were less favourable, although still well below £20,000 per QALY. Increasing the cost of LATP with a freehand device by assuming the cost of the most expensive device, the ICER remained below £20,000 per QALY for the highest-risk subgroup but not for the other subgroups.

Conclusions

Transperineal prostate biopsy under local anaesthetic is equally efficient at detecting prostate cancer as transrectal ultrasound-guided prostate biopsy under local anaesthetic but evidence from one RCT, supported by observational studies, suggests that it might be better when using a freehand device. Local anaesthetic transperineal prostate biopsy is associated with urinary retention-type complications, whereas local anaesthetic transrectal ultrasound-guided prostate biopsy has a higher infection rate. Economic evaluation suggests that LATP with a freehand device is likely to be cost-effective compared with LATP with other methods, LATRUS and GATP for patients with no previous biopsy at high risk of having prostate cancer indicated by previous MRI results. This result is sensitive to the estimated cost of the freehand device, the number of and cost of core samples taken, and the sources for biopsy complication rates.

Recommendations for research

- *Evidence for freehand devices*. There was no comparative evidence for several of the freehand devices in the NICE scope. The TRANSLATE study is expected to help address this question, as it is evaluating the PrecisionPoint, UA1232 and 'any ultrasound probe-mounted needle guidance device'.
- *Outcomes not covered in included available evidence*. We suggest that incidence of defined complications (standardised for grading of severity and length of follow-up), health-related quality of life and longer-term clinical outcomes could be defined in a core outcome set.
- *LATP versus GATP*. Evidence for this comparison is sparse (we identified one RCT reporting cancer detection rates).

- *Repeat biopsy population*. There is a need for separate reporting of results for this subgroup, or a separate prospective RCT.
- *UK NHS setting*. The three UK studies included in our review were single-centre observational studies with a limited set of outcomes. The TRANSLATE study is expected to remedy this; it is a multicentre randomised study across nine NHS Trusts in England.

Study registration

This study is registered as PROSPERO CRD42021266443.

Funding

This awardproject was funded by the National Institute for Health and Care Research (NIHR) Evidence Synthesis programme (NIHR award ref: NIHR134220) and is published in full in *Health Technology Assessment* Vol. 28, No. 60. See the NIHR Funding and Awards website for further award information.

Health Technology Assessment

NICE DAR

ISSN 2046-4924 (Online)

Impact factor: 3.6

A list of Journals Library editors can be found on the NIHR Journals Library website

Launched in 1997, *Health Technology Assessment* (HTA) has an impact factor of 3.6 and is ranked 32nd (out of 105 titles) in the 'Health Care Sciences & Services' category of the Clarivate 2022 Journal Citation Reports (Science Edition). It is also indexed by MEDLINE, CINAHL (EBSCO Information Services, Ipswich, MA, USA), EMBASE (Elsevier, Amsterdam, the Netherlands), NCBI Bookshelf, DOAJ, Europe PMC, the Cochrane Library (John Wiley & Sons, Inc., Hoboken, NJ, USA), INAHTA, the British Nursing Index (ProQuest LLC, Ann Arbor, MI, USA), Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and the Science Citation Index Expanded™ (Clarivate™, Philadelphia, PA, USA).

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta.

Criteria for inclusion in the *Health Technology Assessment* journal
Manuscripts are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

This article

The research reported in this issue of the journal was funded by the HTA programme as award number NIHR134220. The contractual start date was in June 2021. The draft manuscript began editorial review in December 2021 and was accepted for publication in December 2022. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' manuscript and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this article.

This article presents independent research funded by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care.

This article was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Newgen Digitalworks Pvt Ltd, Chennai, India (www.newgen.co).