Local anaesthetic transperineal biopsy versus transrectal prostate biopsy in prostate cancer detection (TRANSLATE): a multicentre, randomised, controlled trial

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Summary

Background Prostate cancer diagnosis requires biopsy, traditionally performed under local anaesthetic with ultrasound guidance via a transrectal approach (TRUS). Local anaesthetic ultrasound-guided transperineal biopsy (LATP) is gaining popularity in this setting; however, there is uncertainty regarding prostate sampling, infection rates, tolerability, side-effects, and cost-effectiveness. TRANSLATE was a randomised clinical trial that aimed to compare detection of Gleason Grade Group (GGG) 2 or higher prostate cancer, side-effects, tolerability, and patient-reported outcomes, after LATP versus TRUS biopsy.

Methods In this randomised clinical trial which was done at ten hospitals in the UK, patients aged 18 years or older were eligible if investigated for suspected prostate cancer based on elevated age-specific prostate-specific antigen or abnormal digital rectal examination, and if biopsy-naive having received pre-biopsy MRI on a 1·5 or higher Tesla scanner. Individuals were excluded if they had any previous prostate biopsy, extensive local disease easily detectable by any biopsy (prostate-specific antigen >50 ng/mL or entire gland replaced by tumour on MRI), symptoms of concurrent or recent urinary tract infection, history of immunocompromise, need for enhanced antibiotic prophylaxis, absent rectum, or inability to position in lithotomy. Participants were randomly assigned in a 1:1 ratio to receive LATP or TRUS biopsy, using web-based software with a randomisation sequence using a minimisation algorithm to ensure balanced allocation across biopsy groups for minimisation factors (recruitment site, and location of the MRI lesion). The primary outcome was detection of GGG 2 or higher prostate cancer, analysed in the modified intention-to-treat population (all randomly assigned to treatment who had a biopsy result available). Key secondary endpoints assessing post-biopsy adverse events were infection, bleeding, urinary and sexual function, tolerability, and patient-reported outcomes. This trial is registered with ClinicalTrials.gov (NCT05179694) and at ISRCTN (ISRCTN98159689), and is complete.

Findings Between Dec 3, 2021, and Sept 26, 2023, 2078 (76%) of 2727 assessed individuals were eligible, and 1126 (41%) of 2727 agreed to participate. 1044 (93%) of the 1126 participants were White British. Participants were allocated to TRUS (n=564) or LATP (n=562) biopsy, and were followed up at time of biopsy, and at 7 days, 35 days, and 4 months post-biopsy. We found GGG 2 or higher prostate cancer in 329 (60%) of 547 participants with biopsy results randomly assigned to LATP compared with 294 (54%) of 540 participants with biopsy results randomly assigned to TRUS biopsy (odds ratio [OR] 1·32 [95% CI 1·03–1·70]; p=0·031). Infection requiring admission to hospital within 35 days post-biopsy occurred in 2 (<1%) of 562 participants in the LATP group compared with 9 (2%) of 564 in the TRUS group. No statistically significant difference was observed in the reporting of overall biopsy-related complications (LATP 454 [81%] of 562 *vs* TRUS 436 [77%] of 564, OR 1·23 [95% CI 0·93 to 1·65]), urinary retention requiring catheterisation (LATP 35 [6%] of 562 *vs* TRUS 27 [5%] of 564), urinary symptoms (median International Prostate Symptom Score: LATP 8 [IQR 4–14] *vs* TRUS 8 [4–13], OR 0·36 [95% CI –0·38 to 1·10]), nor sexual function (median International Index of Erectile Function score: LATP 5 [2–25] *vs* TRUS 8 [3–24], OR –0·60 [–1·79 to 0·58]) at 4 months after biopsy. Trial participants more commonly reported LATP biopsy to be immediately painful and embarrassing compared with TRUS (LATP 216 [38%] of 562 *vs* TRUS 153 [27%] of 564; OR 1·84 [95% CI 1·40 to 2·43]). Serious adverse events occurred in 14 (2%) of 562 participants in the LATP group and 25 (4%) of 564 in the TRUS group.

Interpretation Among biopsy-naive individuals being investigated for possible prostate cancer, biopsy with LATP led to greater detection of GGG 2 or higher disease compared with TRUS. These findings will help to inform patients, clinicians, clinical guidelines, and policy makers regarding the important trade-offs between LATP and TRUS prostate biopsy.

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Introduction

Prostate biopsy is key for prostate cancer diagnosis,[1,2] with more than 1 million procedures done annually in the USA alone.[3] Prostate biopsy has been performed mostly via the transrectal route, using transrectal ultrasound (TRUS) guidance. Local anaesthetic transperineal (LATP) biopsy is now gaining popularity,[4–7] given concerns about infectious complications following TRUS biopsy,[8–10] expedited during the COVID-19 pandemic,[11] and the perceived superiority of transperineal targeting of MRI-visible anterior and apical lesions.

Until recent randomised controlled trial evidence published in the last year, the shift from TRUS to LATP biopsy was based on evidence from cohort studies.[4–6,12–15] Randomised controlled trials comparing these approaches have reported inconclusive findings for cancer detection (PERFECT[16]) and infection rates (PROBE-PC[17] and PREVENT[18]), which might be indicative of the trials' designs, inadequate power, and low event rates.

We conducted the Transrectal versus Local Anaesthetic Transperineal Prostate Biopsy Evaluation (TRANSLATE) Trial to compare LATP and TRUS biopsy for the detection of clinically significant prostate cancer.[19] We aimed to investigate whether improved ability of LATP to target anterior and apical lesions, and the coaxial route parallel to the long axis of the prostate, results in greater detection of Gleason Grade Group (GGG) 2 or higher prostate cancer.

Methods

Study design and participants

TRANSLATE was a multicentre, UK-wide, pragmatic, open-label, randomised, controlled superiority trial,[19] with a research question shaped by involvement of patient representatives, and with internal feasibility and main phases done in ten hospitals across the UK (appendix 1 p 8). We aimed to open recruitment centres representing as diverse a population of recruited participants as possible, however many large urban conurbations such as London had already wholly transitioned to LATP by the time the study commenced; despite this, the trial was able to open recruitment centres in three of the four Home Nations of the UK (England, Scotland, and Wales). Biopsy-naive individuals aged 18 years or older with suspected prostate cancer based on elevated age-specific prostate-specific antigen, an abnormal digital rectal examination, or a pre-biopsy MRI on a 1·5 or higher Tesla scanner, were eligible. Individuals were excluded if they had any of the following: previous prostate biopsy, extensive local disease easily detectable by any biopsy (prostate-specific

Research in context

Evidence before this study

Currently, approximately 70 000 prostate biopsies are performed each year in the UK, and 350 000 per year in the USA, to investigate men at risk of having prostate cancer. There is an ongoing debate and considerable uncertainty regarding the best approach to undertake prostate biopsies in the diagnostic pathway. For decades, the conventional approach to prostate biopsies has been through the transrectal route (TRUS). However, in recent years, transperineal prostate biopsy under local anaesthetic (LATP) has been developed as an alternative approach, aiming to improve cancer detections and reduce rates of post-biopsy infection. However, there has been a absence of level 1 evidence to inform clinical practice, with adoption of LATP on an ad-hoc basis, driven by enthusiasts, leading to inequality of access to each type of biopsy. We searched PubMed with no language restrictions using the search terms ("transperineal" and "prostate" and "RCT or randomised trial" and "2023 or 2024") and identified three prospective randomised controlled trials comparing LATP and TRUS. The primary outcomes were rates of infectious complications (PROBE-PC, n=718 participants; PREVENT, n=567 participants) and detection rate of clinically significant prostate cancer (Gleason grade group [GGG] ≥2 prostate cancer; PERFECT, n=250 participants). The results of these three randomised controlled trials showed similar rates of infectious and other complications, and similar rates of detection of GGG 2 or higher prostate cancer, although they were potentially underpowered to detect a difference between the two biopsy approaches.

Added value of this study

To our knowledge, TRANSLATE is the largest randomised controlled trial of LATP versus TRUS (n=1126) in biopsy-naive individuals being investigated for possible prostate cancer. All participants received pre-biopsy MRI. To our knowledge, this is the first trial to show the superiority of LATP versus TRUS in detection of GGG 2 or higher prostate cancer. We also evaluated the rates of infection, other post-biopsy complications such as post-procedure bleeding, acute urinary retention, and impact on urinary and sexual function. Additional outcomes measured included procedure tolerability, quality of life, and secondary histopathological findings.

Implications of all the available evidence

The TRANSLATE trial provides randomised controlled trial evidence regarding which type of prostate biopsy to perform in the outpatient setting in the diagnostic evaluation of men with possible prostate cancer. These findings will help to inform patients, clinicians, clinical guidelines, and policy makers regarding the important trade-offs between LATP and TRUS prostate biopsy.

antigen >50 ng/mL or entire gland replaced by tumour on MRI), symptoms of concurrent or recent urinary tract infection, history of immunocompromise, need for enhanced antibiotic prophylaxis, absent rectum, inability to position in lithotomy, or inability to undergo MRI. Participants were required to provide informed written electronic or paper-based consent.

The trial was coordinated by the University of Oxford, overseen by a Trial Steering Committee and independent Data Safety and Monitoring and Committee. The Oxford 'C' Research Ethics committee approved the trial (REC reference number: 21/SC/0274), which was conducted according to local regulations using principles outlined in the Declaration of Helsinki and Good Clinical Practice. The trial is registered on ClinicalTrials.gov (NCT05179694) and with the ISRCTN (ISRCTN98159689). The protocol has been published previously.[19]

Randomisation and masking

After a research nurse or delegated member of the research team obtained informed consent, web-based randomisation software assigned patients in a 1:1 ratio to LATP or TRUS. The randomisation sequence was generated using a minimisation algorithm to ensure balanced allocation across biopsy groups for minimisation factors: recruitment site, and location of the MRI lesion ("no significant lesion"; "significant lesion, including anterior"; or "significant lesion, but not anterior"). Minimisation was performed on a secure web-based form in the study randomisation system RRAMP version 3.4.12, which was accessible to the statisticians and programmers for the purpose of monitoring randomisation. 20 participants randomly assigned by simple randomisation seeded the minimisation programme. The minimisation algorithm allowed for an 80% chance of allocating the minimised treatment. TRANSLATE was an open-label study; thus, no-one was masked to treatment assignment.

Procedures

An important aim of TRANSLATE was to obtain equivalent average numbers of systematic and target biopsy cores with either LATP or TRUS, to avoid bias. Biopsies were performed in the outpatient setting by clinicians or specialist nurses, with practitioners having performed at least 50 LATPs and certified competent by the Principal Investigator at each recruitment site. Anatomical location of MRI-visible lesions on imaging informed the cognitive targeting of those radiological lesions at LATP or TRUS biopsy in the outpatient setting.

LATP biopsy was performed with chlorhexidine-based skin preparation, without antibiotics.[20] Practitioners performed an average of 12 systematic cores in six sectors (modified Ginsburg protocol[21]), with two biopsy cores per anterior, mid, and posterior sector, left-sided and right-sided, depending on prostate size, using an ultrasound probe-mounted LATP needle guidance device, plus between three and five (average of four) target biopsies per lesion sent for histopathology assessment in a separate pot.[19] Practitioners used judgement regarding whether same sector systematic biopsies were required, depending on size of lesion and size of prostate. Each centre used its existing LATP biopsy technique and ultrasound probe-mounted LATP needle guide devices (either PrecisionPoint, BXTAccelyon; or BK UA1232, BK Medical) access system, or similar probe-mounted device.

TRUS biopsy was performed using local anaesthetic infiltration, with pre-procedure and post-procedure antibiotics as standard-of-care at each recruitment centre.[19] None of the TRANSLATE recruitment centres used enhanced prophylaxis or rectal culture-guided prophylaxis, as this is not routinely used in the UK. Practitioners performed an average of 12 systematic biopsy cores (six per side; two cores per base, mid, and apical regions, left-sided and right-sided) using a TRUS probe, plus between three and five (average of four) target biopsies per lesion sent for histopathological assessment in a separate pathology pot.[19] Practitioners used judgement regarding how many additional systematic biopsies were required on the side of a target lesion.

GGG 2 or higher prostate cancer was reported by a histopathologist upon diagnostic assessment of the biopsy specimens. Patient-reported tolerability of the procedure was assessed using the ProBE questionnaire. Health-related quality of life was assessed at baseline, and at 7 days, 35 days, and 4 months post-biopsy procedure, using the International Index of Erectile Function (IIEF; domain A, assessing sexual function [scale 0 to 30, lower score being worse]), International Prostate Symptom Score (IPSS [scale 0 to 35, higher score being worse]), and the 5-level EQ-5D (EQ-5D-5L [EQ-5D VAS values are between 0 and 100, where 0 represents worst imaginable health and 100 best imaginable health, and the EQ-5D utility score follows a similar direction]) using patient-completed online or paper questionnaires.

Participant follow-up questionnaires and adverse event assessments were completed at the time of biopsy, and at 7 days, 35 days, and 4 months post-biopsy as per protocol.[19]

Patients could be withdrawn from the study at any time based upon either patient request (eg, due to intolerable serious adverse events, inability to comply with study procedures, or participant decision) or based on investigator discretion (eg, if they did not meet the inclusion criteria; appendix 1 p 11). Serious adverse events (defined as any adverse events that results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or consists of a congenital anomaly or birth defect) were recorded if reported to the central trial team by any of the recruiting centres, or if identified by the central trial

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See Online for appendix 1

team during completion or reporting of either a patient-reported or clinician-reported case report form, including review of the case report forms by the study team at the end of each patient's 4-month follow-up period.

According to CONSERVE 2021 guidance, we report that recruitment to the TRANSLATE Trial commenced in December, 2021, while COVID-19 restrictions remained in place, but these had no material impact on the conduct of the study.

Outcomes

The primary outcome was detection of clinically significant (GGG ≥2) prostate cancer (any Gleason pattern 4 disease) on biopsy, compared between randomised groups. Secondary outcomes were infection rates (the primary definition of infection being any symptoms or signs of infection resulting in hospitalisation; the secondary, broader definition of infection was symptoms or signs of infection resulting in hospitalisation, plus infection not requiring hospitalisation); patient-reported outcomes including sexual function (assessed using IIEF domain A), biopsy complications (urinary retention requiring catheterisation; visible blood in bowel movements; blood in urine; pain in the biopsy area; or hospital admission due to bleeding or pain), urinary symptoms (assessed using the IPSS and IPSS quality of life), and tolerability (using the Prostate Biopsy Effects: PROBE questionnaire[22]); histological parameters (ISUP grade group, cancer core length, core involvement, and biopsy cancer parameters); re-biopsy (number of subsequent prostate biopsy procedures required and associated pathology results); burden and rate of detection of clinically insignificant (GGG 1) prostate cancer; burden and rate of detection of additional definition of clinically significant (GGG ≥3) prostate cancer; health-related quality of life using the EQ-5D-5L cost-effectiveness, and serious adverse events.[23] Cost-effectiveness, and detailed histological parameters and other pathology results, including those of repeat biopsy where performed, will be reported separately.

Statistical analysis

A minimum sample of 1042 patients was selected to detect a between-group improvement of 10% in detection rate of GGG 2 or higher prostate cancer from 45% for TRUS[24] to 55% for LATP,[5] with 90% power and a two-sided type I error rate of 5%. A 10% improvement in detection of GGG 2 or higher prostate cancer from TRUS to LATP was considered clinically meaningful by the trial team at the outset of the study. The original sample size calculation did not allow withdrawal or crossover of participants. Therefore, as it became apparent that there were some withdrawals and crossovers, we extended the study (with the approval of the Trial Steering Committee before the end of recruitment of the participants) and continued to recruit to 1126 participants, to maintain statistical power to detect a statistically significant difference in diagnosis of GGG 2 or higher prostate cancer, if such a difference exists.

The primary outcome in TRANSLATE was detection of GGG 2 or higher prostate cancer (any Gleason pattern 4 disease) on biopsy and is presented as the proportion of patients with a biopsy positive for GGG 2 or higher prostate cancer, compared across the two randomised groups (LATP and TRUS).[25] The primary outcome was compared between randomised groups as a binary variable using a mixed effects logistic regression model adjusted for minimisation factors (recruitment centre fitted as a random effect, and site of MRI lesion fitted as a fixed effect). Differences between groups are reported as odds ratios (ORs) and absolute proportions, with 95% CIs. An independent covariance structure was used to model the within-centre errors with random intercept. The Satterthwaite approximation was used to estimate denominator degrees of freedom.

Secondary outcomes were analysed using mixed effect logistic regression models for binary data and mixed effects linear regression for continuous data, adjusted for minimisation variables (recruitment centre fitted as a random effect, and site of MRI lesion fitted as a fixed effect) and additionally adjusted for baseline outcome score where available (IIEF, IPSS, and EQ-5D-5L). Where outcomes were measured at multiple timepoints, repeated measures within participant were accounted for in the model as a random effect. Analyses were done on the modified intention-to-treat (ITT) population (composed of all participants in the group they were randomised to regardless of actual intervention received, using only cases with a biopsy result available), as outlined in the statistical analysis plan[25] agreed early in the trial and before any data analysis, with Trial Steering Committee and Data Safety and Monitoring and Committee review. The primary analysis was repeated for the per-protocol population, with excluded patients (those with major protocol deviations) as pre-specified in the statistical analysis plan.[25] The trial was powered for a single pre-specified primary endpoint and pre-specified analysis plan, and therefore no adjustment for multiple testing was conducted.

All comparative outcomes are presented as summary statistics, reported with 95% CIs, and all tests were done using a 5% two-sided significance level. Prespecified subgroup analyses for prostate cancer detection were conducted across levels of MRI lesion ("lesion including anterior"; "lesion not including anterior"; and "no lesion") and prostate volume (<50 cc; 50–79 cc; and ≥80 cc).[25] Post hoc analysis included an exploratory subgroup analysis of detection of an alternative definition of clinically significant prostate cancer (GGG ≥3 disease) according to lesion location and prostate size. Descriptive statistics were used for demographics between the two biopsy groups, reporting means and SDs or medians and IQRs as appropriate for continuous variables, and

numbers and percentages for binary and categorical variables. As supporting analyses we also carried out an unadjusted analysis, and a further adjusted analysis accounting for additional important prognostic factors (prostate-specific antigen level, MRI tumour stage, and cancer risk group), of the modified ITT population. All statistical analyses were performed using Stata version 18.0. No formal interim analyses were performed. The final version of the trial protocol (Feb 29, 2024, version 4) is provided in appendix 2 and includes a full amendment history, and details of all protocol amendments, as listed on page 50 of that document.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Dec 3, 2021, and Sept 26, 2023, 2727 participants were assessed for eligibility. 2078 (76·2%) of 2727 individuals were eligible (reasons for ineligibility of 649 patients are shown in the figure); 1126 (41·3%) of 2727 individuals were randomly assigned to TRUS (n=564) or LATP (n=562) biopsy (figure, table 1, and appendix 1 pp 1–7). 1044 (92·7%) of 1126 participants were White British, 800 (71·0%) of 1126 were overweight or obese (BMI ≥25 kg/m²), 885 (78·6%) of 1126 had two or more comorbidities, 27 (2·4%) of 1126 were taking finasteride, and 264 (23·4%) of 1126 had a first-degree family history of prostate cancer (table 1, appendix 1 pp 1–4). The median age of the participants was 66 years (IQR 61–72) and we did not specifically collect data on the sex or gender of recruited participants. 1054 (93·6%) of 1126 participants had a prostate-specific antigen of 20 ng/mL or less and 384 (37·6%) of 1021 had an abnormal digital rectal examination noted at time of biopsy (table 1 and appendix 1 pp 1–4). The number of patients recruited at each of the ten recruitment centres is in appendix 1 p 8, and the the demographics of the per-protocol population are in appendix 1 pp 5–7). All recruited participants received pre-biopsy MRI (814 [72·3%] of 1126 multiparametric and 307 [27·3%] of 1126 biparametric; details of the biparametric or multiparametric nature of the pre-biopsy MRI scan were unavailable for five cases). 1016 (90·2%) of 1126 had at least one significant radiological lesion (appendix 1 pp 9–10).

All participants were biopsy-naive. 43 (3·8%) of 1126 recruited individuals withdrew from the study (appendix 1 p 11). 540 of participants allocated to LATP and 511 allocated to TRUS received their allocated biopsy. Participants who did not receive their allocated biopsy and details of the LATP and TRUS biopsies performed are summarised in appendix 1 (pp 12–14). Physicians delivered more LATP biopsies than nurses (404 [71%] of 567 for physicians versus 163 [29%] of 567 for nurses);

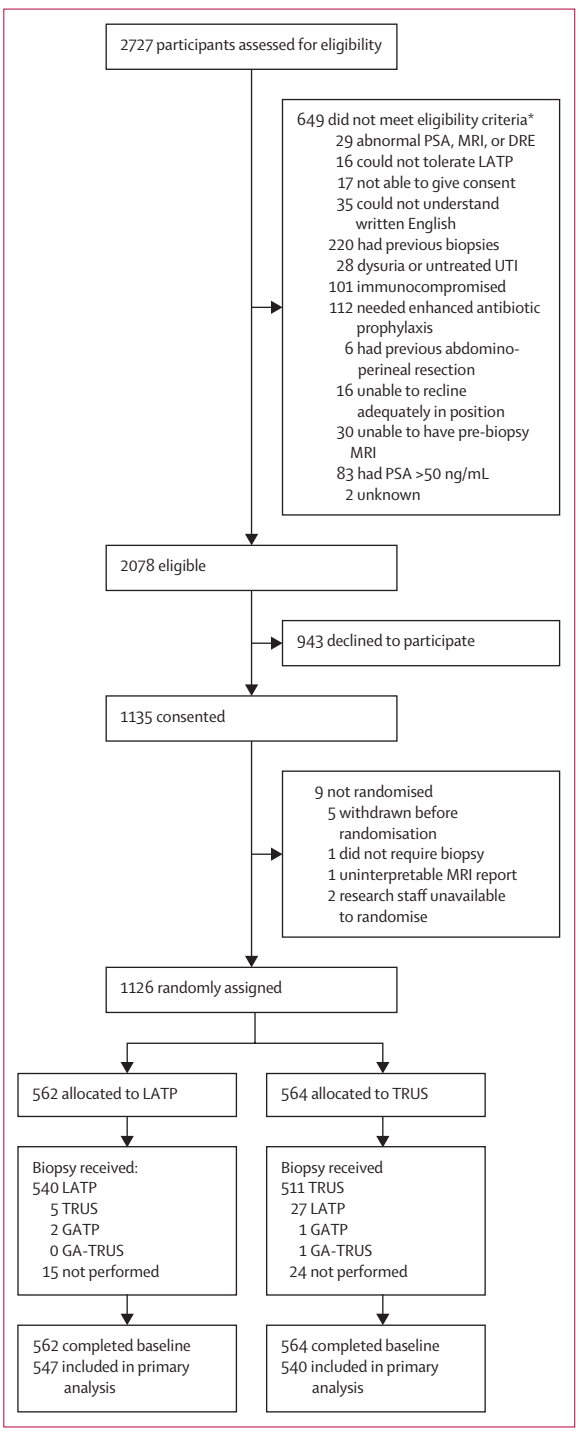

Figure: **Trial profile**

Note: of 39 individuals without a biopsy, 38 withdrew before biopsy was performed. Reasons for an alternative type of biopsy being performed, rather than the allocated biopsy, can be found in the appendix (p 12). DRE=digital rectal examination. GATP=transperineal biopsy under general anaesthetic. GA-TRUS=transrectal biopsy under general anaesthetic. LATP=local anaesthetic ultrasound-guided transperineal biopsy. PSA=prostate-specific antigen. TRUS=transrectal approach. URI=urinary tract infection. *Patients could be ineligible for more than one reason.

See Online for appendix 2

	LATP group (n=562)		TRUS group (n=564)		All patients (n=1126)	
BMI, kg/m²*	548	27 (25–29); 27·3 (4·1)	543	27 (25–30); 27·7 (4·4)	1091	27 (25–30); 27·5 (4·3)
White British ethnicity†	527	93·8%	517	91·7%	1044	92·7%
Charlson Comorbidity Index Score*	559	2 (2–3); 2·4 (1·3)	557	2 (2–3); 2·5 (1·4)	1116	2 (2–3); 2·5 (1·3)
Anticoagulants†	27	4·8%	28	5·0%	55	4·9%
Finasteride†	14	2·5%	13	2·3%	27	2·4%
Prostate-specific antigen level, ng/mL*	561	7 (5–10); 8·8 (7·5)	559	7 (5–10); 8·8 (6·8)	1120	7 (5–10); 8·8 (7·1)
Age, years*	562	66 (60–72); 66·1 (8·1)	564	66 (61–71); 66 (7·3)	1126	66 (61–72); 66·1 (7·7)
IIEF (domain A)‡	531	19 (3–29)	530	18 (4–28)	1061	19 (4–29)
IPSS‡	468	7 (3–13)	461	7 (3–13)	929	7 (3–13)
IPSS quality of life‡	478	2 (1–3)	477	2 (1–3)	955	2 (1–3)
EQ-5D utility score‡	540	0·89 (0·81–0·99)	537	0·89 (0·8–0·99)	1077	0·89 (0·81–0·99)
EQ-5D VAS‡	540	82 (75–90)	537	85 (75–90)	1077	83 (75–90)
DRE result pre-biopsy†§						
Benign	249	44·4%	289	51·7%	538	48·0%
Suspicious	148	26·4%	119	21·3%	267	23·8%

Data are for the modified intention-to-treat population (ie, according to type of biopsy randomised). DRE=digital rectal examination. IIEF (domain A)=International Index of Erectile Function Domain A (score 0–30, lower values being worse). IPSS=International Prostate Symptom Score (score range 0–35, higher values being worse). VAS=visual analogue scale. Data are: *n, median (IQR), mean (SD) shown for each; †n, % shown for each; ‡n, median (IQR). §Denominators are 561 for the LAPT group and 559 for the TRUS group because data were not available for six patients (n=1; n=5 respectively).

Table 1: **Baseline characteristics**

	LATP (n=562)	TRUS (n=564)	Total (n=1126)
Biopsy procedures performed	567 (100·9%)	516 (91·5%)	1083 (96·2%)
Left side systematic biopsy cores (range 0–15)	6 (6–6); 6·4 (2); 0 to 15; n=565	6 (4–6); 5·2 (1·7); 0 to 9; n=516	6 (5–6); 5·8 (1·9); 0 to 15; n=1081
Right side systematic biopsy cores (range 0–14)	6 (6–7); 6·4 (2); 0 to 14; n=565	6 (5–6); 5·2 (1·6); 0 to 9; n=516	6 (5–6); 5·8 (1·9); 0 to 14; n=1081
Total systematic biopsy cores from both sides (range 0–29)	12 (12–13); 12·7 (3·7); 0 to 29; n=565	12 (8–12); 10·4 (3); 0 to 18; n=516	12 (10–12); 11·6 (3·6); 0 to 29; n=1081
Less than 6 systematic cores taken	6 (1·1%)	33 (6·4%)	39 (3·6%)
Reason for less than 6 cores taken			
Patient intolerance	0	4 (12·1%)	4 (10·3%)
High cancer burden	2 (33·3%)	12 (36·4%)	14 (35·9%)
Prostate size	0	17 (51·5%)	17 (43·6%)
Clinical decision	1 (16·7%)	1 (3%)	2 (5·1%)
Unknown	2 (33·3%)	12 (36·4%)	14 (35·9%)
More than 18 systematic cores taken	31 (5·5%)	0	31 (2·9%)
Reason for more than 18 cores taken			
High cancer burden	3 (9·7%)	0	3 (9·7%)
Prostate size	19 (61·3%)	0	19 (61·3%)
Clinical decision	4 (12·9%)	0	4 (12·9%)
Patient not identified as being in TRANSLATE	3 (9·7%)	0	3 (9·7%)
Unknown	2 (6·5%)	0	2 (6·5%)

Data are n (%), or median (IQR), mean (SD), and range. The denominators are the numbers randomised to each group. The actual numbers for the biopsy performed indicate the small number of deviations from the allocated biopsy.

Table 2: **Details of trial biopsy cores**

for TRUS, physicians and nurses delivered similar proportions of biopsies (264 [51%] of 516 for physicians versus 251 [49%] of 516 for nurses). LATP procedures took longer than TRUS, including time in the room (median 28 min [IQR 23–35] for LATP *vs* 22 min [19–26] for TRUS) and time to perform the biopsy (median 12 min [10–15] for LATP *vs* 8 min [6–10] for TRUS; appendix 1 pp 13–14). The median number of target (appendix 1 pp 15–16) and systematic cores for LATP and TRUS biopsy were equivalent (table 2). Most target biopsies were sent for histopathological assessment in separate pots (appendix 1 pp 15–16). Most participants who received LATP underwent biopsy without antibiotics according to protocol (503 [89%] of 567). All participants in the TRUS group received antibiotics (appendix 1 p 17).

In the primary modified ITT analysis population, GGG 2 or higher prostate cancer was detected in 329 (60·1%) of 547 participants allocated to LATP versus 294 (54·4%) of 540 allocated to TRUS biopsy (OR 1·32 [95% CI 1·03–1·70], p=0·031; table 3). In the per-protocol analysis population, GGG 2 or higher prostate cancer was detected in 323 (60·3%) of 536 participants allocated to LATP versus 273 (53·6%) of 509 allocated to TRUS biopsy (1·38 [1·06–1·78]; p=0·016).

According to the pre-defined primary definition of post-biopsy infection (infection requiring admission to hospital), in the first 7 days post-biopsy this occurred in one (<1%) of 562 individuals allocated to LATP versus seven (1%) of 564 allocated to TRUS biopsy (OR 0·14 [95% CI 0·02–1·15]; table 4). In the 4-month post-biopsy period there were fewer infectious complications overall with LATP than with TRUS (six [1%] of 562 for LATP versus 13 [2%] of 564 for TRUS, adjusted 0·45 [0·17–1·20]). Analysis of the secondary, broader definition

	LATP (n=562)	TRUS (n=564)	Odds ratio (95% CI)	p value
Gleason Grade Group ≥2 prostate cancer detection				
Modified ITT population*	329/547 (60·1%)	294/540 (54·4%)	1·32 (1·03–1·70)	0·031
Per-protocol population†	323/536 (60·3%)	273/509 (53·6%)	1·38 (1·06–1·78)	0·016
Supporting analyses				
Modified ITT population unadjusted‡	329/547 (60·1%)	294/540 (54·4%)	1·26 (0·99–1·61)	0·058
Modified ITT population additionally adjusted§	316/528 (59·8%)	285/526 (54·2%)	1·43 (1·08–1·90)	0·014

ITT=intention-to-treat. *Modified ITT (as randomised and with biopsy result available) with output from a logistic regression model adjusted for biopsy type and minimisation factors (recruitment centre, and location of pre-biopsy MRI prostatic lesion). †Per-protocol population excludes participants with major protocol deviations; major protocol deviations are those where participants did not receive their randomised intervention, did not satisfy the eligibility criteria, or where the biopsy was not conducted in accordance with the protocol as reported by sites. ‡Output from a logistic regression model adjusted for biopsy type only. §Output from a logistic regression model adjusted for biopsy type, minimisation factors (recruitment centre, and location of pre-biopsy MRI prostatic lesion) and important prognostic factors (prostate-specific antigen level, MRI tumour stage, and cancer risk group).

Table 3: **Primary outcome, analysed in the modified ITT and per-protocol populations**

of post-biopsy infection (symptoms or signs of infection with or without hospital admission) showed no evidence of a statistically significant difference in the 4-month post-biopsy period (113 [20%] of 562 for LATP versus 120 [21%] of 564 for TRUS, 0·93 [0·70–1·25]).

There was no statistically significant difference in the proportion of participants reporting at least one biopsy-related complication (urinary retention requiring catheterisation; visible blood in bowel movements; blood in urine; pain in the biopsy area; hospital admission due to bleeding or pain) during the 4-month post-biopsy follow-up period (454 [81%] of 562 for LATP and 436 [77%] of 564 for TRUS, OR 1·23 [95% CI 0·93–1·65]; table 5). There was no statistically significant difference in post-biopsy urinary symptoms in participants allocated to LATP versus TRUS at follow-up time-points following biopsy, as measured by patient-reported IPSS scores (table 5). IPSS scores at baseline, day 7, day 35, and 4 months post-biopsy were similar for LATP compared with TRUS (table 5, appendix 1 pp 22–23). There was no statistically significant difference in post-biopsy sexual function, as measured by patient-reported IIEF scores (domain A), in participants allocated to LATP versus TRUS at any of the follow-up timepoints (table 5). IIEF scores were lower at day 7 post-biopsy compared with pre-biopsy baseline and did not return to baseline by day 35 or 4 months post-biopsy for LATP or TRUS (table 5, appendix 1 p 24).

Participants more commonly reported LATP biopsy to be problematic immediately post-procedure using a PROBE perception evaluation than TRUS (216 [38%] of 562 *vs* 153 [27%] of 564, OR 1·84 [95% CI 1·40–2·43]). Procedure-related pain, discomfort, and embarrassment were more commonly reported as occurring "a lot" for LATP versus TRUS (table 5). At 7 days post-biopsy, procedure-related symptoms were higher in participants allocated to TRUS versus LATP (140 [25%] of 564 *vs* 99 [18%] of 562, OR 0·59 [95% CI 0·44–0·80]). The percentage of participants reporting a general post-biopsy symptom using a PROBE general symptoms evaluation tool was higher in most domains (feeling feverish; nausea or vomiting; pain in biopsy area; feeling shivery or unwell; blood in the urine, semen, or stool) for participants allocated to TRUS versus LATP at 7-days post-procedure (table 5). No statistically significant difference in quality of life was observed between participants allocated to LATP versus TRUS at post-biopsy evaluation time-points, measured using EQ-5D utility and VAS evaluation tools (table 5, appendix 1 pp 25–26).

Any-grade prostate cancer was detected in 390 (69%) of 562 participants allocated to LATP, compared with 361 (64%) of 564 allocated to TRUS (appendix 1 p 18). GGG 3–5 prostate cancer was detected in 123 (22%) of 562 participants allocated to LATP versus 129 (23%) of 564 allocated to TRUS (OR 0·93 [95% CI 0·70–1·24]; appendix 1 p 18). GGG 2 or higher prostate cancer was detected in target biopsies in 472 (41·9%) of 1126 trial participants (appendix 1 p 18), and only in systematic biopsy cores (ie, where there is a radiological target, the target biopsies are benign or contain GGG 1 disease, or

	LATP (n=562)	TRUS (n=564)	Odds ratio (95% CI)
Primary definition*			
By 7 days	1 (<1%)	7 (1%)	0·14 (0·02–1·15)
By 35 days	2 (<1%)	9 (2%)	0·22 (0·05–1·01)
By 4 months	6 (1%)	13 (2%)	0·45 (0·17–1·20)
Secondary definition†			
By 7 days	54 (10%)	72 (13%)	0·73 (0·5–1·06)
By 35 days	85 (15%)	102 (18%)	0·81 (0·59–1·11)
By 4 months	113 (20%)	120 (21%)	0·93 (0·7–1·25)

*Primary definition of infection is any symptoms or signs of infection resulting in hospital admission. Output is adjusted odds ratio using a mixed effects logistic regression model fitted at each timepoint accounting for biopsy type and lesion location as fixed effects, and recruitment site as random effect. †Secondary (broader) definition of infection is symptoms or signs of infection resulting in hospital admission, plus infection not requiring hospital admission. Output is adjusted odds ratio using a mixed effects logistic regression model fitted at each timepoint accounting for biopsy type and lesion location as fixed effects, and recruitment site as a random effect.

Table 4: **Infection rate, in the modified intention-to-treat population**

	LATP (n=562)		TRUS (n=564)		Odds ratio/between group difference (95% CI)
At least one biopsy-related complication*					
Overall	454	81%	436	77%	1·23 (0·93 to 1·65)
By 7 days	447	80%	433	77%	..
By 35 days	448	80%	435	77%	..
By 4 months	454	81%	436	77%	..
Urinary retention requiring catheter					
Overall	35	6%	27	5%	..
By 7 days	11	2%	12	2%	..
By 35 days	20	4%	17	3%	..
By 4 months	35	6%	27	5%	..
Visible blood in bowel movements					
Overall	62	11%	174	31%	..
By 7 days	34	6%	161	29%	..
By 35 days	51	9%	171	30%	..
By 4 months	62	11%	174	31%	..
Urology admission due to haematuria					
Overall	0	..	0	..	..
By 7 days	0	..	0	..	..
By 35 days	0	..	0	..	..
By 4 months	0	..	0	..	..
Urology admission due to pain					
Overall	1	<1%	2	<1%	..
By 7 days	1	<1%	1	<1%	..
By 35 days	1	<1%	2	<1%	..
By 4 months	1	<1%	2	<1%	..
PROBE (Perception) score post-biopsy†					
Yes (biopsy problematic)	216	38%	153	27%	1·84 (1·40 to 2·43)
Biopsy procedure painful					
Not at all	82	15%	142	25%	..
A little	235	42%	221	39%	..
Somewhat	105	19%	73	13%	..
A lot	37	7%	15	3%	..
Missing	103	18%	113	20%	..
Biopsy procedure physically uncomfortable					
Not at all	69	12%	63	11%	..
A little	246	44%	262	46%	..
Somewhat	97	17%	101	18%	..
A lot	45	8%	25	4%	..
Missing	105	19%	113	20%	..
Biopsy procedure embarrassing					
Not at all	295	52%	320	57%	..
A little	108	19%	99	18%	..
Somewhat	41	7%	23	4%	..
A lot	15	3%	9	2%	..
Missing	103	18%	113	20%	..

(Table 5 continues on next page)

where there was no radiological lesion) in 151 (13·4%; calculated from the total number of any GGG 2 or higher cases [n=623] minus the number of GGG 2 in target biopsies [n=472]) of 1126 participants (appendix 1 p 18). A total of ten (2%) of 562 participants allocated to LATP, and 29 (5%) of 564 allocated to TRUS, received a further biopsy during the 4-month follow-up period (appendix 1 p 19).

Prespecified subgroup analyses of GGG 2 or higher prostate cancer detection according to lesion location

	LATP (n=562)		TRUS (n=564)		Odds ratio/between group difference (95% CI)
(Continued from previous page)					
Biopsy procedure loss of dignity					
Not at all	325	58%	369	65%	..
A little	95	17%	72	13%	..
Somewhat	32	6%	7	1%	..
A lot	6	1%	3	1%	..
Missing	104	19%	113	20%	..
Problem having another biopsy procedure in the future					
Not a problem	306	54%	342	61%	..
A minor problem	84	15%	75	13%	..
A moderate problem	53	9%	29	5%	..
A major problem	16	3%	6	1%	..
Missing	103	18%	112	20%	..
Describing biopsy procedure					
A minor procedure	158	28%	230	41%	..
A moderate procedure tolerable under local anaesthetic	261	46%	200	35%	..
Quite a major procedure but tolerable under local anaesthetic	34	6%	18	3%	..
A major procedure that requires a general anaesthetic (being put to sleep)	6	1%	4	1%	..
Missing	103	18%	112	20%	..
PROBE (General symptoms) overall score, past 7 days†	99	18%	140	25%	0·59 (0·44 to 0·80)
PROBE (general symptoms), number of participants indicating moderate or major problem					
Feverish	8	1%	20	4%	..
Nausea or vomiting	10	2%	10	2%	..
Pain in biopsy area	44	8%	54	10%	..
Shivery	9	2%	20	4%	..
Unwell in any other way	16	3%	32	6%	..
Blood in urine	23	4%	37	7%	..
Blood in stool	0	..	4	1%	..
Blood in semen	42	7%	44	8%	..
Urinary function‡					
IPSS (scored from 0 to 35)					
Baseline	468	7 (3–13)	461	7 (3–13)	
7 days	479	8 (4–14)	448	7 (3–13)	0·41 (–0·30 to 1·13)
35 days	479	8 (4–13)	443	8 (4–13)	0·06 (–0·66 to 0·78)
4 months	446	8 (4–14)	410	8 (4–13)	0·36 (–0·38 to 1·10)
IPSS QoL (scored from 0 "delighted" to 6 "terrible")					
Baseline	478	2 (1–3)	477	2 (1–3)	
7 days	481	2 (1–3)	453	2 (1–3)	0·08 (–0·08 to 0·24)
35 days	485	2 (1–3)	452	2 (1–3)	–0·01 (–0·17 to 0·15)
4 months	455	2 (1–3)	420	2 (1–3)	0·06 (–0·10 to 0·23)
Sexual function§ (IIEF domain A)					
Baseline	531	19 (3–29)	530	18 (4–28)	
7 days	464	4 (3–12)	437	4 (3–13)	0·21 (–0·90 to 1·32)
35 days	468	9 (3–26)	424	11 (3–25)	0·10 (–1·02 to 1·22)
4 months	407	5 (2–25)	373	8 (3–24)	–0·60 (–1·79 to 0·58)

(Table 5 continues on next page)

and prostate size are shown in appendix 1 (pp 20, 27). No statistically significant difference in detection between biopsy groups was observed according to subgroups (appendix 1 p 27). Further secondary outcome analysis results reporting a cost-effectiveness comparison of LATP versus TRUS prostate biopsy will be published elsewhere, due to the large volume of data in the full health economics evaluation.

	LATP (n=562)		TRUS (n=564)		Odds ratio/between group difference (95% CI)
(Continued from previous page)					
EQ-5D utility¶					
Baseline	540	0·893 (0·808–0·989)	537	0·893 (0·797–0·987)	..
7 days	477	0·868 (0·788–0·987)	451	0·868 (0·788–0·987)	–0·015 (–0·03 to 0·00)
35 days	476	0·868 (0·788–0·987)	434	0·891 (0·793–0·987)	–0·021 (–0·04 to 0·00)
4 months	408	0·891 (0·778–0·987)	382	0·891 (0·793–0·987)	–0·008 (–0·03 to 0·01)
EQ-5D VAS¶					
Baseline	540	82 (75–90)	537	85 (75–90)	..
7 days	476	80 (70–86)	451	80 (70–87)	0·50 (–1·31 to 2·32)
35 days	475	80 (70–87)	431	80 (70–89)	–0·16 (–1·99 to 1·67)
4 months	408	79 (70–87)	382	80 (70–87)	0·11 (–1·82 to 2·03)

Data are n, %, median (IQR), or odds ratio (95% CI). IIEF=International Index of Erectile Function. IPSS=International Prostate Symptom Score. QoL=quality of life. VAS=visual analogue scale. *Includes urinary retention, or visible blood in bowel movements, or urology admission due to bleeding, or urology admission due to pain, or blood in urine (as per PROBE questionnaire), or pain in biopsy area (as per PROBE questionnaire), or blood in motions (as per PROBE questionnaire). Output is adjusted odds ratio using a mixed effects logistic regression model accounting for biopsy type and lesion location as fixed effects, and recruitment site as random effect. †PROBE perception and PROBE general symptoms output is adjusted odds ratio using a mixed effects logistic regression model accounting for biopsy type and lesion location as fixed effects, and recruitment site as a random effect. ‡IPSS values range from 0 to 35, higher score is worse (0–7=mildly symptomatic; 9–19 moderately symptomatic; 20–35=severely symptomatic); IPSS QoL range is 0 to 6. Between group difference: output from a mixed effects linear regression model adjusted for baseline IPSS, minimisation factors (recruitment centre as random effect, and location of pre-biopsy MRI prostatic lesion as fixed effect), with repeated measures within participant and timepoint by biopsy type interaction. §IIEF range is 0 to 30, lower values are worse. Between-group difference: output from a mixed effects linear regression model adjusted for baseline IIEF, minimisation factors (recruitment centre as a random effect, and location of pre-biopsy MRI prostatic lesion as a fixed effect), with repeated measures within participant and timepoint by biopsy type interaction. ¶EQ-5D utility range is between –0·594 to 1, and VAS between 0 and 100; lower values are worse scores. Between group difference: output from a model adjusted for baseline EQ-5D utility or VAS depending on outcome, minimisation factors (recruitment centre as a random effect, and location of pre-biopsy MRI prostatic lesion as a fixed effect), with repeated measures within participant and timepoint by biopsy type interaction.

Table 5: **Secondary non-infectious complication outcomes, in the modified intention-to-treat population**

An exploratory post hoc subgroup analysis of detection of an alternative definition of clinically significant prostate cancer (GGG ≥3 disease) according to lesion location and prostate size is shown in appendix 1 (p 20). Serious adverse events reported during the conduct of the trial are presented in appendix 1 (p 21). Serious adverse events occurred in 14 (2%) of 562 participants in the LATP group and 25 (4%) of 564 in the TRUS group, the most common being renal and urinary disorders and infection.

Discussion

Physicians are considering shifting from TRUS to LATP for diagnostic prostate biopsies[3,7,11,12,15] to reduce infectious complications.[7–12,15] However, diagnostic accuracy of biopsy sampling remains paramount.[1] The TRANSLATE study compared the effectiveness of these biopsy approaches in detecting clinically significant (GGG ≥2) prostate cancer in biopsy-naive men. We found superiority of LATP over TRUS in this aim, with a 5·7% higher rate of GGG 2 or higher prostate cancer detection with LATP versus TRUS. The PERFECT randomised controlled trial (n=250) did not demonstrate non-inferiority of LATP over TRUS (targeted biopsies identifying GGG ≥2 prostate cancer in 47·2% [60/127] of participants allocated to LATP *vs* 54·2% [71/131] to TRUS; p=0·6235[16]). PERFECT found that posterior lesion location yielded higher GGG 2 or higher prostate cancer detection for TRUS (59·0% [59/100] *vs* 44·3% [39/88], p=0·0443), and more frequent (albeit not significantly so) detection of anterior lesions via LATP versus TRUS (40·6% versus 26·5%, p=0·2228).[16] PROBE-PC[17] (n=840) reported GGG 2 or higher prostate cancer detection as a secondary outcome,[26] with no evidence of a difference for LATP versus TRUS.[26] In that trial, 46% (333/718) of PROBE-PC participants had previous biopsies, and 4% (31/718) were without pre-biopsy MRI,[26] whereas all TRANSLATE participants were biopsy-naive and received pre-biopsy MRI. TRANSLATE was powered as a superiority trial for LATP versus TRUS to detect GGG 2 or higher prostate cancer. These factors could explain the different results between TRANSLATE and other randomised controlled trials investigating these two biopsy approaches.

The GGG 2 or higher prostate cancer detection rates were higher than anticipated in TRANSLATE (observed *vs* hypothesised: TRUS: 54·4% *vs* 45%; LATP: 60·1% *vs* 55%). The 5·7% uplift in GGG 2 or higher prostate cancer detection with LAPT compared against TRUS was lower than the 10% hypothesised for the sample size calculation, mainly due to the almost 10% increase in the observed versus expected TRUS biopsy detection rate. Nonetheless, the difference still reached statistical significance with LATP detection rates of over 60%. We believe there are several reasons for this difference, including the improved targeting of radiological lesions via LATP, and improved detection of GGG 2 or higher prostate cancer with LATP in patients with anterior lesions on pre-biopsy MRI.

Diagnostic yield increases with more biopsies taken.[21] Maintaining equivalent biopsy numbers in each trial group is important when comparing modalities. PERFECT reported a lower number of biopsy cores for LATP versus TRUS; but numbers were equivalent in PROBE-PC and PREVENT.[17–18] TRANSLATE acquired equivalent numbers of systematic and target biopsy cores in the two groups to avoid bias.[9] TRANSLATE provides level 1 evidence for a minimum LATP biopsy template and number of cores required for GGG 2 or higher prostate cancer detection.

Infectious complications from biopsy, and concerns regarding the development of post-biopsy urinary sepsis, have driven the transition from TRUS to LATP. PROBE-PC and PREVENT reported infection-related complications as primary outcomes[17,18] and found no difference between the techniques (PROBE-PC: n=718, 3% [10/367] LATP *vs* 3% [9/351] TRUS; PREVENT: n=567, 0% [0/287] LATP *vs* 1% [4/280] TRUS, p=0·059). There were fewer infections (both resulting, and not resulting, in hospital admission) in TRANSLATE for LATP versus TRUS. This difference was not statistically significant, although as this was a secondary outcome, the trial was not powered around this outcome. The 7-day and 35-day "hospitalisation for infection" rates in both groups were likely to be related to biopsy. Rates of post-biopsy infection in TRANSLATE were low and similar to PROBE-PC[17] and PREVENT.[18] TRANSLATE demonstrates fewer post-biopsy infection hospitalisations following LATP versus TRUS, with 89% of LATP biopsies not receiving antibiotics (the 11% of LATP cases receiving antibiotics being largely protocol deviations). Thus, TRANSLATE demonstrates that most LATP biopsies can be safely performed without antibiotics, which is important for antibiotic stewardship.[15,27–29] We recognise that excluding participants at higher risk of infection, necessary for successful randomisation, likely reduced the infection event rate in both groups of this study. Furthermore, this UK study did not incorporate regular use of targeted antibiotic prophylaxis using pre-procedure rectal swabs, which might be a practice undertaken in some other countries. Overall, the rates of "all infections" reported in this study are higher than reported in other studies, reflecting our approach to data collection which included patient-reported primary care attendances and investigator-reported events.

TRANSLATE has comprehensively evaluated LATP against TRUS biopsy for non-infectious complications (post-procedure bleeding and acute urinary retention, effects on urinary and sexual function, and procedure tolerability) immediately post-procedure, at 7 and 35 days, and at 4 months. We observed no difference between LATP and TRUS in participants reporting one or more biopsy-related complication. There was no difference in post-biopsy urinary symptoms (IPSS) or sexual function (IIEF). Participants more commonly reported pain and embarrassment immediately after LATP biopsy, consistent with the PREVENT trial.[18] Notably, in TRANSLATE we found that less men in the LATP group received less than six systematic biopsy cores compared with the TRUS group, despite also demonstrating that LATP was less well tolerated than TRUS. This finding implies that patient-reported poor tolerance does not necessarily lead to suboptimal biopsy sampling of the gland. At 7 days, procedure-related symptoms were higher for TRUS versus LATP, with no difference in quality of life (EQ-5D-5L). LATP biopsy took longer to perform than TRUS. A full health economics and cost-effectiveness analysis will be reported separately.

Increased detection of GGG 4–5 prostate cancer was observed for TRUS versus LATP, although TRANSLATE was not powered to detect statistically significant differences in this subgroup. There was a slightly higher detection of GGG 1 prostate cancer for TRUS versus LATP. The TRANSLATE protocol defined clinically significant prostate cancer as the presence of any Gleason pattern 4 or higher disease, although this definition is evolving.

Discussion is ongoing around omitting systematic biopsies in men with suspected prostate cancer,[2] and solely targeting MRI-visible lesions. TRANSLATE detected GGG 2 or higher prostate cancer in target biopsies in 42% of participants, and in only systematic biopsy cores (the target biopsies being benign or GGG 1) in a further 13%. If systematic biopsies were omitted, we would have seen lower overall detection of GGG 2 or higher prostate cancer, speaking in favour of continuing to perform systematic biopsies. During the course of the trial, further data have emerged emphasising the value of regional biopsies in addition to target-only biopsies.[30] Further analysis of the TRANSLATE trial data will help to advance the understanding of detection rates of targeted versus peri-lesional versus systematic biopsies.[30]

TRANSLATE has several limitations. First, the 12-core biopsy approach[21] might not apply to 24-core systematic Ginsburg, plus target lesion, sampling practice. Second, the clinical significance of the 6% uplift in GGG 2 or higher prostate cancer detection is unknown, and the primary outcome of GGG 2 or higher prostate cancer did not assess involved numbers or length or percentage of cores. The definition of clinically significant prostate cancer continues to evolve in light of findings from studies such as ProtecT. This study, in which approximately one third of participants had intermediate-risk clinically localised disease, demonstrated no difference in disease-specific mortality in men allocated to radical surgery, radiotherapy, or active monitoring at a median of 15 years of follow-up.[31] Third, 93% of participants were White British, with under-representation of multi-ethnic groups. TRANSLATE couldn't include London and many other major UK cities, to increase diversity, since the hospitals in these cities had already wholly transitioned to LATP. It would be valuable to see if the results from TRANSLATE can be

generalised to patients from ethnic groups other than White British, which would require another study. Fourth, we did not assess the individual skills of clinicians versus specialist nurses undertaking trial biopsies. We anticipated that a large number of practitioners would perform the biopsy and therefore we did not account for a clustering effect within clinicians. Fifth, the broader TRANSLATE definition of infection might have captured patient-reported symptoms that were not true post-biopsy infections.

Strengths of TRANSLATE include the following: 90% statistical power to detect a difference in detection of GGG 2 or higher prostate cancer; pre-biopsy MRI in all participants, who were all biopsy-naive; quality assurance regarding competency requirements for all practitioners conducting biopsy procedures during the trial, be they nurse practitioners or doctors; both nurses and doctors performed both LATP and TRUS biopsy in TRANSLATE, which is common practice in the UK; reporting of post-biopsy infection-related complications as hospitalisation, and non-hospitalisation, events; very high rates of acceptance of allocated biopsy; equivalence in targeted and systematic biopsy cores between LATP and TRUS.

In summary, LATP results in greater detection of GGG 2 or higher prostate cancer versus TRUS biopsy, but with higher immediate post-procedure pain and embarrassment, and takes longer to perform. TRUS biopsy results in higher procedure-related symptoms than LATP beyond 7 days. TRANSLATE provides the evidence necessary when considering trade-offs and deciding which biopsy to adopt.

Contributors

RJB and ADL wrote the first draft of the manuscript. IRM and AOoms independently undertook the statistical analysis, and independently verified the data in the study. RJB, ADL, JFL, CM, MR, CB, JW, TC, MPCL, TAL, JWFC, DJR, AOmer, SG, DWG, RHRG, SK, HW, DC, KN, BE, and HY recruited participants or directed clinical activities at the participating clinical centres. CV was lead histopathologist and REM was lead radiologist for the study. ST was patient and public involvement lead for the study. FCH and JMR provided senior advice throughout the conduct of the study. RW, VSB, JS, AH, and AT undertook trial co-ordination and database activities at the University of Oxford Surgical Intervention Trials Unit and Oxford Clinical Trials Research Unit. RJB is Chief Investigator, and RJB and ADL are co-Leads, of the TRANSLATE study, and led the design of the protocol. FL, ML, and JW undertook the health economics analysis. All authors were permitted to access the underlying data if they wished, and contributed to data interpretation and drafting and review of the final manuscript and had final responsibility for the decision to submit for publication.

Declaration of interests

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Data sharing

Individual patient data from this trial will not be published in the public domain. The trial protocol[19] and statistical analysis plan[25] have been published previously. Requests for data sharing will be reviewed on a case-by-case basis, and subject to data sharing agreements. Any data to be shared will be fully anonymised.

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