

# Thulium laser transurethral vaporesection versus transurethral resection of the prostate for benign prostatic obstruction: the UNBLOCS RCT

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## Scientific summary

### The UNBLOCS RCT

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# Scientific summary

## Background

Transurethral resection of the prostate (TURP) is the gold-standard operation for men with benign prostate obstruction (BPO). Although it is generally a successful procedure, it is associated with small but significant risks of both morbidity and mortality. Thulium laser transurethral vaporessection of the prostate (ThuVAP) is a new laser procedure in which the prostate is vaporised and resected using a surgical technique similar to TURP. The small number of published data suggest that ThuVAP may have certain advantages over TURP, but the evidence base is limited.

## Objectives

The key aim of this research was to determine whether ThuVAP is equivalent to TURP in men with BPO treated in the NHS in terms of a patient-reported symptom severity score [International Prostate Symptom Score (IPSS)] and the clinical measure of maximum urine flow rate (Qmax) 12 months after surgery. The secondary aims were to compare the procedures in terms of cost-effectiveness, surgical outcomes, patient-reported lower urinary tract symptoms (LUTS), erectile function, quality of life, general health, satisfaction and patient experience.

## Methods

### *Design*

This was a multicentre, pragmatic, randomised controlled parallel-group trial, including an embedded qualitative study and a within-trial economic evaluation from a NHS secondary care and a NHS perspective.

### *Setting*

Participants were recruited and underwent operations at seven UK centres: four university teaching hospitals and three district general hospitals.

### *Participants*

Participants were men who were suitable for TURP and either in urinary retention or with bothersome LUTS secondary to BPO. Men were excluded if they had neurogenic LUTS, previous prostate or urethral surgery, prostate cancer, or a prostate-specific antigen outside the normal age-related range without having had prostate cancer excluded, and if they were unable to give informed consent or complete trial documentation.

### *Interventions*

Participants were randomised 1 : 1 to receive either TURP or ThuVAP. As this was a pragmatic trial, centres continued to use their usual practices, for example in how they undertook the TURP procedure (e.g. use of monopolar or bipolar TURP). All trial surgeons underwent training in the ThuVAP technique. Participants were blinded to which procedure they received during their involvement in the trial.

### *Outcome measures*

The two key co-primary outcomes were the patient-reported IPSS and the clinical measure of Qmax. The key secondary outcomes were surgical complications, length of hospital stay and blood transfusion rates, cost-effectiveness, patient-reported LUTS, sexual symptoms, quality of life, general health, satisfaction and patients' experiences obtained using structured interviews.

Follow-up was at 6 weeks and 3 and 12 months after surgery for IPSS, and at 3 and 12 months for Qmax, with 12 months being the primary end point. Other patient-reported outcomes, including the EuroQol-5-dimensions, five-level version (EQ-5D-5L), were also collected at 6 weeks, 3 months and 12 months after surgery. Resource use was collected for the 12 months following surgery using trial case report forms, hospital patient-linked information costing systems and patient-completed questionnaires.

## Results

A total of 410 patients were randomised: 205 in each surgical arm. Primary IPSS outcome data were available for 151 (74%) and 159 (78%) participants and primary Qmax data were available for 168 (82%) and 176 (86%) participants in the TURP and ThuVARP arms, respectively. In terms of the primary outcomes, both arms showed significant improvements in both IPSS and Qmax. The two procedures were demonstrated to be equivalent in terms of the IPSS; participants in the ThuVARP arm had a mean IPSS of 6.43 and those patients in the TURP arm had a mean IPSS of 6.26 points [adjusted mean difference 0.28 higher in ThuVARP (favouring TURP), 95% confidence interval (CI)  $-0.92$  to  $1.49$ ]. However, the two procedures were not equivalent in terms of Qmax, with TURP deemed superior. Participants in the ThuVARP arm had a mean Qmax of 20 ml per second, whereas those patients in the TURP arm had a mean Qmax of 23 ml per second at 12 months post surgery [adjusted mean difference of 3.12 ml per second in favour of TURP, 95% CI  $0.45$  to  $5.79$  ml per second]. These conclusions were strengthened by various sensitivity analyses that were in agreement with the conclusions, including a per-protocol and a complier average causal effect analysis. There was no evidence to suggest that subgroup interactions were present; however, the beneficial effect of TURP in terms of Qmax was strengthened in younger men (i.e. those aged  $< 70$  years) and in those diagnosed with LUTS rather than urinary retention.

Other surgical outcomes were found to be similar between the arms. No difference was detected in the frequency or severity of surgical complications, or in the rate of blood transfusions, change in haemoglobin (indicating blood loss) or serum sodium (indicating absorption of irrigation fluid) postoperatively. The length of hospital stay was also similar after both procedures.

No obvious differences in individual patient-reported urinary symptoms were seen between the arms, with the exception of some evidence to indicate a potential reduction in nocturia incidence at 12 months post surgery in the TURP arm [ $p = 0.102$  when treated as binary (getting up to urinate more than once per night) and  $p = 0.031$  when treated as ordinal]. There was no apparent difference in sexual symptoms experienced by participants post surgery between the two arms, or in participants' quality of life or satisfaction with treatment, which were high.

The high satisfaction with treatment was mirrored in the qualitative study. Interviews were undertaken with 37 men using an open-ended interview schedule until data saturation was achieved and no new themes were emerging. The findings confirmed that both procedures resulted in a fairly equal patient experience as men reported similar journeys of recovery and outcomes. As the majority of participants specified that their expectations regarding outcomes had been met, it appeared that most were generally satisfied with the outcomes and the extent to which their initial symptoms had been alleviated. The provision of information was highlighted as a key requirement in order to understand the recovery period fully. The need to be aware of concerns regarding sexual matters when undergoing these procedures was also highlighted. Concerns were raised regarding the ability to conduct a satisfactory sex life, which was perceived to be related to, and to predate, surgery.

When the number of men diagnosed with prostate cancer in each arm from routine histology was reviewed, this was found to be greater in the TURP arm than in the ThuVARP arm. Following the procedure, 193 participants per arm had a prostate histology available. In the TURP arm 13% of participants were diagnosed with prostate cancer, compared with only 5% in the ThuVARP arm (odds ratio 0.35, 95% CI  $0.16$  to  $0.75$ ). The weight of resected prostate tissue was also much lower in the ThuVARP arm (difference in means  $-15.4$  ml, 95% CI  $-19.3$  to  $-11.5$  ml) as ThuVARP not only resects but also vaporises tissue.

The number of participants undergoing the procedure to which they had been randomised differed: 98% of participants in the TURP arm received their randomised procedure, compared with only 75% in the ThuVAP arm. Among the 51 participants who did not receive ThuVAP as randomised, the most common reason for this ( $n = 18$ ) was equipment failure, which led to either a change to TURP immediately or a conversion mid-procedure. In addition, large prostate size resulted in nine of these conversions to TURP.

In terms of the health economic analysis, the total adjusted mean secondary care NHS cost in the ThuVAP arm was slightly higher (£4253) than in the TURP arm (£4244), but with a difference of only £9 (95% CI –£359 to £376) this was consistent with chance. This difference reduced to £4 (95% CI –£367 to £375) when all NHS costs were included. The ThuVAP operation took, on average, 21 minutes longer than the TURP procedure. The higher cost of the time in theatre for ThuVAP is, to some extent, offset by the higher cost of recovery in the TURP arm.

The adjusted mean differences between the arms were similar in terms of quality-adjusted life-years (QALYs) (0.01 favouring TURP, 95% CI –0.04 to 0.01), equivalent to an extra 4 days of perfect health. The TURP arm weakly dominates the ThuVAP arm, and at a willingness to pay threshold of £20,000 per QALY, there is only a 24% probability that ThuVAP is more cost-effective than TURP.

## Strengths and limitations

The main strengths of this study were recruiting to the target sample size in a multicentre study, successful blinding of participants in a surgical trial, inclusion of patients presenting with urinary retention and exceptional follow-up rates, resulting in informative and robust conclusions.

Limitations included the reporting of complications, which were recorded according to prespecified categories; those complications reported as free text, and thus not prespecified, were excluded as a result of variable reporting. Serious adverse events are reported separately. It was also not possible to collect Qmax and IPSS data for those participants with indwelling catheters, making adjustment for baseline difficult. In addition, a pragmatic approach was taken to the measurement of prostate size, which was carried out by digital rectal examination at the start of surgery rather than by ultrasound scanning or magnetic resonance imaging, to adhere to NHS usual practice. A statistical limitation was that the data collected at 3 months could not be utilised in the imputation model, as originally planned, owing to modelling issues (collinearity and lack of convergence).

## Conclusions

Overall, the outcomes for both procedures were positive, with clinical improvements in IPSS and Qmax, as well as positive reporting of quality of life after the operation, and satisfaction with surgery. Although ThuVAP was demonstrated to be equivalent to TURP in terms of IPSS, the study was unable to demonstrate equivalence in Qmax between the surgical procedures, with TURP shown to be superior. However, the improvement in Qmax in both arms would be considered clinically successful. A reduction in the detection of prostate cancer from routine histology was also indicated in the ThuVAP arm. Length of stay, which was anticipated to be a key benefit for ThuVAP, was found to be equal to TURP in this trial. There was weak evidence for cost-effectiveness for the TURP arm, but this was very marginal. The difference in operative time between ThuVAP and TURP should be noted, with ThuVAP procedures taking an additional 21 minutes on average, which has implications for patients because of the longer period under anaesthetic, and for NHS service delivery. Overall, both ThuVAP and TURP were effective procedures for BPO, with minor benefits favouring TURP, suggesting that it may remain appropriate that new alternative treatments continue to be compared with TURP.

## Future work

Longer-term follow-up of trial participants would demonstrate whether or not there is any sustained difference between the arms in reoperation rates over time. This would provide a more comprehensive perspective on whether or not the lower Qmax achieved by ThuVAP has any relevance in terms of requiring further future interventions for LUTS, especially at an earlier time span than TURP. Also of interest would be future research into the comparative effectiveness of ThuVAP and TURP in large prostates of > 80–100 ml, as would a comparison between the enucleation procedures of thulium and holmium lasers.

## Trial registration

The trial is registered as ISRCTN00788389.

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## This report

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