Treating male lower urinary tract symptoms in primary healthcare using conservative interventions: the TRIUMPH cluster randomised controlled trial

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Treating male lower urinary tract symptoms in primary healthcare using conservative interventions: the TRIUMPH cluster randomised controlled trial

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Abstract

Objective(s): To determine whether a standardised and manualised intervention for Lower Urinary Tract Symptoms (LUTS) achieves superior symptomatic improvement versus usual care.

Design: 2-arm cluster randomised controlled trial where sites were randomised 1:1 to the intervention and control arms.

Setting: 30 NHS General Practice sites in England with an adequate number of potentially eligible patients.

Participants: 1,077 adult men (≥18) with bothersome LUTS recruited between June 2018 and August 2019 (524 in the intervention arm (n=17 sites) and 553 in the usual care arm (n=13 sites)).

Intervention: Standardised information booklet, developed with patient and expert input, providing guidance on conservative and lifestyle interventions for male LUTS. Participants were directed to relevant sections by general practice nurses/healthcare assistants or research nurses following urinary symptom assessment (manualised element) with subsequent contacts over 12 weeks to assist adherence.

Main outcome measures: Patient-reported International Prostate Symptom Score (IPSS) primary outcome 12 months after participant consent. Secondary patient-reported outcomes of quality of life (QoL), urinary symptoms and LUTS perception, hospital referrals and adverse events. The primary intention-to-treat analysis included 887 participants (82% of those recruited) and used a mixed effects multilevel linear regression model adjusting for site-level variables used in the randomisation and baseline scores.

Results: Participants in the intervention arm had a lower mean IPSS score at 12 months (adjusted mean difference of -1.81 points, 95% Confidence Interval (CI) -2.66 to -0.95) indicating less severe urinary symptoms than those in the usual care arm. LUTS-specific QoL, incontinence and LUTS perception also improved more in the intervention arm at 12 months. The proportion of urology referrals and numbers of adverse events were comparable between arms.

Conclusions: The standardised and manualised intervention in a UK primary care setting showed a sustained reduction in LUTS (difference in mean IPSS of -1.81 at 12 months (95% CI: -0.95 to -2.66)), which was less than the predefined target reduction of 2.0.

Trial registration: ISRCTN registry – ISRCTN11669964

Print abstract

Study question

Does a standardised and manualised intervention for Lower Urinary Tract Symptoms (LUTS) achieve superior symptomatic improvement versus usual care?

Methods

TRIUMPH is a 2-arm cluster randomised controlled trial with sites randomised 1:1 to intervention and control arms. The study was conducted in 30 NHS General Practice sites in England. 1,077 adult men with bothersome LUTS were recruited (524 in the intervention arm (n=17 sites) and 553 in the usual care arm (n=13 sites)). The intervention is a standardised information booklet, developed with patient and expert input, providing guidance on conservative and lifestyle interventions for male LUTS. Participants were directed to relevant sections by general practice nurses/healthcare assistants or research nurses following urinary symptom assessment (manualised element) with subsequent contacts over 12 weeks to assist adherence. The primary outcome is patient-reported International Prostate Symptom Score (IPSS) at 12 months. Secondary outcomes include patient-reported quality of life, urinary symptoms and LUTS perception, hospital referrals and adverse events.

Study answer and limitations

Participants in the intervention arm had a lower mean IPSS score at 12 months (adjusted mean difference: -1.81 points, 95% Confidence Interval: -2.66 to -0.95) indicating less severe urinary symptoms than in the usual care arm. Other LUTS symptoms also improved more in the intervention arm, with urology referrals comparable between arms.

What this study adds

This study developed a practical resource to support symptom assessment and conservative treatment for LUTS in primary care. The intervention showed a sustained reduction in LUTS (difference in mean IPSS of -1.81), which was less than the predefined target reduction of 2.0.

Funding, competing interests and data sharing:

This study was funded by the National Institute for Health Research, Health Technology Assessment programme (16/90/03). Competing interests are declared in the paper. Data requests should be submitted to the corresponding author.

Trial registration: ISRCTN11669964

Table for print abstract

	Intervention		Usual care		Analysis adjusted for baseline scores and minimisation variables
	N	Mean (SD) [Min, Max]	N	Mean (SD) [Min, Max]	Difference (95% CI); p-value
IPSS score: 12 months	442	11.6 (6.2) [1, 33]	473	13.9 (6.8) [2, 34]	-1.81 (-2.66 to -0.95); p<0.001
Secondary outcomes					
IPSS score: 6 months	471	11.5 (6.1) [1, 35]	501	13.8 (6.6) [1, 32]	-1.68 (-2.34 to -1.02); p<0.001
ICIQ: 12 months	453	3.7 (3.6) [0, 18]	480	4.5 (4.1) [0, 18]	-0.74 (-1.15 to -0.33); p<0.001
IPSS Quality of life: 12 months	463	2.9 (1.3) [0, 6]	483	3.3 (1.25) [0, 6]	-0.34 (-0.50 to -0.18); p<0.001

Introduction

Lower urinary tract symptoms (LUTS) relate to the storage and passing of urine as summarised in Box 1. The severity and prevalence of LUTS in men increases with age (up to 30% in men over 65 years)[1], with greater numbers therefore likely to be affected as the population ages. LUTS can have a substantial impact on quality of life;[2] with such problematic LUTS referred to as 'bothersome'. Men usually present with a range of LUTS, which can relate to storage, voiding or post-voiding urinary symptoms, and most men are assessed and managed by their General Practitioner (GP) in the first instance. Male LUTS can be caused by prostate obstruction and/or bladder dysfunction, but are also influenced by lifestyle factors. Assessments to exclude serious medical conditions, categorise and assess the impact of precise symptoms are recommended by the UK National Institute of Health and Care Excellence (NICE)[1] and the European Association of Urology (EAU).[3] However, LUTS assessment is time-consuming, and the level undertaken in general practice is variable.[4]

Conservative therapies, including bladder training, advice on fluid intake and lifestyle advice are recommended in the first instance by NICE[1] and the EAU[5] for the treatment of LUTS, although there is a lack of evidence on their effectiveness. An NHS Evidence Update in 2012[6] indicated a role for self-management in the treatment of LUTS, based on a post-hoc analysis[7] of a single centre randomised controlled trial (RCT)[8] of 140 men. However, NICE Clinical Guideline 97[1] recommended that a multicentre RCT would be needed to determine effectiveness in clinical practice. Delivery of conservative treatments in primary care is also limited,[4] which can result in men simply receiving medication to treat the prostate, potentially inappropriate referral to secondary care, or enduring persistent bothersome symptoms.

As provision for male LUTS in primary care is inconsistent, primary care health professionals require practical resources to support urinary symptom assessment, and to enhance patient engagement with conservative management interventions. The TRIUMPH study aimed to address this need in primary care. The key aim was to determine whether a standardised and manualised care intervention achieves superior symptomatic outcome compared with usual care for male LUTS, with a primary outcome of overall International Prostate Symptom Score (IPSS) measured 12 months after participant consent.

Box 1

Lower urinary tract symptoms (LUTS) in men can be caused by structural or functional abnormalities in the bladder, prostate or urethra.

"Voiding LUTS" are problems passing urine, such as hesitancy, slow urinary stream and dribbling.

"Storage LUTS" include urgency, increased urinary frequency and nocturia.

Storage LUTS can result from increased urine volumes, due to high fluid intake or systemic conditions (cardiovascular, respiratory, renal, or endocrine).

Patients may experience one or more LUTS. Severity for each individual symptom may not correlate with how much it bothers the patient.

LUTS can be measured with the International Prostate Symptom Score (IPSS); scores of 0-7 are categorised as mild overall severity, 8-19 as moderate, 20-35 as severe.

Methods

Trial Design

The TRIUMPH study was a multicentre, pragmatic, two-arm cluster randomised controlled trial (RCT) in UK primary care. The trial was conducted in thirty general practice sites, recruiting patients from June 2018 to August 2019. The trial design included an internal pilot recruitment phase of 4 months' duration, primarily to verify that recruitment was achievable before progression to the main phase of the trial. Specification of an exact figure for the number of eligible patients required by GP practices to take part in the trial, as determined by a pre-randomisation practice database search, was removed for the main phase of the trial, to allow flexibility according to patient response rate.

The trial protocol was submitted for publication before recruitment ended[9] and the trial registered prospectively (ISRCTN11669964) on 12 April 2018. The Statistical Analysis Plan[10] was finalised in July 2020, prior to completion of participant follow up (August 2020).

General practice sites

General practices were recruited from across the National Institute for Health Research (NIHR) West of England and Wessex Clinical Research Network (CRN) regions by the CRNs. Practices were eligible if they had an adequate number of eligible patients determined by a pre-randomisation practice database search (to achieve site target recruitment of 35 participants), with suitable treatment room space and availability for healthcare professional (HCP) training/baseline visits. In the final selection of practices for randomisation, consideration was also given to representative practice list size, social deprivation score (Index of Multiple Deprivation (IMD) determined using the general practice postcode) and preference for how the intervention would be delivered (practice staff or trial research nurses) if the practice was randomised to the intervention arm.[9] Groups of practices who shared nurse resource were randomised as a single site.

Participants

Adult men (18 years or over) who had presented to primary care with LUTS within the past 5 years according to GP records, currently with at least one symptom of bothersome LUTS, were potentially eligible for the study. Men were excluded due to a lack of capacity to consent, inability to pass urine without a catheter (indwelling or intermittent catheterisation), a relevant neurological disease or referral, undergoing urological testing for LUTS, currently being treated for prostate or bladder cancer, previous prostate surgery, poorly controlled diabetes mellitus, recently referred or currently under urology review, visible haematuria, or unable to complete trial assessments in English.

General practices conducted a single study-specific database search to identify potentially eligible patients, which was then manually verified by GPs using electronic medical records. A single mail out was conducted to potentially eligible patients by each site, before the site was notified of their randomisation outcome, to avoid any bias in patient selection. Patients expressing an interest in taking part in the study were contacted by phone by NIHR CRN nurses or clinical practitioners trained by the trial team, whilst masked to the allocation of the practice and therefore the patient, to avoid any bias. Calls were conducted to confirm eligibility, particularly the subjective criteria of whether the patient's LUTS were currently bothersome to them, as initial GP screening only identified men coded with LUTS within the preceding 5 years. The calls were also to ensure patient understanding of the study, answer any questions and confirm willingness to participate.

Patients deemed willing and eligible completed a consent form and questionnaire containing baseline measures via post. All patients received the same consent form and questionnaires, but those in the intervention arm also received a bladder diary to be completed before their face-to-face visit for symptom assessment. Patients remained blinded to arm whilst completing their baseline measures, and were not aware that bladder diary completion indicated randomisation to the intervention arm. The intervention arm did not have sight of the intervention booklet until after consent, and the usual care arm remained unaware of the content of the booklet throughout the trial.

Intervention

The TRIUMPH intervention employed a standardised information booklet, within which participants were directed to applicable information through HCP assessment and discussion, providing the manualised element of the intervention. The booklet was developed for the study from the British Association of Urological Surgeons patient information sheets, in collaboration with patients, healthcare professionals and health psychologists (supplementary material). The printed booklet provides targeted guidance on conservative and lifestyle interventions for male LUTS, and is water-resistant and able to lie flat when open for bathroom use. Sections are tabbed and colour coded for specific LUTS symptoms and advice.

The TRIUMPH booklet was provided to participants by either a general practice clinical nurse, research nurse or healthcare assistant, or trial research nurse depending on site preference. Training and ongoing support was provided to the HCPs delivering the intervention from the trial research nurses. The HCP reviewed the participant's baseline urinary symptoms, utilising their

completed IPSS, International Consultation on Incontinence Questionnaire Urinary Incontinence-Short Form Symptoms score (ICIQ-UI-SF) and ICIQ bladder diary before the participant then attended for one intervention visit. During this visit the HCP discussed their individual symptoms and level of bother. The HCPs were provided with decision tools (supplementary material) to assist them in directing the participant to relevant sections of the booklet based on their symptoms. A maximum of three sections were recommended to each participant and tabbed with discreet stickers. The sections were: 1) advice on drinks and liquid intake; 2) advice on controlling an urgent need to urinate; 3) exercising the muscles between the legs (pelvic floor) to help stop bladder leakage; 4) advice on emptying the bladder as completely as possible; 5) advice on getting rid of the last drops of urine; 6) reducing sleep disturbance caused by needing to urinate.

To encourage and gauge adherence to the intervention, follow-up contacts with the HCP were conducted by phone with participants at 1 week, and then by phone, email or text at 4 and 12 weeks according to participant preference. Participants retained the intervention booklet thereafter. Participants in the intervention arm continued to receive usual care from their GP for their LUTS.

The usual care practices were requested to continue their standard local practice for the management of LUTS. At the end of the study, usual care arm participants were provided with a copy of the booklet alongside a summary of trial results.

Participants in both randomised groups were provided with overall study progress updates at 3 and 9 months via a newsletter to maintain engagement with the trial and encourage completion of follow-up questionnaires.

Outcomes

The primary outcome measure was the validated patient-reported IPSS at 12 months after participant consent, which is extensively used in LUTS research and also widely employed in urology services.[11] The IPSS score ranges from 0 to 35, with higher scores indicating more severe symptoms. The endpoint of 12 months was chosen to measure whether the effect of the TRIUMPH intervention on LUTS was sustained after the initial 12-week delivery period.

Secondary outcomes collected by questionnaire at baseline, and 6 and 12 months after consent comprised of the IPSS Quality of Life (LUTS QoL score, 6 and 12m), the IPSS (overall urinary symptom score, 6m), the ICIQ-UI-SF (International Consultation on Incontinence Questionnaire Urinary

Incontinence-Short Form Symptoms score, 6 and 12m,[12] which supplements the IPSS with measurement of incontinence and post-void dribble), the EQ-5D (five-level version, EQ-5D-5L, measure of health status, 6 and 12m, used to create quality-adjusted life years for the health economic evaluation)[13] and the Brief Illness Perception Questionnaire (B-IPQ, participant cognitive and emotional perception of their LUTS, which was modified slightly, with developers' permission, to ask about "urinary symptoms" rather than "illness", 6 and 12m).[14]

The number of expected adverse events (specified as urinary tract infections, catheterisations, urinary retention, prostatitis or death) and the number of referrals to secondary care (urology) at 12 months post-consent were extracted from primary care electronic medical records through trial specific automated database searches, conducted a minimum of one month after the final participant for each site had completed follow up. Anonymised data extracts were provided by sites to the central trial team for analysis.

Study designed case report forms (CRFs) were completed by the HCPs for the intervention arm only, at the intervention visit and during the 12-week treatment phase to collect details of the booklet sections advised to the participant, and feedback on the booklet.

Health economic and qualitative outcomes are reported separately.

Sample size calculation

TRIUMPH was designed to detect a mean between-arm difference of 2 points on the IPSS score at 12 months post-randomisation with 90% power, as this is the mean decrease in IPSS among men rating the condition as slightly improved when the baseline scores are less than 20 points.[15] As outlined in the study protocol,[9] this is less than the previously observed minimum clinically important difference of 3 points for the IPSS[16] but allows for a difference in just one symptom. Based on a scoping search of local general practices we estimated a mean cluster size of 35 participants and proposed an estimated intraclass correlation (ICC) of 0.05 based on other primary care studies.[17] Prior trials centre experience suggested that allowing for up to 30% loss to follow-up would be prudent. Based on this we estimated that 840 participants would be needed from at least 24 sites to achieve 90% power under the assumptions outlined above.

We observed early in the study, however, that there was variability between sites in the number of participants recruited thus necessitating a revision of the sample size calculation. Using recruitment

data available at the time, we estimated that the mean number of participants consented at each site would be 26 and that the coefficient of variation of the mean cluster size would be 0.26. Ignoring clustering and loss to follow-up 263 patients in total would be required to detect a 2-unit difference in IPSS scores with 90% power assuming a common standard deviation of 5. Our updated design effect assumed (i) an ICC of 0.05; (ii) the mean number of patients consenting per site would be 26 but that only 70% would provide primary outcome data resulting in a mean cluster size of 18.2; (iii) the coefficient of variation in cluster sizes is 0.26. This gives a design effect of 1.92 meaning that the total number of patients required to provide primary outcome data is 506. Given our assumed loss to follow-up, this meant that 724 patients needed to be consented to the study and since each site was expected to consent 26 patients this translated to 28 sites in total. Allowing for some not to perform as expected, 30 practices were ultimately recruited in agreement with the trial management group, funder and steering committee.

Randomisation and blinding

General practice sites were the units of allocation and practices were randomised on a 1:1 basis to deliver either the TRIUMPH intervention or usual care arm by a statistician blind to the identity of practices. Randomisation was conducted after the practices had completed their screening and invitation to eligible patients. Randomisation was minimised by centre (West of England and Wessex CRN regions) practice size (number of patients registered at the practice) and area-level deprivation (Index of Multiple Deprivation score, IMD) of the practice. A random element was incorporated in the minimisation procedure such that there was a 40% probability that allocation was random with a 50-50 chance of practices being allocated to either arm. Area-level deprivation assessed at the lower super output area level (LSOA; geography comprising between 400 and 1200 households) can estimate deprivation for individuals (using home postcodes to identify the LSOA), but middle layer super output area level (MSOA; geography made up of 4 or 5 LSOAs) data better reflect the area-level deprivation of General practices since the catchment area of a General practice is generally wider than the area covered by the LSOA.[18] As such, General practice postcodes were mapped onto LSOAs then MSOAs. Population-averaged IMD scores (2015) were then calculated based on the scores of LSOAs within each MSOA.

Staff conducting patient eligibility calls were blinded to practice allocation, to minimise selection and recruitment bias. Participants were blinded to their allocation until their completed baseline questionnaire and consent form were received.

Safety

General practices were responsible for reporting Serious Adverse Events (SAEs) for their trial participants, however participants were also asked to report any inpatient stays in their follow up questionnaires, which prompted GP review. The study independent Data Monitoring Committee reviewed serious adverse events on a 6-monthly basis. All other adverse events were collected from participant primary care electronic medical records (EMR), as part of the secondary outcomes.

Statistical analysis

Statistical analyses were conducted keeping all consenting participants in the randomised arm of their general practice. Baseline characteristics at the individual- and practice-level were summarised using means, standard deviations (SD), medians (interquartile ranges (IQR)) or number (%) depending on the nature and distribution of the data.

The primary analysis of IPSS scores at 12 months was conducted on a modified intention-to-treat (ITT) basis and comparisons between treatment arms were made using mixed-effect multilevel linear models (individuals (level 1) nested within General practices (level 2)) adjusting for individual-level baseline IPSS and practice-level variables used in the randomisation based on those providing non-missing data for the variables included in the model. The results are presented as the mean between-arm difference, 95% confidence interval (CI), p-value and model ICC (95% CI).

The secondary outcomes were also analysed on a modified ITT basis. IPSS scores at 6 months were analysed using a mixed-effect multilevel linear model (individuals (level 1) nested within General practices (level 2)) adjusting for individual-level baseline IPSS and practice-level variables used in the randomisation. Additionally, and separately, a repeated measures analysis was conducted using a repeated measures linear mixed model (IPSS scores at 6 and 12 months (level 1), nested within participants (level 2) and nested within General practices (level 3)) adjusting for individual level baseline IPSS scores and practice-level variables used in the randomisation. Minimal clinically important differences for male LUTS patients are not established in the literature for the secondary outcomes included.

Seven sensitivity analyses were planned to assess the robustness of the primary analysis to varying assumptions. Each of these sensitivity analyses was compared to the primary analysis.

- Descriptive statistics were used to assess whether baseline characteristics were balanced between the two arms and, if differences were observed, the primary analysis would be re-

run adjusting for those imbalanced variables. This analysis was not performed, however, since there was no evidence of imbalance in variables not already included in the primary analysis.

- To allow for possible clustering of outcomes within nurses/HCAs delivering the intervention, patient-level data was grouped according to the combination of practice and nurse/HCA delivering the intervention. The primary analysis was then re-run using a single random effect for this level of clustering.
- While the target recruitment was reached prior to the COVID-19 outbreak, we wished to allow for participation and symptom reporting to have been influenced by the outbreak and subsequent lockdowns. To do this the primary analysis was repeated including a binary variable for whether or not the outcome measure was taken before or after 11 March 2020 (date the World Health Organisation declared the outbreak a pandemic).
- A small number of participants recruited to the study were subsequently found to be ineligible. They were included in the primary analysis and a sensitivity analysis was performed excluding those individuals.
- A series of per protocol analyses were performed using different definitions of protocol compliance. The definitions of compliance are outlined with the results of these analyses in the supplementary materials.
- Recognising the biases inherent to per protocol analyses a complier-average causal analysis (CACE) was also performed. Compliers were those who received the intervention booklet by the time of the primary outcome follow-up. The CACE estimates were obtained using instrumental variable regression using the same variables used in the primary analysis with the randomised arm as the instrumental variable and an indicator variable for compliance.
- We explored the impact of missing primary outcome data using different assumptions regarding missingness: “best” and “worst” case scenarios as well as multiple imputation by chained equations (MICE) to impute missing data.

To explore whether the effectiveness of the intervention on the primary outcome differed by participant sub-group we performed four pre-specified sub-group analyses. In each case, effect modification was assessed by including a sub-group-treatment interaction term and performing a likelihood ratio test comparing the model with and without the interaction term. A significance level of 5% was used, but as these analyses were not statistically powered, they are interpreted with caution. Sub-group analyses assessed (i) whether effectiveness differed by the nature of LUTS at baseline measured by the ratio of the IPSS voiding score to the storage score, (ii) whether a practice nurse/HCA or trial nurse delivered the intervention, (iii) the participant’s preferred method of contact

at baseline and (iv) the number of contacts between the practice nurse/HCA and participant at intervention practices.

Patient and public involvement

Patient and public involvement (PPI) representatives have been involved at all stages from a patient co-applicant at the grant application stage to help shape the project, to patient representative members of our Trial Management Group and Trial Steering Committee who helped steer the trial throughout. Wider patient advisory group meetings were also held over the course of the study. Development of our TRIUMPH intervention booklet was one of the key roles for PPI, resulting in important changes to aid clarity and usability, and recommendations on what patients would consider a manageable level of advice to follow. PPI review of our patient-facing study materials was also undertaken, including patient questionnaires to assess clarity and participant burden, newsletters and the study website. Further PPI involvement has included discussion of some of our initial qualitative findings relating to men's experiences of the patient pathways for LUTS within the NHS, as well as routes for implementation and dissemination, and patients will continue to be involved as this progresses.

Results

30 primary care sites (32 General Practices; one group of 3 practices were randomised as a single site) were recruited and all contributed to the intention-to-treat analysis (figure 1); 17 were randomised to the intervention arm and 13 to the usual care arm. At the time of recruitment, they provided estimated (pre-screening) practice list sizes ranging from 7,600 to 48,623 patients (mean=19,576) reflecting some of the larger practices in the Wessex and West of England regions (combined regional median practice size in June 2019: 9,440). Area-level IMD scores ranged from 4.22 to 33.62 for practices and the mean was slightly higher in usual care practices, suggesting greater levels of socio-economic deprivation than in intervention ones (table 1).

7,872 potentially eligible patients were identified from database searches by General practices. A random selection of 160 patients were not screened due to agreed limits on screening numbers by large practices, and 97 patients were not screened due to practice capacity. Of the remaining 7,615 patients manually screened by GPs, 2,047 were ineligible (figure 1) with reasons for ineligibility outlined in table S1 (supplementary). Of the eligible patients identified, 4,808 were invited to join the study with a maximum of 150 (pilot phase) or 220 (main phase) invited patients per site, to avoid over-representation of larger sites.

2,300 of the 4,808 (48%) participants invited into the study responded to the single invitation (no reminder was issued). Of those who responded 1,671 were interested in taking part (73%). On further screening for eligibility (in particular current bothersome LUTS) 1,293 (77%) of those interested were eligible. Of these 524 participants were recruited from intervention sites and 553 from usual care sites (83% of those interested & eligible) (figure 1). Patients remained blinded to their randomised arm until after consent. Men were, on average, in their late 60s, with a strong predominance of white and married or civil-partnered men (table 1). The distribution of clinical characteristics was comparable between treatment arms. The median number of GP consultations in the last 12 months before baseline was the same in both arms, but the proportion with a referral to urological services in that period was slightly lower in the intervention arm (intervention: 2.93%; usual care: 3.49%). Baseline IPSS scores were slightly lower in the intervention arm than in the usual care arm, indicating a lower symptom burden; but this was not reflected in the ICIQ-UI-SF focused on incontinence. Quality of life (IPSS quality of life) was comparable between the two arms, as was patient perception of their LUTS (B-IPQ).

Primary outcome: IPSS at 12 months

915 participants (84.96% of those randomised) provided primary outcome data of whom 887 provided sufficient baseline data to be included in the analysis. In both randomised arms there was some improvement in LUTS symptoms at 12 months, but this was greater in the intervention arm (IPSS difference=-1.81 (95% CI: -2.66 to -0.95), p<0.001) after adjustment for baseline values and minimisation variables (table 2).

In a planned sensitivity analysis, accounting for clustering by nurse/HCA had little effect on the primary outcome results (difference=-1.79 (95% CI: -2.53 to -1.06), p<0.001), nor did excluding three participants who were found to be ineligible after follow-up began (difference=-1.81 (95% CI: -2.65 to -0.96), p<0.001) or adjusting for whether the outcome data was collected during the COVID-19 pandemic (difference=-1.89 (95% CI: -2.69 to -1.09), p<0.001). Imputation of missing data also yielded comparable results to the complete case analysis (table 3).

Secondary outcomes

The difference in IPSS score means was also evident between the two arms at 6 months, although slightly less than at 12 months, and in the repeated measures analysis of IPSS scores (6 and 12 months) (table 2). Incontinence scores were also lower in the intervention arm compared to usual care at 6 and 12 months (as assessed with the ICIQ-UI-SF) with the improvement in the intervention arm being greater at 12 months than at 6 months (table 2). Mean IPSS LUTS-specific quality of life (QoL) scores at 6 and 12 months were near the middle of the range of scores for this measure, but showed evidence of small differences between the arms (table 2). Patient perception of their LUTS (B-IPQ) showed a greater improvement in the intervention arm at both 6 and 12 months than the usual care arm (table 2).

Similar proportions of men were referred to secondary care over the following 12 months (intervention: 7.32%, usual care: 7.90%), and after adjusting for randomisation variables and pre-baseline referrals there was no evidence of a difference between the arms (adjusted OR=0.91 (95% CI: 0.51 to 1.62); p=0.757) (table 4).

A low number of patients reported LUTS-related adverse events or other urinary “expected” adverse events, but reporting was similar in both arms (table 5). All study serious adverse events were unrelated to the intervention with the exception of five which were deemed unlikely to be related to the intervention (supplementary table S3).

Subgroup analyses

Including the ratio of storage: voiding LUTS at baseline as a continuous interaction term in the model of IPSS scores at 12 months showed no evidence of effect modification (p=0.971). Similarly, distinguishing between those men receiving the intervention via a study nurse (n=249) or a practice nurse/healthcare assistant (n=190) also yielded no evidence of difference (p=0.387). There was, however, very weak evidence (p=0.094) of effect modification by how intervention participants preferred follow-up by the clinical team (telephone=310; text or email=210) with contact by text or email showing a greater improvement from usual care.

Intervention delivery

Almost all participants at intervention sites received the intervention booklet (98.47%) and 91.67% received all three planned follow-up contacts, with the majority (79.01%) received in the protocolised format (week 1 by phone call, weeks 4 and 12 as preferred by the participant). Given the high level of fidelity to the intervention, the planned per protocol analyses on amount of follow up had very small numbers, thus were underpowered, but were also consistent with a greater change in IPSS scores at 12 months in the intervention arm (supplementary table S2). As only nine participants in the intervention arm were deemed non-adherent, the planned CACE analysis was not performed.

TABLES AND FIGURES

Table 1: Site and participant characteristics at baseline

	Intervention		Usual care	
	n[a]		n[a]	
SITE-LEVEL CHARACTERISTICS				
Total number of sites; n		**17**		**13**
Practice size; mean (SD)	17	20,694 (9,714)	13	18,114 (7,998)
Number of participants consented per site; mean (SD)	17	31 (12.00)	13	43 (12.71)
Area-level deprivation of the practice based on practice postcode; mean (SD)	17	11 (5.00)	13	16 (8.39)
PARTICIPANT-LEVEL CHARACTERISTICS				
Total number of participants; n		**524**		**553**
Demographic characteristics				
Age (years); mean (SD) [min – max]	524	*68.9 (9.3) [32 – 94]*	553	*68.4 (9.2) [30 – 95]*
Ethnicity; n(%)	522		550	
White		*513 (98.28)*		*542 (98.55)*
Non-white		*8 (1.53)*		*5 (0.91)*
Disclosure declined		*1 (0.19)*		*3 (0.55)*
Marital status; n(%)	517		543	
Single		21 (4.06)		25 (4.60)
Married or civil partnered		436 (84.33)		455 (83.79)
Divorced		31 (6.00)		32 (5.89)
Widowed		27 (5.22)		28 (5.16)
Disclosure declined		2 (0.39)		3 (0.55)
IMD Quintile ; n(%)	506		525	
Quintile 1 (most deprived)		17 (3.36)		21 (4.00)
Quintile 2		33 (6.52)		37 (7.05)
Quintile 3		67 (13.24)		106 (20.19)
Quintile 4		141 (27.87)		136 (25.90)
Quintile 5		248 (49.01)		225 (42.86)
IMD Score; median (IQR)		8.80 (5.75-13.71)		9.89 (6.21 – 15.45)
Clinical characteristics				
Height (cm); mean (SD) [min – max]	518	176.72 (6.77) [152.40, 198.12]	550	176.93 (7.41) [157.48, 208.28]
Weight (kg); mean (SD) [min – max]	510	83.35 (14.45) [55.02, 152.41]	549	83.89 (14.29) [53.98, 136.98]
BMI; mean (SD) [min – max]	508	26.71 (4.40) [18.91, 52.31]	549	26.76 (4.00) [17.57, 42.18]
Number of co-morbidities; n(%)	478		544	
None		151 (31.59%)		171 (31.43%)
One		160 (33.47%)		197 (36.21%)
More than 1		167 (34.94%)		176 (32.35%)
Most recent urine analysis results in the 6 months pre-baseline; n(%)	79		52	
Abnormal		1 (1.27%)		2 (3.85%)
Kidney function: most recent eGFR (ml/min/1.73m^2) measure in the 6 months pre-baseline	170		215	
Number of patients with an eGFR measure		170		215
eGFR: mean (SD)		73.5 (15.7)		74.6 (13.2)
eGFR: median (IQR)		76.5 (65, 87)		75 (66, 87)
eGFR: min - max		28, 98		36, 100
Chronic kidney disease (CKD) stages based on most recent eGFR in the 6 months pre-baseline; n(%)	170		215	
≥90 ml/min/1.73m^2 (normal)		28 (16.47%)		33 (15.35%
90-60 ml/min/1.73m^2 (CKD stages G1-G2)		114 (67.06%)		154 (71.63%)

30-59 ml/min/1.73m² (CKD stage G3)		27 (15.88%)		28 (13.02%
<30 ml/min/1.73m² (CKD stages G4- G5)		1 (0.59%)		0 (0%)
Number of GP consultations in the 12 months before baseline	478		544	
Mean (SD)		4.4 (3.7)		4.8 (5.0)
Median (IQR)		4 (2, 6)		4 (2, 6)
[min – max]		0, 23		0, 58
Referrals to urology in the 12 months pre-baseline; n(%)	478		544	
None		464 (97.07%)		525 (96.51%)
One		14 (2.93%)		19 (3.49%)
More than one		0 (0%)		0 (0%)
Patient reported symptoms and quality of life				
IPSS symptoms; mean (SD) [min – max]				
Incomplete emptying	512	*1.7 (1.5) [0-5]*	549	*1.9 (1.5) [0-5]*
Frequency	514	*2.7 (1.3) [0-5]*	551	*2.9 (1.4) [0-5]*
Intermittency	514	*1.9 (1.6) [0-5]*	549	*2.0 (1.7) [0-5]*
Urgency	513	*2.1 (1.6) [0-5]*	549	*2.3 (1.7) [0-5]*
Weak stream	510	*1.9 (1.5) [0-5]*	549	*2.0 (1.7) [0-5]*
Straining	513	*0.8 (1.2) [0-5]*	548	*1.0 (1.3) [0-5]*
Nocturia	516	*2.6 (1.4) [0-5]*	551	*2.4 (1.2) [0-5]*
Total IPSS score; mean (SD) [min – max]	501	*13.6 (5.8) [1, 33]*	541	*14.6 (6.6) [2, 34]*
Mildly symptomatic (score ≤7); n(%)		*76 (15.17)*		*74 (13.68)*
Moderately symptomatic (score: 8-19); n(%)		*342 (68.26)*		*338 (62.48)*
Severely symptomatic (score ≥ 20); n(%)		*83 (16.57)*		*129 (23.84)*
IPSS quality of life score *(If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?)*; mean (SD) [min – max]	516	*3.5 (1.2) [0, 6]*	551	*3.6 (1.1) [0, 6]*
ICIQ-UI-SF total score; mean (SD) [min – max]	513	*3.6 (3.6) [0, 14]*	542	*3.9 (3.7) [0, 15]*
ICIQ-UI-SF: when does urine leak?; n (%)	523		553	
Never		*185 (35.37)*		*162 (29.29)*
Leaks before you can get to the toilet		*205 (39.20)*		*237 (42.86)*
Leaks when you cough/sneeze		*24 (4.59)*		*24 (4.33)*
Leaks when you are asleep		*12 (2.29)*		*15 (2.71)*
Leaks when you are physically active		*23 (4.40)*		*27 (4.88)*
Leaks when you have finished urinating/ are dressed		*175 (33.46)*		*205 (37.07)*
Leaks for no obvious reason		*36 (6.88)*		*42 (7.59)*
Leaks all of the time		*1 (0.19)*		*1 (0.18)*
B-IPQ total score; mean (SD) [min – max]	440	*38.7 (11.0) [1, 75]*	478	*39.4 (10.4) [6, 72]*
Bladder diary[b]; n(%)			N/A	N/A
Incontinence	502	*100 (19.92%)*		
Urgency	507	*364 (71.79%)*		
Nocturia[c]	261	*222 (85.07%)*		

[a] Number of sites/participants providing non-missing data at baseline

[b] Bladder diary completed as part of initial assessment in intervention

[c]For description purposes at baseline, nocturia is defined as waking up in the night to urinate at least once on two nights, or waking up in the night to urinate twice or more on one night. Where waking or sleeping data were not provided by the participant the variable is set to missing.

Table 2: Analyses of treatment effectiveness on patient-reported primary and secondary outcomes

	Intervention		Usual care		Analysis adjusted for baseline scores and minimisation variables		
	N*	Mean (SD) [Min, Max]	N*	Mean (SD) [Min, Max]	Difference (95% CI); p-value	N contributing to analysis	ICC (95% CI)
Primary outcome							
IPSS[†] score: 12 mo. **	442	11.6 (6.2) [1, 33]	473	13.9 (6.8) [2, 34]	-1.81 (-2.66 to -0.95); p<0.001	887	0.011 (0.0001 to 0.086)
Secondary outcomes							
IPSS[†] score: 6 mo. **	471	11.5 (6.1) [1, 35]	501	13.8 (6.6) [1, 32]	-1.68 (-2.34 to -1.02); p<0.001	942	<0.001 (<0.001 to <0.001)
IPSS[†] scores at 6 and 12 mo. (repeated measures analysis) ***	913	11.6 (6.2) [1, 35]	974	13.8 (6.7) [1, 34]	-1.70 (-2.35 to -1.05); p<0.001	1829	0.005 (0.0002 to 0.115)
ICIQ[†]: 6 mo. ***	476	3.6 (3.5) [0, 15]	504	4.5 (4.1) [0, 20]	-0.53 (-1.02 to -0.04); p=0.03	961	0.022 (0.007 to 0.072)
ICIQ[†]: 12 mo. ***	453	3.7 (3.6) [0, 18]	480	4.5 (4.1) [0, 18]	-0.74 (-1.15 to -0.33); p<0.001	915	<0.001 (<0.001 to <0.001)
IPSS[†] QoL: 6 mo. **	483	3.0 (1.2) [0, 6]	511	3.35 (1.25) [0, 6]	-0.28 (-0.41 to -0.14); p<0.001	984	Could not be estimated
IPSS[†] QoL: 12 mo. **	463	2.9 (1.3) [0, 6]	483	3.3 (1.25) [0, 6]	-0.34 (-0.50 to -0.18); p<0.001	937	0.004 (<0.001 to 0.274)
B-IPQ[†]: 6 mo.**	450	33.4 (11.9) [2, 73]	430	38.3 (11.5) [1, 76]	-5.34 (-6.69 to -3.99); p<0.001	777	<0.001 (<0.001 to <0.001)
B-IPQ[†]: 12 mo. **	419	33.8 (12.0) [0, 69]	427	38.4 (12.2) [0, 71]	-4.78 (-6.31 to -3.25); p<0.001	746	<0.001 (<0001 to <0.001)

*n reflects the number of participants in each arm providing non-missing outcome data except in the repeated measures analysis of IPSS scores (6 and 12 months) where this reflects the number of repeated measures of IPSS in each arm. [†]IPSS scores can range between 0 and 35; ICIQ scores can range between 0 and 21; IPSS QoL scores can range between 0 and 6; B-IPQ scores can range between 0 and 90.

** analysed using *mixed-effect multilevel linear model (individuals (level 1) nested within General practices (level 2)) adjusting for individual-level baseline outcome measure and practice-level variables used in the randomisation*

*** *analysed using a repeated measures linear mixed model (IPSS scores at 6 and 12 months (level 1), nested within participants (level 2) and nested within General practices (level 3)) adjusting for individual level baseline IPSS scores and practice-level variables used in the randomisation*

Table 3: Sensitivity analysis: comparison of results of ITT analysis of complete cases with ITT analyses where missing IPSS data were imputed

	N imputed in intervention arm	N imputed in usual care arm	N used in analysis	Mean (overall)	SD	Difference in means[a]	95% CI	p-value
Complete case ITT	0	0	887	12.79	6.64	-1.81	(-2.66 to -0.95)	<0.001
"Best" case scenario	77	78	1,042	10.89	7.63	-1.89	(-2.89 to -0.88)	<0.001
"Worst" case scenario	77	78	1,042	14.82	7.82	-1.14	(-2.08 to -0.20)	0.02
MICE[b]	82	80	1,077			-1.61	(-2.57 to -0.66)	0.001

[a] Analysis adjusted for baseline IPSS score and minimisation variables

[b] Data is imputed using baseline and 6 month IPSS, treatment arm, practice size, centre and deprivation (IMD). To allow for clustering in Stata, imputations were performed separately for each practice.

Table 4: Secondary outcome: percentage and OR of referral to secondary care (urology)

	N	N	%[a]	OR[b] (95% CI)	p-value	ICC (95% CI)	OR[c] (95% CI)	p-value	ICC (95% CI)
Intervention	478	35	7.32	0.91 (0.51 to 1.62)	0.76	0.02 (0.00 to 0.41)	0.89 (0.52 to 1.54)	0.69	0.04 (0.01 to 0.26)
Usual care	544	43	7.90						
Total N	1,022	78	7.63						

[a] number with referral (n) in relation to number in treatment arm (N)

[b] modified ITT analysis adjusted for whether or not the patient had a referral pre-baseline and minimisation variables restricted to those providing non-missing data for the variables included in the model

[c] modified ITT analysis adjusted for whether or not the patient had a referral pre-baseline restricted to those providing non-missing data for the variables included in the model

Table 5: Expected adverse events identified from GP electronic medical records search

	Received intervention	**Received usual care**
Prostatitis; n	2 (one patient had 1 occurrence and the other had 4 occurrences)	2 (one patient had one occurrence and the other had 6 occurrences)
LUTS-related urinary tract infection; n	2 (one patient had 3 occurrences and the other had 2 occurrences)	3 (each patient had one occurrence)
Urinary retention; n	1 (one patient had 1 occurrence)	2 (one patient had 2 occurrences and the other had 4 occurrences)
Catheterisations; n	0	0
Deaths; n	2	1

Figure 1: Study flow diagram

Discussion

This large, pragmatic RCT in primary care showed a range of bothersome LUTS improved over 12 months in men with moderate LUTS severity, using a standardised booklet and manualised approach to symptom management. The mean patient reported primary outcome (IPSS) was 1.81 points lower in the intervention arm than usual care. The secondary outcomes of ICIQ and IPSS-QoL also showed improvement against usual care, demonstrating the overall impact on LUTS through incontinence, post-void dribble, and quality of life. In addition, patient perception of their LUTS improved over 12 months in the intervention arm (B-IPQ) and as shown in the embedded qualitative research (in preparation). Referral rates to urology and adverse events did not differ greatly between the arms, possibly reflecting alternative reasons for referral, such as suspected prostate cancer. The health economic analysis showed similar costs in the intervention and usual care arms (to be submitted).

The response rate of patients invited into the study was 48%, which may reflect men historically coded as LUTS in primary care in the previous five years no longer being bothered by symptoms, or inaccuracies in coding. In addition, only a single invitation was sent, with no reminder. Of those who responded 73% were interested in taking part. Response rates were unrelated to acceptability of the intervention as men were blinded to their randomisation group until they had consented to the study, without sight of the intervention booklet.

The mean IPSS score at baseline was 13.6/14.6 in the two randomised groups which is moderate by the accepted symptom severity categories (8-19). The TRIUMPH study accepted men who were still bothered by any type of LUTS despite having previously consulted their GP in the previous five years. This included storage or voiding LUTS, post-void dribble and monosymptomatic nocturia (a symptom that can be caused by a wide range of medical causes unrelated to the lower urinary tract).[19, 20] Obtaining symptom improvement in such a mixed population, using assessments and guidance in the form of a booklet provided by nurses or healthcare assistants, is a considerable challenge. The population mean IPSS reduction was 1.81 points greater than that obtained with usual care and was sustained for at least nine months beyond the final healthcare professional input into the intervention. Hence, a considerable number of men saw improvement in symptoms, with low risk, low cost (to be reported separately) and low requirement for GP input.

The target reduction of 2.0 points on which TRIUMPH was powered is less than the more generally used minimum clinically important difference of 3.0 points for the IPSS[16] , as the threshold change for “slight improvement” in symptoms is affected by baseline IPSS scores.[15] Two is the threshold where baseline IPSS is below 20.The study pragmatically included LUTS in all in its manifestations, potentially including men with just one symptom requiring treatment (e.g. nocturia). For such men, the baseline

IPSS score could be as low as 2 (i.e. nocturia twice per night, the severity of nocturia generally accepted as impairing quality of life).[19] These men could see improved quality of life by reducing their nocturia severity down to once per night [21] (i.e. a reduction in IPSS from 2 to 1).

The observed reduction of 1.81 (95% CI -2.66 to -0.95) was smaller than the predefined target reduction of 2.0 points thus the improvement in symptoms due to the intervention may be small. [10] The symptom score reduction was relative to usual care, where a small overall reduction in IPSS was also seen at a year. By participating in the study, the usual care arm completed patient-reported outcomes, received newsletters, and were potentially influenced to reflect on their LUTS, hence triggering health-seeking behaviour that could improve their symptoms. The clinical importance of this result is potentially increased given that this pragmatic study of a non-drug intervention was unselective of type or severity of LUTS and was based in primary care. In addition, the result is sustained, with a long interval (minimum of 9 months) between the end of healthcare professional input and measurement of the primary outcome.

We did not identify other studies of similar size directed at this issue. A non-randomized pilot study of men with uncomplicated LUTS in secondary care gave access to an online self-management programme in the intervention arm, versus usual care from a urologist.[22] No significant differences between cohorts was found for the IPSS, and uptake of the intervention was only 53%. A randomised trial determined the effects of a health education strategy for older adults living at home, providing a booklet on five common health problems including LUTS,[23] showing the health education strategy did not change GP attendances within 3 months. Both these studies suggest primary care is the most appropriate context to support self-care in LUTS.

Post-void dribble affects about half of men,[24] and incontinence affects about one man in eight.[25] These are bothersome symptoms[26], so they were included in the standardised booklet used in the intervention. However, neither symptom is captured by the IPSS, so the ICIQ-UI-SF was used when men were assessed by the healthcare professional, to indicate which should be directed to the applicable section(s) of the booklet. At 12 months, the mean ICIQ-UI-SF score in the intervention arm was 3.7 and in the usual care arm it was 4.5 (out of a maximum score of 12). This small difference is unlikely to be clinically significant overall, but it does not exclude the possibility that individuals may have obtained a useful benefit. Similar benefits of likely low significance were observed for the IPSS QoL (difference of 0.34 at 12 months) and possibly also men's perception of LUTS (difference of 4.78 at 12 months).

A strong focus on pharmaceutical management of male LUTS persists,[27] perhaps causing clinicians to rely on their use, however men have tended previously to express a preference for conservative and

less risky treatment for LUTS.[28] The TRIUMPH study has identified that symptomatic improvement can be sustained in the medium term using clear written materials. Key features were practical relevant assessment, interpretation by a suitably-trained HCP, focus on the most applicable elements for the individual's symptoms and supportive follow up. The type of healthcare professional (nurse or healthcare assistant) undertaking the assessment and intervention did not appear to affect outcomes. Accordingly, the intervention appears well-suited to delivery in clinical practice by either type of HCP.

Strengths and limitations of the study

This was a large pragmatic RCT conducted in a range of general practices in two English regions. Recruitment of practices and men was high and intervention delivery successful, including follow up contacts to 12 weeks. Follow up was timed to capture whether the impact of the intervention was sustained, with missing data low for a patient reported outcome at 12 months.

Some considerations are needed in interpreting the findings. The preference for conservative and less risky treatment for LUTS is potentially affected by baseline symptom severity,[29] and the study randomised men regardless of baseline severity, provided they considered the symptoms bothersome. The study could not distinguish which symptoms specifically benefitted most. Nocturia was included, but it can also have a multifactorial bases driven by several medical influences.[19, 20] and a qualitative exploration has been published finding that men with long-term disruptive symptoms, perception that the booklet content was novel or worthwhile, and a belief that self-management might help, were more receptive to the intervention.[30] The study is not able to distinguish which elements of the intervention are necessary for its success, for example whether reduced follow up contacts would have been sufficient. The white ethnic predominance in the demographic constitution of the study populations may restrict applicability, particularly for different ethnic groups. This merits additional evaluation.

Conclusions and future research

Conservative treatment is recommended by guidelines as first line treatment of male lower urinary tract symptoms. The TRIUMPH study showed that the standardised and manualised intervention achieved a sustained reduction in LUTS (difference in mean IPSS scores at 12 months of -1.81 (95% CI -0.95 to -2.66)), which was less than the predefined target reduction of 2.0.

Future research is directed at integrating the TRIUMPH intervention into general practice infrastructure, adapting it for patients with low literacy or non-English versions, including training materials, approaches to interpretation and access to the standardised booklet. Potentially, many of the symptoms managed in this way are also experienced by women, raising the possibility of developing an equivalent standardised and manualised approach to managing female LUTS.

Summary box

What is already known on this topic

- Assessment of male LUTS and use of conservative treatments in primary care are limited and variable.
- There is limited evidence that conservative treatments are effective for male LUTS, despite their recommendation in national guidelines.

What this study adds

- This study developed an intervention which provides a practical resource to support symptom assessment and conservative treatment for LUTS in primary care.
- The TRIUMPH intervention achieved a sustained reduction in LUTS in a UK primary care setting (difference in mean IPSS scores at 12 months of -1.81 (95% CI -0.95 to -2.66)), which was less than the predefined target reduction of 2.0.

Ethics statements

Ethical approval

Acknowledgments

This study was designed and delivered in collaboration with the Bristol Randomised Trials Collaboration (BRTC), a UKCRC registered clinical trials unit which, as part of the Bristol Trials Centre, is in receipt of NIHR CTU support funding. The University of Bristol acted as the Sponsor for this trial and the trial was hosted by the NHS Bristol, North Somerset and South Gloucestershire Clinical Commissioning Group (CCG). The TRIUMPH Research team acknowledges the support of the National Institute for Health Research Clinical Research Network (NIHR CRN). Study data were collected and managed using REDCap hosted at the University of Bristol.

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Data availability statement

Footnotes

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Contributors: MJD was the Chief Investigator of TRIUMPH; he conceived the study, participated in its design and coordination, and drafting the manuscript. JAL, NC, MF, LM, HH, SJM, MJR, SN, JR, MJD, LAR and GT also assisted with the study design. JW and JF developed the trial procedures, protocol and manuscript and managed the coordination of the study. MM and JT also assisted with the coordination of the study. SJM designed the statistical analysis and ES conducted the statistical analysis. MC contributed to the data extraction from GP medical records. All authors contributed to the oversight of the study via the TMG, read and commented on manuscript drafts and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Ethical approval: Approval from the NRES North West Preston Ethics Committee (18/NW/0135) was received on 11 April 2018 and applied to all NHS sites who took part in the study. All participants provided their written, informed consent to participation before entering the study.

Data sharing: All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Transparency: The lead author (MD) affirms that this manuscript is an honest, accurate, and transparent account of the trial being reported; that no important aspects of the trial have been omitted; and that any discrepancies from the trial as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities: Participants of the TRIUMPH study will be informed of the results through the website (bristol.ac.uk/triumph-study), they will be sent details of the results in a study newsletter, and we will also disseminate through the media.

Provenance and peer review: Not commissioned; externally peer reviewed.

Trial registration: Trial registration was prospective before enrolling the first patient. ISRCTN registry number: ISRCTN11669964. Registration date: 12/04/2018.

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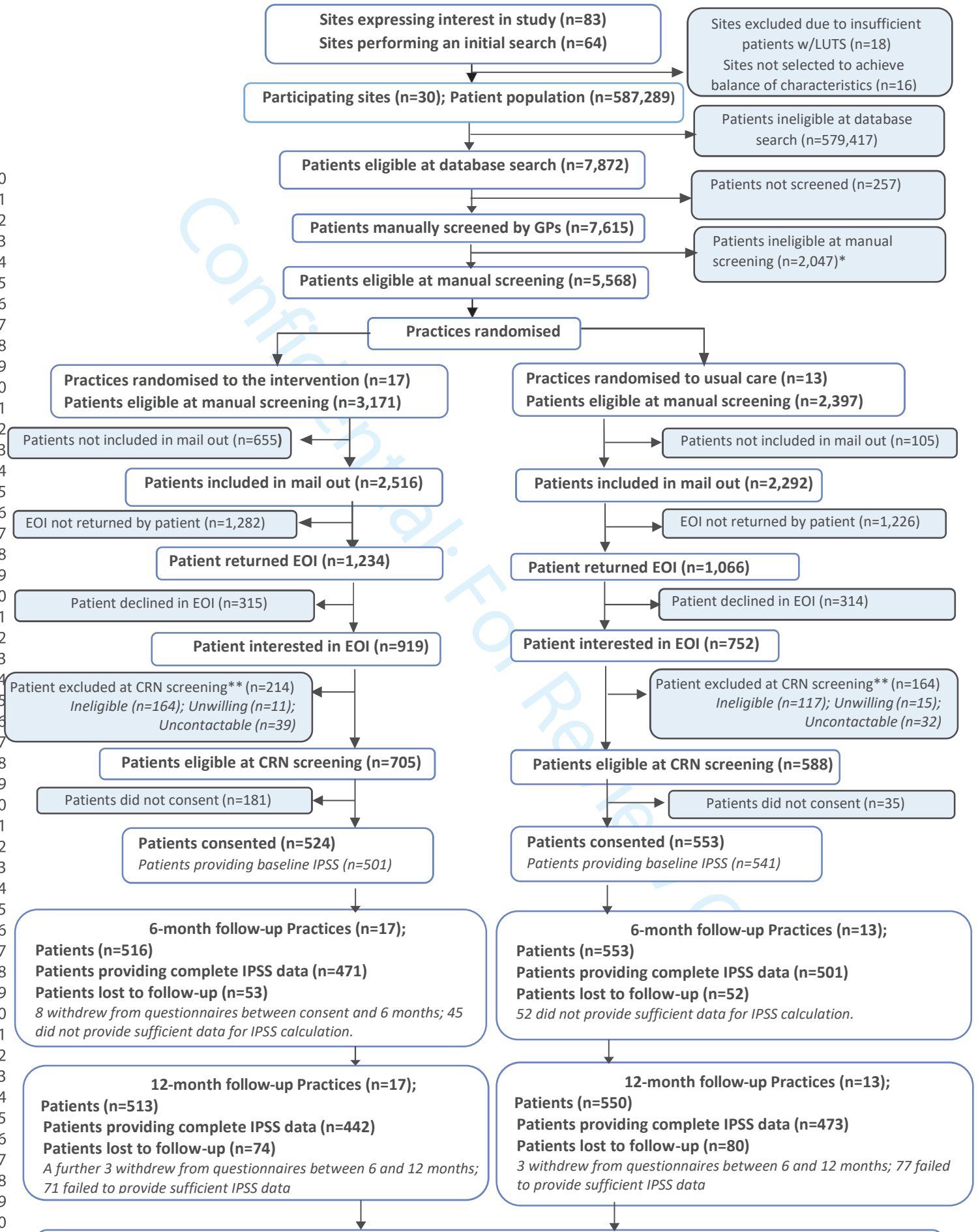

*Reasons for exclusion detailed in table S1.

**Participants remained blinded to arm through all screening processes, until point of consent.

SUPPLEMENTARY TABLES

Table S1: Reasons for exclusion at GP manual screening

Reason for exclusion	**Patients excluded at GP manual screening;** n (% of all exclusions)
Currently being treated for prostate or bladder cancer	50 (2.4)
Lack of capacity	85 (4.2)
Patient does not have LUTS	871 (42.6)
Patient is under 18 years of age	4 (0.2)
Patient has poorly-controlled diabetes mellitus	18 (0.9)
Previous prostate surgery	71 (3.5)
Recently referred or currently under urological review	441 (21.5)
Relevant neurological disease or referral	56 (2.7)
Unable to complete assessments in English	9 (0.4)
Unable to pass urine without a catheter	61 (3.0)
Undergoing neurological testing for LUTS	38 (1.9)
Visible haematuria	42 (2.1)
*Other**	301 (14.7)
	2,047

**Other: Awaiting surgery or had previous surgery (n=2), COPD (n=3), cancer (n=17), cognitive impairment (n=14), deceased (n=4), declined research (n=6), declined treatment for LUTS (n=4), under palliative care (n=6), family bereavement/illness (n=6), frail (n=39), housebound (n=19), may not be able to comply with follow-up (n=2), mental health or substance use issues (n=29), no symptoms (n=13), not living at home (n=17), no longer at practice (n=13), involved in another trial (n=50), permanent catheter (n=1), prostatitis (n=3), UTI (n=6), under bladder/bowel services (n=1), reason not given (n=9) and other (n=37).*

Table S2: Sensitivity analysis: Comparison of the results of ITT analysis with per protocol analyses

	N (int) *	N (usual care)*	Total	Mean	SD	Min - Max	Difference in means 95% CI	p-value
ITT	424	463	887	12.79	6.64	0 - 35	-1.81 (-2.66, -0.95)	<0.001
Per protocol 1: Including all in the usual care arm and those in the intervention who received the intervention booklet and had 3 follow-up contacts	391	463	854	12.84	6.67	0 - 35	-1.84 (-2.70, -0.99)	<0.001
Per protocol 2: Including all in the usual care arm and those in the intervention who received the intervention booklet and had 2 follow-up contacts	24	463	487	13.76	6.80	0 - 32	-0.83 (-3.16, 1.50)	0.484
Per protocol 3: Including all in the usual care arm and those in the intervention who received the intervention booklet and had 1 follow-up contact	5	463	468	13.88	6.85	0 - 32	-0.57 (-5.12, 3.99)	0.807
Per protocol 4: Including all in the usual care arm and those in the intervention who received the intervention booklet and had no follow-up contacts	2	463	465	13.90	6.83	0 - 32	-4.25 (-11.38, 2.89)	0.243
Per protocol 5: : Including all in the usual care arm and those in the intervention who received the intervention in the protocolised format (all 3 follow-ups, week 1 was delivered on the phone and week 4 or 12 delivered in the participants preferred follow-up method (not done face-to-face))	344	463	807	12.83	6.63	0-35	-2.06 (-2.92, -1.20)	<0.001

*Ns included in analysis (dependent on completion of IPSS at baseline and 12 month follow-up)

Table S3 Serious Adverse Events (identified through trial SAE reporting procedures)

	Received Intervention	Received Usual care	Overall
Adverse events			
Total number of SAEs; n	47	47	94
Total number of related AEs; n	0	0	0
Total number of deaths; n	2	1	3
Status of SAEs; n(%)[a]			
Resolved	45 (95.74%)	44 (93.62%)	89
Ongoing	0	2 (4.26%)	2
Died	2 (4.26%)	1 (2.13%)	3

[a] Denominator for the proportion is the total number of SAEs in treatment arm