The management of lower urinary tract symptoms in men

Appendices A – H

Produced by the National Clinical Guidelines Centre for Acute and Chronic Conditions

Contents

Appendix A - Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

The management of lower urinary tract symptoms in men

1.1 Short title

Lower urinary tract symptoms in men

2 Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Acute Care to develop a clinical guideline on the management of lower urinary tract symptoms (LUTS) in men for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (see appendix). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) The Institute's clinical guidelines support the implementation of National Service Frameworks (NSFs) in those aspects of care for which a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued will have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

a) Lower urinary tract symptoms (LUTS) are a collection of symptoms related to problems with the voiding, storage and post-micturition of urine. They generally arise as a result of abnormalities or inadequate functioning of the prostate, urethra, bladder or sphincters. The pathophysiology of LUTS are diverse. In men, benign prostate enlargement, which is secondary to benign prostatic hyperplasia and causes bladder outlet obstruction, is frequently considered to be the major cause of LUTS. However, many other conditions can cause LUTS, including detrusor muscle weakness or overactivity, prostatitis, urinary tract infection, malignancy and neurological disease. In acknowledgement of the non-specific nature of many male LUTS, this clinical guideline will advise on the effective evidence-based management of male LUTS in general, with a specific focus on LUTS associated with benign prostatic disease (presumed benign prostatic hyperplasia).

b) LUTS in men are best categorised into voiding, storage or post-micturition symptoms to help define the source of the problem. Voiding symptoms (previously known as obstructive symptoms) include weak or intermittent urinary stream, straining, hesitancy, terminal dribbling and incomplete emptying. Storage symptoms (previously known as irritative symptoms, and currently often considered as a symptom complex known as 'overactive bladder') include urgency, frequency, urgency incontinence and nocturia. The major post-micturition symptom is dribbling, which is common and bothersome. Although LUTS do not usually cause severe illness, they can considerably reduce patients' quality of life, and may point to serious pathology of the urogenital tract.

c) LUTS are a major burden for the ageing male population. Approximately 30% of men aged 50 and older have moderate to severe LUTS. This is a very large group potentially requiring treatment. Age is an important risk factor for LUTS and the prevalence of LUTS increases as men get older. Other risk factors include hormonal status (presence of androgens), increased size of the prostate gland and bladder decompensation. Ethnicity may also be a risk factor: men of black origin seem to be more likely to need surgery for prostate enlargement than men of white origin. Men of Asian origin seem to be less likely than men of white origin to need surgery.

d) Because prevalence increases with age, the figure above will continue to rise with increasing life expectancy and the resulting growth of the elderly population. This will place increasing demands on health service resources in the coming years. The past 25 years have seen an increase in the use of pharmacotherapy for LUTS, with a considerable decline in surgical rates. Nevertheless, in England, for the year 2003–2004, there were almost 30,000 endoscopic resections of the

male bladder outlet, accounting for more than 138,000 bed days. Although transurethral resection of the prostate is often effective in reducing symptoms in men, it is associated with considerable morbidity and a significant overall annual cost. In addition, a significant proportion of men (25–30%) do not benefit from prostatectomy and have poor post-surgical outcome with no improvement of symptoms. Some failures can be attributed to poor surgical technique, whereas others may be due to incorrect diagnosis of the cause of LUTS. Therefore, to minimise the number of unnecessary operations, predicting the outcome of transurethral resection of the prostate is important.

e) The British Association of Urological Surgeons primary care guidelines (2004) include recommendations on management and referral to secondary care. There are no specific recommendations on urodynamic studies. The European Association of Urology guidelines (2004) recommend the routine use of uroflowmetry before prostatectomy, and that pressure-flow studies should be used in certain circumstances (but not routinely). According to expert opinion, most UK clinicians carry out uroflowmetry and, in appropriate patients in secondary care, pressure-flow studies are done before surgical intervention in units with access to the equipment. However, experts agree that there is wide variation in clinical practice in the UK. This is due to individual clinicians' belief in the value of urodynamic studies, and also due to staffing issues and access to the technology. There are many national and international guidelines concerned with the management of men with LUTS; however, these vary in quality.

f) This NICE clinical guideline will address the variations in practice to allow equitable and appropriate treatment for all affected men. There may be cost savings in defining the appropriate use of suitable investigational modalities and existing pharmacotherapy, and by potentially preventing unnecessary surgical treatment and the costs of failed prostatectomy. However, costs incurred would include the cost of equipment, carrying out the tests and associated staff time. Uncertainty over the effectiveness of urodynamic studies makes it impossible to estimate resource impact.

4 The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

b) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health (see appendix).

c) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Adult men (18 years or older) with a clinical working diagnosis of LUTS.

b) Men who have a higher prevalence of LUTS or may be at higher risk including:

- older men
- men who are of black origin.

4.1.2 Groups that will not be covered

a) Women.

b) Men younger than 18 years.

4.2 Healthcare setting

Primary, secondary and tertiary care settings.

4.3 Clinical management

a) The clinical and cost effectiveness, and possibly morbidity, of intervention in the management of LUTS.

b) Initial diagnostic assessments of LUTS, including:

- digital rectal examination (DRE)
- symptom scores assessments
- prostate-specific antigen
- urinary flow rate
- post-void residual
- appropriate use of pressure/flow urodynamics
- cystoscopy.

c) Monitoring of chronic LUTS.

d) Non-pharmacological interventions:

- active observation ('watchful waiting')
- devices (such as catheters, pads and clamps)
- lifestyle and behavioural changes (such as diet, bladder retraining and pelvic floor exercises).

e) Pharmacological interventions as first- and/or second-line treatment:

- 5-alpha reductase inhibitors
- alpha blockers
- anticholinergics
- other pharmacotherapeutic agents (such as phytotherapy and phosphodiesterase inhibitors)
- combination therapy.

f) Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

g) Surgical interventions or minimally invasive alternatives:

- transurethral electrovaporisation of the prostate
- transurethral radiofrequency needle ablation of the prostate

- all forms of laser therapy directed at the prostate, including enucleation and vaporisation
- transurethral resection of the prostate, including newer forms of therapy such as bipolar excision
- transurethral incision of the prostate
- open prostatectomy.

h) Combinations of the above interventions.

i) Condition-specific information, support and communication needs of patients, carers and families with LUTS.

j) General advice on the appropriate evaluation and management of LUTS in men.

k) The Guideline Development Group will consider making recommendations on the principal complementary and alternative interventions or approaches to care relevant to male LUTS. This will include phytotherapy.

l) The Guideline Development Group will take reasonable steps to identify ineffective interventions and approaches to care. If robust and credible recommendations for re-positioning the intervention for optimal use, or changing the approach to care to make more efficient use of resources can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

4.4 Status

4.4.1 Scope

This is the final version of the scope.

The NICE has published the following related guidance:

- Urinary incontinence: the management of urinary incontinence in women. NICE clinical guideline 40 (2006)
- Referral guidelines for suspected cancer. NICE clinical guideline 27 (2005)
- Potassium-titanyl-phosphate (KTP) laser vaporisation of the prostate for benign prostatic obstruction. NICE interventional procedure guidance 120 (2005)
- Holmium laser prostatectomy. NICE interventional procedure guidance 17 (2003)
- Transurethral radiofrequency needle ablation of the prostate. NICE interventional procedure guidance 15 (2003)
- Transurethral electrovaporisation of the prostate. NICE interventional procedure guidance 14 (2003).

NICE is in the process of producing the following related guidance:

- Prostate cancer: diagnosis and treatment. NICE clinical guideline (publication expected February 2008).

4.4.2 Guideline

The development of the guideline recommendations will begin on 12 December 2007.

5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

6 Referrals from the Department of Health

The Department of Health asked the Institute:

'To prepare a clinical guideline on the management of benign prostatic hyperplasia.'

'To prepare a guideline on the assessment, investigation, management and onward referral of men with lower urinary tract symptoms (including male incontinence) within primary care.'

Appendix B – Declarations of interest

1 Declarations of interests

1.1 Introduction

All members of the GDG and all members of the NCGC-ACC staff were required to make formal declarations of interest at the outset, and these were updated at every subsequent meeting throughout the development process.

1.2 Declarations of interests of the GDG members

1.2.1 Chris Chapple (Chair)

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	CC declared a personal pecuniary interest, his attendance in National and International conferences for BAUS, EAU and AUA. He declared a personal pecuniary interest in private practice. He declared that he knew of no personal family interest. He declared his non-personal pecuniary interest, consultancy and research honoraria up to 6 months age from Allergan, AMS, Astellas, Novartis, Pfizer and UCB – this was put into the department to provide funding for a researcher. He declared a personal non-pecuniary interest as principal investigator and author on pharmaceutical sponsored papers. He is a member of the committee of the BAUS section of female and functional urology and the Adjunct Secretary General of EAU- responsible for their educational activities. He has written books on the subject of BPH/LUTS. He is editor in chief of the Neurourology and Urodynamics journal (official journal of ICS and SUFU).
Second GDG Meeting **(13th December 2007)**	No change
Third GDG Meeting **(17th March 2008)**	No change
Fourth GDG Meeting **(30th April 2008)**	CC declared a personal pecuniary interest, his attendance in National and International conferences for ICS.
Fifth GDG Meeting **(6th June 2008)**	No change
Sixth GDG Meeting **(14th July 2008)**	No change
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	No change
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	No change
Eleventh GDG Meeting **(23rd February 2009)**	CC declared a non-personal pecuniary interest as a consultant for Astellas, Pfizer, Allergen, Xention, Ono, Recordati and Ranbaxy. He declared a personal non-

GDG meeting	Declaration of Interests
	pecuniary interest that any concerns over his views should be expressed at any stage. He declared that he knew of no personal pecuniary interest or personal family interest, above those declared at the previous meeting.
Twelfth GDG Meeting **(25th March 2009)**	No change
Thirteenth GDG Meeting **(1st May 2009)**	No change
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	CC declared a personal non-pecuniary interest; he spoke as invited speaker at Astellas symposium at the British Association of Urological Surgeons meeting. He was a speaker at a symposium provided by the European Association of Urology on behalf of Astellas. He was a speaker at a symposium organised by Allergan at the American urology Association meeting. He declared that he had no personal pecuniary interest, personal family interest or non-personal pecuniary interest above those previously declared.
Actions	None required.

1.2.2 Angela Billington

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	She did not attend this meeting.
Second GDG Meeting **(13th December 2007)**	AB declared a personal pecuniary interest, Pfizer education support committee. AB did not declare a personal family interest. AB did not declare a non-personal pecuniary interest. She did not declare a personal non-pecuniary interest.
Third GDG Meeting **(17th March 2008)**	She did not attend this meeting.
Fourth GDG Meeting **(30th April 2008)**	AB declared a personal pecuniary interest, attended conferences for Pfizer, Coloplast, Rochester Medical and Bard. Faculty for Pfizer sense of leadership conference and CARE program for nurses. She did not declare a personal family interest, non-personal pecuniary interests or personal non-pecuniary interest.
Fifth GDG Meeting **(6th June 2008)**	She did not attend this meeting.
Sixth GDG Meeting **(14th July 2008)**	AB declared a personal pecuniary interest; she is involved in an educational package for Pfizer and educational symposium for Coloplast. Articles for nursing press on catheters. She had dinner courtesy of Pfizer at the ICI meeting. She did not declare a personal family interest, non-personal pecuniary interest or personal non-pecuniary interest.
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	She did not attend this meeting
Ninth GDG Meeting **(27th November 2008)**	No change

GDG meeting	Declaration of Interests
Tenth GDG Meeting **(16th January 2009)**	No change
Eleventh GDG Meeting **(23rd February 2009)**	No change
Twelfth GDG Meeting **(25th March 2009)**	She did not attend this meeting
Thirteenth GDG Meeting **(1st May 2009)**	No change
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	No change
Actions	During both the 14th GDG on the 8 June 2009 and the 15th GDG on the 29 June 2009, The Chair noted that AB had personal pecuniary interests and required AB to be present in an observatory role during the discussion of the pharmacologic recommendations.

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2 **1.2.3 Paul Joachim**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	PJ did not declare a personal pecuniary interest or personal family interest. He declared a non-personal pecuniary interest, trustee of Incontact, a charity that benefits from grants from the industry. He declared a personal non-pecuniary interest, trustee of Incontact (as above) Chair of the patient advisory board. He declared that he has had personal and family experience of symptoms.
Second GDG Meeting **(13th December 2007)**	No change
Third GDG Meeting **(17th March 2008)**	No change
Fourth GDG Meeting **(30th April 2008)**	No change
Fifth GDG Meeting **(6th June 2008)**	No change
Sixth GDG Meeting **(14th July 2008)**	No change
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	No change
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	No change

GDG meeting	Declaration of Interests
Eleventh GDG Meeting **(23rd February 2009)**	No change
Twelfth GDG Meeting **(25th March 2009)**	No change
Thirteenth GDG Meeting **(1st May 2009)**	No change
Fourteenth GDG Meeting **(8th June 2009)**	PJ declared that his interests have not changed, but he informed the group that 'Incontact' had changed its name to 'The Bladder and Bowel Foundation' in September 2008.
Fifteenth GDG Meeting **(29th June 2009)**	No change
Actions	None required

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2 **1.2.4 Malcolm Lucas**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	He did not attend this meeting
Second GDG Meeting **(13th December 2007)**	He did not attend this meeting
Third GDG Meeting **(17th March 2008)**	ML declared a personal pecuniary interest; I have received lecture fees from Pfizer, UCB Pharma and Astellas within the last 12 months and sponsorship to attend national and international meetings also from Pfizer, Gynecare and AMS. I am not involved in private practice and I am not now accepting invitations to serve on advisory boards. Any current income from lecturing will be payable to a research fund which pays expenses for research fellow and nurses. He did not declare a personal family interest. He declared a non-personal pecuniary interest, I am Principle local investigator for trials with Astellas, Plethora and Bioxell and Lead investigator for trials with Astra. All income goes to Clinical Research Unit, Swansea NHS Trust. He declared a personal non-pecuniary interest, current chairman of Section of Female and Reconstructive Urology, BAUS.
Fourth GDG Meeting **(30th April 2008)**	No change
Fifth GDG Meeting **(6th June 2008)**	No change
Sixth GDG Meeting **(14th July 2008)**	No change
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	He did not attend this meeting
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	No change

GDG meeting	Declaration of Interests
Eleventh GDG Meeting **(23rd February 2009)**	No change
Twelfth GDG Meeting **(25th March 2009)**	ML declared a non-personal pecuniary interest of departmental research fund receiving income from the UK Continence Society Conference April 2009. The primary source of income in this conference derives from healthcare companies (pharmaceutical and device manufactures). He declared that he knew of no personal pecuniary interest, personal non-pecuniary interest or personal family interest, above those declared at the previous meeting.
Thirteenth GDG Meeting **(1st May 2009)**	ML declared a non-personal pecuniary interest of the clinical research unit receiving research income from Astra tech, Pfizer and Astellas. He declared that he knew of no personal pecuniary interest, personal non-pecuniary interest or personal family interest, above those declared at the previous meeting.
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	He did not attend this meeting.
Actions	None required

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2 **1.2.5 Roy Latham**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	RL declared a personal pecuniary interest, he acted as a Lay Member on an Invited Service Review carried out by the Royal College of Physicians (July 07). He received a fee for this. He did not declare a personal family interest or non-personal pecuniary interest. He declared a personal non-pecuniary interest, he is personally affected by BPH/LUTS as a patient and as the relative/friend of affected people.
Second GDG Meeting **(13th December 2007)**	No change
Third GDG Meeting **(17th March 2008)**	No change
Fourth GDG Meeting **(30th April 2008)**	No change
Fifth GDG Meeting **(6th June 2008)**	No change
Sixth GDG Meeting **(14th July 2008)**	No change
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	No change
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	He did not attend this meeting

GDG meeting	Declaration of Interests
Eleventh GDG Meeting **(23rd February 2009)**	He did not attend this meeting
Twelfth GDG Meeting **(25th March 2009)**	No change
Thirteenth GDG Meeting **(1st May 2009)**	No change
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	No change
Actions	None required

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2 **1.2.6 Thomas Ladds**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	He did not attend meeting
Second GDG Meeting **(13th December 2007)**	He did not attend meeting
Third GDG Meeting **(17th March 2008)**	TL declared a personal pecuniary interest, regular attendance at national and international conferences. BAUS, BAUN, EAU and AUA. Advisory board member for Bard UK Ltd – January 2008. He did not declare a personal family interest or non-personal pecuniary interest. He declared a personal non-pecuniary interest, member and current president of British Association of Urological Nurses (BAUN). Ex officio member BAUS Council Editorial Board member of International Journal of Urological Nursing and Urology News.
Fourth GDG Meeting **(30th April 2008)**	TL declared a personal pecuniary interest, sponsorship to attend EAU from Bayer. Lecture fee from Astra Zenecu Marhcin in 2008.
Fifth GDG Meeting **(6th June 2008)**	He did not attend this meeting
Sixth GDG Meeting **(14th July 2008)**	TL declared that he knew of no personal pecuniary interest, personal family interest or personal non-pecuniary interest. He declared a non-personal pecuniary interest, lecture fees for Astrazeneca and Coloplast Ltd, which were paid to departmental charitable research fund.
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	No change
Ninth GDG Meeting **(27th November 2008)**	He did not attend this meeting
Tenth GDG Meeting **(16th January 2009)**	TL declared a personal pecuniary interest, that he has notified his NHS employer, Central Manchester University Hospitals NHS Foundation Trust that he wished to terminate his contract with them on 27th March 2009. He is in the process of setting up a limited company, TL Consulting Ltd, of which he will be the director and sole

GDG meeting	Declaration of Interests
	shareholder; he will be employed there from April 1 2009. TL Consulting Ltd. has entered into a contract with ProstaLund Operations AB of Sweden to supply services, including advising them on clinical issues and potential business activities in the UK and overseas. This contract will be operational from April 1 2009. ProstaLunc AB currently develops, manufacture and supply equipment, consumables and software in the field of microwave thermotherapy for BPH. TL Consulting may also negotiate and enter into contracts with other suppliers in urology pharmaceutical and medical technical sectors in the future. He declared that he knew of no non-personal pecuniary interest, personal non-pecuniary interest or personal family interest, above those declared at the previous meeting.
Eleventh GDG Meeting **(23rd February 2009)**	TL withdrew from the GDG due to new interests declared in the 10th GDG meeting.
Actions	None required

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2 **1.2.7 James N'Dow**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	JN declared a personal pecuniary interest, principle investigator (PI) on a clinical trial with payment per patient going to the urology department. Involved in private practice. He is a member of BAUS Academic Section. He did not declare a personal family interest. He declared a non-personal pecuniary interest, PI of commissioned research with University of Aberdeen by CYTOSYSTEMS on evaluation of a urinary diagnostic marker for bladder cancer. He declared a personal non-pecuniary interest; he led HTA commissioned research on systematic review of surgical treatments of BPH (in press).
Second GDG Meeting **(13th December 2007)**	No change
Third GDG Meeting **(17th March 2008)**	No change
Fourth GDG Meeting **(30th April 2008)**	JN declared a non-personal pecuniary interest, principle investigator (PI) on a clinical trial with payment per patient going to the urology department.
Fifth GDG Meeting **(6th June 2008)**	He did not attend this meeting
Sixth GDG Meeting **(14th July 2008)**	He did not attend this meeting
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	He did not attend this meeting
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	No change
Eleventh GDG Meeting **(23rd February 2009)**	No change

GDG meeting	Declaration of Interests
Twelfth GDG Meeting **(25th March 2009)**	He did not attend this meeting
Thirteenth GDG Meeting **(1st May 2009)**	No change
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	No change
Actions	None required

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2 **1.2.8 Jon Rees**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	JR declared a personal pecuniary interest, involved in private urological practice. He declared that he knew of no personal family interest, non-personal pecuniary interest or personal non-pecuniary interest.
Second GDG Meeting **(13th December 2007)**	No change
Third GDG Meeting **(17th March 2008)**	No change
Fourth GDG Meeting **(30th April 2008)**	No change
Fifth GDG Meeting **(6th June 2008)**	No change
Sixth GDG Meeting **(14th July 2008)**	No change
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	He did not attend this meeting
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	He did not attend this meeting
Eleventh GDG Meeting **(23rd February 2009)**	No change
Twelfth GDG Meeting **(25th March 2009)**	He did not attend this meeting
Thirteenth GDG Meeting **(1st May 2009)**	No change

GDG meeting	Declaration of Interests
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	No change
Actions	None required

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2 **1.2.9 Mark Speakman**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	MS declared a personal pecuniary interest, he is involved in giving lectures for drug companies at national and international meetings in last 12 months (Astellas, GSK, Boehringer Ingelheim, Pfizer). No new consulting work and new projects declined for duration of guideline. Involved in private practice. He did not declare a personal family interest. He declared a non-personal pecuniary interest, investigator in BPH trials (Astellas, Bayer, GSK, Pfizer, MSD, Allergan). None in last 12 months (sponsorship). Previous research sponsorship from Yamanouchi and MSD in last 5 years. He declared a personal non-pecuniary interest, his clear opinion - author of BAUS BPH Guideline 2004. Author of a number of peer-reviewed LUTS/BPH papers.
Second GDG Meeting **(13th December 2007)**	No change
Third GDG Meeting **(17th March 2008)**	No change
Fourth GDG Meeting **(30th April 2008)**	MS declared a personal non-pecuniary interest, he is a member of the editorial board for European Urology.
Fifth GDG Meeting **(6th June 2008)**	No change
Sixth GDG Meeting **(14th July 2008)**	MS declared a personal pecuniary interest, single lecture (debate) on anticholinergics for Astellas. He declared that he knew of no personal family interest, non-personal pecuniary interest or personal non-pecuniary interest, above those declared at the previous meeting.
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	No change
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	He did not attend this meeting
Eleventh GDG Meeting **(23rd February 2009)**	No change
Twelfth GDG Meeting **(25th March 2009)**	MS declared a non-personal pecuniary interest of future research studies planned with Allergan and GSK. He declared a personal non-pecuniary interest as national investigator for new LUTS/BPH Registry for the European Association of Urology. He declared that he knew of no personal pecuniary interest or personal family

GDG meeting	Declaration of Interests
	interest, above those declared at the previous meeting.
Thirteenth GDG Meeting **(1st May 2009)**	He did not attend this meeting.
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	MS declared a non-personal pecuniary interest, new supported research studies with Allergan, Astellas and GSK. He declared participation in EAU LUTS/BPH database. He declared that he knew of no personal pecuniary interest, personal family interest or personal non-pecuniary interest, above those declared at the previous meeting.
Actions	None required

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2 **1.2.10 Julian Spinks**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	JS declared a personal pecuniary interest, he is a member of advisory boards on LUTS and received honoraria from Boehringer Ingeliheim (March 07). He has attended advisory boards on Restless legs syndrome organised by RLS UK with payment from Boehringer Ingelheim. He has been paid for attendance at a focus group on faecal incontinence by Continence UK (Nov 07). He has been paid to speak and chair meetings by Astellas, BMS and ALK. He is a paid member of the editorial boards of Continence UK. He has received payment for attending focus meetings on child growth hormone. He did not declare a personal family interest of non-personal pecuniary interest. He declared a personal non-pecuniary interest, member of the strategy board of Incontact, Chairman of the local division of the BMA and board member of RLS UK.
Second GDG Meeting **(13th December 2007)**	No change
Third GDG Meeting **(17th March 2008)**	No change
Fourth GDG Meeting **(30th April 2008)**	JS declared a personal pecuniary interest, I have received sponsorship to attend the EAU congress in Milan from Pfizer. I have received speaker fees to speak at a conference from Pfizer on GPs and OAB. He is a member of advisory boards on LUTS and received honoraria from Boehringer Ingeliheim (March 07). He has attended advisory boards on Restless legs syndrome organised by RLS UK with payment from Boehringer Ingelheim. He has been paid for attendance at a focus group on faecal incontinence by Continence UK (Nov 07). He has been paid to speak and chair meetings by Astellas, BMS and ALK. He is a paid member of the editorial boards of Continence UK. He has received payment of attending focus meetings on child growth hormone. He did not declare a personal family interest of non-personal pecuniary interest. He declared a personal non-pecuniary interest, member of the strategy board of Incontact, Chairman of the local division of the BMA and board member of RLS UK.
Fifth GDG Meeting **(6th June 2008)**	No change
Sixth GDG Meeting **(14th July 2008)**	No change
Seventh GDG Meeting **(8th September 2008)**	No change

GDG meeting	Declaration of Interests
Eighth GDG Meeting **(15th October 2008)**	No change
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	JS declared a personal non-pecuniary interest, he attended a planning meeting for the "Sense of Leadership" organised by Pfizer. He declared that he knew of no personal pecuniary interest, personal family interest or non-personal pecuniary interest, above those declared at the previous meeting.
Eleventh GDG Meeting **(23rd February 2009)**	No change
Twelfth GDG Meeting **(25th March 2009)**	No change
Thirteenth GDG Meeting **(1st May 2009)**	JS declared that he had no current personal pecuniary interests. He declared that he knew of no non-personal family interest, personal non-pecuniary interest or personal family interest, above those declared at the previous meeting.
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	No change
Actions	During the 12th GDG on the 25th March 2009, JS was only present as an observer for the presentations on medical interventions and did not participate in discussion due to previously declared interest.

1

2 **1.2.11 William Turner**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	WT declared a personal pecuniary interest, private practice in urology. He did not declare a personal family interest. He declared a non-personal pecuniary interest, he is the principal local investigator in clinical trials with Allergan (not yet opened), Dianippo Sumuto, Yamanouchi (now Astellas), Schwarz Pharma. He is the principal local investigator in clinical trial with Novartis 2005-6. He declared a personal non-pecuniary interest, executive committee member section of female and reconstructive urology, British Association of Urological Surgeons. Author of papers, chapters and books on urology. Member of NICE Topic Selection Panel and Technology Appraisal Committee.
Second GDG Meeting **(13th December 2007)**	No change
Third GDG Meeting **(17th March 2008)**	No change
Fourth GDG Meeting **(30th April 2008)**	No change
Fifth GDG Meeting **(6th June 2008)**	No change

GDG meeting	Declaration of Interests
Sixth GDG Meeting **(14th July 2008)**	No change
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	No change
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	No change
Eleventh GDG Meeting **(23rd February 2009)**	No change
Twelfth GDG Meeting **(25th March 2009)**	No change
Thirteenth GDG Meeting **(1st May 2009)**	No change
Fourteenth GDG Meeting **(8th June 2009)**	No change
Fifteenth GDG Meeting **(29th June 2009)**	He declared a non-personal pecuniary interest; he stated that his participation in the clinical trial with Allergan never materialised. He declared that he knew of no personal pecuniary interest, personal family interest or personal non-pecuniary interest above those declared at the previous meeting.
Actions	None required.

1

2 **1.2.12 Adrian Wagg**

GDG meeting	Declaration of Interests
First GDG meeting **(12th December 2007)**	He did not attend this meeting
Second GDG Meeting **(13th December 2007)**	AW declared a personal pecuniary interest, Astellas pharmaceutical – consultant. Pfizer – occasional consultant. He did not declare a personal family interest. He declared a non-personal pecuniary interest, fees for lectures/writing to research healthcare commission – research fund for Pfizer, Astellas, UCB. He declared a personal non-pecuniary interest, Chairman of trustees of the Continence Foundation and Vice Chairman trustees of Incontact. Researcher for Astellas. Plethora, Boehringer Ingelheim –Lilly. Associate Director CEEU, Royal College of Physicians. He is the National leader for audit of the Continence care.
Third GDG Meeting **(17th March 2008)**	He declared a non-personal pecuniary interest, he declared a Pfizer research study, European CI and UK PI.
Fourth GDG Meeting **(30th April 2008)**	AW declared a personal pecuniary interest, Astellas pharmaceutical – consultant. Pfizer – occasional consultant. Pfizer pharmaceutical advisory board. Sense of leadership course for Pfizer. SCA conference. Lecture fees from Astellas and telephone symposium on LUTS on geriatric medicine. He did not declare a personal family interest. He declared a non-personal pecuniary interest, fees for lectures/writing to research healthcare commission – research fund for Pfizer,

GDG meeting	Declaration of Interests
	Astellas, and UCB. Pfizer research study, European C.I. and UK principal investigator. BUPA grant for research £13K. Sponsorship to EAU by Astellas. He declared a personal non-pecuniary interest, Vice-chairman of the Continence Foundation and Incontact (merged). Researcher for Astellas. Plethora, Boehringer Ingelheim –Lilly. Associate Director CEEU, Royal College of Physicians. He is the National leader for audit of the Continence care. Papers for Pharma funded studies.
Fifth GDG Meeting **(6th June 2008)**	AW declared a personal pecuniary interest, since last declaration, speaker for Pfizer at launch meeting for Fesoterodine. Astellas pharmaceutical – consultant. Pfizer – occasional consultant. Pfizer pharmaceutical advisory board. Sense of leadership course for Pfizer. SCA conference. Lecture fees from Astellas and telephone symposium on LUTS on geriatric medicine. He did not declare a personal family interest. He declared a non-personal pecuniary interest, fees for lectures/writing to research healthcare commission – research fund for Pfizer, Astellas, and UCB. Pfizer research study, European C.I. and UK principal investigator. BUPA grant for research £13K. Sponsorship to EAU by Astellas. He declared a personal non-pecuniary interest, Vice-chairman of the Continence Foundation and Incontact (merged). Researcher for Astellas. Plethora, Boehringer Ingelheim –Lilly. Associate Director CEEU, Royal College of Physicians. He is the National leader for audit of the Continence care. Papers for Pharma funded studies.
Sixth GDG Meeting **(14th July 2008)**	AW declared a non-personal pecuniary interest, Chairman of Bladder Master class for Astellas Pharma. He declared a personal non-pecuniary interest; he had dinner courtesy of Pfizer at the ICI meeting in Paris and BAUS. He declared that he knew of no personal pecuniary interest or personal family interest, above those declared at the previous meeting.
Seventh GDG Meeting **(8th September 2008)**	No change
Eighth GDG Meeting **(15th October 2008)**	No change
Ninth GDG Meeting **(27th November 2008)**	No change
Tenth GDG Meeting **(16th January 2009)**	AW declared a non personal pecuniary interest, donation to fellows research fund from Astellas. He declared that he knew of no personal pecuniary interest, personal family interest or personal non-pecuniary interest, above those declared at the previous meeting.
Eleventh GDG Meeting **(23rd February 2009)**	He did not attend this meeting
Twelfth GDG Meeting **(25th March 2009)**	He did not attend this meeting
Thirteenth GDG Meeting **(1st May 2009)**	No change
Fourteenth GDG Meeting **(8th June 2009)**	AW declared a personal pecuniary interest and had received fees for a talk from Glaxo, he did not declare a personal family interest. He declared a non-personal pecuniary interest for research from Pfizer. He declared a personal non-pecuniary interest that a donation from Astellas for filming.
Fifteenth GDG Meeting **(29th June 2009)**	AW declared a non-personal pecuniary interest, Pfizer talk at BAUS – payment into the department. He declared that he had no personal pecuniary interest, personal family interest or personal non-pecuniary interest above those previously declared.
Actions	During both the 14th GDG on the 8 June 2009 and the 15th GDG on the 29 June 2009, The Chair noted that AW had personal pecuniary interests and required AW

GDG meeting	Declaration of Interests
	to be present in an observatory role during the discussion of the pharmacologic recommendations.

1.3 Personal pecuniary interests

ML, MS and CC personal pecuniary interests that were deemed significant conflicts of interest had expired before medical intervention recommendations were discussed in the 10th GDG meeting on the 16th January 2009. Further details of the GDG meetings can be found in the minutes on the NICE website.

Appendix C – Search Strategies

Overview of Search Strategies

Search Strategies

Searches were constructed by using the following groups of terms. These groups are expanded in full in Section 1.2 below.

All searches were run in Medline, Embase and Cochrane Library. Additionally Cinahl and PsychINFO were searched where this was deemed appropriate. Economic searches were conducted in Medline, Embase, NHS EED and the HTA (Health Technology Reports) database from the Cochrane Library. Additionally in HEED (Health Economic Evaluations Database).

Medications search

BPH/LUTS terms
AND
Medication terms
AND
RCT filter or systematic review filter
NOT
Animal/publication filter

Surgery search

BPH/LUTS terms
AND
Surgery terms
AND
RCT filter or systematic review filter
NOT
Animal/publication filter

Laser search

BPH/LUTS terms
AND
Laser terms
AND
RCT filter or systematic review filter
NOT
Animal/publication filter

Conservative treatment search

BPH/LUTS terms

AND
Conservative treatment terms
AND
RCT filter or systematic review filter
NOT
Animal/publication filter

Diagnosis search

BPH/LUTS terms
AND
Diagnosis terms
NOT
Animal/publication filter

Monitoring search

BPH/LUTS terms
AND
Monitoring terms
NOT
Animal/publication filter

Economic searches (Medline and Embase)

BPH/LUTS terms
AND
Economic filter
NOT
Animal/publication filter

Economic searches (NHS EED and HEED)

BPH/LUTS terms

Patient education search

BPH/LUTS terms
AND
Patient education terms
NOT
Animal/publication filter

Patient views search

BPH/LUTS terms
AND
Patient view terms

Search terms

Animal/publication filter

Animal/publication filter - OVID Embase

1	Case-Study/ or Abstract-Report/ or Letter/ or (case adj report).tw. or ((exp Animal/ or Nonhuman/ or exp Animal-Experiment/) not exp Human/)

Animal/publication filter - OVID Medline

1	(Case-Reports NOT Randomized-Controlled-Trial OR Letter OR Historical-Article OR Review-Of-Reported-Cases).PT. OR (exp Animals/ NOT Humans/)

Benign Prostatic Hyperplasia (BPH) / Lower Urinary Tract Infection (LUTS) Terms

BPH/LUTS terms – Cochrane Library

1	MeSH descriptor Prostatic Hyperplasia, this term only
2	(Benign prostat* disease or prostatism or benign prostat* hyperplasia or benign prostat* enlargement or prostat* hypertrophy or prostat* obstruct* or enlarged prostate):ti,ab
3	(Lower urinary tract symptom* or urinary symptom* or LUTS or irritable bladder syndrome):ti,ab
4	MeSH descriptor Urinary Retention, this term only
5	(Bladder obstruct* or incomplete bladder emptying or impaired bladder emptying or storage symptom* or (retention adj5 (chronic or urinary or acute)) or residual urine):ti,ab
6	MeSH descriptor Urinary Bladder, Overactive, this term only
7	MeSH descriptor Urinary Incontinence, this term only
8	MeSH descriptor Enuresis explode all trees
9	((micturition or urin* or bladder or voiding) near (disorder or dysfunction or symptom* or urgency or incontinen*)):ti,ab
10	(post micturition dribble or enuresis or nocturia or pollakisuria or weak bladder or overactive bladder or bedwetting):ti,ab
11	(haematuria or hematuria):ti,ab
12	male or man or men
13	((#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11) AND #12)
14	#1 OR #2 OR #13

BPH/LUTS terms - OVID Embase

1	Prostate Hypertrophy/
2	(Benign prostat$ disease or prostatism or benign prostat$ hyperplasia or benign prostat$ enlargement or prostat$ hypertrophy or prostat$ obstruct$ or enlarged prostate).tw.
3	(Lower urinary tract symptom$ or urinary symptom$ or LUTS or irritable bladder syndrome).tw.
4	exp Micturition Disorder/
5	(Bladder obstruct$ or incomplete bladder emptying or impaired bladder emptying or storage symptom$ or (retention adj5 (chronic or urinary or acute)) or residual urine).tw.
6	Urinary Frequency/
7	((micturition or urin$ or bladder or voiding) adj2 (disorder or dysfunction or symptom$ or urgency or incontinen$)).tw.
8	(post micturition dribble or enuresis or nocturia or pollakisuria or weak bladder or overactive bladder or bedwetting).tw.

9	(haematuria or hematuria).tw.
10	(male or man or men).mp.
11	((or/3-9) and 10)
12	1 or 2 or 11

1

BPH/LUTS terms - OVID Medline

1	prostatic hyperplasia/
2	(Benign prostat$ disease or prostatism or benign prostat$ hyperplasia or benign prostat$ enlargement or prostat$ hypertrophy or prostat$ enlargement or enlarged prostate).tw.
3	(Lower urinary tract symptom$ or urinary symptom$ or LUTS or irritable bladder syndrome).tw.
4	urinary retention/
5	(Bladder obstruct$ or incomplete bladder emptying or impaired bladder emptying or storage symptom$ or (retention adj5 (chronic or urinary or acute)) or residual urine).tw.
6	urinary bladder, overactive/ or urinary incontinence/ or exp enuresis/
7	((micturition or urin$ or bladder or voiding) adj2 (disorder or dysfunction or symptom$ or urgency or incontinen$)).tw.
8	(post micturition dribble or enuresis or nocturia or pollakisuria or weak bladder or overactive bladder or bedwetting).tw.
9	(haematuria or hematuria).tw.
10	(male or man or men).mp.
11	((or/3-9) and 10)
12	1 or 2 or 11

2

3 **Conservative**

Conservative terms – Cochrane Library

1	(conservative next (management or treatment* or therap*))
2	MeSH descriptor Pelvic Floor, this term only
3	MeSH descriptor Exercise Therapy, this term only
4	((Pelvic floor or pelvic muscle) next (exercise or training))
5	MeSH descriptor Behavior Therapy, this term only
6	(bladder next (training or education or exercise*))
7	Post void milking or post-void milking
8	MeSH descriptor Drinking Behavior, this term only
9	MeSH descriptor Drinking, this term only
10	MeSH descriptor Beverages, this term only
11	(Fluid* or water) near (consumption or intake)
12	MeSH descriptor Caffeine, this term only
13	MeSH descriptor Sweetening Agents, this term only
14	MeSH descriptor Carbonated Beverages, this term only
15	alcohol* or caffeine or tea or coffee or artifical sweetener* or carbonated drink* or fizzy drink* or beverage*
16	MeSH descriptor Catheterization, this term only
17	MeSH descriptor Catheters, Indwelling, this term only
18	MeSH descriptor Absorbent Pads, this term only
19	MeSH descriptor Incontinence Pads, this term only
20	Catheter*
21	Sheath* or penile clamp*

22 (Absorbent or incontinence or continence or protective or bed) near (pad* or pants or product*)
23 (bed or seat or chair) near (protection or pad* or sheet*)
24 MeSH descriptor Biofeedback (Psychology), this term only
25 (biofeedback or bio feedback or bio-feedback)
26 MeSH descriptor Electric Stimulation, this term only
27 Electric stimulation
28 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27

1

Conservative terms - OVID Embase

1 (conservative adj (management or treatment$ or therap$)).tw.
2 Pelvic floor muscle training/
3 ((Pelvic floor or pelvic muscle) adj (exercise or training)).tw.
4 Bladder training/
5 (bladder adj (training or education or exercise$)).tw.
6 (Post void milking or post-void milking).tw.
7 Fluid intake/ or exp beverage/ or drinking behavior/
8 ((Fluid$ or water) adj (consumption or intake)).tw.
9 Alcohol consumption/ or caffeine/ or sweetening agent/ or carbonated beverage/
10 (alcohol$ or caffeine or tea or coffee or artifical sweetener$ or carbonated drink$ or fizzy drink$ or beverage$).tw.
11 Catheter/
12 Catheter$.tw.
13 (Sheath$ or penile clamp$).tw.
14 ((Absorbent or incontinence or continence or protective or bed) adj (pad$ or pants or product$)).tw.
15 ((bed or seat or chair) adj2 (protection or pad$ or sheet$)).tw.
16 Feedback system/
17 (Biofeedback or bio feedback or bio-feedback).tw.
18 Electrostimulation/
19 Electrical stimulation.tw
20 or/1-19

2

Conservative terms - OVID Medline

1 (conservative adj (management or treatment$ or therap$)).tw.
2 Pelvic floor/ or exercise therapy/
3 ((Pelvic floor or pelvic muscle) adj (exercise or training)).tw.
4 behavior therapy/
5 (bladder adj (training or education or exercise$)).tw.
6 (Post void milking or post-void milking).tw.
7 Drinking behavior/ or Drinking/ or Beverages/
8 ((Fluid$ or water) adj (consumption or intake)).tw.
9 Caffeine/ or sweetening agents/ or carbonated beverages/
10 (alcohol$ or caffeine or tea or coffee or artifical sweetener$ or carbonated drink$ or fizzy drink$ or beverage$).tw.
11 Catheterization/ or catheters, indwelling/ or absorbent pads/ or incontinence pads/
12 Catheter$.tw.
13 (Sheath$ or penile clamp$).tw.

14	((Absorbent or incontinence or continence or protective or bed) adj (pad$ or pants or product$)).tw.
15	((bed or seat or chair) adj2 (protection or pad$ or sheet$)).tw.
16	"Biofeedback (Psychology) /"
17	(biofeedback or bio feedback or bio-feedback).tw
18	Electric stimulation/
19	Electrical stimulation.tw.
20	or/1-19

1

2 **Diagnosis**

Diagnosis terms - Central

1	(IPSS or I-PSS or (symptom near score))
2	((American Urological Association or AUA*) near (symptom or score or index or questionnaire)).tw.
3	MeSH descriptor Urinalysis, this term only
4	MeSH descriptor Kidney Function Tests explode all trees
5	kidney function test* or renal function test* or serum creatinine or eGFR or urea or serum biochemistry or blood test* or dipstick test* or urine analys* or urinalys*
6	MeSH descriptor Digital Rectal Examination, this term only
7	rectal exam*
8	MeSH descriptor Prostate-Specific Antigen, this term only
9	(prostate specific antigen or PSA) and (test* or assess*)
10	MeSH descriptor Urodynamics, this term only
11	urinary flow rate* or urodynamics or pressure flow studies or post void residual measurement* or uroflowmetry
12	(Frequency volume chart* or ((bladder or volume or void* or urine or urinary or incontinence) adj (diar* or record*)))
13	MeSH descriptor Cystoscopy, this term only
14	Cystoscopy or cystometry or cystourethroscopy or videocystogram or cystometrogram
15	MeSH descriptor Ultrasonography, this term only
16	ultrasound or non-invasive test*
17	pad test*
18	MeSH descriptor X-Rays, this term only
19	abdominal x-ray*
20	KUB
21	MeSH descriptor Urography, this term only
22	IVU or IVP
23	(intravenous or intra-venous) near (urogram* or pyelogram* or urography)
24	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23

3

Diagnosis terms - OVID Embase

1	international prostate symptom score/
2	(IPSS or I-PSS or (symptom adj3 score)).tw.
3	((American Urological Association or AUA) adj3 (symptom or score or index or questionnaire)).tw.
4	urinalysis/ or kidney function test/
5	(kidney function test$ or renal function test$ or serum creatinine or eGFR or urea or serum biochemistry or blood test$ or dipstick test$ or urine analys$ or urinalys$).tw.
6	digital rectal examination/

7	rectal exam$.tw.
8	Prostate Specific Antigen/
9	((prostate specific antigen or PSA) and (test$ or assess$)).tw.
10	urodynamics/
11	(urinary flow rate$ or urodynamics or pressure flow studies or post void residual measurement$ or uroflowmetry).tw.
12	(Frequency volume chart$ or ((bladder or volume or void$ or urine or urinary or incontinence) adj (diar$ or record$))).tw.
13	cystoscopy/ or urethrocystometry/
14	(Cystoscopy or cystometry or cystourethroscopy or videocystogram or cystometrogram).tw.
15	(ultrasound or ultrasonography or non-invasive test$).tw.
16	pad test$.tw.
17	X Ray/
18	abdominal x-ray$.tw.
19	KUB.tw.
20	Intravenous Urography/ or Intravenous Pyelography/
21	(IVU or IVP).tw.
22	((intravenous or intra-venous) adj (urogram$ or pyelogram$ or urography)).tw.
23	or/1-22

1

Diagnosis terms - OVID Medline

1	(IPSS or I-PSS or (symptom adj3 score)).tw.
2	((American Urological Association or AUA) adj3 (symptom or score or index or questionnaire)).tw.
3	urinalysis/ or exp kidney function tests/
4	(kidney function test$ or renal function test$ or serum creatinine or eGFR or urea or serum biochemistry or blood test$ or dipstick test$ or urine analys$ or urinalys$).tw.
5	digital rectal examination/
6	rectal exam$.tw.
7	prostate specific antigen/
8	((prostate specific antigen or PSA) and (test$ or assess$)).tw.
9	urodynamics/
10	(urinary flow rate$ or urodynamics or pressure flow studies or post void residual measurement$ or uroflowmetry).tw.
11	(Frequency volume chart$ or ((bladder or volume or void$ or urine or urinary or incontinence) adj (diar$ or record$))).tw.
12	cystoscopy/
13	(Cystoscopy or cystometry or cystourethroscopy or videocystogram or cystometrogram).tw.
14	ultrasonography/
15	(ultrasound or non-invasive test$).tw.
16	pad test$.tw.
17	X-Rays/
18	abdominal x-ray$.tw.
19	KUB.tw.
20	Urography/
21	(IVU or IVP).tw.
22	((intravenous or intra-venous) adj (urogram$ or pyelogram$ or urography)).tw.
23	or/1-22

2

1 Economic

	Economic filter - OVID Embase
1	exp economic aspect/
2	cost$.tw.
3	(price$ or pricing$).tw.
4	(fee or fees).tw.
5	(financial or finance or finances or financed).tw.
6	(value adj2 (money or monetary)).tw.
7	resourc$ allocat$.tw.
8	expenditure$.tw.
9	(fund or funds or funding or fundings or funded).tw.
10	(ration or rations or rationing or rationings or rationed).tw.
11	(saving or savings).tw.
12	or/1-11
13	Quality of Life/
14	quality of life.tw.
15	life quality.tw.
16	quality adjusted life.tw.
17	(qaly$ or qald$ or qale$ or qtime$).tw.
18	disability adjusted life.tw.
19	daly$.tw.
20	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
21	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
22	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
23	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
24	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
25	(euroqol or euro qol or eq5d or eq 5d).tw.
26	(hql or hqol or h qol or hrqol or hr qol).tw.
27	(hye or hyes).tw.
28	health$ equivalent$ year$.tw.
29	(hui or hui1 or hui2 or hui3).tw.
30	health utilit$.tw.
31	disutilit$.tw.
32	rosser.tw.
33	(quality of wellbeing or quality of well being).tw.
34	qwb.tw.
35	willingness to pay.tw.
36	standard gamble$.tw.
37	time trade off.tw.
38	time tradeoff.tw.
39	tto.tw.
40	factor analy$.tw.
41	preference based.tw.
42	(state adj2 valu$).tw.
43	Life Expectancy/
44	life expectancy$.tw.
45	((duration or length or period of time or lasting or last or lasted) adj4 symptom$).tw.

46	or/13-46
47	exp model/
48	exp Mathematical Model/
49	markov$.tw.
50	Monte Carlo Method/
51	monte carlo.tw.
52	exp Decision Theory/
53	(decision$ adj2 (tree$ or anlay$ or model$)).tw.
54	model$.tw.
55	or/47-55
56	12 or 46 or 55

1

Economic filter - OVID Medline

1	exp "Costs and Cost Analysis"/
2	Economics/
3	Economics, Nursing/ or Economics, Medical/ or Economics, Hospital/ or Economics, Pharmaceutical/
4	exp "Fees and Charges"/
5	exp Budgets/
6	budget$.tw.
7	cost$.ti.
8	(cost$ adj2 (effective$ or utilit$ or benefit$ or minimi$)).ab.
9	(economic$ or pharmacoeconomic$ or pharmaco-economic$).ti.
10	(price$ or pricing$).tw.
11	(financial or finance or finances or financed).tw.
12	(fee or fees).tw.
13	(value adj2 (money or monetary)).tw.
14	Value of Life/
15	quality adjusted life.tw.
16	(qaly$ or qald$ or qale$ or qtime$).tw.
17	disability adjusted life.tw.
18	daly$.tw.
19	Health Status Indicators/
20	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
21	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
22	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
23	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
24	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
25	(euroqol or euro qol or eq5d or eq 5d).tw.
26	(hql or hqol or h qol or hrqol or hr qol).tw.
27	(hye or hyes).tw.
28	(hui or hui1 or hui2 or hui3).tw.
29	utilit$.tw.
30	disutilit$.tw.
31	rosser.tw.
32	quality of wellbeing.tw.
33	qwb.tw.
34	willingness to pay.tw.

35	standard gamble$.tw.
36	time trade off.tw.
37	time tradeoff.tw.
38	tto.tw.
39	exp models, economic/
40	models, theoretical/ or models, organizational/
41	economic model$.tw.
42	markov chains/
43	markov$.tw.
44	Monte Carlo Method/
45	monte carlo.tw.
46	exp Decision Theory/
47	(decision$ adj2 (tree$ or anlay$ or model$)).tw.
48	or/1-47

1

2 **Laser**

	Laser terms - Central
1	MeSH descriptor Prostatic Hyperplasia, this term only with qualifier: SU
2	MeSH descriptor Prostatic Hyperplasia, this term only
3	MeSH descriptor Urinary Bladder Neck Obstruction, this term only
4	benign prostat* near (hyperplas* or hypertroph* or obstruct* or enlarge* or disease)
5	bph or bpo or bpe
6	(bladder neck or bladder outlet or bladder outflow) near obstruct*
7	#2 or #3 or #4 or #5 or #6
8	MeSH descriptor Prostatectomy explode all trees
9	MeSH descriptor Transurethral Resection of Prostate, this term only
10	Transurethral near (resect* or electroresect* or incision* or diatherm* or vapori* or electrovapori* or evapori* or ablat* or thermo* or inject* or coagulat*)
11	MeSH descriptor Electrosurgery explode all trees
12	MeSH descriptor Laser Therapy, this term only
13	MeSH descriptor Laser Coagulation, this term only
14	laser near (resect* or ablat* or coagulat* or incision* or vaporis*)
15	laser near (enucleat* or prostatect*)
16	laser near (holmium or yag or nd or ktp or green light)
17	photoselectiv* near vapori*
18	needle near ablat*
19	microwave near thermo*
20	coretherm or prostatron or targis or thermatrx or prolieve
21	ethanol near inject*
22	(water or cooled) near thermotherapy
23	MeSH descriptor Ultrasound, High-Intensity Focused, Transrectal, this term only
24	high intensity near ultrasound
25	MeSH descriptor Stents, this term only
26	prostat* near (stent* or spiral*)
27	turp or tvap or tevap or tvp or tuevap
28	tuip or vlap or holrp or holep or tuna or tumt
29	ilc or tulip or hifu
30	#11 or #12 or #13 or #14 or #16 or #17 or #18 or #19 or #21 or #22 or #23 or #24 or #25 or #29

31	#7 AND #30
32	#1 or #8 or #9 or #10 or #15 or #20 or #26 or #27 or #28 or #31

1

Laser terms - OVID Embase

1	Prostate hypertrophy/su
2	Prostate hypertrophy/
3	bladder obstruction/
4	(benign prostat$ adj1 (hyperplas$ or hypertroph$ or obstruct$ or enlarge$ or disease)).tw.
5	(bph or bpo or bpe).tw.
6	((bladder neck or bladder outlet or bladder outflow) adj1 obstruct$).tw.
7	or/2-6
8	exp prostate surgery/
9	(Transurethral adj3 (resect$ or electroresect$ or incision$ or diatherm$ or vapori$ or electrovapori$ or evapori$ or ablat$ or thermo$ or inject$ or coagulat$)).tw.
10	exp laser/
11	laser prostatectomy/
12	laser surgery/
13	Laser Coagulation/
14	(laser adj3 (resect$ or ablat$ or coagulat$ or incision$ or vapori$)).tw.
15	(laser adj3 (enucleat$ or prostatect$)).tw.
16	(laser adj3 (holmium or yag or ktp or nd or green light)).tw.
17	(photoselectiv$ adj1 vapori$).tw.
18	(needle adj3 ablat$).tw.
19	(microwave adj3 thermo$).tw.
20	(coretherm or prostatron or targis or thermatrx or prolieve).tw.
21	(ethanol adj3 inject$).tw.
22	Laser thermotherapy/
23	((water or cooled) adj3 thermotherapy).tw.
24	high intensity focused ultrasound/
25	(high intensity adj3 ultrasound).tw.
26	stents/
27	(prostat$ adj3 (stent$ or spiral$)).tw.
28	(turp or tuvp or tevap or tvp or tuevap).tw.
29	(tuip or vlap or holrp or holep or tuna or tumt).tw.
30	(ilc or tulip or hifu).tw.
31	or/10-14,16-19,21-26,30
32	7 and 31
33	or/1,8-9,15,20,27-29,32
34	prostate cancer/ or bladder cancer/
35	(cancer$ or carcinoma$ or neoplasm$).tw.
36	34 or 35
37	36 not 7
38	33 not 37

2

Laser terms - OVID Medline

1	Prostatic hyperplasia/su
2	Prostatic hyperplasia/

3	Bladder neck obstruction/
4	(benign prostat$ adj1 (hyperplas$ or hypertroph$ or obstruct$ or enlarge$ or disease)).tw.
5	(bph or bpo or bpe).tw.
6	((bladder neck or bladder outlet or bladder outflow) adj1 obstruct$).tw.
7	or/2-6
8	exp prostatectomy/
9	Transurethral resection of prostate/
10	(Transurethral adj3 (resect$ or electroresect$ or incision$ or diatherm$ or vapori$ or electrovapori$ or evapori$ or ablat$ or thermo$ or inject$ or coagulat$)).tw.
11	exp electrosurgery/
12	laser therapy/
13	laser coagulation/
14	(laser adj3 (resect$ or ablat$ or coagulat$ or incision$ or vaporis$)).tw.
15	(laser adj3 (enucleat$ or prostatect$)).tw.
16	(laser adj3 (holmium or yag or nd or ktp or green light)).tw.
17	(photoselectiv$ adj1 vapori$).tw.
18	(needle adj3 ablat$).tw.
19	(microwave adj3 thermo$).tw.
20	(coretherm or prostatron or targis or thermatrx or prolieve).tw.
21	(ethanol adj3 inject$).tw.
22	((water or cooled) adj3 thermotherapy).tw.
23	ultrasound, high-intensity focused, transrectal/
24	(high intensity adj3 ultrasound).tw.
25	stents/
26	(prostat$ adj3 (stent$ or spiral$)).tw.
27	(turp or tvap or tevap or tvp or tuevap).tw.
28	(tuip or vlap or holrp or holep or tuna or tumt).tw.
29	(ilc or tulip or hifu).tw.
30	or/11-14,16-19,21-25,29
31	7 and 30
32	or/1,8-10,15,20,26-28,31
33	prostatic neoplasms/ or bladder neoplasms/
34	(cancer$ or carcinoma$ or neoplasm$).tw.
35	33 or 34
36	35 not 7
37	32 not 36

1

2 **Medications**

Medication terms - Central

1	MeSH descriptor Adrenergic alpha-Antagonists, this term only
2	(Alpha near (blocker or blocking agent or antagonist)):ti,ab
3	MeSH descriptor Doxazosin, this term only
4	MeSH descriptor Indoramin, this term only
5	MeSH descriptor Prazosin, this term only
6	(Doxazosin or Tamsulosin or Alfusozin or Terazosin or Indoramin or Prazosin or Cardura or Stronazon or Flomaxtra or Flomax or Xaltral or Hytrin or Doralese or Hypovase):ti,ab
7	(5-Alpha reductase inhibitor* or Alpha V reductase inhibitor*):ti,ab

8 MeSH descriptor Finasteride, this term only
9 (Finasteride or Dutasteride or Avodart or Proscar):ti,ab
10 MeSH descriptor Cholinergic Antagonists, this term only
11 (Anticholinergic* or cholinergic antagonist* or antimuscarininc*):ti,ab
12 (Oxybutynin or Tolterodine or Darifenacin or Propiverine or Solifenacin or Trospium or Cystrin or Ditropan or Lyrinel or Detrusitol or Emselex or Detrunorm or Vesicare or Regurin):ti,ab
13 MeSH descriptor Cyclic Nucleotide Phosphodiesterases, Type 5, this term only
14 (Phosphodiesterase 5 inhibitor* or Phosphodiesterase V inhibitor*):ti,ab
15 (PDE5 or sildenafil or viagra or vardenafil or levitra or tadalafil or cialis):ti,ab
16 MeSH descriptor Phytotherapy, this term only
17 MeSH descriptor Plant Extracts, this term only
18 MeSH descriptor Plants, Medicinal, this term only
19 (Phytotherapy or plant extract*):ti,ab
20 MeSH descriptor Serenoa, this term only
21 MeSH descriptor Sterols, this term only
22 MeSH descriptor Sitosterols, this term only
23 (Saw palmetto or serenoa or sabal or s repens or sitosterol* or b-sitosterol* or sitosteryl* or phytosterol*):ti,ab
24 MeSH descriptor Secale cereale, this term only
25 (pollen or secale cereale or rye or cernitin or cernilton):ti,ab
26 MeSH descriptor Cucurbita, this term only
27 (pumpkin seed$ or cucurbita or pepita):ti,ab
28 MeSH descriptor Urtica dioica, this term only
29 (nettle or urtica):ti,ab
30 MeSH descriptor Pygeum, this term only
31 (pygeum africanum or prunus or tadenan or docosonal or pigenil):ti,ab
32 (cranberry AND (juice or extract)):ti,ab
33 MeSH descriptor Diuretics, this term only
34 Diuretic*:ti,ab
35 MeSH descriptor Furosemide, this term only
36 MeSH descriptor Bumetanide, this term only
37 (Frusemide or furosemide or bumetanide or burinex):ti,ab
38 (Desmopressin or DDAVP or desmotabs or desmomelt or desmospray or octim):ti,ab
39 MeSH descriptor Anti-Inflammatory Agents, Non-Steroidal, this term only
40 (Aceclofenac or acemetacin or azapropazone or celecoxib or dexibuprofen or dexketoprofen or diclofenac or etodolac or etoricoxib or fenbufen or fenobufen or flurbiprofen or ibuprofen or indometacin or ketoprofen or mefenamic acid or meloxicam or nabumetone or naproxen or piroxicam or sulindac or tenoxicam or tiaprofenic acid or aspirin):ti,ab
41 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #'40

1

Medication terms - OVID Embase

1 Alpha Adrenergic Receptor Blocking Agent/
2 (Alpha adj3 (blocker or blocking agent or antagonist)).ti,ab.
3 Doxazosin/ or Tamsulosin/ or Alfuzosin/ or Terazosin/ or Indoramin/ or Prazosin/
4 (Doxazosin or Tamsulosin or Alfusozin or Terazosin or Indoramin or Prazosin or Cardura or Stronazon or Flomaxtra or Flomax or Xaltral or Hytrin or Doralese or Hypovase).ti,ab.

5	Steroid 5alpha Reductase Inhibitor/
6	(5-Alpha reductase inhibitor$ or Alpha V reductase inhibitor$).ti,ab.
7	Dutasteride/ or Finasteride/
8	(Finasteride or Dutasteride or Avodart or Proscar).ti,ab.
9	(Anticholinergic$ or cholinergic antagonist$ or antimuscarininc$).ti,ab.
10	Oxybutynin/ or Tolterodine/ or Darifenacin/ or Propiverine/ or Solifenacin/ or Trospium/
11	(Oxybutynin or Tolterodine or Darifenacin or Propiverine or Solifenacin or Trospium or Cystrin or Ditropan or Lyrinel or Detrusitol or Emselex or Detrunorm or Vesicare or Regurin).ti,ab.
12	Phosphodiesterase V Inhibitor/
13	(Phosphodiesterase 5 inhibitor$ or Phosphodiesterase V inhibitor$).ti,ab.
14	Sildenafil/ or Vardenafil/ or Tadalafil/
15	(PDE5 or sildenafil or viagra or vardenafil or levitra or tadalafil or cialis).ti,ab.
16	Phytotherapy/ or Plant extract/ or Medicinal plant/
17	(Phytotherapy or plant extract$).ti,ab.
18	Sabal/ or Sterol/ or Sitosterol derivative/
19	(Saw palmetto or serenoa or sabal or s repens or sitosterol$ or b-sitosterol$ or sitosteryl$ or phytosterol$).ti,ab.
20	Rye/ or Grass pollen extract/
21	(pollen or secale cereale or rye or cernitin or cernilton).ti,ab.
22	(pumpkin seed$ or cucurbita or pepita).ti,ab.
23	Urtica extract/
24	(nettle or urtica).ti,ab.
25	Pygeum Africanum extract/
26	(pygeum africanum or prunus or tadenan or docosonal or pigenil).ti,ab.
27	Cranberry extract/ or Cranberry juice/
28	(cranberry adj1 (juice or extract)).ti,ab.
29	Diuretic Agent/
30	Diuretic$.ti,ab.
31	Furosemide/ or Bumetanide/
32	(Frusemide or furosemide or bumetanide or burinex).ti,ab.
33	Desmopressin Acetate/ Or Desmopressin/
34	(Desmopressin or DDAVP or desmotabs or desmomelt or desmospray or octim).ti,ab.
35	Nonsteroid Antiinflammatory Agent/
36	(Non steroidal anti inflammator$3 or NSAID$).ti,ab.
37	Aceclofenac/ or acemetacin/ or azapropazone/ or celecoxib/ or dexibuprofen/ or dexketoprofen/ or diclofenac/ or etodolac/ or etoricoxib/ or fenbufen/ or fenobufen/ or flurbiprofen/ or ibuprofen/ or indometacin/ or ketoprofen/ or mefenamic acid/ or meloxicam/ or nabumetone/ or naproxen/ or piroxicam/ or sulindac/ or tenoxicam/ or tiaprofenic acid/ or aspirin/
38	(Aceclofenac or acemetacin or azapropazone or celecoxib or dexibuprofen or dexketoprofen or diclofenac or etodolac or etoricoxib or fenbufen or fenobufen or flurbiprofen or ibuprofen or indometacin or ketoprofen or mefenamic acid or meloxicam or nabumetone or naproxen or piroxicam or sulindac or tenoxicam or tiaprofenic acid or aspirin).ti,ab.
39	or/1-38

1

Medication terms - OVID Medline

1	Adrenergic alpha-Antagonists/
2	(Alpha adj3 (blocker or blocking agent or antagonist)).ti,ab.
3	Doxazosin/ or Indoramin/ or Prazosin/

4	(Doxazosin or Tamsulosin or Alfusozin or Terazosin or Indoramin or Prazosin or Cardura or Stronazon or Flomaxtra or Flomax or Xaltral or Hytrin or Doralese or Hypovase).ti,ab.
5	(5-Alpha reductase inhibitor$ or Alpha V reductase inhibitor$).ti,ab.
6	Finasteride/
7	(Finasteride or Dutasteride or Avodart or Proscar).ti,ab.
8	Cholinergic Antagonists/
9	(Anticholinergic$ or cholinergic antagonist$ or antimuscarininc$).ti,ab.
10	(Oxybutynin or Tolterodine or Darifenacin or Propiverine or Solifenacin or Trospium or Cystrin or Ditropan or Lyrinel or Detrusitol or Emselex or Detrunorm or Vesicare or Regurin).ti,ab.
11	Cyclic Nucleotide Phosphodiesterases, Type 5/
12	(Phosphodiesterase 5 inhibitor$ or Phosphodiesterase V inhibitor$).ti,ab.
13	(PDE5 or sildenafil or viagra or vardenafil or levitra or tadalafil or cialis).ti,ab.
14	Phytotherapy/ or Plant extracts/ or Plants, medicinal/ or serenoa/
15	(Phytotherapy or plant extract$).ti,ab.
16	Serenoa/ or Sterols/ or Sitosterols/
17	(Saw palmetto or serenoa or sabal or s repens or sitosterol$ or b-sitosterol$ or sitosteryl$ or phytosterol$).ti,ab.
18	Secale Cereale/
19	(pollen or secale cereale or rye or cernitin or cernilton).ti,ab.
20	Cucurbita/
21	(pumpkin seed$ or cucurbita or pepita).ti,ab.
22	Urtica dioica/
23	(nettle or urtica).ti,ab.
24	Pygeum/
25	(pygeum africanum or prunus or tadenan or docosonal or pigenil).ti,ab.
26	(cranberry adj1 (juice or extract)).ti,ab.
27	Diuretics/
28	Diuretic$.ti,ab.
29	Furosemide/ or Bumetanide/
30	(Frusemide or furosemide or bumetanide or burinex).ti,ab.
31	(Desmopressin or DDAVP or desmotabs or desmomelt or desmospray or octim).ti,ab.
32	Anti-Inflammatory Agents, Non-Steroidal/
33	(Non steroidal anti inflammator$3 or NSAID$).ti,ab.
34	(Aceclofenac or acemetacin or azapropazone or celecoxib or dexibuprofen or dexketoprofen or diclofenac or etodolac or etoricoxib or fenbufen or fenobufen or flurbiprofen or ibuprofen or indometacin or ketoprofen or mefenamic acid or meloxicam or nabumetone or naproxen or piroxicam or sulindac or tenoxicam or tiaprofenic acid or aspirin).ti,ab.
35	or/1-34

1

2 **Monitoring**

Monitoring terms – Cochrane Library

1	(review* near (interval* or visit* or inspect* or examin* or attend* or check-up* or recall*))
2	(routine* near (interval* or visit* or inspect* or examin* or attend* or check-up* or recall*))
3	(periodic* near (interval* or visit* or inspect* or examin* or attend* or check-up* or recall*))
4	(regular near (visit* or inspect* or examin* or attend* or check-up*))
5	recall* near interval*

6 visit* near clinic*

7 #1 or #2 or #3 or #4 or #5 or #6

1

Monitoring terms – OVID Embase and Medline

1 (review$ adj (interval$ or visit$ or inspect$ or examin$ or attend$ or check-up$ or recall$)).tw.

2 (routine$ adj (interval$ or visit$ or inspect$ or examin$ or attend$ or check-up$ or recall$)).tw.

3 (periodic$ adj (interval$ or visit$ or inspect$ or examin$ or attend$ or check-up$ or recall$)).tw.

4 (regular adj (visit$ or inspect$ or examin$ or attend$ or check-up$)).tw.

5 (recall$ adj interval$).tw.

6 (visit$ adj5 clinic$).tw.

7 or/1-6

2

3 **Patient education**

Patient education - OVID Embase

1 Patient/ or Hospital patient/ or Outpatient/

2 Caregiver/ or exp Family/ or exp Parent/

3 (patients or carer$ or famil$).tw.

4 or/1-3

5 Information Service/ or Information center/ or Publication/ or Book/ or Counseling/ or Directive counseling/

6 4 or 5

7 ((patient or patients) adj3 (education or educate or educating or information or literature or leaflet$ or booklet$ or pamphlet$)).ti,ab.

8 Patient information/ or Patient education/

9 or/6-8

4

Patient education OVID Medline

1 Patients/ or Inpatients/ or Outpatients/

2 Caregivers/ or exp Family/ or exp Parents/ or exp Legal-Guardians/

3 (patients or carer$ or famil$).tw.

4 or/1-3

5 Popular-Works-Publication-Type/ or exp Information-Services/ or Publications/ or Books/ or Pamphlets/ or Counseling/ or Directive-Counseling/

6 4 or 5

7 ((patient or patients) adj3 (education or educate or educating or information or literature or leaflet$ or booklet$ or pamphlet$)).ti,ab.

8 Patient-Education/ or Patient-Education-Handout-Publication-Type/

9 or/6-8

5

6 **Patient views**

Patient views - OVID Embase

1 Consumer attitude/ or patient satisfaction/ or patient compliance/ or patient right/ or health survey/ or questionnaire/ or interview/

2 (patient$ adj3 (view$ or opinion$ or awareness or tolerance or perception or persistenc$ or attitude$ or compliance or satisfaction or concern$ or belief$ or feeling$ or position or idea$ or preference$ or choice$)).tw.

3	(Discomfort or comfort or inconvenience or bother$4 or trouble or fear$ or anxiety or anxious or embarrass$4).tw.
4	or/1-3

1

Patient views - OVID Medline

1	exp Consumer-Satisfaction/ or Personal-Satisfaction/ or exp Patient-Acceptance-Of-Health-Care/ or exp Consumer-Participation/ or exp Patient-Rights/ or Health Care Surveys/ or Questionnaires/ or Interview/ or Focus groups/
2	(patient$ adj3 (view$ or opinion$ or awareness or tolerance or perception or persistenc$ or attitude$ or compliance or satisfaction or concern$ or belief$ or feeling$ or position or idea$ or preference$ or choice$)).tw.
3	(Discomfort or comfort or inconvenience or bother$4 or trouble or fear$ or anxiety or anxious or embarrass$4).tw.
4	or/1-3

2

3 **RCT filter**

RCT filter Embase

1	Clinical-Trial/ or Randomized-Controlled-Trial/ or Randomization/ or Single-Blind-Procedure/ or Double-Blind-Procedure/ or Crossover-Procedure/ or Prospective-Study/ or Placebo/
2	((((((((((clinical or control or controlled) adj (study or trial)) or (single or double or triple)) adj (blind$3 or mask$3)) or randomised or randomized or random$) adj (assign$ or allocat$ or group or grouped or patients or study or trial or distribut$)) or crossover) adj (design or study or trial)) or placebo or placebos).ti,ab.
3	1 or 2

4

RCT filter Medline

1	Randomized-Controlled-Trials/ or Random-Allocation/ or Double-Blind-Method/ or Single-Blind-Method/ or exp Clinical-Trials as topic/ or Cross-Over-Studies/ or Prospective-Studies/ or Placebos/
2	(Randomized-Controlled-Trial or Clinical-Trial or Controlled-Clinical-Trial).pt.
3	((((((((((clinical or control or controlled) adj (study or trial)) or (single or double or triple)) adj (blind$3 or mask$3)) or randomised or randomized or random$) adj (assign$ or allocat$ or group or grouped or patients or study or trial or distribut$)) or crossover) adj (design or study or trial)) or placebo or placebos).ti,ab.
4	or/1-3

5

6 **Surgery**

Surgery terms – Cochrane Library

1	MeSH descriptor Surgery, this term only
2	MeSH descriptor Urologic Surgical Procedures, this term only
3	MeSH descriptor Botulinum Toxins, this term only
4	botulinum or botox
5	Cystoplasty or bladder neck incision
6	Neuromodulation
7	Sacral nerve stimulation
8	Myectomy
9	MeSH descriptor Suburethral Slings, this term only
10	sling

11	injectable
12	MeSH descriptor Urinary Diversion, this term only
13	(Continent or incontinent) and diversion
14	MeSH descriptor Urinary Sphincter, Artificial, this term only
15	Artificial sphincter
16	Compression device
17	MeSH descriptor Catheterization, this term only
18	Suprapubic catheter*
19	Sphincterotomy
20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19

1

Surgery terms - OVID Embase

1	Urologic Surgery/ or Male Genital System Surgery/ or Surgery/ or Bladder Surgery/ or Prostate Surgery/
2	Botulinum Toxin/
3	(botulinum or botox).tw.
4	Bladder Reconstruction/
5	(Bladder neck incision or cystoplasty).tw.
6	Neuromodulation/
7	neuromodulation.tw.
8	sacral nerve stimulation/
9	Sacral nerve stimulation.tw.
10	muscle resection/
11	Myectomy.tw.
12	sling.tw.
13	injectable.tw.
14	Urinary Diversion/
15	((Continent or incontinent) and diversion).tw.
16	Bladder Sphincter Prosthesis/
17	Artificial sphincter.tw.
18	Compression device.tw.
19	Ureter Catheterization/ or Catheterization/
20	Suprapubic Catheter/
21	Suprapubic catheter$.tw.
22	Sphincterotomy/
23	Sphincterotomy.tw.
24	or/1-23

2

Surgery terms - OVID Medline

1	Surgery/
2	Urologic Surgical Procedures/
3	Botulinum Toxins/
4	(botulinum or botox).tw.
5	(Cystoplasty or bladder neck incision).tw.
6	Neuromodulation.tw.
7	Sacral nerve stimulation.tw.
8	Myectomy.tw.

9	Suburethral Slings/
10	sling.tw.
11	injectable.tw.
12	Urinary Diversion/
13	((Continent or incontinent) and diversion).tw.
14	Urinary Sphincter, Artificial/
15	Artificial sphincter.tw.
16	Compression device.tw.
17	Catheterization/
18	Suprapubic catheter$.tw.
19	Sphincterotomy.tw.
20	or/1-19

1

2 **Systematic review filter**

Systematic review filter - OVID Medline

1	meta-analysis/
2	(metaanalys$ or meta-analys$ or meta analys$).tw.
3	exp "review literature"/
4	(systematic$ adj3 (review$ or overview$)).tw.
5	(selection criteria or data extraction).ab. and review.pt.
6	(cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or bids or cancerlit).ab.
7	(reference list$ or bibliograph$ or hand search$ or hand-search$ or manual search$ or relevant journals).ab.
8	or/1-7

3

Systematic review filter - OVID Embase

1	meta analysis/
2	(metaanalys$ or meta-analys$ or meta analys$).tw.
3	systematic review/
4	(systematic$ adj3 (review$ or overview$)).tw.
5	(selection criteria or data extraction).ab. and Review.pt.
6	(cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or bids or cancerlit).ab.
7	(reference list$ or bibliograph$ or hand search$ or manual search$ or relevant journals).ab.
8	or/1-7

4

5

Appendix D – Evidence Tables

1 **Abbreviations**
2

5-ARI	5-Alpha-Reductase Inhibitors
AB	Alpha-Blockers
AUA	American Urological Association
AUASS	American Urological Association Symptom Score
AUR	Acure Urinary Retention
BOO	Bladder outlet obstruction
BPE	Benign prostatic enlargement
BPH	Benign prostatic hyperlasia
BPO	Benign prostatic obstruction
CI 95%	95% Confidence interval
DRE	Digital rectal examination
ED	Erectile dysfunction
GP	General Practitioner
HIFU	High Intensity Focused Ultrasound
HoLAP	Holmium Laser Ablation of the Prostate
HoLEP	Holmium Laser Enucleation of the prostate
HoLRP	Holmium Laser Resection of the Prostate
ICER	Incremental Cost-Effectiveness Ratio
ICS	International Continence Society
ILC	Interstitial Laser Coagulation
Int	Intervention
IPSS	International prostate symptom score
IQR	Interquartile range
ITT	Intention to treat analysis
KTP	Potassium-Titanyl-Phosphate
LOS	Length Of Stay
LUTS	Lower urinary tract symptoms
M/F	Male/female
N	Total number of patients randomised
NA	Not Applicable
NR	Not reported
OAB	Overactive bladder
PFMT	Pelvic floor muscle training
PMD	Post micturition dribble
PPP	Purchasing Power Parities
PSA	Prostate specific antigen
PVM	Post-void milking
PVP	Photoselective vaporisation of the prostate
PVR	Post voidal residual
QALY	Quality-Adjusted Life Years
Qmax	Maximum urinary flow rate
QoL	Quality of life
RBC	Red blood cells
RCT	Randomised controlled trial
RR	Relative risk

SA	Sensitivity Analysis
SD	Standard Deviation
SE	Standard Error
Sig	Statistically significant at 5%
TEAP	Transurethral ethanol ablation of the prostate
TUIP	Transurethral incision of the prostate
TUMT	Transurethral microwave thermotherapy
TUNA	Transurethral needle ablation
TURP	Transurethral resection of the prostate
TUVP	Transurethral vaporisation of the prostate
TUVRP	Transurethral vaporisation resection of the prostate
TVP	Transurethral electroVaporisation of the Prostate
TWOC	Trial Without Catheter
UI	Urinary incontinence
UTI	Urinary Tract Infection
Vs	Versus
WW	Watchful Waiting

Evidence Table 1: Diagnostic accuracy for urinalysis

Study details	Patients	Diagnostic tools	Measure of Disorders	Results	Comments
Ezz et al., 1996[85] **Study design:** Cross sectional study **Evidence level:** Level-2 study (II) **Duration of follow-up:** NR. Tests carried out over 2 visits.	**Patient group:** Consecutive men at one outpatient department (Department of Urology, Nijmegen, The Netherlands) with BPE and LUTS, either irritative or obstructive. **Exclusion criteria:** Patients excluded from further assessment for BPH once a prostate carcinoma suspected. **<u>All patients</u>** **N:** 750 **Av Age (range):** 64 years (40-85) **Drop outs:** 0	**Assessment tool under investigation:** Urinalysis by dipstick readings from clean mid-stream specimen, If revealed erythrocytes urine sediment microscopy was completed. Sediment grading completed by number of red blood cells (RBC): Grade 1 = 0 RBC Grade 2 = 1-5 RBC Grade 3 = 6-10 RBC Grade 4 = 10+ RBC **Results:** Grade 1: 516 (68.8%) Grade 2: 207 (27.2%) Grade 3: 15 (2%) Grade 4:12 (1.6%) **Gold standard:** Cystoscopy and histology. **Additional tests:** All patients underwent: History, IPSS, physical examination with Digital rectal examination, biochemistry (PSA and serum creatinine), urine culture and cytology, trans rectal ultrasonography, plain abdominal X-ray, renal ultrasound, flexible cystoscopy, flow, post void residual (PVR) and urodynamic investigations.	**Bladder tumours** **Sensitivity** **Specificity** **PPV** **NPV** **Prevalence** **Positive LR** **Negative LR** **Pre-test Odds (CI 95%)** **Post-Test Odds +ve result** **Post-Test Odds -ve result**	Grade 1: 1/516 (0.2%) Grade 2, 3 & 4: 2/234 (0.9%) Grade 2: 2/207 Grade 3: 0/15 Grade 4: 0/12 66.7% 68.9% 0.9% 99.8% 3/750 (0.4%) 2.15 0.48 0.004(0-0.01) 0.01 0.01	**Funding:** NR. **Limitations:** Cystoscopy performed on second visit after initial tests. **Additional tests:** Correlation of grades of RBC to age, prostate volume, IPSS, residual urine and outlet obstruction. Papillary lesion and dilatation were reported. One renal tumour was reported. **Notes:** All patients with positive dipstick readings were found to have red cells on microscopy. Sensitivity and specificity values calculated by NCGC using no RBC found (negative) compared to any RBC (positive). All values calculated to 1d.p.
			Urinary tract infection by urine culture **Sensitivity** **Specificity** **PPV** **NPV** **Prevalence** **Positive LR** **Negative LR** **Pre-test Odds (CI 95%)** **Post-Test Odds +ve result** **Post-Test Odds -ve result**	Grade 1: 7/516 (1.4%) Grade 2, 3 & 4: 10/234 (4.3%) Grade 2: 9/207 Grade 3: 0/15 Grade 4: 1/12 58.8% 69.4% 4.3% 98.6% 17/750 (2.3%) 1.9 0.6 0.02 (0.01-0.03) 0.04 0.03	
			Urinary calculi (Stones) by abdominal X-ray **Sensitivity** **Specificity**	Grade 1: 35/516 (6.8%) Grade 2, 3 & 4: 14/234 (6.0%) Grade 2: 12/207 Grade 3: 1/15 Grade 4: 1/12 28.6% 68.6%	

Study details	Patients	Diagnostic tools	Measure of Disorders	Results	Comments
			PPV	6.0%
			NPV	93.2%
			Prevalence	49/750 (6.5%)
			Positive LR	0.91
			Negative LR	1.04
			Pre-test Odds (CI 95%)	0.07 (0.05-0.09)
			Post-Test Odds +ve result	0.06
			Post-Test Odds -ve result	0.07
			Cyst by renal ultrasound	Grade 1: 39/516 (7.6%) Grade 2, 3, & 4: 22/234 (9.4%) Grade 2: 11/207 Grade 3: 10/15 Grade 4: 1/12
			Sensitivity	36.1%
			Specificity	69.2%
			PPV	9.4%
			NPV	92.4%
			Prevalence	61/750 (8.1%)
			Positive LR	1.17
			Negative LR	0.92
			Pre-test Odds (CI 95%)	0.09 (0.07-0.11)
			Post-Test Odds +ve result	0.10
			Post-Test Odds -ve result	0.10

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Evidence Table 2: How does PSA predict symptom progression (in terms of symptom score)?

Study details	Patients	Outcome measures & Analysis	Effect size	Comments
Carter et al., 2005[46] **Study design:** Longitudinal Cohort **Duration of follow-up:** Long-term from 1959	**Patient group:** cohort of men from the Baltimore Longitudinal Study of Aging (BLSA). **Setting:** USA **Interventions:** Not applicable **Inclusion criteria:** • < 70 years **Exclusion criteria:** • Medical or surgical treatment of BPH • Development of prostate cancer **<u>All patients</u>** **N:** 704 **Drop outs:** **<u>Group 1 (age <50)</u>** **N:** 370 **Age (median + range):** 37.4 (22.5 – 49.9) **25th percentile PSA (ng/mL):** 0.3 **50th percentile PSA (ng/mL):** 0.5 **75th percentile PSA (ng/mL):** 0.8 **Median symptom evaluation (range):** 6 (1-18) **<u>Group 2 (age 50 – 69.9)</u>** **N:** 334 **Age (median + range):** 59.3 (50.1 – 69.9) **25th percentile PSA (ng/mL):** 0.5 **50th percentile PSA (ng/mL):** 0.9 **75th percentile PSA (ng/mL):** 2.0 **Median symptom evaluation (range):** 10.5 (0-28)	**Change in IPSS over time with PSA** Mixed effect Poisson model (because of repeated measures between subjects) used to test whether there was a significant relationship between PSA percentile grouping and symptom score with time	**No correlation – analysis not shown**	**Funding:** National Institute on Aging Intramural Research Program and gift from GSK. **Limitations:** No results for regression analysis of IPSS score and PSA **Additional outcomes:** • Symptom score distribution by percentile against PSA percentile grouped by age • Correlation plot of medical history symptom score with IPSS. • Plot of symptom score vs. age for each PSA percentile **Notes:** Baseline PSA was divided into percentiles: <25th 25th – 50th >75th Patients also divided into age groups at the time of 1st PSA measurement PSA measurements at visits started in 1991otherwise measured retrospectively from serum samples Medical history questionnaire used from 1959 – 1991 and IPSS also used from 1991 – 2000. Questions relating to lower urinary tract score from medical history were used to devise score 0 - 13

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Study details	Patients	Outcomes			Analysis conducted	Results	Comments
Laguna et al. 2002[157] **Study design:** Cohort **Duration of follow-up:** Minimum of 1 year. Evaluated every 3 months during year 1 and every 6 months in year 2 and thereafter	**Patient group:** Consecutive patients treated with transurethral thermotherapy **Setting:** Secondary care, Netherlands **Interventions:** transurethral thermotherapy **Inclusion criteria:** - Treated with transurethral thermotherapy between February1992 to June1999, when data were available on pre-treatment determination of PSA, free uroflowmetry, voided and post-void residual urine, ultrasound measurement of prostate volume, and IPSS scores. **Exclusion criteria:** - Previously treated with transurethral thermotherapy, medical therapy or manipulation of the lower urinary tract interfering with baseline PSA. - Neurogenic or systemic disorder that may have impaired bladder function. **<u>All patients</u>** **N:** 404 **M/F:** 404/0 **Age (mean, range):** 66.3 (44.8-89.7) **Drop outs:** 16/404, 388 analysed		**Pre-treatment**	**Change at 12 months**	**Linear regression:** Change in IPSS vs. pretreatment PSA	**Spearman r:** -0.004 **"linear regression coefficient":** -0.04 **P value:** 0.58	**Funding:** not stated **Limitations:** - Patients received surgical treatment (TUMT) - "Retreated patients", analysed as having unchanged values at 12 months - Report: "no relevant linear correlation was noted for baseline PSA with changes in IPSS, QoL or Qmax." **Additional outcomes:** - Values for a subgroup of patients, who have similar inclusion criteria for Djavan 2004 was reported. **Notes:** - Seems to address the question of" does baseline PSA predict TUMT surgery outcomes"? - Retrospective study, on "prospectively collected data".
		Age (years):	66.3 (44.8-89.7)	-			
		PSA (ng/Ml):	5.3 (0.1-45)	-			
		IPSS:	19.1 (3-35)	9.4(0-32)	**Linear regression:** Change in QoL vs. pretreatment PSA	**Spearman r:** -0.135 **"linear regression coefficient":** -0.04 **P value:** 0.01	
		QoL (IPSS)	3.9(0-6)	1.9(0-5)			
		Prostate volume, PV (cm3)	57.7(25-178) 18 (11-31)	-	**Linear regression:** Change in Qmax vs. pretreatment PSA	**Spearman r:** 0.105 , **"linear regression coefficient":** 0.105 **P value:** 0.1	
		Qmax (mL/s):	9.4 (2-19.9)	14.6(2.4-50.3)			
		Voided vol (ml)	226(22-763)				
		Post-void vol (ml)	86(0-755)		**Mann Whitney test:** Baseline PSA vs. these outcomes at I year - IPSS>7 vs. les - Qmax >12 vs. less - QoL 1 or 2 (or 1 or 0)	Box and whisker plots shown, reported as "no association"	
		All values reported were mean (range), unless otherwise specified					

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
McConnell et al., 2003[191] MTOPS research group NCT00021814 **Setting:** multi-centre, 17 centres USA **Study design:** RCT double blinded (4 arms) **Evidence level:** 1+ **Duration of follow-up:** Mean follow up 4.5 years Study also reported in Bautista et al., 2003[25]	**Patient group:** Men with BPH **Inclusion criteria:** • ≥ 50 years • Qmax between 4 - 15 mL/sec; and voided volume ≥ 125 ml. • AUA-7 Symptom Score 8 - 30. • Voluntarily signed the informed consent agreement prior to the performance of any study procedures. **Exclusion criteria:** • Serum PSA > 10 ng/ml. • Supine blood pressure < 90/70 mmHg • Orthostatic hypotension. • Prior medical/surgical intervention for BPH. • Received prior experimental intervention (either medical or surgical) for prostate disease or enrolled in any other study protocol. **<u>All patients</u>** **N:** 3047 out of 4391 screened **Mean age:** 62.6 ± 7.3 **Drop outs:** ? **<u>Group 1 (Doxazosin)</u>** **N:** 756 **Age Mean (± SD):** 62.7 ± 7.2 **White race (%):** 82.5 **AUA-7 (± SD):** 17.0 ± 5.8	**Group 1: Doxazosin 10 mg (+ placebo)** Single daily dose at bedtime. Dose doubled at 1 week intervals starting at 1 mg/day for the 1st week until final dose of 8 mg/day. Men who could not tolerate 8mg were given 4 mg. Those who could not tolerate 4 or 8 mg were discontinued. **Group 2: Finasteride 5mg (+ placebo)** Single daily dose at bedtime **Group 3: Doxazosin 10 mg + finasteride 5 mg** Single daily dose at bedtime **Group 4: placebo for Doxazosin and placebo for finasteride** Single daily dose at bedtime **Examination methods:** Vital signs, AUA	**Cumulative incidence of clinical progression defined as first occurrence of increase of ≥ 4 points AUA-7 score over baseline at 4 years** log rank test	**Grp 1:** 55/756 **Grp 2:** 65/768 **Grp 3:** 36/786 **Grp 4:** 97/737 **P value:** grp 1 v grp 4 <0.001, **P value:** grp 2 v grp 4 <0.016 **P value:** grp 3 v grp 4 <0.001 No significant differences between grps 1, 2 or 3	**Funding:** National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) National Institutes of Health, National Centre for Minority Health & Health Disparities, Merck and Pfizer. **Limitations:** • Standard deviations were not reported for mean changes from baseline for secondary outcomes • Number of patients discontinuing in the placebo group were not reported. **Additional outcomes:** Median changes from baseline for symptom score, Qmax and serum PSA at 1 year and 4 years. Percentage discontinued therapy (most of them due to adverse events) Doxazosin: 27% % Finasteride:24%
			Cumulative incidence of clinical progression defined as incidence of acute urinary retention at 4 years log rank test	**Grp 1:** 9/756 **Grp 2:** 6/768 **Grp 3:** 4/786 **Grp 4:** 18/737 **P value:** grp 1 v grp 4 =0.23 **P value:** grp 2 v grp 4 =0.009 **P value:** grp 3 v grp 4 <0.001	
			Mean change in AUA ± SD at 4 years	**Grp 1:** 6.6 ± 5.8** **Grp 2:** 5.6 ± 5.0** **Grp 3:** 7.4 ± 5.7* **Grp 4:** 4.9 ± 4.1* **P value:** grp 1 v grp 4 <0.001 **P value:** grp 2 v grp 4 =0.001* **P value:** grp 3 v grp 4 <0.001 **P value:** grp 1 v grp 3 =0.006* **P value:** grp 2 v grp 3 <0.001 **P value:** grp 1 v grp 2 =0.001*	
			Mean change in Qmax ± SD at 4 years	**Grp 1:** 4.0 ± NR **Grp 2:** 3.2 ± NR **Grp 3:** 5.1 ± NR **Grp 4:** NR P values were only available for median change from baseline	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Qmax (± SD), mL/s:10.3 ± 2.5 **Prostate volume (± SD),** mL: 36.9 ± 21.6 **PVR (± SD), mL:** 69.2 ± 88.2 **PSA serum(± SD), ng/mL:** 2.4 ± 2.1 **Dropouts:** 204/756 (27%) **Group 2 (Finasteride)** **N:** 768 **Age Mean (± SD):** 62.67 ± 7.3 **White race (%):** 83.7 **AUA-7 (± SD):** 17.6 ± 5.9 **Qmax (± SD), mL/s:**10.5 ± 2.5 **Prostate volume (± SD),** mL: 36.9 ± 20.6 **PVR (± SD), mL:** 66.2 ± 80.0 **PSA serum(± SD), ng/mL:** 2.4 ± 2.1 **Dropouts:** 174/768 (24%) **Group 3: (Doxazosin + finasteride 5 mg)** **N:** 786 **Age Mean (± SD):** 62.7 ± 7.1 **White race (%):** 80.8 **AUA-7 (± SD):** 16.8 ± 5.8 **Qmax (± SD), mL/s:**10.6 ± 2.5 **Prostate volume (± SD),** mL: 36.4 ± 19.2 **PVR (± SD), mL:** 67.5 ± 81.1 **PSA serum(± SD), ng/mL:** 2.3 ± 1.9 **Dropouts:** 141/786 (18%) **Group 4: (placebo for Doxazosin and placebo for Finasteride)** **N:** 737 **Age Mean (± SD):** 62.5 ± 7.5 **White race (%):** 82.4	symptom score, Qmax, compliance, adverse events measured every 3 months. DRE, Serum PSA and urinalysis performed annually. Prostate volume assessed by TRUS at baseline and 5 year follow up.	**Change of prostate volume compared to baseline,** mean±sd (ml) [Calculated by NCC-AC from Kaplan2008B[135]]	**Group 1:** 8.00±16.07 **Group 2:**-2.76±14.42 **Group 3:**-1.91±13.63 **Group 4:** 6.67±15.98	Combination: 18% (discontinued both) **Notes:** Urn method of randomisation and stratified according to centre. Merck and Pfizer supplied active drugs and placebo designed to look and taste like Doxazosin and Finasteride. Allocation concealment preserved by coded medications distributed by drug company. Eligible patients entered 2 week single blind placebo run-in. Patients discontinued were followed for primary and secondary outcomes * P values between comparisons were used along with mean differences to estimate standard deviations for groups. Where possible exact p values were used. As numbers of patients as each follow up point not clear the ITT numbers were used. Methods were following Cochrane Handbook.
			Adverse events$ **Total no. of person-year** **Erectile Dysfunction** **Libido decrease** **Ejaculation disorder** **Postural hypotension** **Asthenia** **Dizziness** **Peripheral oedema** **Dyspnea** **Allergic reaction** **Somnolence** $ 10 most frequently reported adverse expressed as rate per 100 person-year of follow up.	**Grp 1** / **Grp 2** / **Grp3** / **Grp4** **3489** / **3600** / **3832** / **3489** 3.56 / 4.53 / 5.11 / 3.32 1.56 / 2.36 / 2.51 / 1.40 1.10 / 1.78 / 3.05 / 0.83 4.03 / 2.56 / 4.33 / 2.29 4.08 / 1.56 / 4.20 / 2.06 4.41 / 2.33 / 5.35 / 2.29 0.88 / 0.72 / 1.25 / 0.66 0.93 / 0.56 / 1.20 0.57 0.85 / 0.58 / 0.73 0.46 0.82 / 0.39 / 0.78 0.37	
			Prognosis value of PSA, based on placebo arm *[Data from Crawford2006, [57]]* Overall BPH progression was defines as the first occurrence of an increase of at least 4 points in the AUASS, AUR, urinary incontinence or renal insufficiency or recurrent UTI	**Cumulative probability of BPH progression (4 year follow up)** PSA≥1.6ng/ml: 24% PSA<1.6ng/ml: 13.5% P<0.001 (values read from graph) **Incidence rate of overall BPH progression** (events/100 person year) PSA≥1.6ng/ml: 5.9 PSA<1.6ng/ml: 3.1 P=0.0002 **Incidence rate of ≥4 points increase in AUASS** (events/100 person year) PSA≥1.6ng/ml: 4.5 PSA<1.6ng/ml: 2.8	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	AUA-7 (± SD): 16.8 ± 5.9 **Qmax (± SD), mL/s:**10.5 ± 2.6 **Prostate volume (± SD),** mL: 35.2 ± 18.8 **PVR (± SD), mL:** 69.6 ± 82.1 **PSA serum(± SD), ng/mL:** 2.3 ± 2.0 **Dropouts:** Not reported			P=0.028 **Incidence rate of AUR** (events/100 person year) PSA≥1.6ng/ml: 1.0 PSA<1.6ng/ml: 0.3 P=0.0029 **Incidence rate of invasive therapy** (events/100 person year) PSA≥1.6ng/ml: 1.8 PSA<1.6ng/ml: 0.8 P=0.018	**Where >1 possible standard deviations were calculated for a group the mean was used

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Roehrborn et al., 2006[255] **Study design:** RCT **Setting:** multi-centre in US, Europe, Australia, Middle-east and South Africa. **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient group:** Men at risk of having progression events from LUTS/BPH enrolled between May 2001 and March 2005. **Inclusion criteria:** ≥55 years with a ≥6 month history of LUTS related to BPH, an IPSS of ≥13, a Qmax of 5-12mL/s for a voided volume of ≥150mL, a PVR of ≥350mL, a prostate of ≥30g estimated by DRE, and a PSA level of 1.4-10ng/mL. **Exclusion criteria:** previous occurrence of AUR or prostatic surgery; concomitant urological diseases; diagnosed or suspected prostate carcinoma; previous x-ray therapy of the pelvic region; history of postural hypotension or syncope; concomitant use of medications that my alter the voiding pattern; and clinically relevant biochemical abnormalities. **<u>All patients</u>** **N:** 1522 **<u>Group 1</u>** **N:** 759 (ITT analysis N: 749) Mean (±SD) **Age:** 66.4 (6.7) **Dropouts:** 230 (Lack of efficacy or disease progression 75; adverse events 71; patients request=39; poor compliance with protocol=8, lost to follow-up=6; other 31)	**Group 1: alpha-blocker** Alfuzosin 10mg once daily **Group 2: Placebo**	**Number (%) progressed to AUR**	Group1: 16 (2.1%) Group 2: 14 (1.8%) P=0.82	**Funding:** Sanofi-Aventis **Limitations:** Method of randomisation and allocation concealment unclear. **Additional outcomes:** Haematological or biochemical measurement s-reported that there were no significant changes. **Notes:** Baseline variables analysed as predictors of IPSS worsening, AUR or BPH related surgery.
			Number (%) men with BPH-related surgery	Group1: 38 (5.1%) Group 2: 49 (6.5%) P=0.18 RR: 22 (-18 to 48)%	
			Number (%) patients with symptom progression of ≥ 4points	Group1: 88 (11.7%) Group 2: 127 (16.8%) P=0.0013 RR with alfuzosin: 30 (10-46)%	
			Number (%) of men having any LUTS/BPH progression event (AUR and/or surgery and/or IPSS deterioration of ≥4 points)	Group1: 122 (16.3%) Group 2: 167 (22.1%) P<0.001 RR with alfuzosin: 26 (9-40)%	
			Mean (SD) decrease from baseline in IPSS	Group1: -5.9 (6.9) Group 2: -4.7 (6.9)	
			Mean (SD) decrease from baseline in bother score	Group1: -1.3 (1.5) Group 2: -0.9 (1.6) P<0.001	
			Mean (SD) decrease from baseline in Qmax, mL/s at 12 months	Group1: 2.0 (3.8) Group 2: 1.3 (3.6) P=0.001	
			Median change in serum PSA levels	Group 1: -0.6% Group 2: 3.6%; P=0.07	
			Treatment emergent adverse events	Group 1: 400 (53.1%) Group 2: 390 (51.2%)	
			Discontinuation after TEAE	Group 1: 69 (9.2%) Group 2: 58 (7.6%)	
			Adverse events	**Dizziness** Group 1: 45 (6.0%) Group 2: 35 (4.6%) **Headache** Group 1: 25 (3.3%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2 **N:** 763 (ITT analysis N: 757) Mean (±SD) **Age:** 66.5 (7.0) **Dropouts:** 283 (Lack of efficacy or disease progression=111; adverse events=62; patients request=58; poor compliance with protocol=13, lost to follow-up=12; other=27)			Group 2: 17 (2.2%) **Hypotension** Group 1: 9 (1.2%) Group 2: 4 (0.5%) **Syncope** Group 1: 5 (0.7%) Group 2: 2 (0.3%) **Malaise** Group 1: 1 (0.1%) Group 2: 0 **Ejaculatory dysfunction** Group 1: 15 (2.0%) Group 2: 14 (1.8%) **Ejaculatory disorders** Group 1: 3 (0.4%) Group 2: 0 **Asthenia/fatigue** Group 1: 16 (2.1%) Group 2: 8 (1.1%) **Somnolence** Group 1: 0 Group 2: 3 (0.4%)	
			Mean (SD) changes in SBP/DBP, mmHg	Supine Group 1: -3.2 (15.6)/-2.9 (10.1) Group 2: -0.1 (15.3)/-0.8 (9.3) Standing Group 1: -3.8 (15.5)/ -2.8 (10.3) Group 2: -0.2 (15.5)/-0.5 (10.0)	
			Number (%) symptom worsening (IPSS worse ≥4 points) by baseline PSA	**Group 1:** PSA<2.3: 22/248 (8.9%) PSA 2.3-3.9: 33/261 (12.6%) PSA >3.9: 32/228 (14.8%) P=NS **Group 2:** PSA<2.3: 36/242 (14.9%) PSA 2.3-3.9: 49/237 (20.7%); PSA >3.9: 39/264 (14.0%) P=NS	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Roehrborn et al., 1999[256] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 4 years	**Patient group:** men with clinical BPH diagnosed on the basis of moderate to severe symptoms. **Setting:** 95 centres (Finasteride Long-Term Efficacy & Safety Study Group) **Inclusion criteria:** • Moderate to severe symptoms • Peak flow rate <15 mL/s with voided volume ≥ 150 mL • Enlarged prostate by digital rectal examination • Serum PSA 4 -9.9 ng/mL with negative biopsy **Exclusion criteria:** • Current therapy of α-blocking agents or anti-androgens • History of chronic prostatitis • Recurrent urinary tract infections • Surgery for prostate or bladder cancer • Serum PSA >10ng/mL **<u>All patients</u>** **N:** 3040 **Drop outs:** 1157 **<u>Group 1</u>** **N:** 1524 **Age (mean ± SD):** 64 ± 7 **Quasi-AUA**: 15 ± 6 **Serum PSA (ng/mL):** 2.8 ± 2.1 (n=1512)* **1st tertile PSA (ng/mL):** 0.83 ± 0.3 (n=	**Group 1** Finasteride (Proscar) 5mg 1/day **Group 2** Placebo **Assessment:** 1 month single blind placebo run in after which randomisation and baseline measurements performed Quasi AUA symptom score (1-34), adverse events, urinary flow were assessed every 4 month. PSA was measured at baseline and every 4 months in year 1 and every 8 months thereafter. Physical examinations and routine haematological and serum chemistry tests performed yearly. MRI to determine prostate volume performed at baseline and yearly in a subset of 10% of patients	**Mean Change in Quasi-AUA Symptom Score (± SE) v baseline PSA at 4 years** Within tertile group and between treatment group analysis of variance performed to compare effect of baseline PSA and prostate volume on symptom changes over time	**1st Tertile** **Group 1:** -3.2 ± 0.4 **Group 2:** -2.4 ± 0.3 Group1 v Group 2 p=0.128 **Not sig.** (ANOVA) **2nd Tertile** **Group 1:** -3.4 ± 0.3 **Group 2:** -0.4 ± 0.4 Group1 v Group 2 p<0.001 (ANOVA) **3rd Tertile** **Group 1:** -3.4 ± 0.3 **Group 2:** -0.2 ± 0.4 **P** Group1 v Group 2 p<0.001 (ANOVA)	**Funding:** Merck & Co., Inc. **Limitations:** No adjustment mentioned and no regression analysis **Additional outcomes:** • Mean Change in Quasi-AUA Symptom Score (± SE) v baseline prostate volume tertile at 4 years • Mean Change in Quasi-AUA Symptom Score (± SE) v PSA tertile over time • Mean Change in Quasi-AUA Symptom Score (± SE) v prostate volume tertile over time • Mean Change in Qmax (± SE) v PSA tertile over time • Mean Change in Qmax (± SE) v prostate volume tertile over time **Notes:** Baseline PSA was divided into 3 tertiles: First (0.2 - 1.3) Second (1.4 – 3.2) Third (3.3 – 12.0)
			Mean Change in Quasi-AUA Symptom Score (± SE) over time (years 1-4) for each PSA tertile in placebo patients (group 2)	1st tertile had a significantly better long-term symptom improvement than those in other tertiles p < 0.001 There was no significant difference between long term symptom improvement between 2nd and 3rd tertiles p=0.65	
			Mean Change in Quasi-AUA Symptom Score (± SE) over time (years 1-4) for each PSA tertile group 1 v group 2	1st tertile Not sig. 2nd tertile (p=0.004) 3rd tertile (p=0.001)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	472) **2nd tertile PSA (ng/mL):** 2.21 ± 0.6 (n= 536) **3rd tertile PSA (ng/mL):** 5.39 ± 1.7 (n= 504) **Qmax (mL/s):** 11 ± 4 **Prostate Volume (mL):** 54 ± 25 (n=157) **Drop outs:** 524 **Group 2** **N:** 1516 **Age (mean ± SD):** 64 ± 6 **Quasi-AUA:** 15 ± 6 **Serum PSA (ng/mL):** 2.8 ± 2.1 (n=1498)* **1st tertile PSA (ng/mL):** 0.86 ± 0.3 (n= 511) **2nd tertile PSA (ng/mL):** 2.24 ± 0.6 (n= 514) **3rd tertile PSA (ng/mL):** 5.36 ± 1.7 (n= 473) **Qmax (mL/s):** 11 ± 4 **Prostate Volume (mL):** 55 ± 26 (n=155) **Drop outs:** 633				Quasi AUA symptom score: Had all components of the AUA score but the score differed from AUA per question: 0-5 for six questions and 0-4 for one question. Total 0-34 *Patients numbers quoted for baseline characteristics were different in Roehborn 1999 paper from original study report McDonnell et al 1998 (NEJM).

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Study details	Patients	Outcomes		Analysis conducted	Results	Comments
Tubaro et al., 2004[298] **Study design:** Cross sectional, observational **Duration of follow-up:** Nil	**Patient group:** Men with LUTS, ambulatory **Setting:** 45 urological centres in Italy between Feb 1998 and Jan 1999 **Interventions:** Not applicable **Inclusion criteria:** - Age: 50-80 years - Persistent LUTS/BPH and BPE (as estimated by DRE) - Minimal voided volume (VV)of 150ml **Exclusion criteria:** - Associated urological diseases, psychiatric or mental illness, previous surgical or minimally invasive treatments of BPH, indwelling catheter, - Pharmacological treatments (e.g. tricyclic amtidepressants, anticholinergic and sympathomimetic drugs) - Current or previous treatment for LUTS/BPH (e.g. alpha adrenoreceptor antagonists, finasteride, plant extracts) **<u>All patients</u>** **N:** 866 **M/F:** 866/0 **Age (mean, range):64**(50-80) **Drop outs:** 64/866, 802 analysed, dropouts are due to missing data **Mean duration of LUTS:** 30.2 months, median 24 months	**Age (range)** (years):	66.3 (44.8-89.7)	**Multiple logistic regressions:** IPSS >7 vs. PSA (ng/ml), IPSS<7 is the reference	**Odds ratio (95%CI)** **PSA≤2:** 1.0 **PSA>2-4:** 1.62(1.2-2.2) **PSA>4-10:** 2.64 (1.5-4.7) **PSA >10:** 4.28 (1.8-10.3) ≤2	**Funding:** not stated **Limitations:** - Cross sectional study - Answers the questions of association of PSA vs. IPSS, rather than ability of PSA to predict IPSS over time (prognosis) **Additional outcomes:** Logistic regression of IPSS vs. prostate related variables- PVR, PV, Qmax, Abrams-Griffiths number etc.. **Notes:** - All values reported were mean ±standard deviation unless otherwise specified
		PSA (ng/ml)**:**	2.23±2.36			
		IPSS: - **Voiding** - **Storage**	13.4 ±6.1 7.6±4.4 5.8±2.9			
		Prostate volume, PV (cm3)	34.5±18.8			
		Uroflowmetry Qmax (ml/s) Qave (ml/s) Flow time(s) VV(ml) Post void volume, PVR (ml)	 13.6±6.6 6.8±3.7 46.3±27.3 265.9±123.4 58.3±72.6			

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Evidence Table 3 Diagnosistic accuracy of uroflowmetry

Study details	Patients	Diagnostic tools	Measure of Disorders	Results	Comments
Ref ID: Oelke et al., 2007[231] **Study design:** Cross-sectional study **Evidence level:** Level-2 study (II) **Duration of follow-up:** 1-3 weeks duration between the index test and the gold standard	**Patient group:** Men with LUTS, clinical BPH and/or prostate volume >25ml **Setting:** single centre – urologic outpatient clinic - Germany **Inclusion criteria:** • > 40 years • with LUTS, clinical BPH and/or prostate volume >25ml **Exclusion criteria:** Patients with: • Prostate cancer • Acute urinary retention • Neurological disease • Previous prostatic or urethral surgery • Medication treating BPH α- blockers, α-reductase inhibitors **<u>All patients</u>** **N:** 160 **Age median (range):** 62 (40-89) **Drop outs:** 0	**Assessment tool under investigation:** Uroflowmetry – number of voids not specified. **Gold standard:** Pressure flow studies (PFS) performed using Ellipse (Andromeda) machine with CHESS used to classify obstruction	**Qmax threshold < 10 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result **Qmax threshold < 15 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result	 68% (51/75) CI95% 57 - 79 73% (62/85) CI95% 64 - 82 69% (51/74) 72% (62/86) **47%** 75/160 2.51 0.44 **0.88** (CI95%: 0.81-0.96) 2.22 0.39 99% (74/75) CI95% 97 - 100 39% (33/85) CI95% 29 - 49 59% (74/126) 97% (33/34) **47%** 75/160 1.61 0.03 **0.88** (CI95%: 0.81-0.96) 1.42 0.03	**Funding:** NR **Limitations:** Details of Uroflowmetry methods not reported 1-3 week delay between Uroflowmetry as index test and PFS No mention whether the procedures tested were conducted by the same investigator(s) **Additional outcomes:** This study also reports Detrusor Wall Thickness measured by 7.5 MHz ultrasound, Post Void Residual measured with 3.5 MHz ultrasound. Prostate Volume measured with TRUS **Notes:** None

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Study details	Patients	Diagnostic tools	Measure of Disorders	Results	Comments
Ref ID: Poulsen et al., 1994[241] **Study design:** Cross-sectional study **Evidence level:** Level-2 study (II) **Duration of follow-up:** NA	**Patient group:** Men with symptomatic BPH (94% uncomplicated), 5% also with recurrent urinary tract infection and 1% with previous AUR **Setting:** single centre Denmark **Exclusion criteria:** NR **All patients** **N:** 188 **Age median (range):** 68 (32-90) **Drop outs:** Free flow missing for 35/188 (19%) and PFS data missing for 5/188 (3%)	**Assessment tool under investigation:** Void into Dantec Urodyn 1000 uroflowmeter. Number of voids not reported **Gold standard:** Pressure flow studies (PFS) performed using Dantec Urodyn 1000 uroflowmeter after filling with Foley 14F catheter. Patients characterised for BOO using Abrams-Griffiths nomogram.	**Qmax threshold < 10 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result **Qmax threshold < 15 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result	 69% (68/99) CI95%: 59 - 78 57% (31/54) CI95%: 44 - 70 75% (68/91) 50% (31/62) **65%** (99/153) 1.61 0.55 **1.83** (CI95%: 1.76 -1.91) 2.96 1.00 90% (89/99) CI95%: 84 - 96 31% (17/54) CI95%: 19 - 43 71% (68/91) 63% (31/62) **65%** (99/153) 1.31 0.32 **1.83** (CI95%: 1.76 -1.91) 2.41 0.59	**Funding:** NR **Limitations:** Masking of assessors to test results NR Not clear whether tests were independent (implies PFS before entry into study) Number of voids NR **Additional outcomes:** DAN-PSS Symptom Score also recorded **Notes:** None

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Study details	Patients	Diagnostic tools	Measure of Disorders	Results	Comments
Ref ID: Reynard et al., 1996[248] **Study design:** Cross-sectional study **Evidence level:** Level-2 study (II) **Duration of follow-up:** NA	**Patient group:** Men > 45 years with) LUTS suggestive of benign prostatic obstruction (BPO) **Setting:** 2 centres UK **Exclusion criteria:** Patients with: • Prostate cancer (DRE + TRUS) • Diabetes • Lower urinary tract infection • Previous prostatic or urethral surgery • Medication affecting lower urinary tract **<u>All patients</u>** **N:** 165 **Age median (range):** 68 (50-84) **Drop outs:** PFS data missing for 8/165 (5%) patients	**Assessment tool under investigation:** Uroflowmetry 4 voids into Dantec Urodyn 1000 uroflowmeter. Qmax below threshold indicates BOO **3 voids:** 17 (10%) **4 voids:** 148 (90%) **Gold standard:** Pressure flow studies (PFS) performed using Dantec Menuet or Dantec 5500 multichannel recorder. Patients characterised for BOO using Abrams-Griffiths nomogram as obstructed or equivocal/ unobstructed.	***Qmax threshold < 10 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result ***Qmax threshold < 12 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result ***Qmax threshold < 15 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result	 49% (47/95) CI95% 39 - 59 87% (54/62) CI95% 79 - 95 85% 53% **61%** (95/157) 3.83 0.58 **1.53** (CI95%:1.46 -1.61) 5.88 0.89 65% (62/95) CI95% 55 - 75 74% (46/62) CI95% 79 - 95 79% 58% **61%** (95/157) 2.53 0.47 **1.53** (CI95%:1.46 -1.61) 3.88 0.72 85% (81/95) CI95% 78 - 92 53% (33/62) CI95% 63 - 85 74% 70% **61%** (95/157) 1.82 0.38 **1.53** (CI95%:1.46 -1.61) 2.79 0.42	**Funding:** NR **Limitations:** No indication of who carried out the tests-whether by the same people, or whether the investigator or patients were masked to the results of other tests. Results of individual centres not compared, and inter-rater agreement (presumably tests in different tests done by different people) was not addressed **Notes:** *Qmax taken as highest value on voids 1 & 2. **Also reported < 8 mL/s** Study suggests increasing specificity and decreasing specificity with increasing number of voids

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Evidence Table 4: Diagnostic accuracy of post void residual

Study details	Patients	Diagnostic tools	Measure of Disorders	Results	Comments
Ref ID: REYNARD1998 (ICS-'BPH' study) **Study design:** Cross-sectional study **Evidence level:** Level-2 study (II) **Duration of follow-up:** NA	**Patient group:** Men with LUTS and benign prostatic enlargement (BPE) **Setting:** multi-centre 12 centres in Europe, Australia, Canada, Taiwan & Japan **Inclusion criteria:** • > 45 years • Symptoms of BOO secondary to BPH **Exclusion criteria:** Patients with: • Prostate cancer • Neurological disease • Previous prostatic or urethral surgery • Medication affecting lower urinary tract **<u>All patients</u>** **N:** 1271 **Age mean (range):** 66.5 (45-88) **Drop outs:** Uroflowmetry data missing for 81/1271 (6%) PFS data missing for 338/1271 (27%)	**Assessment tool under investigation:** Uroflowmetry 3 voids **1 void:** 211 (17%) **2 voids:** 443 (35%) **3 voids:** 537 (42%) Details of technique not reported **Gold standard:** Pressure flow studies (PFS) performed according to International Continence Society guidelines with diagnosis of BOO using Schafer classification Ratings 0-2 categorised as non-obstructive while 3-6 were obstructed. Definition of Schaefer method: 0 no obstruction, 1 slightly obstructed, 2-6 obstructed with increasing severity	***Qmax threshold < 10 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result ***Qmax threshold < 15 mL/s** Sensitivity Specificity Positive predictive value Negative predictive value Prevalence Positive Likelihood Ratio Negative Likelihood Ratio Pre-test Odds (CI 95%) Post-Test Odds +ve result Post-Test Odds -ve result	 47% (252/540) CI95% 42 - 51 70% (250/357) CI95% 65 - 75 70% (252/359) 46% (250/538) **60%** 540/897 1.56 0.76 **1.51** (CI95%:1.48 -1.54) 2.36 1.15 81% (440/540) CI95% 78 - 85 38% (136/357) CI95% 33 - 43 67% (440/661) 58% (136/236) **60%** 540/897 1.32 0.49 **1.51** (CI95%:1.48 -1.54) 1.99 0.74	**Funding:** International Continence Society (ICS) **Limitations:** No information provided about the specific protocol followed in carrying out tests, who carried them out, whether they were blinded and also interval between the tests. **Notes:** *Qmax taken as highest value for each patient from voids

See Evidence Table 3 Diagnosistic accuracy of uroflowmetry for Oelke et al., 2007[231] .

Evidence Table 5: Pelvic floor exercises (with or without electrical stimulation or biofeedback)

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Bales et al., 2000[22] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 months after surgery Outcome assessment was masked	**Patient group:** Men with stages T1c-T2c prostate cancer who were to undergo radical retropubic prostatectomy by a single surgeon **Inclusion criteria:** Men with stages T1c-T2c prostate cancer who were to undergo radical retropubic prostatectomy by a single surgeon. None of the men had undergone transurethral resection of the prostate or had pre-existing neurologic disease. **Exclusion criteria:** See above, exclusion criteria not specifically stated. **<u>All patients</u>** **N:** 100 **Drop outs:** 3 **<u>Group 1:</u>** **N:** 50 **Age (mean):** 59.3 **Drop outs:** 3 **<u>Group 2:</u>** **N:** 50 **Age (mean):** 60.9 **Drop outs:** 0	**Group 1: Biofeedback** 45-minute session with a nurse trained in biofeedback techniques 2 to 4 weeks prior to radical prostatectomy. Patients instructed how to perform graded PFMT using biofeedback. Surface electrodes were used to assess muscle strength and contractions of 5 to 10 seconds, and 10 to 15 repetitions were performed. Patients advised to practice these exercises 4/day until their surgery. **Group 2: Control** Patients underwent radical prostatectomy without any biofeedback training. These patients received only written and brief verbal instructions on how to perform PFMT to isolate the muscle that starts and stops urine flow and to practice contractions 4/day with 10 to 15 repetitions. Patients were given written instructions and briefly reviewed these instructions with a nurse. **All patients:** Postoperatively, the urethral catheter was removed approximately 2 weeks following surgery in both groups. Patients in both groups were encouraged to perform pelvic muscle strengthening exercises 4/day after catheter removal. No patient in either group received adjuvant radiation therapy or hormonal therapy within 6 months following surgery.	**Incidence of urinary continence at 6 months post op.**	**Group 1:** 44/47 (94%) **Group 2:** 48/50 (96%) **p value:** 0.60	**Funding:** NR **Limitations:** This study is poorly reported: Method of randomisation and allocation concealment not described, there is insufficient information about patients' baseline characteristics, no description of sample size calculation. Assessments methods could be unreliable. Other limitations stated by authors: - no effort was made to assess pelvic muscle floor strength prior to surgery - incidence of incontinence in Group 2: was very low - patients received only one preoperative biofeedback session. - subtle differences in results might have been detected if more rigorous measures of incontinence had been used, such as weighted pad testing. No objective measurement of continence was used. **Notes:** Patients wearing one pad or less per day were considered to be continent. Those using two or more pads per day were considered incontinent.
			Incidence of urinary continence at 3 months post op	**Group 1:** 27/47 **Group 2:** 31/50 **p value:** 0.64	
			Proportion of still incontinent at 3 months (ITT analysis)	**Group 1:** 23/50 **Group 2:** 19/50 **p value:** NR	
			Proportion of still incontinent at 6 months (ITT analysis)	**Group 1:** 6/50 **Group 2:** 2/50 **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Burgio et al., 2006[39] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 months post surgery	**Patient group:** Men elected for radical prostatectomy for prostate cancer **Setting:** single centre university urology clinic(USA) **Inclusion criteria:** Ambulatory and continent **Exclusion criteria:** • If reporting > 2 episodes of urinary incontinence in past 6 months • Had documented incontinence in a bladder diary • Previous prostatectomy • Mental impaired status (<20 on the Mini-Mental State Examination) • <1 week before scheduled surgery **<u>All patients</u>** **N:** 112 **Age (mean ± SD):** 60.9 ± 6.9 **Drop outs:** 0 **<u>Group 1</u>** **N:** *57** **Age (mean ± SD):** 60.7 ± 6.6 **M:** *57* **Black**: 13 **Previous TURP**: 2 **Drop outs:** 0 **<u>Group 2</u>**	**Group 1** Single session of preoperative biofeedback enhanced behavioural training on pelvic floor muscle control and instructions on daily PMFT. Rectal probe used to provide feedback of rectal pressure. Daily practice 3 x 15 exercises. Also instructed to interrupt stream when voiding. Postoperatively patients were reminded to resume exercise regimen **Group 2** Brief instructions on how to interrupt stream when voiding and usual care. **All patients** Instructed on use of bladder diaries and use of pads to record incontinence. Patients sent a weekly bladder diary to investigators during follow up. Patients were contacted for follow-up at 6 weeks, 3 and 6 months after surgery. They completed patient questionnaire on bladder	**Proportion of patients with severe/continual leakage at 6 months**	**Group 1:** 3/50 (6%) **Group 2:** 9/47 (19%) **p value:** 0.04 (Chi squared) not ITT NCGC Chi-squared calculation p=0.058 using ITT	**Funding:** National Institute for Diabetes and Digestive Kidney Diseases, National Institute of Health **Limitations:** There were significantly more men in the control group with preserved urethral length. P=0.03 favouring continence. At 6 months data was not presented as an ITT analysis **Notes:** Bladder diaries were scored by an individual kept blind to group assignment. Those performing intervention were blinded to next group assignment. Randomisation by computer. Kaplan-Meier data extraction by Hunter et al., 2007[123] et al Cochrane review
			Number of patients wearing pads at 6 months	**Group 1:** 16/50 (32%) **Group 2:** 24/46 (52%) **p value:** <0.05 not ITT NCGC Chi-squared calculation p=0.086 using ITT	
			Mean days ± SD with no leakage at 6 months	**Group 1:** 72.6 ±0.39 **Group 2:** 54.2 ± 0.47 **p value:** 0.04 not ITT NCGC t-test with equal variance test calculation p<0.00001 using ITT	
			Kaplan-Meier survival curve of proportion of still incontinent at < 3 months (data from Hunter et al., 2007[123])	**Group 1:** 49/54 **Group 2:** 51/53 **p value:** 0.25 (NCGC Chi-squared calculation – not ITT)	
			Kaplan-Meier survival curve of proportion of still incontinent at 3 - 6 months (data from Hunter et al., 2007[123])	**Group 1:** 32/53 **Group 2:** 40/51 **p value:** 0.046 (NCGC Chi-squared calculation – not ITT)	
			Kaplan-Meier survival curve of proportion of still incontinent at 6 - 12 months (data from Hunter et al., 2007[123])	**Group 1:** 22/51 **Group 2:** 30/50 **p value:** 0.09 (NCGC Chi-squared calculation – not ITT)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 55* **Age (mean ± SD):** 61.1 ± 7.2 **M:** 55 **Black:** 18 **Previous TURP:** 1 **Drop outs:** 0 * excludes patients with cancelled operations	control, 7-day bladder diary, QoL score, and Incontinence Impact Questionnaire modified for men. ***Continence defined as 3 consecutive weekly bladder diaries returned with no leakage.***			

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Filocamo et al., 2005[91] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men undergoing retropubic radical prostatectomy for localised prostate cancer **Setting:** urology clinic, University of Florence, Italy **Inclusion criteria:** NR **Exclusion criteria:** • Prior bladder or prostate surgery • Prior urinary or faecal incontinence • Neurogenic dysfunction of lower urinary tract • Preoperative history of overactive bladder **<u>All patients</u>** **N:** 300 **Age (mean ± SD):** NR **Drop outs:** 0 **<u>Group 1</u>** **N:** 150 **Age (mean ± SD):** 65 ± 4.79 (51-75) **M:** 150 **Mean preop PSA (ng/ml):** 8.13 **Drop outs:** 0 **<u>Group 2</u>** **N:** 150 **Age (mean ± SD):** 66.8 ± 5.33 (45-75) **M:** 150	**Group 1** In 1st treatment session PFMT was taught using verbal and visual feedback. Strength of muscles evaluated by digital anal control. Patients instructed to perform 3x10 sets/day at home for 6 months. In 2nd treatment session PMFT taught in all positions and patients asked to identify movements causing incontinence. Patients asked to practice new exercises at home for 7 days. At 3rd treatment session patients asked to practise PFMT before any activity that may cause incontinence. **Group 2** No treatment **All patients** Asked to complete a bladder diary and counselled to prevent leakage by increasing frequency of micturation. All patients were assessed at 1,3 ,6 and 12 months.	**Proportion of patients still incontinent at 1 month (using subjective ICS male questionnaire)**	**Group 1:** 121/150 (81%) **Group 2:** 138/150 (92%) **p value:** NR NCGC Chi-squared calculation p=0.004 using ITT analysis **signif.**	**Funding:** NR **Limitations:** • Randomisation method not described • Masking of outcome assessment not mentioned • Proportion of patients still incontinent reported as subjective measurement using ICS questionnaire **Additional outcomes:** Correlation between patient age and continence at each time interval **Notes:** Study reports numbers of patients continent at time intervals but data are presented as number of patients ***still incontinent***
			Proportion of patients still incontinent at 3 months (using subjective ICS male questionnaire)	**Group 1:** 39/150 (26%) **Group 2:** 105/150 (70%) **p value:** NR NCGC Chi-squared calculation p<0.00001using ITT analysis **signif.**	
			Proportion of patients still incontinent at 6 months (using subjective ICS male questionnaire)	**Group 1:** 6/150 (4%) **Group 2:** 53/150 (35%) **p value:** NR NCGC Chi-squared calculation p<0.00001using ITT analysis **signif.**	
			Proportion of patients still incontinent at 12 months (using subjective ICS male questionnaire)	**Group 1:** 2/150 (1%) **Group 2:** 18/150 (12%) **p value:** NR NCGC Chi-squared calculation p=0.0002 using ITT analysis **signif.**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean preop PSA (ng/ml): 8.11 **Drop outs:** 0	Incontinence was assessed objectively using 1h and 24h pad test – number of pads used daily. Subjective assessment by completion of International Continence Society (ICS) questionnaire. All patients still incontinent at 6 months underwent urodynamic evaluation ***Continence defined as 1 precautionary pad***			

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Floratos et al., 2002[93] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** Patients undergoing radical retropubic prostatectomy for localised prostate cancer. **Setting: multi-centre.** Greece and Netherlands **Inclusion criteria:** Patients with objectively confirmed urinary incontinence, no significant perioperative complications (ureteric or rectal injury, urine leakage from anastomosis, thrombo-embolism), no history of preoperative incontinence and pelvic or lower urinary tract operations, no psychiatric history, a recognised ability to participate in a learning programme, good general condition and willingness to participate in the study. **<u>All patients</u>** **N:** 42 **Age (mean ± SD):** **Drop outs:** Unclear **<u>Group 1:</u>** **N:** 28 **Age (mean ± SD):** 63.1 +/- 4 **Received Oxybutynin:** n=3 **<u>Group 2:</u>** **N:** 14 **Age (mean ± SD):** 65.8 +/- 4.3 **Received Oxybutynin:** n=2	**<u>Group 1: Biofeedback</u>** Patients referred to a specialist in physical therapy and rehabilitation to have 15 sessions of electromyographic (EMG) biofeedback (2 channel Totem Biofeedback, BEAC, Italy) 3/week of 30 min duration each. During the initial 2/3 sessions, a strong emphasis was placed on the specificity of muscle contraction. During the sessions the exercises were designed to increase the power, endurance and coordination of the pelvic floor muscles. In parallel, patients practised 50-100 exercises daily at home. **<u>Group 2: Control</u>** Patients were taught how to contract their pelvic muscles without contracting abdominal muscles simultaneously. Patient was placed in the lateral decubitus position and the instructor inserted index finger into patient's rectum to check for simultaneous contraction whilst palpating the abdominal muscles. Verbal feedback used to instruct the patient how to correctly and selectively contract the anal sphincter while. Patients received an informative leaflet with these instructions. Home practise comprised 80-100 exercises daily, divided in four sessions of 20-25 exercises each. The duration of each constriction was 3-5 s with submaximal strength (70%) and relaxation period of 6-10 s between the exercises. Initially patients practised these exercises while supine but later when sitting and standing. After the first month patients were encouraged to practise the exercises during normal daily activities, including movements that provoked incontinence.	**Mean urine loss as assessed by the 1-h pad test** Patients were evaluated at 1,2, 3 and 6 months of treatment using 1-h pad test. For the best intra- and inter-patient estimates in the pad test, a special type of 'pocket pad' was used which covered only the penis, thus reducing the interference from sweat on the pad weight gained during the test.	**Group 1:** Baseline: 39 g 1st month: 18 g 2nd month: 7 g 3rd month: 4 g 6th month: 3 g **Group 2:** Baseline: 31 g 1st month: 11 g 2nd month: 3 g 3rd month: 1 g 6th month: 0 g **P value** > 0.05	**Funding:** NR **Limitations:** Randomisation and allocation concealment is not described. There is insufficient information about patients' baseline characteristics, no description of sample size calculation. Masking of outcome assessment is not reported. **Additional outcomes:** No additional outcomes reported **Notes:** **All patients:** During the study, patients with irritative symptoms and a negative urine culture received empirical anticholinergic medication (oxybutynin). **Continence defined as <1 g loss / 1hour pad test or < 2 pads per day**
			Mean no. pads/ day Patients were evaluated subjectively with a questionnaire (to determine the number and extent of incontinence episodes, number of pads used per day, and any LUTS).	**Group 1:** Baseline: 3.9 1st month: 3.4 2nd month: 1.2 3rd month: 0.8 6th month: 0.4 **Group 2:** Baseline: 3.6 1st month: 1.8 2nd month: 0.9 3rd month: 0.4 6th month: 0.2 **P value** > 0.05	
			Number of men still incontinent at 3-6 months (data from Hunter et al., 2007[123])	**Group 1:** 4/28 **Group 2:** 0/14	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Franke at al., 2000[96] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 24 weeks (6 months)	**Patient group:** Incontinent men after radical prostatectomy **Setting:** Urology department, Vanderbuilt Medical Centre, Tennessee, USA **Inclusion criteria:** 2 weeks post prostatectomy **Exclusion criteria:** • Previous TURP • Neurological condition affecting the urinary tract. • Men with residual urine greater than 50ml or urinary tract infection were excluded at 6 week visit. **<u>All patients</u>** **N:** 30 **Drop outs:** 5 withdrew after randomisation **<u>Group 1</u>** **N:** 15 **Age (mean):** 62.3 **Dropouts:** At 3 months= 2, 6 months= 8 **<u>Group 2</u>** **N:** 15 **Age (mean): 60.7** **Drop outs:** 3 months: 5, 6 months: 7	**Group 1** 45 minute biofeedback behavioural therapy session 6, 7, 9, 11 and 16 weeks postoperatively. Perineal patch electromyography biofeedback was performed using abdominal electromyography leads to ensure proper isolation. Patients instructed to continue pelvic floor muscle exercises at home (20 contractions 3 times a day). A timed voiding schedule was encouraged and patients instructed in techniques tot decrease urgency and urge incontinence. **Group 2** No instruction and asked to return voiding diary and 48 hour pad test at the routine follow-up visits. **All patients:** Urinalysis and post void residual urine volume tests at 6 week visit. Completed voiding diary and 48 hour pad test at 6, 12 and 24 weeks postoperatively.	**Number still incontinent at 3 months**	**Group 1:** 6/13 (46%) **Group 2:** 3/10 (30%) **P value:** NR NCGC Chi-squared calculation p=0.23 using ITT analysis **Not sig.**	**Funding:** NR **Limitations:** • Randomisation method not described • Masking of outcome assessment not mentioned • Not an ITT analysis **Additional outcomes:** Improvement in pelvic muscle work using electromyography training effect (only assessed in intervention group). **Notes:** Study reports number of patients continent at time intervals but data are presented as number of patients ***still incontinent***. Incontinent defined as still using pads in the study.
			Number still incontinent at 6 months	**Group 1:** 1/7 (14%) **Group 2:** 1/8 (12%) **P value:** NR NCGC Chi-squared calculation p=1.00 using ITT analysis **Not sig.**	
			Mean incontinence (gm/24hours) using pad tests	**At 6 weeks** **Group 1:** 162 **Group 2:** 152, **p value:** 0.91(CI95%: 193-214) **At 3 months:** **Group 1:** 58 **Group 2:** 93, **p value:** 0.67(CI95%: 199-128) **At 6 months:** **Group 1:** 8 **Group 2:** 62, **p value:** 0.41(CI95%: 200-90)	
			Mean incontinent episodes/day (mean voiding diary differences)	**At 6 weeks** **Group 1:** 7.2 **Group 2:** 5.2, **p value:** 0.48 (-3.7-7.7) **At 3 months:** **Group 1:** 1.3 **Group 2:** 0.8, **p value:** 0.38 (-0.7-1.6) **At 6 months:** **Group 1:** 0.3 **Group 2:** 0.1, **p value:** 0.45 (-0.3-0.6)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Manassero et al., 2007[180] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months Masked outcome assessment and computer generated random numbers	**Patient group:** men undergoing retropubic radical prostatectomy for localised prostate cancer **Setting:** urology clinic, University of Pisa, Italy **Inclusion criteria:** • Compliance with protocol clinic attendance • Objectively confirmed urinary incontinence (>2g urine on 24h pad test) **Exclusion criteria:** • History of preoperative incontinence • Significant perioperative complications • Active rectal lesions or infections • Psychiatric or neurological disorders • Inability to contract pelvic floor muscles or weak contraction • Detrusor over activity **<u>All patients</u>** **N:** 107 **Age (mean):** **M:** 107 **Drop outs:** 13 **<u>Group 1</u>** **N:** 54 **Age (mean ± SD):** 66.8 ± 6.3	**Group 1** Pelvic floor muscle training programme by trained urologists with verbal feedback and measurement of muscle strength using digital anal control. Patients with weak muscles had additional electrical stimulation. Home practice 3x15 sessions/day increasing to 3x30 sessions in supine, sitting and standing positions. After 1 month patients were encourage to integrate exercise into daily life. **Group 2** No treatment. **All patients** Assessed at 1 week and 1,3,6,9 and 12 months after catheter removal including a physical examination and IPSS score. At home patients weighed pads and residual incontinence assessed subjectively using visual analogue score (VAS) where 0=completely continent, 10=completely incontinent. Patients also filled out frequency volume charts ***Continence defined as <2g urine***	**Proportion of patients still incontinent at 1 month**	**Group 1:** 45/54 (83%) **Group 2:** 39/40 (98%) **p value:** 0.04 (Fishers exact test) **signif.** NCGC Chi-squared calculation p=0.21 using ITT analysis **Not sig.**	**Funding:** NR **Limitations:** High drop out rate 13/53 (28%) in control group and results for control group are not presented as intention to treat (ITT) analysis **Additional outcomes:** Correlation between VAS score subjective assessment and 24h pad test at each time interval. Multivariate logistic regression to find variables that predict incontinence at 12 months (adjusting for age, IPSS score, blood loss, baseline QoL, incontinence at 1 week, tumour stage & nerve preservation) **Notes:** None
			Proportion of patients still incontinent at 3 months	**Group 1:** 29/54 (54%) **Group 2:** 31/40 (76%) **p value:** 0.03 (Fishers exact test) **signif** NCGC Chi-squared calculation p=0.61 using ITT analysis **Not sig.**	
			Proportion of patients still incontinent at 6 months	**Group 1:** 18/54 (33%) **Group 2:** 24/40 (60%) **p value:** 0.01 (Fishers exact test) **signif** NCGC Chi-squared calculation p=0.21 using ITT analysis **Not sig.**	
			Proportion of patients still incontinent at 12 months	**Group 1:** 9/54 (17%) **Group 2:** 21/40 (53%) **p value:** 0.0003 (Fishers exact test) **signif** NCGC Chi-squared calculation p=0.008 using ITT analysis **signif.**	
			Proportion of patients still incontinent at 12 months (incontinence severity)	**Group 1:** 1 mild (2-9g), 1 moderate (10-49g), 7 severe (≥50g) **Group 2:** 7 mild (2-9g), 10 moderate (10-49g), 4 severe (≥50g)	
			Subjective comparison of incontinence at 12 months using VAS score	**Group 1:** NR **Group 2:** NR **p value:** 0.01 (Wilcoxon Rank Sum Tets) **signif**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	M: 54 **Mean urine leakage/day:** 247 ± 505g **Drop outs:** 0 **<u>Group 2</u>** **N:** 53 **Age (mean ± SD):** 67.9 ± 5.5 (n=40) **M:** 53 **Mean urine leakage/day:** 97 ± 138g **Drop outs:** 13 (social reasons and refusal to complete follow-up) Baseline data only available for 40 patients	***lost per day on 24h***	**Subjective comparison of incontinence at 12 months using Quality of Life (QoL) question from IPSS symptom score.**	**Group 1:** NR **Group 2:** NR **p value:** 0.03 (Wilcoxon Rank Sum Tets) **signif**	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Mathewson-Chapman 1997[185] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** Men with a radical retropubic prostatectomy (RP) for localised prostate cancer **Setting:** University of Florida College of Nursing **Inclusion criteria:** • Incontinent on day 15 after surgery after catheter removal • Able to regularly attend hospital appointments **<u>All patients</u>** **N:** 53 **Age (mean):** 62 (range 47-75) **M:** 53 **Drop outs:** 2 (unaccounted for in report) **<u>Group 1</u>** **N:** 27 **Age (mean):** NR **M:** 27 **Drop outs:** NR **<u>Group 2</u>** **N:** 24 **Age (mean):** NR **M:** 24 **Drop outs:** NR	**Group 1** Preoperative education and instruction* Then postoperative Pelvic Muscle Exercise protocol (PME) practiced 3/week for 36 sessions starting at week 3. 15 repetitions performed at home, increasing by 10 every 4 weeks to a maximum of 35 Biofeedback using an anal probe (PRS 8900 Incare). Evaluations were done at baseline, weeks 5, 12 and any other times requested by the patient. **Group 2** Preoperative education and instruction* Postoperatively no intervention. **Examination methods:** Bladder diary was used to measure the number of pads used, number of episodes of incontinence /day over a 3 day period and frequency of episodes of urine loss. 24h pad test measured	**Mean ± SD number of episodes of incontinence at week 2**	**Group 1:** 25.1 ± 39.5 **Group 2:** 12.5 ± 26.3 **p value:** 0.17 (t test) **Not sig.**	**Funding:** In part by a Geriatric Nurse Fellowship from Dept. Veteran Affairs, USA **Limitations:** • The results from the intervention arm are potentially confounded by the preoperative instruction on pelvic floor muscle contraction given to both groups • No allocation concealment • No blinding • Not an ITT analysis – report says 53 randomised but only 51 in patient groups. Drop outs not explained. **Notes:** *Both groups were taught preoperatively how to contract perineal muscle prior to lifting, standing, coughing or sneezing and also to limit tea, coffee, chocolate and alcohol uptake.
			Mean ± SD number of episodes of incontinence at week 5	**Group 1:** 13.4 ± 31.1 **Group 2:** 10.4 ± 26.8 **p value:** 0.71 (t test) **Not sig.**	
			Mean ± SD number of episodes of incontinence at week 9	**Group 1:** 1.5 ± 3.2 **Group 2:** 5.6 ± 26.3 **p value:** 0.34 (t test) **Not sig.**	
			Mean ± SD number of episodes of incontinence at week 12	**Group 1:** 0.84 ± 1.99 **Group 2:** 1.00 ± 0.27 **p value:** 0.68 (t test) **Not sig.**	
			Mean ± SD number of pads used at week 2	**Group 1:** 3.88 ± 3.15 **Group 2:** 3.84 ± 3.3 **p value:** 0.95 (t test) **Not sig.**	
			Mean ± SD number of pads used at week 5	**Group 1:** 2.35 ± 2.97 **Group 2:** 2.84 ± 3.1 **p value:** 0.56 (t test) **Not sig.**	
			Mean ± SD number of pads used at week 9	**Group 1:** 1.1 ± 2.1 **Group 2:** 2.04 ± 2.7 **p value:** 0.2 (t test) **Not sig.**	
			Mean ± SD number of pads used at week 12	**Group 1:** 0.6 ± 1.6 **Group 2:** 1.8 ± 2.7 **p value:** 0.07 (t test) **Not sig.**	
			Mean ± SD time to continence - no pad needed (days)	**Group 1:** 51 ± 28.9 **Group 2:** 56 ± 30.47 **p value:** 0.59 (t test) **Not sig.**	
			Mean amount of urine (ounces ± SD) lost in 24h at week 5	**Group 1:** 4.3 ± 8.9 (4.3 oz = 121g) **Group 2:** 4.5 ± 7.7 (4.5 oz = 128g) **p value:** 0.95 (t test) **Not sig.**	
			Mean amount of urine (ounces ± SD) lost in 24h at week 12	**Group 1:** 0.0 ± 80.0 **Group 2:** 0.5 ± 1.7 (1.7 oz = 48g) **p value:** 0.22 (t test) **Not sig.**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
		amount of urine lost. Volume of urine lost (ounces), number of pads used, number of episodes of urine loss, number of episodes of incontinence and length of time urine loss was experienced were all evaluated at weeks 2, 5, 9 and 12.	**Proportion of still incontinent at 0 – 3 months (60-79 days)** Data from Hunter et al., 2007[123]	**Group 1:** 8/27 **Group 2:** 10/24 **p value:** NR	. Included study in SR by Hunter et al., 2007[123].

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Moore et al., 1999[203] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 24 weeks Computer generated randomisation sequence and allocation concealment	**Patient group:** Patients who had undergone radical retropubic prostatectomy **Setting:** University-affiliated hospitals in Edmonton, Canada **Inclusion criteria:** • >= 4 weeks after radical prostatectomy (RP) • (>2 g of urine loss on pad test) • Neurologically normal • Within 2 h drive of study centre • Able to speak and read English • Willing to comply with protocol • No current treatment • Not seeking other treatment **Exclusion criteria:** • Demand pacemaker • Previous pelvic muscle stimulation • Active rectal lesions or infections • Known detrusor instability **All patients** **N: 63** **Drop outs:** 5	**Group 1 (PFMT)** Pre and postoperative verbal + written instructions about PFMT by nurses in preadmission clinic and follow-up visits to urologist. **Also** Intensive physiotherapy 30 min 2/week for 12 weeks. Initial contractions were of 5-10 s + a 10-20 s rest, with 12-20 repetitions. For endurance exercises the 'hold' time was 20-30 s + equal rest time, with 8-10 repetitions. Speed was achieved by sets of quick repetitive contractions in a 10 s span with a 20-s rest. Finally, purposeful control occurred in 3 stages, with a 5-s hold each stage and a slow release, with a rest period of 15-30s. **Group 2 (PFMT+ ES)** Pre and postoperative verbal + written instructions about PFMT by nurses in preadmission clinic and follow-up visits to urologist **Also** patients met with the same physiotherapist 2/week for 30 min. Electrical stimulation (ES) with a surface anal electrode (InCare) was alternated with PMFT as for Group 1. Stimulation parameters were 50 Hz, a	**Mean (median) [SD, range] urinary loss (g) in 24 h at baseline*** **Mean (median) [SD, range] urinary loss (g) in 24 h at 3 months*** **Mean (median) [SD, range] urinary loss (g) in 24 h at 4 months*** **Mean (median) [SD, range] urinary loss (g) in 24 h at 6 months*** **QOL** Objective QoL measures (IIQ-7 and EORTC QLQ	**Group 1 (PFMT): n=18:** 565.6 (513.9) [403.3, 21.5-1538.6] **Group 2 (PFMT+ ES) n= 19:** 452.5 (492.1) [385.1, 5.3-1344.8] **Group 3(Control) n=21:** 385.9 (395.5) [256.9, 6.3-921.5] **Total n=58:** 463.5 (419.8) [352.2, 5.3-1538.6] **p value:** Not sig **Group 1 (PFMT): n=18:** 86.9 (32.50) [123.0, 2.2-385.9] **Group 2 (PFMT+ ES) n= 19:** 155.5 (87.5) [168.1,1.0-509.3] **Group 3 (Control) n=21:** 103.8 (23.8) [176.3, 1.0-702.4] **Total n=58:** 115.5 (27.2) [158.7, 1.0-702.4] **p value:** Not sig **Group 1 (PFMT): n=18:** 73.5 (10.35) [131.4, 1.0-494.6] **Group 2 (PFMT+ ES) n= 19:** 202.2 (85.7) [242.23, 1.0-753.4] **Group 3 (Control) n=21**: 67.3 (11.5) [137.4, 2.0-530.3] **Total n=58:** 114.2 (14.1) [185.6, 1.0-595.7] **p value:** Not sig **Group 1 (PME): n=18:** 69.9 (8.7) [113.5, 1.0-362.8] **Group 2 (PME+ ES) n= 19:** 98.2 (8.95)[132.1, 1.0-424.2] **Group 3 (Control) n=21:** 54.1 (6.9) [103.1, 1.0-277.3] **Total n=58:** 72.5 (7.5) [115.7, 1.0-424.2] **p value:** Not sig There were no significant group differences in either IIQ-7 or the QLQ C30	**Funding:** Oncology Nurses' Society, Canadian Nurses' Foundation, Caritas Health, Alberta Physiotherapy Association, Edna Minton Foundation, and the University of Alberta, Edmonton, Canada. **Limitations:** • Masking of outcome assessment was not reported • The results from the intervention arm are potentially confounded by the preoperative instruction on pelvic floor muscle contraction given to all groups **Notes:** ***Data from text for median urinary loss:** A one-way repeated-measures ANOVA using a general linear model was computed to test the difference between and within groups, as well as the change over time at 12, 16 and 24

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	3 because of bladder neck contractures 1 because of rectal pain when he did the exercises 1 because he went on vacation for 4 months and could not continue therapy **Age (mean):** 67 (range 49-77) **<u>Group 1 (PFMT)</u>** **N:** 20 **Age (mean):** 67.4 **Drop outs:** 2 **<u>Group 2 (PFMT+ ES)</u>** **N:** 22 **Age (mean):** 65.7 **Drop outs:** 3 **<u>Group 3 (Standard treatment)</u>** **N:** 21 **Age (mean):** 66.8 **Drop outs:** 0	biphasic pulse shape with 1-s bursts, a 1 s pulse width and 1 s pulse trains. **Group 3(Standard treatment)** Pre and postoperative verbal + written instructions about PFMT by nurses in preadmission clinic and follow-up visits to urologist ***Continence was defined as a loss of <= 2 g of urine; socially acceptable continence was considered as <= 10 g***	C-30)	P NR Other data for QoL is reported in text for the whole population and not per group.	weeks. There were no differences among the groups (F=0.23, P=0.80) at any of the measurements Data for proportion of patients still incontinent was taken from Hunter et al., 2007[123] Cochrane Review though it is unclear how this data was extracted from the paper.
			Proportion of still incontinent at 0 – 3 months (data from Hunter et al., 2007[123])	**Group 1:** 12/20 **Group 2:** 11/22 **Group 3:** 14/21 **p value:** NR	
			Proportion of still incontinent at 3 – 6 months (data from Hunter et al., 2007[123])	**Group 1:** 8/20 **Group 2:** NR **Group 3:** 7/21 **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Parekh et al., 2003[233] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men scheduled to undergo radical prostatectomy for localised prostate cancer **Setting:** Urology clinic, USA **Exclusion criteria:** Prior bowel or bladder incontinence **<u>All patients</u>** **N:** 38 **Age (mean ± SD):** NR **Drop outs:** 0 **<u>Group 1</u>** **N:** 19 **Age (mean ± SD):** 61.6 **M:** 19 **Mean preop PSA (ng/ml):** 8.3 **Drop outs:** 0 **<u>Group 2</u>** **N:** 19 **Age (mean ± SD):** 55.5 **M:** 19 **Mean preop PSA (ng/ml):** 8.1 **Drop outs:** 0	**Group 1** PMFT using verbal and visualisation techniques and biofeedback using rectal probe was delivered by a physiotherapist comprising initial evaluation and 2 treatment sessions prior to surgery and then every 3 weeks for 3 months postoperatively. Home exercise programme was followed for 6 months or longer. **Group 2** No treatment. **All patients** Completed urinary incontinence questionnaire by telephone or when questioned by medical students at weeks 6, 12, 16, 20, 28 and 52. Incontinence measured by number of pads used daily with ***continence defined as 0-1 precautionary pad***	**Median time to regain continence**	**Group 1:** 12 weeks **Group 2:** 16 weeks **p value:** <0.05 (2 tailed *t*-test)	**Funding:** NR **Limitations:** • Randomisation method not described • Masking of outcome assessment not mentioned **Notes:** Study reports numbers of patients continent at time intervals but data are presented as number of patients ***still incontinent***
			Proportion of patients still incontinent at 3 months	**Group 1:** 6/19 (32%) **Group 2:** 12/19 (63%) **p value:** NR NCGC Chi-squared calculation p=0.051 using ITT analysis **Not sig.**	
			Proportion of patients still incontinent at 6.5 months	**Group 1:** 4/19 (21%) **Group 2:** 7/19 (37%) **p value:** NR NCGC Chi-squared calculation p=0.28 using ITT analysis **Not sig.**	
			Proportion of patients still incontinent at 13 months	**Group 1:** 3/19 (16%) **Group 2:** 4/19 (21%) **p value:** NR NCGC Chi-squared calculation p=0.68 using ITT analysis **Not sig.**	
			Severe incontinence (>3 pads) at 12 months	**Group 1:** 2/19 (11%) **Group 2:** 3/19 (16%) **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Paterson et al., 1997[237] **Study design:** RCT Observer masked **Evidence level:** 1+ **Duration of follow-up:** 13 weeks	**Patient group:** Men with post-micturation dribbling (PMD) **Setting:** Repatriation General Hospital, South Australia **Inclusion criteria:** Patients with an history of post-micturation dribbling (PMD) **Exclusion criteria:** No history of surgery on the bladder, prostate or urethra, or had a history of urgency or stress incontinence. All were able to comply with instructions **<u>All patients</u>** **N:** 49 **Drop outs:** 6 **Group 1 (counselling)** **N:** 15 **Age (mean [SEM]):** 69.5 [2.4] **Initial pad weight gain (g) (mean [SEM]):** 7.56 [1.27] **Initial pelvic muscle (mean [SEM]):** 2.5 [0.21] **Group 2 (milking)** **N:** 15 **Age (mean [SEM]):** 69.3 [3.1] **Initial pad weight gain (g) (mean [SEM]):** 10.43 [2.99] **Initial pelvic muscle (mean [SEM]):**	**Group 1 (counselling)** Advice on drinking patterns, types of beverages, aperient use, toileting habits, hints to alleviate oedema, dietary advice and relaxation therapy **Group 2 (milking)** Patients were given insights into the anatomy of the urethra and where the urine pools. They performed the procedure in the clinic to ensure that they did so correctly. An education sheet based on the technique outlined by Millard was issued to this group to reinforce their understanding of the procedure. **Group 3 (PFMT)** Pelvic muscle exercise: Patients were given simple education on the anatomy and physiology of the act of micturition. Time and effort were taken to enable correct identification of the pelvic muscles. Participants were taught to tighten and lift these muscles as if they were controlling flatus or interrupting the flow of urine mid-stream. They were encouraged to do them in front of the mirror to observe penile and scrotal lift and to recognize inappropriate tightening of abdominal and gluteal muscles. The fast-twitch muscle fibres were exercised by a series of 1-second contractions (usually five) and gradually extending the number of repetitions, depending on the individual ability of each participant. The slow-twitch fibres	**Urinary loss measured by difference in mean pad weight gain** Urinary loss was measured at baseline and at 5, 7, and 13 weeks using pad weighing method. Participants were given instruction on how to wear the pads, seal them in plastic bags and how to complete a bladder chart. The weighing and coding of the pads was the responsibility of the research assistant who was unaware of the participant's group allocation. **Crude and adjusted mean (SEM) improvement in pad weight gain (g)** Adjusted for initial pad weight gain	Data is reported in figures. The mean pad weight initially decreased rapidly in the exercise group and less so in the milking group but did not changed dramatically in the counselling group (p values not reported). **Counselling:** n=15 Crude 0.019 (1.04) Adjusted: -1.387 **Milking:** n=15 Crude 3.97 (2.07) Adjusted: 2.877 p<0.01 compared to counselling **Exercise:** n=13 Crude 4.28 (2.47) Adjusted: 4.707 p<0.001 compared to	**Funding:** Cello Paper Pty donated weighing scales. Sancella Pty Ltd supplied the male incontinent pads **Limitations:** • Randomisation method and allocation concealment were not reported. • Standard deviations were not available for adjusted improvement in pad weight again. • Sample size calculation is not reported. **Notes:** Authors report compliance of participants was excellent, with all patients completing pad wearing and bladder charts, and 99.6% attendance of the required number of clinic visits.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	2.6 [0.30] **Group 3 (PFMT)** **N:** 14 (1 patient completed 9 of the 13 weeks of the study) **Age (mean [SEM]):** 70.8 (2.7) **Initial pad weight gain (g) (mean [SEM]):** 11.68 [5.43] **Initial pelvic muscle (mean [SEM]):** 2.5 [0.23] Height and weight reported not included in this table. Differences in initial pad weight gain was Not sig.	were exercised by repeating the maximum contraction as many times as possible without weakening of the length and strength of the contraction. Participants were instructed to spread exercise sessions throughout the day and to vary the positions from lying to sitting and standing.		counselling Improvement in pad weight gain was strongly influenced by initial pad weight gain, or degree of urine loss at the start of the study. After allowing for the effects of initial pad weight gain, the counselling group showed no improvement, the urethral milking group showed an adjusted mean improvement in urine loss of 2.9 g after 13 weeks, compared with 4.7 in the exercise group.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Porru et al., 2001[240] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 1 month Blinded outcome assessment for pelvic muscle strength	**Patient group:** diagnosis of symptomatic BPH selected to undergo TURP **Setting:** single centre, university urology clinic, Italy **Exclusion criteria:** • > 80 years • History of urethral or pelvic surgery • Neurogenic bladder • Prostate carcinoma **All patients** **N:** 58 **Age (mean):** NR **M:** 58 **Drop outs:** 5 **Group 1:** **N:** 30 **Age (mean):** 66 (range 53-71) **M: 30** **Drop outs:** 2 **Group 2** **N:** 28 **Age (mean):** 67.5 (range 55-73) **M:** 28 **Drop outs:** 3	**Group 1** Pelvic floor muscle training through verbal instructions and feedback on contractions. Patients received verbal and written instructions for home PFMT with a regimen of 3x15 exercises/day **Group 2** No treatment **All patients** Pelvic floor muscle strength was measured using digital examination and graded from 0 (none) to 4 (strong) preoperatively and at follow up visits on week 1, 2, 3 and 4. Patients began voiding diaries immediately post TURP over 48 hour periods The AUA symptom score was administered preoperatively and at 30 days postoperatively. ICS male questionnaire was used to assess Quality of Life Uroflowmetry was performed pre and 30 days post TURP and pressure flow studies confirmed existence of BOO Incontinence assessed by voiding diary.	**Proportion of patients still incontinent at 4 weeks**	**Group 1:** 1/30 (3%) **Group 2:** 3/28 (11%) **p value:** NR NCGC Fishers exact test calculation p=0.34 using ITT analysis **Not sig.**	**Funding:** NR **Limitations:** • Randomisation method not described • Masking of outcome assessment not mentioned • Incontinence was not clearly defined **Notes:** Urologist measuring pelvic floor muscle strength was masked to treatment allocation
			Change in AUA symptom score at 30 days	**Group 1:** from 22 to 9 **Group 2:** from 24 to 10 **p value:** reported as **Not sig. ANOVA**	
			Change in ICS-Male Quality of Life score at 30 days	**Group 1:** from 5.8 to 1.5 **Group 2:** from 5.5 to 3.2 **p value:** <0.001 **signif. ANOVA**	
			Mean muscle contraction strength (grade 0-4) ± SD at 4 weeks	**Group 1:** 3.8 ± 0.3 **Group 2:** 2.4 ± 0.2 **p value:** NR. NCGC calculation using a two-sample t test with unequal variances p <0.00001 **signif.**	
			Mean voiding interval at 4 weeks (± SD)	**Group 1:** 110 ± 23 **Group 2:** 118.5 ± 24 **p value:** reported as **Not sig.**	
			Proportion of patients with post micturation dribbling and incontinence episodes at 4 weeks	**Group 1:** NR **Group 2:** NR **p value:** reported as **Not sig.**	

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Study details	Patients	Interventions	Outcome measures	Effect size				Comments
Tibaek et al., 2007[294] **Study design:** RCT single blinded **Evidence level:** 1+ **Duration of follow-up:** 3 months after TURP	**Patient group:** Men with uncomplicated BPO (benign prostatic obstruction) scheduled for TURP (transurethral resection of the prostate). **Setting:** single centre, university hospital, Denmark **Inclusion criteria:** Fit, ambulatory, uncomplicated BPO scheduled for TURP **Exclusion criteria:** Prostate cancer, previous lower urinary tract surgery and neurological disease **<u>All patients</u>** **N:** 58 **Drop outs:** 9/58 (before intervention – group not specified) **<u>Group 1</u>** **N:** 26 **Age**, median (range): 70(58-77) **DAN-PSS-1** - **Symptom score:** 15(7-24) - **Bother score:** 17 (8-28) - **Total Score:** 28 (10-61) **Urine output per 24 h (ml):** 1827(1023-3187) **Voided volume (ml):** 165(50-350) **Frequency (no. of voidings/24hr):** 12(5-21) **Max flow (ml/s):** 7(3-15) **Residual urine (ml):** 116(0-877) **1st sensation (ml):** 64(10-270)	**Group 1 (PFMT)** Pre-TURP pelvic floor muscle training (digital-anal guided) lasting 4 consecutive weeks Program consisted of : - **Individual information:** 1 hour session including symptoms, anatomy and instructions on PFMT - **3 group treatments** 1 hour of isolated PFM contractions, strength exercises, endurance exercises repeated 4-8x in the supine, standing and sitting positions and PFM contractions before and during rising from sitting position and walking - **Home exercises:** PFM strength and endurance exercises repeated gradually 6 - 10 x in the supine, standing and sitting positions, 1 or 2/day. Patients received new	**DansPSS-1 total score** (values range from 0-108) Results presented as median (range).		**2 weeks**	**4 weeks**	**3 months**	**Funding:** Prof Jens C Christoffersen's Memory Fund, Danish Physiotherapist Research Fund, SCA Hygiene Products A/s. Astra Tech Denmark and Coloplast **Limitations:** • Physiotherapists assessing the PFM outcomes were masked. However, no mention on whether urological nurses who measured the subjective and objective voided parameters were blinded. • No mention whether urologists performing the TURP were blinded • Both groups received information
				Group 1:	15(3-61)	11(0-52)	3 (0-24)	
				Group 2:	13.5(0-51)	6 (0-37)	4.5(0-51)	
				P value:	0.927	0.452	0.754	
			Leakage in pad test (g/24 hours)		**2 weeks**	**4 weeks**	**3 months**	
				N#	12/26	12/23		
				Group 1:	1(0-188)	12(0-374)	-	
				Group 2:	0(0-23)	4(0-56)	-	
				P value:	0.656	0.755		
				#The others were continent and refused to do the test				
			Patients who used pads per 24hours, n(%)		**2 weeks**	**4 weeks**	**3 months**	
				Group 1:	9/25 (36)	4/26(15)	3/26(12)	
				Group 2:	6/21(29)	4/21(19)	5/22(23)	
				Relative risk: (95%CI)	()	()	()	
				p value:				
			Urine output/24hours (ml)		**2 weeks**	**4 weeks**	**3 months**	
				Group 1:	1985(1050-3415)	1694(923-3003)	1875(775-3387)	
				Group 2:	1887(583-3557)	1903(617-3803)	1820(367-2716)	
				p value:	0.638	0.412	0.640	
			Voiding volume (diary) (ml)		**2 weeks**	**4 weeks**	**3 months**	
				Group 1:	165.5(40-250)	150(30-250)	200(50-300)	
				Group 2:	127.5(50-360)	150(50-350)	155(50-360)	

Study details	Patients	Interventions	Outcome measures	Effect size				Comments
	Max cystometric bladder capacity (ml): 131(38-406) **Unstable detrusor; n(%):** 22/26(85) **Pressure flow AG number (ml/s):** 79.5(33-170) **Weight of prostate specimen (g):** 22(4-61) **Histology; no with prostate cancer:** 2 **Time from randomisation to TURP (days):** 42(18-140) **Group 2** **N:** 23 **Age,** median (range): 68(52-79) **DAN-PSS-1** - **Symptom score:** 15(6-22) - **Bother score:** 15(3-28) - **Total Score:** 26(3-64) **Urine output per 24 h (ml):** 1650 (418-3180) **Voided volume (ml):** 140 (50-350) **Frequency (no. of voidings per 24 hour):** 11.7(5-21) **Max flow (ml/s):** 7(1.5-17) **Residual urine (ml):** 108(0-875) **First sensation (ml):** 97(13-238) **Max cystometric bladder capacity (ml):** 174(42-338) **Unstable detrusor; n(%):** 19/23(83) **Pressure flow AG number (ml/s):** 76(22-228) **Weight of prostate specimen (g):** 24(10-58) **Histology; no with prostate cancer:** 2 **Time from randomisation to TURP (days):** 35(5-162)	progressive programme after the weekly lessons and motivated to continue until at lest 4 weeks after surgery. **Group 2 (control) -**no preoperative physiotherapy treatment Both groups received brief information regarding the anatomy and physiology of the bladder and PFM, and were given verbal, instructions about PFMT in the ward 2-3 days after TURP		**P value:**	0.563	0.599	0.510	about PMFT after TURP. Confounding **Additional outcomes:** Attendance was 100% for 24/26 and 75% for 2/26 All men had good initial PFM function (minimum rating 2), but did not improve to optimum function post-test. At 2 weeks, 41 men "improved", and 8 "worse". At 3 months, 3 patients still had higher DAN-PSS-1 score than before surgery Significant difference (p=0.049) between groups on dynamic muscle endurance. **Notes:** None.
			Frequency of voiding, times/24 hours		**2 weeks**	**4 weeks**	**3 months**	
				Group 1:	11.85(7.5-28.3)	10.3(4.3-26.3)	10.0(6.0-17.3)	
				Group 2:	13.2(5.7-20.7)	11.3(6.7-17.3)	10.7(4.3-19.0)	
				P value:	0.657	0.499	0.794	
			Maximal Urine Flow (ml/s)		**2 weeks**	**4 weeks**	**3 months**	
				Group 1:	-	-	16.6(4.1-47)	
				Group 2:	-	-	16.8(5.3-36.5)	
				P value:	-	-	0.726	
			Residual urine (ml)		**2 weeks**	**4 weeks**	**3 months**	
				Group 1:	-	-	22(0-661)	
				Group 2:	-	-	1(0-56)	
				P value:	-	-	0.127	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Van Kampen et al., 2000[304] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months Blinded outcome assessment and allocation concealment	**Patient group:** Men with a radical retropubic prostatectomy (RP) for localised prostate cancer **Setting:** Department of Urology, Leuven University Hospital, Belgium **Inclusion criteria:** • Incontinent on day 15 after surgery after catheter removal • Able to regularly attend hospital appointments **Exclusion criteria:** NR **<u>All patients</u>** **N:** 102 **Age (mean):** 65 range (52-76) **M:** 102 **Drop outs:** 4 **<u>Group 1</u>** **N:** 50 **Age (mean):** 64.4 ± 0.8 **M:** 50 **Drop outs:** 2 **Previous TURP**: 2 (4%) **Preoperative micturation (IPSS):** <10: 37 (74%) 10-20: 9 (18%)	**Group 1** Pelvic floor re-education programme extending for as long as incontinence persisted within time limit of 1 year. Programme comprised anatomical education pelvic floor and function, active pelvic floor muscle training (PFMT) with biofeedback. Strength of pelvic-floor muscles assessed using digital anal control and scored. 7 patients who could not contract were given electrical stimulation by anal probe. Patients were required to do 90 home exercises/day supine, sitting or standing. Each patient received treatment at weekly outpatient clinic **Group 2** Attendance of weekly outpatient clinic receiving education on aetiology of UI and placebo electrotherapy that couldn't affect muscle function. **Examination methods:** Continence measured by 24h weighed pad test after catheter removal and everyday until patient was	**Number of men achieving continence at 3 months**	**Group 1:** 43/48 (not ITT) **Group 2:** 29/52 **p value:** 0.001 (Fishers Exact test) NCGC check using ITT analysis p=0.0008 (Chi-squared) **signif.**	**Funding:** Grant from Fund of Scientific Research, Flanders, Belgium **Limitations:** No IPSS change data. No QoL score **Notes:** Patients placed in 6 subgroups according to amount of initial urine loss (>50g, <250g, >250g) and whether they had had a previous TURP. They were then randomised using permuted blocks by an independent person. Sealed envelopes but no statement of opacity. All patients treated by same physiotherapist. All continence assessments done by therapist who was not involved in the study.
			Number of incontinent* patients at 12 months	**Group 1:** 2/50 **Group 2:** 9/52 **p value:** 0.001 (Wald test) NCGC check using ITT analysis p=0.03 (Chi-squared) **Not sig.**	
			Duration of incontinence (Kaplan-Meier Survival Analysis)	**Group 1:** NR **Group 2:** NR **p value:** 0.0001 (log rank test)	
			Number of patients with VAS score=0 completely dry at 1 month	**Group 1:** 15/50 **Group 2:** 8/52 **p value:** NR NCGC check using ITT analysis p=0.08 (Chi-squared) **Not sig.**	
			Number of patients with VAS score=0 completely dry at 6 months	**Group 1:** 29/50 **Group 2:** 27/52 **p value:** NR NCGC check using ITT analysis p=0.5 (Chi-squared) **Not sig.**	
			Number of patients with VAS score=0 completely dry at 12 months	**Group 1:** 26/50 **Group 2:** 22/52 **p value:** NR NCGC check using ITT analysis p=0.3 (Chi-squared) **Not sig.**	
			Proportion of still incontinent at 0 – 3 months	**Group 1:** 5/48 **Group 2:** 23/52 **p value:** NR	
			Proportion of still incontinent at 3 - 6 months	**Group 1:** 2/48 **Group 2:** 12/52 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	>20: 4 (8%) **<u>Group 2</u>** **N:** 52 **Age (mean):** 66.6 ± 0.8 **M:** 52 **Drop outs:** 2 **Previous TURP**: 5 (10%) **Preoperative micturation (IPSS):** <10: 41 (81%) 10-20: 9 (17%) >20: 2 (2%)	continent. ***Continence defined as <2g urine lost per day on 24h and 1 h pad test as well as patients indicating no incontinence in past 3 days*** Confirmation was by 1h pad test in hospital with additional assessment. Continence was also assessed subjectively by visual analogue scale (0=completely continent, 10=completely incontinent) Continence assessed preoperatively and at 1, 6, 12 months	**Proportion of still incontinent at 6 - 12 months**	**Group 1:** 2/48 **Group 2:** 9/49 **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Willie et al., 2003[321] **Study design:** RCT **Evidence level:** 1 + **Duration of follow-up:** 12 months post.op	**Patient group:** Men with clinically localized prostate cancer who were scheduled for radical prostatectomy. **Setting:** Department of urology **Inclusion criteria:** Patient willingness to make 2 visits 3 and 12 months postoperatively. Patients who underwent previous transurethral prostatic resection were not excluded from the study. **Exclusion criteria:** NR **<u>All patients</u>** **N:** 139 **Drop outs:** see outcomes **<u>Group 1: PFMT</u>** **N:** 47 **Age (no units reported):** 65.9 **Prostate wt (gm):** 58.5 **% pathological tumor stage:** **pT1a-2b:** 71.7 **pT3a-3b:** 28.3 **pT4:** 0 **patients continent at baseline according to questionnaire:** 20.5% **Patients continent at baseline according to pad test:** 29% **Drop outs:** see outcomes	**Group 1: PFMT:** Patients received verbal and written instructions about postoperative PFMT from a physiotherapist. After this introduction each patient received intensive physiotherapy for 20 to 30 minutes for 3 days. All patients encouraged to perform the exercises twice daily for 3 months after discharge. **Group 2: PFMT + Electrical Stimulation (ES)** Patients received PFMT and ES and shown how to use the device by a dedicated nurse. ES was provided with a bioimpulser (Haynl Elektronik, Schonebeck, Germany) surface anal electrode. Therapy time was set for 15 minutes in the device. After this time the device was automatically downloaded to ensure that each patient had same therapy duration. Stimulation parameters were 27 Hz, biphasic pulse shape with 1-second bursts, a 5-second pulse width and 2-second pulse trains. Intensity was controlled by each patient from 10% to 100%. **Group 3: PFMT +ES and Biofeedback:** These patients were additionally	**% patients continent at 3 months according to questionnaires to determine number of pads daily** Results available at 3 months for questionnaires: n= 120	**Group 1: PFMT:** 3 months: 60% **Group 2: PFMT + ES:** 3 months: 65% **Group 3: PMFT + ES + Biofeedback:** 3 months: 53% p= 0.8	**Funding:** NR **Limitations:** Method of randomisation, allocation concealment and sample size calculation not described. **Additional outcomes:** **Compliance to treatment** Measured by asking the patients how long they had done the recommended treatment. **Notes:** Subjective continence was defined as no or 1 pad used daily. Objective continence <1 g/20 minute pad test
			% patients continent at 12 months according to questionnaires to determine number of pads daily Results available at 12 months for questionnaires: n= 129	**Group 1: PFMT:** 12 months: 88% **Group 2: PFMT + ES:** 12 months: 81% **Group 3: PMFT + ES + Biofeedback:** 12 months: 88.6% p= 0.50	
			% patients continent at 3 months according to 20 minute pad test Results available at 3 months for pad test: n= 79	**Group 1: PFMT:** 3 months: 64% **Group 2: PFMT + ES:** 3 months: 78% **Group 3: PMFT + ES + Biofeedback:** 3 months: 73% p= 0.5	
			% patients continent at 12 months according to 20 minute pad test Results available at 12 months for pad test: n= 124	**Group 1: PFMT:** 3 months: 76% **Group 2: PFMT + ES:** 3 months: 82% **Group 3: PMFT + ES + Biofeedback:** 3 months: 90.5% p= 0.24	
			Number of men still incontinent at 3 months (ITT analysis)	**Group 1: PFMT:** 17/47 (36%) **Group 2: PFMT + ES:** 10/46 (22%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	<u>Group 2: PFMT + Electrical Stimulation</u> **N:** 46 **Age (no units reported):** 64.6 **Prostate wt (gm):** 53.7 **% pathological tumor stage:** **pT1a-2b:** 70.4 **pT3a-3b:** 27.3 **pT4:** 2.3 **Patients continent at baseline according to questionnaire:** 22.9% **Patients continent at baseline according to pad test:** 36.4% **Drop outs:** see outcomes **<u>Group 3: PFMT +ES and Biofeedback</u>** **N:** 46 **Age (no units reported):** 64.6 **Prostate wt (gm):** 55.4 **% pathological tumor stage:** **pT1a-2b:** 55.6 **pT3a-3b:** 42.2 **pT4:** 2.2 **Patients continent at baseline according to questionnaire:** 20.7% **Patients continent at baseline according to pad test:** 33% **Drop outs:** see outcomes	treated with biofeedback (BFB) 15 minutes twice daily for 3 months using the same device and the same anal probe. Each contraction of the anal sphincter and pelvic flood led to a corresponding signal in the device display to ensure that the patient had control over training. The combined ES and BFB programme consisted of a stimulation time of 5 seconds, and a contracting the relaxing time of 5 and 15 seconds, respectively. **All patients:** Patients were encouraged to perform the treatment they were randomised to for 3 months. There was regular personal interaction between the patient and a health professional during the 6 weeks of surgery. After that time they had no further support.		**Group 3: PMFT + ES + Biofeedback:** 12/46 (27%)	
			Number of men still incontinent at 12 months (ITT analysis)	**Group 1: PFMT:** 11/47 (24%) **Group 2: PFMT + ES:** 8/46 (18%) **Group 3: PMFT + ES + Biofeedback:** 5/46 (10%)	

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Evidence Table 6 Post void milking vs. no intervention or other conservative intervention

See Evidence Table 5: Pelvic floor exercises (with or without electrical stimulation or biofeedback) for Paterson et al., 1997[237]

1 **Evidence Table 7: Product vs. no product or other conservative intervention**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Fader et al, 2006[87] **Study design:** Cross over RCT **Evidence level:** 3+ **Duration of follow-up:** 4 weeks, 1 week for each design	**Patient group:** Men with light urinary incontinence **Setting:** United Kingdom **Inclusion criteria:** - ≥18 years old - usually use an absorbent product for light urinary incontinence or had been accessed by a health care professional to as suitable to use such products <u>**All patients**</u> **N:** 74 **Age:** median 70 years (range 23-92) **Dropouts:** 6 (did not return any data) **Type of incontinence:** - 50% did not know type - 21% stress, 16% urge, 13% mixed **Output type:** 90% described as "dribbled", 7% as "gush" and 3% as constant flow **Time of incontinence:** - 31(46%) both day and night - 37(54%) during the day only **Usual products:** <u>Leaf:</u> 38%	**Products:** All products available for leaf (6 types) and pouch (6 types) design. The best product for pads and pants with inserts were chosen. Products in random order for up to 1 week. Total test time was 14 weeks. **Product performance:** Rated using product performance questionnaire (developed from earlier study) **Wet product weights** Measured and recorded using pad leakage diaries.	**Prioritisation of product performance characteristics** (% of patients rated it as top 5): - Ability to hold urine (Absorbance without leakage-82%) - Comfort (88%) – leaf design allowed the scrotum to stay wet, and this can cause skin irritation and discomfort. - Fit (71%) – designs which are flatter preferred - Discreteness and ability to stay in place (23%) -- elastics help product to stay in place. If a product fall off (ie down the trouser leg), it can be very embarrassing. **Other issues: Ease of use and practical issues** - Absorbent products can be difficult to manage away from home when wet. o Men's toilet cubicles may not have the equivalent of sanitary disposal unit. Discrete disposal difficult o For washables, need to bring home for washing. Washing and drying can be problematic and embarrassing o Pouches fiddly to apply, especially through a trouser fly, and difficult to reinsert when it is swollen with absorbent gel. Some men may need a cubicle instead of urinal. **Design performance results*:** <u>Very good/good:</u> Leaf : 59% Pouch: 24% Pantegral: 50% Small pad: 51% <u>Okay:</u> Leaf : 25% Pouch: 21% Pantegral: 12% Small pad: 31% <u>Poor/very poor:</u> Leaf : 16% Pouch: 55%		**Funding:** The products were provided from manufacturers. **Limitations:** - Not a blinded study. - Method of qualitative analysis not well described **Additional outcomes:** Specific product performance measured by product performance questionnaire provided for each brand of leaf or pouches tested. **Related outcomes** Fader et al 2008 [86] reported that men and women have different preferences of products. The suitability of products may depend on time of use (day vs. night) due to the position of the penis and whether when going out or staying at home. For overall acceptability, men preferred pull ups or diapers to pads. Washable diapers were most popular among men for use at night. **Notes:**

	<u>Small disposable pads :</u> 35% <u>Other methods (including pouches or Pantegral)</u>: 27% Most use 1-2 products during the day (66%), and during the night (87%). **Other characteristics:** 76% walked independently, 21% use walking aids routinely, 3% use occasionally. 32% reported penile retraction		Pantegral: 38% Small pad: 18% <u>Leakage performance (10g)</u> 96(90-98)% 88(78-94)% 57(43-70)% 93(84-97)% <u>Leakage performance (50g)</u> 87(76-93)% 85(75-91)% 7(0-56)% 87(76-93)% *Results from best products in each design category. **Leaf products:** - Varied in performance within group. Tena Level 2 significantly better (score of 79% in overall opinion) compared to others brands (19-40%) in the same leaf design group - Leakage performance was generally better for disposables compared to washables (88-96% vs. 59% do not leak when holding 10g of urine) **Pouches:** - Least successful design - More homogenous in performance (range of 15-28%). Generally lower score than leafs. - 74-88% do not leak when holding 10g of urine.	None

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Jakobsson et al, 2002[126] **Study design:** qualitative study **Evidence level:** 3+ **Duration of follow-up:** Questionnaire	**Patient group:** sample selected from men with prostate cancer and BPH that were part of larger questionnaire study. **Setting:** They were randomly selected from 2 urological clinic registers in Sweden. **Inclusion criteria:** Men with experience of indwelling urinary catheter treatment. **All patients** **N:** 108 Group 1: n=37 Group 2: n=71 **Treatment duration:** **Group 1: Men with BPH** <1 week=48.6 2-4 weeks=18.9 1-2 months=27.0 >3 months=5.4 **Group 2: Men with prostate cancer** <1 week=11.3 2-4 weeks=54.9 1-2 months=24.0 >3 months=8.5	**Questionnaire** – questions on experiences of indwelling catheter installation, wearing and handling and background data. Response format was on nominal (no-yes) and ordinal (ranging from 'not at all' to 'much') scale levels. **Assessment of health related quality of life** with the QLQ-C30 questionnaire – which includes five functional scales (physical, role, emotional, social and cognitive functioning), three symptoms scales (fatigue, pain, and nausea and vomiting) a global health status and additional single items. Response format comprised yes-no questions and assessment ranging from 'very bad' to 'excellent' (1-7). All scores linearly transformed to a 0-100 scale. **Sense of Coherence Questionnaire**, 13 item format used in the study (1-7 score to disagree completely to agree completely).	**Information about wearing a catheter:**	Little or less than wanted: Group 1: 23.9% Group 2: 29.9% Satisfaction with information: Group 1: 24.3% Group 2: 52.1% Question not applicable: Group 1: 35.1% Group 2: 16.9%	**Funding:** Supported by the medical faculty, Lund University, the Swedish Foundation for Health Care Science sand Allergy Research, the County Council of Kristianstad, and Kristianstad University college. **Limitations:** - Aim of study to compare results from men with BPH to men with prostate cancer. - QLQ C-30 score is cancer specific. - study only looked at negative views of catheters. **Additional outcomes:** Factor solution of indwelling catheter treatment and mean values. Single items on health related quality of life scores. **Notes:** None
			Information about handling a catheter	Little or less than wanted: Group 1: 22.6% Group 2: 23.9% Satisfaction: Group 1: 24.3% Group 2: 56.3% Not applicable: Group 1: 40.5% Group 2: 14.1%	
			Mean (SD) functional scales: higher score better function): Feelings of discomfort, tagging, smarting and pain at catheter instalment, resting, moving and problems related to indwelling catheter treatment:	**Physical:** 85.5 (22) / 84.3 (24.1) **Role:** 83.3 (28) / 83.3 (29) **Emotional:** 85.4 (19.5) / 86.0 (17.8) **Cognitive:** 85.1 (15) / 85.2 (18.3) **Social:** 85.0 (14.6) / 85.2 (18.3) **QoL:** 69.0 (26) / 72.0 (23.0) Discomfort: % Rather much / much Instalment: 38 / 5.6% Resting: 32.4 / 1.9% Moving:40.8 / 7.4% Tagging: % Rather much / much Instalment: 25.9 / 0.9% Resting: 19.4 / 2.8% Moving:38.9 / 5.6%	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				<u>Smarting: % Rather much / much</u> Instalment: 25 / 2.8% Resting: 15.7 / 1.9% Moving:23.2 / 1.9% <u>Pain: % Rather much / much</u> Instalment: 26.9 / 2.8% Resting: 14.8 / 1.9% Moving:20.3 / 2.8% Infections % Rather often / often: 18.5 / 7.4% Smeary urethra: 25 / 6.5% Difficulties attaching catheter comfortably: 30.5 / 1.9% Difficulties attaching drainage bag comfortably: 31.5 / 0.9% Difficulties changing drainage bag: 13.9 / 0.9% Fear of leaking urine: 25.9 / 4.6% Fear of drainage bag rupture: 16.7 / 3.7% Difficulties finding comfortable resting/sleeping position: 46.3 / 1.9%	
			Bivariate significant relationship between health related quality of life and sense of coherence	Global quality of life had a moderate correlation to sense of coherence: r=.0.52	
			Multiple logistic regression test:	No association between global quality of life, QOL, and the independent variables under study in any of the groups.	

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Study details	Patients	Intervention (Methodology)	Outcomes	Comments
Macaulay et al, 2004[177,177] **Study design:** 2 interviews (pre and post tests), and a survey (questionnaire) **Evidence level:** 3+ **Duration of follow-up:** Not stated. Up to 8 washes for each product	**Patient group:** Men/Women who had moderate/ eavy incontinence. Fully mobile. Participants recruited from advertisement in a consumer journal (Incontact) **Cause of incontinence:** Varied, not specified. **Setting:** UK **All participants** **N: 14** **Age (mean):** 43.6 , range 28-67 years **M/F:** 10/4	**Purpose:** To evaluate all the reusable products for moderate/heavy incontinence and compare them with disposable alternatives. **Methods:** Order of product testing was randomized. Subjects tests products one after another based on randomization order, and repeat the process until each product tested a maximum of 8 times. **Sequence of follow up:** Pretests interview – to determine attributes of products considered to be important Testing period: Completion of product performance questionnaire and pad leakage diary. Questionnaire was designed based on the pretest interview. Post test interview Feedback regarding reusables	**Difference in men vs. women in fitting of pads.** - Men were not always happy with a product they perceived to be designed for women. - Fitting of insert pads (for pants with integral pads), shaping of pads did not reflect anatomy. - Some reversed the inset pads thereby having their larger end situated to their front. This left the smaller end feeling uncomfortable around the buttocks. **Problems with washing** - A man who had to use a launderette found it difficult. Even when washed at home, this could lead to some embarrassment when they are part of the family laundry, in a bucket or on a drying line. **Most important product attributes:** - Leakage/absorbency, discreteness, comfort and fit. - More details about the specific performance attributed were reported.	**Funding:** conducted by Continence Product Evaluation (CPE) Network , funded by MHRA **Limitations:** - Selection of participants from specialized consumer journal – not certain how this is representative of men with LUTS. Patients noted to be relatively young. - This was a pilot study with small sample size. - Feedback from men and women were not reported separately. - Method of qualitative analysis not well described **Additional outcomes:** More details about the specific performance attributed were reported **Notes:** A full report on the product performances are detailed in a report to MHRA: MHRA. A pilot study to evaluate reusable absorbent body- word products for adults with moderate/heavy urinary incontinence. Med healthcare Prod Reg Agency. 2003:IN11

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Moore et al., 2004[204] **Study design:** Cross over randomised **Evidence level:** 1+ **Duration of follow-up:** 4 days, 1 day for each product/control	**Patient group:** Men with radical prostatectomy ≤ 6 months ago **Setting:** Canada **Inclusion/Exclusion criteria:** - Men with stress incontinence who required continuous incontinence pad protection after radical prostatectomy - Normal perineal and penile sensation, intact penile skin, no neurologic disorders that could affect sensation or peripheral circulation, sufficient manual dexterity to manage the penile compression device - No overactive bladder - No cognitive impairment that could affect their ability to follow instructions or perceive penile discomfort (Mini-Mental State Examination score ≥27), ability to read and speak English **<u>All patients</u>** **N:** 12 Mini Mental State Score (Mean29.6±1.2) No other baseline data provided	**Group 1:** Control- no device **Group 2:** Timms C-3 penile compression device **Group 3:** Cunningham Clamp **Group 4:** U-Tex Male Adjustable Tension Band All these interventions were randomly carried out on 4 sequential days. Subjects were instructed to standardise their activities, time of day for wearing the devices and the amount of fluid intake.	**Mean urine loss** (grams loss in 4 hour pad test)	**Group 1(No device):** 122.8 ± 130.8 **Group 2(C-3):** 32.3 ± 24.3 **Group 3(Cunningham):** 17.1 ± 21.3 **Group 4 (U-Tex):** 53.3 ± 65.7 **p value:** <0.05 for all groups vs. Group 1 **Note:** The standard deviation sizes were larger than the mean values, indicating that the data was potentially skewed and not normally distributed.	**Funding:** University of Alberta: Internal Allocations Fund and Department of Radiology. One investigator was supported by the Ministry of Health of the Province of British Columbia. **Limitations:** - Data analysis – Data was potentially not normally distributed, but a parametric test (analysis of variance, Dunnet's procedure for post hoc) was used. Interpretation of results need to be treated with caution since n=12. - The duration of intervention was only 4 hours or each product, or the control (1 pad test each). - The value for Doppler tests for Cunningham clamp was reported for the loosest setting, but setting for others was not reported. - The outcome for patient satisfaction was measured using Male Continence Device Satisfaction Questionnaire, which was adapted from another product testing questionnaire. It is unclear whether this is a fully validated instrument. The criteria for determining "rated positively" were not stated. **Additional outcomes:** None of the clamps completely eliminated urine loss.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Patient satisfaction (rating device positively, using Male Continence Device Satisfaction Questionnaire)	**Group 1(Control):** NR **Group 2(C-3):** 2/12 **Group 3(Cunningham):** 10/12 **Group 4 (U-Tex):** 0/12 **p value:** NR For U-Tex, none reported it "positively" because it was difficult to apply, did not stay on with activity and did not control urine leakage satisfactorily. The patient satisfaction for no control was not reported.	**Safety data:** **Blood flow** (Systolic velocity)- measured using Doppler Ultrasound. Right: **Group 1(Control):** 12.4±2.8 **Group 2(C-3):** 12.4±5.5 **Group 3(Cunningham):** 9.5±2.3* **Group 4 (U-Tex):** 11.9±4.4 **p value:** * <0.05 vs. control Left: **Group 1(Control):** 12.3±3.0 **Group 2(C-3):** 11.7±4.7 **Group 3(Cunningham):** 7.3±3.0* **Group 4 (U-Tex):** 13.8±7.3 **p value:** * 0.05 vs. control **Resistance Index-** measured using Doppler Ultrasound. Right: **Group 1(Control):** 0.90±0.10 **Group 2(C-3):** 0.92±0.10 **Group 3(Cunningham):** 0.92±0.13 **Group 4 (U-Tex):** 0.93±0.08 **p value:** * 0.05 vs. control) Left: **Group 1(Control):** 0.87±0.10 **Group 2(C-3):** 0.92±0.11 **Group 3(Cunningham):** 0.86±0.29 **Group 4 (U-Tex):** 0.91±0.11 **p value:** * 0.05 vs. control **Notes:** Information from author: Patient satisfaction data was based on the reply to a single question "What is your overall opinion of the penile compression device?" Response choices for this question was not provided.

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Study details	Patients	Methodology	Outcomes	Comments
Paterson et al, 2003[236] **Study design:** Qualitative Study Semi structured interviews and focus groups **Evidence level:** 3+ **Duration of follow-up:** NR	**Patient group:** Participants included people who had incontinence or cared for someone with incontinence, or were part of an advocacy group that had significant numbers of people with incontinence in its membership, from metropolitan, rural and remote Australia. Included people of minority backgrounds and indigenous Australians. Purposive and snowballed sampling. Participant recruitment ceased once no new themes emerged. **Cause of incontinence:** Varied widely and included congenital malformations, chronic debilitating diseases, sever spinal cord injuries and degenerative diseases. **<u>All participants</u>** **N: 82** NR **Age (mean):** NR **M/F:** NR **Dropouts:** NR	**Purpose:** To understand issues, needs and concerns of people with incontinence to inform development of comprehensive Australian consumer guide to continence products. **Analysis method:** Key issues transcribed from audio tapes. Constant comparison, thematic data analysis was commenced concurrently with data collection enabling the opportunity to follow up an emerging theme. (grounded theory) Transcriptions and notes taken during sessions Integrated into common themes, shared meanings, similarities and difference. 3 researchers conducted analysis, cross- validated with another. Analysis focused on the similarities in experiences and concerns of consumers across the group.	**Overall:** Striking similarities in experiences and concerns about selection of consumer products. **Seeking information:** - <u>Did not know how to begin to search for information and had problems finding it:</u> Most gathered information themselves, and these are usually not all available in one place. - <u>Feeling vulnerable:</u> Most felt discussing about incontinence management and shopping for products very personal and embarrassing. Some reluctant to speak to professionals. - <u>Lack of confidence in healthcare professional's knowledge:</u> Although dependent on healthcare professionals for assessment and referral, they had not received much helpful advice on products or directed to sources of advice. The most satisfactory help was from specialist continence nurse advisers. Local doctors knew little about assessment and management and many participants were dissatisfied. There was a pervasive "grin and bear with it" attitude and participants were expected to purchase a supermarket product and learn to live with it. - <u>Assessment and management:</u> Participants expressed a need for these to be standardised and coordinated. **Finding a suitable product:** - <u>Trialed different products</u> to find one which enable them to remain socially continent. - <u>Advice for product selection:</u> Most had limited product knowledge in early stages and selected from limited range accessible to them in shops, hospital suppliers and recommendations of professionals. However, participants in support networks benefited from exchange of information. - <u>Key factors influencing selection of continence products</u> were quality, comfort and design balanced against availability and cost. Specific product features of concern including noise, allergy, trouble of keeping on, leakage around the seams	**Funding:** National Continence Management Strategy, an initiative of the Commonwealth of Australia Department of Health and Aged Care **Limitations:** Possible selection bias as details of demography, disease, disease severity and role of participants not reported. Not clear whether their target group of 'incontinent' patients is for urinary or faecal incontinence or both. **Notes:** Analysis did not use verbatim transcripts.

Study details	Patients	Methodology	Outcomes	Comments
			Information about product use and disposal required: - Instructions for use and wear - Best methods for care and disposal of products	
			Suggestions for content and format of the consumer guide to products: - Detailed product description - More information in general about incontinence (causes, treatments and sources of help) and - Use simple layman's language throughout guide. - Make available a variety of formats and a wide distribution throughout the community	

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1 **Evidence Table 8: Catheters vs. no catheters**
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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Logan et al, 2008[170] **Study design:** Qualitative study **Evidence level:** 3+ **Duration of follow-up:** NR	**Patient group:** selected from case lists of a continence and urology service. Patients with experiences of learning clean intermittent self catheterisation (CISC). Patients selected to include maximum variation of characteristics likely to impact on views, attitudes and access to services. **Setting:** Continence and urology service in Wales. **<u>All patients</u>** **N:** 15 **M/F**: 8/7 **Median age (range):** 65 (33-81) Duration of use: 6m to >2y Frequency: weekly to four times per day. Reasons for catheterisation: MS, urethral stricture, urine retention.	In depth interviews from January to June 2006 in the UK by two of authors and by a continence nurse. Interview guide developed based on the literature and experience and expertise of the research team. Topics helped guide the interviewer to explore reasons for CISC duration and frequency of CISC, experience of being taught, location, teaching aids, information, ongoing support and follow-up. Guide covered all relevant areas but allowed interviews to pursue themes emerging during the interview.	**Psychological-embarrassment and privacy:** Views not separated out for men and women. **Physical:** Technical difficulties were expressed by both sexes. Men's difficulties were related to negotiating the penile anatomy and handling the lengthy catheters. Generally men had no problem in visualising the urethra. One man experienced muscle spasms and urethral 'clamping', causing difficult insertion and frustration in the first few months. The entire sample used coated catheters, commonly describing them as 'slippery'. To overcome this, some men developed practical handling strategies; another recruited his wife to help. Men with urethral strictures described complications such as discomfort, bleeding and problems negotiating the stricture: 'Sometimes you (have) got to twiddle, twirl it in around it and just sort of ease it in the best way I can'. Both sexes avoided touching the catheter tip for fear of contamination and infection, illustrating concerns about hygiene and the development of a good technique. In the beginning, respondents found CISC emotionally and technically difficult. Gaining confidence was related to pace of skill acquisition. Men were squeamish at the thought of inserting a catheter for the first time, because of psychological issues and fear of causing internal damage. Q: You were going weak at the knees were you? A: Yes, definitely yes, and the perspiration… I was afraid to blink, I wouldn't see… you know, from a man's point of view to think you got something that long to push into yourself! Only two men in study felt confident immediately while the majority took considerably longer to accept CISC as part of their lives. **Service interaction:** <u>Information-giving:</u> Participants were unfamiliar with CISC, and on		**Funding:** Gwent Health Care Trust research and development small grant scheme. **Limitations:** Mix of views from men and women. **Additional outcomes:** Service interaction was also covered.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			hearing the word catheter feared it would involve a permanent 'catheter and bag': 'I didn't know enough about it – I was just told that I had to start using a catheter and I didn't know any thing at the point…I didn't know that there was a much simpler, straight forward version that you could use yourself and that point I was not at all happy about it' . Practical demonstration was an important component of learning CISC, and a few participants felt that their demonstrations had been insufficient: 'I would have liked more than one demonstration or more time spent…I was only shown once and I had to get on with it then.'		

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Saint et al, 1999[266] **Study design:** Qualitative study **Evidence level:** 3+ **Duration of follow-up:** NR	**Patient group:** Consecutive male patients between May and November 1998 who were using an indwelling or condom urinary catheter. **Setting:** Patients housed on the medical, rehabilitation and nursing home units of Puget Sound VA health Care System. **Inclusion criteria:** patients with a urinary catheter in use for at least 24 hours were eligible to participate. **<u>All patients</u>** **N:** 116 **Mean age** (SD): 71 (12) **Drop outs:** 12 90% response rate. **Group 1: n = 21** **Group 2: n = 83** **Location:** Hospitalised on an acute care ward: 72% Other ward (nursing home, surgery, neurology, rehabilitation): 28%	Face to face interviews with a simple instrument requiring only yes or no answers for each of the 5 questions. **Group 1: men using a condom catheter** **Group 2: men using an indwelling catheter**	**% of men reporting yes to questions at interview:** Question: Is the current urinary catheter… 1. Comfortable? 2. Painful? 3. Convenient? 4. Restricting your daily activity? 5. Causing you embarrassment? **Logistic regression:** **Condom catheters compared to indwelling were found to be:** More comfortable: Less painful: Less restrictive: Convenience or embarrassment: Patients were also asked if they remembered having another type	 Group 1: 86% Group 2: 58%, p=0.04 Group 1: 14% Group 2: 48%, p=0.008 Group 1: 86% Group 2: 75%, p=0.40 Group 1: 24% Group 2: 61%, p=0.002 Group 1: 24% Group 2: 30%, p=0.50 OR=4.2; 95% CI: 1.1 to 15.6, p=0.03 OR=0.17; 95% CI: 0.05 to 0.64, p=0.008 OR=0.23; 95% CI: 0.07 to 0.75, p=0.01 Catheter type not significantly related. N=36 Preferred condom: 17 (47%)	**Funding:** Supported, in part, by the Department of Veterans Affairs and the Robert Wood Johnson Clinical Scholars Program. **Limitations:** Not population of interest. **Additional outcomes:** Nurses views by questionnaire. **Notes:** Logistic regression analysis using each 'yes' or 'no' answer as the dependent variable with patient age, hospital service and current catheter type as independent variables.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			of urinary collection device in the past (alternative catheter or disposable diaper). If yes, we asked whether they preferred current or previous device. Previous experience of disposable diapers, n=27 Men with experience of condom catheter (n=43)	Preferred indwelling: 14 (39%) No preference: 5 (14%) Group 1: n=10 preferred current catheter Group 2: n=17; 9 preferred current catheter, four preferred diapers and four had no preference. N=7 (16%) offered spontaneously that main drawback was the associated leaking.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Shaw et al, 2008[273] Same trial as Logan, et al (see evidence table above) reporting more outcomes on QOL **Study design:** Qualitative study **Evidence level:** 3+ **Duration of follow-up:** NR	**Patient group:** selected from case lists of a continence and urology service. Patients with experiences of learning clean intermittent self catheterisation (CISC). Patients selected to include maximum variation of characteristics likely to impact on views, attitudes and access to services. **Setting:** Continence and urology service in Wales. **All patients** **N:** 15 **M/F**: 8/7 **Median age (range):** 65 (33-81) Duration of use: 6m to >2y Frequency: weekly to four times per day. Reasons for catheterisation: MS, urethral stricture, urine retention.	In depth interviews from January to June 2006 in the UK by two of authors and by a continence nurse. Interview guide developed based on the literature and experience and expertise of the research team. Topics helped guide the interviewer to explore reasons for CISC duration and frequency of CISC, experience of being taught, location, teaching aids, information, ongoing support and follow-up. Guide covered all relevant areas but allowed interviews to pursue themes emerging during the interview.	**Impact on QoL:** **Positive impacts** Specific comments from men: There were reports of relief from symptoms such as recurrent urinary tract infections. "I would rather do this than put up with the symptoms of infection." CISC was also deemed to be a preferable option compared to other management strategies, such as permanent catheters with leg bags. "I said, 'I don't want a catheter fixed to me permanent, this bag on the leg or whatever they use'". **Negative impacts** Specific comments from men: "..if I found a disabled toilet where you can go into the room and wash your hands and whatever, and in a normal toilet you can't do that" "I have a problem when I am out…Finding water… If you go to a public toilet you have to fill it and then go into the toilet." Difficulty experienced in travelling Carrying the necessary equipment was a particular problem: "Yes. I can't travel light. Where I would much prefer to get on the train and go over and come back again, I now drive" **Physical impacts** Specific comments from men: Some reported occasional bleeding, or ongoing discomfort: "Oh it still gets sore now…especially with the withdrawal, insertion and withdrawal. And, of course, when you empty your bladder for the first time after the procedure, it's grit your teeth.." **Carrying out CISC**		**Funding:** Gwent Health Care Trust research and development small grant scheme. **Limitations:** Mix of views from men and women. **Additional outcomes:** Same trial as Logan, et al (see evidence table above) reporting more outcomes on QOL

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Specific comments from men: One man had a common problem of muscle spasm preventing insertion of the catheter. Whilst he had learned how to manage this, he found it an inconvenience as he had to wait before trying to catheterize again. **Factors explaining variation in QoL impacts** **Reasons for carrying out CISC and sex issues:** More men found CISC to be a nuisance and time-consuming. This was related to the reasons carrying out CISC. More women carried is out to relive previously severe urinary tract symptoms, whereas men tended to have problems with urethral stricture or voiding difficulties in the absence of severe symptoms. Because of differences in physiology and the longer urethra, men were more likely to be anxious about the catheter causing discomfort or pain, or about inadvertent damage because of poor technique. **Type of catheter and sex issues** There were sex differences related to type of catheter as male catheters are longer and more unwieldy. This had implications for carrying catheters discreetly. Women easily carried catheters in their handbags, whereas men were less likely to carry a bag and had difficulty carrying catheters in their pockets.		

See Evidence Table 7 Product vs. no product or other conservative intervention for Jakobsson et al., 2002[126].

1 **Evidence Table 9 Alpha-blockers vs. placebo**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Andersen et al., 2000[16] **Study design:** RCT **Setting:** Multi-centre, Scandinavia. **Evidence level:** 1+ **Duration of follow-up:** 13 weeks	**Patient group:** Men between 50-80 years with evidence of BPH. **Inclusion criteria**: Maximum urinary flow rate ≥5ml/s and ≤ 15ml/s in a total voided volume of ≥ 150ml and IPSS score of 12 or more. **Exclusion criteria:** Patients who had undergone prostate surgery, had a prostatic stent, or had undergone microwave thermotherapy were excluded, as were those who had had balloon dilation within the previous 6 months. Suspected or known malignancy and or PSA>10ng/ml; any known cause of urinary symptoms or reduced flow rate other than BPH; known acute urinary retention within the year, major residual urine, bladder stones, recurrent urinary tract infections, or large bladder diverticulum. Hepatic, renal, cardiac and gastrointestinal dysfunction or disease; uncontrolled diabetes, hypotension; and known allergy to study drugs. Use of prespecified drugs that might interfere with treatment or of an investigational drug or donation of blood 4 weeks prior to or during the study and conditions precluding good compliance were also cause for exclusion. **<u>All patients</u>** **N:** 795	**Phase 1:** 2 week wash out **Phase 2:** Run-in period 2-week single blind placebo run-in period **Phase 3:** Treatment period: 13 weeks double blind **Group 1: Doxazosin Gastrointestinal therapeutic system (GITS)** 4mg or 8mg once daily with a doxazosin standard placebo tablet. Initially 4mg dose given for at least 7 weeks. At week 7 the dose was increased to 8mg once daily if subjects had not experienced an increase in the maximum urinary flow are of at least 3ml/s and a 30% reduction in IPSS. **Group 2: Doxazosin standard** 1 to 8mg once daily Initial dose 1mg that was increased at the end of 1 week to 2mg, at week to	**Mean (SE) adjusted change from baseline to final visit for total IPSS score** (per-protocol analysis)	Group1 (n=310): -8.0±0.3; p<0.01 Group 2 (n=311): -8.4±0.3; p<0.01 Group 3 (n=151): -6.0±0.4	**Funding:** Pfizer Inc. **Limitations:** Method of randomisation and allocation concealment was NR. **Additional outcomes:** Mean changes from baseline in individual symptom IPSS score. Graphical presentation of IPSS and Qmax over each visit. Blood pressure and heart rate, pharmacokinetics. **Notes:** Mean changes are adjusted and can not be combined for meta-analysis. **Per protocol analysis:** Group 1 GITS: 44.2% remained at the 4mg and 55.8% received 8mg at the final visit. Group 2: doxazosin standard group 14.9% were receiving 2mg;day, 34% were on 4mg/day and 51.1% were receiving 8mg/day. Mean final dose for Group 1: 6.2mg/day
			IPSS Mean difference ±SEM (95% CI) **in change from baseline at the final visit for Group 1-Group 2** [least squares difference]	0.39±0.39 (-0.38, 1.15)	
			Mean (SE) adjusted change from baseline to final visit for Qmax (per-protocol analysis)	Group1 (n=300): 2.6±0.2 Group 2 (n=303): 2.2±0.2 Group 3 (n=151): 0.8±0.3	
			Mean (SD) adjusted change from baseline to final visit for urinary flow (per-protocol analysis)	Group1 (n=300): 1.2±2.4; p<0.04 Group 2 (n=303): 1.1±2.0; p<0.05 Group 3 (n=151): 0.6±2.1	
			Mean (SD) adjusted change from baseline to final visit for total quality of life IPSS question (per-protocol analysis) – least squares difference	Group1 (n=310): -1.3±0.1 Group 2 (n=311): -1.4±0.1 Group 3 (n=151): -0.9±0.1 P<0.001	
			Adverse events	**Dizziness** Group1: 18/317 (5.7%) Group 2: 27/322 (8.4%) Group 3: 3/156 (1.9%) **Headache** Group1: 18/317 (5.7%) Group 2: 13/322 (4.0%) Group 3: 7/156 (4.5%) **Asthenia** Group1: 10/317 (3.2%) Group 2: 16/322 5.0%) Group 3: 2/156 (1.3%) **Vertigo** Group1: 8/317 (2.5%) Group 2: 24/322 (7.5%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	ITT analysis: 784 Per protocol analysis: 780 Mean **age**: 65.2 years **Drop outs:** **<u>Group 1</u>** **N:** 317 ITT analysis =311 Mean (±SD) Age: 64.9 Baseline IPSS: 17.7±4.3 Race: White=311 Dropouts:22 (treatment related adverse events=11) **<u>Group 2</u>** **N:** 322 (ITT analysis =318) Mean (±SD) Age: 65.3 Baseline IPSS: 17.8±4.5 Race: White=318 Dropouts:38 (treatment related adverse events=20; insufficient clinical response=1) **<u>Group 3</u>** **N:** 156 (ITT analysis =155) Mean (±SD) Age: 65.4 Baseline IPSS: 18.0±4.3 Race: White=153; Asian=1; Other=1 Dropouts: 8 (treatment related adverse events=1)	4mg and at week 7 the dose was increased to 8mg once daily if required to achieve the target increasing urinary flow and decrease in IPSS. **Group 3: Placebo** once daily Received double-dummy matching placebo Study medications taken once daily at breakfast, except on study visit days, when medication was administered after study assessments.		Group 3: 1/156 (0.6%) **Flu syndrome** Group1: 4/317 (1.3%) Group 2: 6/322 (1.9%) Group 3: 7/156 (4.5%) **Back pain** Group1: 4/317 (1.3%) Group 2: 4/322 (1.2%) Group 3: 4/156 (2.6%) **Postural hypotension** Group1: 4/317 (1.3%) Group 2: 7/322 (2.2%) Group 3: 1/156 (0.6%) **Nausea** Group1: 3/317 (0.9%) Group 2: 8/322 (2.5%) Group 3: 1/156 (0.6%) **Discontinuation - adverse events** Group 1: 11 (3.5%) Group 2:20 (6.2%) Group 3: 1 (0.6%)	Group 2: 5.7mg/day
			Reduction from baseline IPSS of ≥30%	Group1: 73.5% Group 2: 74.7% Group 3: 53.5%	
			Increase in maximum urinary flow rate ≥3ml/s	Group1: 38.8% Group 2: 38.7% Group 3: 21.4%	
			Investigator s assessment of efficacy (intention to treat analysis)	**Excellent or good rating** Group 1: 193 (62.3%) Group 2:207 (65.5%) Group 3: 57 (37.5%) **Poor rating** Group 1: 39 (12.6%) Group 2:48 (15.2%) Group 3: 47 (30.9%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Carbin et al., 1991[42] **Study design:** Randomised controlled trial. **Setting:** NR **Evidence level:** 1+ **Duration of follow-up:** 8 weeks	**Patient group:** Males from 50 to 76 years of age with a known diagnosis of BPH. **<u>All patients</u>** **N:** 33 **Drop outs:** 3 (1 did not enter trial due to pneumonia, 2 discontinued treatment due to palpations and tachycardia) **<u>Group 1</u>** **N:** 16 Mean (±SD) Age: 68.7 (5.0) Prostatic size, g: 41 (15) Dropouts: 1 **<u>Group 2</u>** **N:** 16 Mean (±SD) Age: 64.6 (6.4) Prostatic size, g: 61 (40) Dropouts: 1	**Group 1: Alpha-blocker** Alfzosin 2.5mg X 3 If no effect of therapy noticed by the patient after 3 weeks of treatment and body weight more than 80kg the dose was increased to 4 tablets daily (e.g. 10mg). **Group 2: Placebo**	**Mean urinary flow rate, ml/sec**	**Baseline** Group1: 8.1 (2.2) Group 2: 8.4 (3.0) **3 weeks** Group1: 9.2 (3.3) Group 2: 8.2 (3.8) **8 weeks** Group1: 8.9 (2.8) Group 2: 8.9 (3.4) P=NS	**Funding:** NR **Limitations:** Method of randomisation, allocation concealment and blinding were unclear. **Additional outcomes:** Serum concentration, heart rate and blood pressure reported. **Notes:** Baseline number in each group not reported in methods. The table for adverse events reports that 15 in the intervention group.
			Timed micturition seconds	**Baseline** Group1: 19.6 (13.1) Group 2: 23.9 (15.4) **3 weeks** Group1: 14.7 (10.4) Group 2: 22.6 (13.2) **5 weeks** Group1: 14.3 (9.8) Group 2: 23.9 (17.8) **8 weeks** Group1: 15.8 (11.7) Group 2: 21.8 (10.6) P=0.023	
			Residual urine	**Baseline** Group1: 97.9 (115) Group 2: 92.7 (86) **3 weeks** Group1: 30.9 (32) Group 2: 114 (167) **8 weeks** Group1: 42.8 (51) Group 2: 94.2 (121) P=0.02	
			Frequency number	**Baseline** Group1: 8.9 (3) Group 2: 10.7 (3.0)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				3 weeks Group1: 7.1 (2) Group 2: 10.4 (3) **5 weeks** Group1: 8.6 (3) Group 2: 9.5 (3) **8 weeks** Group1: 7.4 (2) Group 2: 9.4 (3) P=NS	
			Boyarsky score	**Baseline** Group1: 11.3 (3.0) Group 2: 11.7 (3.7) **3 weeks** Group1: 7.3 (3.0) Group 2: 8.9 (2.6) **5 weeks** Group1: 6.3 (3.2) Group 2: 7.9 (2.6) **8 weeks** Group1: 5.9 (3.6) Group 2: 7.1 (2.2) P=NS	
			% of patients that had the dose increased	Group 1: 27% Group 2: 47%	
			Patients/physicians correct guess of treatment given	Group 1: 60% / 60% Group 2: 67% / 58%	
			Adverse events	**Vertigo** Group 1: 3/15 Group 2: 2/15 **Headache** Group 1: 1/15 Group 2: 1/15 **Weakness** Group 1: 1/15	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group 2: 0/15 **Weight gain** Group 1: 1/15 Group 2: 0/15 **Indigestion** Group 1: 2/15 Group 2: 0/15 **Diarrhoea** Group 1: 1/15 Group 2: 2/15 **Constipation** Group 1: 1/15 Group 2: 0/15 **Dry mouth** Group 1: 0/15 Group 2: 1/15 **Dry hands** Group 1: 1/15 Group 2: 0/15 **Herpes simplex** Group 1: 1/15 Group 2: 0/15 **Conjunctivitis** Group 1: 1/15 Group 2: 0/15	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Chapple et al., 1994[50] **Study design:** Randomised controlled study **Setting:** Multi-centre, UK **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** **Inclusion criteria:** Maximum urinary flow rate<15ml/s accompanied by symptoms of bladder outflow obstruction and in whom outflow obstruction at the level of the prostate was confirmed by means of videocystometrography. Only patients with a functioning detrusor muscle were included (residual urine <200ml). **Exclusion criteria:** Patients with other conditions giving rise to urinary symptoms and reduced urine flow rates, such as carcinoma of the prostate. Previous prostatic surgery, serum creatinine>200mmol/l, poorly controlled diabetes, a history of myocardial infarction or a cerebrovascular accident within the preceding 6 months. **<u>All patients</u>** **N:** 135 **<u>Group 1</u>** **N:** 67 Mean (±SD) **Age:** 67 (7.3) **Race:** Caucasian=55, other=12 Dropouts: 7 (drop out during 2 week run-in=2, withdrew due to concomitant or associated illness=3; adverse events=2) Data for efficacy=60 [Evaluable in	**Baseline evaluation:** Lasting 2 weeks during which patients received one doxazosin or placebo tablet each morning. **Group 1: Alpha-blocker** Doxazosin commenced with daily dose 1mg, increased to 2mg after 2 weeks and to maximum of 4mg after 4 weeks **Group 2: Placebo**	**Mean (SEM) maximum flow rate, ml/s**	**Baseline** Group1: 9.1 (0.5) Group 2: 9.1 (0.5) **Change** Group1: 2.6 (0.7) Group 2: 1.1 (0.6) P=0.09	**Funding:** Pfizer provided medications and material support for study. **Limitations:** Method of randomisation and allocation concealment unclear. **Additional outcomes:** Maximum bladder capacity, volume of first unstable contraction, end filling pressure reported. Modified Boyarsky scale used to report obstructive and irritative symptoms but figures not provided. **Notes:** Headache and dizziness reported as most frequent side effects but actual figures not reported.
			Mean (SEM) maximum detrusor voiding pressure, cmH2O	**Baseline** Group1: 78.5 (2.7) Group 2: 74.2 (4.6) **Change** Group1: -4.6 (3.2) Group 2: 7.9 (3.0) P=0.007	
			Mean flow rate, ml/s	**Baseline** Group1: 4.4 (0.3) Group 2: 4.3 (0.3) **Change** Group1: 1.0 (0.3) Group 2: 0.2 (0.3) P=0.04	
			Number of reported adverse events in number of patients with adverse events	**Group 1: 44/25** **Group 2: 12/11**	
			Withdrawn due to adverse events	**Group 1: 2** **Group 2: 0**	
			% Improvement in symptoms (evaluation in response to questioning at tend of study)	**Hesitancy** Group 1: 59% Group 2: 26% P=0.003 **Nocturia** Group 1: 39% Group 2: 19% P=0.017	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	2 of 12 that withdrew; inevaluable in 1 due to protocol violations] **<u>Group 2</u>** **N:** 68 Mean (±SD) Age: 67 (7.5) **Race**: Caucasian=64, other4 Dropouts: 5 (drop out during 2 week run-in=1, withdrew due to concomitant or associated illness=4) Data for efficacy=62 [inevaluable in 2 due to protocol violations]			**Urgency** Group 1: 60% Group 2: 38% P=0.041 **Impaired urinary stream** Group 1: 56% Group 2: 33% P=0.019 **Frequency** Group 1: 44% Group 2: 27% P=0.062	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Chapple et al., 2005[49] **Study design:** RCT **Setting:** Multi national (18 countries), multi-centre (138 mainly European) **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** Men with lower urinary tract symptoms suggestive of BPH. **Inclusion criteria:** Men aged 45 years or over with voiding and storage symptoms diagnosed as LUTS/BPH with a total IPSS ≥13 and a maximum flow rate ≥4ml/s and ≤12ml/s. **Exclusion criteria:** any other urological procedures or conditions what may cause LUTS ; patients with hepatic or renal insufficiency, clinically significant cardiovascular or cerebrovascular diseases within 6 months prior to enrolment, central nervous system conditions or life-threatening diseases. Patients taking or had taken other drugs for LUTS or were hypersensitive to a1 AR antagonists or their recipients, were taking drugs which could interfere with the pharmacodynamics of tamsulosin OCAS or were taking or had taken other investigational drugs within the previous 3 months. **<u>All patients</u>** **N:** 2152 **Mean age:** 65 years **Mean IPSS:** 18.5 **Mean prostate volume:** 43-45ml **Drop outs:** 107 (5%) due to treatment emergent adverse events=57, insufficient	**Group 1:** **Tamsulosin:** Oral controlled absorption system 0.4mg once daily **Group 2:** **Tamsulosin:** Old modified release tamsulosin: 0.4mg once daily **Group 3:** **Tamsulosin:** Oral controlled absorption system 0.8mg once daily **Group 4: placebo** Placebo once daily	**Mean (SD) IPSS at baseline**	**Baseline:** Group1: 18.5 (4.4) Group 2: 18.5 (4.5) Group 3: 18.6 (4.5) Group 4: 18.3 (4.5) **End point:** Group1 (n=355): 10.8 (6.2) Group 2 (n=703): 10.6 (5.9) Group 3 (n=709): 10.6 (5.9) Group 4 (n=351): 12.4 (6.4)	**Funding:** NR. **Limitations:** None. **Additional outcomes:** Blood pressure was reported. **Notes:** Additional information retrieved from the authors. Outcomes reported for group 1 and 2 combined for meta-analysis by NCGC.
			IPSS reduction at endpoint	**Group1 (n=354):** -7.7 (5.8); p<0.001 **Group 2 (n=700):** -8.0 (5.6); p<0.001 **Group 3 (n=707):** -8.0 (5.9) **Group 4 (n=350):** -5.8 (5.6)	
			Mean (SD) change at endpoint IPSS- QOL	**Baseline:** Group1 (n=354): 3.8 (1.1) Group 2 (n=699): 3.8 (1.1) Group 3 (n=706): 3.8 (1.1) Group 4 (n=350): 3.8 (1.0) **Change at endpoint:** Group1 (n=354): -1.4 (1.3) Group 2 (n=699): -1.4 (1.3) Group 3 (n=706): -1.4 (1.4) Group 4 (n=350): -1.1 (1.3)	
			Investigator reported as slightly improved	Group1: 33.1% Group 2: 33.5% Group 3: 33.0% Group 4: 35.7%	
			Investigator reported as much improved	Group1: 46.5% Group 2: 48.7% Group 3: 48.4% Group 4: 35.7%	
			Treatment-emergent Adverse events attributable to alpha-blocker	**Non cardiovascular** Group1: 16 (4.4%) Group 2: 36 (5.1%) Group 3: 57 (7.9%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	response=18, lost to follow-up=9, protocol violations=3, adverse events starting during the placebo run in =3, death=3, abnormal laboratory values=1, non-specified reasons=13 **Group 1** **N:** 361 Dropouts:18 **Group 2** **N:** 710 Dropouts: 25 **Group 3** **N:** 724 Dropouts: 45 **Group 4** **N:** 357 Dropouts: 19			Group 4: 7 (2.0%) **Cardiovascular** Group1: 9 (2.5%) Group 2: 23 (3.2%) Group 3: 28 (3.9%) Group 4: 8 (2.2%) **All:** Group1: 25 (6.9%) Group 2: 55 (7.8%) Group 3: 80 (11.1%) Group 4: 13 (3.7%)	
			Number (%) Dizziness	**Group1:** 5/360 (1.4%) **Group 2:** 9/709 (1.3%) **Group 3:** 17/722 (2.4%) **Group 4:** 5/356 (1.4%)	
			Number (%) Retrograde ejaculation	**Group1:** 6/360 (1.7%) **Group 2:** 10/709 (1.4%) **Group 3:** 18/722 (2.5%) **Group 4:** 1/356 (0.3%)	
			Number (%) of at least one Treatment-emergent adverse events	**Group1:** 93/360 (26.0%) **Group 2:** 168/709 (24.0%) **Group 3:** 192/722 (27.0%) **Group 4:** 71/356 (20.0%)	
			Number (%) at least one treatment-related adverse events	**Group1:** 40/360 (11.0%) **Group 2:** 82/709 (12.0%) **Group 3:** 103/722 (14.0%) **Group 4:** 25/356 (7.0%)	
			% **Responders** (defined as patients who had at least a 25%j improvement in total IPSS vs. baseline)	**Group1:** 71.2% **Group 2:** 75.4% **Group 3:** 73.8% **Group 4:** 60.9%	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Serious adverse events	**Group 1:** 7/360 **Group 2:** 9/709 **Group 3:** 12/722 **Group 4:** 3/356	
			Discontinuation due to adverse events	**Group 1:** 14/360 **Group 2:** 11/709 **Group 3:** 28/722 **Group 4:** 6/356	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Christensen et al., 1993[53] **Study design:** Randomised controlled trial **Setting:** Denmark **Evidence level:** 1+ **Duration of follow-up:** 9 weeks	**Patient group: consecutive** patients from Feb 1988-May 1989 referred to the out patient clinics of the 2 participating surgical departments for BPH. **Inclusion criteria:** All had moderate or severe symptoms resulting from infravesical obstruction, an obstructive flow curve pattern as determined by uroflowmetry and were candidates for TURP. **Exclusion criteria:** previous prostatic/bladder neck surgery, suspicion of prostatic cancer on DRE, non-prostatic obstruction on the urethra, overflow incontinence, renal dysfunction, positive urine cytology, hematuria, urinary infection, symptomatic hypotension, previous or present cerebrovascular disease, history of intolerance to doxazosin, prazosin or other quinazolines, current treatment with alpha adrenoceptor blocking agents, severe psychiatric or neurologic disease. **<u>All patients</u>** **N:** 100 **Drop outs:** 9 **<u>Group 1</u>** **N: 52** Mean (±SD) Age: 66.7 (7.9)	**Run-in period** One week **Group 1: alpha-blocker** Doxazosin once daily at bed time. 1mg week 1,2mg week 2-5 and 4mg week 6-9. **Group 2: Placebo** Once daily at bedtime	**Mean (SEM) maximum urinary flow rate (estimated from graph)**	**Baseline** Group1 (n=52): 7.6 (SD 3.7) Group 2 (n=48): 7.5 (SD 3.5) **0 weeks** Group1 (n=46): 7.4 Group 2 (n=43): 8.0 **5 weeks** Group1 (n=47): 9.5 (0.7) Group 2 (n=42): 9.1 (0.8) **9 weeks** Group1 (n=46): 9.4 (0.7) Median improvement: **1.5 (range: -9.0, 22.0)** Group 2 (n=42): 8.0 (0.5) Median improvement: **-0.3 (-7.0 to 7.2)**	**Funding:** NR **Limitations:** Method of allocation concealment unclear. **Additional outcomes:** Mean urinary flow rate – reported but actual figures not provided. Changes in blood pressure and weight were reported. **Notes:** Maximum urinary flow rates were estimated from a graph.
			Median reduction in voiding frequency chart (3 days average 24-hour voiding frequencies)	**9 weeks** Group1: 2.3 Group 2: 1.2 P=0.005	
			Median (range) baseline and change in frequency (daytime)	**Baseline** Group1 (n=52): 8 (3/18) Group 2 (n=48): 7 (3/16) **Week 9** Group1 (n=48): -1.5 (-9/3) Group 2 (n=43): 0.3 (-7/7) **P=0.001**	
			Median (range) baseline and change in nocturia	**Baseline** Group1 (n=52): 2.5 (0/6) Group 2 (n=48): 2.5 (0/7) **Week 9** Group1 (n=48): -1.1 (-4/1) Group 2 (n=43): -1.0 (-4/1) **P=0.12**	
			Baseline and change in residual urine	**Baseline** Group1 (n=52): 100 (10/450)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Dropouts: 4 (diabetes=1, withdrew consent=2, urinary tract infection=1) **<u>Group 2</u>** **N:** 48 Mean (±SD) Age: 68.1 (7.4) Dropouts: 5 (S-creatinine>130micromoles/l, withdrawn due to side effects=2, urinary retention=1, lost to follow-up=1).			Group 2 (n=48): 85 (10/340) **Week 9** Group1 (n=48): -15.0 (-430/150) Group 2 (n=43): -1.0 (-305/355) **P=0.56**	
			Median (range) Bladder capacity (ml)	**Baseline** Group1 (n=52): 288 (134/490) Group 2 (n=48): 271 (124/660) **Week 9** Group1 (n=48): 0.0 (-228/197) Group 2 (n=43): 3.0 (-297/159) **P=0.34**	
			Number of symptoms improved (%) - all symptoms pooled for each group	**Baseline:** Group 1: 239 Group 2: 270 **Week 9:** Group 1:159 (67) Group 2: 95 (35) P=0.023	
			Number of obstructive symptoms improved (%) - all symptoms pooled for each group	**Baseline:** Group 1: 177 Group 2: 196 **Week 9:** Group 1:112 (63) Group 2: 62 (32) P=0.015	
			Number of irritative symptoms improved (%) - all symptoms pooled for each group	**Baseline:** Group 1: 62 Group 2: 74 **Week 9:** Group 1:47 (76) Group 2: 33 (45) P=0.12	

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				Group 1: 11 patients reported 13 events Group 2: 10 patients reported 11 events P=Not sign **Dizziness/vertigo** Group 1:5 Group 2: 5 (2 withdrew due to dizziness)	
			Patients subjective overall assessment at 9 weeks	**Group 1** Much worse: 0/48 Worse: 1/48 Unchanged: 9/48 Better: 28/48 Much better: 10/48 **Group 2** Much worse: 1/43 Worse: 0/43 Unchanged: 23/43 Better: 12/28 Much better: 7/43	

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Djavan et al., 2005D[73] **Study design:** RCT **Setting:** European multi-centre (3 countries) **Evidence level:** 1+ **Duration of follow-up:** 8 week	**Patient group:** Men aged 45 years or over with voiding and storage symptoms diagnosed as LTUS/BPH. **Inclusion criteria:** After a 2 week placebo run in, men 45 years or older, with lower urinary tract symptoms (IPSS: 13 or above suggestive of BPH (maximum flow rate 4-12ml/s and 2 or more nocturnal voids per night. **Exclusion criteria:** any other urological procedures or conditions, which may cause LUTS; hepatic or renal insufficiency, clinically significant cardiovascular or cerebrovascular diseases within six months prior to enrolment, central nervous system conditions or life-threatening diseases. Alcohol consumption of more than 15 units per week; post voiding residual volume of >250ml in at least two assessment over the last 3 months. Patient taking or had taken other drugs for BPH; hypersensitive to alpha-blockers, were taking drugs with could interfere with the pharmacodynamics of tamsulosin or were taking or had taken over investigational drugs within previous 3 months. **<u>All patients</u>** **N:** 117	**Group 1: Alpha-blocker** Tamsulosin oral controlled absorption system 0.4mg once daily **Group 2: Placebo**	**Mean (SD) IPSS symptom scores**	**Baseline** Group1: 18.2 (4.0) Group 2: 18.1 (3.3) **Change at endpoint** Group1: -8.0 (5.2) Group 2: -5.6 (4.7) **Difference:** 2.4; p=0.0099	**Funding:** NR **Limitations:** Method of randomisation and allocation concealment was unclear. **Additional outcomes:** Analysis of IPSS by sub-group of voiding and storage symptoms. **Notes:** None.
			Mean change in nocturia question on IPSS questionnaire	Group1: 1.1 Group 2: 0.7 **Difference:** 0.4; p=0.028	
			Mean IPSS quality of life question reduction at endpoint	Group1: 2.0 Group 2: 1.3 **OR:** 2.4; p=0.0087	
			Adverse events	**Treatment-emergent adverse events (TEAE)** Group1 (n=61): 10 Group 2 (n=56): 8 **At least one TEAE** Group1: 5 (8.2%) Group 2: 7 (12.5%) **Dizziness** Group1: 2 (3.3%) Group 2: 0 **Nasopharingitis** Group1: 0 Group 2: 2 (3.4%) **Orthostatic hypotension** Group 1: 0 Group 2: 0 **Discontinuations due to AE** Group 1:0 Group 2: 0	
			Mean change in total hours of undisturbed	Group1: 81 minutes (60%) Group 2: 60 minutes (40%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean age: 67 **<u>Group 1</u>** **N:** 61 Mean (±SD) Age: 66.8 (8.5) Baseline IPSS: 19.0 (5.1) Dropouts: 1 (discontinued due to non compliance) **<u>Group 2</u>** **N:** 56 Mean (±SD) Age: 67.6 (7.6) Baseline IPSS: 18.1 (3.5) Dropouts: 0		**sleep** (defined as time between falling asleep and first awakening to void)	Difference: 21 minutes; p=0.198	
			Mean decrease in nocturnal voids as measured by means of voiding diary (defined as time between falling asleep and first awakening to void)	Group1: 1.0 Group 2: 0.7 OR: 0.56; p=0.099	
			Questionnaire to assess level of tiredness or alertness during the day (not validated)	**Group 1:** 0.49 **Group 2:** 0.32 **OR:** 0.672; p=.27	
			Correlation between number of nocturnal void and the hours undisturbed sleep	**Spearman's rank coefficient: -0.63**	
			Correlation between IPSS nocturia and IPSS QoL domains	**Spearman's rank coefficient: 0.64**	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Fawzy et al., 1995[89] **Study design:** RCT **Setting:** Multi-centre, US. **Evidence level:** 1+ **Duration of follow-up:** 16 week	**Patient group:** normotensive patients (sitting diastolic blood pressure <90mm.Hg) with BPH. **Inclusion criteria:** AUA of 10 or greater , maximum urinary flow rate of 5-15ml/s in a voided volume of 125-500ml and post void residual volume of 250ml or less on 2 consecutive weeks of the placebo run in period. aged 45 years or over **Exclusion criteria:** recent urinary retention, sever outflow obstruction, or non BPH conditions that caused obstruction or symptoms. Patients who had serious concurrent disease, history of clinically significant cardiovascular, hepatic or renal dysfunction, poorly controlled diabetes, urinary calculi or intolerance/sensitivity to quinazoline derivatives. **<u>All patients</u>** **N:** 100 **Race:** 96% white, 2% Asian, 1% Hispanic and 1% Black. **Drop outs:** 2 (did not undergo any efficacy measurement). Patient withdrawal: 22 **<u>Group 1</u>** **N:** 50 Mean (±SD) Age: 62.1 (7.8) Withdrawals: 11 (adverse events –	**Placebo run-in:** 2 weeks **Group 1: Alpha-blocker** Doxazosin: 8 week dose titration phase the initial dose of doxazosin was 1mg, increasing to 2mg, 4mg, or 8mg at 2-week intervals until the optimum dose was attained. During the final 6-week phase of the study the dose was held constant at the optimum level. 41 patients in the study dosage was titrated to a maximally efficacious s and/or tolerated, stable level of doxazosin; 36 reached dose of 8mg, 1 reached a daily dose of 4mg and 4 reached a daily dose of 2mg. **Group 2: Placebo**	**Mean change in AUA6 symptom score**	Group1: -5.7 Group 2: -2.5 P<0.001	**Funding:** Pfizer **Limitations:** Method of randomisation and allocation concealment unclear. Frequency of nocturia significantly greater in placebo arm. **Additional outcomes:** Graphical presentation of Qmax by week. Intervention arm significantly improved compared to placebo by 2 weeks. Boyarsky modified score also reported. **Notes:** None.
			Mean change from baseline in Qmax, ml/s	Group1: 2.9 Group 2: 0.7 P<0.01	
			Mean change from baseline in average urinary flow rate, ml/s	Group1: 1.4 Group 2: 0.3 P<0.01	
			Percent improvement in patient assessed symptoms (AUA)	**Total symptoms** Group1: 39 Group 2: 17 **Obstructive symptoms** Group1: 43 Group 20 **Irritative symptoms** Group1: 35 Group 2: 15	
			Adverse events	**Total** Group 1: 44% Group 2: 30% **Events in patients over 65 years** Group 1: 28% Group 2: 37% **Discontinuation due to adverse events** Group 1: 1 Group 2: 0 **Dizziness** Group 1: 15/50 Group 2: 2/50 **Fatigue** Group 1: 6/50 Group 2: 2/50 **Headache** Group 1: 6/50	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	related and unrelated=7; other=4) **<u>Group 2</u>** **N:** 48 Mean (±SD) Age: 61.6 (8.7) Withdrawals: 11 (adverse events – related and unrelated=1; patient request=3; protocol violation=4; entry criteria not me=1; other=2)			Group 2: 2/50 **Somnolence** Group 1: 5/50 Group 2: 2/50 **Hypotension** Group 1: 4/50 Group 2: 0 **Nausea** Group 1: 4/50 Group 2: 0	
			Mean sitting blood pressure change, mmHg	Group 1: -5.6/-4.1 Group 2: 0.7/-0.4 P<0.05	
			Mean standing blood pressure change, mmHg	Group 1: -6.0/-4.5 Group 2: 1.9/-0.4 P<0.05	
			Mean change in daytime micturition frequency from patient daily diary	Group 1: -1.3 Group 2: -0.7 P=0.043	
			Mean change in nocturia frequency from patient daily diary	Group 1: -0.5 Group 2: -0.5 P=0.470	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Gillenwater et al., 1995[101] **Study design:** Randomised controlled trial **Setting:** Multi-centre, USA **Evidence level:** 1+ **Duration of follow-up:** 16 weeks	**Patient group:** men 45 years or older with BPH and mild to moderate essential hypertension. **Inclusion criteria:** maximum urinary flow rte of 5-15ml/s in a voided volume of 150-500ml, post void residual volume of less than 200ml, daytime micturition frequency of 4 or more, nocturia of more than 2 times per night and a sitting diastolic blood pressure of 90-114 mm.Hg. **Exclusion criteria:** Any other conditions casuing urinary symptoms or decreased flow rate, previous or imminent prostatic surgery , prostate specific antigen level greater than 10ng/ml, acute urinary retention, recent catheterisation for outflow obstruction or prostate malignancy were excluded from the study. Insulin-dependent or poorly controlled noninsulin-dependent diabetes, significant hepatic, renal or cardiovascular dysfunction; secondary hypertension, concurrent serious disease or malignancy, or significant psychiatric disorders. Intolerance/sensitivity to quinazoline derivatives, substance abuse, recent blood donation, obesity, antihypertensive drug therapy or any treatment known to affect vesicourethral function, and recent therapy with any other investigational drug or any prior	**Screening:** **0**-4 week period allowed for the discontinuation and wash out of excluded medication, including any other antihypertensive agents. **Placebo- run in phase:** 2 weeks. **Group 1: Alpha-blocker** Doxazosin 2, 4, 8 or 12mg once daily in the morning. The initial dose was 1mg, increasing sequentially at weekly intervals during a 5-week titration phase to the randomised, fixed dose level. The dose then remained constant during the 9-week efficacy phase. **Group 2: Placebo**	**Mean (SD) Qmax at trough and peak measurements, ml/s** Trough defined as assessment approximately 24 hours following the previous morning dose. Peak defined as assessment 2 -6 hours following administration of medication	**Trough** **Group1:** 2mg (n=39): 10.5 (2.1) 4mg (n=46): 9.8 (2.0) 8mg (n=45): 10.7 (2.1) 12mg (n=45): 10.5 (2.2) **Group 2** (n=41): 10.3 (2.3) **Peak** **Group1:** 2mg (n=39): 10.1 (2.7) 4mg (n=46): 9.4 (2.9) 8mg (n=45):10.3 (2.6) 12mg (n=45): 9.7 (2.4) **Group 2** (n=41):10.5 (2.6)	**Funding:** Gillenwater, Conn, Chrysant and Roy, and the Multicenter Study Group have participated in clinical studies sponsored by Pfizer Central Research, new York. **Limitations:** Method of randomisation and allocation concealment unclear. Method states that compliance assessed by tablet count of returned medication – results not reported. **Additional outcomes:** Obstructive and irritative sub-groups results for Boyarsky score. Qmax also reported as adjusted mean change. **Notes:** Boyasrsky score was reversed so that lower scores indicated improvement, as with other commonly used symptom scores. Treatment effect tested
			Patients with ≥3ml/s increase in Qmax	**Trough** **Group 1:** 8mg: 37% 2mg: 39% **Group 2:** 13% **Peak** **Group 1:** 8mg: 42% 2mg: 51% **Group 2:** 17% * 2mg and 4mg Not sig.ly different from placebo group	
			Mean (adjusted) change in average flow rate (* significantly different from placebo p<0.05, ** p<0.01)	**Trough** **Group1:** 2mg: 0.6 4mg: 0.6 8mg: 1.5** 12mg: 1.3* **Group 2**: 0.2 **Peak**	

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	doxazosin therapy. **<u>All patients</u> N:** 248 Efficacy analysis Group 1: 175 Efficacy analysis Group 2: 41 Drop outs: 32 (no efficacy follow-up measurements=7; not meet inclusion criterion for maximum urinary flow rate=25). **<u>Group 1</u>** **N:** 199 Efficacy analysis: 175 2mg: 39 4mg: 46 8mg: 45 12mg: 45 **Mean** (±SD) **Age:** **Dropouts:** 69 (adverse events 11%, lack of blood pressure efficacy 7%, and protocol violations 9%) **<u>Group 2</u>** **N:** 49 Efficacy analysis: 41 **Mean** (±SD) **Age:** 64.5 (7.7) **Dropouts:**18 (adverse events 4%, lack of blood pressure efficacy 12%, lack of BPH efficacy 4% and protocol violations 10%)			**Group1:** 2mg: 0.9 4mg: 1.1 8mg: 1.6** 12mg: 2.1** **Group 2**: 0.2	for significance after adjusting for the baseline effect. Intervention at 1 week of treatment with 1mg dose - Qmax +0.8ml/s.
			BPH symptom questionnaire (modified Boyarsky) mean change from baseline (adjusted for baseline effect) Key: * significantly different from placebo mean changes, p<0.01; $significantly different from placebo mean changes, p<0.05	**End point analysis of severity** **Group 1** 2mg (n=34): -2.8 4mg(n=38): -5.0* 8mg(n=42): -4.2$ 12mg(n=39): -3.6 **Group 2** (n=37): -0.25 **End point analysis of bothersomeness** **Group 1** 2mg (n=34): -3.4 4mg (n=38):-5.3$ 8mg (n=42): -4.7 12mg (n=39): -4.9 **Group 2** (n=37): -3.0	
			% of patients with adverse events	**Total** Group 1 (n=199): 48% Group 2 (n=49): 35% **Dizziness** Group 1 (n=199): 19% Group 2 (n=49): 4% **Headache** Group 1 (n=199): 14% Group 2 (n=49): 18% **Fatigue** Group 1 (n=199): 10% Group 2 (n=49): 0% **Hypotension** Group 1 (n=199): 2.5% Group 2 (n=49): NR **Withdrawal due to adverse events** Group 1 (n=199): 11.1% Group 2 (n=49): 4.1%	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hansen et al., 1994[112] **Study design:** RCT **Setting:** Multi-centre, Denmark and Netherlands **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** Men with BPH enrolled from November 1991 to March 1993. **Inclusion criteria:** Madsen-Iversen symptom score >6; urinary peak flow rate <10ml/s with a voided volume of at least 100ml. Men with very low urinary flow rates were included. **Exclusion criteria:** patients whose digital rectal examination suggested presence of prostatic cancer, or patients suffering from other urological diseases such as neurogenic bladder, urethral stricture, current urinary tract infection, macroscopic or microscopic hematuria, prostatitis or previous prostatectomy were excluded. Incidence of total urinary retention, history of bladders tones, repeated urinary tract infections, overflow incontinence, azotemia, abnormal acid phosphatise, a history of orthostatic hypotension or know hypersensitivity to alpha-	**Run-in phase:** All patients entered a four week placebo run-in phase. Single blind. **Group 1: Alpha-blocker** Alfuzosin 2.5mg TID **Group 2: Placebo** Three times a day	**Median (25% and 75% quartiles) Madsen-Iversen symptom score**	**Baseline** Group1: 7 (6-8.5) Group 2: 7 (6-9) **12 weeks** Group1: 5 (3.5-7) Group 2: 6 (5-7.5)	**Funding:** Research grant from Synthelabo International. **Limitations:** Method of randomisation and allocation concealment was not reported. **Additional outcomes:** Blood pressure reported. Small but significant decrease in diastolic blood pressure in alfuzosin group compared to placebo. **Notes:** None
			Median (25% and 75% quartiles) peak flow rate, ml/s	**Baseline** Group1: 9 (7-11) Group 2: 9 (7-11) **12 weeks** Group1: 11 (7.6-13.5) Group 2: 10 (8-11)	
			Median (25% and 75% quartiles) residual urinary volume, ml	**Baseline** Group1: 50 (20-89) Group 2: 42 (20-100) **12 weeks** Group1: 30 (15-80) Group 2: 45 (15-80)	
			Adverse events – vasodilatory events	**Dizziness** Group 1: 3 Group 2: 0 **Headache** Group 1: 2 Group 2: 2 **Postural hypotension** Group 1: 1 Group 2: 0 **Fatigue** Group 1: 1 Group 2: 1 **Syncope** Group 1: 2 Group 2: 0	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	blockers. **<u>All patients:</u> N:** 205 Mean age: 45-81 **<u>Group 1</u>** **N:** 104 (91 completed study) Median (±SD) Age: 65 (47-81) Withdrawals: 5 (lost to follow-up=1; adverse event=1; other=3) **<u>Group 2</u>** **N:** 101 (87 completed study) Median (±SD) Age: 64 (45-81) Withdrawals: 12 (lack of efficacy=4; lost to follow-up=2; adverse events=1; other=5)		**Adverse events – gastro-intestinal disorders**	**Nausea** Group 1: 2 Group 2: 1 **Diarrhoea** Group 1: 4 Group 2: 1 **Vomiting** Group 1: 0 Group 2: 0 **Pyrosis** Group 1: 1 Group 2: 0 **Abdominal pain** Group 1: 5 Group 2: 0 **Obstipation** Group 1: 0 Group 2: 1 **Flatulence** Group 1: 1 Group 2: 0 **Haematemesis** Group 1: 1 Group 2: 0	
			Adverse events – urinary tract disorders	**Cystitis** Group 1: 1 Group 2: 0 **Urinary tract infection** Group 1: 0 Group 2: 0 **Hameatura** Group 1: 0 Group 2: 0	
			Other adverse events (including pain in arm, lympth disease, pneumonia, hypertension)	Group 1: 2 Group 2: 9	
			Discontinuation due to adverse events	Group 1: 1 Group 2: 1	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kaplan et al., 2006[136] Also reported in Kaplan2008[134] and Rovner2008A[264] Study identifier: NCT00147654 **Study design:** RCT,Double blind Patients, investigators and researchers masked to treatment allocation **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** Men with overactive bladder or other LUTS recruited between Nov 2004 – Feb 2006 **Setting:** multi-centre, USA **Inclusion criteria:** • ≥ 40 years • IPSS ≥ 12 • Self-rated bladder condition of 'some moderate problems', 'severe problems' or 'many severe problems' based on the validated Patient Perception of Bladder Condition questionnaire. • Micturition frequency ≥8/24 hrs and urgency ≥ 3/24 hrs for ≥ 3 months **Exclusion criteria:** • Clinically significant bladder outlet obstruction defined as PVR ≥200 mL and Qmax < 5 mL/s • Serum PSA > 10 ng/mL with risk of prostate cancer • History of postural hypotension or syncope • Significant hepatic or renal disease • Neurological conditions such as MS, spinal cord injury and Parkinson disease • Prostate cancer • Prostate surgery or other intervention	**Group 1:** Tolterodine ER 4mg/day in evening **Group 2:** Tamsulosin 0.4 mg/day in evening **Group 3:** Tolterodine ER 4mg + Tamsulosin 0.4 mg/day in evening **Group 4:** Placebo in evening **Examination methods:** A Perception of Treatment Benefit question was posed at weeks 1, 6 and 12. "Have you had any benefit from your treatment? – YES/NO" and if so "How much benefit (little/a lot)?" Bladder diaries for 5 days were assessed prior to each visit at baseline and weeks 1, 6 and 12. IPSS measured at baseline and weeks 1, 6 and 12. PVR and Qmax measured at baseline and at week 12.	**Change in IPSS from baseline at 12 weeks** (estimated from graph) Analysis of covariance with covariates – smoking status, age, baseline score, duration of OAB, centre	**Grp 1:** -6.7 ± NR, n=206 **Grp 2:** -7.6 ± NR, n=197 **Grp 3:** -8.0 ± NR,n=203 **Grp 4:** -6.2± NR, n=213 **P values:** Grp 1 vs Grp 4: not sig. Grp 2 vs Grp 4: =0.007 Grp 3 vs Grp 4: =0.003	**Funding:** Pfizer **Limitations:** Incomplete reporting of outcomes: ▪ Only the statistical significance of Combination vs placebo was reported. The statistical significance of difference between active arms unknown ▪ There were inconsistencies in the results reported within the paper ▪ Standard deviations were not reported. **Additional outcomes:** Number of patients reporting treatment benefit from Perception of Treatment Benefit Question: **Grp 1:** 136/217 **Grp 2:** 146/215 **Grp 3:** 172/225 **Grp 4:** 132/222 Not sig, except : Grp 1 v Grp 3 p value 0.02, Grp 3 v Grp 4 p value 0.01
			Change in IPSS QoL from baseline at 12 weeks (estimated from graph) Analysis of covariance with covariates – smoking status, age, baseline score, duration of OAB, centre	**Grp 1:** -1.4 ± NR, n=206 **Grp 2:** -1.4 ± NR, n=198 **Grp 3:** -1.6 ± NR, n=205 **Grp 4:** -1.2 ± NR, n=213 **P values:** Grp 1 vs Grp 4: not sig. Grp 2 vs Grp 4: not sig Grp 3 vs Grp 4 =0.003	
			Change in Qmax from baseline at 12 weeks Analysis of covariance with covariates – centre, treatment, baseline value.	**Grp 1:** -0.60 ± NR **Grp 2:** -0.22 ± NR **Grp 3:** 0.07 ± NR **Grp 4:** -0.53 ± NR **P values:** Grp 1 vs Grp 4: not sig. Grp 2 vs Grp 4: not sig Grp 3 vs Grp 4: not sig.	
			Change in urgency incontinence/24h from baseline at 12 weeks (estimated from graph) Analysis of covariance with covariates – treatment, centre, PVR, Qmax and baseline value	**Grp 1:** -0.7. ± NR [n=48] **Grp 2:** -0.8 ± NR [n=46] **Grp 3:** -0.9 ± NR [n=47] **Grp 4:** -0.3 ± NR [n=43] **P values:** Grp 1 vs Grp 4= 0.008 Grp 2 vs Grp 4: Not sig Grp 3 vs Grp 4 p value =0.005	
			Change in urgency	**Grp 1:** -2.9 ± NR, n=209	

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	• History of acute urinary retention requiring catheterisation • BOO due to diseases other than BPH • Any condition for which antimuscarinics are contraindicated • Men treated with alpha-blockers with 2 weeks or antimuscarinics, phytotherapy or electrical stimulation within 1 month, any investigational drug within 2 months or 5-alpha reducatase within 3 months **<u>All patients</u>** **N:** 879 out of 1531 evaluated **Mean age:** 61.8±9.9 **Drop outs:** 851/879 included in efficacy analysis, 754 /879 completed the study **IPSS ± SD:** 19.9±5.3 **IPSS QoL ± SD:** 4.57 ± 0.93 **Qmax ± SD, mL/s:** 12.9 ± 7.2 **<u>Group 1 (Tolterodine ER)</u>** **N:** 217 (baseline data/efficacy analysis for N=210) **Mean (± SD) Age:** 61.8 ± 9.6 (range 41-91) **Urge urinary incontinence :** 53/217 **Urgency episodes/24h:** 7.58 ± 3.49 **Micturitions/24h:** 11.79 ± 2.83 **Micturitions/night:** 1.97 ± 1.27 **IPSS ± SD:** 19.53 ± 5.15 **IPSS QoL ± SD:** 4.57 ± 0.94		**episodes/24h from baseline at 12 weeks** (estimated from graph) Analysis of covariance with covariates – treatment, centre, PVR, Qmax and baseline value	**Grp 2:** -2.4 ± NR, n=205 **Grp 3:** -3.3 ± NR , n=211 **Grp 4:** -2.5 ± NR , n=210 **P values:** Grp 1 vs Grp 4: not sig. Grp 2 vs Grp 4: not sig Grp 3 vs Grp 4: = 0.03	Pair wise analysis using Fishers 2 sided test **Notes:** The study reported the adverse events based on the safety population, ie patients who had received at least one dose of the allocated treatment. The average IPSS score puts the patients in the study in the severely symptomatic category Sample size based on projected treatment difference of 15% between Tolterodine ER + Tamsulosin group compared to placebo for number of patients reporting treatment benefit at week 12. Randomisation sequence using block method prepared by statistician. Study medication kits were identical in appearance and smell. Missing data imputed for treatment benefit
			Change in micturitions/24h from baseline at 12 weeks (estimated from graph) Analysis of covariance with covariates – treatment, centre, PVR, Qmax and baseline value	**Grp 1:** -1.7 ± NR, n=209 **Grp 2:** -1.8 ± NR, n=205 **Grp 3:** -2.5 ± NR, n=211 **Grp 4:** -1.4 ± NR, n=212 **P values:** Grp 1 vs Grp 4: not sig. Grp 2 vs Grp 4: not sig Grp 3 vs Grp 4: <0.001	
			Change in micturitions/night from baseline at 12 weeks (estimated from graph) Analysis of covariance with covariates – treatment, centre, PVR, Qmax and baseline value	**Grp 1:** -0.36 ± NR, n=209 **Grp 2:** -0.54 ± NR, n=205 **Grp 3:** -0.59 ± NR, n=209 **Grp 4:** -0.39 ± NR, n=212 **P values:** Grp 1 vs Grp 4: not sig. Grp 2 vs Grp 4: not sig Grp 3 vs Grp 4: =0.02	
			Reasons for discontinuation	**Grp 1** **Grp 2** **Grp 3** **Grp 4** Adverse event 5 7 20 7 Lack of efficacy 8 0 4 7 Withdrew consent 9 9 2 5 Protocol deviation 2 4 0 4 Lost to follow up 1 4 6 4 Death 1 0 0 0 Other 1 5 2 5	
			All cause adverse events **N** **Constipation**	**Grp 1** **Grp 2** **Grp 3** **Grp 4** ***216*** ***215*** ***225*** ***220*** 9 2 8 5	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Qmax ± SD, mL/s: 13.3 ± 7.8 **PVR ± SD, mL:** 50.5 ± 55.8 **Dropouts:** 28/217 (12.9%) 1 patient did not receive study medication **Group 2 (Tamsulosin)** **N:** 215 (baseline data/efficacy analysis for N=209) **Mean (± SD) Age:** 61.7 ± 10.5 (range 40-90) **Urge urinary incontinence :**50/215 **Urgency episodes/24h:** 7.10 ± 3.83 **Micturitions/24h:** 12.10 ± 3.51 **Micturitions/night:** 1.74 ± 1.20 **IPSS ± SD:** 20.04 ± 5.02 **IPSS QoL ± SD:** 4.57 ± 0.86 **Qmax ± SD, mL/s:** 13.4 ± 7.6 **PVR ± SD, mL:** 56.5 ± 55.0 **Dropouts:** 29/215 (13.5%) **Group 3 (Tolterodine ER + Tamsulosin)** **N:** 225 (baseline data/efficacy analysis for N=217) **Mean (± SD) Age:** 61.0 ± 9.6 (range 40-92) **Urge urinary incontinence :** 52/225 **Urgency episodes/24h:** 6.72 ± 3.95 **Micturitions/24h:** 11.92 ± 3.35 **Micturitions/night:** 2.07 ± 1.32 **IPSS ± SD:** 20.10 ± 5.49 **IPSS QoL ± SD:** 4.55 ± 0.93 **Qmax ± SD, mL/s:** 12.7 ± 6.8 **PVR ± SD, mL:** 58.8 ± 53.8 **Dropouts:** 34/225 (15.1%) **Group 4 (Placebo)**		**Diarrhoea** 7 6 5 3 **Dizziness** 3 12 6 2 **Dry mouth** 16 15 47 5 **Dyspepsia** 2 1 3 5 **Ejaculation failure** 0 4 7 0 **Fatigue** 2 3 2 6 **Headache** 2 9 14 7 **Nasal congestion** 0 3 10 2 **Somnolence** 2 5 4 2 **Urinary retention** 2 0 2 3 *See Notes		question (YES/NO), bladder diary variables, IPSS and IPSS QoL using Last observation carried forward (LOCF) PPBC is a single item global measure questionnaire with sex options to the question of " which of the following statements described your bladder condition best at the moment"?
			Number of patients reporting treatment benefit at 12 weeks (ITT post hoc figures with imputed data) Pair wise analysis using Fishers 2 sided test	**Grp 1:** 136/217 **Grp 2:** 146/215 **Grp 3:** 172/225 **Grp 4:** 132/222 Grp 1 v Grp 4 p value 0.49 Grp 1 v Grp 2 p value 0.27 Grp 1 v Grp 3 p value 0.002 Grp 2 v Grp 4 p value 0.07 Grp 2 v Grp 3 p value 0.06 Grp 3 v Grp 4 p value <0.001	
			PPBC at week 12 (%) **Major improvement** **Minor improvement** **No change** **Deterioration**	**Grp 1 Grp 2 Grp 3 Grp 4** 32 35 35 27 32 27 32 30 28 30 27 38 8 8 5 5	
			Willingness to continue at week 12 (%) **Very willing** **Little bit willing** **Little bit unwilling** **Very unwilling**	**Grp 1 Grp 2 Grp 3 Grp 4** 44 39 51 38 21 19 15 21 12 20 12 12 23 21 23 30	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 222 (baseline data/efficacy analysis for N=215) **Mean (± SD) Age:** 62.8 ± 9.7 (range 40-88) **Urge urinary incontinence :**48/220 **Urgency episodes/24h:** 7.33 ± 3.82 **Micturitions/24h:** 11.86 ± 3.24 **Micturitions/night:** 2.02 ± 1.19 **IPSS ± SD:** 20.00 ± 5.42 **IPSS QoL ± SD:** 4.58 ± 0.95 **Qmax ± SD, mL/s:** 12.2 ± 6.6 **PVR ± SD, mL:** 47.1 ± 47.7 **Dropouts:** 34/222 (15.3%) 2 patients did not receive study medication				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kirby et al., [147] **Study design:** RCT double blinded(4 arms) **Setting:** 90 European centres **Evidence level:** 1+ **Duration of follow-up:** 1 year(52 weeks)	**Patient group:** Symptomatic BPH **Inclusion criteria:** ▪ Aged 50 to 80 years ▪ IPSS≥ 12 ▪ Qmax of ≥5 mL/s but ≤15 mL/s in a total voided volume of ≥150 mL ▪ Enlarged prostate as determined by DRE. **Exclusion criteria:** ▪ Previous prostate surgery or other invasive procedures for treating BPH ▪ Prostate cancer or a PSA level exceeding 10 ng/mL. If PSA was between 4.1 to 10 ng/mL, need to have ≥2 of the following : negative DRE *or* transrectal ultrasound findings(within the past 3 months) *or* negative biopsy findings(within the past 4 weeks) ▪ lower urinary tract symptoms or reduced urinary flow rates resulting from a condition other than BPH ▪ large bladder diverticulum, bladder stones, recurrent urinary tract infection, or two or more episodes of AUR requiring catheterization within the year	**Group 1: Doxazosin 4 mg(+ placebo)** Initiated on 1 mg/day, titrated to 2 mg at end of week 2 and, 4 mg from end of week 6. At the end of week 10, the 4-mg dose was maintained in subjects who met the following two criteria: (a) total IPSS had decreased by 30% or more from baseline, and(b) Qmax had increased by 3 mL/s or more from baseline. For subjects who did not meet these goals, the doxazosin dose was increased to 8 mg/day and maintained for the remaining 42 weeks. Doses were reduced to the next lower dose if the SBP/diastolic BP(DBP) fell to less than 90/60 mm Hg or tolerability was limited. Subjects unable to tolerate a 2-mg/day dose of	**IPSS, mean ±SD** at 1 year	**Group 1:** 8.7 ± 5.8 **Group 2:** 10.9 ± 6.2 **Group 3:** 8.7 ± 6.2 **Group 4:** 11.8 ± 6.9	**Funding:** Grant provided by Pfizer Ltd. Finasteride & placebo provided by Merck & Co **Limitations:** Randomisation allocation and concealment methods not stated. **Additional outcomes:** Mean change in sitting and SBP and DBP: Normotensive subjects: Not sig Hypertensive subjects (sitting DBP≥90mmHg, SBP≥140mmHg): LS mean change (sitting SBP/DBP, mmHg) for doxazosin: -11.8/-5.7 Doxazosin + finasteride: -9.2/-5.6 (P<0.05, clinically sig)
			IPSS LS mean change ±SEM at 1 year	<u>Compared to baseline value</u> **Group 1:** -8.3 ± 0.4## **Group 2:** -6.6 ± 0.4 **Group 3:** -8.5 ± 0.4## **Group 4:** -5.7 ± 0.4 ##P<0.0001 compared to placebo, <0.01 compared to finasteride	
			Qmax, ml/s mean ±sd at 1 year	**Group 1:** 14.0 ± 4.9 **Group 2:** 12.1 ± 4.7 **Group 3:**14.5 ± 5.1 **Group 4:**12.1 ± 4.2	
			Qmax, ml/s change from baseline at endpoint, LS mean change ±sem	**Group 1:** 3.6 ± 0.3 ## **Group 2:** 1.8 ± 0.3 **Group 3:** 3.8 ± 0.3 ## **Group 4:** 1.4 ± 0.3 **P<0.0001 compared to placebo or finasteride	

Reason for withdrawal	Grp 1	Grp 2	Grp 3	Grp4
Total withdrawals	78(28.4)	81(30.7)	89(31.1)	76(28.1)
Reasons				
Adverse Events	32(11.6)	34(12.9)	35(12.2)	30(11.1)
Death**	0(0.0)	2(0.8)	1(0.3)	2(0.7)
Inadequate response	3(1.1)	6(2.3)	3(1.0)	9(3.3)
Noncompliance	7(2.5)	12(4.2)	6(2.1)	9(3.3)
Protocol violation	5(1.8)	4(1.5)	6(2.1)	3(1.1)
Failed screening guidelines	3(1.1)	2(0.8)	1(0.3)	1(0.4)
Other therapy indicated	5(1.8)	3(1.1)	6(2.1)	5(1.9)
Lost to follow-up	4(1.5)	15(5.7)	5(1.7)	4(1.5)
Other	19(6.9)	15(5.7)	26(9.1)	13(4.8)

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	before study entry ▪ residual urine volumes greater than 200 ml ▪ Active urinary tract infection. ▪ Serious diseases ▪ History of drug or alcohol abuse ▪ History of sensitivity to alpha-adrenergic blocking agents, quinazolines, or finasteride. ▪ Hypotension(sitting BP less than 95/60 mm Hg) or orthostatic hypotension(greater than a 20-mm Hg decrease in systolic BP [SBP] when changing from a supine to standing position ▪ Concomitant therapy with anticholinergics, cholinergics, other alpha-blockers, calcium channel blockers, antiandrogens, other 5-alpha-reductase inhibitors, and plant extract preparations was prohibited during the study. **<u>All patients</u>** **N:** 1095(79.5%) out of 1378 screened **Age**, mean ±sd,(yr): 64 **IPSS** mean ± sd: 17.2 **Qmax**, ml/s mean±sd: 10.5 **Mean PSA**, ng/ml, mean= 2.6 **Prostate volume**, g, mean= 36.3 **Drop outs:**	doxazosin were withdrawn. Mean final dose: 6.4mg/day 8mg: 63.2% 4mg: 31.2% 2 mg: 4.8% 1 mg: 0.8% **Group 2: Finasteride 5mg(+ placebo)** **Group 3: Doxazosin 4 mg + finasteride 5 mg** Mean final dose: 6.1mg/day 8mg: 57.0% 4mg: 35.5% 2 mg:6.0% 1 mg:1.5% **Group 4: placebo for terazosin and placebo for finasteride** All subjects advised to take medications at about 8am **<u>Concomitant treatment:</u>** Diuretic and beta-blocker dosages which were stable for 4		**Grp 1 N=275** **Grp 2 N=264** **Grp 3 N=286** **Grp4 N=269** AUR 0(0) 3(1.1) 0(0) 4(1.5) TURP 1(0.4) 3(1.1) 0(0) 7(2.6) Either AUR or TURP 1(0.4) 5(1.9) 0(0) 7(2.6)	For Finasteride: -5.7/-2.7 Placebo: -4.0/-2.1 Not sig **Notes:** Analysis of covariance was used for efficacy data, which included effects of treatment, centre(pooled by country), and treatment by centre interaction Last observed carried forward algorithm was used for subjects who discontinued early. **No overall baseline differences were found except for Qmax.* †P *<0.0001 vs. placebo.* ‡P _*<0.09 vs. finasteride.* §*Estimated by DRE(in increments of 5 g).* ** Excludes one post therapy death, which
			Dizziness	**Group 1:** 43/275(15.6%)# **Group 2:** 21/264(8.0%) **Group 3:** 39/286(13.6%)# **Group 4:** 20/269(7.4%) P<0.01 vs. finasteride and placebo	
			Postural hypotension	**Group 1:** 16/275(5.8%)# **Group 2:** 2/264(0.8%) **Group 3:** 8/286(2.8%) **Group 4:** 4/269(1.5%) P<0.01 vs. finasteride and placebo	
			Hypertension	**Group 1:** 5/275(1.8%)# **Group 2:** 11/264(4.2%) **Group 3:** 4/286(1.4%)# **Group 4:** 15/269(5.6%) P=0.02 *vs. placebo.*	
			Hypotension	**Group 1:** 14/275(5.1%)# **Group 2:** 2/264(0.8%) **Group 3:** 8/286(2.8%) **Group 4:** 4/269(1.5%) P=0.01 vs. finasteride & placebo	
			Syncope	**Group 1:** 2/275(0.7%) **Group 2:** 0/264(0.0%) **Group 3:** 6/286(2.1%)# **Group 4:** 1/269(0.4%) P=0.04 *vs. finasteride*	
			Asthenia	**Group 1:** 29/275(10.5%) # **Group 2:** 11/264(4.2%) **Group 3:** 26/286(9.1%) # **Group 4:** 11/269(4.1%) P<0.01 vs. finasteride & placebo	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1(Doxazosin) **N:** 250 **Dropouts:** **Age,** mean ±sd,(yr): 63 ±7 **Dropouts:** **Duration of BPH at baseline,** mean(yr): 1.7 ± 2.9 **Prostate Vol by DRE,(g)§:** 36 ± 14 **IPSS** mean ± sd: 17.1 ± 4.2 **Qmax**(ml/s): 10.4 ± 2.5†‡ **PSA** serum, mean(ng/ml): 2.5 ± 2.0 **Group 2(Finasteride)** **N:** 239 **Dropouts:** **Age,** mean ±sd,(yr): 63 ±7 **Duration of BPH at baseline,** mean(yr) = 1.4 ± 2.2 **Prostate Vol by DRE,(g)§:** 36 ± 14 **IPSS** mean ± sd: 17.1 ± 4.4 **Qmax**(ml/s): 10.2 ± 2.5† **PSA** serum, mean(ng/ml): 2.6 ± 2.1 **Group 3: Terazosin 10 mg + finasteride 5 mg** **N:** 265 **Dropouts:** **Age,** mean ±sd,(yr): 64 ±7 **Duration of BPH at baseline,** mean(yr) = 1.8 ± 2.9 **Prostate Vol by DRE,(g)§:** 37 ± 14 **IPSS** mean ± sd 17.3 ± 4.7 **Qmax**(ml/s): 10.4 ± 2.7† **PSA** serum, mean(ng/ml): 2.7 ± 2.3 **Group 4: placebo for terazosin and**	weeks before the initial screening and were maintained during the study.	**Somnolence**	**Group 1:** 11/275(4.0%) **Group 2:** 8/264(3.0%) **Group 3:** 9/286(3.1%) **Group 4:** 6/269(2.2%) Not sig	occurred approximately 35 days after discontinuation of doxazosin therapy
			Vertigo	**Group 1:** 8/275(2.9%) **Group 2:** 6/264(2.3%) **Group 3:** 8/286(2.8%) **Group 4:** 3/269(1.1%) Not sig	
			Impotence	**Group 1:** 16/275(5.8%) **Group 2:** 13/264(4.9%) **Group 3:** 30/286(10.5%)#‡ **Group 4:** 9/269(3.3%) P<0.01 vs. finasteride, finasteride and doxazosin	
			Decreased libido	**Group 1:** 10/275(3.6%) **Group 2:** 9/264(3.4%) **Group 3:** 6/286(2.1%) **Group 4:** 5/269(1.9%) Not sig	
			Ejaculatory abnormality	**Group 1:** 1/275(0.4%) **Group 2:** 6/264(2.3%) **Group 3:** 7/286(2.4%) **Group 4:** 4/269(1.5%) Not sig	
			PSA at end point , mean±sd ng/ml	Group 1: 2.8 ± 2.3 Group 2: 1.5 ± 1.0 Group 3: 1.4 ± 1.2 Group 4: 2.9 ± 2.6	
			PSA change from baseline at endpoint , mean ±sd ng/ml	Group 1: 0.3 ± 1.0 Group 2: 1.2 ± 1.4 Group 3: 1.3 ± 1.6 Group 4: 0.3 ± 1.3	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	placebo for finasteride **N:** 253 **Dropouts:** **Age Mean(±SD):** 64±7 **Duration of BPH at baseline,** mean(yr) = 1.6 ± 3.0 **Prostate Vol by DRE,(g)§:** 36 ± 15 **IPSS** mean ± sd: 17.2 ± 4.5 **Qmax**(ml/s): 10.8 ± 2.5 **PSA** serum, mean(ng/ml): 2.6 ± 2.1				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Martorana et al., 1997[184] **Study design:** RCT **Setting:** Multi-centre **Evidence level:** 1+ **Duration of follow-up:** 4 weeks	**Patient group:** Men with clinical diagnosis of BPH. **Inclusion criteria**: Men aged 50-80 years with a clinical diagnosis of BPH confirmed by digital rectal examination and transrectal ultrasound examination showing prostate enlargement,; at least a 6 month history of BPH related symptoms with a 9-item Boyarsky score>6 before entry and after placebo run-in; peak flow rate between 5-12ml/s with a voided volume>150ml. **Exclusion criteria:** concomitant urological diseases, had undergone prostatectomy or were scheduled to have prostatectomy within 6 months had systolic blood pressure<100,,Hg or history off orthostatic hypotension, had either renal or severe hepatic insufficiency, a psychiatric disorder, insulin dependent diabetes mellitus, history of sever heart disease, myocardial infarction or cerebrovascular accident within 6 months, had hypersensitivity to afluzosin, had treatment with other drugs for BPH during the 2 weeks prior to inclusion, or concomitant treatment with other alpha-blockers, calcium antagonists, monoamine oxidase inhibitors or anticholinergic drugs. **<u>All patients</u>** **N:** 94	**Group 1: alpha-blocker** Alfuzosin2.5mg t.i.d. **Group 2: Placebo**	**Mean (±SEM) Qmax, ml/s**	**Baseline** Group1: 10.55 (0.43) Group 2: 10.4 (0.50) **4 weeks** Group1 (n=25): 13.16 (0.80) Group 2 (n=25): 11.75 (0.62) P=NS	**Funding:** NR **Limitations:** ITT analysis completed but only the per-protocol analysis reported in the study. This is the patient population that complied with the selection criteria and with the complete urodynamic evaluation at baseline and end point. **Additional outcomes:** Detrusor opening pressure and maximum detrusor pressure reported. Reported that blood pressure and heart rate measurement found no statistically significant changes. **Notes:** 2 week placebo run-in phase before trial. After double blind study there was an 8 week single blind treatment extension study.
			Mean (±SEM) flow, ml/s	**Baseline** Group1: 5.92 (0.34) Group 2: 6.30 (0.43) **4 weeks** Group1 (n=25): 7.80 (0.70) Group 2 (n=24): 6.90 (0.47) P=NS	
			Mean (±SEM) maximum flow rates, ml/s (from pressure/flow study)	**Baseline** Group1: 7.76 (0.44) Group 2: 8.52 (0.57) **4 weeks** Group1 (n=25): 10.01 (0.91) Group 2 (n=26): 10.26 (0.92) P=NS	
			Mean (±SEM) detrsor pressure at maximum flow, cmH20 (pressure/flow study)	**Baseline** Group1: 77.88 (5.61) Group 2: 82.27 (5.91) **4 weeks** Group1 (n=25): 54.36 (4.97) Group 2 (n=26): 76.84 (7.78) P<0.05	
			Mean (SEM) Boyarsky score	**Baseline** Group1: 10.7 (0.7) Group 2: 10.5 (0.5) **4 weeks** Group1 (n=25): 8.0 (0.4) Group 2 (n=26): 8.0 (0.5) P=NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1 **N:** 47 Evaluable for efficacy analysis: 26 Mean (±SD) **Age:** 62.5 (1.0) **Dropouts:** 21 (10 lack of complete urodynamic evaluation; 6 lack of compliance with selection criteria at baseline; 5 lack of compliance with protocol treatment requirements; 1 lack of correspondence between treatment drug and blood detection; 2 lost to follow up; 1 lack of uroflowmetric evaluation. **Group 2** **N:** 47 Evaluable for efficacy analysis: 26 Mean (±SEM) **Age:** 63.1 (1.1) **Dropouts:** 21 (9 lack of complete urodynamic evaluation; 8 lack of compliance with selection criteria at baseline; 2 lack of compliance with protocol treatment requirements; 3 lack of correspondence between treatment drug and blood detection, 2 lost to follow up. **Note:** 5 patients had two reasons and 1 had three reasons of non evaluability.		**Adverse events**	**Total** Group 1: 4/47 (8.5%) Group 2: 1/47 (2.1%) **Hypertension** Group 1: 1(2.1%) Group 2: 1 (2.1%) **arthralgia** Group 1: 1(2.1%) Group 2: 0 **Vertigo** Group 1: 1(2.1%) Group 2: 0 **Pathological fracture** Group 1: 1(2.1%) Group 2: 0	

See Evidence Table 2: How does PSA predict symptom progression (in terms of symptom score)? for McConnell et al., 2003[170].

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Mohanty et al., 2003[201] **Study design:** RCT **Setting:** India **Evidence level:** 1+ **Duration of follow-up:** 2 months	**Patient group:** male patients between 40-80years having lower urinary tract obstructive symptoms suggestive of BPH were recruited. **Inclusion criteria:** IPSS>10, maximum flow rate 5-13mL/s and average flow rate<6mL/s with post residual urine volume >100mL and PSA<4ng/mL **Exclusion criteria:** patients with renal or hepatic failure, carcinoma prostate, stricture urethra, neurogenic bladder, bladder neck stenosis, previous surgery on prostate **<u>All patients</u>** **N:** 72 Mean age: 61years **Drop outs:** 3 **<u>Group 1</u>** **N:** 38 Mean (±SD) Age: 61.3 (8.5) Dropouts:2 **<u>Group 2</u>** **N:** 34 Mean (±SD) Age: 62.7 (13.8) Dropouts:1	**Group 1: ALPHA-BLOCKER** Tamsulosin 0.4mg daily (sustained capsules) **Group 2: PLACEBO** Identical capsules once daily	**Mean (SD) IPSS**	**Baseline** Group1: 19.53 (3.2) Group 2: 18.52 (5) **2 weeks** Group1: 12.67 (4.3) Group 2: 15.3 (4.7) **4 weeks** Group1: 9.8 (4.4) Group 2: 13.8 (4.8) **8 weeks** Group1 (n=36): 6.9 (4.4) Group 2 (n=33): 12.7 (4.0)	**Funding:** NR **Additional outcomes:** Vital signs reported. **Notes:** Adverse events reported at end point but study included figures for each time interval.
			Mean (SD) Qmax, mL/s	**Baseline** Group1: 10.5 (2.1) Group 2: 11.6 (2.3) **8 weeks** Group1 (n=36): 15.7 (4.6) Group 2 (n=33): 12.5 (2.6)	
			Average urinary flow rate, mL/s	**Baseline** Group1: 4.5 (1.5) Group 2: 5.3 (1.7) **8 weeks** Group1 (n=36): 7.7 (2.1) Group 2 (n=33): 5.8 (1.7)	
			Maximum voided volume, mL	**Baseline** Group1: 341.7 (137.6) Group 2: 310.3 (105.4) **8 weeks** Group1 (n=36): 353.1 (154.3) Group 2 (n=33): 336.9 (149.4)	
			Mean (SD) post voided residual volume, mL	**Baseline** Group1: 100.6 (46) Group 2: 97.6 (46.4) **8 weeks** Group1 (n=36): 53.1 (19.2) Group 2 (n=33): 91.8 (40.1)	

			Adverse events at end point	**Dizziness** Group 1: 9 Group 2: 11 **Headache** Group 1: 8 Group 2: 9 **Fatigue** Group 1: 14 Group 2: 14 **Postural hypotension** Group 1: 2 Group 2: 0 **Syncope** Group 1: 1 Group 2: 0 **Somnolence** Group 1: 1 Group 2: 1 **Abdominal** pain Group 1: 2 Group 2: 1 **Dyspnea** Group 1: 0 Group 2: 3 **Retrograde ejaculation** Group 1: 0 Group 2: 0 **Constipation** Group 1: 7 Group 2: 0 **Withdrawn due to adverse events** Group 1: 0 Group 2: 0	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Nordling et al., 2005[225] **Study design:** RCT **Setting:** Multi-centre, Europe and Israel **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** Men were recruited between Feb 1998 and August 1999. **Inclusion criteria:** men aged ≥50 years with a clinical diagnosis of symptomatic BPH and at least a 6 month history of LUTS, with all the following criteria met only a the beginning of the placebo run-in period: an IPSS of ≥13, nocturia twice or more, a peak flow rate of 5-12ml/s for a voided volume of 150mL or more, and a residual urine volume of 350mL or less. Patients were not required to these criteria again at the time of randomisation, simulating real-life practice. **Exclusion criteria:** concomitant urological diseases; diagnosed or suspected carcinoma of the prostate; previous prostate surgery; invasive BPH treatments; previous x-ray therapy of the pelvic region; patients previously showing no improvement with treatment with an alpha-blocker; patients with Parkinson's disease, insulin-dependent diabetes, diagnosed or suspected MS, unstable angina or sever heart failure, history of stroke or myocardial infarction within 5 months of day -28 of day 0, known hypersensitivity to alpha blockers or patients taking concomitant medications that might alter voiding	**Run in period:** 28 day single blind, placebo run in period. One placebo tablet matching Alfuzosin 10mg and one matching Tamsulosin 0.4mg at the end of the evening meal. **Group 1: Alpha-blocker** Alfuzosin 10mg once daily (one tablet plus one placebo tamsulosin capsule) **Group 2: Alpha-blocker** Alfuzosin 15mg once daily (one tablet plus one placebo tamsulosin capsule) **Group 3: Alpha-blocker** Tamsulosin 0.4mg once daily (one capsule plus one placebo alfuzosin tablet) **Group 4: Placebo** One placebo alfuzosin tablet plus one placebo tamsuosin capsule. At the end of the evening meal	**Mean (SD) IPSS**	**Baseline** Group1: 18.0 (5.4) Group 2: 17.4 (5.6) Group3: 17.4 (6.2) Group 4: 17.7 (5.0) **Change from baseline** Group1: -6.5 (5.2); p=0.007 Group 2: -6.0 (5.6); p=0.050 Group 3: -6.5 (6.2); p=0.014 Group 4: -4.6 (5.8)	**Funding:** NR. **Limitations:** Method of randomisation and allocation concealment not reported. **Additional outcomes:** Blood pressure changes were reported. Standard laboratory test results were taken but the study did not report figures but stated no significant changes. **Notes:** Alfuzosin 10mg improvement of IPSS was apparent at the first assessment at 4 weeks. Not reported for other groups.
			% of patients with a total IPSS improvement (defined as 3 or more points)	Group1: 81 Group 2: 69 Group3: 77 Group 4: 64	
			Mean (SD) Qmax, mL/s	**Baseline** Group1: 9.2 Group 2: 8.9 Group3: 9.4 Group 4: 9.0 **Change from baseline** Group1: 1.5 (3.3) ; p=0.22 Group 2: 1.6; (3.8) p=0.09 Group3: 2.4 (4.3); p=0.02 Group 4: 0.9 (3.0)	
			Number (%) adverse events (AE)	**Treatment emergent (TE) AE≥ one** Group 1: 58 (38) Group 2: 61 (39) Group 3: 58 (37) Group 4: 52 (34) **TEAE ≥ one serious** Group 1: 3 (2) Group 2: 7 (4) Group 3: 6 (4) Group 4: 3 (2) **Discontinuation because of TEAE**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	patterns. **<u>All patients</u>** **N:** 625 **Patients in ITT analysis:** 611 Dropouts: 47 **<u>Group 1</u>** **N:** 154 Mean (±SD) Age: 65 (51-85) Dropouts: 9 (adverse events=4; other=5) **<u>Group 2</u>** **N:** 159 Mean (±SD) Age: 65 (50-84) Dropouts: 17 (adverse events=14; other=3) **<u>Group3</u>** **N:** 158 Mean (±SD) Age: 64 (50-87) Dropouts: 9 (adverse events=6, other=3) **<u>Group 4</u>** **N:** 154 Mean (±SD) Age: 64 (50-82) Dropouts:12 (adverse events=5; lack of efficacy=2; other=5)			Group 1: 4 (3) Group 2:13 (8) Group 3: 6 (4) Group 4: 5 (3) **Discontinuation because of serious vasodilatory TEAE** Group 1: 0 Group 2: 1(1) Group 3: 1 (1) Group 4: 0 **Dizziness** Group 1: 9 (6) Group 2: 11 (7) Group 3: 3 (2) Group 4: 6 (4) **Headache** Group 1: 3 (2) Group 2: 4 (3) Group 3: 7 (4) Group 4: 5 (3) **Syncope** Group 1: 0 Group 2: 2 (1) Group 3: 1 (1) Group 4: 0 **Hypotension** Group 1: 0 Group 2: 1 (1) Group 3: 1(1) Group 4: 0 **Malise** Group 1: 0 Group 2: 1 (1) Group 3: 0 Group 4: 0 **Impotence** Group 1: 2 (1) Group 2: 2 (1) Group 3: 7 (4)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group 4: 0 **Ejaculation disorder** Group 1: 2 (1) Group 2: 0 Group 3: 5 (3) Group 4: 0 **Abnormal semen** Group 1: 0 Group 2: 0 Group 3: 1 (1) Group 4: 0 **Asthenia/ Fatigue** Group 1: 4 (3) Group 2: 10 (6) Group 3: 6 (4) Group 4: 3 (2) **Somnolence** Group 1: 0 Group 2: 1 (1) Group 3: 0 Group 4: 2 (1)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Resnick et al., 2007[245] **Study design:** RCT **Setting:** Multi-centre, US **Evidence level:** 1+ **Duration of follow-up:** 29 days	**Patient group:** Men aged≥50 years with LUTS suggestive of BPH, including a history of storage and/or voiding symptoms. **Inclusion criteria:** IPSS of ≥13 points and IPSS bother score of ≥3 pints; Qmax between 5 and 12ml/s with a voided volume ≥150ml and post void residual ≤350ml. **Exclusion criteria:** Conditions that affect urinary functioning, such as Parkinson's disease, MS, poorly controlled diabetes, severe heart failure, stroke recent myocardial infarction or concomitant lower urinary tract disease. Previous prostatic surgery or radiation therapy, an endoscopic procedure within 1 month of screening, spontaneous urinary retention during the preceding 12 months, an ongoing episode of urinary retention requiring an indwelling catheter, postural hypotension, syncope or non-responders to previous alpha blocker therapy. Concomitant use of medications. Evidence of clinically relevant biochemical abnormalities or a PSA>10ng/ml. **All patients N:** 372 **Group 1** **N:** 186 Mean (±SD) **Age:** 63.5 (8.4)	**Run-in phase:** 28 days patients received one tablet of placebo. **Group 1: Alpha-blocker** Alfuzosin 10mg One tablet taken once daily after the evening meal, at approximately 0700 h or as late as possible. **Group 2: Placebo** One tablet taken once daily	**Mean improvement in Qmax, ml/s**	**24 hours** Group1: 1.58 Group 2: 0.71; p<0.021 **Day 8** Group1: 1.92 Group 2: 0.39; p<0.001 **Day 29** Group1: 1.76 Group 2: 0.36; p<0.001	**Funding:** Sanofi-Aventis **Limitations:** Adverse events figures reported differently in text and table. **Additional outcomes:** BPH impact score reported. Method of randomisation and allocation concealment unclear. **Notes:** No clinically significant changes in blood pressure were observed (figures not provided). One serious adverse event (non-insulin dependent diabetes mellitus) in intervention group. Considered not to be due to treatment.
			Mean change in IPSS (acute version of IPSS: to allow evaluation of symptom relief after one week)	**Day 8** Group1: -3.4 Group 2: -2.7; p=0.071 **Day 29** Group1: -4.5 Group 2: -3.1; p=0.003	
			Mean change in IPSS quality of life score	**Day 29** Group1: -0.7 Group 2: -0.6 **P=0.125**	
			Treatment emergent adverse events (with > 1% incidence in either group)	**Total** Group 1: 46/185 (24.9%) Group 2: 43/185 (23.2%) **Dizziness** Group 1: 11/185 (5.9%) Group 2: 0 **Headache** Group 1: 5/185 (2.7%) Group 2: 2/185 (1.1%) **Upper respiratory tract infection** Group 1: 4/185 (2.2%) Group 2: 2/185 (1.1%) **Orthostatic hypotension** Group 1: 3/185 (1.6%) Group 2: 4/185 (2.2%) **Fatigue** Group 1: 2/185 (1.1%)	

	Ethnicity: Black/African: 161 *American:* White/Caucasian: 10 Other: 14 **Dropouts:** 10 **<u>Group 2</u>** **N:** 186 Mean (±SD) **Age:** 64.4 (8.0) **Ethnicity:** Black/African: 166 *American:* White/Caucasian: 6 Other: 13 **Dropouts:** 7			Group 2: 1/185 (0.5%) **Insomnia** Group 1: 2/185 (1.1%) Group 2: 0 **Erectile dysfunction** Group 1: 1/185 (0.5%) Group 2: 2/185 (1.1%) **Cough** Group 1: 0 Group 2: 2/185 (1.1%) **Dry mouth** Group 1: 0 Group 2: 2/185 (1.1%) **Gastroesophageal reflux disease** Group 1: 0 Group 2: 2/185 (1.1%) **Discontinuation due to adverse events** Group 1: 3/185 (24.9%) Group 2: 1/185	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Roehrborn et al., 2001a[254] **Study design:** RCT **Setting:** Multi-centre, US and Canada. **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** Men with LUTS/BPH recruited between Jan 1998-Aug 1999. **Inclusion criteria:** men aged 50 years or older with a history of lower urinary tract symptoms consistent with clinical BPH for 6 months or longer, an IPSS of at least 13, a Qmax between 5-12mL/s with a voided volume of 150mL or more, a residual urine volume of 350mL or less, and a quality of life of at least 3 points. Patients had to meet inclusion criteria on day 1 of placebo run-in period (4 weeks) and did not need to re-qualify on randomisation. **Exclusion criteria:** Concomitant lower urinary tract disease; previous prostate surgery; history of postural hypotension or syncope; concomitant use of medications that may alter the voiding pattern; and clinically relevant biochemical abnormalities. Serum PSA >10ng/mL were excluded and those with an elevated serum PSA 4-10 had to have prostate cancer excluded to the satisfaction for the investigator. **<u>All patients</u>** **N:** 536 Mean age: 63.6 (49-92) **Drop outs:** 72 (13%)	**Group 1: Alpha-blocker** Alfuzosin 10mg once daily without initial dose titration. **Group 2: Alpha-blocker** Alfuzosin 15mg once daily without initial dose titration. **Group 3: Placebo**	**Mean (SD) IPSS** [Note: * adjusted p-value compared to placebo]	**Baseline** Group1: 18.2 (6.3) Group 2: 17.7 (5.7) Group 3: 18.2 (6.4) **Change** Group1 (n=170): -3.6 (4.8); p=0.001* Group 2 (n=165): -3.4 (5.7); p=0.004 Group 3 (n=167): -1.6 (5.8)	**Funding:** Sanofi-Synthelabo **Limitations:** Method of randomisation or allocation concealment unclear. Prostate volume in alfuzosin 10mg significantly larger than other 2 groups. **Additional outcomes:** IPSS voiding and filling sub-scores were reported. Reported that there were no significant changes in the hematologic or biochemical measurement were observed. Blood pressure changes reported (reported that no patient experienced clinically relevant changes). **Notes:** Significant improvement in IPSS for treatment groups by first post treatment assessment (day 28) and maintained throughout study.
			% of patients showing an improvement in IPSS of 3 or more points	Group1: 56% Group 2: 52% Group 3: 39%	
			Mean (SD) quality of life	**Baseline** Group1: 3.8 (1.1] Group 2: 3.7 (1.1) Group 3: 3.7 (1.1) **Change** Group1 (n=170): -0.7 (1.1); p=0.002 Group 2 (n=165): -0.7 (1.2); p=0.002 Group 3 (n=167): -0.3 (1.1)	
			% of patients showing an improvement in IPSS quality of life question of 2 or more points	Group1: 21%; p=0.004 Group 2: 21%; p=0.003 Group 3: 12%	
			Mean (SD) Qmax, mL	**Baseline** Group1: 9.9 (3.9) Group 2: 10.0 (3.2) Group 3: 10.2 (4.0) **Mean change** Group1 (n=170): 1.7 (4.2); p=0.0004 Group 2 (n=165): 0.9 (3.6); p=0.12 Group 3 (n=167): 0.2 (3.5) **Optimal mean change** Group1 (n=170): 1.7; p=0.0004	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1 **N:** 177 Mean [range] Age: 64.3 (50-92) Prostate volume: 40.2 Dropouts: 11% (adverse events=8; **Group 2** **N:** 181 Mean [range] Age: 63.9 (50-81) Prostate volume: 38.3 Dropouts: 18% (adverse events=8; insufficient efficacy=2 **Group 3** **N:** 178 Mean [range] Age: 62.7 (49-85) Prostate volume: 36.8 Dropouts: 11% (adverse events=4; insufficient efficacy=2			Group 2 (n=165): 1.2; p=0.03 Group 3 (n=167): 0.3 **Median change** Group1 (n=170): 1.1 (4.2); p=0.0006 Group 2 (n=165): 1.0 (3.6); p=0.0006 Group 3 (n=167): **Median optimal change** Group1 (n=170): 1.3 Group 2 (n=165): 1.1 Group 3 (n=167): 0.3	Qmax was not normally distributed so median values were also reported. Men over 65 years who received alfuzosin 15mg reported more adverse events potentially related to vasodilation (dizziness, malaise, hypotension) than younger patients (17% v 5%). This was not observed in the 10mg group.
			% of patients showing an improvement in Qmax of 2mL/s or more	Group1: 40% Group 2: 41% Group 3: 26%	
			Number (%) treatment emergent adverse events (≥2%) of the exposed population	**Total** Group 1: 52% Group 2:43% Group 3:43% **Dizziness** Group1: 13 (7.4) Group 2: 16 (9.0) Group 3: 5 (2.9) **Headache** Group1: 9 (5.1) Group 2: 4 (2.3) Group 3: 4 (2.3) **Respiratory tract infection** Group1: 6 (3.4) Group 2: 5 (2.8) Group 3: 4 (2.3) **Back pain** Group1: 2 (1.1) Group 2: 6 (3.4) Group 3: 4 (2.3) **Rhinitis** Group1: 3 (1.7) Group 2: 4 (2.3) Group 3: 4 (2.3)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Fatigue Group1: 4 (2.3) Group 2: 3 (1.7) Group 3: 4 (2.3) **Inflicted injury** Group1: 4 (2.3) Group 2: 3 (1.7) Group 3: 1 (0.6) **Impotence** Group1: 5 (2.8) Group 2: 2 (1.1) Group 3: 2 (1.1) **Somnolence** Group1: 4 (2.3) Group 2: 3 (1.7) Group 3: 0 **Sinusitis** Group1: 5 (2.8) Group 2: 1 (0.6) Group 3: 4 (2.3) **Constipation** Group1: 4 (2.3) Group 2: 1 (0.6) Group 3: 1 (0.6) **Pain** Group1: 5 (2.8) Group 2: 0 Group 3: 1 (1.1) **Nausea** Group1: 4 (2.3) Group 2: 1 (0.6) Group 3: 1 (0.6) **Abdominal pain** Group1: 2 (1.1) Group 2: 2 (1.1) Group 3: 4 (2.3) **Arthralgia**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group1: 2 (1.1) Group 2: 1 (0.6) Group 3: 4 (2.3) **Dyspepsia** Group1: 3 (1.7) Group 2: 0 Group 3: 4 (2.3) **Orthostatic hypotension** (decrease in systolic BP of 20mmHg or more when standing) Group1: 3.4% Group 2:2.3% Group 3: 3.4%	

See Evidence Table 2: How does PSA predict symptom progression (in terms of symptom score)? for Roehborn et al., 2006[255]

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Schulman et al., 1994[269] **Study design:** Randomised cross over trial **Setting:** Multi-centre **Evidence level:** 1+ **Duration of follow-up:** 4 weeks	**Patient group:** men with clinical symptoms of BPH **Inclusion criteria:** urinary peak flow of <12.5ml/sec; prostate volume >20ml. **Exclusion criteria:** men suffering from urogenital diseases other than BPH or from neurological diseases that might influence the parameters measured during the trial were excluded. **All patients** **N:** 161 Mean age: 31-79 **Drop outs:** 19 (lost to follow-up=6; intercurrent disease=2; patient withdrawal=2; adverse event=8; lack of efficacy=1) **Group 1** (alfuzosin-placebo) **N:** 79 Mean Age: 63.5 **Group 2** (placebo-alfuzosin) **N:** 82 Mean Age: 61.9	**Group 1: Alpha-blockers** Alfuzosin 2.5mg three times daily **Group 2: Placebo** Three times daily	**Peak flow, ml/sec**	**Baseline** Group 1: 9.06 (2.9) Group 2: 9.14 (2.8) **4 weeks** Group1(n=68): 13.95 (6.3) Group 2(n=73): 11.69 (5.5)	**Funding:** NR **Limitations:** Method of randomisation and allocation concealment unclear. No washout period between cross over of treatments. **Additional outcomes:** Results after the cross over period. Adverse events – not reported as unclear whether in phase 1 before cross over of treatments. **Notes:** After 4 weeks of treatment each group then had 4 more weeks on the opposite treatment. There was no wash out period and the effect of the initial treatment could not be distinguished from any new effects. Therefore, only the first 4 weeks of this trial are reported to limit bias.
			Mean flow, ml/sec	**Baseline** Group1: 4.72 (1.9) Group 2: 5.00 (1.9) **4 weeks** Group1(n=68): 6.85 (3.4) Group 2(n=73): 6.01 (2.5)	
			Post voiding volume, ml	**Baseline** Group1: 90.65 (82.2) Group 2: 83.86 (67.4) **4 weeks** Group1 (n=61): 50.88 (47.76) Group 2 (n=68): 71.13 (77.0)	
			Boyarsky symptoms score	**Baseline** Group1: 12.33 (2.55) Group 2: 12.42 (2.36) **4 weeks** Group1 (n=61): 50.88 (47.76) Group 2 (n=69): 7.65 (3.58)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
VanKerrebroeck et al., 2000[305] **Study design:** RCT **Setting:** 48 Urology centres, Europe **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** Men over 50 years with micturition disorders related to BPH from April 1997 to July 1998. **Inclusion criteria:** IPSS ≥13 and a maximum urinary flow rate between 5 and 12ml/s for a voided volume of at least 150ml and a residual urine volume of ≤350ml. **Exclusion criteria:** concomitant urinary tract disease, previous prostatic surgery or other invasive procedures for the treatment of BPH, associated severe visceral disease, history of postural hypotension or syncopes, clinically relevant biological abnormalities, alpha blockers in the month preceding the selection, androgen, antiandrogens, 5 alpha reductase inhibitors and LHRH analogues in the 3 months preceding the selection. **<u>All patients</u>** **N:** 447 **Drop outs:** 40 (8.9%) **<u>Group 1</u>** **N:** 143 Mean (±SD) Age: 64.9 (7.4) Dropouts: 16 **<u>Group 2</u>** **N:** 150 Mean (±SD) Age: 64.7 (7.5) Dropouts: 14	**Run-in period:** One moth, placebo controlled period' **Group 1: Alpha-blockers** Alfuzosin 10mg once daily at the end of the evening meal **Group 2: Alpha-blockers** Alfuzosin 7.5mg (2.5mg thrice daily) **Group 3: Placebo**	**Mean (SD) IPSS**	**Baseline** Group1: 17.3 (3.5) Group 2: 16.8 (3.7) Group 3: 17.7 (4.1) **3 months** Group1: 10.4 (4.7) Group 2: 10.5 (6.1) Group 3: 12.8 (6.7)	**Funding:** NR **Limitations:** Qmax was significantly lower in alfuzosin 2.5mg group at baseline. Method of randomisation and allocation concealment unclear. **Additional outcomes:** IPSS sub-scores for filling and voiding symptoms. Changes in haemodynamic parameters in normotensive and hypertensive patients (no significant differences reported). **Notes:** NCGC calculated means for Group 1 and 2 for the meta-analysis.
			Mean (SD) IPSS quality of life question	**Baseline** Group1: 3.3 (0.9) Group 2: 3.3 (1.0) Group 3: 3.3 (1.0) **3 months** Group1: 2.2 (1.1) Group 2: 2.2 (1.1) Group 3: 2.6 (1.3)	
			Mean (SD) Qmax	**Baseline** Group1: 9.4 (1.9) Group 2: 8.7 (1.9) Group 3: 9.2 (2.0) **3 months** Group1: 11.7 (3.9) Group 2: 11.9 (4.3) Group 3: 10.6 (3.3)	
			Adverse events	**Vasodilatory events** Group1: 9/143 (6.3%) Group 2: 14/149 (9.4%) Group 3: 4/154(2.6%) **Drop outs due to Vasodilatory events (syncope)** Group1: 0 Group 2: 1/149 (0.7%) Group 3: 0 **Dizziness** Group1:3/143 (2.1%) Group 2: 7/149 (4.7%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 3 **N:** 154 Mean (±SD) Age: 64.2 (7.8) Dropouts: 10			Group 3: 2/154 (1.3%) **Headache** Group1: 2/143 (1.4%) Group 2: 3/149 (2%) Group 3: 1/154 (0.6%) **Hypotension/postural hypotension** Group1: 1/143 (0.7%) Group 2: 2/149 (1.3%) Group 3: 0/154 **Malaise** Group1: 2/143 (1.4%) Group 2: 1/149 (0.7%) Group 3: 0/154 **Asthenia/fatigue** Group1: 5/143 (3.5%) Group 2: 1/149 (0.7%) Group 3: 4/154 (2.6%) **Sexual dysfunction** Group1: 0 Group 2: 1/149 (0.7%) Group 3: 2/154 (1.3%) **Acute urinary retention** Group1: 0 Group 2: 0 Group 3: 1/154	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Wilt et al., 2000a[325] **Study design:** Systematic Review – Cochrane. This comparison includes 10 randomised controlled trials. **Setting:** Europe, Canada and US. **Evidence level:** 1++ **Duration of follow-up:** Range 4-52 weeks	**Patient group:** Men with symptomatic benign prostatic hyperplasia. **Inclusion criteria:** treatment duration of at least 4 weeks. **Exclusion criteria:** NR. **<u>All patients</u>** **N:** 5151 Mean age: 65 (45-94) **Racial characteristics** (reported in 6 trials): White: 82%, Asian: 10%, Black 6%, Other : 2% **Discontinuation:** 26% (5-42%) **Mean symptoms score** (7 trials)= 18.8 **Drop outs:** 23 (lost to follow-up, reported as erroneously randomised or unaccounted for and not included in outcome analysis) **<u>Group 1</u>** **N:** 2438 **<u>Group 2</u>** **N:** 1821 **<u>Group 3</u>** **N:** 990	**Group 1: Alpha-blocker** Terazosin (hytrin) – non-uroselective alpha-blocker **Group 2: Placebo** **Group 3: Active controls** Includes phytotherapy, pharmacological or surgical therapies	**AUA symptoms score** (0-35) * extrapolated from graphs	Group1 (n=275): 10.1 (6.35) Group 2 (n=265): 13.2 (6.3) Mean difference: -3.10 [-4.17, -2.03]; 1study P<0.00001	**Funding:** Minneapolis/VISN-13 Centre for Chronic Diseases Outcomes Research (CCDOR), USA. Department of Veterans Affairs Health Services Research and Development Program, USA. **Limitations:** Only 3 of 10 studies described their method of allocation concealment (unclear in remaining 7) **Additional outcomes:** Boyarsky symptom score was reported. **Notes:** Baseline values for symptoms scores, peak urine flow did not differ by treatment group. * NCGC used fixed effect meta-analysis model rather than
			Mean change in AUA symptom score (fixed dose studies, 10mg only)	Group1 (n=976): -7.6 (7.17) Group 2 (n=973): -3.7 (7.16) Mean difference: -3.90 [-4.54, -3.26]; 1study P<0.00001	
			Mean change in peak flow rate (10mg), mL/s	**Flexible dose studies:** MD: 1.40 [0.56, 2.24]; n=424; 2 studies **Fixed dose: 10mg** MD: 1.53 [0.35, 2.70]; n=148; 2 studies **Total:** MD: 1.44 [0.76, 2.13]; 4 studies; p<0.0001	
			Mean change in Peak flow rate (5mg), mL/s	**Flexible dose studies:** MD: 1.40 [0.56, 2.24]; n=424; 2 studies **Fixed dose: 5mg** MD: 0.46 [-0.76, 1.69]; n=153; 2 studies **Total:** MD: 1.10 [0.41, 1.79]; 4 studies; p=0.002	
			Mean peak flow rate (up to 10mg), mL/s	**Dose escalation/Flexible dose studies:** MD: 1.75 [1.09, 2.41]; n=424; 2 studies **Fixed dose:** MD: 0.90 [-1.06, 2.86]; n=153; 1 study **Total:** MD: 1.66 [1.03, 2.29]; 3 studies; p<0.00001	
			Discontinuations, all causes*	**Dose escalation/flexible-dose studies** RR: 0.86 [0.78, 0.95]; 4 studies **Fixed doses: all doses** RR: 0.93 [0.55, 1.55]; 3 studies **Total:** Group 1: 521/1904 (27.4%) Group 2: 555/1621 (34.2%) RR: 0.87 [0.79, 0.95]; p=0.003; 7 studies	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Discontinuations, due to adverse events	**Dose escalation/flexible-dose studies** RR: 1.51 [1.24, 1.85]; 4 studies **Fixed doses: all doses** RR: 1.77 [0.58, 5.40]; 2 studies **Total:** Group 1: 229/1817 (12.6%) Group 2: 140/1607 (8.7%) RR: 1.52 [1.25, 1.86]; p<0.00001	random effect used by Cochrane. Fixed model used as there was no heterogeneity present. Cochrane model detected no significant difference between the interventions.
			Dizziness	Group 1: 252/1802 (14.0%) Group 2: 98/1586 (6.2%) RR: 2.40 [1.92, 3.00]; 6 studies; p=<0.00001	
			Asthenia	Group 1: 153/1736 (8.8%) Group 2: 62/1566 (4.0%) RR: 2.42 [1.78, 3.28]; 5 studies; p=<0.00001	
			Headache	Group 1: 40/749 (5.3%) Group 2: 25/555 (4.5%) RR: 1.24 [0.76, 2.01]; 5 studies; p=0.39	
			Postural hypotension	Group 1: 57/1655 (3.4%) Group 2: 8/1487 (%) RR: 5.52 [2.71, 11.24]; 4 studies; p=<0.00001	
			Impotence/erectile dysfunction	Group 1: 24/386 (6.2 %) Group 2: 15/384 (3.9%) RR: 1.59 [0.85, 2.99]; 2 studies; p=0.15	
			Flu syndrome	RR: 1.22 [0.49, 3.06]; 3 studies; p=0.67	
			Abnormal ejaculation	RR: 1.50 [0.05, 40.91]; 2 studies; p=0.81	
			Rhinitis	RR: 1.34 [0.77, 2.31]; 2 studies; p=0.30	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Wilt et al., 2002[324] **Study design:** Systematic Review – Cochrane. 14 RCTs identified; 6 included in this comparison. **Setting:** Europe, Japan and US. **Evidence level:** 1++ **Duration of follow-up:** Range 4-26 weeks.	**Patient group:** Men with symptomatic benign prostatic hyperplasia. **Inclusion criteria:** treatment duration at least 30 days. **Exclusion criteria:** NR. **<u>All patients</u>** **N:** 3418 **Mean age:** 64 (45 to 85) **Drop outs:** 395 (lost to follow-up, reported as erroneously randomised or unaccounted for and not included in outcome analysis) **Mean IPSS/AUA:** 19.5 (6 studies) **Mean discontinuation rate:** 12% Racial characteristics from one study: White > 99% **<u>Group 1</u>** **N:** 2486 **<u>Group 2</u>** **N:** 781 **<u>Group 3</u>** **N:** 851	**Group 1: Alpha-blockers** Tamsulosin **Group 2: Placebo** **Group 3: Active control** Medical, phytotherapeutic or surgical therapies.	**IPSS/AUA final score by dose**	**Tamsulosin 0.4mg:** MD: -2.55[-3.46, -1.63]; p<0.00001; 2 studies **Tamsulosin 0.8mg:** MD: -3.42 [-4.32, -2.52]; p<0.00001; 2 studies	**Funding:** internal sources: Minneapolis/VISN-23 centre for chronic Disease Outcomes Research, USA. Dept of Veterans Affairs Health Service research and Development Program, USA. **Limitations:** Allocation concealment unclear in all of the studies. **Additional outcomes:** Boyarsky scores. Mean urine flow. Comparisons by dose for adverse events. **Notes:** Converted pooled analysis to fixed model rather than random effect model reported in Cochrane review – expect when there was heterogeneity.
			Mean change in IPSS/AUA	**Tamsulosin 0.4mg:** MD: -2.14[-3.42, -0.87]; p=0.001; 2 studies **Tamsulosin 0.8mg:** MD: -3.15 [-5.01, -1.28]; p=0.0009; 2 studies	
			Qmax	**Tamsulosin 0.4mg:** MD: 0.91 [0.51, 1.32]; p<0.00001; 5 studies **Tamsulosin 0.8mg:** MD: 0.96 [0.50, 1.43]; p<0.00001; 2 studies	
			Mean change in Qmax	**Tamsulosin 0.4mg:** MD: 1.02 [0.68, 1.35]; p<0.00001; 4 studies **Tamsulosin 0.8mg:** MD: 1.07 [0.65, 1.48]; p<0.00001; 2 studies	
			Discontinuation due to adverse events	RR: 1.08 [0.73, 1.62]; p=0.69; 3 studies	
			Discontinuation – all men	RR: 1.02 [0.80, 1.31]; p=0.85; 3 studies	
			Serious adverse events	RR: 1.18 [0.57, 2.43]; p=0.65; 3 stuies	
			Adverse events – cardiovascular	RR: 0.78 [0.40, 1.53]; p=0.47; 1 study	
			Adverse events – digestive system	RR: 0.86 [0.65, 1.12]; p=0.27; 2 studies	
			Adverse events – nervous system	RR: 1.55 [1.24, 1.95]; p=0.0002; 3 studies	
			Adverse events – urogenital system	RR: 2.67 [0.89, 7.96]; p=0.08; 3 studies	
			Adverse events - drug related	RR: 1.07 [0.71, 1.62]; p=0.75; 2 studies	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Dizziness	Group 1: 176/1473 (11.9%) Group 2: 56/714 (7.8%) RR: 1.53 [1.15, 2.02]; p=0.003; 4 studies	
			Headache	Group 1: 211/1473 (14.3%) Group 2: 104/714 (14.6%) RR: 1.00 [0.81, 1.24]; p=1.00; 4 studies	
			Abnormal ejaculation	Group 1: 148/1375 (10.8%) Group 2: 3/686 (0.4%) RR: 21.13 [7.33, 60.87]; p<0.00001; 3 studies	
			Rhinitis	Group 1: 154/1375 (11.2%) Group 2: 41/686 (6.0%) RR: 1.86 [1.34, 2.57]; p=0.0002; 3 studies	
			Asthenia	Group 1: 89/1473 (6.0%) Group 2: 31/714 (4.3%) RR: 1.38 [0.93, 2.04]; p=0.11; 4 studies	
			AUA bother score	**Tamsulosin 0.4mg:** MD: -1.60 [-2.44, -0.76]; 0.00018; 1 study **Tamsulosin 0.8mg:** MD: -2.00 [-2.83, -1.17]; p<0.00001; 1 study	

1 **Evidence Table 10: Alpha blocker vs. 5-alpha reductase inhibitors**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Debruyne et al., 1998[69] ALFIN study **Study design:** RCT double blinded(3 arms) **Setting:** European, multicenter (104 centres). Conducted from Sept 1994 to Dec1996 **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** Lower urinary tract symptoms related to BPH **Inclusion criteria:** ▪ Men 50-75 years ▪ IPSS≥7 ▪ Qmax of ≥5 mL/s but ≤15 mL/s in a total voided volume of >150 mL (no threshold for prostate size was specified, patients with hypertension included) **Exclusion criteria:** ▪ Other concomitant urinary tract disease (prostate cancer, neurogenic bladder dysfunction, bladder stones, chronic bacterial prostatitis, untreated urinary tract infection) ▪ Previous invasive procedure to treat BPH ▪ Associated severe visceral disease ▪ Postural hypotension ▪ Any concomitant medication affecting voiding pattern ▪ Clinically relevant biological abnormalities (aspartate aminotransferase and alanine aminotransferase > 2 times the upper limit of normal, blood creatinine ≥160 micromol/l) ▪ Serum PSA>20ng/ml **<u>All patients</u>** **N:** 1051 **Dropouts:** 133(13%) **Age,** mean ±sd,(yr): 63.3±6.5	All patients received placebo during a 2-week, single blinded run in period **Group 1: Alfuzosin SR** 5mg twice daily **Group 2:** finasteride 5mg once daily **Group 3: Alfuzosin** SR 5mg twice daily + finasteride 5 mg once daily <u>Duration:</u> 6 months	**IPSS change, at 6 months** (mean ±SD)	**Group 1:** -6.3±5.8 **Group 2:** -5.2±5.7 **Group 3:** -6.1±5.6 **P values:** Group 1 vs. 2: 0.01 Group 2 vs. 3: 0.03 Group 1 vs. 3: NR	**Funding:** Synthelabo Recherche, France **Limitations:** ▪ Method of randomisation allocation and concealment was not reported ▪ No report of placebos being used to mask the different number of pills and treatment regimens **Additional outcomes:** Supine blood pressure (systolic and diastolic), change compared to baseline. There were no sig. difference between groups **Notes:** None.
			IPSS improved by >50% at 6 months (% of patients)	**Group 1:** 43 **Group 2:** 33 **Group 3:** 42 **P values:** Group 1 vs. 2: 0.008 Group 2 vs. 3: 0.009 Group 1 vs. 3: NR	
			Qmax change, at 6 months (mean ±SD), ml/s	**Group 1:** 1.8±3.8 **Group 2:** 1.8±4.5 **Group 3:** 2.3±4.7 **P values:** Not sig	
			Qmax increase >30% compared to baseline, % (Subgroup analysis in 497/1051 men who had Qmax <10ml/s at baseline (most likely to be obstructed))	**Group 1:** 51 **Group 2:** 38 **Group 3:** 49 **P values:** Group 1 vs. 2: 0.02 Group 2 vs. 3: 0.06 Group 1 vs. 3: NR	
			Prostate volume change, at 6 months (mean ±SD), ml	**Group 1:** -0.2±14.3 **Group 2:** -4.3±15.0 **Group 3:** -4.9±12.4 **P values:** Group 1 vs. 2: <0.001 Group 2 vs. 3: Not sig Group 1 vs. 3: <0.001	
			PSA change, at 6 months (mean ±SD), ng/ml	**Group 1:** 0.1±2.7 **Group 2:** -1.7±1.9 **Group 3:** -1.4±1.7 **P values:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	IPSS mean ± sd: 15.4±5.5 **Duration of symptoms,** mean ± sd, (yr): 3.4±3.2 **Prostate vol** ,mean ± SD (ml): 41.2±24.0 **PSA serum,** mean ± sd:(ng/ml): 4.0 ± 2.08 **Qmax** mean±sd (ml/sec): 9.9±3.0 **Group 1(Alfuzosin SR)** **N:** 358 **Dropouts:** 40(11%) **Age,** mean ±sd,(yr): 63.2±6.4 **IPSS,** mean ± sd: 15.3±5.5 **Duration since first LUTS,** mean ± sd, (yr): 3.5±3.0 **Prostate vol** ,mean ± SD (ml):41.4±25.7 **PSA serum,** mean ± sd:(ng/ml): 3.0±2.5 **Qmax** mean±sd (ml/sec): 9.7±2.8 **Group 2 (Finasteride)** **N:** 344 **Dropouts:** 39(11%) **Age,** mean ±sd,(yr): 63.0±6.4 **IPSS,** mean ± sd: 15.5±5.2 **Duration since first LUTS,** mean ± sd, (yr): 3.3±3.2 **Prostate vol** ,mean ± SD (ml): 40.9±23.5 **PSA serum,** mean ± sd:(ng/ml): 3.4±2.5 **Qmax** mean±sd (ml/sec): 9.8±2.6 **Group 3: Alfuxosin SR + finasteride** **N:** 349 **Dropouts:** 54(15%) **Age,** mean ±sd,(yr): 63.7±6.7			Group 1 vs. 2: <0.001 Group 2 vs. 3: Not sig Group 1 vs. 3: <0.001	
				Grp 1 N=358 / **Grp 2** N= 344 / **Grp 3** N=349 Withdrawals: 40 / 54 / 39 Withdrawal due to adverse events: 25 / 24 / 18 Lack of efficacy: 3 / 2 / 2	
			Adverse events: **Vasodilatory events (%)** Vertigo/dizziness Headache Postural hypotension/ hypotension Malaise **Sexual disorders (%)** Impotence Ejaculatory failure Decreased libido **Others (%)** Somnolence Asthenia/fatigue Myocardial infarction Acute urine retention	**Grp 1** / **Grp 2** / **Grp 3** 6(1.7) / 4(1.2) / 8(2.3) 7(2.0) / 4(1.2) / 5(1.4) 2(0.6) / 3(0.9) / 2(0.6) 1(0.3) / 1(0.3) / 1(0.3) 8(2.2) / 23(6.7) / 26(7.4) # - (-) / 5(1.5) / 3(0.9) 2(0.6) / 6(1.7) / 7(2.0) -(-) / 2(0.6) / 1(0.3) 4(1.1) / -(-) / 2(0.6) -(-) / 1(0.3) / 1(0.3) 2(0.6) / 1(0.3) / 1(0.3) # p>0.002	
			Asymptomatic orthostatic hypotension during at least one visit **All** **Hypertensive** **≥65 years**	**Grp 1** / **Grp 2** / **Grp 3** (9)/358 / (8)/344 / (8)/349 (13)/112 / (13)/109 / (12)/115 (10)/165 / (10)/147 / (10)/169	

Study details	Patients	Interventions	Outcome measures	Effect size			Comments
	IPSS, mean ± sd: 15.6±5.7 **Duration since first LUTS,** mean ± sd, (yr): 3.4±3.3 **Prostate vol** ,mean ± SD (ml):41.1±22.6 **PSA serum,** mean ± sd:(ng/ml): 3.1±2.7 **Qmax** mean±sd (ml/sec): 10.1±3.5		**Study withdrawals**	**Grp 1** N=358	**Grp 2** N= 344	**Grp 3** N=349	
			Withdrawals	40(11%)	39(11%)	54(15%)	
			Adverse events	25	18	24	
			Lost to follow up	3	6	6	
			Lack of efficacy	3	2	2	
			Other reasons	9	13	22	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Lepor et al., 1996[163] Also reported in Lepor 1998[164] and Lepor 2000[162] **Study design:** RCT double blinded (4 arms) **Setting:** US , outpatient clinics, multicentre (Dec 1992 to March 1995) **Evidence level:** 1+ **Duration of follow-up:** 1 year	**Patient group:** Symptomatic BPH **Inclusion criteria:** ▪ Age 45 to 80 years old ▪ Mean AUA symptom score ≥8 ▪ Mean Qmax ≥4ml/s, ≤15 ml/s, with a minimal voided volume 125ml and a mean residual volume after voiding <300ml **Exclusion criteria:** ▪ Taken the following drugs within the specified time periods: experimental drug < 4 weeks before screening; alpha adrenergic agonist, cholinergic agonist or antagonist, topical beta adrenergic antagonist drug for glaucoma, or any hypertensive drug other than a diuretic or angiotensin converting enzyme inhibitor within 2 weeks before lead in period; estrogens, androgens or androgen inhibitors within 3 months. ▪ Unstable angina, myocardial infarction, transient ischaemic attack, stroke within past 6	**Group 1: Terazosin 10 mg (+ placebo)** (Titrated from 1 mg from days 1 to 3, 2 mg from days 4 to 7, 5 mg from days 8 to 14 and 10 mg from day 15 to end of study. Patients allowed to reduce to 5 mg in the event of adverse events observed) **Group 2: Finasteride 5mg (+ placebo)** Single daily dose at bedtime **Group 3: Terazosin 10 mg + finasteride 5 mg** **Group 4: placebo for terazosin and placebo for finasteride**	**IPSS/AUASS mean ±SD** at 1 year (SD calculated from SEM presented in Lepor1998[164]*	**Group 1:** 10.2 ± 4.97, n=275 **Group 2:** 13.0 ±4.84, n=260 **Group 3:** 9.80 ±5.00, n=278 **Group 4** 13.2±4.88, n=265	**Funding:** Veterans Affairs Medical Research Service, Merck and Abbott **Limitations:** ▪ Values for Qmax and AUA/IPSS had to be extrapolated from graphs, no actual values reported. **Additional outcomes:** AUA symptoms scores started to be significantly different between arms containing terazosin vs. finasteride only or placebo at week 2, reached nadir at week 13 and maintained until week 52. There were no significant differences between terazosin only vs. terazosin + finasteride arm through out study period. The Qmax outcomes had a similar trend, expect that statistical
			IPSS/AUASS mean change (95% CI) at 1 year * [calculated by NCGC team from baseline and 1 year follow up values]	<u>Compared to baseline value</u> **Group 1:** -6.00 [-6.85, -5.15] **Group 2:** -3.20 [-4.04, -2.36] **Group 3:** -6.10 [-3.97, -5.23] **Group 4:** -2.60 [-3.45, -1.75]	
			Difference in IPSS/AUA mean change (95% CI) at 1 year, between groups [calculated by NCGC team]	**MD Gp1-2:** -2.80 [-3.99, -1.61]** **MD Gp1-3:** 0.10 [-1.31, 1.11] **MD Gp1-4:**-3.40 [-4.60, -2.20]** **MD Gp2-3:** 2.90 [1.70, 4.10]** **MD Gp2-4:**-0.60 [-1.79, 0.59] **MD Gp3-4:** -3.50 [-4.71, -2.29]** **p value:<0.001	
			Qmax, ml/s mean ±SD at 1 year (SD calculated from SEM presented in Lepor1998[164]*	**Group 1:** 13.2±4.97, n=275 **Group 2:** 12.1±4.76, n=252 **Group 3:** 13.6±1.66, n=277 **Group 4:** 11.8±4.87, n=264	
			Qmax, ml/s mean change (95% CI) at 1 year compared to baseline* [calculated by NCGCAC team from baseline and 1 year follow up values]	<u>Compared to baseline value</u> **Group 1:** 2.70[2.04, 3.36] **Group 2:** 1.50[0.85, 2.15] **Group 3:** 3.20[2.54, 3.86] **Group 4:** 1.40[0.74, 2.06]	
			Difference in Qmax mean change (95% CI) at 1 year, between groups* [calculated by NCGC team]	**MD Gp1-2:** 1.20 [0.28, 2.12]** **MD Gp1-3:** -0.50 [-1.43, 0.43] **MD Gp1-4:** 1.30 [0.37, 2.23]** **MD Gp2-3:** -1.70 [-2.62, -0.78]** **MD Gp2-4:** 0.10 [-0.82, 1.02] **MD Gp3-4:** 1.80 [0.87, 2.73]** **p value:<0.001	
			Discontinuation due to adverse events	**Group 1:** 18/305 (5.9%) **Group 2:** 15/310 (4.8%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	months, insulin dependent diabetes mellitus, orthostatic hypotension ▪ Previous BPH, obstruction or pelvic surgery ▪ Prostate carcinoma ▪ Urinary tract infections ▪ Renal or hepatic impairment ▪ **<u>All patients</u>** **N:** 1229 (73%) out of 1686 screened **Age Mean (±SD):** **Drop outs:** **<u>Group 1 (Terazosin)</u>** **N:** 305 **Age Mean (±SD):** 65±6 **Dropouts:**49/305 **Prostate volume** (cm^3)**:** 37.5±1.1 **White race** (%)**:** 81 **AUASS:** 16.2±5.5 **Qmax** (ml/s):10.5±2.6 **PSA** serum (ng/ml): 2.2±1.9 **<u>Group 2 (Finasteride)</u>** **N:** 310 **Age Mean (±SD):** 65±7 **Dropouts:**67 **Prostate volume** (cm^3): 36.2±1.0 **White race** (%): 79 **AUASS:**16.2±5.4 **Qmax** (ml/s):10.6±2.5 **PSA** serum (ng/ml): 2.2±1.8			**Group 3:** 24/309 (7.8%) **Group 4:** 5/305 (1.6%) P<0.05	significance between terazosin containing arms vs. finasteride only and placebo arms started at week 4. (based on graph, no actual values reported) **Notes:** Slight differences in values of differences between baseline and 1 year values between Lepor1996 and Lepor1998. Postural hypotension and other adverse events values reported in Lepor1996 was slightly different from 1998 † P values for overall difference among all 4 groups * Values for Qmax and AUASS was obtained from Lepor1998[164]. There are some discrepancies in differences between baseline and 1 year follow up. Values in Lepor 1998 were used.
			Discontinuation – all men	**Group 1:** 49/305 (16%) **Group 2:** 67/310 (22%) **Group 3:** 55/309 (18%) **Group 4:** 51/305 (17%)	
			Reason for withdrawal *	**Grp 1 / Grp 2 / Grp 3 / Grp4** **Total withdrawals** 49 / 67 / 55 / 51 **Reasons** **Adverse Events** 18 / 15 / 24 / 5 **Absolute indication for surgery** 2 / 5 / 2 / 4 **Unrelated medical problem** 4 / 10 / 8 / 10 **Death** 2 / 7 / 2 / 3 **Lost to follow up** 9 / 9 / 5 / 3 **Other** 14 / 21 / 14 / 26	
			Dizziness	**Group 1:** 79/305 (26%) **Group 2:** 26/310 (8%) **Group 3:**66/309 (21%) **Group 4:** 22/305 (7%) P<0.001†	
			Postural hypotension (determined by principal investigator, involving light headedness when standing and not measurable change in blood pressure)	**Group 1:** 23/305 (8%) **Group 2:** 7/310 (2%) **Group 3:** 27/309 (9%) **Group 4:** 3/305 (1%) P<0.001†, Gp 1 +- 2: P=0.004	
			Orthostatic hypotension, at least once during study (A fall of more than 20 mmHg in the systolic blood pressure when patient changed from supine to upright position)	**Group 1:** 45% **Group 2:** 26% **Group 3:** 39% **Group 4:** 30% (Information was provided in replies and correction section NEJM1997; 336:293)	
			Syncope	**Group 1:** 3/305 (1%) **Group 2:** 3/310 (1%) **Group 3:** 5/309 (2.3%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 3: Terazosin 10 mg + finasteride 5 mg **N:** 309 **Age Mean (±SD):** 65±7 **Dropouts:**55 **Prostate volume** (cm^3): 37.2±1.1 **White race** (%): 80 **AUASS:**15.9±5.7 **Qmax** (ml/s):10.4±2.7 **PSA** serum (ng/ml): 2.3±2.0 **Group 4: placebo for terazosin and placebo for finasteride** **N:** 305 **Age Mean (±SD):** 65±7 **Dropouts:**51 **Prostate volume** (cm^3): 38.4±1.3 **White race** (%): 79 **AUASS:**15.8±5.5 **Qmax** (ml/s):10.4±2.6 **PSA** serum (ng/ml): 2.4±2.1			**Group 4:** 0/305 (0%) Not sig
			Asthenia	**Group 1:** 42/305 (14%) **Group 2:** 23/310 (7%) **Group 3:** 43/309 (14%) **Group 4:** 21/305 (7%) P<0.002†, Gp 1 +- 2: P= 0.01
			Headache	**Group 1:** 18/305 (6%) **Group 2:** 19/310 (6%) **Group 3:** 16/309 (5%) **Group 4:** 10/305 (3%) Not sig
			Decreased libido	**Group 1:** 8/305 (3%) **Group 2:** 14/310 (5%) **Group 3:** 15/309 (5%) **Group 4:** 4/305 (1%) P=0.05†, Grp 1 vs. 2: Not sig
			Ejaculatory abnormality	**Group 1:** 1/305 (0.3%) **Group 2:** 6/310 (2%) **Group 3:** 21/309 (7%) **Group 4:** 4 /305 (1%) P<0.001†, Grp 1 vs. 2: Not sig
			Rhinitis	**Group 1:** 20/305 (7%) **Group 2:** 8/310 (3%) **Group 3:** 24/309 (8%) **Group 4:** 14/305 (5%) P=0.02† Grp 1 vs. 2: Not sig
			Sinusitis	**Group 1:** 6/305 (2%) **Group 2:** 4/310 (1%) **Group 3:** 7/309 (2%) **Group 4:** 4/305 (1%) Grp 1 vs. 2: 0.02
			BPH impact index (BII) mean ±SD at 1 year (SD calculated from SEM presented in Lepor1998[164]*	**Group 1:** 2.4±1.66 n=276 **Group 2:** 3.0±1.61 n=259 **Group 3:** 2.0±1.67 n=279 **Group 4:** 3.0±1.63 n=265	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			BPH impact index (BII) mean change (95% CI) at 1 year * [calculated by NCGC team from baseline and 1 year follow up values]	Compared to baseline value Group 1: -1.2±2.4 Group 2: -0.5±2.4 Group 3: -1.7±2.4 Group 4: -0.5±2.4	
			BPH impact index (BII) mean change ±SD(95% CI) at 1 year, between groups [calculated by NCGC team]	MD Gp1-2: -0.7±3.4(-1.0,-0.4)** MD Gp1-3: 0.5±3.4 (0.2,0.8)** MD Gp1-4: -0.5±3.4 (-1.0,-0.4)** MD Gp2-3: 1.2±3.4 (0.9,1.5)** MD Gp2-4: 0.0±3.4 (-0.3,0.3) MD Gp3-4: -1.2±3.0 (-1.5,-0.9)** **P<0.001	
			Prostate volume, ml, ±SD at 1 year (SD calculated from SEM presented in Lepor1998[164]*	**Group 1:** 38.0±21.5 n=271 **Group 2:** 30.1±20.8, n=252 **Group 3:** 30.2±21.7, n=275 **Group 4:** 38.9±25.2, n=258	
			Prostate volume, ml, mean change (95% CI) at 1 year * [calculated by NCGC team from baseline and 1 year follow up values]	Compared to baseline value Group 1: 0.5±21.57 Group 2: -6.1±20.80 Group 3: -7.0±21.72 Group 4: 0.5±25.20	
			Difference in prostate volume mean change (95% CI) at 1 year, between groups [calculated by NCGC team]	Change in AUA between groups, at 1 year MD Gp1-2: 6.6(3.0, 10.2) ** MD Gp3-1: -7.5(-11.1,-3.9) ** MD Gp1-4: 0(-4.0, 4.0) MD Gp3-2: -0.9(-4.5, 2.7)** MD Gp2-4: -6.6(-10.6, -2.6) ** MD Gp3-4: -7.5(-11.5,-3.5) ** **p value:<0.001	

See Evidence Table 9 Alpha-blockers vs. placebo for Kirby et al., 2003[147]

See Evidence Table 2: How does PSA predict symptom progression (in terms of symptom score)? for McConnell et al., 2003[170].

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Rigatti et al, 2003[252] MICTUS study **Study design:** RCT double blinded **Setting:** Italian, multicenter (50 centres) **Evidence level:** 1+ **Duration of follow-up:** 52 weeks	**Patient group:** Lower urinary tract symptoms related to benign prostatic hyperplasia **Inclusion criteria:** ▪ men between 50 and 80 y with symptomatic LUTS/BPH ▪ I-PSS ≥13 ▪ Qmax between 4 and 15 ml/s Total Symptom Problem Index (SPI) score ≥7. ▪ Post-void residual volume (PVR: evaluated by ultrasonography) <400 ml ▪ PSA level <3 or 3–10 ng/ml (provided that prostate cancer was ruled out by the investigator according to the usual procedure in the centre). **Exclusion criteria:** ▪ Known history or a diagnosis of urological disturbances, cardiovascular diseases, neurological diseases, hepatic or renal insufficiency ▪ Clinically significant abnormalities in haematological and biochemical tests ▪ Took an alpha-1-adrenoreceptor antagonist (A-1-ARA) or phytotherapy in the 6 weeks prior to the study or finasteride in the 6 months prior to the study. ▪ Required concomitant medications influencing pharmacodynamic or pharmacokinetic properties of tamsulosin, in particular A-1-ARA,	During the 2-week, single-blind, placebo run-in period, patients took one capsule of tamsulosin-matching placebo and one tablet of finasteride-matching placebo once daily. **Group 1: Tamsulosin** One capsule of tamsulosin 0.4 mg + one tablet of finasteride-matching placebo once daily **Group 2: Finasteride** One tablet of finasteride 5 mg + one capsule of tamsulosin-matching placebo once daily. Patients were assessed at visit 1 (screening visit) and 2 weeks later (randomisation/baseline visit) during the placebo run-in period.	**IPSS change from baseline at 26 weeks** (mean ±SD)	**Group 1:** -6.3 ±5.5 (-32.0%) **Group 2:** -5.7 ±5.7 (-37.3%) **P value:** 0.080	**Funding:** Boehringer Ingelheim Italy SpA **Limitations:** Method of randomisation allocation and concealment was not reported **Notes:** None.
			IPSS improved by ≥50% at 26 weeks compared to baseline (% of patients)	**Group 1**: 42.5% **Group 2:** 35.6% **P value:** Not sig	
			I-PSS-QoI change from baseline at 26 weeks, (mean±sd)	Group 1: -1.1±1.2 (-31.2%) Group 2: -1.0±1.2 (-25.8%) P value: 0.163	
			Qmax change from baseline at 26 weeks, (mean±sd) ,ml/s	Group 1: 2.4±5.9 (30.7%) Group 2: 1.9±5.1 (21.7%) P value: 0.271	
			Voided volume, change from baseline at 26 weeks, (mean±sd), ml	Group 1: 21.3±152.4 (29.9%) Group 2: 5.2±141.0 (16.4%) P value: 0.043	
				Grp 1 **Grp 2**	
			Number of patients treated	N=196 N= 204	
			Any AE	63 (32.1) 60 (29.4)	
			Serious AE	15 (7.6) 15 (7.4)	
			Discontinued due to AE	19 (9.7) 13 (6.4)	
			Adverse events reported in more than 3% patients)		
			Influenza-like symptoms	12 (6.1) 7 (3.4)	
			Impotence	6 (3.1) 7 (3.4)	
			Abdominal pain	6 (3.1) 5 (2.5)	
			Ejaculation disorder	6 (3.1) 2 (1.0)	
			Study withdrawals	**Grp 1** **Grp 2** N=199 N= 204	
			Adverse events	19(9.7%) 13(6.4%)	
			Lost to follow up	13(6.6) 9(4.4)	
			Lack of efficacy	4(2.0%) 8(3.9%)	
			Non compliance to protocol	4(2.0%) 1(0.5%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	mixed alpha- beta-antagonists, alpha-agonists and anticholinergics. **<u>All patients</u>** **N:** 403 randomised from 441 enrolled Dropouts: see study withdrawals **Age**, mean ±sd,(yr): 63±7.1 **Prostate vol** ,mean ± SD (ml): 39±18.9 **<u>Group 1(Tamsulosin)</u>** **N:** 199 **Dropouts:** 34(17%) at week 26, 63 (31%) at week 52 **IPSS**, mean ± sd: 16.3±5.1 **IPSS-QoL**, mean ± sd: 3.2 (1.0) ***Prostate vol** < 50 ml): 68% **Qmax** mean±sd (ml/sec):10.8±3.7 **Voided volume**, mean±sd, ml 239.5 (118.4) **<u>Group 2(Finasteride)</u>** **N:** 204 **Dropouts:** 24(11.8%) at 26 weeks, 45 (22%) at 52 weeks **IPSS**, mean ± sd: 16.9±5.0 **IPSS-QoL**, mean ± sd: 3.1 (1.1) ***Prostate vol** < 50 ml): 75% **Qmax** mean±sd (ml/sec): 10.8±3.4 **Voided volume**, mean±sd,ml:226.5 ±93.1 * Not statistically significant, calculated by NCGC team using Fisher's exact test	**Treatment period:** 26 weeks + 26 weeks	**Withdrawal of consent** **Other reasons**	16(8.2%) 9(4.4%) 7(3.6%) 5(2.5%)	
			Symptom Problem Index (SPI) ITT population	<u>Baseline</u> **Group 1:** 13.6 ± 4.4, n=193 **Group 2:** 14.0 ± 4.2, n=202 <u>Change at week-26</u> **Group 1:** -5.2±5.0 (-37.4%), n=193 **Group 2:** -4.5±5.0 (-31.5%), n=202 **P value:** 0.055	
			Symptom Problem Index (SPI)): Per protocol population	<u>Baseline</u> **Group 1:** 13.6 ± 4.4, n=130 **Group 2:** 14.1 ± 4.2, n=152 <u>Change at week-26</u> **Group 1:** -5.5 ± 5.0 (-39.6%) **Group 2:** -4.5 ± 4.9 (-31.5%) **P value:** 0.032	
			% Symptom Problem Index (SPI) responders (50% improvement from baseline)	<u>% Patients at week-26</u> **Group 1:** 43.5%, n=193 **Group 2:** 35.1%, n=202	
			Symptom Problem Index (SPI) -storage	<u>Baseline</u> **Group 1:** 6.1 ± 2.4 **Group 2:** 6.2 ± 2.2 <u>Change at week-26</u> **Group 1:** -2.3±2.5 (-34.3%), n=193 **Group 2:** -1.9±2.7 (-22.0%), n=202 **P value:** 0.09	
			Symptom Problem Index (SPI) -voiding	<u>Baseline</u> **Group 1:** 7.5 ± 3.0, n=193 **Group 2:** 7.8 ± 2.7, n=202 <u>Change at week-26</u> **Group 1:** -3.0 ± 3.2(-35.0%) **Group 2:** -2.6 ± 3.1(-27.3%) **P value:** 0.069	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Roehrborn et al 2008 [263] for the 2 year results **Study design:** RCT double blinded(3 arms) **Setting:** International, multicenter (446 investigators in 35 countries) **Evidence level:** 1+ **Duration of follow-up:** This is the results from the 2-year interim results Total: 208 weeks treatment + 16 weeks additional safety follow up(224 total)	**Patient group:** Clinical diagnosis of BPH, prostate size ≥30cc **Inclusion criteria:** ▪ Men 50 years or older ▪ Clinical diagnosis of BPH by medical history and physical examination, including digital rectal examination ▪ IPSS≥ 12 ▪ Qmax of ≥5 mL/s but ≤15 mL/s in a total voided volume of ≥125 mL ▪ Prostate volume≥ 30 cc on TRUS ▪ Total serum PSA ≥1.5 ng/ml **Exclusion criteria:** ▪ Total serum PSA > 10.0 ng/ml ▪ A history or evidence of prostate cancer ▪ Previous surgery to treat BPH ▪ History of AUR within 3 months before study entry. ▪ Postvoid volume >250mL (suprapubic ultrasound) ▪ Use of phytotherapy for BPH within 2 weeks of screening visit or /and predicted need for phytotherapy ▪ Use of any alpha adrenoceptor blockers within 2 weeks of screening visit and/or predicted need to any alpha blocker other than tamsulosin during study ▪ History of postural hypotension, dizziness, vertigo or any other signs and symptoms or orthostasis, which in the opinion of the investigators, could	All patients received placebo run in the 4 weeks run in period. **Group 1: Tamsulosin 0.4mg (+ placebo dutasteride)** **Group 2: dutasteride 0.5mg(+ placebo tamsulosin)** **Group 3: Tamsulosin 0.4 mg + dutasteride 0.5 mg** Duration: 4 years (208 weeks) All administered once daily	**IPSS, at 24 months (mean ±SD) SE**	**Group 1:** 11.9±6.8, SE 0.17 **Group 2:** 11.4±6.4, SE 0.16 **Group 3:** 10.1±6.4, SE 0.16	**Funding:** GSK **Limitations:** ▪ Only interim results available. Final 4-year results will be published at a later date (Autumn2009) **Additional outcomes:** % of responders defined as ▪ 25% or greater, 2points of more improvement in IPSS ▪ 30% or greater improvement in Qmax Qmax improved significantly greater from baseline for combination vs. monotherapies from month-6. IPSS score improvement from baseline of combination vs. dutasteride was
			IPSS, change from baseline at 24 months (mean ±SD) SE	Compared to baseline value **Group 1:** -4.3 ±6.0, SE 0.15 **Group 2:** - 4.9±6.0, SE 0.15 **Group 3:** - 6.2±6.0, SE 0.15 **P value:** < 0.001 for Grp 3 vs Grp1 and Grp 2, P=0.0113 for Grp 1 vs Grp 2	
			IPSS, adjusted mean difference between groups at 24 months**	Group 3 vs Group 1: -1.8 Group 3 vs Group 2: -1.3	
			IPSS-QoL, change from baseline at 24 months (mean ±SD) SE	Compared to baseline value **Group 1:** -1.1 **Group 2:** -1.1 **Group 3:** -1.4 **P value:** < 0.001 for Grp 3 vs Grp1 and Grp 2	
			Patients who improved by more than 3 points on the IPSS at 24 months compared to baseline (%)	**Group 1:** 62 **Group 2:** 65 **Group 3:** 72 **P value:** < 0.001 for Grp 3 vs Grp1 and Grp 2	
			Qmax, ml/s adjusted mean change from baseline** ±sd at 24 months	**Group 1:** 0.9 ± 4.8, SE 0.12 **Group 2:** 1.9 ± 4.8, SE 0.12 **Group 3:** 2.4 ± 4.8, SE 0.12 **P value:** ≤0.003 for Grp 3 vs Grp 1 and Grp 2, P<0.001 for Grp 1 vs Grp 2	
			Prostate volume change from baseline at 24 months, mean %	**Group 1:** 0.0% ± 33.4 SE 0.84% **Group 2:** -28.0% ± 24.3 SE 0.61%	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	be be exacerbated by tamsulosin and putting the subject at risk **<u>All patients</u>** **N:** 4,844 **Dropouts:** **Age**, mean ±sd,(yr): 66.1 ± 7.01 **No. white ethnicity (%):** 4,259 (88) **IPSS** mean ± sd: 16.4 ± 6.16 **Duration since first LUTS** mean±sd, (yr): 5.4 ± 4.84 **<u>Prostate vol</u>** (cc): Mean ± SD total: 55.0 ± 23.58 Median total: 48.9 Mean ± SD transition zone* 29.5 ± 21.97 **PSA serum**, mean ± sd:(ng/ml): 4.0 ± 2.08 **Qmax** mean±sd (ml/sec): 10.7 ± 3.62 **Post-void residual vol**, mean±sd, (ml): 67.7 ± 64.87 **No. sexually active (%):** 3,529 (73) **No. previous α-blocker use (%):** 2,444 (50) **No. previous 5-ARI use (%):** 531 (11) **<u>Group 1(Tamsulosin)</u>** **N:** 1,611 **Dropouts:** **Age**, mean ±sd,(yr): 66.2 ± 7.00 **No. white ethnicity (%):** 1,405 (87) **IPSS**, mean ± sd: 16.4 ± 6.10 **Duration since first LUTS** mean ± sd, (yr): 5.4 ± 4.76 **Prostate vol** (cc): Mean ± SD total: 55.8 ± 24.18 Median total: 49.6			**Group 3:** -26.9% ± 24.6 SE0.62% **P value** < 0.001 for Grp 3 vs Grp 1	significant from month 3, vs. tamsulosin was significant from month 9. IPSS-QOL improvement was significant from months 3 and 12 respectively. **Notes:** "investigator blinding to the treatment was maintained by an independent, unblended reviewer who doubled the PSA values in subjects receiving dutatsteride or combination therapy with the value randomly stated as the doubled value, or 0.1 units higher or lower. Methods published in Siami et al [279] The study recruitment was completed in 2005. The standard deviation values in the results were calculated by the NCCAC team from the SE values reported.
			PSA change from baseline at 24 months , mean %	**Group 1:** +12.1% **Group 2:** -55.0% **Group 3:** -56.0%	
			Any **Serious** **Drug related †** **Leading to study withdrawal** **Drug related, leading to study withdrawal**	**Grp 1** N=1611: 1039(64); 1015(63); 195(12); 209(13); 292(18); 258(16); 130(8); 145(9); 49(3); 48(3) **Grp 2** N= 1623: 1047(65); 193(12); 386(24); 161(10); 81(5) **Grp 3** N=1610 **P value:** P<0.001 for combination vs single treatments for any drug related event †	
			Adverse events occurring in >1% patients Erectile dysfunction Retrograde ejaculation Ejaculation failure Loss of libido Semen volume decreased Altered (decreased) libido Dizziness Breast enlargement Nipple pain Breast tenderness	**Grp 1** N=1611: 61(3.8); 18(1.1); 13(0.8); 14(0.9); 13(0.8); 27(1.7); 27(1.7); 13(0.8); 5(0.3); 5(0.3) **Grp 2** N= 1623: 97(6.0); 10(0.6); 8(0.5); 21(1.3); 5(0.3); 45(2.8); 11(0.7); 29(1.8); 10(0.6); 16(1.0) **Grp 3** N=1610: 119(7.4); 68(4.2); 39(2.4); 27(1.7); 29(1.8); 55(3.4); 26(1.6); 23(1.4); 19(1.2); 16(1.0)	

Study details	Patients	Interventions	Outcome measures	Effect size			Comments
	Mean ± SD transition zone*: 30.5 ± 24.47 **PSA serum,** mean ± sd:(ng/ml): 4.0 ± 2.08 **Qmax mean** ± sd (ml/sec): 10.7 ± 3.66 **Post-void residual vol,** mean ± sd, (ml): 67.7 ± 65.14 **No. sexually active (%):** 1,164 (72) **No. previous α-blocker use (%):** 819 (51) **No. previous 5-ARI use (%):** 172 (11) **Group 2(Finasteride)** **N:** 1,623 **Dropouts:** **Age,** mean ±sd,(yr): 66.0 ± 6.99 **No. white ethnicity (%):** 1,433 (88) **IPSS,** mean ± sd: 16.4 ± 6.03 **Duration since first LUTS** mean ± sd, (yr): 5.3 ± 4.69 **Prostate vol** (cc): Mean ± SD total: 54.6 ± 23.02 Median total: 48.4 Mean ± SD transition zone*: 30.3 ± 21.02 **PSA serum,** mean ± sd:(ng/ml): 3.9 ± 2.06 **Qmax mean** ± sd (ml/sec): 10.6 ± 3.57 **Post-void residual vol,** mean ± sd, (ml): 67.4 ± 63.49 **No. sexually active (%):** 1,189 (73) **No. previous α-blocker use (%):** 820 (51) **No. previous 5-ARI use (%):** 188 (12) **Group 3: Tamsulosin + finasteride** **N:** 1,610 **Dropouts:**		Other adverse events Breast neoplasm Floppy iris syndrome	 0(0) 0(0)	 0(0) 0(0)	 0(0) 0(0)	* In a subset of 656 men. The baseline values were taken 4 weeks after screening, when all men received placebo treatment ** General linear model adjusted for treatment, investigative site cluster, and baseline IPSS

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Age, mean ±sd,(yr): 66.0 ± 7.05 **No. white ethnicity (%):** 1,421 (88) **IPSS**, mean ± sd: 16.6 ± 6.35 **Duration since first LUTS** mean ± sd, (yr): 5.4 ± 5.07 **Prostate vol** (cc): Mean ± SD total: 54.7 ± 23.51 Median total: 48.9 Mean ± SD transition zone*: 27.7 ± 20.20 **PSA serum**, mean ± sd:(ng/ml): 4.0 ± 2.05 **Qmax mean** ± sd (ml/sec): 10.9 ± 3.62 **Post-void residual vol**, mean ± sd, (ml): 68.1 ± 66.01 **No. sexually active (%):** 1,176 (73) **No. previous α-blocker use (%):** 805 (50) **No. previous 5-ARI use (%):** 171 (11)				

Evidence Table 11: Alpha-blockers vs. anticholinergics

See Evidence Table 9 Alpha-blockers vs. placebo for Kaplan et al., 2006[123]

1 **Evidence Table 12 Alpha-blockers vs. phosphodiesterase-5 inhibitors**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kaplan et al., 2007[132] **Study design:** RCT open label **Setting:** single-centre, Department of Urology, Weill Cornell Medical College, NY, USA **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** consecutive men with moderate to severe untreated LUTS and erectile dysfunction **Inclusion criteria:** • Moderate to severe untreated LUTS and self reported erectile dysfunction (not specific cut off points) **Exclusion criteria:** • Contraindications to the study drugs **<u>All patients</u>** **N:** 62 **Mean age:** 63.4 ± 7.6 **Drop outs:** 7 (11%) due to adverse events **<u>Group 1 (Sildenafil)</u>** **N:** 21 **Mean (± SD) Age:** 64 ± 5.9 **Duration of LUTS, mths:** 14.3 ± 2.4 **Duration of ED, mths:** 25.6 ± 5.4 **Frequency:** 9.3 ± 2.6 **Nocturia:** 2.9 ± 0.6 **IPSS, mean± SD:** 17.3 ± 4.3 **IPSS moderate (8-19):** 43% **IPSS severe (>20):** 57% **IIEF-EF domain, mean ± SD:** 14.3 ± 5.2 **IIEF Q3, mean ± SD:** 2.1 ± 1.1 **IIEF Q5, mean ± SD:** 2.3 ± 1.3 **Qmax, mean ± SD, mL/s:** 9.7 ± 3.7 **PVR, mean ± SD, mL:** 46 ± 14.3 **Dropouts:** 2 (10%) **<u>Group 2 (Alfuzosin)</u>** **N:** 20 **Mean (± SD) Age:** 62.6 ± 8.2 **Duration of LUTS, mths, mean ± SD:**	**Group 1:** Sildenafil citrate 25 mg one daily at night **Group 2:** Alfuzosin 10mg once daily after the same meal **Group 3:** Sildenafil citrate 25 mg/day + Alfuzosin 10 mg/day **Examination methods:** Patients assessed at baseline and 12 weeks. IPSS taken and frequency and nocturia quantified with bladder diary. Qmax and PVR also assessed. Q3 frequency of penetration and Q4 frequency of maintained erection were analysed separately.	**IPSS ± SD at 12 weeks** P value calculated by NCGC as *t*-test with equal variances	**Grp 1:** 14.9 ± 4.2 **Grp 2:** 14.6 ± 3.7 **Grp 3:** 13.5 ± 4.2 P value grp 1 v grp 2 = 0.81	**Funding:** NR **Limitations:** ▪ This was an open label study with no randomisation allocation and concealment methods reported. The outcomes are mainly subjective outcomes, and this makes it particularly at risk of biases. **Additional outcomes:** % change from baseline for Qmax, PVR, frequency and nocturia IIEF Q3 % change from baseline and IIEF Q5 % change from baseline **Notes:** **Erectile Dysfunction assessed using the Erectile Function domain score of the 15-question IIEF, ie , ie Q1-5 and Q15 (Maximum score 30).
			IPSS change (%) from baseline at 12 weeks (p change from baseline t-test) Change (mean ±sd) calculated by NCGC from the difference in baseline and follow up values. % values as reported	**Grp 1:** -2.40 ±4.25 (11.8%) p=0.03 **Grp 2:** -2.30 ±3.91(15.6%) p=0.01 **Grp 3:** -2.70 ±3.96 (24.1%) p=0.002	
			Qmax mean± SD P value calculated by NCGC as *t*-test with equal variances	<u>at 12 weeks</u> **Grp 1:** 10.3 ± 2.4 **Grp 2:** 10.5 ± 2.3 **Grp 3:** 11.5 ± 2.9 <u>Change from baseline</u> **Grp 1:** 0.3±3.1 **Grp 2:** 1.1±2.3 **Grp 3:** 2.0±2.6	
			Frequency ± SD at 12 weeks P value calculated by NCGC as *t*-test with equal variances	**Grp 1:** 7.8 ± 1.7 **Grp 2:** 6.4 ± 2.1 **Grp 3:** 6.1 ± 2.2 P value grp 1 v grp 2 = 0.02	
			Nocturia ± SD at 12 weeks P value calculated by NCGC as *t*-test with equal variances	<u>at 12 weeks</u> **Grp 1:** 2.1 ± 0.9 **Grp 2:** 1.8 ± 0.9 **Grp 3:** 1.8 ± 1.1 <u>Change from baseline</u> **Grp 1:**-0.8±0.8 **Grp 2:**-1.3±1.0 **Grp 3:**-1.1±1.0	
			IIEF erectile function domain ± SD at 12 weeks**	**Grp 1:** 21.4 ± 5.7 **Grp 2:** 20.3 ± 5.2	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	12.4 ± 2.3 **Duration of ED, mths, mean ± SD:** 22.5 ± 4.9 **Frequency, mean ± SD:** 8.9 ± 2.5 **Nocturia, mean ± SD:** 3.1 ± 1.1 **IPSS, mean ± SD:** 16.9 ± 4.1 **IPSS moderate (8-19):** 45% **IPSS severe (>20):** 55% **IIEF-EF , mean ± SD:** 17.4 ± 4.9 **IIEF Q3 , mean ± SD:** 2.3± 1.3 **IIEF Q5, mean ± SD:** 2.4 ± 1.2 **Qmax , mean ± SD, mL/s:** 9.4 ± 2.2 **PVR, mean ± SD, mL:** 54 ± 17.8 **Dropouts:** 2 (10%) **<u>Group 3 (Sildenafil + Alfuzosin)</u>** **N:** 21 **Mean (± SD) Age:** 63 ± 6.9 **Duration of LUTS, mths mean±SD:** 13.9±2.7 **Duration of ED, mths, mean±SD:** 26.9±5.4 **Frequency, mean ± SD:** 9.1 ± 2.2 **Nocturia, mean ± SD:** 2.89 ± 0.9 **IPSS , mean ± SD:** 16.2 ± 3.7 **IPSS moderate (8-19):** 48% **IPSS severe (>20):** 52% **IIEF-EF mean± SD:** 16.2 ± 3.7 **IIEF Q3 , mean ± SD:** 2.1 ± 1.1 **IIEF Q5 , mean ± SD:** 2.3 ± 1.3 **Qmax , mean ± SD, mL/s:** 9.5 ± 2.3 **PVR , mean ± SD, mL:** 53 ± 19.8 **Dropouts:** 3 (14%)		P value calculated by NCGC as *t*-test with equal variances	**Grp 3:** 25.7 ± 4.9 P value grp 1 v grp 2 = 0.52	This is different from IIEF-5, which consists of question Q2, Q4, Q5, Q7 and Q15 of the IIEF (maximum score 25). *Q3 - frequency of penetration and Q4 - frequency of maintained erection from the IIEF were analysed separately. % of IIEF change from baseline had been updated to correct publication error in original article.
			IIEF erectile function domain % change from baseline at 12 weeks** (p change from baseline t-test)	**Grp 1:** 49.79%, p=0.01 **Grp 2:** 16.7%, p=0.11 **Grp 3:** 58.6%, p=0.002	
			Adverse Events / **N** / **Withdrawals due to adverse events** / **Dizziness** / **Flushing** / **Dyspepsia** / **Gastric upset**	**Grp 1** / **21** / 2 / 0 / 1 / 1 / 0 **Grp 2** / **20** / 2 / 2 / 0 / 0 / 0 **Grp 3** / **21** / 3 / 1 / 0 / 0 / 2	

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1 **Evidence Table 13: 5-alpha reductase inhibitors vs. placebo**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Abrams et al., 1999[7] **Setting:** multi-centre, world wide **Study design:** RCT double blinded **Evidence level:** 1+ **Duration of follow-up:** 1 year	**Patient group:** Men meeting objective evidence of obstruction after pressure flow studies **Inclusion criteria:** • > 55 years • Ambulatory • Enlarged prostate by DRE • Presence of LUTS **Exclusion criteria:** • PSA > 10 ng/mL • Need for immediate surgery • PVR ≥300 mL • Urethral strictures • Chronic Bacterial prostatitis • Neurogenic bladder • Previous prostate or testicular surgery • Prostate cancer or suspect • Neurogenic bladder • Acute UTI • Use of drugs with anti-androgenic properties or alpha-blockers or plant extracts • History of drug or alcohol abuse • Evidence of renal or hepatic impairment • History of recurrent renal or prostatic calculi **<u>All patients</u>** **N:** 121 (out of 201 screened) **Mean age:** **Drop outs:** 15/121 (12.4%)	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** Uroflowmetry performed at 4, 8, 12 months with voided volume of ≥ 150 mL. Prostate volume measured at baseline and month 12. IPSS assessed at 4, 8, 12 months	**Mean change in IPSS ± SD from baseline at 1 year** **Mean change in Qmax ± SD from baseline at 1 year** **Withdrawals due to adverse events**	**Grp 1:** -4.8 ± 6.4* (n=69) **Grp 2:** -3.3 ± 6.4* (n=37) **P value:** NS **Grp 1:** 1.1 ± 2.5 (n=69) **Grp 2:** -0.1 ± 1.5 (n=37) **P value:** 0.02 **Grp 1** 3 **Grp 2** 3	**Funding:** NR **Limitations:** • Randomisation & allocation concealment method not reported. • Unclear whether examiners or investigators are masked. • Primary outcomes are not changed in symptom score or adverse events **Additional outcomes:** Detrusor pressure Free maximum flow rate **Notes:** Study was designed to detect differences in urodynamic parameters rather than symptom score. Randomisation was on a 2:1 basis * Standard deviation for change from baseline calculated using reported mean difference and confidence intervals for the between group comparison following methods from Cochrane Handbook

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1 (Finasteride 5mg/dayl) **N:** 81 **Mean (± SD) Age:** 68.1 ± 6.1 **IPSS ± SD:** 19.4 ± 6.3 **Qmax ± SD, mL/s:** 6.7 ± 2.4 **Prostate volume ± SD, mL:** 45.4 ± 21.9 **Number obstructed:** 61 **Number equivocal:** 19 **Dropouts:** 12/81 (14.8%) **Group 2 (Placebo 1/day)** **N:** 40 **Mean (± SD) Age:** 67.4 ± 7.2 **IPSS ± SD:** 17.4 ± 6.8 **Qmax ± SD, mL/s:** 7.0 ± 2.0 **Prostate volume ± SD, mL:** 44.8 ± 20.2 **Number obstructed:** 33 **Number equivocal:** 7 **Dropouts:** 3/40 (7.5%)				Study reports that analysis of variance was used to compare baseline to follow up with treatment centre and treatment group as variables.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Andersen et al., 1995[15] **Setting:** multi-centre, 59 centres in 5 Scandinavian countries (Denmark, Finland, Iceland, Norway and Sweden) **Study design:** RCT double blinded **Evidence level:** 1+ **Duration of follow-up:** 24 months	**Patient group:** Men moderate symptoms of BPH **Inclusion criteria:** • ≤ 80 years • Ambulatory and good physical and mental health • Qmax ≥5 ≤ 15 mL/s (at screening or start of placebo run-in) • Enlarged prostate by DRE • At least 2 symptoms indicting moderate BPH (increased frequency of urination or difficulty in urination) but not more than 2 severe symptoms • Serum PSA ≤ 10 ng/mL • PVR ≤ 150 mL **Exclusion criteria:** • Haematuria associated with UTI, prostatitis or bladder carcinoma • Serum creatinine > 150 mmol/L or liver function tests ≥50% above normal • Urethral strictures • Chronic Bacterial prostatitis • Previous prostate or testicular surgery • Prostate cancer • Neurogenic bladder • ≥2 catheterisations for AUR in previous 2 years • Significant abnormalities detected in screening examination • Untreated UTI • Use of drugs with anti-androgenic properties	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** Physical examination including DRE was performed at baseline and months 12 and 24. Symptoms measured at baseline and months 1, 4, 8, 12, 16, 20 and 24 using modified Boyarsky scale (9 questions max score is 54) and obstructive symptoms totalled for Q1-5 as impairment in size and force of urinary stream, hesitancy or delay in starting urination, dribbling, interruption of stream, feeling of incomplete emptying (max score is 30) Flow rates measured using Dantec Urodyn 1000, PVR measured using portable ultrasound device at baseline and 12 & 24 months. Serum PSA at baseline and months 12 & 24. Subset of 416 patients had prostate volume measured by TRUS.	**Mean change in total symptom score from baseline at 24 months** (Boyarsky scale)	**Grp 1:** -2.0 ± 6.2 *(n=347) **Grp 2:** 0.2 ± 7.6 * (n=346) **P value:** <0.01	**Funding:** Merck & Co, Inc. **Limitations:** • Randomisation & allocation concealment method not reported. • Unclear whether examiners or investigators are masked. • Median changes from baseline reported. **Additional outcomes:** Change in total symptom score at 12 months **Notes:** Eligible patients entered 1 month single blind placebo run-in to reduce placebo effect then randomised. Patients who withdrew were included in
			Mean change in obstructive symptom score from baseline at 24 months (Boyarsky scale)	**Grp 1:** -1.5 ± 4.3 * (n=348) **Grp 2:** -0.2 ± 4.7 * (n=344) **P value:** <0.01	
			Mean change in Qmax from baseline at 12 months estimated from graph with confidence intervals	**Grp 1:** 1.2 ± 3.1* (n=308) **Grp 2:** -0.3 ± 3.6* (n=309) **P value:** <0.01	
			Mean change in Qmax from baseline at 24 months	**Grp 1:** 1.5 ± 3.6* (n=308) **Grp 2:** -0.3 ± 3.1* (n=309) **P value:** <0.01	
			Mean change in Prostate volume from baseline at 24 months	**Grp 1:** -19.2 ± 23.1* (n=197) **Grp 2:** 11.5 ± 47.3 * (n=197) **P value:** <0.01	
			Median % change in PSA from baseline at 24 months	**Grp 1:** -52% **Grp 2:** 6% P value < 0.0001	
			Reason for withdrawal § **N** **Adverse Events** **Insufficient response** **Other (lost to follow up, protocol deviation, uncooperative)**	**Grp 1 Grp 2** **353 354** 39 30 13 22 14 12	
			Adverse events – sexual dysfunction	**Grp 1:** 67/353 **Grp 2:** 34/354 P value < 0.01	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	All patients **N:** 707 **Mean age:** 65.5 (range 46-80) **Drop outs:** 130 (18.4%) **Group 1 (Finasteride 5mg/dayl)** **N:** 353 **Mean (range) Age:** NR **Total symptom score:** 13.4 ± NR (n=347) **Total obstructive score:** 8.8 ± NR (n=348) **Qmax ± SD, mL/s:** 10.2 ± NR (n=308) **Prostate volume ± SD, mL:** 40.6 ± NR (n=197) **Dropouts:** 66 (18.7%) see withdrawals**§** **Group 2 (Placebo 1/day)** **N:** 354 **Mean (range) Age:** NR **Total symptom score:** 13.1 ± NR (n=346) **Total obstructive score:** 8.6 ± NR (n=344) **Qmax ± SD, mL/s:** 10.5 ± NR (n=309) **Prostate volume ± SD, mL:** 41.7 ± NR (n=197) **Dropouts:** 64 (18.1%) see withdrawals**§**				analysis using Last observation Carried Forward. Study reports that analysis of variance used to compare outcomes but it unclear what variables were used in the model.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Beisland et al., 1992[28] **Setting:** multi-centre (8) in Sweden and Norway Scandinavian finasteride study group **Study design:** RCT double blinded. Patients and investigators. **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** men with symptomatic urinary obstruction **Inclusion criteria:** • 40-80 years in good physical and mental health with symptoms of urinary obstructions and Qmax <15 ml/s documented by two measurements at screening. • Enlarged prostate by DRE **Exclusion criteria:** • Clinical or laboratory abnormalities **<u>All patients</u>** **N:** 182 **Mean age:** NR **Drop outs:** 14/182 (7.65) **<u>Group 1 (Finasteride 5mg/dayl)</u>** **N:** 94 **Mean (range) Age:** 66.6 (46-80) **Total symptom score, mean ± SD:** 8.8 ± 6.1 **Total obstructive score, mean ± SD:** 2.2 ± 4.0 **Troublesome score, mean ± SD:** **Qmax ± SD, mL/s:** 8.0 ± 3.0 **Prostate volume ± SD, cm³:** 44.2 ± 22.4 **Drop outs:** 7/94 (7.4%) see withdrawals**§** **<u>Group 2 (Placebo 1/day)</u>**	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day Symptoms were assessed using a modified Boyarksy scale modified which comprises 9 questions (max score is 36). Patients were treated as mild if the score was <6, moderate (6-13) and severe if scores were >13. Obstructive symptoms totalled for the following questions: ▪ impairment of size and force of urinary stream ▪ hesitancy or delay in starting the flow of urine ▪ dribbling after urination ▪ feeling of incomplete emptying of the bladder ▪ interruption of urinary stream	**Mean change in Qmax(ml/s) from baseline at 24 weeks**	**Grp 1:** 1.6 ± 1.4* (n=87) **Grp 2:** 1.1 ± 1.4* (n=81) **P value:** 0.022(as reported)	**Funding:** Not stated. Most likely Merck Laboratories, as 4/12 authors were from Merck. . **Limitations:** • Method of randomisation and concealment not reported • A modified Boyarksy scale was used **Additional outcomes:** Change of to total symptom score (Boyarsky scale) from baseline at 12 weeks for finasteride (-2.1) vs. placebo (-0.8) was significant (0=0.0046) for 12 weeks. Change for obstructive symptoms scores were -2.0 vs. -0.7 for 24 weeks (p=0.05) using analysis of covariance DHT level changes from baseline were also reported **Notes:** *Standard deviations for changes from baseline calculated from reported p values between groups using Cochrane methodology Analysis of covariance used to compare baseline parameters
			Median % change in PSA from baseline at 12 weeks months	**Grp 1:** -22.4 **Grp 2:** No change P value < 0.001	
			Median % change in PSA from baseline at 24 weeks months	**Grp 1:** -32.4 **Grp 2:** No change P value < 0.001	
			Mediun % decrease iun prostate volume from baseline at 24 weeks	**Grp 1:** 22.5 **Grp 2:** 1.0 P value < 0.001	
			§ **Reason for withdrawal** (see notes)** **N** **Adverse Events** **No response** **Other**	**Grp 1 Grp 2** 7 7 6 1 0 3 1 3	
			Withdrawal due to sexual adverse events	**Grp 1 Grp 2** 1 1	
			Adverse events **N** **Insomnia and depression** **Deep vein thrombosis** **Urinary retention** **Decreased libido** **Impotence**	**Grp 1 Grp 2** **93 48** 1 0 1 0 1 0 1 0 4 4	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 88 **Drop outs:** 3/88 (3.4%) **Mean (range) Age:** 68.0 (54-79) **Total symptom score, mean ±S D:** 7.8 ± 4.9 **Total obstructive score, mean ± SD:** 1.1 ± 3.3 **Troublesome score, mean ± SD:** 6.8 ± 3.9 **Qmax ± SD, mL/s:** 7.6 ± 3.1 **Prostate volume ± SD, cm³** 43.8 ± 24.1				and % change from baseline. **6 year follow up reported by Ekman et al.,1998 [78]. The number of drop outs reported in this report was 14. Adverse events reported in more detail in BEISLAND1992.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Byrnes et al., 1995[40] **Setting:** multicentre, USA **Study design:** RCT double blinded **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Men attending community-based clinics for treatment of BPH **Inclusion criteria:** • Clinical diagnosis of BPH based on moderate to severe symptoms with prostate gland enlargement on DRE • PSA ≤ 10 ng/mL **Exclusion criteria:** • Urethral strictures • Previous prostate surgery • Pelvic radiotherapy • Chronic Bacterial prostatitis • Neurogenic bladder • Recurrent UTI • Use of drugs with anti-androgenic properties • Use of hormonal therapy affecting prostate • Prostate cancer or suspected **<u>All patients</u>** **N:** 2417 included in safety analysis, 2342 in efficacy analysis **Mean age:** 65 **Drop outs:** 465 (19.2%) **<u>Group 1 (Finasteride 5mg/dayl)</u>** **N:** 1821 randomised 1759 efficacy **Mean (range) Age:** 65 (42-91) **White/other:** 1226 **Black:** 285 **Hispanic:** 248 **AUA symptom score mild (<8):** 33	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** Physical examination including DRE was performed at baseline and 12 mths. Serum dihydrotestosterone measured at baseline and mths 6 & 12 AUA-7 Symptom score, BPH Impact Index (BII) used for HRQoL, Patient satisfaction with urinary condition as extra question (0-6) and additional questions from modified BSIA instrument to measure interference with activities and extra question about adjustment of activities to cope	**Mean change in AUA-7 symptom score from baseline at 3 months** Estimated from graph with confidence intervals. Numbers at follow up not clear so total for efficacy analysis used.	**Grp 1:** -3.3 ± 7.7* (n=1759) **Grp 2:** -2.6 ± 7.8* (n=583) **P value:** <0.05	**Funding:** Merck & Co, Inc. **Limitations:** • Randomisation & allocation concealment method not reported.. • Unclear whether examiners or investigators are masked. • Numbers of patients remaining at each time point not clear for AUA score. **Additional outcomes:** BPII + patient satisfaction question at 12 mths, activities of living score at 12 mths, general adjustment question at 12 mths, investigator global assessment at 12 mths **Notes:** Eligible patients entered 1 month single blind placebo run-in. Men with moderate to severe symptoms after run-in with good compliance were randomised in 3:1 ratio. *Standard deviations for
			Mean change in AUA-7 symptom score from baseline at 6 months estimated from graph with confidence intervals	**Grp 1:** -4.1 ± 7.7* (n=1759) **Grp 2:** -3.3 ± 7.8* (n=583) **P value:** <0.05	
			Mean change in AUA-7 symptom score from baseline at 12 months estimated from graph with confidence intervals	**Grp 1:** -4.6 ± 9.6* (n=1759) **Grp 2:** -3.3 ± 8.6* (n=583) **P value:** <0.05	
			Mean change in BPII at 12 months	**Grp 1:** -1.2 ± 4.2* (n=1711) **Grp 2:** -0.9 ± 3.7* (n=575) **P value:** <0.04 (ANOVA)	
			Mean change in patient global assessment at 12 months	**Grp 1:** 4.9 ± 2.1.2* (n=1714) **Grp 2:** 4.7 ± 1.2* (n=575) **P value:** 0.0001 (ANOVA)	
			% Patients rating themselves "better" at 12 mths	**Grp 1:** 56.2 % **Grp 2:** 44.2 % **P value:** <0.001	
			% Investigators rating patients "better" at 12 mths	**Grp 1:** 55.3 % **Grp 2:** 45.8 % **P value:** <0.001	
			Reason for withdrawal § **Total withdrawals** **Adverse Events** **Lost to follow up** **Treatment failure**	**Grp 1 Grp 2** **343 122** 100 28 81 30 62 24	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	AUA symptom score moderate (8-19): 1001 **AUA symptom score severe (20-35):** 724 **AUA symptom score unknown:** 1 **BII:** 5.1 CI95% 4.9-5.2 **BII + patient satisfaction:** 8.8 CI95% 8.6-9.0 **Activities of living score:** 13.3 CI95% 12..8-13.8 **Adjustment question:** 1.4 CI95% 1.3-1.5 **Dropouts:** 343 (19.4%) for reasons see**§** **<u>Group 2 (Placebo 1/day)</u>** **N:** 596 randomised 583 efficacy **Mean (range) Age:** 65.1 (45-91) **White/other:** 397 **Black:** 95 **Hispanic:** 91 **AUA symptom score mild (<8):** 13 **AUA symptom score moderate (8-19):** 335 **AUA symptom score severe (20-35):** 235 **AUA symptom score unknown:** 0 **BII:** 5.0 CI95% 4.8-5.3 **BII + patient satisfaction:** 8.6 CI95% 8.3-9.0 **Activities of living score:** 12.8 CI95% 11.9-13.7 **Adjustment question:** 1.3 CI95% 1.2-1.4 **Dropouts:** 122 (20.4%) for reasons see**§**	with urinary symptoms were taken at baseline and 3 mth intervals. Patient and investigator global assessment of change in urologic status also rated from 1 (much worse) to 7 (much better) every 3 mths. Patients with visual impairment had questionnaires read to them and Spanish versions provided.	**Protocol violation or other** **Adverse events** **N randomised** **Impotence**** **Libido decrease**** **Ejaculation disorder**** **Withdrawal due to sexual adverse events** **Acute urinary retention** ** Possibly, probably or definitely drug related	100 40 no significant differences between groups **Grp 1 Grp 2** **1821 596** 102 13 p < 0.0001 53 6 p = 0.008 38 3 p = 0.009 27 3 p = 0.06 11 4 p = 0.77	changes from baseline calculated using confidence intervals and Cochrane methodology Study reports that analysis of variance was used to compare baseline to follow up with race and treatment-by-race as variables. It is unclear whether the results presented have been adjusted for these variables.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Finasteride Study Group, 1993[92] **Setting:** multicentre worldwide **Study design:** RCT double blinded **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Men with BPH and symptoms of BOO **Inclusion criteria:** • 40-80 years • Good physical and mental health • Qmax < 15 mL/s (from 2 measurements) • Prostate volume ≥ 30 mL **Exclusion criteria:** • Bacterial prostatitis • Previous prostate or testicular surgery • Prostate cancer • PSA ≥ 40 ng/mL • PVR > 350 mL • Neurogenic bladder • Repeated catheterisations • Use of drugs with anti-androgenic properties **<u>All patients</u>** **N:** 750 (all treatment arms) **Mean age:** NR **Drop outs:** NR **<u>Group 1 (Finasteride 5mg/dayl)</u>** **N:** 249 **Mean (range) Age:** 66 (46-83) **Total obstructive score (max 20):** 11.2 ± 3.8 **Total symptom score (max 36):** 18.6 ± 6.0 **Qmax ± SD, mL/s:** 9.2 ± 4.0	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Group 3:** Finasteride 1 mg 1/day Results and baseline characteristics reported for normal dose finasteride arm 5mg/day only **Examination methods:** At baseline and months 3, 6 & 12 prostate volume measured by TRUS and Qmax measured at by Dantec Urodyn 1000 uroflowmeter, Boyarsky symptom questionnaire taken (9 questions). Testosterone, dihydrotestosterone, luteinising hormone measured at baseline and weeks 2, 8, 16, 24 and 9 and 12 months. Thyroxine and thyroid stimulating hormone measured at baseline and months 3 & 6. PSA measured at -2, 12, 24 weeks and 9 & 12 months	**Median change in total symptom score** (Boyarsky scale) **from baseline at 12 months** Estimated from graph	**Grp 1:** 3.3 **Grp 2:** 2.0 P value = signif (value NR)	**Funding:** Merck **Limitations:** • Randomisation & allocation concealment method not reported. Unclear whether examiners or investigators are masked. • Median changes from baseline reported. • Dropouts not clearly reported **Additional outcomes:** % change from baseline for plasma dihydrotestosterone **Notes:** Eligible patients entered a 2 week month single blind placebo run-in to reduce placebo effect then
			Median change in Qmax from baseline at 12 months Estimated from graph	**Grp 1:** 1.38 **Grp 2:** 0.42 P value = 0.025	
			% patients achieving ≥ 3 mL/s flow increase	**Grp 1:** 31.0 % **Grp 2:** 21.0 %	
			Median % change in prostate volume from baseline at 12 months	**Grp 1:** 22.4 % **Grp 2:** 5.0 % P value < 0.001	
			Median % change in PSA from baseline at 12 months	**Grp 1:** 46.0 % **Grp 2:** 0 (no change) % P value < 0.001	
			Adverse Events **N** **Withdrawals due to adverse events** **Impotence** **Acute urinary retention**	**Grp 1 Grp 2** **249 255** 1 0 12 1 p <0.001 3 3	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Prostate volume ± SD, mL: 47.0 ± 20.8 **PSA ± SD, ng/mL:** 5.8 ± 6.7 **Dropouts:** Not clear. 1 patients withdrew due to impotence but others not mentioned **<u>Group 2 (Placebo 1/day)</u>** **N:** 255 **Mean (range) Age:** 66 (46-81) **Total obstructive score (max 20):** 11.1 ± 3.7 **Total symptom score (max 36):** 18.2 ± 5.9 **Qmax ± SD, mL/s:** 8.6 ± 3.4 **Prostate volume ± SD, mL:** 46.3 ± 23.4 **PSA ± SD, ng/mL:** 5.7 ± 7.2 **Dropouts:** NR				randomised. Analysis of variance used to compare outcomes with treatment centre and treatment group and treatment-centre interaction as model parameters

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Gormley et al., 1992[105] Finasteride study group **Setting:** multi-centre, 25 centres in USA and 5 in Canada **Study design:** RCT double blinded **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Men with BPH and symptoms of urinary obstruction **Inclusion criteria:** • 40-83 years • Enlarged prostate gland enlargement on DRE • Qmax < 15 mL/s with voided volume of ≥ 150 mL • Men with very low urinary flow rates unless at risk for total obstruction **Exclusion criteria:** • Prostate cancer or suspected • PVR > 350 mL • Serum PSA ≥ 40 µg/L • UTI • Chronic prostatitis • Neurogenic bladder **<u>All patients</u>** **N:** 895 (all study arms) **Mean age:** 64 **Drop outs:** 105/895 (11.7%) **<u>Group 1 (Finasteride 5mg/dayl)</u>** **N:** 297 **Mean (range) Age:** 64 (40-80) **White:** 286 **Black:** 6 **Other:** 5 **Total Symptom score ± SD:** 10.2 ± 5.5 **Obstructive symptom score ± SD:** 7.0 ± 3.6 **Qmax ± SD, mL/s:** 9.6 ± 3.7	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Group 3:** Finasteride 1 mg 1/day Results and baseline characteristics reported for normal dose finasteride arm 5mg/day only **Examination methods:** Men were examined monthly by the same investigator for symptoms (Boyarsky – 9 questions max score 36), obstructive symptoms (Boyarsky – first 5 questions max score 20), side effects and compliance. Flow rate measured using Urodyn 1000, PVR using TRUS. Prostate volume measured using MRI at baseline, 3, 6 & 12 mths;, ophthalmic examination at 12 mths; serum amino-transferases, urea	**Mean symptom score(Boyarsky) at 12 months** **Mean obstruction score(Boyarsky) at 12 months** **Mean Qmax at 12 months** **Mean Prostate volume at 12 months** **Reason for withdrawal *** **Adverse events **** ** Possibly, probably or definitely drug related	**Grp 1:** 7.5 ± 5.2 (n=257) **Grp 2:** 8.8 ± 6.1 (n=263) **P value:** <0.05 **Grp 1:** 5.1 ± 3.6 (n=257) **Grp 2:** 5.9 ± 3.8 (n=263) **P value:** <0.001 **Grp 1:** 11.2 ± 4.7 (n=257) **Grp 2:** 9.8 ± 3.7 (n=263) **P value:** <0.001 **Grp 1:** 47.5 ± 23.6 (n=257) **Grp 2:** 59.8 ± 39.4 (n=263) **P value:** <0.001 **Grp 1 / Grp 2** **Total: 40 / 37** **Adverse Events:** 16 / 18 **Lost to follow up:** 3 / 4 **Treatment failure:** 12 / 9 **Other:** 9 / 6 **Grp 1 / Grp 2** **N randomised: 297 / 300** **Impotence:** 10 / 5 **Libido decrease:** 14 / 4 p <0.05 **Ejaculation disorder:** 13 / 5 p <0.05 **Breast pain:** 1 / 0 **Digestive system:** 8 / 6 **Dizziness:** 0 / 2 **Headache:** 2 / 2 **Asthenia:** 3 / 3 **lens opacity:** 0 / 2 **lens change:** 2 / 0 **Withdrawal due to sexual dysfunction:** 4 / 1	**Funding:** Merck & Co, Inc. **Limitations:** • Randomisation & allocation concealment method not reported. • Unclear whether key examiners or investigators are masked. **Additional outcomes:** Median PSA at follow up, Median change in prostatic volume % at follow up. Mean Qmax + SE at follow up as graph. **Notes:** Eligible patients entered 2 week single blind placebo run-in. ITT analysis with missing data from last observation carried forward.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Prostate volume, mL: 58.6 ± 30.5 **Serum PSA ± SD, µg/L:** 3.6 ± 4.2 **PVR ± SD, mL:** 73 ± 89 **Dropouts:** 40 (13%) for reasons see* **<u>Group 2 (Placebo 1/day)</u>** **N:** 300 **Mean (range) Age:** 64 (45-82) **White:** 288 **Black:** 8 **Other:** 4 **Total Symptom score ± SD:** 9.8 ± 5.3 **Obstructive symptom score ± SD:** 6.7 ± 3.5 **Qmax ± SD, mL/s:** 9.6 ± 3.5 **Prostate volume, mL:** 61.0 ± 36.5 **Serum PSA ± SD, µg/L:** 4.1 ± 4.8 **PVR ± SD, mL:** 73 ± 91 **Dropouts:** 37 (12%) for reasons see*	nitrogen, creatinine, Na, K, Ca and glucose measured every 3 mths. Compliance determined by counting number of tablets remaining and serum dihydrotestosterone measurements			Analysis of variance used to compare outcomes with treatment centre and treatment group as model parameters..

See Evidence Table 10 Alpha blocker vs. 5-alpha reductase inhibitors for Lepor et al., 1996[163] .

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Marberger et al., 1998[181] PROWESS study group **Setting:** multi-centre, 285 worldwide **Study design:** RCT double blinded (patients and investigators) **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient group:** Men moderate symptoms of BPH **Inclusion criteria:** • 50 - 75 years • Good general health • Enlarged prostate gland enlargement on DRE • Qmax 5 - 15 mL/s with a voided volume ≥ 150mL (2 measurements) • No more than 2 severe symptoms on modified Boyarsky scale • PSA < 10 ng/mL • PVR < 150 mL **Exclusion criteria:** • Dysuria, haematuria • Previous prostate or bladder surgery • Concurrent use of alpha-blockers or anti-androgens • Recurrent UTI • Chronic prostatitis • Bladder cancer • Abnormalities on clinical examination • Liver function tests >50% above upper limit of normal • Allergies • History of drug or alcohol abuse • Prostate cancer or suspected • Neurogenic bladder • Urinary catheterisation for AUR twice during previous 2 years	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** Total and obstructive symptom score on modified Boyarksy scale measured at baseline and every 4 months. Prostate volume measured at baseline and 1 and 2 years by TRUS.	**Mean change ± SD in total symptom score at 1 year (Boyarsky scale)**	**Grp 1:** -2.9 ± NR **Grp 2:** -1.9 ± NR **P value:** ≤0.001 (ANOVA)	**Funding:** Merck & Co, Inc. manufacturers of finasteride **Limitations:** Standard deviations for Qmax were not reported. **Additional outcomes:** Change in obstructive symptom score at 1 and 2 years % change in prostate volume **Notes:** Eligible patients entered 1 month single blind placebo run-in prior to computer generated randomisation. Sample size of 3000 to detect change in symptom score of 1.4 ± 7 from baseline and change of 1.1 ± 5 mL/s in Qmax
			Mean change ± SD in total symptom score at 2 years(Boyarsky scale)	**Grp 1:** -3.2 ± NR **Grp 2:** -1.5 ± NR **P value:** ≤0.001 (ANOVA)	
			Mean change in Qmax ± SD at 1 year	**Grp 1:** 1.2 ± NR **Grp 2:** 0.6 ± NR **P value:** 0.01 (ANOVA)	
			Mean change in Qmax ± SD at 2 year	**Grp 1:** 1.5 ± NR **Grp 2:** 0.7 ± NR **P value:** 0.002 (ANOVA)	
			Mean % change in prostate volume from baseline at 1 year	**Grp 1:** -13 ± NR **Grp 2:** +5 ± NR **P value:** ≤0.01 (ANOVA)	
			Mean % change in prostate volume from baseline at year	**Grp 1:** -15 ± NR **Grp 2:** +9 ± NR **P value:** ≤0.001(ANOVA)	
			Reason for withdrawal *	**Grp 1** **Grp 2** **Total discontinuations** **331** **360** **Adverse Events** 111 144 **Lack of improvement** 50 64 **Protocol deviation** 25 14 **Patient compliance** 40 40 **Loss to follow up** 70 55 **Other** 36 47	
			Drug related adverse events (>1%)	**Grp 1** **Grp 2** **Total in safety analysis** **1577** **1591** **Decreased libido** 63 44 **Impotence** 104 74 p <0.05 **Ejaculation disorder** 33 9 p <0.05 **Urinary retention** 17 35 p <0.05	

Study details	Patients	Interventions	Outcome measures	Effect size			Comments
	• Poor compliance during placebo run in. • Planned fatherhood **<u>All patients</u>** **N:** 2902 in efficacy analysis (368 excluded from some centres for poor clinical practice) and 3168 included in safety analysis **Mean age:** **Drop outs:** **<u>Group 1 (Finasteride 5mg/dayl)</u>** **N:** 1450 **Mean (± SD) Age:** 63.0 ± 6.3 **Total Symptom score (Boyarksy) ± SD:** 14.5 ± 7.3 **Obstructive score ± SD:** 9.3 ± 4.6 **Qmax ± SD, mL/s:** 11.2 ± 5.9 **Prostate volume, mL:** 38.7 ± 20.1 **Dropouts:** 331/1450 (23%) see* **<u>Group 2 (Placebo 1/day)</u>** **N:** 1452 **Mean (± SD) Age:** 63.4 ± 6.1 **Total Symptom score (Boyarksy) ± SD:** 14.3 ± 7.2 **Obstructive score ± SD:** 9.1 ± 4.5 **Qmax ± SD, mL/s:** 10.9 ± 3.6 **Prostate volume, mL:** 39.2 ± 20.2 **Dropouts:** 360/1452 (23%) see*		**Asthenia/fatigue** **Rash** **Headache** **Withdrawal due to sexual problem** **UTI** **Hypertension** **Myocardial infarction or angina** **Abdominal Pain** **Gastric problems (pain, gastritis, diarrhoea)** **Respiratory (infection or bronchitis)** **Influenza or pharyngitis** **Back pain** **Dysuria** **Haematuria** **BPH worsening**	11 17 33 22 28 48 44 38 72 55 57 27 16 10 35	24 21 36 16 40 58 29 36 64 61 55 46 13 24 64	p <0.05 p <0.05 p <0.05	and 11% ± 40 change in prostate volume of power=99% and α 0.05. Data collected for those patients that discontinued ** Mean change and SD from baseline were estimated from graphs for mean change and standard error. Analysis of variance used to compare outcomes but it's not clear what variables have been included in the model

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
McConnell et al., 1998[190] Study also reported in Roehrborn et al., 2000[258] PLESS study group **Setting:** multi-centre, 95 centres in USA **Study design:** RCT double blinded **Evidence level:** 1+ **Duration of follow-up:** 4 years	**Patient group:** Men moderate to severe symptoms of BPH **Inclusion criteria:** • Enlarged prostate gland enlargement on DRE • Qmax < 15 mL/s • PVR < 300 mL **Exclusion criteria:** • Previous prostate or bladder surgery • Concurrent use of alpha-blockers or anti-androgens • Recurrent UTI • Chronic prostatitis • PSA >10 ng/mL (those with PSA > 4 ng/mL had a TRUS biopsy to rule out prostate cancer) **<u>All patients</u>** **N:** 3040 randomised but 1 centre closed (n=24) so data available for 3016 patients **Mean age:** **Drop outs:** 1157/3040 (38%) **<u>Group 1 (Finasteride 5mg/dayl)</u>** **N:** 1524 **Mean (± SD) Age:** 64.0 ± 6.3 **White:** 94.9 % **Black:** 3% **Other:** 2.1% **Quasi AUA Symptom score ± SD:** 15.2 ± 5.6 **Qmax ± SD, mL/s:** 10.9 ± 3.9	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** Patients were evaluated every 4 months fpr symptom score, flow rate (>150mL) and side effects. PSA was measured every 4 months for 1 year and every 8 months thereafter. Blood components and DRE performed every year and biopsy if clinically indicated. Prostate volume was measured in a subset of 10% of patients at 13 sites using MRI. At the beginning of the study symptom score was assessed using a symptom score validated by Bolognese et al., 1992 comprising the same components as the AUA but with a slightly different score. The AUA symptom score was then adopted and the data from both	**Mean change ± SD in Quasi-AUA score at 1 year****	**Grp 1:** -2.4 ± 4.5 (n=1314) **Grp 2:** -1.6 ± 4.5 (n=1296) **P value:** NR	**Funding:** Merck & Co, Inc. manufacturers of finasteride **Limitations:** • High discontinuation rate at >30% for both arms though efforts were made to retrieve data (see notes) • Unclear whether key examiners or investigators are masked. **Additional outcomes:** % change in prostate volume **Notes:** Eligible patients entered 1 month single
			Mean change ± SD in Quasi-AUA score at 2 year**	**Grp 1:** -2.9 ± 6.4 (n=1153) **Grp 2:** -1.3 ± 6.2 (n=1101) **P value:** NR	
			Mean change ± SD in Quasi-AUA score at 3 year**	**Grp 1:** -3.1 ± 6.1 (n=1047) **Grp 2:** -1.3 ± 5.8 (n=961) **P value:** NR	
			Mean change ± SD in Quasi-AUA score at 4 year**	**Grp 1:** -3.3 ± 5.8 (n=965) **Grp 2:** -1.1 ± 5.5 (n=853) **P value:** NR	
			Mean change in Qmax ± SD at 1 year**	**Grp 1:** 1.3 ± 3.1 (n=928) **Grp 2:** 0.2 ± 3.0 (n=899) **P value:** NR	
			Mean change in Qmax ± SD at 2 year**	**Grp 1:** 1.8 ± 5.6 (n=786) **Grp 2:** 0.4 ± 5.4 (n=720) **P value:** NR	
			Mean change in Qmax ± SD at 3 year**	**Grp 1:** 1.8 ± 5.3 (n=691) **Grp 2:** 0.0 ± 4.9 (n=608) **P value:** NR	
			Mean change in Qmax ± SD at 4 year**	**Grp 1:** 2.0 ± 4.9 (n=588) **Grp 2:** 0.2 ± 4.9 (n=496) **P value:** NR	
			Mean change (%) in prostate volume at 1 year	**Grp 1:** -16 (n=144) **Grp 2:** +5 (n=136) **P value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Prostate volume, mL: 54 ± 25 **Serum PSA ± SD, µg/L:** 2.8 ± 2.1 **Dropouts:** 524/1524 (34%) see* **<u>Group 2 (Placebo 1/day)</u>** **N:** 1516 **Mean (± SD) Age:** 63.9 ± 6.6 **White:** 995.5.9 % **Black:** 3% **Other:** 1.5% **Quasi AUA Symptom score ± SD:** 15.2 ± 5.8 **Qmax ± SD, mL/s:** 11.1 ± 4.8 **Prostate volume, mL:** 55 ± 26 **Serum PSA ± SD, µg/L:** 2.8 ± 2.1 **Dropouts:** 633/1516 (42%) see *	scores combined as a Quasi AUA 0-34 points (1-5 for 6 questions and 1-4 for1 question)	**Mean change (%) in prostate volume at 2 year**	**Grp 1:** -18 (n=130) **Grp 2:** +9 (n=119) **P value:** NR	blind placebo run-in prior to computer generated randomisation stratified according to centre Those discontinuing study were also contacted at 6 months after discontinuing study and at the 4 year end point. Complete outcome data was collected for 92% in both treatment groups including discontinuations. ** Mean change and SD from baseline were estimated from graphs for mean change and standard error.
			Mean change (%) in prostate volume at 3 year	**Grp 1:** -17 (n=116) **Grp 2:** +11(n=98) **P value:** NR	
			Mean change (%) in prostate volume at 4 year	**Grp 1:** -17 (n=102) **Grp 2:** +14 (n=85) **P value:** NR	
			Reason for withdrawal *	**Grp 1** **Grp 2** **Total discontinuations** **524** **633** **Adverse Events** 176 166 **Lack of improvement** 99 104 **Worsening of disease** 23 56 **Need for surgery or medical therapy** 80 172 **Loss to follow up** 52 36 **Other** 94 99	
			Spontaneous or precipitated AUR Acute urinary retention defined as spontaneous (no precipitating factors) or precipitated (stroke, UTI, pre surgery etc)	**Grp 1:** 42/1503 **Grp 2:** 99/1513 **P value:** NR	
			Drug related adverse events (>1%) in year 1	**Grp 1** **Grp 2** **1503** **1513** **Decreased libido** 96 51 p =0.002 **Impotence** 122 56 p <0.001 **Ejaculation disorder** 12 2 p =0.003 **Breast tenderness** 6 2 NR **Breast enlargement** 8 2 p=0.04 **Rash** 8 3 NR	

See Evidence Table 2: How does PSA predict symptom progression (in terms of symptom score)? for McConnell et al., 2003[170].

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Nickel et al., 1996[220] **Setting:** multi-centre, 28 sites in Canada PROSPECT study **Study design:** RCT double blinded. Patients and investigators. **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient group:** Men moderate symptoms of BPH **Inclusion criteria:** • ≤ 80 years • Ambulatory and in good health • Qmax 5 - 15 mL/s (at screening or start of placebo run-in) • Enlarged prostate by DRE • At least 2 symptoms indicting moderate BPH (increased frequency of urination or difficulty in urination) but not more than 2 severe symptoms • Serum PSA ≤ 10 ng/mL • PVR ≤ 150 mL **Exclusion criteria:** • Prostate cancer or suspect • Neurogenic bladder • ≥2 catheterisations for AUR in previous 2 years • Previous prostate or testicular surgery • Urethral strictures • Chronic Bacterial prostatitis • Serum creatinine > 150 mmol/L or liver function tests ≥50% above normal • Use of drugs with anti-androgenic properties • Haematuria associated with UTI, prostatitis or bladder carcinoma	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** At baseline and 12 and 24 months patients received a physical examination including DRE, urodynamics, serum PSA, liver function tests, and urinalysis. Primary outcomes for symptom score and flow rates measured every 4 months. Symptoms assessed using the Boyarksy scale modified by Bolognese et al. which comprises 9 questions (max score is 54) and obstructive symptoms totalled for Q1-5 as impairment in size and force of urinary stream, hesitancy or delay in starting urination, dribbling, interruption of stream, feeling of incomplete emptying (max score is 30) A quasi IPSS score was also developed using the seven items that corresponded from the Boyarsky scale and condensing the 2 highest values on the 6 point scale to	**Mean change in Quasi-IPSS ± SD from baseline at 4 months** Number of patients remaining is unclear so use ITT figures	**Grp 1:** -1.0 ± 4.9* **Grp 2:** -1.0 ± 5.3* **P value:** NS	**Funding:** Merck Frost Canada, inc. **Limitations:** • Quasi IPSS score • Data estimated from graph. • Unclear how many patients remaining at each time interval. **Additional outcomes:** Mean change in total symptom score and obstructive score from baseline and % change in prostate volume from baseline. **Notes:** Eligible patients entered 1 month single blind placebo run-in to reduce placebo effect then
			Mean change in Quasi-IPSS ± SD from baseline at 1 year Number of patients remaining is unclear so use ITT figures	**Grp 1:** -1.5 ± 5.4* **Grp 2:** -1.0 ± 5.3* **P value:** <0.05	
			Mean change in Quasi-IPSS ± SD from baseline at 2 year Number of patients remaining is unclear so use ITT figures	**Grp 1:** -1.7 ± 6.7* **Grp 2:** -0.5 ± 6.3* **P value:** <0.01	
			Mean change in Qmax ± SD from baseline at 4 months Number of patients remaining is unclear so use ITT figures	**Grp 1:** 0.7 ± 3.8* **Grp 2:** 0.65 ± 6.2* **P value:** NS	
			Mean change in Qmax ± SD from baseline at 1 year Number of patients remaining is unclear so use ITT figures	**Grp 1:** 0.95 ± 6.0* **Grp 2:** 0.3 ± 4.2* **P value:** <0.05	
			Mean change in Qmax ± SD from baseline at 2 years Number of patients remaining is unclear so use ITT figures	**Grp 1:** 1.25 ± 4.3* **Grp 2:** 0.25 ± 4.9* **P value:** <0.01	
			Mean change in % prostate volume from baseline at 1 year	**Grp 1:** -19 **Grp 2:** +7 **P value:** ≤0.01	
			Mean change in % prostate volume from baseline at 2 year	**Grp 1:** -21 **Grp 2:** +9 **P value:** ≤0.01	
			Median % change in PSA from baseline at 24 months	**Grp 1:** -52% **Grp 2:** 6% P value < 0.0001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	• Any condition that might jeopardise the patient's ability to complete the study **<u>All patients</u>** **N:** 613 **Mean age:** NR **Drop outs:** 141 (23%) **<u>Group 1 (Finasteride 5mg/dayl)</u>** **N:** 310 **Mean (range) Age:** 63 (46-79) **Total symptom score:** 15.8 ± 7.6 **Total obstructive score:** 10.2 ± 4.8 **Qmax ± SD, mL/s:** 11.1 ± 3.7 **Prostate volume ± SD, mL:** 44.1 ± 23.5 **Dropouts:** 64/310 (20.6%) see withdrawals**§** **<u>Group 2 (Placebo 1/day)</u>** **N:** 303 **Mean (range) Age:** 63.5 (47-80) **Total symptom score:** 16.6 ± 7.2 **Total obstructive score:** 10.7 ± 4.5 **Qmax ± SD, mL/s:** 10.9 ± 3.5 **Prostate volume ± SD, mL:** 45.8 ± 22.4 **Dropouts:** 77/303 (25.4%) see withdrawals**§**	1.	**Reason for withdrawal §** **N** **Adverse Events** **Insufficient response** **Lost to follow up** **Protocol violation** **Other**	**Grp 1** **Grp 2** **64** **77** 28 40 16 19 5 9 6 3 9 6	randomised by computer generated sequence. Allocation preserved using sealed opaque envelopes. Analysis was ITT *Standard deviations for changes from baseline calculated using confidence intervals and Cochrane methodology Analysis of variance used to compare outcomes with treatment centre and treatment group as model parameters.
			Other adverse events **Urinary retention or surgery** **Non-drug related mortality**	**Grp 1** **Grp 2** 19 31 p=0.08 5 3	
			Adverse events related to sexual function **N** **Decreased libido** **Impotence** **Ejaculation disorder**	**Grp 1** **Grp 2** **104** **43** 31 19 49 19 p <0.01 24 5 p <0.01	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Polat et al.,1997[239] **Setting:** single centre, Turkey **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men with BPH **Inclusion criteria:** • 50-80 years • In good health • Prostate volume >30 ml • Qmax <15 mL/s **Exclusion criteria:** • Prostate cancer or suspect **<u>All patients</u>** **N:** 123 **Mean age:** NR **<u>Group 1 (Finasteride 5mg/dayl)</u>** **N:** 62 **Mean (range) Age:** 61 (45-80) **AUA symptom score:** 15.1 ± NR **Qmax ± SD, mL/s:** 9.9 ± NR **Prostate volume ± SD, mL:** 39.1 ± NR **PVR ± SD, mL:** 96.2 ± NR **Serum PSA ± SD, ng/mL:** 2.2 ± NR **Dropouts:** 23/62 (37%) **<u>Group 2 (Placebo 1/day)</u>** **N:** 61 **Mean (range) Age:** 59 (44-80) **AUA symptom score:** 15.3 ± NR **Qmax ± SD, mL/s:** 10.1 ± NR **Prostate volume ± SD, mL:** 38.2 ± NR **PVR ± SD, mL:** 100.0 ± NR **Serum PSA ± SD, ng/mL:** 2.32 ± NR **Dropouts:** 0	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** Prostate volume (TRUS), AUA symptom score, Qmax, serum PSA, PVR and adverse events were recorded at 3, 6, 9 and 12 months	**Mean AUA score ± SD at 3 months**	**Grp 1:** 11.6 ± 5.3* **Grp 2:** 14.1 ± 5.3* **P value:** <0.01	**Funding:** Merck Frost Canada, inc. **Limitations:** • Randomisation method, allocation concealment and blinding not reported. • High dropout rate in Finasteride arm • Reasons for withdrawal not explained. **Additional outcomes:** % reduction in PSA **Notes:** * Standard deviations for changes from baseline calculated using p values for intergroup comparison following the Cochrane methodology
			Mean AUA score ± SD at 6 months	**Grp 1:** 10.9 ± 6.4* **Grp 2:** 13.9 ± 6.4* **P value:** <0.01	
			Mean AUA score ± SD at 12 months	**Grp 1:** 10.5 ± 9.0* **Grp 2:** 13.7 ± 9.0* **P value:** <0.05	
			Mean Qmax ± SD at 3 months	**Grp 1:** 10.5 ± NR **Grp 2:** 10.3 ± NR **P value:** NS	
			Mean Qmax ± SD at 6 months	**Grp 1:** 10.6 ± NR **Grp 2:** 10.4 ± NR **P value:** NS	
			Mean Qmax ± SD at 12 months	**Grp 1:** 13.2 ± 4.6* **Grp 2:** 10.4 ± 4.6* **P value:** <0.001	
			Mean PSA (ng/dl) at 3 months	**Grp 1:** 1.6 ± NR **Grp 2:** 2.3 ± NR **P value:** ≤0.01	
			Mean PSA (ng/dl) at 6 months	**Grp 1:** 1.4 ± NR **Grp 2:** 2.3 ± NR **P value:** ≤0.001	
			Mean PSA (ng/dl) at 12 months	**Grp 1:** 1.2 ± NR **Grp 2:** 2.3 ± NR **P value:** ≤0.001	
			Prostate volume (cm^3) at 3 months	**Grp 1:** 32.4 ± NR **Grp 2:** 38.1 ± NR **P value:** ≤0.01	
			Prostate volume (cm^3) at 6 months	**Grp 1:** 31.1 ± NR **Grp 2:** 38.0 ± NR **P value:** ≤0.01	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Prostate volume (cm^3) at 12 months	**Grp 1:** 30.0 ± NR **Grp 2:** 38.0 ± NR **P value:** ≤0.01	
			Adverse events **Impotence**	**Grp 1** **Grp 2** 1/62 0/61	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Roehrborn et al., 2002[257] A priori design for pooled analysis of parallel studies ARIA 3001, 3002, 3003 with identical inclusion/exclusion criteria. Study also reported in O'Leary et al., 2003[229] and O'Leary et al., 2008[230] **Setting:** multi-centre, 400 sites in 19 countries **Study design:** RCT double blind. Patients and investigators masked. **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient group:** Men with a clinical diagnosis of BPH (according to medical history, DRE and physical examination) **Inclusion criteria:** • ≥ 50 years • Prostate volume (TRUS) ≥ 30 mL • AUA-7 ≥ 12 • Qmax ≤ 15 mL/s on 2 consecutive voids of ≥125 mL **Exclusion criteria:** • PVR > 250 mL • History of prostate cancer • Previous prostate or bladder surgery • Previous AUR within 3 months of screening • Serum PSA <1.5 ng/mL or >10 ng/mL • Concurrent use of alpha-blockers or anti-androgens **<u>All patients</u>** **N:** 4325 **Mean age:** NR **Drop outs:** 1374/4325 (32%) **<u>Group 1 (Dutasteride 0.5mg/day)</u>** **N:** 2167 **White:** 91% **Mean (± SD) Age:** 66.5 ± 7.6	**Group 1:** Dutasteride 0.5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** AUA score and Qmax were evaluated at baseline and months 1, 3, 6 and every 6 months thereafter. Total prostate volume by TRUS was measured at baseline and months 6, 12, 24 and additionally in month 1 for ARIA 3001 and in month 3 for ARIA 3002. PSA analysis was completed at baseline and months 1, 3, 6, 12, 18 and 24. O'Leary at al., 2008[230] reports quality of life measures. **Symptom Problem Index SPI** - 7questions about frequency and urgency with a scale of 0-28 where 0= no problem and 4=big problem. SPI is similar to AUA. **BPH-specific interference**	**Mean change ± SD in AUA score from baseline at 2 years (ITT analysis)** **Mean change in Qmax ± SD from baseline at 2 years (ITT analysis)** **Mean change in total prostate volume ± SD from baseline at 2 years (ITT analysis)** **Mean change in Serum PSA ± SD from baseline at 2 years (ITT analysis)** **Mean change SPI ± SD from baseline at 2 years (ITT analysis)** **Mean change BSIA ± SD from baseline at 2 years (ITT analysis)** **Mean change BPWB ± SD from baseline at 2 years (ITT analysis)** **Reason for withdrawal *** **Total discontinuations** **Adverse Events** **Lack of improvement** **Protocol violation** **Consent withdrawn** **Loss to follow up** **Other/missing**	**Grp 1:** -4.5 ± 6.6 (n=2167) **Grp 2:** -2.3 ± 6.8 (n=2158) **P value:** <0.001 **Grp 1:** 2.2 ± 5.2 (n=2167) **Grp 2:** 0.6 ± 4.7 (n=2158) **P value:** <0.001 **Grp 1:** -14.6 ± 13.5 (n=2167) **Grp 2:** 0.8 ± 14.3 (n=2158) **P value:** <0.001 **Grp 1:** -3.1 ± 2.0 (n=2167) **Grp 2:** 0.5 ± 2.1 (n=2158) **P value:** <0.001 **Grp 1:** -2.2 ± 5.8 (n=2167) **Grp 2:** -0.8 ± 5.8 (n=2158) **P value:** <0.001 **Grp 1:** -1.7 ± 5.5 (n=2167) **Grp 2:** -1.5 ± 6.0 (n=2158) **P value:** <0.001 **Grp 1:** -1.5 ± 3.9 (n=2167) **Grp 2:** -0.6 ± 4.0 (n=2158) **P value:** <0.001 **Grp 1 / Grp 2** **657 / 717** 193 / 192 134 / 212 43 / 50 129 / 135 67 / 52 91 / 76	**Funding:** GSK of dutasteride **Limitations:** **Additional outcomes:** Serum DHT and transition zone volume. BSLA – BPH Specific lifestyle adaptations. (19 questions) **Notes:** Eligible patients entered 1 month single blind placebo run-in prior to randomisation by computer generated block sequence. Author confirms allocation concealment was preserved. Paper reports that a linear model was used to compare baseline and

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	AUA Symptom score ± SD: 17.0 ± 6.0 **Qmax ± SD, mL/s:** 10.1 ± 3.5 **Prostate volume, mL:** 54.9 ± 23.9 **Serum PSA ± SD, ng/L:** 4.0 ± 2.1 **SPI (QoL):** 11.7 ± 6.1 **BSIA (QoL):** 8.7 ± 6.2 **BPWB (QoL):** 11.0 ± 4.2 **Dropouts:** 657/2167 (30%) see* **<u>Group 2 (Placebo 1/day)</u>** **N:** 2158 **White:** 92% **Mean (± SD) Age:** 66.1 ± 7.4 **AUA Symptom score ± SD:** 17.1 ± 6.1 **Qmax ± SD, mL/s:** 10.4 ± 3.6 **Prostate volume, mL:** 54.0 ± 21.9 **Serum PSA ± SD, ng/L:** 4.0 ± 2.1 **SPI (QoL):** 11.8 ± 6.1 **BSIA (QoL):** 8.9 ± 6.2 **BPWB (QoL):** 11.0 ± 4.3 **Dropouts:** 717/2158 (33%) see *	**with activities BSIA** – 7 questions about how often urinary problems interfered with everyday activities with a scale of 0-28 where 0= none of the time and 4=all of the time. **BPH-Specific Psychological Well Being (BPWB)** – 6 questions about how often urinary condition has affected mental health with a scale of 5-25 where 1=not at all and 5=almost always	**Spontaneous or precipitated AUR** Acute urinary retention defined as spontaneous (no precipitating factors) or precipitated (stroke, UTI, pre surgery etc) **Drug related adverse events over 2 years**	**Grp 1:** 42/1503 **Grp 2:** 99/1513 **P value:** NR **Grp 1 Grp 2** **2167 2158** **N** 91 46 p <0.001 **Decreased libido** 158 86 p <0.001 **Impotence** 48 17 p <0.001 **Ejaculation disorder** 50 16 p <0.001 **Gynaecomastia**	follow up data for continuous variables with baseline values, treatment, protocol and investigator cluster as model parameters.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Tenover et al.,1997[293] **Setting:** multi-centre, 97 centres in the USA recruitment from April 1993 to October 1994. **Study design:** RCT double blind. Patients and investigators masked. **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men seeking treatment for symptomatic BPH from a primary care physician. **Inclusion criteria:** • ≥ 45 years • Moderate to severe AUA • Enlarged prostate gland on DRE • PSA ≤ 10 ng/mL **Exclusion criteria:** • Urethral stricture • History of repeated catheterisations • Previous pelvic radiotherapy • Recurrent urinary retention • Previous prostate or bladder surgery • Chronic prostatitis • Neurogenic bladder • Recurrent UTI • Concurrent use of alpha-blockers or anti-androgens • Prostate cancer suspects unless biopsy ruled out cancer **<u>All patients</u>** **N:** 2315 (2112 in efficacy analysis and baseline characteristics) **Mean age:** NR **Drop outs:** **<u>Group 1 (Finasteride 5mg/day)</u>**	**Group 1:** Finasteride 5 mg 1/day **Group 2:** Placebo 1/day **Examination methods:** Physical examination including DRE was performed at baseline and 12 mths. Serum dihydrotestosterone measured at baseline and mths 6 & 12 AUA-7 Symptom score, BPH Impact Index (BII) used for HRQoL, Patient satisfaction with urinary condition as extra question (0-6) and additional questions from modified BSIA instrument to measure interference with activities and extra question about adjustment of activities to cope with urinary symptoms were taken at baseline and 3 mth intervals. Patient and investigator global assessment of change in urologic status also rated from 1 (much worse) to 7 (much better) every 3 mths. Patients with visual impairment had	**Adjusted mean change in AUA score* from baseline at 12 months**	**Grp 1:** -4.96 ± NR **Grp 2:** -3.71 ± NR **P value:** <0.01	**Funding:** Merck & Co., Inc **Limitations:** • Randomisation method and allocation concealment was not clear **Additional outcomes:** Changes in lipid profiles from baseline **Notes:** Eligible patients entered 1 month single blind placebo run-in prior to randomisation in a 3:1 ratio * Mean AUA symptom score was adjusted for treatment, centre and baseline age. ** Mean BII score, general adjustment question, BSIA, Patient global assessment and
			Adjusted mean change in BII score from baseline at 12 months**	**Grp 1:** -1.12 CI95% -1.32 to -0.92 **Grp 2:** -0.70 CI95% -1.00 to -0.40 **P value:** 0.007	
			Adjusted mean change in general adjustment question from baseline at 12 months**	**Grp 1:** -0.26 CI95% -0.35 to -0.17 **Grp 2:** -0.10 CI95% -0.23 to 0.03 **P value:** 0.019	
			Adjusted mean change in BSIA score from baseline at 12 months**	**Grp 1:** -2.65 CI95% -3.25 to -2.06 **Grp 2:** -2.21 CI95% -3.09 to -1.32 **P value:** 0.343	
			Reason for withdrawal $ **Total discontinuations** **Adverse Events (all)** **Lack of improvement** **Protocol violation or patient request** **Loss to follow up**	**Grp 1 / Grp 2** **288 / 95** 118 / 36 43 / 14 54 / 20 73 / 25	
			Acute urinary retention	**Grp 1:** 34/1736 **Grp 2:** 23/579 **P value:** 0.644	
			Drug related adverse events (possibly, probably or definitely drug related) **N Randomised** **Withdrawals due to drug related** **AE** **Decreased libido** **Impotence** **Ejaculation disorder** **Withdrawal due to sexual AE**	**Grp 1 / Grp 2** **1736 / 579** 54 / 13 p =0.243 85 / 17 p =0.038 128 / 19 p <0.001 57 / 5 p =0.001 38 / 8 p =0.213	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 1589 **Mean (± SD) Age:** 63.6 ± 8.7 **White/other:** 1473 **Black:** 76 **Hispanic:** 40 **AUA symptom score*** ± **SD:** 19.03 ± NR **BII**:** 4.76 CI95% 4.61-4.9 **General adjustment question**:** 1.29 CI95% 1.21-1.36 **BSIA**:** 12.7 CI95% 12.16-13.24 **Dropouts:** 288/1736 (16.65) for reasons see**§** **<u>Group 2 (Placebo 1/day)</u>** **N:** 523 **Mean (± SD) Age:** 62.7 ± 8.9 **White/other:** 482 **Black:** 28 **Hispanic:** 13 **AUA symptom score*** ± **SD:** 18.35 ± NR **BII**:** 4.67 CI95% 4.45-4.9 **General adjustment question**:** 1.21 CI95% 1.09-1.33 **BSIA**:** 12.75 CI95% 11.93-13.57 **Dropouts:** 95/579 (16.4%) for reasons see**§**	questionnaires read to them and Spanish versions provided.			investigator global assessment were adjusted for treatment, centre, baseline AUA and age covariates. A graph was presented in the study with adjusted AUA score at follow up but it was not clear if the mean was with a standard deviation or CI95%

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Evidence Table 14 Anticholinergics vs. placebo

See Evidence Table 9 Alpha-blockers vs. placebo for Kaplan et al.,2006[123].

1 **Evidence Table 15: Phosphodiesterase-5 inhibitors vs. placebo**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
McVary et al., 2007b[197] **Study design:** Randomised controlled trial **Setting:** US **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** Men 45 years and older with a history of LUTS secondary to BPH of 6 months or longer were recruited from 21 centres in US from November 2004 to July 2005. Patients agreed not to use other BPH medications during this study. **Inclusion criteria**: IPSS of 13 or greater and a Qmax of 4-15ml/s on a voided volume of 125ml or greater was required. **Exclusion criteria:** patients without treatment compliance during run in phase (<70%) were excluded. Men with PSA >10ng/ml, recent finasteride or dutasteride treatment, history of radical prostatectomy or other pelvic surgery; neurological condition affecting bladder function; recent lower urinary tract instrumentation, urinary retention or bladder stones; history of urethral obstruction due to strictures, valves, sclerosis or tumour; detrusor-sphincter dyssynergia; urinary tract inflammation or infection; intravesical obstruction secondary to the prostate median lobe; prostate cancer; PVR 200ml or greater; certain cardiovascular diseases, clinically significant renal or hepatic insufficiency;	**Run-in period:** Eligible patients entered 4 week single blind run in period with placebo dosed once daily. **Group 1: PHOSPHODIESTERASE 5 INHIBITORS** Tadalafil 5mg once daily for six weeks, followed by dose escalation to 20mg for remaining 6 weeks. Medication ingested at same time every day. **Group 2: PLACEBO**	**Mean (SE) IPSS at 6 weeks**	**Baseline** Group1 (n=138): 17.4 Group 2 (n=143): 18.5 **6 weeks** Group1 (n=135): 14.5 Group 2 (n=136): 17.0 **Change from baseline:** Group 1: -2.8 (0.5) Group 2: -1.2 (0.5); p=0.003 **Difference between change from baseline:** 1.7 (95% CI: 0.5-2.9); p=0.003	**Funding:** NR **Limitations:** Randomisation method and allocation concealment unclear. **Additional outcomes:** Comparisons from before placebo run-in to endpoint were reported. BII reported and IPSS results for obstructive and irritative domains reported separately. Voided volume and average urinary flow were also reported. **Notes:** * All reports of erection increased were from 1 study site, reported in response to specific questioning by the investigator and described as secondary to sexual stimulation. Least square means calculations used for
			Mean (SE) IPSS at 12 weeks	**Baseline** Group1 (n=138): 17.5 Group 2 (n=143): 18.3 **12 weeks** Group1 (n =136): 13.3 Group 2 (n=138): 16.1 **Change:** Group 1: -3.8 (0.5) Group 2: -1.7 (0.5); p<0.001 **Difference between change from baseline**: 2.1 (95% CI: 0.9-3.3); p<0.001	
			Responders (defined as patients with an IPSS change from baseline or 3 points or greater)	**6 weeks:** Group 1: 49.3% Group 2: 36.4%; p=0.03 **12 weeks:** Group 1: 60.9% Group 2: 42.7%; p<0.01	
			Mean (SE) IPSS quality of life question at 6 weeks	**Baseline** Group1 (n=138): 3.6 Group 2 (n=143): 3.8 **6 weeks** Group1 (n=136): 3.1 Group 2 (n=138): 3.5	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	recent history of stroke or spinal cord injury; current treatment with nitrates, cancer chemotherapy, antiandrogens or a potent cytochrome P450 3A4 inhibitor; or uncontrolled diabetes. **<u>All patients</u>** **N:** 281 **<u>Group 1</u>** **N:** 138 **Ethnicity/race:** Black 10.9%, white 79%, Hispanic 6.5%, other 3.6% **Mean (range) Age:** 62 (45.1-82.4) **Dropouts:** 13 (adverse events=5, lost to follow up=1, patient decision=2, other =5) **<u>Group 2</u>** **N:** 143 **Mean (range) Age:** 61 (45.0-82.3) **Ethnicity/race:** Black 8.4%, white 83.2%, Hispanic 7%, other 1.4% **Dropouts:** 17 (adverse events=2, lack of efficacy=1, lost to follow up=5, patient decision=6, other=3)			**Change from baseline:** Group1: -0.5 (0.1) Group 2: -0.2 (0.1); p=0.017	analysis. NCGC calculated SD for meta-analysis from Cochrane calculations.
			Mean (SE) IPSS quality of life question at 12 weeks	**Baseline** Group1 (n=136): 3.6 Group 2 (n=138) : 3.8 **12 weeks** Group1 (n=136): 2.8 Group 2 (n=138): 3.3 **Change from baseline:** Group1: -0.7 (0.1) Group 2: -0.3 (0.1); p=0.004	
			% of yes responses to question: Has the treatment you have been taking since your last visit improved your urinary symptoms?	**6 weeks** Group 1 (n=136): 55.9 Group 2 (n=138): 32.6; p<0.001 **12 weeks** Group 1 (n=136): 57.4 Group 2 (n=138): 37.7; p<0.001	
			Mean (SE) Qmax, ml/sec at 6 weeks	**Baseline** Group1 (n=110): 11.7 Group 2 (n=111) : 11.2 **12 weeks** Group1 (n=110): 12.2 Group 2 (n=111): 11.8 **Change from baseline:** Group1: 1.1 (0.6) Group 2: 1.0 (0.6); p=0.46	
			Mean (SE) Qmax, ml/sec at 12 weeks	**Baseline** Group1 (n=116): 11.8 Group 2 (n=121) : 11.1 **12 weeks** Group1 (n=116): 12.3 Group 2 (n=121): 12.1 **Change from baseline:** Group1: 0.5 (0.5) Group 2: 0.9 (0.5); p=0.72	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Mean (SE) PVR, ml at 6 weeks	**Baseline** Group1 (n=132): 58.0 Group 2 (n=135) : 58.5 **12 weeks** Group1 (n=132): 57.2 Group 2 (n=136): 53.8 **Change from baseline:** Group1: 3.6 (7.0) Group 2: 0.1 (6.7); p=0.66	
			Mean (SE) PVR, ml at 12 weeks	**Baseline** Group1 (n=132): 58.0 Group 2 (n=135) : 58.2 **12 weeks** Group1 (n=132): 57.9 Group 2 (n=136): 54.2 **Change from baseline:** Group1: 1.4 (6.5) Group 2: -2.6 (6.2); p=0.69	
			Mean (SE) IPSS change from baseline in men that were sexually active	**6 weeks** Group 1 (n=80): -3.2±0.7 Group 2 (n=76): -0.7±0.7; p=0.001 **12 weeks** Group 1 (n=80): -4.4± 0.7 Group 2 (n=76): -1.8± 0.7; p=0.001	
			Mean (SE) IIEF EF domain change from baseline in men that were sexually active	**6 weeks** Group 1(n=80): 6.0±0.9 Group 2(n=76): 0.6±0.9; p<0.001 **12 weeks** Group 1(n=80): 7.7± 0.9 Group 2 (n=76): 1.4± 1.0; p<0.001	
			Discontinuation due to treatment emergent adverse events	Group 1: 3.6% Group 2: 1.4%	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Treatment emergent adverse events with a frequency of 2% or greater at 12 weeks	**Erection increased*** Group 1: 7 (5.1%) Group 2: 2 (1.4%) **Dyspepsia** Group 1: 6 (4.3%) Group 2: 0 **Back pain** Group 1: 5 (3.6%) Group 2: 2 (1.4%) **Headache** Group 1: 4 (2.9%) Group 2: 1 (0.7%) **Nasopharyngitis** Group 1: 3 (2.2%) Group 2: 0 **Upper respiratory tract infection** Group 1: 3 (2.2%) Group 2: 1 (0.7%) **Serious adverse events:** Group 1: 0 Group 2: 1 (0.7%) **AUR:** Group 1: 0 Group 2: 0	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
McVary et al., 2007c[196] **Study design:** Randomised controlled trial. **Setting:** USA **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** men with erectile dysfunction and LUTS/BPH from 41 urology clinics and clinical research centres. **Inclusion criteria**: Men≥45 years, had a clinical diagnosis of ED (score≤25 on the erectile function domain of the International Index of Erectile Function) and IPSS ≥12. **Exclusion criteria:** Men with confirmed or suspected prostate malignancy, serum prostate-specific antigen >10ng/ml, previous invasive intervention for BPH, ore previous prostate or bladder/pelvic rations or surgery. Those with PSA between 4-10ng/ml required two additional forms of documentation to confirm the absence of clinically evident malignancy. Men with acute urinary tract disease or cystoscopy with in 4 weeks of the trial, calculi in the urinary tract or acute urinary retention within 6 months of the trial, recurrent urinary tract infections or catheterisation for outflow obstruction in the year before the trial, or other known or suspected causes of urinary symptoms other than BPH, hypotension, hypertension orthostatic hypotension or significant cardiovascular disease. Men were excluded if used	**Group 1: Phosphodiesterase 5 inhibitors** Sildenafil citrate: 50mg once daily with each night at bedtime or 30 minutes to 1hr before sexual activity. After 2 weeks the does increased to 100mg but could be decreased to 50mg if the higher dose was not tolerated. **Group 2: Placebo**	**Mean (SD) IIEF – erectile function domain (1-30; higher scores indicate better treatment outcome)**	**Baseline** Group1: 13.4 Group 2: 13.2 **Change from baseline** Group1: 9.2 (1.0) Group 2: 1.9 (1.0) **Mean change:** 9.17, 95% CI: 7.25-11.09 vs. 1.86, 95% CI: -0.03, 3.74;p<0.0001	**Funding:** Supported by Pfizer, Inc. **Limitations:** Actual figures and SD not provided for IPSS, Qmax and IPSS QoL question. **Additional outcomes:** BPHII score, SEAR questionnaire (self-esteem and relationship questionnaire) **Notes:** 8 week open label extension study after this 12 week study. Least square means calculations used for analysis. NCGC calculated SD for meta-analysis from Cochrane calculations.
			Least mean change in IPSS score	Group 1 (n=182): -6.3 (-8.1, -4.6) Group 2 (n=178): -1.9 (-3.7, -0.2) P<0.001	
			Least mean change in Qmax, ml	Group 1: 0.31 (-1.6, 2.2) Group 2: 0.16 (-1.7, 2.1) P=0.8	
			Least mean change in IPSS quality of life score	Group 1: -0.97 (-1.32, -0.62) Group 2: -0.29 (-0.64, 0.05) P<0.001	
			LS mean (SE) EDITS score (end of treatment satisfaction score; 0-100)	Group 1: 71.2±3.2 Group 2: 41.7±3.2; p<0.0001	
			Number (%) of patients reporting adverse events	Group 1: 100/189 (53%) Group 2: 78/180 (43%)	
			Number (%) of treatment related adverse events	Group 1: 86/189 (%) Group 2: 25/180 (%)	
			Headache	Group 1: 21/189 (11%) Group 2: 6/180 (3%)	
			Flushing	Group 1: 9/189 (5%) Group 2: 1/180 (1%)	
			Dyspepsia	Group 1: 12/189 (6%) Group 2: 2/180 (1%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	nitrates, had hepatic or renal dysfunction, poorly controlled diabetes or a history of retinitis pigmentosa. Use of antimuscarinics, 5-alpha-reductase inhibitors within 6 months or alpha blockers within 4 weeks during study. PDE5 inhibitor or any other treatment for ED must have terminated therapy 4 weeks or more before the study. **<u>All patients</u>** **N:** 370 **Mean age**: 60 (9) **Drop outs:** 1 not treated/withdrew **<u>Group 1</u>** **N:** 187 **Mean (±SD) ED**: 5.7 (4.6) years **Ethnicity/race:** White: 84%; Black: 10% **Discontinuations**:21 **<u>Group 2</u>** **N:** 179 **Mean (±SD) ED**: 5.6 (5.1) years **Ethnicity/race:** white: 80%; black: 13% **Discontinuations**: 25		**Rhinitis**	Group 1: 8/189 (4%) Group 2: 3/180 (2%)	
			Discontinuations due to adverse events	Group1: 9/189 (5%) Group 2: 2/180 (1%)	
			Serious adverse events	Group1: 2/189 (1%) Group 2: 3/180 (2%)	
			Discontinuations due to serious adverse events	Group1: 1/189 (1%) Group 2: 0	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Roehrborn et al., 2008b[261] **Study design:** RCT **Setting:** 92 centres in 10 countries **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** Men with a history of LUTS secondary to BPH of 6 months longer. **Inclusion criteria:** • At least 45 years old • IPSS of 13 or greater • Qmax of 4-15ml/s from pre-void bladder volume between 150-550ml with a voided volume of 125ml or greater. **Exclusion criteria:** • PSA > 10ng/ml • PVR volume was 300ml or greater at screening visit 1 • Patients reporting use of other BPH or ED treatments underwent a 4 week treatment free screening/ washout period. • Penile or pelvic surgery, radiotherapy, lower urinary tract malignancy, trauma or recent instrumentation, urinary retention or bladder stones, • History of urethral obstruction • Neurological condition • Detrusor sphincter dyssynergia, intravesical obstruction secondary to the prostate median lobe, • Urinary tract inflammation or infection • Prostate cancer. • Renal or hepatic insufficiency,	**Group 1: PDE5I** Tadalafil 2.5mg once daily **Group2: PDE5I** Tadalafil 5 mg once daily **Group 3: PDE5I** Tadalafil 10 mg once daily **Group 4: PDE5I** Tadalafil 20 mg once daily **Group 5: Placebo** once daily	**Least squares mean (SE) IPSS change from baseline**	Group1 (n=208): -3.88 (0.50) Group 2 (n=212): -4.87 (0.49) Group 3 (n=216): -5.17 (0.49) Group 4 (n=208): -5.21 (0.50) Group 5 (n=210): -2.27 (0.49) P<0.001 (tad v placebo)	**Funding:** Eli Lilly and Co. **Limitations:** method of randomisation and allocation concealment unclear. **Additional outcomes:** BPH-II score **Notes:** None.
			Least squares mean (SE) IPSS quality of life change from baseline	Group1 (n=208): -0.74 (0.11) Group 2 (n=212): -0.86 (0.11) Group 3 (n=216): -0.92 (0.10) Group 4 (n=208): -0.88 (0.11) Group 5 (n=210): -0.49 (0.11) P<0.01 (tad v placebo)	
			Least squares mean (SE) Qmax change from baseline	Group1 (n=208): 1.41 (0.39) Group 2 (n=212): 1.64 (0.39) Group 3 (n=216): 1.58 (0.38) Group 4 (n=208): 1.96 (0.39) Group 5 (n=210): 1.24 (0.40) P=Not sig. (tad v placebo)	
			% Yes LUTS GAQ end point (GAC question: Has the treatment you have been taking since your last visit improved your urinary symptoms)	Group1 (n=208): 61.9 Group 2 (n=212): 69.2 Group 3 (n=216): 73.0 Group 4 (n=208): 74.2 Group 5 (n=210): 54.8 P<0.05 (tad v placebo)	
			Lease squares mean (SE) sexually active ED IIEF-EF change from baseline (55% of patients)	Group1 (n=208): 5.59 (1.01) Group 2 (n=212): 6.97 (1.01) Group 3 (n=216): 7.98 (1.0) Group 4 (n=208): 8.34 (1.01) Group 5 (n=210): 2.20 (1.03) P<0.001 (tad v placebo)	
			Treatment emergent adverse events	**Headache** Group1: 5/209 Group 2: 6/212 Group 3: 11/216	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	• Cardiovascular conditions, history of stroke or spinal cord injury, cancer chemotherapy, uncontrolled diabetes **<u>All patients</u>** **N:** 1058 **<u>Group 1</u>** **N:** 209 **Mean Age:** 62.03 **Ethnicity/race:** White 88.46%, Hispanic 9.62%, black 1.44%, other 0.48% **Mean % ED history:** 64.9% **Dropouts:** 27 **<u>Group 2</u>** **N:** 212 **Mean Age:** 61.95 **Ethnicity/race:** White 84.43%, Hispanic 11.79%, black 3.30%, other 0.47% **Mean % ED history:** 67.92% **Dropouts:** 30 **<u>Group 3</u>** **N:** 216 **Mean Age:** 62.22 **Ethnicity/race:** White 86.11%, Hispanic 11.11%, black 2.31%, other 0.46% **Mean % ED history:** 69.44% **Dropouts:** 41 **<u>Group 4</u>** **N:** 209 **Mean Age:** 62.55			Group 4: 7/209 Group 5: 6/211 **Dyspepsia** Group1: 2/209 Group 2: 10/212 Group 3: 6/216 Group 4: 10/209 Group 5: 0/211 **Back Pain** Group1: 3/209 Group 2: 2/212 Group 3: 10/216 Group 4: 12/209 Group 5: 1/211 **Myalgia** Group1: 3/209 Group 2: 3/212 Group 3: 6/216 Group 4: 6/209 Group 5: 0/211 **Nasopharyngitis** Group1: 7/209 Group 2: 4/212 Group 3: 2/216 Group 4: 5/209 Group 5: 2/211 **Diarrhoea** Group1: 2/209 Group 2: 6/212 Group 3: 1/216 Group 4: 5/209 Group 5: 3/211 **Gastroesophageal reflux disease** Group1:2/209 Group 2: 2/212 Group 3: 6/216 Group 4: 3/209 Group 5: 0/211 **Extremity pain**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Ethnicity/race: White 84.21%, Hispanic 11.96%, black 2.39%, other 1.44% **Mean % ED history:** 69.38% **Dropouts:** 47 **<u>Group 5</u>** **N:** 212 **Mean Age:** 61.75 **Ethnicity/race:** White 84.83%, Hispanic 13.74%, black 1.42%, other 0% **Mean % ED history:** 67.30% **Dropouts:** 27			Group1: 3/209 Group 2: 5/212 Group 3: 2/216 Group 4: 3/209 Group 5: 0/211 **Influenza** Group1: 4/209 Group 2: 4/212 Group 3: 1/216 Group 4: 2/209 Group 5: 1/211 **Bronchitis** Group1: 3/209 Group 2: 1/212 Group 3: 5/216 Group 4: 0/209 Group 5: 1/211 **Muscle spasms** Group1: 2/209 Group 2: 0/212 Group 3: 2/216 Group 4: 5/209 Group 5: 0/211 **Urinary retention** Group1: 0/209 Group 2: 0/212 Group 3: 0/216 Group 4: 0/209 Group 5: 1/211	
			Discontinuation due to adverse events	Group1: 4/209 Group 2: 12/212 Group 3: 11/216 Group 4: 14/209 Group 5: 5/211	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Stief et al.,2008[287] **Study design:** Randomised control trial. **Setting:** multi-centre, Germany **Evidence level:** 1+ **Duration of follow-up:** 8 weeks.	**Patient group:** Men with BPH/LUTS from 16 centres in Germany from October 2005-June 2006. **Inclusion criteria:** Men aged 45-64 years with a history of BPH/LUTS for at least 6 months before commencing the study and an IPSS≥12 at screening. Patients completed a 4 week run-in phase during which no study medications was administered. **Exclusion criteria:** contraindications to vardenafil, spinal cord injury, prostatitis, history of prostate or bladder cancer, bladder o r urethra stricture, urinary retention (PVR≥100ml), pelvic trauma or surgery, history of any malignancies, and life expectancy of less than 3 yr. concomitant use of nitrates or NO donors, androgens or anti-androgens, anticoagulants, cytochrome P-50 3A4 inhibitors, any treatment for ED or alpha1-adrenocoetpro antagonists were prohibited. Alpha blockers – if withdrawn at screening, subjects would fail o be eligible for study drug treatment, precious or current use of 5-alpha reductase inhibitors. **<u>All patients:</u> N:** 222 **<u>Group 1</u>** **N:** 109 **Mean** (±SD) **Age:** 56.5 (5.4) years **Ethnicity:** White 100%	**Group 1: Phosphodiesterase 5 (PDE5) inhibitors** 10mg Vardenafil twice daily **Group 2: Placebo** Matched placebo tablet twice daily (12-h dosing interval).	**Mean IPSS symptom score***	**Baseline** Group1: 16.8 Group 2: 16.8 **8 weeks** Group1 (n=105): 11.0 Group 2 (n=110): 13.2 **Between group difference in change from baseline:** 2.3 (0.90-3.64), p=0.0013	**Funding:** This study was sponsored by Bayer Healthcare AG, Leverkusen, Germany. Bayer healthcare AG involved in the design and conduct of the study; management, analysis and interpretation of the data; and preparation, review and approval of the manuscript. **Limitations:** No SD values provided for further analysis. [NCC emailed author for this information] **Additional outcomes:** IPSS also reported by irritative and obstructive sub score. **Notes:** Serious adverse events reported included myocardial infarction, chest pain, and cardiac rehabilitation therapy (one patient) and hypertensive crisis in the intervention group. The placebo group comprised of haematochezia, a meniscus injury and knee
			Mean Qmax, ml/s*	**Baseline** Group1: 15.9 Group 2: 15.9 **8 weeks** Group1 (n=105): 17.5 Group 2 (n=110): 16.9 **Between group difference in change from baseline:** -0.6 (-2.62–1.43), p=0.5614	
			Mean PVR volume	**Baseline** Group1: 28.0 Group 2: 26.9 **8 weeks** Group1 (n=105): 27.0 Group 2 (n=110): 28.8 **Between group difference in change from baseline:** 1.8 (-7.39 to 10.99); p=0.6994	
			International Index of Erectile Function – Erectile function (IIEF-EF) score	**Baseline** Group1: 15.9 Group 2: 15.9 **8 weeks** Group1 (n=105): 23.4 Group 2 (n=110): 17.4 **Between group difference in change from baseline:** -6.0 (-7.77 to 4.16), p=0.0001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Dropouts: 4 (1=not received medication, 3=did not provide efficacy data) Premature discontinuation=13 ITT population=105 **<u>Group 2</u>** **N:** 113 **Mean** (±SD) **Age**: 55.4 (5.7) years **Ethnicity**: White 98.2%; Black 0.9%; Asian 0.9%. **Dropouts**: 3 (3=did not provide efficacy data) Premature discontinuation=14 ITT population=110		**Total Urolife Qulatiy of life-9 score**	-9.3 (95% CI: -12.79, -5.71) P<0.0001	surgery. None were considered related to study medication. * Least square means analysis reported for outcomes. NCGC calculated estimated SD for mean change in IPSS/Qmax from Cochrane handbook formula.
			Number (%) of adverse events (treatment-emergent adverse events affecting at least 2% of patients)	**Any event:** Group 1 (n=108): 32 (29.6%) Group 2 (n=113):18 (15.9%) **Headache:** Group 1:14 (13.0%) Group 2: 2 (1.8%) **Dyspepsia:** Group 1: 8 (7.4%) Group 2: 0 **Flushing:** Group 1: 7 (6.5%) Group 2: 1 (0.9%) **Diarrhoea:** Group 1: 5 (4.6%) Group 2: 1 (0.9%) **Gastrointestinal reflux disease:** Group 1: 3 (2.8%) Group 2: 0 **Back pain:** Group 1: 3 (2.8%) Group 2: 0 **Serious adverse events** Group 1: 2 Group 2: 3	

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1 **Evidence Table 16: Diuretics vs. placebo**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Reynard et al., 1998a[249] **Study design:** Randomised controlled trial **Setting:** Hospital, UK **Evidence level:** 1+ **Duration of follow-up:** 4 weeks.	**Patient group:** elderly men presenting with lower urinary tract symptoms and completed 7day frequency volume chart. **Inclusion criteria:** aged over 50 years, with nocturnal polyuria (defined as night time diuresis defined as the production of >33% of the 24-h urine volume between midnight and 8am). **Exclusion criteria:** serum creatinine >150umol.L, previous lower urinary tract surgery, symptomatic heart failure, taking medication active on the lower urinary tract including those taking any diuretic, concomitant neurological disease which could potentially affect lower urinary tract function, and clinical evidence of prostate cancer or diabetes mellitus. **<u>All patients</u>** **N:** 49 Number obstructed: 19/41 **Drop outs:** 6 (withdrew) **<u>Group 1</u>** **N:** 21 Mean (±SD) Age: 70 Dropouts: 3 (evening frequency). **<u>Group 2</u>** **N:** 22 Mean (±SD) Age: 69	Two week placebo period. In second week a frequency volume chart was completed with the IPSS symptom score. **Group 1: Diuretic** Frusemide 40mg Afternoon dose taken 6 hours before their usual bedtime. **Group 2: Placebo**	**Reduction in night time frequency**	Group 1: -0.5 Group 2: 0 P=0.014	**Funding:** NR. **Limitations:** Method of randomisation, allocation concealment not reported. Actual figures not reported. **Additional outcomes:** No significant correlation between the % night time voided volume and changes in night time frequency, night time voided volume or % voided volume. Figures not reported. **Notes:** Day time defined as 08.00 and 23.59h and night time as between 00.00 and 07.59h.
			Increase in daytime frequency	Group1: +1.9 Group 2: -0.1 P<0.001	
			Correlation for % night time voided volume at entry to the study against change in night-time voiding frequency	Spearman's correlation coefficient: 0.25 P=0.3	
			Increase in daytime voided volume, mL	Group 1: +365 Group 2: -31 P=0.002	
			Night time voided volume, mL	Group 1: -120 Group 2: +9 P=0.065	
			Reduction in night-time voiding frequency of one or more	Group 1: 7/19 Group 2: 1/20 P=0.02	
			Night time voiding frequency was reduced 2 or more	4/19 0/20	
			Correlation between % night time voided volume at entry and reduction in night time voided volume	Spearman's correlation coefficient: 0.03 P=0.9	
			Total urine output (24h), mL	Group 1: 1663 Group 2: 1780 P=0.2	
			% change of night time voided volume	Group 1: -18% Group 2: 0%	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Dropouts: 3=(lack of efficacy or evening frequency)			P=0.001	
			Correlation between % night time voided volume and change in % night time voided volume	Spearmans correlation coefficient = 0.43, p=0.08	
			Change in IPSS	Group 1: +1 Group 2: 0 P=0.9	
			Patients reported that intervention 'helped'	Group 1: 14/21 Group 2: 5/22 P<0.001	

Evidence Table 17 Desmospressin vs. placebo

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Cannon et al., 1999[41] **Study design:** RCT-cross over trial **Setting:** UK **Evidence level:** 1+ **Duration of follow-up:** Two-2 week periods	**Patient group:** Men with nocturia **Inclusion criteria:** ▪ Men >50 years ▪ Nocturnal polyuria confirmed after 48 hours of inpatient monitoring or a 1-week FV chart, which showed in excess of a third of their 24-hour urine volume being produced overnight **Exclusion criteria:** ▪ Nocturnal enuresis or incontinence ▪ Significant cardiovascular, renal or hepatic disease, diabetes, UTI or concomitant medication active on the lower urinary tract **<u>All patients</u>** **N:** 20 **Mean age,** mean (range): 70.5(52-80) years **Drop outs:** 2	**Group 1: Desmopressin** 20 microgram nasal spray, administered just before going to bed each evening **Group 2: Placebo** nasal spray, administered just before going to bed each evening	**24-h volume,** (ml) mean, se: (measured using FV-chart*)	**Baseline:** 1646.6 se107.6 **Group 1**: 1567.4 se 96.7 **Group 2**: 1713.5 se 119.4 **P value** (paired t-test)**:** Not sig	**Funding:** Ferring Pharmaceuticals **Limitations:** ▪ Cross over study ▪ Small sample size ▪ Method of randomisation allocation and concealment was not described. **Additional outcomes:** Adverse events: For 20 microgram of desmopressin: dry throat plus cough (1), increased sputum (1), and fluid retention plus hyponatraemia (1). For placebo: headache (1), flu like illness (1). Another 2 patients had fluid retention symptoms while receiving the 40microgram dose. **Notes:** This is a cross over study. Patient had 1 week run in with placebo, and then allocated to desmopressin 20 microgram or placebo for 2 weeks, before crossing over for another 2 weeks. *FV chart resulted were collected at the second week. ** The 24 hour urine collection was done on the last day of the treatment period.
			Nocturnal frequency mean, se: (measured using FV-chart*)	**Baseline:** 3.0 se 0.3 **Group 1**: 2.7 se 0.33 **Group 2**: 3.1 se 0.3 **P value** (paired t-test)**:** Not sig	
			Nocturnal volume (ml)mean, se: (measured using FV-chart*)	**Baseline:** 749.6 se 67.5 **Group 1**: 633.9 se 60.8 **Group 2**: 809.1 se 78.7 **P value** (paired t-test)**:** <0.01	
			Nocturnal percentage (%) (measured using FV-chart*)	**Baseline:** 45.7 se 3.1 **Group 1**: 40.5 se 3.1 **Group 2**: 46.9 se 3.3 **P value** (paired t-test)**:** <0.05	
			24-h volume, (ml) mean, se: (24 hour urine collection**)	**Baseline:** 1487.2 se110.5 **Group 1**: 1419 se 121.20 **Group 2**: 1400.6 se 88.5 **P value** (paired t-test)**:**	
			Nocturnal volume (ml)mean, se: (24 hour urine collection**)	**Baseline:** 718.3 se 79.1 **Group 1**: 562.0 se 73.5 **Group 2**: 726.7 se74 **P value** (paired t-test)**:** <0.01	
			Nocturnal percentage (%) (24 hour urine collection**)	**Baseline:** 47.3 se 3.5 **Group 1**: 39.2 se 3.5 **Group 2**: 50.6 se 3.5 **P value** (paired t-test)**:** <0.001	
			Hyponatremia and hyposmolaemia (withdrawn early from study, sodium 127mmol/L, hypoosmolaemia 263mosmol/kg)	**Group 1:** 1/20 **Group 2:** 0/20	

1 **Evidence Table 18 Non steroidal anti-inflammatory drugs (NSAIDS) vs. placebo**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Falahatkar et al., 2008 [88] **Study design:** RCT, double blinded **Setting:** Iran,Jan to May 2007 **Evidence level:** 1+ **Duration of follow-up:** 1 month	**Patient group:** BPH patients with refractory nocturia **Inclusion criteria:** ▪ BPH with ≥2 voids per night ▪ Mean night time voided volume of <30% of the 24 hour volume ▪ IPSS≥8 ▪ Prostate volume >20cm^3 ▪ Prescribed alpha-blockers or alpha blockers or finasteride (if prostate volume>30cm^3) for 2-3 months but incidence of nocturia remained ≥2 times per night ▪ Negative urine culture findings ▪ Normal renal function **Exclusion criteria:** ▪ Previous prostate surgery or other invasive procedures for testing of BPH ▪ Prostate cancer, or PSA>10ng/ml. Men with PSA 4.1 to 10ng/mL were required to provide ultrasound guided biopsy **<u>All patients</u>** **N:** 80 Mean age: range 49 to 80years **Drop outs:** 0 **<u>Group 1 - Celecoxib</u>** **N:** 40 Mean (±SD) Age: 64.3±7.7 (49-80) Dropouts: 0	**Group 1: COX II selective NSAID (celecoxib)** 100mg capsule at 9PM **Group 2: Placebo**	**IPSS**	**At 1 month** Group 1: 15.5±4.2 Group 2: 18.0±3.9 **P values:**	**Funding:** NR **Limitations:** ▪ Randomisation allocation and concealment not reported ▪ Small sample size ▪ Short length of follow up **Additional outcomes:** Authors reported that not baseline parameters did not influence level of response **Notes:** None
			Qmax, ml/s, mean±sd	**At 1 month** Group 1: 12.9±2.7 Group 2: 12.3±2.5 **P value:**	
			Nocturia frequency	**At 1 month** Group 1: 2.5±1.9 Group 2: 5.1±1.9 **P value:**	
			Nocturia frequency, classified as excellent if decreased ≥2 voids/night or disappeared, improved if decreased by 1 void/night and no change.	**At 1 month** **Excellent improved no change** Group 1: 28(70) 5(12.5) 7(17.5) Group 2: 3(7.5) 6(15) 31(77.5) Values in brackets are percentages	
			Adverse events – mild gastric discomfort	**At 1 month** Group 1: 4/40 Group 2: 0/40 **P value:** 0.11 [calculated by NCGC using Fisher's exact test]	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	IPSS, mean ±sd: 18.2±3.4 **Qmax**, ml/s, mean±sd: 12.5±2.1 Nocturia frequency, mean±sd: 5.17±2.1 **Prostate volume**, ml, mean±sd:18.25 ±4.5 **PSA level**, ng/ml, mean±sd:2.62±1.16 **<u>Group 2 - Placebo</u>** **N:** 40 Mean (±SD) Age: 64.9±7.05 (50-80) Dropouts:0 **IPSS**, mean ±sd: 18.4±3.1 **Qmax**, ml/s, mean±sd:12.1±2.1 Nocturia frequency, mean±sd:5.30±2.4 **Prostate volume**, ml, mean±sd:50.11±5.6 **PSA level**, ng/ml, mean±sd: 2.68±1.18				

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Evidence Table 19 Combination therapy: 5-Alpha reductase inhibitor and alpha-blocker

See Evidence Table 10: Alpha blocker vs. 5-alpha reductase inhibitors

for Debruyne et al., 1998[69].

See Evidence Table 9 Alpha-blockers vs. placebo

Kirby et al., 2003[147].

See Evidence Table 10 Alpha blocker vs. 5-alpha reductase inhibitors

for Lepor et al., 1996[164].

See Evidence Table 2: How does PSA predict symptom progression (in terms of symptom score)?

for McConnell et al., 2003[170].

See Evidence Table 10 Alpha blocker vs. 5-alpha reductase inhibitors

for Roehborn et al., 2008[263]

1 **Evidence Table 20: Combination therapy: Anticholinergic added to alpha-blocker**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Macdiarmid et al., 2008[179] **Study design:** RCT, double blinded , multicentre March2004 to June2005 **Setting:** Double blinded RCT **Evidence level:** 1+ **Duration of follow-up:** 12 weeks post randomisation. All patients received 4 weeks of tamsulosin between screening and randomisation	**Patient group:** Men with LUTS who remained symptomatic despite 4 weeks of alpha blocker therapy **Inclusion criteria:** ▪ Age ≥ 45 years ▪ Diagnosed with LUTS, had urgency and frequency, with or without urge incontinence ▪ Qmax of 4ml/s with voided volumes of 125mL and post void residual volume of ≤ 150mL on at least 2 occasions After receiving ≥4 weeks of 0.4mg tamsulosin, they should still have: ▪ IPSS ≥13 and IPSS storage component (Question 2, 4 and 7) ≥8. **Exclusion criteria:** ▪ History of urinary retention, bladder or prostate cancer ▪ PSA ≥4 ng/ml ▪ Angle closure glaucoma ▪ Surgical or procedural treatment of the prostate **Amendments in protocol in July2004** Inclusion criteria ▪ Qmax of 8 ml/s with voided volumes of 125mL and post void residual volume of ≤ 150mL on at least 2 occasions **Discontinuation criteria:** ▪ Qmax decreased to 5mL/s or	**Group 1: Oxybutynin ER + 0.4 mg tamsulosin** Oxybutynin ER dose was 10mg/day, the recommended starting dose **Group 2: 0.4mg Tamsulosin + placebo** **Note:** All patients received 4 weeks of 0.4mg tamsulosin before randomisation	**IPSS**, mean±sd at various time points and change from baseline P values provided in paper based on ANCOVA using baseline values as the covariates	At week 4 Change Group 1: 15.9±6.7 -4.4±5.6 Group 2: 16.6±5.8 -3.8±5.5 P value: 0.24 At Week 8 Change Group 1: 14.5±7.3 -5.7±6.3 Group 2: 16.0±6.7 -4.4±6.0 P value: 0.03 At week 12 Change Group 1: 13.3±7.4 -6.9±6.5 Group 2: 15.2±6.9 -5.2±6.2 P value: 0.006	**Funding:** Ortho Urology, US (oxybutynin manufacturer) **Limitations:** ▪ Randomisation allocation and concealment not described ▪ The criteria for excluding about ½ of the screened population from randomisation not provided ▪ Characteristics at screening visit not provided ▪ This study only randomised patients who remained symptomatic despite ≥4 weeks of treatment with alpha blocker and should only be generalised to this group of patients (this is likely to augment the difference seen between the two intervention groups) **Additional outcomes:** SPI (symptom problem
			IPSS-QoL (maximum 6 points) at various at various time points and change from baseline P values provided in paper based on ANCOVA using baseline values as the covariates	Week 4 Change Group 1: 3.2±1.3 -0.9±1.4 Group 2: 3.5±1.3 -0.5±1.3 P value: 0.006 Week 8 Change Group 1: 3.0±1.5 -1.2±1.5 Group 2: 3.4±1.4 -0.6±1.3 P value: <.001 Week 12 Change Group 1: 2.8±1.5 -1.3±1.5 Group 2: 3.2±1.5 -0.8±1.4 P value:0.001	
			IPSS-Storage (maximum 15 points), mean ± sd at various time points and change from baseline P values provided in paper based on ANCOVA using baseline values as the covariates	At week 4 Change Group 1: 7.7±2.9 -2.6±2.7 Group 2: 8.2±2.6 -1.9±2.6 P value: 0.008 At Week 8 Change Group 1: 7.0±3.2 -3.3±3.0 Group 2: 7.9±3.0 -2.1±2.8 P value: <.001 At week 12 Change Group 1: 6.5±3.2 -3.7±3.0 Group 2: 7.6±3.1 -2.4±2.9 P value : <.001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	less ▪ Post void residual volume >300mL **<u>All patients</u>** **N:** 420 randomised out of 818 screened Mean age: 62.9±9.1 **Drop outs:** 2 (took <1 dose of medications) **<u>Group 1</u>- Oxybutynin ER + 0.4 mg tamsulosin** **N:** 209 Age, mean ±sd: 62.6±9.0 Dropouts: **Years since LUTS diagnosis**, years, mean±sd:5.0±5.7 **IPSS**, mean±sd:20.2±5.0 **IPSS-QoL**, mean±sd:4.1±1.1 **Qmax**, ml/s, mean±sd:15.7±7.1 **Post void residual volume**, ml, mean±sd: 50.7±42.9 **<u>Group 2</u>** **N:** 209 Age, mean ±sd: 63.3±9.2 Dropouts: **Years since LUTS diagnosis**, years, mean±sd:5.0±4.7 **IPSS**, mean±sd:20.5±4.9 **IPSS-QoL**, mean±sd:4.0±1.0 **Qmax**, ml/s, mean±sd:14.6±6.6 **Post void residual volume**, ml, mean±sd: 45.8±41.4		**Qmax** (ml/s), mean±sd P value and change values calculated by NCGC	<u>At 12 weeks</u> <u>Change</u> Group 1:15.5±8.4 -0.2±7.8 Group 2:14.7±8.4 0.1±7.6 P value: NS	index) values were also reported **Notes:** There were 6/209 vs. 1/209 patients with PVR >300ml (all withdrawn from study) in group 1 vs. group 2 respectively. There were 14/209 vs. 13/209 patients with Qmax<5 ml/s (8/209 vs. 12/209 at endpoint) respectively. The number patients discontinued as per protocol did not tally with the number of patients who had PVR>300ml
			Post void residual volume (ml), mean±sd P value and change values calculated by NCGC	<u>At 12 weeks</u> <u>Change</u> Group 1:69.7±75.3 18.2±77.3 Group 2:53.7±52.9 7.8±47.5 P value: NS	
				Group1 **Group 2** **P value** **Any adverse events** 89(42.6) 89(42.6) NS **Serious adverse events** 5(2.4) 6(2.9) NS **AEs leading to withdrawal** 21(10) 20(9.6) NS **Dry mouth** 32(15.3) 10(4.8) <.001 **Infections and infestations** 18(8.6) 22(10.5) NS **Renal and urinary AEs** 10(4.8) 10(4.8) NS **AUR** (with or without Foley catheter) 0(0) 0(0) NS **Nervous system disorders** 8(3.8) 9(4.3) NS **Constipation** 1(0.5) 4(1.9) NS	
			Reasons for study discontinuation **Adverse events** **Lack of efficacy** **Patient choice** **Others** (include PVR> 300ml and Qmax <5ml/s)	**Group 1** **Group 2** **P value** 21/209 20/209 NS 4/209 6/209 NS 5/209 0/209 NS 14/209 8/209 NS	

Evidence Table 21: Combination therapy: phosphodiesterase-5-inhibitor added to alpha-blocker

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Bechara et al., 2008[27] **Study design:** double blinded, cross over study **Setting:** single-centre in Argentina **Evidence level:** 1+ **Duration of follow-up:** Week 12	**Patient group:** LUTS and erectile dysfunction **Inclusion criteria:** • > 50 years • Clinical diagnosis of LUTS by medical history and physical examination • At least 6 months of LUTS; IPSS≥12, • Total PSA ≤4.0ng/ml • Qmax > 5ml/s with minimum voided volume of >125ml **Exclusion criteria:** • History or evidence of prostate cancer • Previous prostate surgery or other invasive procedure to treat BPH • Post void residual volume >250ml • History of AUR ≤3 months of screening visit • Use of alpha reductase inhibitors or phytotherapy ≤ 6 months; alpha blockers or PDE5-I ≤2 weeks • Cardiovascular comorbidities and uncontrolled diabetes • Comorbidities which may interfere with urinary flow or symptoms. **<u>All patients</u>** **N:** 30 out of 40 patients screened **Drop outs:** 3 (2 adverse events, 1 personal reasons) **Age, mean (range):** 63.7(51-78) **Sexually active:** 28/30 (93.3%) **IPSS, mean (range):** 19.4 (12-34)	**Group 1: Tamsulosin0.4mg/ day+ tadalafil 20mg/day** For 6 weeks, at about the same time each day **Group 2: Tamsulosin 0.4mg/day +placebo** For 6 weeks, at about the same time each day The capsules were identical and prepared by a third party (pharmacist) in numbered containers Cross over design: The patients were randomised to treatment Group 1 or Group 3 at Visit 1 (week 0). At week 6, end point measures were collected and patients switched over to the other treatment group. At week 12, end points	**IPSS change from baseline at end of 6 week treatment,** mean ±SD	**Grp 1:** -9.2±5.08 **Grp 2:** -6.7±3.87 *P value: <0.05	**Funding:** NR **Limitations:** ▪ This is a cross-over RCT. There was no washout period to provide verification that patients had returned to their baseline level. ▪ The sample size is small **Additional outcomes:** IIEF-EF, GAQ (Global Assessment Quality) and a visual analogue scale (no mention of validations) **Notes:** *P values were as reported in paper. Authors reported using Tukey Cramer test with multiple comparisons **IIEF-EF>25 points was reported as 28/30(93.3%) at baseline in Table1. These numbers did not tally with mean IIEF (sexual function domain) of 15 points at baseline (Table3) and number of men with ED who completed study (19/27).
			IPSS-QOL at end of 6 week treatment, mean ±SD	**Grp 1:** 1.6, no SD **Grp 2:** 2.3, no SD *P value: <0.05	
			Qmax, ml/s, mean± SD	**Grp 1:** 12.6, no sd **Grp 2:** 11.7, no sd *P value: >0.05	
			IIEF-EF mean± SD	**Grp 1:** 23.2, no sd **Grp 2:** 16.9, no sd *P value:<0.001	
			Adverse Events **Headache** **Hypotension** **Dizziness** **Dyspepsia** **Diarrhoea** **Ejaculation disorder** **Altered vision**	**Grp 1 Grp 2** 12 0 2 1 0 1 3 1 0 1 0 1 0 1	
			Withdrawals due to adverse events **Headache** **Rashes**	**Grp 1 Grp 2** 1/30 0/30 0/30 1/30	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	IPSS-QoL, mean (range): 4.1 (0-6) **Qmax, ml/s, mean (range):** 9.6 (4 to 14) ****IIEF-EF** mean(range):17(1-29)	were measured again.			Erectile Function domain of the 15-question IIEF (Q1-5 and Q15, maximum score 30) was used. This is different from IIEF-5, which consists of Q2, Q4, Q5, Q7 and Q15 of the IIEF (maximum score 25)

1 See Evidence Table 12 Alpha-blockers vs. phosphodiesterase-5 inhibitors

2 for Kaplan et al., 2007[132]

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Liguori et al., 2009 [167] **Study design:** RCT open label, **Setting:** Multicentre (5) in Italy from Feb to Dec2007 **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** Men with LUTS and previously untreated erectile dysfunction **Inclusion criteria:** ▪ Men aged 50 to 75 years with previously untreated ED and a history of LUTS secondary to BPH for 6 months or longer ▪ IPSS>8 **Exclusion criteria:** ▪ Contraindications to the study drugs ▪ Using medications to control bladder symptoms or had ever taken alpha blockers, PDE5-I, or 5 alpha reductase inhibitors. ▪ Bladder tumours, urethral strictures, neurogenic bladder dysfunction ▪ History of prostatits, prostate cancer; prostate surgery, radiotherapy ▪ PSA level>20 ng/ml ▪ Acute urinary retention or indwelling catheter ▪ Infection on urinalysis **All patients** **N:** 66 **Mean age:** 61 years (range 50 to 75) **Drop outs:** 8/66 (Baseline data excluded patients who dropped out of study) **Group 1 (Tadalafil)** **N:** 21 **Dropouts:**2 /21 **Mean (± SD) Age:** 60.8±8 **IPSS mean± SD:**13.8±5.6	**Group 1:** Tadalafil 20 mg every other day **Group 2:** Alfuzosin 10 mg/day **Group 3:** tadalafil 20 mg every other day + alfuzosin 10 mg/day	**IPSS** **Note:** The change from baseline values were calculated by NCGC	Baseline: **Grp 1:** 13.8±5.6 **Grp 2:** 15.7±4.8 **Grp 3:**15.3±4.5 At 12 weeks **Grp 1:** 12.5±5.6 **Grp 2:** 10.6±3.6 **Grp 3:** 9.0±4.0 Change from baseline **Grp 1:** -1.3±5.6 **Grp 2:** -5.2±4.2 **Grp 3:** -6.3±4.3	**Funding:** Reported no conflicts of interest **Limitations:** ▪ This was an open label study with no randomisation allocation and concealment methods reported. The outcomes are mainly subjective outcomes, and this makes it particularly at risk of biases. **Additional outcomes:** Changes in IPSS (obstructive), IPSS (irritative) IIEF-EF, and IIEF Q15 were also reported **Notes:** **Erectile Dysfunction assessed using the Erectile Function domain score of the 15-question IIEF, ie , ie Q1-5 and Q15 (Maximum score 30). This is different from IIEF-5, which consists of question Q2, Q4, Q5,
			IPSS % change from baseline at 12 weeks The P values reported were for 12 weeks compared to baseline	**Grp 1:** -8.4, p=NS **Grp 2:** -27.2, p=0.003 **Grp 3:** -41.6, p<0.001	
			IPSS-QoL	Baseline: **Grp 1:** 3.5±1.1 **Grp 2:** 3.4±0.9 **Grp 3:** 3.2±1 At 12 weeks **Grp 1:** 2.5±1.2 **Grp 2:** 2.1±0.9 **Grp 3:** 1.6±0.8 Change from baseline **Grp 1:** 1±1.2 **Grp 2:** 1.3±0.9 **Grp 3:** 1.6±0.9	
			Qmax, ml/s mean ±sd	Baseline: **Grp 1:** 13.1±4.3 **Grp 2:** 12.3±5.4 **Grp 3:** 11.9±2.7 At 12 weeks **Grp 1:** 14.3±5.2 **Grp 2:** 14.0±3.7	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	IIEF-EF, mean ±sd: 14.1 **IIEF Q15 mean± SD:** 2.5 **Qmax mean± SD, mL/s:**13.1 **<u>Group 2 (Alfuzosin)</u>** **N:** 22 **Dropouts:** 4/22 **Mean (± SD) Age:** 61.3±6.8 **IPSS mean± SD:**15.7±4.8 **IIEF-EF, mean ±sd:**14.2 **IIEF Q15 mean± SD:** 2.8 **Qmax mean± SD, mL/s:**12.3 **<u>Group 3 (Tadalafil + Alfuzosin)</u>** **N:** 23 **Dropouts:** 2/23 **Mean (± SD) Age:** 63 ± 6.9 **IPSS mean± SD:**15.3±4.5 **IIEF-EF, mean ±SD:** 14.6 **IIEF Q15 mean± SD:** 2.4 **Qmax mean± SD, mL/s:**11.9			**Grp 3:** 15.0±4.0 <u>Change from baseline</u> **Grp 1:** 1.2±4.8 **Grp 2:** 1.7±4.6 **Grp 3:** 3.1±3.4	Q7 and Q15 of the IIEF (maximum score 25).
			Nocturia (as recorded in voiding diary)	<u>Baseline:</u> **Grp 1:** 1.7±1 **Grp 2:** 1.9±0.9 **Grp 3:** 1.9±0.9 <u>At 12 weeks</u> **Grp 1:** 1.1±1.1 **Grp 2:** 1.0±0.7 **Grp 3:** 1.1±0.9 <u>Change from baseline</u> **Grp 1:** -0.6±1.1 **Grp 2:** -0.9±0.8 **Grp 3:** -0.8±0.9	
			Withdrawals due to AE **The reason for withdrawals were**	**Grp 1** **Grp 2** **Grp 3** 1/21 3/22 2/23 **Group 1:** back pain, head aches **Group 2 :**dizziness, constipations **Group 3:** myalgia, dizziness, sensation of heaviness	

Evidence Table 22: Holmium laser enucleation (or resection) of the prostate HoLEP (HoLRP) vs. transurethral resection of the prostate

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Ahyai et al., 2007[11] **Study design:** RCT **Setting:** Urology department, Berlin **Evidence level:** 1+ **Duration of follow-up:** 36 months	**Patient group:** Patients with lower urinary tract symptoms due to BPH. **Inclusion criteria:** AUA of 12 or more, Qmax of 12ml/s or less, PVR volume > 50ml, Schafer grade of II or more in pressure flow studies, and a total prostate volume <100cc in transrectal ultrasound. **Exclusion criteria:** previous prostate or uerthral surgery and voiding disorders not related to benign prostatic hyperplasia. Prostate carcinoma excluded by biopsy. **All patients** **N:** 200 **Group 1** **N:** 100 Mean Age: 68.0 Dropouts: 25 (prostate cancer=3, stricture=4, refused follow-up=6, bladder neck contracture=3, moved away=3, polymorbidity=2, death=3, BPH recurrence=1) **Group 2** **N:** 100 Mean Age: 68.7 Dropouts: 31 (prostate cancer=10, stricture=3, refused follow-up=4, bladder neck contracture=3, moved away=1, polymorbidity=5, death=3, transition cell carcinoma=2)	**Group 1: HoLEP** 40-50 Hz, 80-100W used. Saline used as irrigation fluid and electrolyte-free solution for electrocautery loop tissue fragmentation. Postoperative bladder irrigation used as necessary until haematuria had settled sufficiently to remove catheter. Median postoperative catheterisation=1 day Median Hospital stay=2 days **Group 2: TURP** standard tungsten wire loop with a cutting current o f 160 W and coagulating current of 80 W. Postoperative bladder irrigation used as necessary until haematuria had settled sufficiently to remove catheter. Median postoperative catheterisation=2 day Median Hospital stay=3 days	**Mean (SD) AUA**	**Baseline:** Group1 (n=100): 22.1 (3.8) Group 2 (n=100): 21.4 (5.2); p=0.56 **6 months:** Group1 (n=94): 2.2 (1.6) Group 2 (n=89): 3.7 (3.4); p=0.006 **12 months:** Group1(n=89): 1.7 (1.8) Group 2(n=86): 3.9 (3.9); p<0.001 **18 months:** Group1 (n=82): 1.3 (1.5) Group 2 (n=78): 4.0 (3.8); p<0.0001 **24 months:** Group1 (n=80): 1.7 (1.7) Group 2 (n=75): 3.9 (3.7); p<0.0001 **36 months:** Group1 (n=75): 2.7 (3.2) Group 2 (n=69): 3.3 (3.0); p=0.17	**Funding:** Financial interest and/or other relationship with Lumenis, Inc and Karl Storz, Inc. **Limitations:** Allocation concealment and blinding unclear. **Notes:** Linked to Kuntz 2004[151] – follow up for 24 months.
			Mean (SD) Qmax, ml/s	**Baseline:** Group1: 4.9 (3.8) Group 2: 5.9 (3.9); p=0.08 **6 months:** Group1: 25.1 (6.9) Group 2: 25.1 (9.4); p=0.72 **12 months:** Group1: 27.9 (9.9) Group 2: 27.7 (12.2); p=0.76 **18 months:** Group1: 27.5 (9.2) Group 2: 28.2 (11.2); p=0.89 **24 months:** Group1: 28.0 (9.0) Group 2: 29.1 (10.9); p=0.82 **36 months:** Group1: 29.0 (11.0) Group 2: 27.5 (9.9); p=0.41	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Mean (SD) PVR, ml	**Baseline:** Group1: 237 (163) Group 2: 216 (177); p=0.08 **6 months:** Group1: 4.8 (12.5) Group 2: 16.7 (16.9); p=0.03 **12 months:** Group1: 5.3 (15.3) Group 2: 26.6 (60.4); p<0.001 **18 months:** Group1: 1.6 (11.5) Group 2: 16.3 (28.4); p<0.0001 **24 months:** Group1: 5.6 (19.9) Group 2: 19.9 (29.6); p<0.0001 **36 months:** Group1: 8.4 (16.0) Group 2: 20.2 (33.0); p<0.012	
			Peri-operative complications	**Blood transfusion** Group 1: 0 Group 2: 2 (2%) **Recatheterisation** Group 1: 0 Group 2: 5 (5%) **Mortality** Group 1: 0 Group 2: 0	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Complications at 36 months	**Urethral stricture** Group 1: 4 (4.1%) Group 2: 3 (3.3%) **Bladder neck contracture** Group 1: 3 (3.1%) Group 2: 3 (3.3%) **BPH recurrence:** Group 1: 1 (1.0%) Group 2: 0 **Reoperation:** Group 1: 7.2% Group 2: 6.6%	
			Urinary incontinence at 12 months	**Preoperatively:** Group 1: 27/89 Group 2: 33/86 **Post operatively:** Group 1: 5/89 Group 2: 5/86	
			Stress incontinence developed after surgery	Group 1: 1 Group 2: 1	
			Potency following preoperative erectile dysfunction (insufficient for sexual intercourse)	Group 1: 2/43 Group 2: 0/41	
			Resolved erectile dysfunction postoperatively	Group 1: 1 Group 2: 1	
			Decreased potency at 12 months compared to preoperative level	Group 1:10/89 (11.2%) Group 2: 9/86 (10.5%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Gupta et al., 2006[108] **Study design:** RCT **Setting:** India **Evidence level:** 1+ **Duration of follow-up:** 12 months.	**Patient Group:** Patients with BPH who were candidates for TURP were selected from July 2002 to December 2003. **Inclusion criteria:** glands of >40g **Exclusion criteria:** patients with a previous history of prostatic and urethral surgery, neurovesical dysfunction and carcinoma of the prostate were excluded from the study. **All patients** **N:** 150 **Group 1** **N:** 50 Mean (±SD) Age: 65.88 (10.1) Dropouts: NR **Group 2** **N:** 50 Mean (±SD) Age: 65.67 (7.5) Dropouts: NR **Group 3** **N:** 50 Mean (±SD) Age: 67.68 (9.8) Dropouts: NR	**Group 1: HoLEP** Power settings were 80-100W. Operative duration: 75.4 minutes **Group 2: TURP** 80W cutting and 50W coagulation used. Operative duration: 64.1 minutes **Group 3: TUVRP** 180W cutting and 80W coagulation used. Operative duration: 55.9 minutes	**Mean (SD) IPSS:**	**Baseline:** Group1: 23.4 (4.5) Group 2: 23.3 (3.9) Group 3: 24.9 (3.9) **6 months:** Group1: 5.2 (0.31) Group 2: 6.1 (0.42) Group 3: 5.9(0.25) **12 months:** Group1: 5.2 (0.17) Group 2: 5.6 (0.32) Group 3: 5.4 (0.28)	**Funding:** NR **Limitations:** No mention of drop outs in the study. **Additional outcomes:** Irrigation, haemoglobin decrease, serum sodium decrease. **Notes:** None.
			Mean (SD) Qmax	**Baseline:** Group1: 5.15 (4.4) Group 2: 4.5(3.9) Group 3: 4.65 (3.6) **6 months:** Group1: 23.1(1.2) Group 2:20.7 (1.32) Group 3: 22.5 (0.95) **12 months:** Group1: 25.1 (1.06) Group 2: 23.7 (1.58) Group 3: 23.6(0.96)	
			Mean (SD) PVR, mL	**Baseline:** Group1: 112.0(155.9) Group 2: 84.0(129.7) Group 3: 103 (174.1) **6 months:** Group1: <20 Group 2: <20 Group 3: <20 **12 months:** Group1: <20 Group 2: <20 Group 3: <20	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Mean (SD) blood loss, mL	Group1: 40.6 (37.3) Group 2: 140.5 (60.7) Group 3: 68.6 (42.7)	
			Mean (SD) catheter duration, hours	Group1: 28.6 (20.5) Group 2: 45.7 (12.7) Group 3: 36.2 (8.3)	
			Mean (SD) nursing contact time, minutes	Group 1: 28.1 (8.4) Group 2: 48.3 (9.2) Group 3: 37.2 (6.7)	
			Number (%) complications	**Re-catheterisation:** Group 1: 2 (4) Group 2 3 (6) Group 3: 3 (6) **Fever:** Group 1: 1 (2) Group 2: 1 (2) Group 3: 2 (4) **Hyponatraemia:** Group 1: 0 Group 2: 1 (2) Group 3: 1 (2) **Blood transfusion:** Group 1: 0 Group 2: 1 (2) Group 3: 0 **Capsular perforation:** Group 1: 1 (2) Group 2: 0 Group 3: 0 **Bladder mucsal injury:** Group 1: 2 (4) Group 2: 0 Group 3: 0 **Death (pneumonia):** Group 1: 0 Group 2: 0 Group 3: 1 (2)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Transient dysuria: Group 1: 5 (10) Group 2: 1 (2) Group 3: 9 (18) **Stricture:** Group 1: 1 (2) Group 2: 2 (4) Group 3: 1 (2) **Incontinence:** Group 1: 1 (2) Group 2: 1 (2) Group 3: 0	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Mavuduru RM 2009[187] **Study design:** RCT **Evidence level:** 1+ **Setting:** Chandigarh, India **Duration of follow-up:** 9 months	**Patient group:** Patients who underwent surgery for BPH. **Inclusion criteria:** **Exclusion criteria:** Patients with a history of previous prostatic or urethral surgery, and documented cases of prostate carcinoma. **All patients** **N:** 30 **Group 1: TURP** **N:** 15 **Age (mean):** 66.46±5.79 **Drop outs:** 0 **Group 2: HoLEP** **N:** 15 **Age (mean):** 69.86±9.6 **Drop outs:** 0	**Group 1: Transurethral resection of the prostate (TURP).** TURP was performed by standard technique using a 26-Fr continuous flow resectoscope (Karl Storz) with a cutting current of 100-120 D and coagulating current of 50-60 W. The intraoperative irrigation fluid used was1.5% glycine, the TURP chips were removed by Ellick's evacuator. **Group 2: Holmium laser enucleation of the prostate (HoLEP)** Instrumentation included 550nm end-firing flexible quartz, and a continuous flow resectoscope consisting of a 27-Fr outer sheath, an inner rotating sheath with a self-designed working element. HoLEP was performed by standard technique as described by Gilling et al. The machine used was Versapulse Holmium Laser, with a frequency if 35-40 Hz and a power setting of 2 joules. The irrigant used	**Mean ±SD symptom score- IPSS**	**Baseline:** Group1: 21.4±3.7 Group 2: 22.53±4.79 **3 months:** Group1: 2.86±1.72 Group 2: 2.26±1.57 **p value:** 0.329 **9 months:** Group1: 3.57±1.03 Group 2: 4.32±1.25 **p value:** 0.37	**Funding:** NR **Limitations:** Small study size and duration of follow up is less than 1 year. **Additional outcomes:** Intraoperative data including weight of gland resected and volume of irrigation fluid.
			Mean ± SD PVR volume (ml)	**Baseline:** Group1:103 ±27 Group 2: 91±30 **3 months:** Group1: 13.66±14.0 Group 2: 13±8.61 **p value:** 0.87 **9 months:** Group1: 35.66±15.0 Group 2: 43±10.61 **p value:** 0.97	
			Mean ± SD Uroflowmetry	**Baseline:** Group1:6.9 ±2.5 Group 2: 5.79±2.7 **3 months:** Group1: 27.8±6.5 Group 2: 28.6±6.2 **p value:** 0.721 **9 months:** Group1: 27.8±6.5 Group 2: 28.6±6.2 **p value:** 0.64	
			Operative time (minutes)	**Group1:** 43±9.36 **Group 2:** 53±9.84 **p value:** <0.01	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
		was normal saline.	**Duration of catheterization (hours)**	**Group1:** 78.20±17.84 **Group 2:** 46.42±14.25 **p value:** <0.001	
			Adverse events	**Transient dysuria** Group 1: 3/15 (40%) Group 2: 1/15 (6.66%) **Recatheterization** Group 1: 1/15 (6.66%) Group 2: 1/15 (6.66%) **Bleeding** Group 1: 2/14 (13.33%) Group 2: nil **Incontinence** Group 1: nil Group 2: 2/15 (13.33%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Montorsi et al., 2004[202] **Study design:** RCT **Setting:** 2 centre study (Milan and Bergamo) **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** consecutive patients with symptomatic obstructive BPH from January to October 2002. **Inclusion criteria:** Age<75 years, peak urinary glow rate <15ml/s, post void residual urine <100cc, medical therapy failure, transrectal ultrasound adenoma volume <100gm and urodynamic obstruction. **Exclusion criteria:** Neurogenic bladder, diagnosis of prostate cancer and any previous prostatic, bladder neck or urethral surgery. **All patients** **N:** 100 **Group 1** **N:** 52 Mean Age: 65.14 Mean TRUS volume (gm): 70.3 Dropouts: NR **Group 2** **N:** 48 Mean Age: 64.5 Mean TRUS volume (gm): 56.2 Dropouts: NR	**Group 1: HoLEP** Tissue morcellation of the prostatic lobes into fragments that were retrieved form the bladder cavity. Energy delivered by a 360u fibre. Enucleation performed at 2.0J and 35Hz. Total operative time: 74±19.5 minutes. Catheterisation time 31±13 hours Hospital stay 59±19.9 hours **Group 2: TURP** Using a standard tungsten wire loop with a cutting current of 80W and a coagulation g current of 160W. Following procedure catheter inserted into bladder and irrigation started. Total operative time: 57±15 minutes. Catheterisation time 57.78±17.5 hours Hospital stay 85.8±18.9 hours	**Mean (SD) IPSS**	**Baseline:** Group1: 21.6±6.7 Group 2: 21.9±7.2 **6 months:** Group1: 3.9±2.9 Group 2: 2.9±2.6 **12 months:** Group1: 4.1±2.3 Group 2: 3.9±3.6;p=0.58	**Funding:** NR **Limitations:** Number of drop outs not reported. Prostate size significantly different at baseline. **Additional outcomes:** Average flow reported. Orgasmic function, sexual desire, intercourse satisfaction. **Notes:** Linked with Rigatti 2006[251]
			Mean (SD) QoL question	**Baseline:** Group1: 4.6±1.11 Group 2: 4.7±1.0 **6 months:** Group1: 1±0.8 Group 2: 0.6±0.2 **12 months:** Group1: 1.4±0.9 Group 2: 0.8±1.28;p=0.31	
			Mean (SD) maximum flow (ml/s)	**Baseline:** Group1: 8.2±3.2 Group 2: 7.8±3.6 **6 months:** Group1: 23.1±8.6 Group 2: 26.5±15.5 **12 months:** Group1: 25.1±7.2 Group 2: 24.7±10;p=0.25	
			Mean detrusor pressure at max flow (cmH20)	**Baseline:** Group1: 77.3 Group 2: 81.8 **12 months** Group 1:36.2 Group 2: 38.5 ; p=0.85	
			Mean Schafer grade	**Baseline:** Group1: 3.4 Group 2: 3.5	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				12 months Group 1: 0.9 Group 2: 1.2; p=0.55	
			Mean (SD) Erectile function (International Index of Erectile Function IIEF-15)	**Preoperatively:** Group 1: 22.3±3.6 Group 2: 21.4±3.1 **6 months:** Group 1: 23.5±3.6 Group 2: 23.4±3.5 **12 months:** Group 1: 23.8±3.9 Group 2: 24.1±3.7	
			Number (%) of early Adverse events	**Bladder mucosal injury** Group 1: 10 (18.2%) Group 2: 0 **Re-intervention for bleeding** Group 1: 1 (1.7%) Group 2: 1 (2.2%) **Transurethral resection syndrome** Group 1: 0 Group 2: 1(2.2%) **Early acute urinary retention** Group 1: 3 (5.3%) Group 2: 1 (2.2%) **Dysuria (burning)** Group 1: 33 (58.9%) Group 2: 13 (29.5%) **Transitory urge incontinence** Group 1: 25 (44%) Group 2: 17 (38.6%)	
			Adverse events at 6 & 12 month follow up (%)	**Urethral stricture:** Group 1: 1 (1.7%) Group 2: 4 (7.4%) **Stress incontinence:** Group 1: 1 (1.7%) Group 2: 1 (2.2%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Westenberg et al., 2004[318] **Study design:** RCT **Evidence level:** 1+ **Setting:** Tauranga Hospital, New Zealand. **Duration of follow-up:** 48 months	**Patient group:** Candidates for surgery for LUTS and obstruction due to BPH at Tauranga Hospital from April 1996 to August 1997. **Inclusion criteria:** Age 80 years or younger, AUA score ≥8, peak urinary flow rate ≤15ml/s, transerectal ultrasound volume of the prostate <100ml, post void residual volume <400ml and Schafer grade ≥2. **Exclusion criteria:** Catheterised patients and those who had undergone previous urethral or prostatic surgery. All patients had a digital rectal examination and SPA before enrolment to excluded men with carcinoma of the prostate. **<u>All patients</u>** **N:** 120 **<u>Group 1</u>** **N:** 61 Mean (±SD) Age: 66.9±6.5 Dropouts at 48m: 18 (2 died cardiovascular disease, 5 required reoperation, 6 intercurrent illness, 5 lost to follow up). **<u>Group 2</u>** **N:** 59 Mean (±SD) Age: 66.8±7.4 Dropouts at 48m: 29 (7 died – cardiovascular or malignant disease, 8 required reoperation, 4 intercurrent diseases, 10 lost to	**Group 1** **Holmium laser resection (HoLRP).** Maximum average power of 80W was used. General or spinal anaesthesia required in all cases. Postoperative bladder irrigation was only used if deemed necessary by the surgeon. Catheter removed the morning after surgery. Mean catheter time: 26.2±11.71. **Group 2** **TURP** using a cutting current of 160W and a coagulating current of 80W. General or spinal anaesthesia was used. Bladder irrigation was used and catheter removed before patient discharged from hospital. Mean catheter time: 47.5±17.37.	**AUA score**	**Baseline:** Group1 (n=61): 21.9±6.2 Group 2 (n=59): 23.0±5.9 **3 months:** Group1 (n=61): 5.6±5.1 Group 2 (n=59): 5.7±5.2 **6 months:** Group1 (n=61): 3.8±3.8 Group 2 (n=59): 5.0±4.5 **12 months:** Group1 (n=53): 4.2±6.0 Group 2 (n=49): 4.3±4.1 **18 months:** Group1: 2.9±5.3 Group 2: 4.5±5.3 **24 months:** Group1 (n=45): 3.4±4.9 Group 2 (n=41): 3.7±4.9 **48 months:** Group1 n=43): 5.2±5.9 Group 2 (n=30): 6.6±5.0; P=0.32	**Funding:** Financial interest and/or other relationship with Lumenis, Inc. **Limitations:** Allocation concealment and blinding unclear. **Additional outcomes:** Detrusor pressure at 6 months. **Notes:** Linked to Gilling 1999[104], Gilling 2000[103] and Fraundorfer 2001[97]
			Quality of Life score:	**Baseline:** Group1 (n=61): 4.5±1.1 Group 2 (n=59): 4.7±1.1 **3 months:** Group1 (n=61): 1.4±1.5 Group 2 (n=59): 1.6±1.4 **6 months:** Group1 (n=61): 1.1±1.3 Group 2 (n=59): 1.5±1.4 **12 months:** Group1 (n=53): 0.88±1.4 Group 2 (n=49): 1.6±1.5 **18 months:** Group1 (n=61): 0.72±1.1 Group 2 (n=59): 1.3±1.1 **24 months:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	follow up).			Group1 (n=45): 0.98±1.3 Group 2 (n=41): 1.0±1.3 **48 months:** Group1 n=43): 1.1±1.1 Group 2 (n=30): 1.4±1.4; P=0.37	
			Qmax (ml/s)	**Baseline:** Group1 (n=61): 8.9±3.0 Group 2 (n=59): 9.1±3.2 **3 months:** Group1 (n=61): 22.8±10.0 Group 2 (n=59): 20.2±9.5 **6 months:** Group1 (n=61): 23.9±8.7 Group 2 (n=59): 22.4±9.0 **12 months:** Group1 (n=53): 25.2±11.9 Group 2 (n=49): 20.4±8.5 **18 months:** Group1: 25.1±9.3 Group 2: 19.2±9.3 **24 months:** Group1 (n=45): 25.0±11.1 Group 2 (n=41): 20.9±11.1 **48 months:** Group1 n=43): 22.3±14.2 Group 2 (n=30): 18.5±8.2; P=023	
			TRUS volume (cc)	**Baseline:** Group1: 44.3±19.0 (11-92) Group 2: 44.6±20.7 (11.5-95) **6 months:** Group1: 29.3 (11-61) Group 2: 27.3 (10-75)	
			Post void residual (ml)	**Baseline:** Group1: 87.8±88.4 (0-346) Group 2: 84.7±81.7 (0-373) **6 months:** Group1: 26.7 (0-245) Group 2: 34.3 (0-295)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			<u>Adverse events:</u> **Perioperative blood transfusions:** **Recatheterised** **Reoperations** **Urinary tract infections** **Strictures** **Deep vein thrombosis**	 Group1: 0/61 Group 2: 4/59 Group1: 5/61 Group 2: 8/59 Group1: 5/61 Group 2: 8/59 Group1: 3/61 Group 2: 5/59 Group1: 6/61 Group 2: 6/59 Group1: 0/61 Group 2: 1/59	
			Incontinence	Group 1: 1/61 Group 2: 2/59	
			Deaths (due to cardiovascular or malignant disease)	**12 months:** Group 1: 1/61 Group 2: 1/59 **48 months:** Group1: 2/61 Group 2: 7/59	
			% UI (preoperatively/48 months follow up)	Group 1: 50%/20% Group 2: 47%/17%	
			Patients with decreased erection quality at 48m	Group 1: 8% Group 2: 17%	
			% of men potent	**Baseline:** Group 1: 50% Group 2: 70% **48 months** Group 1: 53% Group 2: 60%	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Retrograde ejaculation	Group 1: 24/25 (96.0%) Group 2: 32/37 (86.5%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Wilson et al., 2006[323] **Study design:** RCT **Setting:** New Zealand **Evidence level:** 1+ **Duration of follow-up:** 24 months	**Patient group:** Men at urology service at Hospital between June 1997 and December 2000 and considered for surgical treatment for bladder outlet obstruction secondary to BPH. **Inclusion criteria**: TRUS volume of 40-200g, Qmax of 15ml/s or less, AUA symptom score of 8 or greater, PVR of less than 400ml and urodynamic Schaffer grade 2 or greater. **Exclusion criteria:** prostatic carcinoma, catheterised patients and those with a history of previous urethral or prostatic surgery. **All patients** **N:** 61 **Group 1** **N:** 31 Mean (±SD) Age: 71.7 (1.1) Dropouts: 9 (one died preoperatively) **Group 2** **N:** 30 Mean (±SD) Age: 70.3 (1.0) Dropouts: 4	**Group 1: HoLEP** Maximum power 100W and a Versacut morcellator was used. Post operative Foley catheter irrigation was performed if deemed necessary; most patients were treated with a Foley catheter, which was normally removed the day after surgery. Mean catheter time: 17.7 hrs Mean hospital time: 27.6 hrs **Group 2: TURP** Tungsten cutting wire at 160W cutting and 80 W coagulating current. Irrigating Foley catheter inserted and bladder irrigation was used as necessary until haematuria had settled sufficiently to remove the catheter. Mean catheter time: 44.9 hrs Mean hospital time: 49.9h hrs	**Mean (SD) AUA symptom score**	**Baseline (n=60)** Group1: 26±6.02 Group 2: 23.7±6.57 **3 months (n=56)** Group1 (n=28) 4.8±4.23 Group 2 (n=29): 3.4±4.85 **6 months (n=54)** Group1 (n=26): 6.0±5.10 Group 2 (n=29): 4.8±3.77 **12 months (n=52)** Group1 (n=25): 4.3±3.5 Group 2 (n=27): 5.0±4.68 **24 months (n=48)** Group1 (n=22): 6.1±4.69 Group 2 (n=26): 5.2±4.08	**Funding:** Supported by Pub Charity, Inc. Financial interest and/or other relationship with Lumenis, Inc, Tel Aviv, Israel. **Limitations:** Reported Tan 2003 results but these differ to some of the figures quoted in Wilson 2006. Used same results as HTA report. **Additional outcomes:** PSA before and after in selected patients. PVR at 6 months. **Notes:** Linked to Tan 2003[292] Calculated SD from SE figures given in study.
			Mean (SD) QoL	**Baseline:** Group1: 4.8±1.1 Group 2: 4.7±1.1 **3 months:** Group1: 1.8±2.12 Group 2: 1.9±3.23 **6 months** Group1: 1.6±1.53 Group 2: 1.5±1.08 **12 months** Group1: 1.5±2.5 Group 2: 1.4±1.56 **24 months** Group1: 1.25±0.94 Group 2: 1.25±1.02	
			Mean (SE) Qmax, ml/s	**Baseline:** Group1: 8.4±0.5 Group 2: 8.3±0.4 **3 months:** Group1: 24.2±1.7 Group 2: 18.9±1.9 **6 months**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group1: 26.4±1.8 Group 2: 20.8±2.3 **12 months** Group1: 21.8±2.1 Group 2: 18.4±2.8 **24 months** Group1: 21.0±2.0 Group 2: 19.3±2.2	
			PdetQmax (cmH20)	**Preoperative** Group1: 73.2±4.4 Group 2: 85.8±5.4 **6 months** Group1: 20.8±2.8 Group 2: 40.7±2.7 **P<0.001**	
			Schaffer grade	**Preoperative** Group1: 3.5±0.2 Group 2: 3.7±0.2 **6 months** Group1: 0.2±0.09 Group 2: 1.2±0.2 **P<0.001**	
			TRUS volume (cc)	**Preoperative** Group1: 77.8±5.6 Group 2: 70.0±5.0 **6 months** Group1: 28.4±1.8 Group 2: 46.6±4.4 P<0.001	
			Onset of erectile dysfunction at 24 months	**Group 1:** 2 **Group 2:** 2	
			Retrograde ejaculation	**Group 1:** 12/16 **Group 2:** 8/13	
			Preoperative incontinence	Group1: 15/31 (48%) Group 2: 11/30 (38%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Patients that regained continence post operatively	Group1: 6/15 Group 2: 8/11	
			Adverse events at 24 months	**Blood transfusion** Group1: 0 Group 2: 1 **Re-catheterisation** Group1: 5 Group 2: 4 **Re-operation** Group1: 0 Group 2: 2 **Urinary tract infections** Group1: 0 Group 2:2 **Strictures** Group1: 1 Group 2: 3 **Deaths (cardiovascular causes)** Group1: 0 Group 2: 1	

1

Evidence Table 23: Thulium laser resection vs. transurethral resection of the prostate

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Xia et al., 2008[330] **Study design:** RCT **Evidence level:** 1+ **Setting:** China **Duration of follow-up:** 12 months	**Patient group:** consecutive BPH patients from November 2004 to December 2005. **Inclusion criteria:** age < 85yr, maximum urinary flow rate <15ml/s, post void residual urine volume <150ml, medical therapy failure, transrectal ultrasound adenoma volume <100g and urodynamic obstruction. **Exclusion criteria:** neurogenic bladder, diagnosis of prostate cancer and any pervious prostatic, bladder-neck or urethral surgery, and the presence of an indwelling catheter. **<u>All patients</u>** **N:** 100 **<u>Group 1</u>** **N:** 52 **Age (mean):** 68.9±7.7 TRUS volume (ml): 59.2±17.7 **Drop outs:** 0 **<u>Group 2</u>** **N:** 48 **Age (mean):** 69.3±7.3 TRUS volume (ml): 55.1±16.3 **Drop outs:** 0	**Group 1: Thulium laser resection of prostate – tangerine technique.** Epidural anaesthesia was achieved. An average power of 50-W thulium lasers operated in continuous wave mode was used. Energy delivered via 550um end-firing fibres. Saline irrigation used. Procedure similar to peeling a tangerine. **Group 2: TURP** Standard tungsten wire loop with a cutting power of 160W and a coagulating current of 80W. Irrigation started until haematuria had sufficiently decreased. **Postoperative care for all patients:** Following both procedures, triple lumen catheter inserted into the bladder. Patients kept in hospital 3 days following catheter removal. 500mg levofloxacin used 1 hour before operation	**Mean ±SD symptom score- IPSS**	**Baseline:** Group1: 21.9±6.7 Group 2: 20.8±5.8 **6 months:** Group1: 4.0±2.4 Group 2: 3.8±2.8 **12 months:** Group1: 3.5±2.9 Group 2: 3.9±2.7	**Funding:** NR **Limitations:** Allocation concealment and method of randomisation unclear. **Additional outcomes:** Haemoglobin, serum sodium decrease, resected weight. **Notes:** None.
			Mean ± SD quality of life	**Baseline:** Group1: 4.7±0.9 Group 2: 4.5±1.1 **6 months:** Group1: 1.1±1.1 Group 2: 0.9±1.0 **12 months:** Group1: 1.0±0.9 Group 2: 0.9±0.8	
			Mean ± SD Qmax (ml/s)	**Baseline:** Group1: 8.0±2.8 Group 2: 8.3±3.0 **6 months:** Group1: 24.5±9.2 Group 2: 23.3±10.5 **12 months:** Group1: 23.7±6.0 Group 2: 24.1±6.4	
			Mean ± SD PVR volume (ml)	**Baseline:** Group1:93.1 ±32.1 Group 2: 85.0±36.7 **6 months:** Group1: 7.1±6.6 Group 2: 6.7±6.3 **12 months:** Group1: 5.2±4.8 Group 2: 6.1±5.6	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
		and in the postoperative days (once a day).	**Catheterisation time (hours)**	**Group1:** 45.7±25.8 **Group 2:** 87.4±33.8 **p value:** <0.0001	
			Hospital stay (hours)	**Group1:** 115.1±25.5 **Group 2:** 161.1±33.8 **p value:** <0.0001	
			Operative time (minutes)	**Group1:** 46.3±16.2 **Group 2:** 50.4±20.7 P=0.28	
			Adverse events	**Blood transfusion** Group 1: 0 Group 2: 2 (4.2%) **TUR** Group 1: 0 Group 2: 1 (2.1%) **Urinary tract infection** Group 1: 2 (3.9%) Group 2: 4 (8.3%) **Recatheterisation** Group 1: 0 Group 2: 0 **Transitory urge incontinence** Group 1: 12 (23.1%) Group 2: 15 (31.3%) **Retrograde ejaculation** Group 1: 18/33 (55%) Group 2: 20/31 (65%) **Urethral stricture** Group 1:1 (1.9%) Group 2: 3 (6.3%) **Stress incontinence** Group 1:0 Group 2: 1 (2.1%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			IIEF-5 scores	**Preoperative:** Group 1: 19.3±6.1 Group 2:20.0±5.2 **6 months** Group 1: 20.4±6.0 Group 2: 21.7±4.8 **12 months:** Group 1: 21.0±5.8 Group 2: 21.4±5.3 P=0.67	
			Mean ± SD PdetQmax(cmH2O)	**Preoperative:** Group 1: 85.9±29.3 Group 2:83.4±33.3 **12 months:** Group 1: 38.1±17.5 Group 2: 38.9±17.3 P=0.80	
			Schafer grade	**Preoperative:** Group 1: 3.8±1.1 Group 2: 3.6±1.2 **12 months:** Group 1: 0.71±0.67 Group 2: 0.79±0.77 P=0.58	

1 **Evidence Table 24: Holmium laser eneucleation of the prostate (HoLEP) vs. transurethral incision of the prostate (HoBNI)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Aho et al., 2005[10] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Men with bladder outflow obstruction (BOO) and small prostate (<40g) **Setting:** Urology department, New Zealand, between July 1998 to May 2001 **Inclusion Criteria:** ▪ Qmax less than 15 ml/s ▪ AUA symptom score ≤8 ▪ Prostate volume (measured by TRUS) ≤40cc ▪ PVR<400ml ▪ Schafer grade ≥2 **Exclusion Criteria:** ▪ Known prostate cancer, or suspected prostate cancer (increased PSA and/or suspicious of DRE underwent TRUS biopsy) ▪ Catheterised patients ▪ History of urethral surgery ▪ On anticoagulants or had coagulation defects **All patients** **N:** 40 **Drop outs:**	**Group 1: HoLEP** Performed under general anaesthesia by 1 of 2 surgeons. (technique described in another paper) Energy used (kJ), mean (range): 74.2 (56-104)* Operative time, mins, mean, SD (range): 29.7±6.1(18-43) * As outpatient procedure: 15/19 (the above values are for 19 patients- 1 died preoperatively) **Group 2: Ho BNI** Performed under general anaesthesia by 1 in 3 surgeons. Incisions made at the 5 and 7 o' clock positions from just distal to each urethral orifice to either side of the verumontanum down to the depth of the surgical capsule. No tissue was excised. Energy used (kJ), mean (range): 13.3 (5-26)* Operative time, mins, mean, SD (range): 7.0±3.3(2-17) * As outpatient procedure:	**IPSS symptom score**, mean ±SD, (range)	At 1 months **Group 1:** 8.7±5.8 (0-21) **Group 2:** 6.2±6.8 (0-30) **Relative risk:** **95% CI:** At 3 months **Group 1:** 6.8±5.5 (1-21) **Group 2:** 6.2±6.7 (0-22) **Relative risk:** **95% CI:** At 6 months **Group 1:** 7.9±6.6 (0-26) **Group 2:** 9.1±8.4 (1-28) **Relative risk:** **95% CI:** At 12 months **Group 1:** 8.9±8.5 (1-31) **Group 2:** 6.1±5.6 (1-16) **Relative risk:** **95% CI:** **p value:** NS at anytime point	**Funding:** Supported by Pub Charity, Inc **Limitations:** ▪ Number of patients with urinary incontinence was significantly different pre-operatively. ▪ Reporting of adverse event – definitions and follow-up period ▪ There was imbalance in the number of incontinence cases at baseline.: 2/20 vs. 11/20 ▪ Retrograde ejaculation outcome was based on the number of patients who were able to comment (sexually active?). The number of patients who were able to comment was not reported. **Additional outcomes:** Death – 1 in HoLEP (pre-operative), 1 in BNI at 6th month (cardiac) **Notes:** Sample size calculation was provided. As sample size of 40 would be required to
			IPSS QoL score mean ±SD, (range)	At 1 months **Group 1:** 2.2±1.6 (0-6) **Group 2:** 1.4±1.6 (0-6) **Relative risk:** **95% CI:** At 3 months **Group 1:** 1.8±1.4 (0-6) **Group 2:** 1.8±1.5 (0-6) **Relative risk:** **95% CI:** At 6 months **Group 1:** 2.0±1.4 (0-5) **Group 2:** 2.1±1.5 (0-5) **Relative risk:** **95% CI:** At 12 months	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1 - HoLEP **N:** 20 **Age (mean):** 65.1±11.5 (range not provided) **Drop outs at 0/1/3/6/12 months:** 0/1/2/3/4, 1 patient died pre-operatively **IPSS symptom:**25.2±5.9(15-34) **IPSS QoL:** 5.2±0.8 (4-6) **Qmax:** 8.3±3.0(4-14) **PdetQmax H_20:** 72.0±29.1(45-145) **Schafer Grade:** 3.2±1.3(2-6) **Prostate Volume, PV:** 30.3±6.6(14-39) **Urinary incontinence:** 2/20# **Erectile dysfunction:** 10/20 **Group 2 - HoBNI** **N:** 20 **Age (mean):** 64.9±10.1 (44-79) **Drop outs at 0/1/3/6/12 months:** 0/0/2/3/8 **IPSS symptom:**24.2±5.1(14-35) **IPSS QoL:** 5.0 ±1.0 (3-6) **Qmax:**9.7±1.3(8-12) **PdetQmax H_20:** 71.0±30.2(40-128) **Schafer Grade:** 3.2±1.3(2-6) **Prostate Volume, PV:**	14/20 **Both groups** ▪ Maximal lasing power: 100 W (2J at 50 Hz) ▪ Versacut™ morcellator ▪ Catheters: Two way catheters unless post-operative bladder irrigation was necessary. Catheters removed at the hospital or in the community the morning following surgery. ▪ Discharged from hospital: the afternoon or evening following surgery *P value<0.001		**Group 1:** 1.7±0.9 (0-5) **Group 2:** 1.5±0.9 (0-3 **Relative risk:** **95% CI:** **p value:** NS at anytime point	detect HoLEP is superior (Qmax change of 12ml/s compared to 8ml/s in BNI), at a power of 80% and p of 0.05
			Qmax , mean ±SD, (range)	At 1 months **Group 1:** 19.9±6.9(9-40) **Group 2:** 18.7±8.0(9-40) **Relative risk:** **95% CI:** At 3 months **Group 1:** 20.7±7.6 (7-36) **Group 2:** 18.5 ±9.2 (10-36) **Relative risk:** **95% CI:** At 6 months **Group 1:** 20.2±8.0 (5-33) **Group 2:** 17.4±7.3 (3-31) **Relative risk:** **95% CI:** At 12 months **Group 1:** 21.6±7.7 (10-38) **Group 2:** 17.4±4.6 (12-24) **Relative risk:** **95% CI:** **p value:** NS at anytime point	
			PdetQmax (cm H_20), mean ±SD, (range)	At 6 months **Group1:** 29.1±11.1 (15-50) **Group 2:** 43.2±25.4 (2-100) **Relative risk:** **95% CI:** **p value:**<0.01	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	30.5±5.9(18-39) **Urinary incontinence:** 11/20# **Erectile dysfunction:** 9/20 #P value =0.006, calculated by NCGC team using Fisher's exact test		**Urodynamic obstruction,** Schafer grade, mean ±SD, (range)	At 6 months **Group1:** 0.5 ±0.7(0-5) **Group 2:** 1.6±1.4 0-5 **Relative risk:** **p value:**<0.01	
			Urodynamically obstructed No definition. 4 patients in HoBNI group subsequently had HoLEP. See "Reoperation"	At 6 months **Group1:** 0/19 **Group 2:** 5/20 (25%) **Relative risk:** **95% CI:** **p value:** NR	
			Prostate Volume, (g) mean ±SD, (range). Measured using TRUS	At 6 months **Group1:** 22.2 ±7.1(11-35) **Group 2:** 31.5±8.0(21-49) **Relative risk:** **p value:**<0.05	
			Catheter duration, mean ± SD (range), hours	**Group1:** 22.9±6.9(12-48) **Group 2:** 23.2±1.9(17-25) **Relative risk:** **95% CI:** **p value:** NS	
			Post-op complications (early): Recatheterisation	**Group1:** 0/19 **Group 2:** 2/20 **Relative risk:** **p value:** NR	
			Post-op complication: Reoperation: Patients had HoLEP between 6-16 months because of persistent LUTS	**Group1:** 0/19 (within 1 year) **Group 2:** 4/20 **Relative risk:** **p value:**	
			Post-op complications: Submeatal Strictures	**Group1:** 1 (dilated) **Group 2:** 1 (meatomy) **Relative risk:** **p value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Incontinence % with incontinence Note: Patients in Group 2 (BNI) who had reoperation was not assessed.	At 12 months **Group1:** 4/16 (44%) - **Group 2:** 0/13 (0%) **Relative risk:** **p value:**<0.01 None of the patients required pads	
			Erectile function: (No change /Worsened/ Improved)	At 12 months **Group1:** 11/2/3 **Group 2:** 10/1/2 **Relative risk:** **p value:** NS	
			Post-op complications: **Retrograde ejaculation in sexually,** % (in patients who are able to "comment" on it, number of patients not stated	**Group1:** 100% **Group 2:** 80% **Relative risk:** **p value:** reported as <0.01	
			Hospital time: mean ± SD (range), hours	**Group1:** 12.3±7.0 (7-28) **Group 2:** 13.7±8.5 (7-28) **Relative risk:** **95% CI:** **p value:** NS	

Evidence Table 25: Holmium laser enucleation of the prostate (HoLEP) vs. open prostatectomy (OP)

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kuntz et al., 2008[152] **Study design:** RCT **Setting:** Department of Urology- Germany **Evidence level:** 1+ **Duration of follow-up:** 5 years	**Patient group:** Candidates for surgical therapy of lower urinary symptoms and obstruction due to a prostate larger than 100 gm. **Inclusion criteria:** AUA>=8, (Q_{max}) of <=12 ml/s, post void residual urine volume >= 50 ml, Schafer grade >= 2. **Exclusion criteria:** Previous prostate or urethral surgery and non-BPH-related voiding disorders. Preoperatively, prostate carcinoma was screened for and excluded by prostate biopsy if indicated. There was no upper limit for prostate size. **<u>All patients</u>** **N:** 120 **Drop outs:** 46 **<u>Group 1:</u>** **N:** 60 Mean ±SD (range) Age: 69.2 +/- 8.4 (56-89) Schaffer grade: 4.3 +/- 1.12 (3-6) Postvoid residual volume (ml): 280 +/- 273 (50-1,000) Peak urinary flow rate (ml/s): 3.8 +/- 3.6 (0-10) Dropouts: 18 (died=3, intercurrent illness=3, moving=6, prostate cancer=3, reoperations=3)	**Group 1: HoLEP** HoLEP was carried out at 80 or 100 W with a high-powered Ho:YAG laser (2.0 J; 40-50 Hz). It involved retrograde enucleation of the median and lateral lobes from the apex toward the bladder. When the trial started, a mechanical tissue morcellator was not yet commercially available. Therefore in the first 50 of the 60 HoLEP patients, fragmentation of the lobes was performed by traditional electrocautery loop resection whilst the devascularised lobes were still connected to the surgical capsule by a narrow pedicle. In the last 10 of the 60 HoLEP patients, the lobes were enucleated in their entirety, pushed into the bladder, and fragmented with the use of a mechanical tissue morcellator. **Group 2: Open prostatectomy (OP)**	**Mean +/- SD AUA symptom score:**	**Preoperatively:** Group 1: 22.1 +/- 3.3 (n=60) Group 2: 21.0 +/- 3.6 (n=60); **3 months** Group 1: 3.3 +/- 2..7 (n=54) Group 2: 3.6 +/- 2..7 (n=50) **6months** Group 1: 2.4 +/- 1.9 (n=54) Group 2: 2.8 +/- 3.9 (n=50) **1-year:** Group 1: 2.3 +/- 2.0 (n=56) Group 2: 2.3 +/- 1.7 (n=49); P value: 0.94 **2-year:** Group 1: 2.3 +/- 2.2 (n=53) Group 2: 2.4 +/- 1.6 (n=46); P value: 0.89 **3 year.** Group 1: 3.0 +/- 3.1 (n=48) Group 2: 2.8 +/- 1.6 (n=40); P value: 0.82 **4-year:** Group 1: 3.0 +/- 3.1(n=45) Group 2: 2.8 +/- 1.9 (n=36); P value: 0.68 **5-year:** Group 1: 3.0 +/- 3.2 (n=42) Group 2: 3.0 +/- 1.7 (n=32); P value: 0.98	**Funding:** Prof. Kuntz is a consultant for the companies Lumenis and Karl Storz. **Limitations:** Allocation concealment and blinding unclear. **Notes:** Linked with Kuntz 2002[150] and Kuntz2004[151]
			Mean +/- SD peak flow (ml/s)	**Preoperatively:** Group 1: 3.8 +/- 3.6 (n=60) Group 2: 3.6 +/- 3.8 (n=60); P value: 0.60 **3 months:** Group 1: 27.6+/- 7.0 (n=54) Group 2: 27.3 +/- 6.2 (n=50); P value: 0.66 **1-year:** Group 1: 27.4+/- 9.7 (n=56) Group 2: 28.3 +/- 7.5 (n=49); P value: 0.86 **2-year:** Group 1: 26.7+/- 8.3 (n=53) Group 2: 27.4 +/- 6.8 (n=46); P value: 0.65 **3-year:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	<u>Group 2:</u> **N:** 60 Mean ±SD (range) Age: 71.2 +/- 8.3 (54-89) Schaffer grade: 4.3 +/- 0.79 (3-6) Postvoid residual volume (ml): 292 +/- 191 (50-1,000) Peak urinary flow rate (ml/s): 3.6 +/- 3.8 (0-12) Dropouts: 28 (died=8, intercurrent illness=3, moving=7, prostate cancer=6, reoperation=4)	Open prostatectomy was performed by a suprapubic transvesical approach via midline incision. The bladder catheter was routinely removed on the seventh postoperative day.		Group 1: 27.0+/- 9.8 (n=48) Group 2: 25.3 +/- 6.9 (n=40); P value: 0.32 **4-year:** Group 1: 27.7 +/- 9.6 (n=45) Group 2: 25.0 +/- 8.3 (n=36); P value: 0.20 **5-year:** Group 1: 24.3 +/- 10.1 (n=42) Group 2: 24.4 +/- 7.4 (n=32); P value: 0.97	
			Mean +/- SD Residual volume (ml)	**Preoperatively:** Group 1: 280+/- 273 (n=60) Group 2: 292 +/- 191 (n=60); P value: 0.43 **1-year:** Group 1: 5.8 +/- 16.7 (n=56) Group 2: 6.4 +/- 12.3 (n=49); P value: 0.83 **2-year:** Group 1: 1.7 +/- 6.5 (n=53) Group 2: 2.4 +/- 6.8; P value: 0.61 **3-year:** Group 1: 6.1 +/- 12.1 (n=48) Group 2: 4.4 +/- 10.5 (n=40); P value: 0.50 **4-year:** Group 1: 8.6 +/- 13.5 (n=45) Group 2: 6.5 +/- 12.1 (n=36); P value: 0.48 **5-year:** Group 1: 10.6 +/- 24.4 Group 2: 5.3 +/- 11.2 (n=32); P value: 0.25	
			Mortality (follow up 60 months) **Mortality (3 months postoperatively)**	**Group 1:** n=3 **Group 2:** n= 8 **Group 1:** n=0 **Group 2:** n= 2	
			Complications (6 months postoperatively):	<u>Blood transfusion</u> **Group 1**: 0 **Group 2:** 8 (13.3%); P value: 0.003 <u>Reoperation for secondary coagulation of bleeding arteries (18)</u> **Group 1**: 3	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group 2: 3; P value: NR Reoperation for secondary apical resections **Group 1**: 2 **Group 2**: 0; P value: NR	
			Re-interventions (60months)	Bladder neck contracture- holium laser incision: **Group 1**: 1 (1.7%) **Group 2**: 3 (5.0); P value: 0.60 Visual urethrotomy (from stricture): **Group 1**: 2 (3.3%) **Group 2**: 1 (1.7); P value: 0.61	
			Mean +/- SD Post-op stay (hrs.)	**Group 1:** 69.6 +/- 36.4 (24-192) **Group 2:** 251.0 +/- 45.5 (216-552) P value: <0.0001	
			Recatheterisation	**Group 1**: 3 (5%) **Group 2**: 3 (5%)	
			Incontinence	**Group 1:** 5/60 **Group 2:** 6/60	
			Erectile dysfunction	**Group 1:** 5/54 **Group 2:** 5/50	
			Retrograde ejaculation (in sexually active patients; 58%)	**Group 1:** 70% **Group 2:** 79%	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Naspro et al., 2006[210] **Study design:** RCT **Setting:** Italy **Evidence level:** 1+ **Duration of follow-up:** 24-months	**Patient group:** Consecutive patients from March 2003 to December 2004 who suffered from BPH-related obstructed voiding symptoms with prostate volume >70 g, as determined by transrectal ultrasound and who had not responded to pharmacologic therapy. **Inclusion criteria:** Postvoiding residue <150 ml, peak urinary flow rate <15 ml/s, and urodynamic obstruction (Schafer grade >2). **Exclusion criteria:** Neurogenic bladder, history of adenocarcinoma of the prostate, or any previous prostatic, bladder-neck, or urethral surgery. **<u>All patients</u>** **N:** 80 **Drop outs:** 15 **<u>Group 1:</u>** **N:** 41 Mean (±SD) Age: 66.26 (+/- 6.55) Total serum PSA ng/ml mean (±SD): 6.33 +/- 3.45 Incidental adenocarcinoma: 2 (4.8%) Dropouts: 6 **<u>Group 2:</u>** **N:** 39	**Group 1: HoLEP** The surgical technique included enucleation of the prostatic lobes with subsequent tissue morcellation into the fragments, which were retrieved from the bladder cavity. Total mean operative time: 72.09 +/- 21.22 **Group 2: OP** Standard transvesicle approach. Total mean operative time: 58.31 +/- 11.95	**Mean (SD) IPSS**	**Baseline:** Group 1: 20.11 +/- 5.84 Group 2: 21.60 +/- 3.24; **p value:** 0.27 **1-month:** Group 1: 6.9 +/- 4.2 Group 2:: 4.7 +/- 2.1; p **value:** 0.20 **3-month:** Group 1: 3.9 +/- 2.9 Group 2:: 2.9 +/- 2.6; **p value:** 0.46 **12-month:** Group 1: 8.45 +/- 5.87 Group 2:: 8.40 +/- 6.0; **p value:** 0.98 **24-month:** Group 1 (n=35): 7.9 +/- 6.2 Group 2: **(n= 30):** 8.1 +/- 7.1; **p value:** 0.44	**Funding:** NR **Limitations:** Allocation concealment and blinding unclear. **Notes:** None.
			Q_{max}	**Baseline:** Group 1: 7.83 +/- 3.42 Group 2:: 8.32 +/- 2.37; p value: 0.64 **1-month:** Group 1: 26.6 +/- 8.7 Group 2:: 24.3 +/- 6.8; p value: 0.53 **3-month:** Group 1: 22.2 +/- 8.6 Group 2:: 25.5+/- 10.5; p value: 0.57 **12-month:** Group 1: 22.32 +/- 3.8 Group 2:: 24.21+/- 6.49; p value: 0.27 **24-month:** Group 1 (n=35): 19.19+/- 6.3 Group 2: (n= 30): 20.11+/- 8.8; p value: 0.91	
			QOL question	**Baseline:** Group 1: 4.07 +/- 0.93 Group 2: 4.44 +/- 0.96; **p value:** 0.17 **1-month:** Group 1: 1.4 +/- 1.4 Group 2: 1.3 +/- 0.7; **p value:** 0.76 **3-month:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean (±SD) Age: 67.27 (+/- 6.72) Total serum PSA ng/ml mean (±SD): 6.99 +/- 4.28 Incidental adenocarcinoma: 3 (7.6%) Dropouts: 9			Group 1: 1 +/- 0.8 Group 2: 0.6 +/- 0.2; **p value:** 0.18 **12-month:** Group 1: 1.7 +/- 0.94 Group 2: 1.77 +/- 0.83; **p value:** 0.85 **24-month:** Group 1 (n=35): 1.5 +/- 0.87 Group 2 (n= 30): 1.66 +/- 0.76; **p value:** 0.76	
			Mean detrusor pressure at maximum flow rate ($P_{detqmax}$)cm H_2O	**Baseline:** Group 1: 80.6 (44-130) Group 2:: 83.1 (41-147); **p value:** 0.94 **12-month:** Group 1: 30.6 (22-80) Group 2:: 34.8 (18-88); **p value:** 0.66	
			Schafer grade (LinPURR):	**Baseline:** Group 1: 3.8 (2-6) Group 2:: 3.1 (2-6); **p value:** 0.33; **12-month:** Group 1: 0.7 (0-4) Group 2:: 0.8 (0-4); **p value:** 0.18	
			Perioperative morbidity (surgery to 3months)	**Bladder mucosal injury:** Group 1: 3 (7.3%) Group 2:: 0 (2-6); **p value:** < 0.001 **Transitory urge incontinence:** Group 1: 14 (34.1%) Group 2:: 17 (38.6%); **p value:** 0.2 **Dysuria (burning):** Group 1: 28 (68.2%) Group 2:: 16 (41.0%); **p value:** <0.001 **Stress incontinence:** Group 1: 1 (2.4%) Group 2: 1 (2.5%); **p value:** 0.9 **Reintervention for bleeding:** Group 1: 1(2.4%) Group 2:: 0; **p value:** 0.9 **Early acute urinary retention:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group 1: 5 (12.1%) Group 2:: 2 (5.1%); **p value:** 0.11	
			Complications 12-month follow-up:	**Urge incontinence:** Group 1: 2 (5.4%) Group 2: 3 (8.5%); **p value:** 0.03 **Dysuria (burning):** Group 1: 4 (10.8%) Group 2: 3 (8.5%); **p value:** 0.02 **Bladder-neck/urethral strictures:** Group 1: 2 (5.4%) Group 2: 2 (5.7%); **p value:** 0.3 **Overall reintervention:** Group 1: 2 (5.4%) Group 2: 2 (5.7%); **p value:** 0.55 **Prostate cancer:** Group 1: 4 (10.8%) Group 2: 4 (11.4%); **p value:** 0.4 **<u>24-month follow-up:</u>** **Prostate cancer:** Group 1: 0 Group 2: 0; **p value:** **Dysuria (burning):** Group 1: 1 (2.8%) Group 2: 1 (3.3%); **p value:** 0.02 **Bladder-neck/urethral strictures:** Group 1: 1 (2.8%) Group 2: 1 (3.3%); **p value:** 0.3	
			Mean +/- SD IIEF domains	**baseline:** Group 1:20.3+/-6.6 Group 2: 21.1 +/- 5.3; **p value:** 0.5 **3 months:** Group 1: 21.4 +/- 2.6 Group 2: 20.6 +/- 5.5; **p value:** 0.67 **6 months:** Group 1: 22.8 +/- 2.1	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group 2: 24.6 +/- 4.0; **p value:** 0.55 **12 months:** Group 1: 25.2 +/- 4.2 Group 2: 23.5 +/- 1.8; **p value:** 0.31 **24 months:** Group 1: 22.3 +/- 4.0 Group 2: 21.9 +/- 5.6; **p value:** 0.21 **Autologous blood transfusion:** Group 1: 2 (4%) Group 2: 5 (12.8%) **p value:** < 0.001 **Homologous blood transfusion:** Group 1: 0 Group 2: **2** (5.1%) **p value:** < 0.007 **Catheterisation time:** Group 1: 1.5 +/- 1.07 Group 2: 4.1 +/- 0.5 **p value:** < 0.0001 **Hospital stay, d:** Group 1: 2.7 +/- 1.1 Group 2: 5.43 +/- 1.05 **p value:** < 0.0001	

Evidence Table 26: Laser coagulation vs. transurethral resection of the prostate (TURP)

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Anson1995 [18] McAllister2000[188] **Study design:** RCT, open label, (multi-centre) **Setting:** United Kingdom **Evidence level:** 1+ **Duration of follow-up:** Up to 5 years	**Patient group:** Patients with BPH **Setting:** From March 1992, UK **Inclusion criteria:** ▪ Age>50 yers old ▪ American Society of Anaesthesiologist (ASA) Grade 1 to 3 ▪ Prostatic urethral length >24mm ▪ Urinary flow rates consistent with outlet obstruction **Exclusion criteria:** ▪ ASA Grade >3 ▪ Known history or suspicion of prostate cancer ▪ Renal impairment ▪ Life expectancy <6 months ▪ On medication such as anticoagulants **<u>All patients</u>** **N:** 151, out of 166 candidates **Age**, mean, (range) (years): 68.1(52-84) **Drop outs** ▪ <u>1 year review</u> : 137/151 ▪ <u>5-year review:</u> 42/151 (109 patients were traced from 151 at the 5-year review) **<u>Group 1-Laser coagulation</u>** **N:** 76	**Group 1- Laser coagulation (ELAP)** **Procedure:** Nd:YAG, using Urolase fibre. Energy was applied at 60W for 6S at the 2, 5, 7, and 10 o clock positions, modified according to prostate length and presence of median lobe. Room temperature sterile water was used for irrigation **Power:** 60W **Group 2 –TURP** **Procedure:** Standard electroresection, by experienced urologists	**All cause mortality**	<u>"immediate post-operative period"</u> **Group 1:** 0/76 **Group 2:** 0/75 **p value:** NS <u>Week 52 (1 year)</u> **Group 1:** 1/76 **Group 2:** 1/75 **p value:** NS	**Funding:** Bard Europe Division **Limitations:** ▪ Open label study ▪ Randomisation concealment method not described ▪ Only 44% of patients available at 5-year follow up, and no sd was provided. **Additional outcomes:** ▪ Pulmonary embolism – 1 patient in TURP group had PE after operation ▪ Deep vein thrombosis: 1 patient in laser group vs. 2 patients in TURP group had DVT **Notes:** 5 year data not used in meta-analysis due to small number of available data compared to original sample size McAllister2000 reported the 5 year follow up period
			AUA-6 symptom score, mean (95% CI):	<u>Week 4</u> **Group 1:** 13.5(95%CI: 12.0 to 15.0) **Group 2:** 8.7 (95%CI: 7.6 to 9.8) **p value:** NS <u>Week 12</u> **Group 1:** 8.7 (95%CI:7.3 to 10.1) **Group 2:** 6.4 (95%CI:5.2 to 7.6) **p value:** NS <u>Week 26</u> **Group 1:** 7.9 (95%CI: 6.4 to 9.4) **Group 2:** 5.9 (95%CI: 4.6 to 7.2) **p value:** NS <u>Week 52</u> **Group 1:** 7.7 (95%CI: 6.3 to 9.1) **Group 2:** 5.1 (95%CI: 3.8 to 6.4) **p value:** <0.05 <u>5 years</u> **Group 1:** 6.3, n=28 **Group 2:** 6.5, n=39 **p value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Drop outs: ▪ At 1-year review: 9/76 (11.8%) ▪ At 5-year review: 19/76 (25%) **Age:** mean (95% CI): 67.9 (66.3-69.5) **Drop outs:** Not stated **AUA-6 symptom score,** mean (95% CI): 18.1(17.1-19.1) **Qmax,** mean (95% CI): 9.6(8.8-10.4) **Post void residual volume:** mean (95% CI): 113(91-135) **Sexually active:** 27/76 (36%) **Group 2 - TURP** **N:** 75 **Drop outs:** ▪ At 1-year review: 5/75(6.7%) ▪ At 5-year review: 24/75(32%) **Age:** mean (95% CI): 68.3(66.5-70.1) **AUA-6 symptom score,** mean (95% CI): 18.2(17.1-19.3) **Qmax,** mean (95% CI): 10.0 (9.1-10.9) **Post void residual volume:** mean (95% CI): 121(93-148) **Sexually active:**24/75 (32%)		**Qmax,** mean (95% CI):	Week 12 **Group 1:** 15.9 (95%CI: 13.6 to 18.2) **Group 2:** 21.3 (95%CI: 19.0 to 23.6) **p value:** <0.05 Week 26 **Group 1:** 15.6 (95%CI:13.7 to 17.5) **Group 2:** 19.9 (95%CI: 17.4 to 22.4) **p value:** NS Week 52 **Group 1:** 15.4 (95%CI: 13.6 to 17.2) **Group 2:** 21.8 (95%CI: 18.5 to 25.1) **p value:** NS 5 years **Group 1:** 17.8, n=24 **Group 2:** 20.0, n=36 **p value:** NS	
			Post void residual volume: mean (95% CI):	Week 12 **Group 1:** 70.3 (95%CI: 51.1 to 89.3) **Group 2:** 21.3 (95%CI: 43.9 to 80.3) **p value:** NS Week 26 **Group 1:** 90.1 (95%CI: 61.6 to 118.0) **Group 2:** 19.9 (95%CI: 17.4 to 22.4) **p value:** <0.05 Week 52 **Group 1:** 69.2 (95%CI:48.1 to 90.3) **Group 2:** 45.9 (95%CI:30.5 to	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				61.3) **p value:** <0.05 5 years **Group 1:** 76, n=24 **Group 2:** 55, n=35 **p value:** NS	
			Post-operative complications: Blood transfusion: (Mean of 2.7 units blood)	**Group 1:** 0/76 **Group 2:** 3/75 **p value:** NS	
			Post-operative complications: Retrograde ejaculation (among patients who were sexually active preoperatively)	Up to week 52 (1 year) **Group 1:** 9/27 (33%) **Group 2:** 15/24 (63%) **p value:** NS	
			Post-operative complications: Clot retention	Up to week 52 (1 year) **Group 1:** 1/76 **Group 2:** 5/75 **p value:** NS	
			Post-operative complications: urinary tract infection (positive culture). 22/28 of patients in the ELAP group received prophylaxis	Up to week 4 **Group 1:** 18/76 **Group 2:** 5/75 **RR:** 3.55 (95% CI: 1.47 to 8.97) **p value:** <0.01 Up to week 52 (1 year) **Group 1:** 28/76 **Group 2:** 7/75 **RR:** 3.95 (95% CI: 1.92 to 8.48) **p value:** <0.01	
			Post-operative complications: Dysuria	Up to week 52 (1 year) **Group 1:** 25/76 **Group 2:** 6/75 **RR:** 4.11 (95% CI: 1.88 to	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				9.42) **p value:** <0.01	
			Post-operative complications: epididymorchitis	Up to week 52 (1 year) **Group 1:** 2/76 **Group 2:** 1/75 **p value:** NS	
			Post-operative complications: Reoperation- by week 52, 2 had bladder neck incision, 3 had TURP	Up to week 52 (1 year) **Group 1:** 5/76 **Group 2:** 0/75 **p value::** 5 years **Group 1:** 18/47 (38%) **Group 2:** 8/51 (16%) **p value:** <0.006	
			Hospitalisation days, mean (95% CI)	**Group 1:** 2.7(95%CI: 2.2 to 3.2) **Group 2:** 4.3 (95%CI: 3.3 to 5.3) **p value:**NS	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Chacko et al., 2001[48] **CLASP** study- acute urinary retention **Study design:** RCT, multicentre, open label **Setting:** UK **Evidence level:** 1+ **Duration of follow-up:** 7.5 months	**Patient group:** men with acute painful, urinary retention **Setting:** 3 centres in UK **Inclusion criteria:** Acute painful, urinary retention. All patients without strong history of LUTS underwent at least one trial without catheter **Exclusion criteria:** ▪ Prostate cancer or previous prostatic surgery; ▪ prostate size > 120ml; ▪ Life expectancy < 6 months; ▪ Urinary retention associated with recent operation, constipation or drugs which could cause acute urinary dysfunction, ▪ Neurogenic bladder dysfunction; ▪ Serum creatinine >250 µmol/L. **<u>All patients</u>** **Number of eligible patients:** 155 **N randomised:** 148 Mean age: **Drop outs:**	**Group 1- Laser coagulation** **Procedure:** Nd:YAG/ Non-contact VLAP, side-firing fibre (Bard Urolase), using standard fixed spot technique **Power:** 60W ND: YAG for 60s, depends on prostate size. For prostate size with urethral length of >25 mm, additional set of laser was used. If median lobe was present, 60W for 30s was applied for each side of lobe. **Energy:** 33.93kJ (mean total delivered) **Catheter protocol:** Suprapubic catheter, voiding trial 1-2 wks after discharge. **Other:** All patients received antibiotic prophylaxis and anti-inflammatory suppository. **Group 2 –TURP** **Procedure:** Standard electroresection **Catheter protocol:** suprapubic; duration depends on success	**All cause mortality** Not treatment related	**Group1:** 2/74 **Group 2:** 4/74 **p value:** NS	**Funding:** Laser machines provided by Bard Diagnostics, Redmond, Washington. **Limitations:** ▪ Open label study, with main outcomes using patient reported measures. ▪ The actual values of data and standard deviations were not reported for many outcomes – only reported p values or whether it was statistically significant – not suitable for meta-analysis **Additional outcomes:** ▪ Myocardial infarction during hospital stay ▪ Composite outcomes categories, and categorical outcomes for IPSS and Qmax **Notes:** ▪ Sample size calculation was performed. ▪ In the laser group, 7/74 patients were converted to the
			IPSS, mean change from baseline (±SD): Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -10.1 (95%CI: -12.8, -7.3), n=54 **Group 2:** -13.5 (95%CI -15.8, -11.2), n=48 **p value:** 0.26 Both groups stats sig compared to baseline	
			IPSS-QoL, mean(±SD): Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -3.10 (95%CI -3.65, -2.55), n=49 **Group 2:** -3.42 (95%CI -3.89, -2.95), n=45 **Adjusted difference:** : 0.26 (0.81-0.30)- page 169 **P value:** 0.37 Both groups stats sig compared to baseline	
			Post-op complications: Transurethral resection syndrome	**Group 1:** 0/74 **Group 2:** 2/74 **P value:** NS	
			Post-op complications: Blood transfusion (units and criteria not stated)	**Group 1:** 0/74 **Group 2:** 4/74 **P value:** NS	
			Post-op complications: Heavy bleeding (criteria not stated)	**Group 1:** 2/74 **Group 2:** 3/74 **P value:** NS	
			Post-op complications: Septicaemia	**Group 1:** 3/74 **Group 2:** 4/74 **P value:** NS	
			Post-op	**Group 1:** 0/74	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1-Laser coagulation **N:** 74 Dropouts: **Received as allocated:** 57/74 **Age, mean (±SD):** 74.2 ± 7.9 **IPSS, mean (±SD):** 20.3 ±9.3 **IPSS-QoL, median(IQR):** 5 (4-6) **Ethnicity (% white):** 97.3 **Group 2 - TURP** **N:** 74 Dropouts: **Received as allocated:** 68/74 **Age, mean (±SD):** 72.7± 7.3 **IPSS, mean (±SD):** 19.4 ± 7.6 **IPSS-QoL, median(IQR):** 5 (4-6) **Ethnicity (% white):** 97.3	voiding after urine is clear. **Other:** All patients received antibiotic prophylaxis and anti-inflammatory suppository.	**complications: Incontinence**	**Group 2:** 3/74 **P value:** NS	standard surgery in theatre, and 3 refused treatment. ▪ In the TURP group, 5 refused or deferred treatment. ▪ A total of 1073 patients were considered for inclusion of the 3 linked CLASP trial, and 570 were entered. 318 (29.5%) were not eligible because of ≥1 exclusion criteria. The rest did not enter for various reasons. There were 240 patients in the uncomplicated LUTS trial, 148 in the acute urinary retention trial and 82 in the chronic retention trial.
			Post-op complications: Reoperation (surgery due to "unacceptable symptoms" or retention after 8 weeks)	**Group 1:** 7/74 **Group 2:** 1/74 **P value:** NS	
			Post-op complications: Urinary retention (>8 weeks)	**Group 1:** 1/74 **Group 2:** 0/74 **P value:** NS	
			LOS, geometric mean, days	**Group 1:** 3.4 (95% CI 2.8 to 4.0) **Group 2:** 5.8 (95% CI 5.2 to 6.5) **Relative risk: 1.73** **95% CI:** 1.40-2.14 **P value:** <0.0001	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Cowles et al.., 1995[56] **Study design:** RCT, open label, multicentre **Setting:** United states **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Bladder outlet obstruction due to BPH **Setting:** Multicentre, United States in August 1991 to June 1992 **Inclusion criteria:** Bladder outlet obstruction due to BPH, not in urinary retention **Exclusion criteria:** ▪ Physical status exceeding category III of the American Society of Anaesthesiologists Adenocarcinoma of the prostate ▪ Bladder neck to verumontanum length less than 2.4cm ▪ Life expectancy of < 6 months ▪ < 50 years ▪ Clinically significant illness ▪ Medication (hormonal therapy, alpha blockers, finasteride) that would have precluded participation in the study ▪ Medical condition (such as recent myocardial infarction, coagulopathy, recent stroke, sepsis) that investigators deemed unsuitable for one or more procedures	**Group 1- Laser coagulation** **Procedure:** Nd; YAG laser, using Urolase fibre to the lateral lobes of the prostate at 3 and 9 o'clock positions for 60s each, and at 6 & 12 o'clock for 30s each, respectively. For patients with length of verumontanum and bladder neck >4 cm, treatment was repeated in 2 transverse planes, one just distal to the bladder and one just proximal to the verumontanum Average number of laser applications: 5.5±2.1 Cumulative duration of laser application: 4.2±1.5 minutes **Power:** 40W **Energy:** 5760-11520 J per patient,	**AUA-6 symptom score**	At 12 months, compared to baseline **Group 1:** -9.0 ±8.9, range -27 to 8 **Group 2:** -13.3 ±7.5, range -29 to 7 **p value:** <0.04	**Funding:** partially funded by CS Bard **Limitations:** ▪ The baseline AUA-6 was significantly lower for laser coagulation group. Statistical adjustment with ANCOVA reported ▪ Not stated which QoL instrument was used ▪ Impotence outcome- not certain if these are newly acquired cases ▪ Time point/period of complication measurement not stated **Additional outcomes:** ▪ Number of patients "non-serious" complications such as pain, hesitancy etc ▪ % of quality of life improved, at 12 months compared to baseline for Laser vs. TURP: 43/55 (78.2%) vs. 53/57 (93.0%) ▪ Post-op complications: (Bleeding (drop> 2.2g/dl of Hb in 24 hours post-procedure):
			Post void residual volume, ml	At 12 months, compared to baseline **Group 1:** -55.4±124.3, range -425 to 220 **Group 2:** 138.8±162.3 range -728 to 130 **p value:** <0.01	
			Qmax, ml/s	At 12 months, compared to baseline **Group 1:** 5.3±6.9 **Group 2:** 7.0±9.5 **p value:** 0.27	
			Reoperation with VLAP or TURP (by 12months)**:** 2 patients had VLAP: 1 patient had residual bladder neck tissue and later diagnosed with cancer. The other had residual apical lobe. 4 others had TURP.	**Group 1:** 2/56 **Group 2:** 0/59 **p value:** NS	
			Post-op complications: Blood transfusions	**Group 1:** 0/56 (0%) **Group 2:** 2/59(3.4%) **p value:** NS	
			Urinary retention	**Group 1:** 17/56 (30.4%) **Group 2:** 5/59 (8.5 %) **Relative risk:** 3.58(95% CI: 1.50, 9.00) **p value:** <0.005	
			Urinary tract infection	**Group 1:** 3/56 (5.4%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	(the protocol had subsequently changed to report patients with urinary retention, but these patients were not part of the cohort reported in this study) **<u>All patients</u>** **N:** 115 **<u>Group 1-Laser coagulation</u>** **N:** 56 Dropouts: **Age, mean (±SD):** 65.8±6.7 ****AUA – 6 symptom score, mean (±SD):** 18.7±6.0 **Prostate volume**, ml:42.2±19.0 **Qmax**, ml/s: 8.9±3.6 **Post void residual volume**, ml: 162.7±126.6 **Previous BPH therapy**: 9/56(9.1%) **<u>Group 2 - TURP</u>** **N:** 59 Dropouts: **Age, mean (±SD):** 67.0±7.8 ****AUA– 6 symptom score, mean (±SD):** 20.8±4.8 **Prostate volume**, ml: 38.6±20.2 **Qmax**, ml/s: 9.5±5.2 **Post void residual volume**, ml: 206.7±181.9 **Previous BPH therapy**: 17/59(28.8%)	depending on prostate size. **Anaesthesia:** Spinal: 36/56 (64.2%) General: 20/56 (35.7%) Intravenous sedation only: 2(3.6%) **Group 2 –TURP Procedure:** Standard prostate resection using wire loop electrocautery under direct vision **Anaesthesia:** Spinal: 54/59(93.1%) General: 5/59(8.6%) Intravenous sedation only: 0/59(0%) **For BOTH groups:** Discharged when deemed medically fit, minimum of 24 hours hospitalisation post surgery for observation		**Group 2:** 1/59 (1.7%) **p value:** NS	1/46 (2.2%) vs. 18/45 (40%). RR= 0.05 (95% CI: 0.01-0.28), p value: <0.01 for Laser vs. TURP ▪ Total number of patients with ≥1 serious complication, (impotence, UTI, meatal stenosis, urethral stricture, clot retention, bladder neck contracture, blood transfusions, TUR syndrome, incontinence, deep vein thrombosis, extravasation of irrigation fluid, prostatitis) was 6/56 in laser vs. 21/59 in TURP, RR = 0.30 (95% CI: 0.13, 0.66), p<0.01. **Notes:** ** AUA-6 score was significantly lower in VLAP group. This required adjustment in data analysis using ANCOVA (analysis of covariance) ***calculated by NCGC team using Fisher's exact test*
			Strictures (urethral and meatal stenosis): 6 patients in TURP group had urethral strictures. 1 patient in laser and 3 in TURP group had meatal stenosis	**Group 1:** 1/56 (0%) **Group 2:** 9/59 (10.2%) **RR:** 0.12 (95% CI: 0.02, 0.67) **p value:** 0.02**	
			Bladder neck contracture	**Group 1:** 0/56 (0%) **Group 2:** 3/59 (5.1%) **p value:** NS	
			Incontinence	**Group 1:** 0/56 (0%) **Group 2:** 2/59 (3.4%) **p value:** NS	
			Impotence (not stated how many were sexually active or whether these are newly acquired cases)	**Group 1:** 3/56 (5.4%) **Group 2:** 2/59 (3.4%) **p value:** NS	
			Deep vein thrombosis	**Group 1:** 0/56 (0%) **Group 2:** 1/59 (1.7%) **p value:** NS	
			Post TURP syndrome	**Group 1:** 0/56 (0%) **Group 2:** 2/59 (3.4%) **p value:** NS	
			Clot retention	**Group 1:** 0/56 (0%) **Group 2:** 3/59 (5.1%) **p value:** NS	
			Hospitalisation duration, days	**Group 1:** 1.8±1.1 **Group 2:** 3.1±0.9 **p value:** <0.01 **	
			Duration of procedure, min	**Group 1:** 23.4±11.1 **Group 2:** 45.2±21.5 **p value:** <0.01 **	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Donovan et al., 2000[74] **CLASP** study-acute urinary retention **Study design:** RCT, multicentre, open label **Setting:** UK **Evidence level:** 1+ **Duration of follow-up:** 7.5 months	**Patient group:** men with uncomplicated LUTS symptoms **Setting:** 3 centres in UK **Inclusion criteria:** ▪ IPSS score of≥8, with physician and patient agreement that the symptoms require intervention ▪ Qmax <15ml.s when voided volume>200ml, <13ml/s when voided volume between 150-200ml and <10ml/s when voided volume between 100 to 149ml measured on two occasions, with the higher value between these two used for analysis ▪ >300ml post void volume urine on ultrasound **Exclusion criteria:** ▪ Prostate cancer or previous prostatic surgery; ▪ prostate size > 120ml; ▪ Life expectancy < 6 months; ▪ Urinary retention associated with recent operation, constipation or drugs which could cause acute urinary dysfunction, ▪ Neurogenic bladder dysfunction; ▪ Serum creatinine >250 μmol/L.	**Group 1- Laser coagulation** **Procedure:** Nd:YAG/ Non-contact VLAP, side-firing fibre (Bard Urolase), using standard fixed spot technique **Power:** 60W ND: YAG for 60s, depends on prostate size. For prostate size with urethral length of >25 mm, additional set of laser was used. If median lobe was present, 60W for 30s was applied for each side of lobe. **Energy:** 28684J **Catheter protocol:** Suprapubic catheter, removed when clinically appropriate. **Other:** All patients received antibiotic prophylaxis and anti-inflammatory suppository. **Group 2 –TURP** **Procedure:** Standard electroresection **Catheter protocol:** Suprapubic catheter. **Group 3 – Conservative management**	**All cause mortality** Not treatment related	**Group 1:** 5/117 **Group 2:** 0/117 **Group 3:** 1/106 **p value:** NS for all groups	**Funding:** Laser machines provided by Bard Diagnostics, Redmond, Washington. **Limitations:** ▪ Open label study, with main outcomes using patient reported measures. However, this paper specified that clinicians measuring outcomes were different from surgeons conducting the surgery **Additional outcomes:** ▪ Composite outcomes categories, and categorical outcomes for IPSS and Qmax **Notes:** Sample size calculation performed Please see Chacko2001 for the acute urinary retention population of CLASP trial and Gujral 2000 for the chronic urinary retention
			IPSS, mean change from baseline (95%CI)**:** Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -10.8 (95% CI: -12.5,-9.0), n=96 **Group 2:** -12.3 (95% CI: -13.8,-10.7), n=89 **Group 3:** -1.3 (95% CI: -2.8,0.2), n=85 **Adjusted difference:** **Group 1 vs. Group 2:** -1.7 (95% CI: -3.6,0.1) **p value:** NS Statistically significant for surgical procedures vs. conservative	
			IPSS-QoL, mean (95%CI)**:** Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -1.9 (95% CI: -2.3, -1.6), n=93 **Group 2:** -2.2 (95% CI: -2.5, -1.8), n=85 **Group 3:** -0.4 (95% CI: -0.7, -0.1), n=85 **Adjusted difference:** **Group 1 vs. Group 2:** -0.2 (95% CI: -0.6,0.2) **p value:** NS	
			Qmax, mean(95%CI)**:** Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** 5.8 (95% CI: 4.5, 7.2), n=102 **Group 2:** 9.7 (95% CI: 7.7, 11.6), n=98 **Group 3:** 0.2 (95% CI: -04, 0.8), n=92 **Adjusted difference:** **Group 1 vs. Group 2:** 3.9 (95% CI:1.9, 5.8) **p value:** <0.05	
			Post void residual volume, mean(95%CI)**:** Adjusted for centre and	**Group 1:** -73.4(95% CI:-91.3, -55.5), n=100 **Group 2:** -74.0 (95% CI:-89.2, -58.8),	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	<u>All patients</u> **N:** 340 **Drop outs:** **<u>Group 1-Laser coagulation</u>** **N:** 117 **Dropouts:**1/117 **Age**, mean (±SD): 67.4±8.1 **IPSS**, mean (±SD): 19.1±6.6 **IPSS-QoL**, median(range): 4(2-6) **Qmax**, mean, (±SD): 10.4±2.9 **Post void residual urine**, mean, (±SD): 123.7±91.8 **Prostate volume**, mean, (±SD): 40.7±21.4 **No obstructed** (%): 90/117 (78.3) **No equivocal and/or unobstructed** (%): 25/117 (21.7) **<u>Group 2 - TURP</u>** **N:** 117 **Dropouts:**2/117 **Age**, mean (±SD): 66.4±7.9 **IPSS**, mean (±SD): 19.2±6.7 **IPSS-QoL**, median(range): 4(0-6) **Qmax**, mean, (±SD): 10.3±2.7 **Post void residual urine**, mean, (±SD): 104.2±69.5 **Prostate volume**, mean, (±SD): 38.1±19.1 **No obstructed** (%): 91/117(78.4) **No equivocal and/or unobstructed** (%): 25/117(21.6) **<u>Group 3 – Conservative management</u>** **N:** 106 **Dropouts:** 5/106	**Procedure:** Men were given general advice and bladder training as deemed clinically appropriate	baseline symptom score, ANCOVA	n=98 **Group 3:** 2.19 (95% CI:-23.1, -27.5, n=90 **Adjusted difference:** **Group 1 vs. Group 2:** -13.4 (95% CI: -32.9, -6.1) **p value:** NS	population.
			Post-op complications: Blood transfusion (units and criteria not stated)	**Group 1: 1/117** **Group 2:** 1/117 **p value:** NS	
			Post-op complications: Perforation	**Group 1:**0/117 **Group 2:** 2/117 **p value:** NS	
			Post-op complications: Septicaemia	**Group 1:** 0/117 **Group 2:** 2/117 **p value:** NS	
			Post-op complications: Urinary tract infection (symptomatic)	**Group 1: 3/117** **Group 2:** 2/117 **p value:** NS	
			Time to catheter removal geometric mean, days	**Group 1:** 2.2(95%CI 1.9 to 2.4) **Group 2:** 3.9(95%CI 3.7 to 4.2) **Relative risk: 1.83** **95% CI:** 1.58 to 2.11 **P value:** <0.0001	
			LOS, geometric mean (95% CI) days	**Group 1:** 11.8(95%CI: 10.2 to 13.7) **Group 2:** 2.4 (95%CI: 2.1 to 2.9) **Relative risk:** 4.79 **95% CI:** 3.88 to 5.91 **p value:** <0.0001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Age, mean (±SD): 67.2±7.8 **IPSS**, mean (±SD): 18.8±6.5 **IPSS-QoL**, median(range): 4(1-6) **Qmax**, mean, (±SD): 9.9±2.7 **Post void residual urine**, mean, (±SD): 119.1±90.4 **Prostate volume**, mean, (±SD): 36.8±17.2 **No obstructed** (%): 82/106(77.4) **No equivocal and/or unobstructed** (%): 24/106(22.6)				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Gujral et al., 2000[107] **CLASP** study-chronic urinary retention **Study design:** RCT, multicentre, open label **Setting:** UK **Evidence level:** 1+ **Duration of follow-up:** 7.5 months	**Patient group:** men with chronic urinary retention **Setting:** 3 centres in UK **Inclusion criteria:** ▪ IPSS score ≥8, suggesting moderate to severe symptoms ▪ Low Qmax; <15ml.s when voided volume>200ml, <13ml/s when voided volume between 150-200ml and <10ml/s when voided volume between 100 to 149ml measured on two occasions, with the higher value between these two used for analysis ▪ >300ml post void volume urine on ultrasound **Exclusion criteria:** CLASP criteria ▪ Prostate cancer or previous prostatic surgery; ▪ prostate size > 120ml; ▪ Life expectancy < 6 months; ▪ dysfunction; ▪ Neurogenic bladder ▪ Serum creatinine >250 µmol/L. Criteria specific to Chronic urinary retention group ▪ Long term medication active on the lower urinary tract **<u>All patients</u>**	**Group 1- Laser coagulation** **Procedure:** Nd:YAG/ Non-contact VLAP, side-firing fibre (Bard Urolase), using standard fixed spot technique **Power:** 60W ND: YAG for 60s, depends on prostate size. For prostate size with urethral length of >25 mm, additional set of laser was used. If median lobe was present, 60W for 30s was applied for each side of lobe. **Energy:** 33.8kJ or 0.94kJ/ml of prostate tissue **Catheter protocol:** Suprapubic catheter, removed when clinically appropriate. **Other:** All patients received antibiotic prophylaxis and anti-inflammatory suppository. **Group 2 –TURP** **Procedure:** Standard electroresection	**All cause mortality** Not treatment related	**Group 1:** 0/38 **Group 2:** 1/44 **p value:** NS	**Funding:** Laser machines provided by Bard Diagnostics, Redmond, Washington. **Limitations:** ▪ Open label study, with main outcomes using patient reported measures. However, this paper specified that clinicians measuring outcomes were different from surgeons conducting the surgery **Additional outcomes:** ▪ Composite outcomes categories, and categorical outcomes for IPSS and Qmax **Notes:** Sample size calculation performed, to detect 30% differences in binary outcomes and SD of 0.63for continuous outcomes at a power of 80% Please see Chacko2001
			IPSS, mean change from baseline (95%CI): Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -12.2 (95%CI: -15.7, -8.7), n=29 **Group 2:** - 14.2, (95% CI: 17.2,-11.2), n=33 **Adjusted difference:** -3.6 (95%CI-7.2 to -0.1) **p value:** 0.048	
			IPSS-QoL, mean (95%CI): Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -2.8(95%CI: -3.4, -2.1), n=30 **Group 2:** -3.2(95%CI: -3.9, -2.6) ,n=33 **Adjusted difference:** -0.6(95% CI:-1.3 to 0.1) **p value:** NS	
			Qmax, mean(95%CI): Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** 5.7 (95%CI: 2.6, 8.8), n=33 **Group 2:** 9.4 (95%CI: 6.5, 12.2) ,n=40 **Adjusted difference:** 1.1 (95%CI: -3.0 to 5.3) **p value:** NS	
			Post void residual volume, mean(95%CI): Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -329 (95%CI: -377, -281), n=33 **Group 2:** - 464(95%CI: -553, -374) ,n=40 **Adjusted difference:** -27.5 (95%CI: -68.1 to 13.0) **p value:** NS	
			Post-op complications: Confusion (TUR syndrome)	**Group 1:** 0/38 **Group 2:** 1/44 **p value:** NS	
			Post-op complications: Blood transfusion (units and criteria not stated)	**Group 1:** 0/38 **Group 2:** 3/44 **p value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 82 **Drop outs:** 2 **<u>Group 1-Laser coagulation</u>** **N:** 38 **Dropouts:**2/38 **Received as allocated:** 30 **Age**, mean (±SD): 70.2±6.8 **IPSS**, mean (±SD): 20.9±6.4 **IPSS-QoL**, , mean, (±SD): 5.0±2.6 **Prostate volume**, mean, (±SD): 40.7±19.9 **Qmax**, mean, (±SD):11.2±5.3 **Post void residual urine**, mean, (±SD): 438±151 **<u>Group 2 - TURP</u>** **N:** 44 **Dropouts:** 0 **Received as allocated:** 44 **Age**, mean (±SD): 70.6±5.8 **IPSS**, mean (±SD): 19.5±7.2 **IPSS-QoL**, mean, (±SD): 4.5±2.6 **Prostate volume**, mean, (±SD): 49.7±21.8 **Qmax**, mean, (±SD): 8.5±3.6 **Post void residual urine**, mean, (±SD): 545±275		**Post-op complications: Heavy bleeding** (4 no termination, 2 cases termination	**Group 1:** 0/38 **Group 2:** 6/44 **p value:** NS	for the acute urinary retention population of CLASP trial and Donovan2000 for the uncomplicated LUTS symptom population.
			Post-op complications: Perforation	**Group 1:** 0/38 **Group 2:** 1/44 **p value:** NS	
			Post-op complications: Septicaemia	**Group 1:** 1/38 **Group 2:** 3/44 **p value:** NS	
			Post-op complications: Urinary tract infection (symptomatic)	**Group 1:** 1/38 **Group 2:** 2/44 **p value:** NS	
			Post-op complications: Reoperation (performed resection after laser therapy due to "unacceptable levels of symptoms")	**Group 1:** 3/38 **Group 2:** 0/44 **p value:** NS	
			Time to catheter removal geometric mean, days	**Group 1:** 25.5(95%CI 20.2 to 28.3) **Group 2:** 3.0 (95%CI 2.3 to 3.9) **Relative risk:** 8.62 **95% CI:** 6.04, 12.29 **p value:** <0.0001	
			LOS, geometric mean (95% CI) days	**Group 1:** 2.2(95%CI 1.7 to 2.8) **Group 2:** 4.4(95%CI 3.9 to 4.9) **Relative risk: 2.01** **95% CI:** 1.54 to 2.61 **P value:** <0.0001	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kursh et al., 2003[156] **Study design:** RCT, open label **Setting:** US, tertiary care hospitals **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient group:** Bladder outflow obstruction secondary to BPH **Setting:** six US tertiary care hospitals between Nov 1997 and Feb 1999 **Inclusion criteria:** ▪ AUASI ≥13 ▪ Qmax <15ml/s for 2 s with an adequately filled bladder ▪ PVR between 30 and 300ml ▪ Prostatic length ≥1.5cm ▪ Prostatic volume ≤75cm^3 **Exclusion criteria:** ▪ Any condition or history of illness or surgery which may pose additional risk to the patient such as unstable angina, significant renal impairment (creatinine >1.8mg/dL), or poorly controlled diabetes mellitus. ▪ History of prostate cancer; suspected prostate cancer (based on digital rectal examination or PSA level > 4 ng/mL) – must be ruled out with biopsy ▪ Acute urinary retention ▪ Acute or chronic prostatitis cystolithiasis, neurogenic bladder, bladder neck contracture, or active urinary tract infection.	**Group 1- Laser coagulation** Performed with the Indigo 830e (830nm) laser system. **Procedure:** Slightly flexible laser fibre was inserted through the urethra and into the prostate using a standard cystoscope. A 1-cm long diffuser tip radiates heat in all directions at a low power (20W). The heat produces an olive-shaped area of coagulation necrosis about 2 x 2.5 cm or a volume of approximately 4 cm^3. **Power:** 20W **Energy:** NR **Catheter protocol:** patients discharged with catheter in place, which was usually removed in	**AUASI score**, median:	At 6 months **Group 1:** 7.0 **Group 2:** 6.0 **Difference:** 1.0 (95% CI: -3.0 to 3.0) **p value:** Not sig At 24 months **Group 1:** 9.0 **Group 2:** 7.0 **Difference:** 2.0 (95% CI: -3.0 to 4.0) **p value:** Not sig	**Funding:** Indigo Medical Inc (the laser system manufacturer). First author a paid consultant of the parent company (Ethicon Endo-Surgery) **Limitations:** ▪ Patient reported outcomes methods were not clearly reported. It was unclear which questionnaires were used to evaluate QoL and sexual function. ▪ Only point estimates (median) were reported for continuous variables. ▪ Only 61% (73/120) of targeted sample size was recruited. Enrolment stopped early because of low patient participation. **Additional outcomes:** ▪ Median prostate volume and PSA
			Qmax (ml/s), median	At 6 months **Group 1:** 14.3 **Group 2:** 16.6 **Difference:** -2.3 (95% CI: -0.4 to -6.5) **p value:** <0.05 At 24 months **Group 1:** 13.9 **Group 2:** 16.5 **Difference:** -2.6 (95% CI: -7.6 to 0.4) **p value:** Not sig	
			Post-void residual volume (ml), mean ± SD (note that the baseline value was significantly different)	At 6 months **Group 1:** 42.4 **Group 2:** 46.0 **Difference:** -3.6 (95% CI: -12.6 to 27.3) **p value:** NS At 24 months **Group 1:** 57.7 **Group 2:** 44.0 **Difference:** 13.7(95% CI: -15.2 to 40.3) **p value:** NS	
			Post-op complications: Blood transfusion	**Group 1:** 0/37 **Group 2:** 0/35 **p value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	▪ Taking terazoxin, doxazosin or tamsulosin within 14 days of enrolment; finasteride or phytotherapy and anticholinergic within one month of enrolment. **<u>All patients</u>** **N:** **Age,** range, years: 50-81 **Drop outs:** 1 patient withdrew consent before treatment group assignment **<u>Group 1-Laser coagulation</u>** **N:** 37 Dropouts: **Age,** mean (years)**:** 67.6 **Ethnicity, white** (%): 30/37 (81%) **AUASI** ,median: 24.0 **Qmax,** median (ml/s)**:** 9.2 **PVR** ,median (ml)**:** 81 **PSA,** median (ng/ml): 2.3 **Prostate volume,** median (cm^3):41.5 **<u>Group 2 - TURP</u>** **N:** 35 Dropouts: **Age,** mean**:** 69.3 **Ethnicity, white (%):** 29/35(83%) **AUASI** ,median: 23.0 **Qmax,** median (ml/s)**:** 9.1 **PVR** ,median (ml)**:** 87.5 **PSA,** median (ng/ml): 2.3 **Prostate volume,** median (cm^3): 40	1 week. **Other:** Usually performed as an outpatient procedure. **Anaesthesia:** general/spinal/topical: 17/15/5 **Group 2 –TURP Procedure:** Standard radiofrequency monopolar loop procedure **Catheter protocol:** Generally removed one day post-operatively, before discharge **Others:** **Anaesthesia:** general/spinal/topical: 11/24/0 **Both groups:** received antibiotics – choice at discretion of individual investigators	**Post-op complications: Development of anaemia** (hematocrite less than 30%)	**Group 1:** 0/37 **Group 2:** 2/35 **p value:** NS	level post surgery were reported. ▪ "Problems from Symptom Index" score and "American Urological Association QoL Assessment" score were reported. However, it what unclear which questionnaire were used from the paper. There was no significant difference between treatment arms in these outcomes. **Notes:** None.
			Post-op complications: reoperation (2 patients retreated within 6 months, 1 with ILC and 1 with TURP. 4 additional patients receive TURP within 1 year)	<u>At 6 months</u> **Group 1:** 2/37 **Group 2:** 0/35 **Relative risk: NE** **p value:**: NS <u>At 12 and 24 months</u> **Group 1:** 6/37 **Group 2:** 0/35 **Relative risk:** NE **p value:** 0.02	
			Post-op complications: Incontinence (1 case of urge incontinence and another case of stress incontinence requiring pads)	**Group 1:** 0/37 **Group 2:** 2/35 **Relative risk: 0 (0-1.77)** **p value:**: NS	
			LOS, median (range), (days)	**Group 1:** 7.0 (3 to 145) **Group 2:** 33.5 (10 to 120) **p value:** NR	
			Sexual function score (Name of questionnaire not provided. Stated that the range was 0-30, higher scores better)	<u>At 6 months</u> **Group 1:** 19.0 **Group 2:** 5.0 **Difference:** 14.0 (95% CI: 3.0 to 14.0) **p value:** <0.05 <u>At 24 months</u> **Group 1:** 19.5 **Group 2:** 10.0 **Difference:** 9.5 (95% CI: -1.0 to 12.0) **p value:** Not sig	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Liedberg et al., 2003[166] **Study design:** RCT, open label **Setting:** Hospital, Sweden **Evidence level:** 1+ **Duration of follow-up:** Up to 1 year	**Patient group:** moderate to severe BPH **Setting:** Department of urology, hospital in Sweden, Dec 1997 to Feb 2000 **Inclusion criteria:** ▪ IPSS ≥12 ▪ Qmax ≤15ml/s **Exclusion criteria:** ▪ Indwelling urinary catheter ▪ Prostatic carcinoma ▪ Clinical suspicion of neurogenic bladder disturbance **All patients** **N:** 38 **Drop outs:** 7/38 (3 due to prostate cancer), one was randomised to ILC but received TURP; 1 did not wish to undergo surgery and 2 could not undergo surgery due to undercurrent illness. **Group 1-Laser coagulation** **N:** 20 **Drop outs:** Not stated **IPSS,** median (IQR): 19(16-24) **Qmax,** median (IQR): 8(7-10) [n=19] **Prostate volume,** median (IQR):49(41-75) **Post void residual volume:** median (IQR): 96(64-190)	**Group 1- Laser coagulation Procedure:** Performed with the Indigo 830e (830nm) laser system. Each puncture site was treated for 3 min with a target temperature of 85C. The prostate was punctured under visual control and the target was one puncture for every 4ml of prostate. Power setting not stated. **Catheter protocol:** suprapubic catheter, removed when PVR <150ml **Others:** Norfloxacin 400mg twice daily while catheter was in place **Group 2 –TURP** **Procedure:** Standard electroresection.	**IPSS,** median (IQR):	At 3 months **Group 1:** 10(4-15), n=20 **Group 2:** 4(2-7), n=11 **p value:** NS At 12 months **Group 1:** 11(6-14), n=19 **Group 2:** 6(3-10), n=9 **p value:** NS	**Funding:** Partly finance by FroU-Kronoberg **Limitations:** ▪ Open label study with subjective patient reported outcomes. ▪ Study stopped early (targeted N=50) due to prolonged rate of catheterisation and high rate of UTI ▪ Large number of exclusions from TURP group resulted in imbalance of sample **Additional outcomes:** Prostate volume post operation **Notes:** Age of subjects not reported
			Qmax (ml/s), median (IQR):	At 3 months **Group 1:** 11(8-15), n=19 **Group 2:** 12(9-18), n=10 **p value:** NS At 12 months **Group 1:** 11(6-12), n=18 **Group 2:** 14(10-19), n=9 **p value:** NS	
			Post void residual volume (ml), median (IQR):	At 3 months **Group 1:** 74(38-140), n=19 **Group 2:** 0(0-53), n=10 **p value:** NS At 12 months **Group 1:** 126(25-190), n=19 **Group 2:** 22(3-62), n=8 **p value:** NS	
			Post-op complications: Clot retention (requiring transurethral clot evacuation under general anaesthesia	**Group 1:** 1/20 **Group 2:** 0/11 **p value:** NS	
			Peri-operative complications: Bleeding (blood loss, median (IQR), (ml))	**Group 1:** 0(0-50) **Group 2:** 350(200-514) **p value:** <0.001	
			Post-op complications: Catheterisation	**Group 1:** 24(14-34) **Group 2:** 2(1-2) **p value:** <0.001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2 - TURP **N:** 11 **Dropouts:** Not stated **IPSS,** median (IQR): 17(17-24) **Qmax,** median (IQR): 8(6-9) [n=10] **Prostate volume,** median (IQR):47(37-61) **Post void residual volume:** median (IQR): 117(67-200)		**Post-op complications: urinary tract infections**	**Group 1:** 13/20 **Group 2:** 1/11 **p value:** <0.007	
			Post-op complications: urethral stricture	**Group 1:** 0/20 **Group 2:** 0/11 **p value:** NS	
			Post-op complications: bladder neck stenosis	**Group 1:** 0/20 **Group 2:** 0/11 **p value:** NS	
			Post-op complications: Retrograde ejaculation	**Group 1:** 1/20 **Group 2:** 3/11 **p value:** NS (0.084)	
			Hospitalisation, median (IQR), (days):	**Group 1:** 2.5 (0.25 to 3.8) **Group 2:** 3 (3 to 4) **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Martenson et al., 1999[183] **Study design:** RCT, open label **Setting:** Netherlands **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient group:** BPH patients **Setting:** Department of Urology, University Hospital Nijmegen, Netherlands Oct 1994 to April 1996 **Inclusion criteria:** ▪ Prostate volume >25 cm^3 ▪ age >45 years ▪ Duration of symptoms> 3 months ▪ IPSS12 ▪ Peak uroflow <15ml/s **Exclusion criteria:** ▪ Prostate carcinoma ▪ Bacterial prostatitis ▪ Urethral stricture ▪ Neurogenic bladder dysfunction ▪ Urinary tract infection ▪ Use of drugs influencing bladder function ▪ History of TURP ▪ Diabetes mellitus ▪ Bladder residual urine >350ml **All patients** **N:** 44 Mean age: NR **Drop outs:** NR **Group 1-Laser coagulation** **N:** 30 **IPSS**, mean ±sd: 21.7±6.1 **IPSS-QoL**, mean ±sd: 4.1±1.4 **Qmax**, mean±sd, (ml/s):7.3±3.8	**Group 1- Laser coagulation** **Procedure:** Performed with the Indigo 830 (830nm) laser system. Each individual fibre placement received 1420 J in a standard for 4 min treatment cycle **Power:** 10 W, decreased to 5 W **Catheter protocol:** Suprapubic catheters were removed when adequate voiding was demonstrated at scheduled follow up (1, 2 or 4 weeks) **Group 2 –TURP** **Procedure:** Standard procedure. 24Fr resectoscope used in combination with glycine irrigation fluid. **Catheter protocol:** Removed according to individual needs	**IPSS**, mean±sd	At 3 months (12 weeks) **Group 1:** 11.8±6.9 **Group 2:** 4.7±4.0 **p value:** NS At 6 months (26 weeks) **Group 1:** 10.3±5.4 **Group 2:** 3.8±2.4 **p value:** NS At 12 months (52 weeks) **Group 1:** 12.4±7.7 **Group 2:** 3.5±2.9 **p value:** NS At 24 months (104 weeks) **Group 1:** 12.0±4.9 **Group 2:** 5.0±4.4 **p value:** NS	**Funding:** Indigo- the laser manufacturer **Limitations:** ▪ Small sample size, with no power calculation provided ▪ Patient age not reported ▪ T-tests were used **Additional outcomes:** The paper also reported the results of another non-randomised phase II study which temperature-sensing laser system **Notes:** The patients were randomised 2:1 in this study.
			IPSS-QoL, mean ±sd	At 3 months (12 weeks) **Group 1:** 2.3±1.4 **Group 2:** 0.9±1.3 **p value:** NS At 6 months (26 weeks) **Group 1:** 2.2±1.4 **Group 2:** 0.5±0.7 **p value:** NS At 12 months (52 weeks) **Group 1:** 2.2±1.5 **Group 2:** 0.6±0.8 **p value:** NS At 24 months (104 weeks) **Group 1:** 2.2±1.5 **Group 2:** 0.7±0.9 **p value:** NS	
			Qmax, mean±sd, (ml/s):	At 3 months (12 weeks) **Group 1:** 12.5±5.4 **Group 2:** 25.8±9.7 **p value:** NS At 6 months (26 weeks)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	PVR, mean±sd, (ml):116±146 **Normal erectile function:** 28/30 **<u>Group 2 - TURP</u>** **N:** 14 **IPSS**, mean ±sd: 21.6±7.7 **IPSS-QoL**, mean ±sd: 4.0±1.3 **Qmax**, mean±sd, (ml/s):9.3±3.2 **PVR**, mean±sd, (ml):88±126 12/14			**Group 1:** 11.1±4.5 **Group 2:** 18.2±6.6 **p value:** NS <u>At 12 months (52 weeks)</u> **Group 1:** 11.9±5.5 **Group 2:** 25.7±11.1 **p value:** NS <u>At 24 months (104 weeks)</u> **Group 1:** 10.3±4.4 **Group 2:** 20.1±13.7 **p value:** NS	
			PVR, mean±sd, (ml):	<u>At 3 months (12 weeks)</u> **Group 1:** 58±103 **Group 2:** 12±19 **p value:** NS <u>At 6 months (26 weeks)</u> **Group 1:** 60±56 **Group 2:** 14±27 **p value:** NS <u>At 12 months (52 weeks)</u> **Group 1:** 59±77 **Group 2:** 14±21 **p value:** NS <u>At 24 months (104 weeks)</u> **Group 1:** 94±128 **Group 2:** 63±100 **p value:** NS	
			Post-op complications: Blood transfusion	**Group 1:** 0/30 **Group 2:** 0/14 **p value:** NS	
			Post-op complications: Clot retention	**Group 1:** 0/30 **Group 2:** 0/14 **p value:** NS	
			Post-op complications: In continence (up to 24 months), definition of incontinence not provided	**Group 1:** 0/30 **Group 2:** 0/14 **p value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Post-op complications: urinary tract infections	**Group 1:** 10/30 **Group 2:** 4/14 **RR**: 4.67(95% CI : 0.94 to 27.8) **p value:** NS	
			Post-op complications: Reoperation (up to 24 months)	**Group 1:** 6/30 **Group 2:** 1/14 **RR**: 2.8(95%CI: 0.51 to 17.5) **p value:** NS	
			Post-op complications: Retrograde ejaculation	**Group 1:** 0/30 **Group 2:** 3/14 **p value:** NS (0.084)	
			Length of catheterisation, mean ±sd (days)	**Group 1:** 27±23 **Group 2:** 3±1	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Rodrigo Aliaga et al., 1998[253] (data extracted from HTA report) **Study design:** **Setting:** Spain **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** ▪ patients with BPH **Inclusion criteria:** ▪ prostate size 20–60 g; symptom score; IPSS score ≥ 15 **Exclusion criteria:** ▪ age < 50 years **All patients** **N:** 41 **Drop outs:** **Group 1 –TUIP** **N:** 20 **Age**, years, mean±sd (range): NR Residual volume, mean ± SD (ml): 89 ± 92 **Group 2 -TURP** **N:** 21 **Age**, years, mean±sd (range): NR Residual volume, mean ± SD (ml): 146 ± 133	**Group 1- TUIP/BNI** **Group 2 - TURP** **All** Patients left hospital 24–72 hours postoperatively if no complications	**IPSS score**, mean ± SD	Baseline **Group 1:** 24.2 ± 7.7 **Group 2:** 24.4 ± 10.3 3 months **Group 1:** 4.3±4.5 **Group 2:** 4.8±4.8 6 months **Group 1:**5.7±6.2 **Group 2:**3.7±3.8	**Funding:** NR **Limitations:** ▪ No information of randomisation allocation and concealment methods ▪ Baseline prognostic factors were reported as not equal in quality assessment (uncertain which factor this referred to) **Additional outcomes:** Irritative symptoms Quality of life score (WHO) Length of hospital stay Catheter duration Residual volume **Notes:** None.
			Qmax, ml/s, mean ±sd (range)	Baseline **Group 1:** 8.7 ± 5.5 **Group 2:** 8.3 ± 4.5 3 months **Group 1:** 22±12.2 **Group 2:**18.6±8.5 6 months **Group 1:** 20.6±8.7 **Group 2:** 20.6±10.1	
			Blood transfusion	**Group 1:** 0/20 **Group 2:** 1/21 **P value:** Not sig	
			Reoperation	**Group 1:** 1/20 **Group 2:** 1/21 **P value:** Not sig	
			Retrograde ejaculation	**Group 1:** 14/20 **Group 2:** 15/21	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Sengor et al., 1996[271] **Study design:** RCT, open label **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** Symptomatic bladder outlet obstruction due to BPH referred to urology clinic **Setting:** urology clinic, single-centre, Istanbul, Turkey **Inclusion Criteria:** • Significant voiding symptoms to request therapy • Qmax ≤15 ml/s and Qave ≤ 10 ml/s from uroflowmetric volume of ≥ 150 ml • Age >50 years **Exclusion Criteria:** • Prostate cancer- Induration or nodularity of prostate on DRE or PSA > 4.0 mg/ml further examined for cancer. • Infections (treated with suitable antibiotics preopreatively) **All patients** **N:** 60 **Age:** 50-85 **Drop outs:** NR **Group 1 - Laser** **N:** 30 **Mean age (yrs):** 66 (range 50-85) **Drop outs:** **Erectile dysfunction:** 7/30 **AUA, mean ± SD:** 21.8 ± 7.6 **Prostate volume (TRUS) ml:** 55 (30-80)	**Group 1** Under spinal or general anaesthesia Ultraline side firing Nd:YAG laser fibre 600μm using SMA-905 adapter and standard Nd:YAG laser generator at 60W through 21F cystoscope. Bladder was continuously irrigated with saline. No indwelling catheter was used but supra public tubes were clamped 4-5 days after treatment and removed after successful urination. **Group 2** TURP in standard manner under spinal anaesthesia using Storz 26F resectoscope with mannitol solution for irrigation. A 3-way Foley catheter was inserted and bladder irrigated with normal saline for 24-48 h. **Examination methods:** Patients followed at 3 and 6 months using AUA symptom score, Qmax	**AUA score**, mean ± SD:	At 3 months **Group 1:** 8.5±4.2 **Group 2:** 9.8±3.1 **p value:** NS (P=0.17), calculated by NCGC team using t-tests. Reported as 0.034 At 6 months **Group 1:**7.8±2.6 **Group 2:** 9.3±4.2 **p value:** NS (P=0.1), calculated by NCGC team using t-tests	**Funding:** NR **Limitations:** ▪ Outcome assessment was not masked. ▪ Randomisation and allocation method not reported. ▪ Statistical methods and sample size calculation not reported ▪ Baseline values of post void residual volume significantly different between groups. **Additional outcomes:** % of mean change was reported for AUA score, Qmax and residual volume but standard deviations were not provided **Notes:** None.
			Qmax (ml/s), mean ± SD:	At 3 months **Group 1:** 18.9±3.1 **Group 2:** 20.7±2.6 **p value:** 0.01, calculated by NCGC team using t-tests. Reported as 0.025 At 6 months **Group 1:** 18.2±2.1 **Group 2:** 19.8±2.5 **p value:** <0.01, calculated by NCGC team using t-tests, reported as NS	
			Post void residual volume (ml), mean ± SD (note that the baseline value was significantly different)	At 3 months **Group 1:** 50.4±30 **Group 2:** 70±27 **p value:** NS At 6 months **Group 1:** 47±19 **Group 2:** 68±22 **p value:** NS	
			Post-op complications: Transurethral resection syndrome	**Group 1:** 0/30 **Group 2:** 0/30 **p value:** NS	
			Post-op complications: Blood transfusion (units and criteria not stated)	**Group1:** 0/30 **Group 2:** 2/30 **p value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	***PVR mean ± SD:** 110 ± 68 **Qmax mean ± SD (ml/s):** 8.7 ± 2.3 **<u>Group 2 - TURP</u>** **N:** 30 **Mean age (yrs):** 61 (55-70) **Drop outs:** **Erectile dysfunction:** 3/30 **AUA, mean ± SD:** 22.1 ± 2.6 **Prostate volume (TRUS) ml:** 47 (30-50) ***PVR, mean ± SD:** 155 ± 40 **Qmax, mean± SD (ml/s):** 8.4 ± 2.8 *P =0.003,calculated by t-test by NCGC team	and PVR measurements	**Post-op complications: urethral strictures** (6 months follow up)	**Group 1:** 0/30 **Group 2:** 0/30 **p value:** NS	
			Post-op complications: Retrograde ejaculation (6 months follow up)	**Group 1:** 1/23 (3%) **Group 2:** 24/27 (80%) **Relative risk::** 0.05 (95% CI: 0.01-0.19) **p value:** <0.001	
			Operation time, mean (range), (min):	**Group 1:** 43 (15-70) **Group 2:** 56 (45-90) **P value :** NR	
			LOS, mean (range), days	**Group 1:** 1.6 (1-3) **Group 2:** 5.9 (4-7) **P value :** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Suvakovic et al., 1996[290] **Study design:** RCT, open label **Evidence level:** 1+ **Duration of follow-up:** 1 year	**Patient group:** Consecutive patients with prostatic symptoms **Setting:** Urology department, South Cleveland University, UK **Inclusion Criteria:** • Qmax ≤15mL/s for a voided volume of ≥150 mL • Age • Significant voiding symptoms (AUA score >15) • PSA level <2.5 ng/mL • Prostate volume <40g (assessed by TRUS, DRE and cystoscopy) • Length of the prostatic urethra >4 cm **Exclusion Criteria:** • Malignancy **<u>All patients</u>** **N:** 40 **<u>Group 1 -</u> VLAP – side fire free beam alone** **N:** 10 **Age (mean):** 67.5(8.7) **IPSS:** 15.7(5.1) **Qmax** ml/s**:** 10.5 (3.7) **Residual Vol** mL**:** 47.4(48.1)	**Group 1: VLAP – side fire free beam alone** 4 spot thermocoagulation at the 10, 2, 4 and 8 o'clock positions. Laser delivered at 60W for 60s. **Group 2 : CLAP- contact laser alone** Nd: YAG laser applied at 40W for vaporising and coagulating the prostate with a minimum depth of penetration. A 16 F two – way catheter was inserted into the bladder and removed after 24 h. **Group 3 : Hybrid – side fire free beam and debridement** As in VLAP, plus debridement of coagulated tiisue using a 26F continuous irrigating resectoscope. At the end of the procedure, a 16 F two –way catheter was inserted into the bladder and removed after 24 h **Group 4 : TURP**	**IPSS symptom score,** mean±sd. Values for 12 months follow up reported in paper, but n was not reported	<u>At 3 months</u> **Group 1:** 16.8±15.0 , n=10 **Group 2:** 9.7±2.6, n=10 **Group 3:** 8.1±5.4, n=8 **Group 4:** 12.8±5.9, n=10 **P value:** NS# P value for Group 1 vs. Group 3 was reported to be <0.01 in paper, but this could not be repeated. <u>At 6 months</u> **Group 1:** 16.2±4.2, n=9 **Group 2:** 18.7±7.5, n=9 **Group 3:** 19.4±3.4, n=4 **Group 4:** 19.0±0.8, n=10 **P value:** NS#	**Funding:** NR **Limitations:** • Small sample size, n of 10 in each arm • Unclear which statistical test was used for data – discrepancies in the stat sig reported for AUA score for 3 months and calculated by NCGC team. • Number of participants followed up at 12 months not reported. **Additional outcomes:** Operation duration for each procedure **Notes:** # values calculated by NCGC team based on mean and sd reported. It was not possible to calculate using Kruskal Wallis test without the
			Qmax ml/s, mean±sd Values for 12 months follow up reported in paper, but n was not reported	<u>At 3 months</u> **Group 1:** 14.8±5.4, n=10 **Group 2:** 15.6±13.5, n=10 **Group 3:** 15.1±7.3, n=8 **Group 4:** 17.8±3.8, n=10 **P value:** NS <u>At 6 months</u> **Group 1:** 16.2±4.2, n=9 **Group 2:** 18.7±7.5, n=9 **Group 3:** 19.4±3.4, n=4 **Group 4:** 19.0±0.8, n=10 **P value:** NS#	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Prostate size (by TRUS), g: 23.6(6.4) **PSA** (ng/ML): 2.3(0.8) **<u>Group 2</u> - CLAP- contact laser alone** **N:** 10 **Age (mean):** 62.6(5.8) **IPSS:** 18 (6.0) **Qmax** ml/s: 12.2 (3.8) **Residual Vol** mL: 139.6(103) **Prostate size** (by TRUS), g: 24(5.8) **<u>Group 3</u> - Hybrid – side fire free beam and debridement** **N:** 10 **Age (mean):** 64.1(6.9) **IPSS:** 17(6.0) **Qmax** ml/s: 11.8(4.1) **Residual Vol** mL: 68.3(64) **Prostate size** (by TRUS), g: 27(12.3) **<u>Group 4</u> - CLAP- TURP Standard resection** **N:** 10 **Age (mean):** 66.1(5.1) **IPSS:** 18.8 (4.5) **Qmax** ml/s: 11.1(6.4) **Residual Vol** mL: 161.8(104) **Prostate size** (by TRUS), g: 22(5)	**Standard resection** using a 26 F continuous irrigating resectoscope. A 22 F three-way urethral catheter was inserted into the bladder and irrigation was continued up to 24 h. The catheter was removed after 48 h and the patients discharged home 3-4 days after the procedure.	**Catheter duration**, mean, hours (range or standard deviations not reported)	**Group 1:** 24, n=10 **Group 2:** 24, n=10 **Group 3:** 20, n=10 **Group 4:** 48, n=10 **p value:** reported as <0.05 between group 4 and "lasers"	raw data. All patients received preoperative oral antibiotics and controlled for more than 5 days post-operatively.
			Length of hospitalisation, (hours)	**Group 1:** 30,n=10 **Group 2:** 30, n=10 **Group 3:** 24, n=10 **Group 4:** 84, n=10 **p value:** reported as <0.05 between group 4 and "lasers"	

1 **Evidence Table 27: Laser vaporisation vs. transurethral resection of the prostate (TURP)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Bouchier-Hayes et al., 2006[32] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 weeks	**Patient group:** Patients referred with LUTS to urology outpatient department **Setting:** single centre, Melbourne, Australia **Inclusion Criteria:** • Age >50 years • Referral by GP • Flow rate ≤ 15 mL/s • IPSS ≥ 12 • Gland 15-85 cm^3 on TRUS • Obstructed Abrams-Griffiths (A-G) nomogram • Able to complete QoL, Bother Score & Baseline Sexual Function Questionnaire (BSFQ) questionnaires • Able to give informed consent **Exclusion Criteria:** • Neurogenic bladder • Known or suspected prostate cancer • Chronic retention • Taking α-blocker or herbal remedy • On anticoagulants • On finasteride or dutasteride **<u>All patients</u>** **N:** 95	**Group 1** Photoselective vaporisation was performed using 80W KTP using Greenlight laser system and StarPulse quasi-continuous wave laser (Laserscope) emitting green light at 532 nm. A 600 μm laser fibre with 70° lateral deflecting quartz element used through continuous flow cystoscope with saline irrigation. Catheters left situ at the discretion of the surgeon. **Group 2** TURP in standard manner through 25F resectoscope sheath using ValleyLab diathermy machine with 3-way 22F Foley catheter on continuous saline irrigation	**Change IPSS symptom score from baseline at 6 weeks****	**Group1:** 14.0 ± 9.8 (n=38) **Group 2:** 12.9 ± 10.6 (n=38) **p value:** Not Signif. (NCGC calculated p=0.63)	**Funding:** NR **Limitations:** • Baseline values for Qmax and IPSS, QoL, bother and BSFQ not reported • **Follow up period not clear for main outcome data or complications. Might be 6 weeks as number of patients with data at 6 weeks is 76 • Outcome assessment was not masked. • Randomisation method not reported. • Allocation concealment not reported **Notes:** 12 months data in publication at October 2008
			Change in flow rate (Qmax) from baseline at 6 weeks**	**Group1:** 11.96 ± 8.23 (n=38) **Group 2:** 8.56 ± 9.08 (n=38) **p value:** Not Signif. (NCGC calculated p=0.09)	
			Change in QoL score from baseline at 6 weeks**	**Group1:** 2.65 ± 2.1 (n=38) **Group 2:** 2.91 ± 2.04 (n=38) **p value:** Not Signif.	
			Change in bother score from baseline at 6 weeks**	**Group1:** 2.65 ± 2.1 (n=38) **Group 2:** 1.61 ± 1.22 (n=38) **p value:** Not Signif.	
			Change in prostate volume from baseline at 6 weeks**	**Group1:** 125 ± 198 (n=38) **Group 2:** 86 ± 124.38 (n=38) **p value:** Not Signif.	
			Post-op complications Failure to void: (follow up period 6 weeks)**	**Group1:** 4/38 **Group 2:** 3/38 **p value:** NR	
			Post-op complications Stricture: (follow up period 6 weeks)**	**Group1:** 0/38 **Group 2:** 5/38 **p value:** NR	
			Post-op complications urine retention: (follow up period 6 weeks)**	**Group1:** 3/38 **Group 2:** 1/38 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Drop outs: 19 (25%)* **<u>Group 1 - Laser</u>** **N:** 38 **Mean age (yrs):** 65.2 range (51-81) **Drop outs:** NR* **IPSS:** NR **Erectile dysfunction:** NR **Prostate volume (TRUS) ml:** 42.4 range (16.5-82.6) **Qmax:** NR **Operation time:** 30.2 mins range (9-70) **Mean catheterisation time (days):** 0.5 ± 0.4 **Mean length of stay (days):** 1.1 ± 0.3 **<u>Group 2 - TURP</u>** **N:** 38 **Mean age (yrs):** 66.2 range (55-80) **Drop outs:** NR* **IPSS:** NR **Erectile dysfunction:** NR **PVR (TRUS) ml:** 33.2 range (15.4-67.5) **Qmax:** NR **Operation time:** 31.3 mins range (5-70) **Mean catheterisation time (days):** 1.9 ± 1.3 **Mean length of stay (days):** 3.4 ± 1.2 *3 patients dropped out after randomisation but groups not defined. Only 76 patients has data at 6 weeks postoperatively	Intervention performed by registrars in training or fellows in the department, all of whom had performed <5 laser prostatectomies each and between 35 & 325 TURPs **Examination methods:** Patients followed at 6 weeks, 3, 6, 12 months by same investigator During follow up Qmax, IPSS, QoL, bother and BSFQ all completed and TRUS, urodynamics and serum PSA measured at 6 months	**Post-op complications number of patients with blood transfusion (follow up period 6 weeks**)**	**Group1:** 0/38 **Group 2:** 1/38 **p value:** NR	
			Post-op complications number of patients Peri-operative urinary tract infections (follow up period 6 weeks)**	**Group1:** 2/38 **Group 2:** 3/38 **p value:** NR	
			Post-op complications number of patients TUR syndrome (follow up period 6 weeks)**	**Group1:** 0/38 **Group 2:** 1/38 **p value:** NR	
			Post-op complication: Haemorrhage necessitating readmission: (follow up period 6 weeks)**	**Group1:** 1/38 **Group 2:** 3/38 **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Carter et al., 1999[44,45] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Patients from urology outpatient department with BPE severe enough to warrant operation **Setting:** single centre, UK **Inclusion Criteria:** (based on British Laser Urological Evaluation Society (BLUES) • Qmax ≤ 15 ml/s • Voided volume > 150 ml • PVR < 300 ml • IPSS≥ 12 **Exclusion Criteria:** • History of acute retention • Histological diagnosis of prostate adenocarcinoma • Prostate volume > 100 ml (TRUS) • Neurogenic bladder **<u>All patients</u>** **N:** 204 **Drop outs:** 13 (9 violated entry criteria, 2 with calculi, 2 with urethral strictures) **<u>Group 1 - Laser</u>** **N:** 95 **Mean age ± SD (yrs):** 67.9 ± 7.8 **Drop outs:** NR **IPSS:** 20.3 ± NR **Erectile dysfunction:** NR **Mean Prostate volume (TRUS) ml ± SD:** 41.6 ± 17.3	**Group 1** Hybrid laser performed using Laserscope 40W KTP/60W Nd:YAG generator system abd AddStat laser delivery fibres producing forward or side beams through a 21 F laser cystoscope (Storz). 30W KTP treatment to create bladder neck incisions and vaporisation then Nd:YAG 60W used to coagulate. Catheter protocol: Urethral catheter removed either 1 or 2 days or 1-2 weeks **Group 2** TURP in standard manner through 24 or 26 Fr resectoscope. Catheters removed postoperatively when clinically indicated **All patients:** Antibiotics: single dose Gentamicin at operation and catheter removal.	**Mean (SD) IPSS symptom score at 6 months**	**Group1 (n=90):** 6.7 (4.0) **Group 2 (n=89):** 6.4 (4.0)	**Funding:** Partially funded by Somerset Health Authority **Limitations:** • Baseline values for were not reported with standard deviations • Follow up outcomes Qmax and IPSS, QoL scores not reported with standard deviations. Only as graphs. • Outcome assessment was not masked. • Allocation concealment not clear if opaque sequential envelopes were used • *Unclear which follow up complications refer to and how many patients remained. ITT analysis used for late complications **Notes:** Mean and standard deviations for IPSS and Qmax data estimated from graphs.
			Mean (SD) IPSS symptom score at 12 months	**Group1 (n=86):** 6.6 (3.6) **Group 2 (n=84):** 5.9 (4.7)	
			Mean (SD) Qmax at 6 months	**Group1 (n=90):** 19.1 (5.1) **Group 2 (n=89):** 19.6 (5.1)	
			Mean (SD) Qmax at 12 months	**Group1 (n=86):** 19.8 (5.8) **Group 2 (n=84):** 20.9 (6.5)	
			Early post-op complications: Failure to void as inpatient following catheter removal (follow up period up to 6 months)	**Group1:** 26/81 **Group 2:** 5/96 **p value:** <0.00001 (calculated by NCGC Fishers exact test)	
			Late post-op complications: urinary tract infection (follow up period > 6 weeks to 1 year)*	**Group1:** 2/95 **Group 2:** 6/96 **p value:** Not signif. (calculated by NCGC Fishers exact test)	
			Late post-op complications: urethral stricture (follow up period > 6 weeks to 1 year)*	**Group1:** 2/95 **Group 2:** 9/96 **p value:** 0.06 (calculated by NCGC Fishers exact test)	
			Late post-op complications: acute retention (follow up period > 6 weeks to 1 year)*	**Group1:** 2/95 **Group 2:** 0/96 **p value:** Not signif. (calculated by NCGC	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean PSA ng/ml ± SD: 3.8 ± 2.7 **Mean Creatinine mmol/l ± SD:** 95.3 ± 15.7 **Qmax:** 9.0 ± NR **PVR:** 109 ± NR **Operation time:** 37.4 ± 12.1 mins 3.4 ± 1.2 **Median catheterisation time (days):** NR **Median length of stay (days):** 2 (0-9) **<u>Group 2 - TURP</u>** **N:** 96 **Mean age ± SD (yrs):** 67.0 ± 7.5 **Drop outs:** NR **IPSS:** 19.8 ± NR **Erectile dysfunction:** NR **Mean Prostate volume (TRUS) ml ± SD:** 41.7 ± 19.4 **Mean PSA ng/ml ± SD:** 3.2 ± 2.4 **Mean Creatinine mmol/l ± SD:** 99.7 ± 27 **Qmax:** 9.5 ± NR **PVR:** 135 ± NR **Operation time:** 35.7 ± 10.8 mins **Median catheterisation time (days):** NR **Median length of stay (days):** 2 (2-14)	**Intervention performed by:** 1 of 3 consultants, 2 Snr registrars, 1 clinical research fellow or 1 staff-grade urologist. **Examination methods:** Patients followed at 6 weeks, 6, 12 months During follow up IPSS, Symptom problem index (SPI), BPH impact Index (BPHII), Short Form 36 (HRQoL) questionnaires completed and uroflometry (Dantec Uroflow 1200), TRUS to find PVR.		Fishers exact test)	
			Late post-op complications: incontinence (follow up period > 6 weeks to 1 year)*	**Group1:** 1/95 **Group 2:** 0/96 **p value:** Not signif. (calculated by NCGC Fishers exact test)	
			Late post-op complications: Re-operation (follow up period > 6 weeks to 1 year)*	**Group1:** 2/95 **Group 2:** 1/96 **p value:** Not signif. (calculated by NCGC Fishers exact test)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Horasanli et al., 2008[122] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** Patients referred to urology clinic with symptoms of BOO due to BPH **Setting:** single centre, dept urology, Memorial Hospital, Istanbul, Turkey **Inclusion Criteria:** • Prostate volume 70-100 mL (TRUS) or PVR >150 mL with IPSS score > 7 **Exclusion Criteria:** • Neurogenic bladder • Urethral strictures • PVR > 400mL • Previous prostatic, bladder or urethral surgery • Prostate malignancy • Indwelling catheters • Refusal of consent **<u>All patients</u>** **N:** 76 **Drop outs:** NR* **<u>Group 1 - Laser</u>** **N:** 39 **Mean age ± SD (yrs):** 69.2 ± 7.1 (range 59-78) **IPSS Score:** 18.9 ± 5.1 **IIEF-5:** 19.9 ± 5.1	**Group 1** Photoselective vaporisation performed using KTP/532 emitting green light at 80W via a 6F side-firing fibre through 24F continuous flow cystoscope. A 20F 3-way Foley catheter was left in place and bladder irrigated with saline for 24 hours. **Group 2** TURP in standard manner under general anaesthesia using Storz 26F continuous flow resectoscope. A 20F 3-way Foley catheter was left in place and bladder irrigated with saline for 24-48 hours. **All patients:** Antibiotics before and after.. **Intervention performed by:** 5 surgeons	**IPSS symptom score at 3 months**	**Group1:** 11.2 ± 7.6 **Group 2:** 6.1 ± 5.4 **p value:** 0.01 (calculated by NCGC as t test with unequal variances using ITT analysis)	**Funding:** NR **Limitations:** • Randoomisatrio n method not reported • Allocation concealment not reported • Masking of outcome assessment not reported • Drop out numbers not clear so ITT analysis used **Notes:** * Drop out numbers not clear so ITT analysis used. .
			Change in IPSS symptom score from baseline at 3 months	**Group1:** 7.7 ± NR **Group 2:** 14.1 ± NR **p value:** NR	
			IIEF-5 at 3 months	**Group1:** 19.0 ± 3.8 **Group 2:** 20.0 ± 4.7 **p value:** Not signif. (calculated by NCGC as t test with equal variances using ITT analysis)	
			Change in IIEF-5 from baseline at 3 months	**Group1:** 0.9 ± NR **Group 2:** 0.1 ± NR **p value:** NR	
			flow rate (Qmax) at 3 months	**Group1:** 14.1 ± 8.7 **Group 2:** 21.3 ± 12.8 **p value:** 0.006 (calculated by NCGC as t test with unequal variances using ITT analysis)	
			Change in flow rate (Qmax) from baseline at 3 months	**Group1:** 5.5 ± NR **Group 2:** 12.1 ± NR **p value:** NR	
			IPSS symptom score at 6 months	**Group1:** 13.1 ± 5.8 **Group 2:** 6.4 ± 7.9 **p value:** 0.0001 (calculated by NCGC as t test with equal variances using ITT analysis)	
			Change in IPSS symptom score from baseline at 6 months	**Group1:** 5.8 ± NR **Group 2:** 13.8 ± NR **p value:** NR	
			IIEF-5 at 6 months	**Group1:** 19.0 ± 5.2 **Group 2:** 21.0 ± 6.8 **p value:** Not signif. (calculated by NCGC as t test with equal variances using ITT analysis)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean Prostate vol (TRUS) ml ± SD: 86.1 ± 8.8 **Mean PSA ng/ml ± SD:** 5.2 ± 4.5 **Qmax ml/s ± SD :** 8.6 ± 5.2 **PVR ml ± SD:** 183.0 ± 50.1 **Operating time (min ± SD):** 87 ± 18.3 **Mean catheterisation time (days):** 1.7 ± 0.8 **Mean length of stay (days):** 2.0 ± 0.7 **Drop outs:** NR **<u>Group 2 - TURP</u>** **N:** 37 **Mean age ± SD (yrs):** 68.3 ± 6.7 (range 58-76) **IPSS Score:** 20.2 ± 6.8 **IIEF-5:** 20.1 ± 5.5 **Mean Prostate vol (TRUS) ml ± SD:** 88.0 ± 9.2 **Mean PSA ng/ml ± SD:** 4.7 ± 3.8 **Qmax ml/s ± SD :** 9.2 ± 5.6 **PVR ml ± SD:** 176.9 ± 45.3 **Operating time (min ± SD):** 51 ± 17.2 **Mean catheterisation time (days):** 3.9 ± 1.2 **Mean length of stay (days):** 4.8 ± 1.2 **Drop outs:** NR	(consultant or experienced SpR) **Examination methods:** Patients followed at 3 and 6 months. All patients were assessed preoperatively and at follow ups for IPSS score, International Index of Erectile Dysfunction (IIEF-5), PSA, Qmax, PVR. In addition, postoperatively, data on length of stay, operating time, catheter removal time, and complications were collected.	**Change in IIEF-5 from baseline at 6 months**	**Group1:** 0.9 ± NR **Group 2:** -0.9 ± NR (IIEF-5 increased) **p value:** NR	
			flow rate (Qmax) at 6 months	**Group1:** 14.1 ± 8.7 **Group 2:** 21.3 ± 12.8 **p value:** 0.002 (calculated by NCGC as t test with unequal variances using ITT analysis)	
			Change in flow rate (Qmax) from baseline at 3 months	**Group1:** 4.7 ± NR **Group 2:** 11.5 ± NR **p value:** NR	
			Early post-op complications: patients requiring transfusion (follow up period up to 6 months)	**Group1:** 0/39 * **Group 2:** 3/37 * **p value:** Not signif (calculated by NCGC Fishers exact test)	
			Early post-op complication: urinary retention (follow up period up to 6 months)	**Group1:** 6/39 * **Group 2:** 1/37 * **p value:** Not signif (calculated by NCGC Fishers exact test)	
			Early post-op complications: urinary tract infection (follow up period up to 6 months)	**Group1:** 6/39 * **Group 2:** 5/37 * **p value:** Not signif (calculated by NCGC Fishers exact test)	
			Early post-op complications: urethral stricture (follow up period up to 6 months)	**Group1:** 2/39 * **Group 2:** 3/37 * **p value:** Not signif (calculated by NCGC Fishers exact test)	
			Early post-op complications: incontinence (follow up period up to 6 months)	**Group1:** 0/72 ** **Group 2:** 1/76 ** **p value:** Not signif. (calculated by NCGC Fishers exact test)	
			Reoperation rate (follow up period up to 6 months)	**Group1:** 7/39 * **Group 2:** 0/37 * **p value:** 0.01 (calculated by NCGC Fishers exact test)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Keoghane et al., 2000[142,144] & Keoghane et al., 1996[140,141,143] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 5 years	**Patient group:** Patients referred to hospital requiring surgery for BPE **Setting:** single centre, UK **Inclusion Criteria:** NR **Exclusion Criteria:** • Previous surgery or instrumentation for BPE • Prostate malignancy • Insufficient knowledge of English to answer questionnaire • Refusal of consent **<u>All patients</u>** **N:** 148 **Drop outs:** *at 5 years 63/148 (43%): 17 (7 laser and 10 TURP) had died., 8 unable to respond to questionnaires through disease and 38 lost to follow up. **<u>Group 1 - Laser</u>** **N:** 72 **Mean age ± SD (yrs):** 69 ± 8 (range 51-95) **Drop outs:** * **AUA 7 Score:** 19.9 ± 7.7 (n=54) **Bother score:** 5.8 ± 3.0 (n=59)	**Group 1** Vaporisation using MD60 Nd:YAG (Selected Laser Technologies) with 600 µm fibre incorporating sapphire-tipped probe. Irrigation using saline. **Group 2** TURP in standard manner using Storz equipment and irrigation with glycine **All patients:** Oral ciprofloxacin prophylaxis before surgery. After treatment 22F 3-way catheter inserted and continuous irrigation commenced. Catheter removed when clinically indicated **Intervention performed by:** 5 surgeons (consultant or experienced SpR) **Examination methods:** Patients followed at 4 weeks, 3, 12, 24, 36 months to 5 years	**AUA 7 symptom score from baseline at 3 months**	**Group1:** 9.6 ± 7.5 (n=55) **Group 2:** 6.5 ± 5.1 (n=62) **p value:** 0.03	**Funding:** Oxford Regional Health Authority **Limitations:** **Patient numbers for primary and secondary outcomes and complications were unclear so ITT analysis used. **Notes:** Randomisation by random number tables and allocation concealment through sealed envelopes although opacity was not reported. Patients and investigators were masked to treatment allocation Change from baseline at 5 years were reported for AUA score but SDs were not reported.
			Change in AUA 7 symptom score from baseline at 3 months	**Group1:** 10.1 ± 9.7 (n=47) **Group 2:** 13.6 ± 6.9 (n=54) **p value:** NS	
			AUA 7 symptom score from baseline at 12 months	**Group1:** 8.7 ± 6.5 (n=53) **Group 2:** 5.8 ± 5.4 (n=60) **p value:** 0.006	
			Change in AUA 7 symptom score from baseline at 12 months	**Group1:** 10.9 ± 8.4 (n=44) **Group 2:** 13.3 ± 7.8 (n=53) **p value:** not signif. (NCGC t-test)	
			AUA 7 symptom score from baseline at 2 years	**Group1:** 7.8 ± 6.6 (n=45) **Group 2:** 5.7 ± 6.0 (n=52) **p value:** 0.018	
			Change in AUA 7 symptom score from baseline at 2 years	**Group1:** 11.7 ± 9.7 (n=35) **Group 2:** 13.7 ± 7.7 (n=47) **p value:** not signif. (NCGC t-test)	
			AUA 7 symptom score from baseline at 3 years	**Group1:** 8.9 ± 6.6 (n=37) **Group 2:** 6.5 ± 6.5 (n=41) **p value:** 0.001	
			Change in AUA 7 symptom score from baseline at 3 years	**Group1:** 11.0 ± 9.7 (n=37) **Group 2:** 12.9 ± 7.9 (n=41) **p value:** not signif. (NCGC t-test)	
			Change in flow rate (Qmax) from baseline at 12 months	**Group1:** 6.2 ± 15.0 (n=32) **Group 2:** 9.4 ± 12.5 (n=37) **p value:** not signif. (NCGC t-test)	
			Change in flow rate (Qmax) from baseline at 24 months	**Group1:** 5.2 ± 7.0 (n=18) **Group 2:** 4.9 ± 7.5 (n=26) **p value:** not signif. (NCGC t-test)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean SF36 (physical) ±SD: 43.69 ±12.58 (n=51) **Mean SF36 (mental) ±SD:** 47.07 ±11.2 (n=51) **Erectile dysfunction (difficulty maintaining erection):** 9/38 (24%) **Mean Prostate volume ml ± SD:** 54.2 ± 26.3 (n=44) **Qmax:** 11.8 ± 4.5 (n=48) **PVR:** NR **Median catheterisation time (days):** 1 (0-9) **Median length of stay (days)**: 3 (1-10) **<u>Group 2 - TURP</u>** **N:** 76 **Mean age ± SD (yrs)**: 70 ± 8 (range 47-84) **Drop outs:** * **AUA 7 Score:** 19.4 ± 6.5 (n=63) **Bother score**: 5.9 ± 2.3 (n=68) **Mean SF36 (physical) ±SD:** 44.66 ±12.12 (n=57) **Mean SF36 (mental) ±SD**: 47.75 ±10.47 (n=57) **Erectile dysfunction (difficulty maintaining erection):** 20/50 (40%) **Mean Prostate volume ml ± SD:** 51.9 ± 24.1 (n=48) **Qmax:** 11.4 ± 5.0 (n=54) **PVR:** NR **Median catheterisation time**	Patients received cysto-urethroscopy after randomisation to assess length of urethra and bladder pathology and residual volume. AUA score assessed preoperatively and at 4 weeks. Qmax was a secondary outcome measurement methods not reported.	**Change in flow rate (Qmax) from baseline at 24 months**	**Group1:** 1.8 ± 6.2 (n=24) **Group 2:** 2.1 ± 6.9 (n=24) **p value:** not signif. (NCGC t-test)	
			Erectile Dysfunction (difficulty maintaining erection) at 3 months	**Group1:** 7/38 **Group 2:** 12/50 **p value:** Not signif. (calculated by NCGC Chi squared test)	
			Bother score at 3 months	**Group1:** 2.9 ± 3.0 (n=54) **Group 2:** 2.4 ± 3.0 (n=64) **p value:** Not Signif.	
			Early post-op complications: Failure to void as inpatient following catheter removal (follow up period first 3 months)	**Group1:** 17/72 ** **Group 2:** 8/76 ** **p value:** Not signif. (calculated by NCGC Chi squared test)	
			Early post-op complications: patients requiring transfusion (follow up period first 3 months)	**Group1:** 0/72 ** **Group 2:** 13/76 ** **p value:** 0.0001 (calculated by NCGC Fishers exact test)	
			Late post-op complications: urinary tract infection (follow up period first 3 months)	**Group1:** 1/72 ** **Group 2:** 3/76 ** **p value:** Not signif. (calculated by NCGC Fishers exact test)	
			Late post-op complications: urethral stricture ((follow up period first 3 months)	**Group1:** 0/72 ** **Group 2:** 3/76 ** **p value:** Not signif. (calculated by NCGC Fishers exact test)	
			Late post-op complications: incontinence (follow up period first 3 months)	**Group1:** 0/72 ** **Group 2:** 1/76 ** **p value:** Not signif. (calculated by NCGC Fishers exact test)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	(days): 2 (1-20) **Median length of stay (days):** 4 (1-8)		**Reoperation rate at 5 years**	**Group1:** 13/72 **Group 2:** 11/76 **p value:** Not signif. (calculated by NCGC Fishers exact test)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Mottet et al., 1999[206] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Patients in urology clinics **Setting:** multi-centre, Nimes & Paris, France **Inclusion Criteria:** • Qmax <12ml/s • age >45 years • PVR <250ml • AUA> 13 • PSA < 10ng/ml • informed consent **Exclusion Criteria:** • history of prostatic or urethral surgery • prostate >60g • diabetes • bladder or neurogenic disease **<u>All patients</u>** **N:** 36 **Age:** 66 (range 50-77) **Drop outs:** 17 (at 12 mths) **<u>Group 1 - Laser</u>** **N:** 23 **Mean age (yrs):** 67 **Drop outs:** 11 without outcome data at 12 months	**Group 1** Dual length VersaPulse Select Laser at 60W-80W of holmium:YAG energy in pulsed mode through 550µm fibre or side-firing fibre in 24F cystoscope. 6 patients also received additional Nd:YAG vaporisation. 20 or 24F Foley placed without irrigation and removed the next day. **Group 2** TURP in standard manner under spinal anaesthesia with glycine irrigation followed by postoperative saline irrigation until urine was clear. Catheter was then removed. Intervention performed by same 2 experienced surgeons **Examination methods:** Patients followed at 1, 3, 6, 12 months	**Mean IPSS at 3 months**	**Group1:** 7.7 ± NR (n=22) **Group 2:** 7.5 ± NR (n=12) **p value** = NR	**Funding:** NR **Limitations:** • Outcomes were reported without standard deviations • Outcome assessment was not masked. • Randomisation method not reported. • Allocation concealment not reported **Additional outcomes:** Madsen score at follow up **Notes:** Randomisation on 2:1 model
			Mean IPSS at 6 months	**Group1:** 6.2 ± NR (n=20) **Group 2:** 7.7 ± NR (n=11) **p value** = NR	
			Mean IPSS at 12 months	**Group1:** 5.9 ± NR (n=12) **Group 2:** 7.5 ± NR (n=7) **p value** = NR	
			Mean Qmax at 3 months	**Group1:** 22.8 ± NR (n=22) **Group 2:** 18.3 ± NR (n=12) **p value** = NR	
			Mean Qmax at 6 months	**Group1:** 17.5 ± NR (n=20) **Group 2:** 16.6 ± NR (n=11) **p value** = NR	
			Mean Qmax at 12 months	**Group1:** 19.3 ± NR (n=12) **Group 2:** 17.6 ± NR (n=7) **p value** = NR	
			Early Post-op complications number of patients with blood transfusion	**Group1:** 0/23 **Group 2:** 0/13	
			Post-op complications number of patients incontinence at 6 months	**Group1:** 1/23 **Group 2:** 0/13	
			Reoperation rate	**Group1:** 1/23 **Group 2:** 2/13	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	IPSS: 20 **Madsen score:** 15 **Erectile dysfunction:** NR **Prostate volume (TRUS) ml:** 39 **Qmax ml/s:** 8 **Operation time mins:** 75 **Mean catheterisation time (days):** 1.6 ± NR **Mean length of stay (days):** 2.2 ± NR **<u>Group 2 - TURP</u>** **N:** 13 **Mean age (yrs):** 64 **Drop outs:** 6 without outcome data at 12 months **IPSS:** 24 **Madsen score:** 17 **Erectile dysfunction:** NR **Prostate volume (TRUS) ml:** 34 **Qmax ml/s:** 8 **Operation time mins:** 40 **Mean catheterisation time (days):** 3.1 ± NR **Mean length of stay (days):** 2.1 ± NR	During preoperative assessment and follow up DRE, Qmax, IPSS and Madsen score, PSA and TRUS all completed. Patients were also questioned about potency and ejaculation status. Length of stay, catheterisation time, reoperation rate also recorded			

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Shingleton et al., 2002[275] & Shingleton et al., 1999[277] & **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 3 years	**Patient group:** Patients with failed α-blockers therapy for voiding symptoms **Setting:** single-centre, Istanbul, Turkey **Inclusion Criteria:** • peak urine flow rate <15ml/s • age >45 years • failure of • medical therapy (α-blockers) • able to undergo regional/general anaesthesia • medical therapy discontinued 1 month before surgery **Exclusion Criteria:** • Prostate cancer **<u>All patients</u>** **N:** 100 **Age:** 66 (range 50-77) **Drop outs:** **<u>Group 1 - Laser</u>** **N:** 50 **Mean age ± SD (yrs):** 68.2± 7.9 **Ethnicity:** 38/50 (76%) white. **Mean AUA score ± SD:** 22.5 ± 6.0 **Erectile dysfunction (full):** 22/50 (44%) **Prostate volume (TRUS) ml:** 32.2 ± 21.4 **Mean PSA ng/ml ± SD:** 2.7 ± 2.3	**Group 1** Laserscope KTP/Nd:YAG with Laserscope ADD or ADD/stat fibre. 36W was used first for vaporisation then 60W for further vaporisation and coagulation. A catheter was placed for between 1-5 days depending on size of prostate and energy used **Group 2** TURP in standard manner using Circon/ACMI continuous flow resectoscope with mannitol solution. Laser intervention performed by one surgeon and TURPs by senior residents under same surgeon. **Examination methods:** All patients had AUA symptom score, serum PSA, TRUS, pressure flow urodynamics preoperatively and were followed up with AUA score, PSA and	**AUA symptom score at 3 months**	**Group 1:** 7.0 ± NR (n=48) **Group 2:** 4.0 ± NR (n=48) **p value** = 0.01	**Funding:** In part by Laserscope **Limitations:** • Reasons for drop out were not reported and there were more patients at 3 years than 2 years • Outcome assessment was not masked. • Allocation concealment not reported • Changes from baseline were not reported **Additional outcomes:** Prostate volume at follow up, serum PSA at follow up Other complications including retrograde ejaculation. **Notes:** Computer generated randomisation. *ITT analysis used for
			AUA symptom score at 6 months	**Group 1:** 7.0 ± NR (n=46) **Group 2:** 4.0 ± NR (n=48) **p value** = 0.01	
			AUA symptom score at 12 months	**Group 1:** 6.0 ± 6.0 (n=40) **Group 2:** 3.8 ± 4.1 (n=33) p value = 0.03 (calculated by NCGC using t test with equal variances *	
			AUA symptom score at 18 - 24 months	**Group 1:** 5.9 ± 5.7 (n=23) **Group 2:** 4.6 ± 4.2 (n=19) p value = 0.19 (calculated by NCGC using t test with equal variances *	
			AUA symptom score at 36 months	**Group 1:** 9.9 ± 6.7 (n=29) **Group 2:** 7.7 ± 5.6 (n=33) p value = 0.07 (calculated by NCGC using t test with equal variances *	
			Qmax at 3 months	**Group 1:** 15.0 ± 5.7 (n=48) **Group 2:** 16.0 ± 8.0 (n=48) **p value** = 0.60	
			Qmax at 6 months	**Group 1:** 15.8 ± 6.9 (n=46) **Group 2:** 16.3 ± 6.4 (n=48) **p value** = 0.77	
			Qmax at 12 months	**Group 1:** 14.6 ± 5.9 (n=40) **Group 2:** 16.2 ± 7.2 (n=33) p value = 0.23 (calculated by NCGC using t test with equal variances *	
			Qmax at 18-24 months	**Group 1:** 14.9 ± 5.4 (n=23) **Group 2:** 14.3 ± 6.3 (n=19) p value = 0.6 (calculated by NCGC using t test with equal variances*	
			Qmax at 36 months	**Group 1:** 12.3 ± 5.3. (n=29) **Group 2:** 12.8 ± 5.6 (n=33) p value = 0.64 (calculated by NCGC using t test with equal variances *	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean Qmax ± SD (ml/s): 8.2± 3.2 **Operation time mins:** 43 (15-70) **Drop outs:** **Mean catheterisation time (days):** NR **Mean length of stay (days):** NR **<u>Group 2 - TURP</u>** **N:** 50 **Mean age ± SD (yrs):** 67.4± 7.3 **Ethnicity:** 34/50 (68%) white. **Mean AUA score ± SD:** 21.2 ± 6.1 **Erectile dysfunction (full):** 21/50 (42%) **Prostate volume (TRUS) ml:** 29.6 ± 15.4 **Mean PSA ng/ml ± SD:** 3.2 ± 2.2 **Mean Qmax ± SD (ml/s):** 7.3± 3.7 **Operation time mins:** 56 (45-90) **Drop outs:** **Mean catheterisation time (days):** NR **Mean length of stay (days):** NR	uroflowmetry measurements at 1, 3, 6, 12, 18, 24, 36, 48, 60 and 72 months	**Post-op complications number of patients with urethral stricture (follow up period 12 months)***	**Group1:** 1/50 **Group 2:** 1/50 **p value:** NR	statistical analysis
			Post-op complications number of patients incontinence (follow up period 12 months)*	**Group1:** 1/50 **Group 2:** 1/50 **p value:** NR	
			Post-op complications number of patients with urinary retention (follow up period 12 months)	**Group1:** 3/50 **Group 2:** 1/50 **p value:** NR	

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Study Details	Patients	Interventions	Outcome measures	Effect size	Comments
Suvakovic & Hindmarsh,1996[290] **Study design:** RCT, open label **Evidence level:** 1+ **Duration of follow-up:** 1 year	**Patient group:** Consecutive patients with prostatic symptoms **Setting:** Urology department, South Cleveland University, UK **Inclusion Criteria:** • Qmax ≤15mL/s for a voided volume of ≥150 mL • Age • Significant voiding symptoms (AUA score >15) • PSA level <2.5 ng/mL • Prostate volume <40g (assessed by TRUS, DRE and cystoscopy) • Length of the prostatic urethra >4 cm **Exclusion Criteria:** • Malignancy **<u>All patients</u>** **N:** 40 **<u>Group 1 -</u> CLAP- contact laser alone** **N:** 10 **Age (mean):** 62.6(5.8) **IPSS:** 18 (6.0) **Qmax** ml/s: 12.2 (3.8) **Residual Vol** mL: 139.6(103) **Prostate size** (by TRUS), g: 24(5.8)	**Group 1 : CLAP-contact laser alone** Nd: YAG laser applied at 40W for vaporising and coagulating the prostate with a minimum depth of penetration. a 16 F two –way catheter was inserted into the bladder and removed after 24 h. **Group 2 : TURP Standard resection** using a 26 F continuous irrigating resectoscope. A 22 F three-way urethral catheter was inserted into the bladder and irrigation was continued up to 24 h. The catheter was removed after 48 h and the patients discharged home 3-4 days after the procedure. All patients received preoperative oral antibiotics and controlled for more than 5 days post-operatively	**IPSS symptom score, mean ± SD at 3 months**	**Group 1:** 9.7 ± 2.6, n=10 **Group 2:** 12.8 ± 5.9, n=10 **p value:** 0.15 (calculated by NCGC using t test with unequal variances using ITT analysis)	**Funding:** NR **Limitations:** • Small sample size, n of 10 in each arm • Unclear which statistical test was used for data – discrepancies in the stat sig reported for AUA score for 3 months and calculated by NCGC team. • Randomisation method and allocation concealment not reported. • Masking of outcome assessment not reported. • Number of participants followed up at 12 months not reported. • Complications were poorly reported **Notes:** None.
			IPSS symptom score, mean ± SD at 6 months	**Group 1:** 8.7 ± 5.4, n=9 **Group 2:** 8.5 ± 3.0, n=10 **p value:** 0.91 (calculated by NCGC using t test with unequal variances using ITT analysis)	
			IPSS symptom score, mean ± SD at 12 months *Values for 12 months follow up reported in paper, but n was not reported	**Group 1:** 8.7 ± 4.9, * **Group 2:** 7.2 ± 6.1, * **p value:** 0.55 (calculated by NCGC using t test with equal variances using ITT analysis)	
			Qmax mean ± SD at 3 months	**Group 1:** 15.6 ± 13.5, n=10 **Group 2:** 17.8 ± 3.8, n=10 **p value:** NR	
			Qmax mean ± SD at 6 months	**Group 1:** 18.7 ± 7.5, n=9 **Group 2:** 19.0 ± 0.8, n=10 **p value:** NR	
			Qmax mean ± SD at 12 months *Values for 12 months follow up reported in paper, but n was not reported	**Group 1:** 23.5 ± 5.9, * **Group 2:** 15.2 ± 2.7, * **p value:** NR	
			Post-op complications: Catheter duration, mean, hours (range or standard deviations NR)	**Group 1:** 24, n=10 **Group 2:** 48, n=10 **p value:** NR	
			Post-op complications	**Group 1:** 30, n=10	

Study Details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean catheterisation time (days): 1 ± NR **Mean length of stay (days):** 1.3 ± NR **<u>Group 2</u> - TURP** **Standard resection** **N:** 10 **Age (mean):** 66.1(5.1) **IPSS:** 18.8 (4.5) **Qmax** ml/s: 11.1(6.4) **Residual Vol** mL: 161.8(104) **Prostate size** (by TRUS), g: 22(5) **Mean catheterisation time (days):** 2 ± NR **Mean length of stay (days):** 3.5 ± NR	**Examination methods:** At 3, 6 12 months AUA score, PSA, flow rate, PVR measured and TRUS performed	**Length of hospitalisation, (hours)**	**Group 2:** 84, n=10	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Tuhkanen et al., 2001[300] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 24 months	**Patient group:** Patients with BPH and BOO that were referred to the outpatient clinic at Kuopio university hospital from January 1995 to November 1997. **Setting:** Urology department, Finland **Inclusion Criteria:** • Obstructed if min. voiding pressure > 40cm water • prostate volume 40-100ml (TRUS) **Exclusion Criteria:** • prostate cancer or surgery • urinary retention **All patients** **N:** 46 **Drop outs:** 9 (20%) **Group 1** **N:** 21 **Age (mean):** 67 (55-78) **Mean (range) symptom score** (DanPSS-1): 18.6 (5-40) **Prostate volume:** 55 (42-83) **Qmax ml/s (range):** 8.5 (2.3-17.2) **PVR ml (range):** 125 (0-350) **Drop outs:** 4 (1=died cardiac infarct 5 months post-operatively; 3=underwent TURP - **Mean prostate size:** 55 (42-83)ml **Mean catheterisation time (days):** NR	**Group 1: laser (hybrid)** Initial noncontact Nd:YAG **coagulation** 40W power asset for 90 sec burn times. Followed by a contact Nd:YAG **vaporisation** to open prostatic urethra. Vaporised at 40W. Urethral catheter was inserted for one day. Postoperatively the suprapubic catheter removed when the patient could urinate and residual urine was less than 150ml. Spinal anaesthesia. **Group 2: TURP** 28 F Storz resectoscope without application of the suprapubic catheter. Spinal anaesthesia. **Examination methods:** Patients reviewed at 3, 6, 12, 24 mths DanPSS-1, urinalysis, serum creatinine, serum PSA, Qmax, PVR, DRE were recorded at each visit. TRUS was performed for suspicious cancer cases	**Mean (range) symptom score** (DanPSS-1)	At 3 months **Group1 (n=21):** 10.0 (0-49) **Group 2 (n=22):** 5.6 (0-27) At 6 months **Group1 (n=19):** 5.5 (0-21) **Group 2 (n=21):** 4.7 (0-22) At 24 months **Group1 (n=17):** 7.2 (0-25) **Group 2 (n=20):** 3.4 (0-21)	**Funding:** NR **Limitations:** • Randomisation method, allocation concealment and masking of outcome assessment were not reported • uses DanPSS-1 score • standard deviations not reported **Additional outcomes:** Average urinary flow rate reported. **Notes:** Linked to Tuhkanen 1999a[301]
			Qmax mL/sec (range)	At 3 months **Group1:** 13.7 (4.9-27.5) **Group 2:** 21.0 (3.2-41.9) At 6 months **Group1:** 14.4 (7.9-20.7) **Group 2:** 19.6 (4.1-43.2) At 24 months **Group1:** **Group 2:** 20.6 (9.5-38.9)	
			Residual urinary volume, ml	At 3 months **Group1:** 77 (0-162) **Group 2:** 54 (0-210) At 6 months **Group1:** 69 (0-160) **Group 2:** 45 (0-177) At 24 months **Group1:** 114 (28-202) **Group 2:** 58 (0-166)	
			Reoperation rate (24 months follow-up):	**Group1:** 3/21 **Group 2:** 2/25	
			Retrograde ejaculation at 3 months	**Group1:** 3/16 **Group 2:** 12/14	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean length of stay (days): 4.0 (2-9) **Group 2** - **N:** 25 **Age (mean):** 67 (46-77) **Mean (range) symptom score** (DanPSS-1): 22.8 (5-69) **Prostate volume:** 55 (40-95) **Qmax ml/s (range):** 7.2 (3.7-14.8) **PVR ml (range):** 138 (0-450) **Drop outs:** 5 (2=prostatic adenocarcinoma at initial operation, 1=internal urethrotomy for distal urethral stricture at 5 months; 1=died unknown causes at 13 months; 1=re-TURP due to overflow incontinence) **Mean prostate size:** 55 (40-94)ml **Mean catheterisation time (days):** NR **Mean length of stay (days)**: 3.5 (1-8)		**Complications**	Transfusion: **Group1:** 1/21 **Group 2:** 2/25 Mortality **Group1:** 1(myocardial infarction at 5 m) **Group 2:** 1 (unknown at 13 m) Stricture (internal urethrotomy treatment) **Group 1:** 0/21 **Group 2:** 1/25 Incontinence (overflow at 13m) **Group 1:** 0/21 **Group 2:** 1/24 Urinary retention (at 17 months and underwent TURP) **Group 1:** 2/21 **Group 2:** 0/25	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Tuhkanen et al., 2003[299] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 4 years	**Patient group:** LUTS with confirmed BOO recruited from September 1994 – January 1998. Prostate volume less than 40ml. **Setting:** Finland **Inclusion Criteria:** • minimum volume of ≥120ml • minimum voiding detrusor pressure>40 cm water **Exclusion Criteria:** • prostate cancer, prostate surgery or history of TUIP or TURP • prostate size>40ml • urethral structure • neurogenic bladder dysfunction • residual volume>350ml **<u>All patients</u>** **N:** 52 **Drop outs:** 10 **<u>Group 1</u>** **N:** 26 **Age (mean):** 68 (56-82) **Median (range) DanPSS-1 symptom score:** 18 (5-54) **Qmax (mean ± SD) ml/s:** 9.0 ± 3.8 **Mean prostate volume (range) ml:** 30 (15-37) **Median PVR ml (range):** 87 (0-331) **Mean catheterisation time (days):** NR **Mean length of stay (days):** 3.4 (2-7) **Drop outs:** 4 (3 died of BPH-unrelated	**Group 1: Contact laser vaporisation** Porsatic urethra vaporised with an Nd:YAG laser at a power setting 40W. Urethral catheter inserted for one day. Spinal anaesthesia. Ciproflaving eve and morning of operation. **Group 2: TURP** Ciproflaving eve and morning of operation. Spinal anaesthesia. **Examination methods:** Patients reviewed at 3, 6, 12, 24 and 48 mths DanPSS-1, urinalysis, serum creatinine, serum PSA, Qmax, PVR, DRE were recorded at each visit. Urodynamics and TRUS were performed at 6 months and 4 years	**Median (range) DanPSS-1 symptom score**	<u>At 3 months: mean</u> **Group1 (n=25):** 6 (7) **Group 2 (n=25):** 5 (6) <u>At 6 months: mean</u> **Group1:** 6 (9) **Group 2:** 5 (7) <u>At 48 months</u> **Group1: (n=22):** 5 (0-34) **Group 2: (n=20):** 4 (0-18)	**Funding:** Financially supported by University of Kuopio. **Limitations:** • Randomisation method, allocation concealment and masking of outcome assessment were not reported • uses DanPSS-1 score • Patient numbers not clear at 6 months • 2 patients in TURP group refused follow-up due to good subjective outcomes. **Notes:** Median values reported at baseline and 48 months in Tuhkanen 2003. Earlier study (Tuhkanen 1999) reports mean (SD) for baseline, 3 months and 6 months.
			Mean (SD) Qmax, mL/s	<u>At 3 months</u> **Group1:** 15.0 (5.2) **Group 2:** 19.0 (9) <u>At 6 months</u> **Group1:** 17.9 (7.1) **Group 2:** 21.1 (9.7) <u>At 48 months – median (range)</u> **Group1:** 14.3 (10.1-33.6) **Group 2:** 16.1 (7.7-39.6)	
			PVR, ml	<u>At 3 months – mean (SD)</u> **Group1:** 44 (39) **Group 2:** 36 (39) <u>At 6 months - mean (SD)</u> **Group1:** 50 (64) **Group 2:** 32 (37) <u>At 48 months – median (range)</u> **Group1:** 60 (0-380) **Group 2:** 10 (0-90) P<0.05	
			UTI (epididymitis) ejaculation at 6 mths	**Group 1**: 0/26 **Group 2:** 1/26	
			Retrograde ejaculation at 6 mths	**Group 1**: 1/16 (6%) **Group 2**: 13/16 (81%)	
			Mortality at 4 years	**Group 1**:3/26 **Group 2:** 1/26	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	causes and one underwent TURP at 2 years postoperatively due to gross haematuria, residual adenoma tissue and bladder stones) **<u>Group 2</u>** - **N:** 26 **Age (mean):** 67 (55-77) **Median (range) DanPSS-1 symptom score:** 18 (4-46) **Qmax (mean ± SD) ml/s:** 8.2 ± 3.2 **Mean prostate volume (range) ml:** 28 (15-38) **Median PVR ml (range):** 83 (8-350) **Mean catheterisation time (days):** NR **Mean length of stay (days):** 2.9 (2-5) **Drop outs:** 6 (1 died of BPH-unrelated causes, 2 diagnosed with prostatic carcinoma, one patient with bladder neck stenosis and underwent a re-TURP, 2 refused reviews due to good subjective outcomes).		**Reoperation rate at 4 years**	**Group 1:**1/26 **Group 2:** 1/26	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Van Melick et al., 2003[309] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** Up to 7 years	**Patient group:** men over 45 years with LTUS associated with BPH that were recruited from their clinic from1996 to 2001 **Setting:** Netherlands **Inclusion Criteria:** patient with lower urinary tract symptoms suggestive of BPH; met ISC criteria for BPH, Schafer obstruction score≥ 2, prostate size between 20-65ml. **Exclusion Criteria:** age ≤45 yrs **<u>All patients</u>** **N:** 95 **<u>Group 1</u>** **N:** 45 **Age (mean) ± SD:** 67 ± 9 **IPSS (mean) ± SD:** 18.9 ± 6.8 **Mean prostate size, ml:** 37 ± 11 **Mean (SD) Global quality of life score:** 3.7 ± 1.6 **Mean Qmax ± SD ml/s:** 12 ± 4 Follow-up 1to 4 years = 15 Follow-up 4 to 7 years=15 ± 0.4 **Mean length of stay (days):** 3.8 ± 1.3 **Mean catheterisation time (days):** 2.1 ± 0.9 **Drop outs:** 8 at one year post-operatively (procedure during surgery changed for medical reasons=3, equipment failure resulting in TURP)=2, reoperation –TURP=1, reoperation – due to stricture =2)	**Group 1: Laser vaporisation** Transurethral catheter post-operation SLT Nd:Yag (MTRL sapphire tip) through Morgenstern scope irrigated with isotonic salt solution. Pre-procedural antibiotics and transurethral catheter postoperatively. **Group 2: TURP** Stabdard 24FR resectoscope using glycine for irrigation. Suprapubic catheter if required peri-operatively. Pre-procedural antibiotics and transurethral catheter postoperatively. **Examination methods:** Urodynamic studies (cystometry and pressure flow) at baseline and 1-6 weeks, 3, 6, 12 months after treatment	**Mean (± SD) symptom score (IPSS) at 6 months**	**Group1 (n=33):** 5.9 ± 5.5 **Group 2 (n=37):** 3.2 ± 2.7	**Funding:** NR. **Limitations:** • Randomisation method was not described and masking of outcome assessment was not reported. • High attrition rate at 1-7 years and 4-7 years **Additional outcomes:** Frequency during day, frequency during night, symptom problem index and BPH impact index. Uroflowmetry also reported. **Notes:** Links with Van Melick 2002 (up to 6 months), Van Melick 2003 Follow up time varied individually as all patients were analysed within a 2 month period. Depending on the individual follow-up time, patient divided into two groups: those with a follow-up time between 1 and 4 years and those with follow up time between 4 and 7 years.
			Mean (± SD) symptom score (IPSS) at 12 months	**Group1 (n=37):** 3.6 ± 3.4 **Group 2 (n=41):** 4.1 ± 4.8	
			Mean (± SD) symptom score (IPSS) at 1-4 years	**Group1 (n=10):** 9.3 ± 5.2 **Group 2 (n=15):** 5.8 ± 7.5	
			Mean (± SD) symptom score (IPSS) at 4-7 years	**Group1 (n=17):** 8.3 ± 6.4 **Group 2 (n=15):** 7.3 ± 7.1	
			Mean (SD) Global quality of life score at 6 months	**Group1:** 0.8 ± 1.0 **Group 2:** 0.5 ± 0.5	
			Mean (SD) Global quality of life score at 12 months	**Group1:** 0.6 ± 0.9 **Group 2:** 0.6 ± 0.8	
			Mean (SD) Global quality of life score at 1-4 years	**Group1:** 2.0 ± 1.0 **Group 2:** 1.1 ± 1.2	
			Mean (SD) Global quality of life score at 4-7 years	**Group1:**1.4 ± 1.2 **Group 2:** 1.3 ± 1.3	
			Qmax mean ± SD at 6 months	**Group1:** 25 ± 9 **Group 2:** 26 ± 6	
			Qmax mean ± SD at 12 months	**Group1:** 27 ± 12 **Group 2:** 23 ± 10	
			Qmax mean ± SD at 1-4 years	**Group1:** 19 ± 6 **Group 2:** 20 ± 5	
			Qmax mean ± SD at 4-7 years	**Group1:** 19 ± 9 **Group 2:** 17 ± 8	
			Post-op complications: urethral stricture (within 12 mths)	**Group1:** 2/45 **Group 2:** 2/50	
			Post-op complications: mortality (within 12 mths)	**Group 1:** 0/45 **Group 2:** 2/50	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2 **N:** 50 **Age (mean) ± SD:** 66 ± 8 **IPSS (mean) ± SD:** 16.8 ± 6.0 **Mean prostate size, ml ± SD**: 37 ± 11 **Mean ± SD Global quality of life score:** 3.8 ± 1.5 **Mean Qmax ± SD ml/s:** 11 ± 4 Follow-up 1to 4 years = 10 Follow-up 4 to 7 years=17 **Mean length of stay (days)**: 3.9 ± 0.9 **Mean catheterisation time (days):** 2.8 ± 3.1 **Drop outs:** 9 at one year post-operatively (surgery cancelled=1, mortality=2, morbidity=2, emigrated=1, reoperation (TURP) =2, reoperation (stricture)=1)		**Post-op complications: transfusion required (within 12 mths)**	**Group 1:** 0/45 **Group 2:** 1/50	
			Post-op complications: urinary retention (within 12 mths)	**Group 1:** 5/45 **Group 2:** 0/50	
			Reoperation rate (TURP) within 12 mths	**Group 1:** 1/45 **Group 2:** 2/50	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Zorn et al., 1999[332] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** military beneficiaries with symptomatic BPH – recruited from June 1995 to June 1996 **Setting:** Walter Reed Army Medical Centre and Madigan Army Medical Centre, US **Inclusion Criteria:** • symptomatic BPH • Qmax<15ml/s • Age > 50 • AUA score 13 or more • PVR>125ml • Prostate volume <45g **Exclusion Criteria:** • previous surgical therapy for BPH • known prostate, bladder, urethral or neurological conditions that could affect the bladder **<u>All patients</u>** **N:** 33 **<u>Group 1</u>** **N:** 21 **Age (mean):** 70.6 **Drop outs:** 3 **IPSS:** 24.0 **Prostate size:** 29.9 **Qmax (mean) ml:** 8.7 **AUA symptom score (mean):** 24.0 **Mean length of stay (days):** 1.2 ± NR **Mean catheterisation time (days):** 1.1 ± NR	**Group 1: Laser vaporisation** contact laser vaporisation of the prostate (CLVP) Nd:YAG laser. Power (w): CLVP 50-60. Performed under general or regional anaesthesia **Group 2 : TURP** Performed under general or regional anaesthesia.	**AUA symptom score**	<u>At 1 month</u> **Group1:** 9.6 (n=20) **Group 2:** 11.0 (n=12) <u>At 6 months</u> **Group1:** 9.1 (n=19) **Group 2:** 8.2 (n=10) <u>At 12 months</u> **Group1:** 8.4 (n=18) **Group 2:** 4.7 (n=7)	**Funding:** NR **Limitations:** • Randomisation method, allocation concealment and masking of outcome assessment were not reported • Standard deviations were not reported. **Additional outcomes:** Results for 5 patients that had CHRP (see notes). **Notes:** There was another group of patients (n=5) with prostate volumes >45 mL that underwent coagulation and haemostatic resection of the prostate (CHRP). 2:1 randomisation method
			Qmax	<u>At 1 month</u> **Group1:** 19.3 (n=20) **Group 2:** 21.4 (n=12) <u>At 6 months</u> **Group1:** 20.0 (n=18) **Group 2:** 23.1 (n=10) <u>At 12 months</u> **Group1:** 20.0 (n=18) **Group 2:** 26.9 (n=6)	
			Transfusions	**Group 1:** 0/21 **Group 2:** 0/12	
			Re-catheterisation	**Group 1:** 3/21 (14.0%) **Group 2:** 3/12 (25.0%)	
			Urethral strictures	**Group 1:** 0/21 **Group 2:** 0/12	
			Reoperations:	**Group 1**: 0/21 **Group 2**: 0/12	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2 - **N:** 12 **Age (mean):** 69.0 **Drop outs:** 5 (1 diagnosed with prostate cancer and had radical prostatectomy so not included in baseline data) **IPSS:** 24.7 **Prostate size:** 33.9 **Qmax (mean) ml:** 9.0 **AUA symptom score (mean):** 24.7 **Mean length of stay (days):** 2.5 ± NR **Mean catheterisation time (days):** 1.7 ± NR				

Evidence Table 28: Laser vs. open prostatectomy

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Skolarikos et al., 2008[281] **Study design:** Randomised controlled trial **Setting:** Greece **Evidence level:** 1+ **Duration of follow-up:** 18 months	**Patient group:** Men recruited from March 2005 to April 2006. **Inclusion criteria:** Age > 50 years, LUTS due to BPH, prostate volume on TRUS >80cc, IPSS>12, medical therapy failure, no alpha blockers during the last month, no 5AR over the last 3 months, post void residual<150ml, peak urinary flow arte<12ml/sec. **Exclusion criteria:** neurogenic bladder, history of adenocarcinoma of the prostate, urethral stricture, previous prostatic, bladder neck or urethral surgery, no urethral catheter at baseline, history of bladder cancer, indwelling urethral catheter. **All patients** **N:** 125 **Drop outs:** NR **Group 1** **N:** 65 Median (25-75 centile) Age: 74 (67-80) **Group 2** **N:** 60 Median (25-75centile) Age:67.5 (65-74)	**Group 1: Laser** Photoselective vaporisation PVP) using high power potassium titanyl phosphate laser (KTP) PVP performed with an 80 watt KTP side-firing laser system. A flexible green light PV ADDStat fiber was used through a modified 23F continuous irrigation 12* Storz cystoscope. Isotonic saline used for irrigation. At end of procedure a 20F triple lumen catheter was inserted into the bladder for irrigation to start. **Group 2: Open prostatectomy (OP)** Transvesical approach used. At end of the procedure a 22F triple lumen catheter inserted into the bladder and irrigation was initiated. A suprapubic catheter was inserted whenever the surgeon thought extra irrigation needed.	**Median (25-75 centile) Symptom score, IPSS**	**Baseline** Group1: 20 (15-22.5) Group 2: 21 (16.2-23.7); p=0.399 **1 month** Group1: 12 (12-13.5) Group 2: 12 (10-16); p=0.019 **3 months** Group1: 10 (8-12 Group 2: 10 (7-12); p=0.743 **6 months** Group1: 9 (7-12) Group 2: 9 (7-12); p=0.224 **12 months** Group1: 9 (7-12) Group 2: 8 (7-12); p=0.128 **18 months** Group1: 10 (7-12) Group 2: 8.5 (7-12); p=0.063	**Funding:** NR **Limitations:** Patients significantly older at baseline in the laser group. Allocation concealment method unclear. **Additional outcomes:** 1, 3, 6, 12 month outcomes for prostate size, PSA, post void residual and IIEF scores. **Notes:** 5 laser patients the resectoscope was used at some 0oint of the operation to achieve hemostatis. When optimal view restored, the KTP laser reused to finish operation.
			Median (25-75 centile) IPSS quality of life question	**Baseline** Group1: 3 (2-4) Group 2: 3 (2.25-4) p=0.520 **1 month** Group1: 2 (1-2) Group 2: 2 (1-2) p=0.283 **3 months** Group1: 1 (1-2) Group 2: 2 (1-2) p=0.995 **6 months** Group1: 1 (1-2) Group 2: 1 (0.25-1) p=0.024 **12 months** Group1: 1 (1-2) Group 2: 1 (1-1) p=0.035 **18 months** Group1: 1 (1-2) Group 2: 1 (1-1) p=0.001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Median (25-75 centile) Qmax, ml/s	**Baseline** Group1: 8.6 (6.7-10.5) Group 2: 8 (5.8-10.2) p=0.283 **1 month** Group1: 13.4 (10.7-15) Group 2: 12.5 (10.7-15) p=0552 **3 months** Group1: 16 (14-18) Group 2: 15.1 (12.6-17) p=0.255 **6 months** Group1: 16 (13.9-18.8) Group 2: 15.6 (12.8-17.1) p=0.220 **12 months** Group1: 16 (13.7-19) Group 2: 15.1 (13-17.5) p=0.186 **18 months** Group1: 16 (13.5-18.9) Group 2: 15 (13-17.4) p=0.271	
			Median (25-75 centile) PVR, ml	**Baseline** Group1: 97 (6-124) Group 2: 89 (50-120) **18 months** Group1: 15 (0-33.5) Group 2: 12 (0-25); p=0.281	
			Median (25-75 centile) IIEF-5	**Baseline** Group1: 12 (8-16 Group 2: 12 (7-16 **18 months** Group1: 12 (7-17) Group 2: 12 (9-17); p=0.987	
			Median (25-75 centile) P-size, ml	**Baseline** Group1: 93 (85-100) Group 2: 96 (86.2-100) **18 months** Group1: 55 (45-65) Group 2:10 (5.5-15); p<0.001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Median (25-75 centile) PSA, ng/dl	**Baseline** Group1: 6.2 (3.1-8.44) Group 2: 6.3 (2.9-8.6) **18 months** Group1: 2.4 (1.8-3.6) Group 2: 2 (1.4-2.6); p=0.025	
			Median (25th-75th centile) Catheter removal (hours)	Group1: 24 (20-36) Group 2: 120 (96-144); p< 0.001	
			Median (25th-75th centile) Hospital stay (hours)	Group1: 48 (24-48) Group 2: 144 (120-144); p< 0.001	
			Median (25th-75th centile) Operation time (minutes)	Group1: 80 (70-90) Group 2: 50 (45-60); p< 0.001	
			Number (%) Adverse events	**Stress/urge incontinence** Group 1: 0 Group 2: 0 **Intra-operative TURP-hemotasis** Group 1: 5 (7.69) Group 2: 0 **Peri-operative blood transfusion** Group 1: 0 Group 2: 8 (13.3) **Transurethral resection syndrome** Group 1: 0 Group 2: NR **Urethrogragia** Group 1: 1 (1.54) Group 2: 0 **Pulmonary infection** Group 1: 0 Group 2: 1 (1.67) **Prolonged dysuria** Group 1: 5 (7.6) Group 2: 7 (11.6) **Culture confirmed UTIs**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group 1:14 (21.5) Group 2: 16 (27) **Re-catheterisation** Group 1: 7 (10.7) Group 2: 10 (16.67) **Re-operation** Group 1: 3 (4.62); urethral strictures (2), persistent bladder outlet flow obstruction symptoms (1) Group 2: 3 (5); urethral stricture (1), bladder neck contracture (2) **Mortality** Group 1: 1 (liver cancer) Group 2: 0	

1 **Evidence Table 29: Laser vs. transurethral microwave thermotherapy (TUMT)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Norby et al., 2002a[223] **Study design:** Randomised controlled trial (RCT) **Evidence level:** 1+ **Setting:** Denmark (two centres) **Duration of follow-up:** 6 months	**Patient group:** Men ≥ 50 years between May 1996 and November 1999. **Inclusion criteria:** IPSS ≥ 7, QoL. ≥ 3, obstructed according to ICS nomogram or Qmax <12mL/s; able to understand project information and have written consent. **Exclusion criteria:** suspicion of prostate cancer; PVR> 350mL or urinary catheter; prostatic urethra <25 mm long, neurological disease or diabetes with abnormal cystometry; previous prostate operation; ongoing UTI; previous diagnosis of rectal cancer, intake of mediation known to influence voiding; sever peripheral arterial insufficiency; previous pelvic radiation therapy; general health condition contraindicating surgery. **<u>All patients</u>** **N:** 118 **Mean age:** 66 **Drop outs:** 8 (6.7%) **<u>Group 1</u>** **N:** 48 **Mean age** (SD): 65 (8) **Median catheter duration:** 3 days	**Group 1: LASER** Interstitial laser coagulation. NdYag: 7-20W. Median length of stay was 3 days. Median catheter duration was 3 days **Group 2: TUMT** Transurethral microwave thermotherapy (TUMT). Prostatron 2.0 (n=8) or 2.5 (n=37). Performed as an outpatient procedure (four stayed overnight and 1 patient for 2 nights). Median catheter duration was 7-14 days **Control:** TUIP (n=3) or TURP (n=18). Median catheterisation was 2 days and hospital stay 5 days.	**Mean (SD) IPSS:**	**Baseline:** Group1: 21.4 (5.8), n=44 Group 2: 20.5 (5.7), n=46 Group 3: 21.3 (6.6), n=22 **6 Months:** Group1: 9.5 (6.6), n=44 Group 2: 9.5 (7.1), n=44 Mean difference: 0.00 [-2.86, 2.86] Group 3: 6.8 (5.7), n=22	**Funding:** Supported by a grant from Vejle County, Denmark. **Limitations:** Had to stop early due to financial restrictions and did not reach target enrolment population. **Additional outcomes:** - Effect on prostatic volume. - Results also compared to control group that had either TURP or TUIP. - Overall satisfaction scores reported in comparison to control group. Figures not provided. - Subgroup analysis comparing results from TUMT 2.0 v TUMT 2.5. **Notes:** Reported in Cochrane Systematic Review by Hoffman 2000. UTI defined as 'symptomatic UTI requiring antibiotic treatment (infections treated both in the outpatient clinical and in primary health care were included)'.
			Median (IQR) IPSS Quality of life:	**Baseline:** Group 1: 4 (4-4) , n=44 Group 2: 4 (4-4), n=46 Group 3: 4 (4-5) , n=22 **6 Months:** Group1: 1 (1-2) , n=44 Group 2: 2 (1-3) , n=44 Group 3: 1 (1-2) , n=22	
			Mean (SD) peak urinary flow (Qmax mL/s):	**Baseline:** Group1: 10.2 (4.0), n=44 Group 2: 9.1 (4.2), n=46 Group 3: 9.6 (3.2) , n=22 **6 Months:** Group 1: 16.2 (8.5), n=43 Group 2: 13.2 (6.9), n=44 Group 3: 20.6 (12.8), n=22	
			Median (IQR) post void residual, mL	**Baseline:** Group1: 117 (50-180), n=44 Group 2: 110 (50-210), n=46 Group 3: 75 (17-193), n=22 **6 Months:** Group 1: 58 (14-118), n=43 Group 2: 48 (24-129)n=44 Group 3: 23 (3-48), n=22	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Median prostate volume, ml = 44 **Dropouts**: 4 (diagnosis changed for 3 and 2 declined surgery, of which one reported IPSS at 6m and included in results). **<u>Group 2</u>** **N:** 46 **Mean age** (SD): 66 (7) **Median catheter duration:** 7-14 days; with longer catheterisation required after higher energy procedures. **Median prostate volume,** ml = 43 **Drop outs**: 2 (one had TURP, other had apoplexy at 4m and only had 3m follow-up) **<u>Group 3</u>** **N:** 24 **Mean age** (SD): 68 (7) **Median prostate volume,** ml = 44 **Drop outs**: 2 (prostate cancer)		**Urinary retention:**	**Group1**: 4/44 (9%) **Group 2:** 3/46 (7%) **Group 3**: 1/22 (5%)	* Erectile dysfunction and retrograde ejaculation was only estimated amongst those who had answered the relevant questions both at baseline and at the 6 month follow-up. Each question was scored from 0 to 3. For evaluation of ejaculation, patients scoring 0, 1 and 2 (i.e. normal amount, slightly reduced and greatly reduced amount of semen) were classified as having antegrade ejaculation. Patients scoring 3 (i.e. no ejaculation) were classified as having retrograde ejaculation.
			Urinary tract infection:	**Group 1:** 27/44 (61%) **Group 2:** 14/46 (30%) **Group 3:** 3/22 (14%)	
			Transurethral resection syndrome (TUR)	**Group 1**: 0/44 (0%) **Group 2**: 0/46 (0%) **Group 3:** 1/22 (5%)	
			Transfusion:	**Group 1**: 0/44 (0%) **Group 2**: 0/46 (0%) **Group 3:** 2/22 (9%)	
			Stricture:	**Group 1:** 1/44 (2%) **Group 2:** 0/46 (0%) **Group 3:** 1/22 (5%)	
			Urinary incontinence:	**Group 1:** 0/44 (0%) **Group 2:** 0/46 (0%) **Group 3:** 1/22 (5%)	
			Development of erectile dysfunction:*	**Group 1:** 4/18 (29%) **Group 2:** 2/22 (9%) **Group 3:** 1/7 (14%)	
			Development of retrograde ejaculation:	**Group 1:** 9/26 (35%) **Group 2:** 6/27 (22%) **Group 3**: 7/14 (50%)	
			Reoperation for BPO	**Group1:** 0/44 (0%) **Group 2:** 1/46 (2%) **Group 3:** 0/22 (0%)	
			Mortality	**Group 1:** 0/44 (0%) **Group 2**: 0/46 (0%) **Group 3:** 0/22 (0%)	

1 **Evidence Table 30: Laser vs. transurethral vaporisation of the prostate (TUVP)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Abdelkhalek et al., 2003[4] **Study design:** RCT, open label **Setting:** Egypt **Evidence level:** 1+ **Duration of follow-up:** Up to 4 years	**Patient group:** Symptomatic bladder outlet obstruction due to BPH **Setting:** Urology and Nephrology Centre, Mansoura University, Egypt. (March1995 to March 1997) **Inclusion criteria:** ▪ Qmax ≤10ml/s ▪ Serum PSA level of < 4 ng/mL ▪ IPSS of ≥15 ▪ Prostate volume of 20-80mL **Exclusion criteria:** ▪ Urethral stricture ▪ Contracted bladder ▪ Large vesicle diverticulum ▪ Neuropathic bladder **<u>All patients</u>** **N:** 180 **Age**, mean ±SD **Drop outs:** 40/180 **<u>Group 1-Laser prostatectomy</u>** **N:** 90 Dropouts: 28/90 **Age**, mean (years): 63.3±6.5 **IPSS**, mean (±SD): 27.9±5.3 IPSS-QoL, mean (±SD): 5±0.8	**Group 1- Laser prostatectomy: combination of coagulation and vaporisation methods:** i) Side firing coagulation of two lateral lobes using fibres with a lateral beam angle of 90° at 40W for 90s at each coagulation spot in the 2, 4, 8, 10 and 12 o clock positions. ii) Vaporisation of the median lobe using contact (sapphire) tips at 60W in a retrograde fashion. **Power:** 40W Nd: YAG for 60s at each lateral lobe at 9 and 3 o'clock positions, and 30s each at 6 and 12 o'clock positions. **Group 2 –TUVP** **Procedure:** TUVP delivered using Vaportrode™ under the 250 to 300 W of pure cutting current in	**All cause mortality** (due to cardiopulmonary disease)	**Group 1**: 1/90 **Group 2:** 2/90 **P value:** NS	**Funding:** Not stated **Limitations:** ▪ Open label study with subjective patient reported outcomes. ▪ Randomisation and concealment methods not reported **Additional outcomes:** ▪ Prostate and adenoma volume at 1 and 4 years ▪ An additional 6 and 2 reoperations were completed for the laser and TUVP groups respectively after the 4-year follow up. **Notes:** None.
			IPSS, mean± SD:	<u>At 1 year</u> **Group 1:** 13.3±6 **Group 2:** 5.6±3.5 **p value:** 0.003 <u>At 2 year</u> **Group 1:** 12.2±5.6 **Group 2:** 5.2±3.3 **p value:** 0.006 <u>At 3 year</u> **Group 1:** 13.1±5.7 **Group 2:** 4.8±2.6 **p value:** 0.002 <u>At 4 year</u> **Group 1:** 11.9±6.1 **Group 2:** 3.7±1.3 **p value:** <0.001	
			IPSS-QoL mean ± SD:	<u>At 1 year</u> **Group 1:** 3.4±0.4 **Group 2:** 1.4±0.5 **p value:** 0.008 <u>At 2 year</u> **Group 1:** 3.2±0.5 **Group 2:** 1.4±0.4 **p value:** 0.009 <u>At 3 year</u> **Group 1:** 3.3±0.6 **Group 2:** 1.4±0.5 **p value:** 0.009 <u>At 4 year</u> **Group 1:** 3.1±1.0 **Group 2:** 1.3±0.5 **p value:** <0.001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Qmax, mean, (±SD): 6.9±2.8 **Post void residual urine**, mean, (±SD): 120±97.5 **Prostate volume**, mean (±SD):43.8±13.4 **Group 2 - TUVP** **N:** 90 **Dropouts**: 12/90 **Age**, mean (years): 62.9±5.9 **IPSS**, mean (±SD): 26.0±5.8 IPSS-QoL, mean (±SD): 4.8±0.9 **Qmax**, mean, (±SD): 6.4±2.5 **Post void residual urine**, mean, (±SD): 125±97.5 **Prostate volume**, mean; 47.4±16.1	an antegrade fashion. The median lobe was vaporised first, and continued down the surgical capsule until a wide prostatic cavity was created, followed by careful coagulation.	**Qmax** (ml/s), mean ± SD:	At baseline **Group 1:** 6.9±2.8 **Group 2:** 6.4±2.5 **p value:** 0.256 At 1 year **Group 1:** 15.1±6.0 **Group 2:** 20.8±7.4 **p value:** 0.029 At 4 year **Group 1:** 13.6±3.6 **Group 2:** 21.4±4.1 **p value:** <0.001	
			Post void residual volume (ml), mean ± SD	At 1 year **Group 1**: 61.3±49.2 **Group 2**: 22.1±22 **p value:** <0.001 At 4 years **Group 1**: 64.6±29.8 **Group 2:** 25.1±12.8 **p value:** <0.001	
			Post-op complications: Bleeding at surgery (definition not provided)	**Group1:** 0/90 **Group 2:** 1/90 **p value:** NS	
			Post-op complications: Haematuria	**Group 1:** 0/90 **Group 2:** 2/90 **p value:** NS	
			Post-op complications: urinary retention	**Group 1:** 9/90 **Group 2:** 2/90 **p value:** NS	
			Post-op complications: Urethral Stricture (urethral stricture, apparent after 6 months)	Up to 1 year **Group 1:** 0/90 **Group 2:** 2/90 **p value:** NS	
			Post-op complications: Bladder neck stenosis	Up to 1 year **Group 1:** 2/90 **Group 2:** 2/90	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				p value: NS	
			Post-op complications: Retrograde ejaculation	At 1 year **Group 1:** 16/90 **Group 2:** 57/90 **p value:** <0.001	
			Post-op complications: Impotence (among patients who were potent at baseline)	At 1 year **Group 1:** 0/49 **Group 2:** 4/53 **p value:** 0.04	
			Post –op complications: Reoperation (cumulative) Details of type reoperation provided.	At 1 year **Group 1:** 10/89 **Group 2:** 3/889 **p value:** 0.04 At 2 year **Group 1:** 18/90 **Group 2:** 5/90 **p value:** <0.05 At 3 year **Group 1:** 27/90 **Group 2:** 8/90 **p value:** <0.05 At 4 year **Group 1:** 35/90 **Group 2:** 11/90 **p value:** <0.001	
			Operation time, mean (range), (min):	**Group 1:** 37.5±15 **Group 2:** 36.6±16.4 **p value:** NS	
			Catheter period (days)mean ±SD	**Group 1:** 6.8 (0.9) **Group 2:** 2.3 (0.5) **p value:** <0.001	
			Length of hospital stay, (days) mean ±SD	**Group 1:** 1.1±0.5 **Group 2:** 2.2±0.8 **p value:** NS	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Shingleton et al., 1998[276] **Study design:** RCT **Setting:** USA **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** consecutive patients with benign prostatic hyperplasia **Inclusion criteria:** Consecutive patients (no further information) **Exclusion criteria:** Not stated **All patients** **N:** 31 Randomised (ratio 2:1) **Group 1** **N:** 11 Mean (range) Age: 67.5 (60-82) Mean prostate volume (cc): 34.6 (9.2 to 87.7) Erectile function: Full: 3/11 (27%) Partial: 5/11(45%) None: 3/11 (27%) Dropouts: Not stated **Group 2** **N:** 20 Mean (range) Age: 66.7 (48-77) Mean prostate volume (cc): 34.6(13.7 to 66.4) Dropouts: Not stated Erectile function: Full: 4/20 (25%) Partial: 7/20(35%) None: 9/20 (47%)	**Group 1: VLAP + KTP** (contact laser – vaporisation) KTP laser set at 40 watts for initial vaporisation of all median and lateral lobe tissue. Nd:YAG beam used at 60 watts for 60 sec to create a series of craters in lateral lobes of the prostate. Catheter protocol: Catheter put in place without accompanying bladder irrigation. **Group 2: Transurethral Electrovaporisation (TVP)** High energy electrical current to vaporise tissue and create a zone of coagulation surrounding vaporised tissue cavity. Catheter protocol Set at initial 275 watts, but increased to 300 watts in all patients. The coagulation setting was 40watts for all patients. Catheter protocol: After procedure a 22F three way catheter was put in place and standard irrigation with normal saline begun.	**AUA symptom score,** mean (range)	**Baseline:** Group1: 19 (13-27) Group 2: 22.1(8-31) **3 months:** Group1: 5.9 (1-12) Group 2: 5.2 (2-24) **6 months:** Group1: 5.0 (0-10) Group 2: 5.2 (1-19) **P value:** NS between arms, stat sig compared to baseline	**Funding:** NR **Limitations:** ▪ Randomisation allocation and concealment not reported ▪ No specific inclusion or exclusion criteria were stated in this paper. ▪ No statistical methods provided. **Additional outcomes:** ▪ 1 month outcomes ▪ % of patients who had improved more than 50 % compared to baseline at 6th month follow up **Notes:** QoL was reported to be collected in method section but was not reported. Shingleton1998A – reported on the urodynamics outcome of a subset of the patients in this cohort (10 patients in each arm). However, the basis of selecting this subset of patients was not provided.
			Qmax, mean (range)	**Baseline:** Group1: 10.7 (0-11.8) Group 2: 7.7 (3.4-13.2) **3 months:** Group1: 17.6 (6.2-22) Group 2: 17.5 (7.6-24.9) **6 months:** Group1: 16.5 (7.1-24.9) Group 2: 14.3 (7.8-27.1) **P value:** NS for all **P value:** NS between arms, stat sig compared to baseline	
			Post-op complications: Clot retention	**Group 1:** 0/11 **Group 2:** 2/20 **p value:** NS	
			Post-op complications: haematuria (2 patient in laser group had clot retention)	**Group 1:** 2/11 **Group 2:** 6/20 **p value:** NS	
			Post-op complications: Post operative urinary retention	**Group 1:** 3/11 **Group 2:** 1/20 **p value:** NS	
			Stricture (urethral stricture0	**Group 1:** 1/11 **Group 2:** 0/20 **p value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Post-op complications: Development of erectile dysfunction	**Group 1:** 1/11 **Group 2:** 2/20 **p value:** NS	Inclusion/exclusion criteria from Shingleton1998A Inclusion: >45 years, Qmax <15ml, no history of carcinoma and ability to undergo general anaesthesia.
			Operation time, mean, (min):	**Group 1:** 27.5 **Group 2:** 46 **p value:** <0.05	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Van Melick et al., 2003[308] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** Up to 7 years:	**Patient group:** men over 45 years with LTUS associated with BPH that were recruited from their clinic from1996 to 2001 **Setting:** Netherlands **Inclusion Criteria:** patient with lower urinary tract symptoms suggestive of BPH; met ISC criteria for BPH, Schafer obstruction score≥ 2, prostate size between 20-65ml. **Exclusion Criteria:** age ≤45 yrs **All patients** **N:** 141 **Group 1** **N:** 45 **Age (mean):** 67±9 **Drop outs:** 8 at one year post-operatively (procedure during surgery changed for medical reasons=3, equipment failure resulting in TURP)=2, reoperation – TURP=1, reoperation – due to stricture =2) **Mean prostate size, ml:** 37±11 Follow-up 1to 4 years = 15 Follow-up 4 to 7 years=15 **Group 2** **N:** 50 **Age (mean):** 66±8 **Drop outs:** 9 at one year post-operatively (surgery cancelled=1, mortality=2, morbidity=2, emigrated=1, reoperation (TURP)	**Group 1: Laser vaporisation** Transurethral catheter post-operation SLT Nd:Yag Pre-procedural antibiotics and transurethral catheter postoperatively. **Group 2: TURP** Suprapubic catheter if required peri-operatively. Pre-procedural antibiotics and transurethral catheter postoperatively. **Group 3: Electrovaporisation** Performed with a Vaportrode element using glycine for irrigation. Pre-procedural antibiotics and transurethral catheter postoperatively.	**Mean (SD) symptom score (IPSS)**	At baseline: **Group1:** 18.3±8.2 **Group 2:** 16.6±5.6 **Group 3:** 20.3±6.8 At 6 months **Group1 (n=33) :** 5.9±5.5 **Group 2 (n=37):** 3.2±2.7 **Group 3:** 3.8±2.7 At 1 year **Group1 (n=37) :** 3.6±3.4 **Group 2 (n=41):** 4.1±4.8 **Group 3:** 4.8±4.9 At 1-4 years **Group1 (n=10):** 9.3±5.2 **Group 2 (n=15):** 5.8±7.5 **Group 3:** 8.4±8.7 At 4-7 years **Group1 (n=17):** 8.3±6.4 **Group 2 (n=15):** 7.3±7.1 **Group 3:** 7.0±5.6	**Funding:** NR. **Limitations:** Open label study **Additional outcomes:** Frequency during day, frequency during night, symptom problem index and BPH impact index. Uroflowmetry also reported. **Notes:** Links with Van Melick 2002[307], Van Melick 2003[308]. Follow up time varied individually as all patients were analysed within a 2 month period. Depending on the individual follow-up time, patient divided into two groups: those with a follow-up time between 1 and 4 years and those with follow up time between 4 and 7 years.
			Mean (SD) Global quality of life score:	At baseline: **Group1:** 3.6±1.6 **Group 2:** 3.9±1.6 **Group 3:** 4.3±1.3 At 6 months **Group1:** 0.8±1.0 **Group 2:** 0.5±0.5 **Group 3:** 1.0±0.8 At 1 year **Group1:** 0.6±0.9 **Group 2:** 0.6±0.8 **Group 3:** 1.0±0.9 At 1-4 years **Group1:** 2.0±1.0 **Group 2:** 1.1±1.2 **Group 3:** 1.0±1.2 At 4-7 years	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	=2, reoperation (stricture)=1) **Mean prostate size, ml:** 38±9 Follow-up 1to 4 years = 10 Follow-up 4 to 7 years=17 **Group 3** **N:** 46 **Age (mean):** 64±10 **Drop outs:** 22 **Mean prostate size, ml:** 35±12 Follow-up 1to 4 years = 12 Follow-up 4 to 7 years=12			**Group1:**1.4±1.2 **Group 2:** 1.3±1.3 **Group 3:** 1.4±0.8	
			Mean (SD) maximal flow (mL/s)	At baseline: **Group1:** 9±3 **Group 2:** 13±4 **Group 3:** 9±3 At 6 months **Group1:** 25±9 **Group 2:** 26±6 **Group 3:** 24±11 At 1 year **Group1:** 27±12 **Group 2:** 23±10 **Group 3:** 28±6 At 1-4 years **Group1:** 19±6 **Group 2:** 20±5 **Group 3:** 23±6 At 4-7 years **Group1:** 19±9 **Group 2:** 17±8 **Group 3:** 16±11	
			Stricture	**Group1:** 2/45 **Group 2:** 2/50 **Group 3:** 1/46	
			Incontinence Reported in HTA (ncc study)	**Group1:** 14/45 (8%) **Group 2:** 4/50 (39%) **Group 3:** 15%	
			Reoperation by TURP	**Group1:** 1/45 **Group 2:** 2/50 **Group 3:** 2/46	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Blood transfusion	**Group1:** 0/45 **Group 2:** 1/50 **Group 3:** 0/46	
			Urinary retention	**Group1:** 5/45 **Group 2:** 0/50 **Group 3:** 0/46	
			Urinary tract infection (after one week)	**Group1:** 4/45 (9%) **Group 2:** 5/50 (10%) **Group 3:** 5%	
			Mean (SD) operative time, minutes:	**Group 1:** 58 (11) **Group 2:** 58 (26) **Group 3:** 50 (16)	
			Mean (SD) postoperative hospital days	**Group 1:** 3.8 (1.3) **Group 2:** 3.9 (0.9) **Group 3:** 3.4 (0.9)	
			Mortality: *cardiac failure, hepatic failure (HTA reports 3 v 4)	**Group 1:** 0/45 **Group 2:** 2/50* **Group 3:** 0/46	

Evidence Table 31: Laser coagulation vs. laser vaporisation

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Bryan et al., 2000[37] **Study design:** RCT, single centre – open study **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient group:** Bladder outlet obstruction, BOO due to benign prostatic hyperplasia, BPH. **Setting:** Urology department, UK hospital **Inclusion Criteria:** Ambulant male patients with BOO due to BPH, confirmed with pressure/flow urodynamics. **Exclusion Criteria:** ▪ Neurological disorders affecting the urinary tract ▪ Previous prostatic or urethral surgery ▪ Clinical evidence of prostatic or vesicle malignancy ▪ Acute urinary tract infection ▪ Prostate gland volume of <20mm^3 On medication known to influence voiding function. **<u>All patients</u>** **N:** 38 **Drop outs:** 0	Laser prostatectomy was carried out using a SLT (Surgical Laser Technologies, Oaks, Pa, USA) neodymium:YAG laser system with semi-rigid endoscopic fibre (SREF15) set a 40W **Group 1-CLAP** A chiselled probe (MD6) with a distal end incorporating a 6 mm sapphire tipped round probe was used. The probe was brought back to the verumontanum and then pushed forward to produce furrows. Mean operating time:37.7min SEM1.6 **Group 2 - VLAP** Laser energy applied using a	**IPSS symptom score** The data was shown in a graph, and values only reported for 6th and 24th month.	<u>At 1, 3, 12th months</u> Group1 : No reported Group 2 : NR **P value:** NS <u>At 6 months</u> **Group1:** 8.3 ± 6.4*** **Group 2:** 12.5** ± 6.4*** **p value:** 0.05 <u>At 24 months</u> **Group1:** 13.5 ± 8.26* **Group 2:** 13.3 ± 7.36* **p value:** NS <u>Compared to baseline</u> Group 1: P value= 0.006 Group 2: P value= 0.002	**Funding:** Not stated **Limitations:** ▪ No sample size calculation provided- small sample size ▪ 38% in CLAP and 24% in VLAP group did not perform urodynamics at 6 months to determine obstruction **Additional outcomes:** ▪ Mean operating time ▪ Increased irritative symptoms which returned to normal after 1 month (5 in VLAP, 4 in CLAP) **Notes:** *SD estimated following the Cochrane handbook method using p values reported for change from baseline. ** estimated from graph shown. Likely
			Qmax	<u>At 12 months</u> **Group1:** 16.6 ± 7.37* **Group 2:** 17.5 ± 6.50* **P value: NS** <u>Compared to baseline</u> Group 1: P value= 0.006 Group 2: P value= 0.002 <u>At 24 months</u> **Group1:** 15.5 ± 7.35* **Group 2:** 15.9 ± 10.15* **P value: NS** <u>Compared to baseline</u> Group 1: P value= 0.02 Group 2: P value= 0.1	
			PdetQmax (cm H_20)	<u>At 6 months</u> **Group1:** 54.6 **Group 2:** 56.4 **p value:** 0.4 Both Sig different compared to baseline p<0.005	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1 - CLAP **N:** 21 **Age (mean):** 72.25, SE1.68 **Drop outs:** 0 **IPSS:** 20.9, SE1.6 **Erectile dysfunction:** 10, SE 21 (47.6%) **Qmax:**10.0, SE 0.68 **PdetQmax H_20:** 79.4, SE 9.4 **Unequivocal obstruction,** proven urodynamically: 19/21 **Group 2 - VLAP** **N:** 17 **Age (mean):** 71.88, SE 1.59 **Drop outs:** 0 **IPSS:** 21.8, SE 1.5 **Qmax:**10.0, SE 0.8 **PdetQmax H_20:** 91.9, SE 9.8 **Erectile dysfunction:** 8/17 (47.1%) **Unequivocal obstruction,** proven urodynamically: 16/17	side firing free beam probe (SFB 1.0), to the lateral lobes 1 cm distal to the bladder neck at 40W for 90s each of 4 quadrants,: 2, 4, 8, and 10 o' clock positions. Mean operating time: 24.5min	**Post-op complications (early): Catheter duration,** mean (range), days	**Group1:** 4.5(1-31) **Group 2:** 13.2 (7-70) **p value:** NR#	error in the value from text (21.3) ***SD estimated from standard error bars from graph because p value for change from baseline was not reported in the results #No SD provided $ 9 in the CLAP and 4 in the VLAP group were infirm or refused to do urodynamics at 6 months post-op
			Post-op complications (early): Required Catheter > 7 days	**Group1:** 2/21 **Group 2:** 7/17 **Relative risk:** NS	
			Post-op complications (early): Bladder irrigation	**Group1:** 5/21 **Group 2:** 0/17 **Relative risk:** 9.00 **95% CI:** 0.53-152.1 **p value:** NS	
			Post-op complications (early): Blood transfusion	**Group1:** 1/21 **Group 2:** 0/17 **Relative risk:** 2.45 **95% CI:** 0.11-56.7 **p value:** NS	
			Post-op complications (early): Peri-operative urinary tract infections	**Group1:** 1/21 **Group 2:** 2/17 **Relative risk:** 0.40 **95% CI:** 0.04-4.09 **p value:** NS	
			Post-op complications: Developed erectile dysfunction	**Group1:** 1/21 **Group 2:** 1/17 **Relative risk:** 0.81 **95% CI:** 0.05-12.01 **p value:** NS	
			Post-op complication: Reoperation:	**Group1:** 1/21 **Group 2:** 2/17 **Relative risk:** 0.40 **95% CI:** 0.04-4.09 **p value:** NS	
			Unequivocal obstruction, proven urodynamically, at 6 months $	**Group1:** 3/13 **Group 2:** 6/13 **Relative risk:** 0.50 **95% CI:** 0.16-1.58 **p value:** NS	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Narayan et al., 1995[209] **Study design:** RCT, multi-centre, open study **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Moderate to severe obstruction, including 8 patients in chronic retention and had indwelling Foley catheter* **Setting:** US, in two Veteran Affairs medical centres **Inclusion Criteria:** ▪ Consecutive patients with moderate to severe obstructive symptoms as defined by AUA symptom score≥13 (midway of the scale between mild and moderate obstructive symptoms) ▪ Qmax <15ml/s, with or without significant post void residual volume **Exclusion Criteria:** ▪ Prostate cancer **All patients** **N:** 64 **Drop outs:**	**Group 1 CLAP- Evaporation** Standard cystourethroscopy was performed before laser ablation. Laser applied initially at the 5 and 7'o clock position at 60W until circular fibres of the bladder neck visible. Next, the median lobe was treated with laser at 45 degrees angle form the lobe form the right to left sides and vice versa. The ablation was completed by laser application at the 6 o'clock position deep enough to visualise the bladder neck muscle fibres and a smooth, bladder neck between 5 and 7 o'clock positions. Prostate evaporation was then performed. Fibre help in contact with area treated and dragged at rate of 1 cm/20 to 30s. At the beginning each furrow dragging was commenced when bubbling was noted signifying evaporation of	**IPSS symptom score,** only mean value reported, no standard deviation provided	At 1 months **Group 1:** 9.9 **Group 2:** 9.8 At 3 months **Group 1:** 7.0 ± 14.81* **Group 2:** 8.4 ± 13.18* At 6 months (N=52) **Group 1:** 5.0 ± 16.73* **Group 2:** 5.1 ± 16.35* At 12 months (N=15) **Group 1:** 5.3 ± 16.45* **Group 2:** 5.2 ± 16.25* **P value:** NR, not sig between arms at all time points (All P<0.001 compared to baseline)	**Funding:** Not stated **Limitations:** ▪ No mention of blinding of outcomes assessors. ▪ Relatively small sample size- not sample size calculation provided. ▪ There was a trend (not statistically significant) of older patients, with larger prostate size, higher number in retention, lower Qmax and higher post void residual volume in the evaporation group. ▪ Most continuous variable outcomes only reported mean values- not standard
			Qmax (ml/s), only mean value reported, no standard deviation provided	At 1 months **Group 1:** 17 **Group 2:** 12.0 At 3 months **Group 1:** 19.7 ± 12.79* **Group 2:** 16.3 ± 14.00* At 6 months (N=52) **Group 1:** 20.0 ± 13.08* **Group 2:** 16.4 ± 9.04* At 12 months (N=15) **Group 1:** 19.9 ± 12.98* **Group 2:** 16.9 ± 11.46* **P value:** <0.05 for all time points. (All P<0.05 compared to baseline)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1 – CLAP-evaporation **N:** 32 **Age (mean, range):** 66.0(49-78) **Prostate volume (mean, range);** 51.7(16-120) **N patient in retention:** 6/32 **Median lobe:** 5/32 Data excluding patients with chronic urinary retention (n=26): **AUA symptom score:** 22.4(14-35) **Qmax:** 6.4(0-15) **Post void residual volume:** 276.6(20-960) **Group 2 – VLAP-Coagulation** **N:** 32 **Age (mean, range):** 64.1(48-92) **Prostate volume (mean, range);** 41.4 (20-62) **N patient in retention:** 3/32 **Median lobe:** 4/32 Data excluding patients with chronic urinary retention (n=29): **AUA symptom score:** 22.1(15-30) **Qmax:** 70(0-14) **Post void residual volume:** 210(0-250) * Patients who were in chronic retention were assigned "0" Qmax and not assigned any AUA score. These results were analysed separately.	tissue. Dragging the fibre at this rate resulted in furrow 5-7 mm deep and with a 3-4mm rim of coagulated tissue. **Group 2 VLAP-Coagulation** (modified visual laser ablation technique) Laser application at 60W for 60s to 11-19 spots (depending on prostate size). Spots included 5 and 7 o' clock positions at the bladder neck, the 6' o clock position for the median lobe and the 5, 7, 11, and 1 o'clock position for each cm length of the prostate. Each spot covered a 1 cm area. Fibre held 2-4 mm away from tissue to ensure coagulation and not evaporation. Antibiotic prophylaxis: All patients received cefazolin 1g/ml perioperatively and trimethoprim-sufamethoxazole double strength twice daily; one hospital provide 24-48 hours of prophylaxis whereas another provided 10 days	**Post void residual volume** (ml), only mean value reported, no standard deviation provided	At 1 months **Group 1:** 49 **Group 2:** 46 At 3 months **Group 1:** 31 **Group 2:** 20 At 6 months(N=52) **Group 1:** 29 **Group 2:** 24 At 12 months (N=15) **Group 1:** 26 **Group 2:** 28 **P value:** NR, not sig between arms at all time points (All P<0.05 compared to baseline)	deviation. **Additional outcomes:** Qmax, AUA symptom score and post void residual volume for 8 patients in chronic retention analysed and reported separately. There was no significant difference in terms of improvement in AUA symptom score or Qmax. **Notes:** # Calculated by NCGC team using Mantel Haenszel test in Rev Man version 5. Values reported in paper were based on chi-square test (Pearson) *SDs estimated following Cochrane methods using p values for change from baseline
			Catheter duration, Median (range), days	**Group 1:** 1.9 (1-10) **Group 2:** 2.1 (1-21) **p value:** NS	
			Post-op complications (early): Blood transfusion	**Group 1:** 0/32 **Group 2:** 0/32 **p value:** NS	
			Post-op complications (early): Epididymitis	**Group 1:** 0/32 **Group 2:** 0/32 **p value:** NS	
			Peri-operative urinary tract infections (patients operated in 2 hospitals, all perioperative UTIs in hospital which only provide 24-48 of prophylaxis.	**Group 1:** 2/32 **Group 2:** 1/32 **Relative risk:** 2.00 **95% CI:** (0.19-20.97) **p value:** NS #	
			Post-op complications: Developed erectile dysfunction	**Group 1:** 0/32 **Group 2:** 0/32 **p value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Post-op complications: Incontinence	**Group 1:** 0/32 **Group 2:** 0/32 **p value:** NS	
			Post-op complication: Reoperation:	**Group 1:** 0/32 **Group 1:** 5/32 **Relative risk:** 0.09 **95% CI:** 0.01-1.58 **p value:** NS	
			Post-op complication: Post operative retention (Longer than 7 days after catheter removal)	**Group 1:** 2/32 **Group 2:** 8/32 **Relative risk:** 0.25 **95% CI:** 0.06-0.94 **p value:** <0.05#	
			"Bothersome irritative symptoms" > 14 days	**Group 1:** 10/32 **Group 2:** 11/32 **Relative risk:** 0.87 **95% CI:** 0.31-2.47 **P value:** NS	

See Evidence Table 26 Laser coagulation vs. transurethral resection of the prostate (TURP)

1 **Evidence Table 32: Holmium laser resection of the prostate (HoLRP) vs. laser coagulation**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Gilling et al., 1998[102] **Study design:** RCT, open study **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Men with symptomatic benign prostatic hyperplasia **Setting:** Urology department, New Zealand **Inclusion Criteria:** ▪ Qmax ≤15ml/s ▪ AUA symptom score >8 ▪ Urodynamically proven bladder outlet obstruction – defined as Schaefer grade of≥2 and at detrusor pressure at peak flow (PdetQmax) value in the obstructed or equivocal region of Abrams-Griffiths nomogram **Exclusion Criteria:** ▪ Age≥85 years ▪ Prostate volume (measured by TRUS), >100ml ▪ **All patients**	**Group 1- HoLRP** Retrograde approach to the incision of the first and median lobe and then each lateral lobe in turn. This was performed using a 550micrometer bare quartz fibre passed down a continuous-flow resectoscope. Power setting was 60W. Energy (kJ), mean (range): 67 (32-165) Mean lasing time, mean (range)*: 27.2min (13-75) Resection weight, g, mean (range): Estimated: 21(10-60) Actual : 5 (2-13) Catheter removed at 6 the following morning and discharged once voided successfully.	**IPSS symptom score**, mean (range). All not sig between treatment arms.	At 1 month **Group1:** 8(0-16) **Group 2:** 11(2-26) **p value:** Not Sig At 3 months **Group1:** 4(0-12) **Group 2:** 8(0-26) **p value:** Not Sig At 6 months **Group1:** 5(1-16) **Group 2:** 7(0-22) **p value:** Not Sig At 12 months **Group1:** 4(0-9) **Group 2:** 5(1-18) **p value:** Not Sig	**Funding:** Not stated **Limitations:** ▪ No details of randomisation method and concealment was provided ▪ Small sample size-sample size calculation not provided ▪ Open study **Additional outcomes:** ▪ % of men requiring analgesia for dysuria symptoms (64% VLAP, 41% for HoLRP) ▪ Mean duration of surgery – stats sig
			Dysuria score , mean, (no SD given) Measured using a visual analogue scale (VAS), ranging from 0 (no voiding symptom), 10 (severe dysuria)	First 10 post-operative days **Group1:** 2 **Group 2:** 4 **p value:** <0.05 First 5 days after catheter removal **Group1:** 2.1 (Day 1- 5) **Group 2:** 3.7 (Day 6-10) **p value:** <0.05	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 44 **Drop outs:** 0 **<u>Group 1 -HoLRP</u>** **N:** 22 **Drop outs:** *All values provided as mean (range)* **Age** : 64 (44-81) **IPSS:** 24(14-33) **Qmax**, ml/s: 8(3-15) **PVR** (TRUS volume), mL: 42(20-72) **PdetQmax H_20:** 72(37-117) **Shaffer Grade:** 4 (2-5) **Residual volume:** 179 (30-40) **Prostate length**, cm: 3(2-5) **<u>Group 2 - VLAP</u>** **N:** 22 **Drop outs: 0** *All values provided as mean (range)* **Age:** 68(45-80) **IPSS:** 23(13-35) **Qmax**, ml/s: 8(3-15) **PVR** (TRUS volume), mL: 49(24-80) **PdetQmax H_20:** 77(42-113) **Shaffer Grade:** 4 (2-5) **Residual volume:** 131 (40-227) **Prostate length**, cm: 3(2-6)	**Group 2 - VLAP** Standard 4-quarant Nd:YAG lasing technique. A total of at least 1kJ/g of measures tissue was delivered using a 60W for 60s at each treatment site. <u>Energy (kJ), mean (range)</u>: 53 (25-102) <u>Mean lasing time, mean (range)*:</u> 27.2min (13-75) <u>Resection weight, g, mean (range):</u> <u>Estimated:</u> 24(5-60) <u>Actual</u> : not stated All patients discharged the morning after surgery. Catheters removed routinely on the 5th post-operative day. * Stats sig between groups	**Qmax**, mL/s, mean (range)	<u>At 1 months</u> **Group1:** 21(10-56) **Group 2:** 13(4-27) **p value:** <0.01 <u>At 3 months</u> **Group1:** 20(12-30) **Group 2:** 15(5-27) **p value:** <0.05 <u>At 6 months</u> **Group1:** 21(12-32) **Group 2:** 15(5-24) **p value:** <0.01 <u>At 12 months</u> **Group1:** 22(8-41) **Group 2:** 18(10-33) **p value:** NS	**Notes:** None.
			Residual volume, mL, mean (range)	<u>At 3 months</u> **Group1:** 40 (5-163) **Group 2:** 73(20-211) **p value:** NS	
			PdetQmax (cm H_20)	<u>At 3 months</u> **Group1:** 39 (21-63) **Group 2:** 51 (37-85) **p value:**<0.05	
			Urodynamic obstruction, at 3 months, Schafer grade Abrams- Griffiths nomogram, % still obstructed, N not provided	**Group1:** 1.9 (0-4) **Group 2:** 1.0 (0-3) **95% CI:** NR **p value:**<0.05 **Group1:** 6% **Group 2:** 21% **95% CI:** NR **p value:** NR	
			Catheter duration, mean (range), days	**Group1:** 1.4 (1-8) **Group 2:** 11.6(3-8) **95% CI:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				p value: <0.0001	
			Post-op complications (early): Recatheterisation	**Group1:** 2/22 (9%) **Group 2:** 8/22 (36%) **Relative risk:** 0.25 **95% CI:** 0.06-1.05 **p value:** NR	
			Post-op complications (early): Blood transfusion	**Group1:** 0/22 **Group 2:** 0/22 **p value:** NS	
			Post-op complications (early): Catheter irrigation (for hematuria)	**Group1:** 0/22 **Group 2:** 0/22 **p value:** NS	
			Post-op complications (early): Peri-operative urinary tract infections	**Group1:** 0/22 **Group 2:** 3/22 (13.6%) **Relative risk:** 0.14 **95% CI:** 0.01-2.61 **p value:** NS	
			Post-op complications: Retrograde ejaculation in sexually active patients (Number sexually active not stated)	**Group1:** 0/NR **Group 2:** 0/NR **p value:** NS	
			Post-op complication: Reoperation: 3 in VLAP group had to be reoperated because of persistent urinary retention. 1 in the HoLRP group – urethral dilatation for submeatal stricture	**Group1:** 1/22 **Group 2:** 3/22 **Relative risk:**0.33 **95% CI:** 0.04-2.96 **p value:** NS	

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1 **Evidence Table 33: Holmium laser enucleation of the prostate (HoLEP) vs. laser vaporisation**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Elzayat 2009[80] **Study design:** RCT **Evidence level:** 1+ **Setting:** Canada **Duration of follow-up:** 12 months	**Patient group:** Between March 2005 and April 2007 men with LUTS secondary to BPH were recruited at McGill University Health centre, Canada. **Inclusion criteria:** prostate size 60cc or smaller, IPSS of 9 or greater, Qmax < 15ml/s. **Exclusion criteria:** previously diagnosed with prostate cancer, urethral stricture or nuerogenic bladder or previous prostate surgery. **<u>All patients</u>** **N:** 109 **<u>Group 1</u>** **N:** 57 **Mean age** ± SD: 72.7±10.3 **Drop outs:** 13 **<u>Group 2</u>** **N:** 52 **Mean age** ± SD: 71.6 ±10.3 **Drop outs:** 10	**Group 1: holmium laser ablation of the prostate (HoLAP)** Performed using an 80 to 100 watt holmium laser generator and 550um side firing laser fibre. Laser setting ranged from 2.0J and 50Hz to 3.2J and 30Hz. **Group 2: photoselective vaporisation (PVP)** Performed using the green light laser system with 80 Watt output and side firing laser fibre with a 600 um core diameter. **Both procedures:** Patient under general or regional anaesthesia and normal saline was used as an irrigant. Continuous flow 26Fr resectoscope with laser fibre stabilising bridge at the tip of the inner sheath was used. After each laser procedure a standard 22Fr 2-way catheter was inserted. Catheter routinely removed the next morning after surgery and when patient is able to void	**Mean (SD) symptom score (IPSS)**	**Baseline:** Group1 (n=57): 20 (6.8) Group 2 (n=52): 18.4 (6.6) **1 month:** Group1(n=54): 8.7 (6.5) Group 2(n=48): 8.9 (5.4) **3 months:** Group1(n=44): 8.4 (7) Group 2(n=39):5.8 (4.4) **6 months:** Group1(n=40):7.8 (5.7) Group 2(n=39):7.7 (6.9) **12 months:** Group1(n=44):6.2 (3.9) Group 2(n=42):8.2 (6.2); p=0.22	**Funding:** Author Elhilali has financial interest and/or other relationship with Lumenis and Laserscope. **Limitations:** Reasons for drop out not reported. Allocation concealment not reported. **Additional outcomes:** IIEF erectile function domain score was reported. Level of haemoglobin and serum Na. PSA was reported. **Notes:** None.
			Mean (SD) quality of life from IPSS score	**Baseline:** Group1 (n=57): 3.8 (1.5) Group 2 (n=52): 3.6 (1.4) **1 month:** Group1(n=54): 1.8 (1.6) Group 2(n=48): 1.9 (1.6) **3 months:** Group1(n=44): 1.5 (1.4) Group 2(n=39): 1.2(1.1) **6 months:** Group1(n=40):1.6 (1.3) Group 2(n=39):1.2 (1.1) **12 months:** Group1(n=44):1.6 (1.2) Group 2(n=42):1.5 (1.4); p=0.81	
			Mean (SD) Qmax	**Baseline:** Group1 (n=57): 6.7 (3.9) Group 2 (n=52): 6.4 (3.9) **1 month:** Group1(n=54): 17.1 (7.5) Group 2(n=48): 18.8 (8.5) **3 months:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
		adequately he is discharged from the hospital.		Group1(n=44): 18.4 (6.4) Group 2(n=39): 18.7 (9.9) **6 months:** Group1(n=40):17.4 (5.9) Group 2(n=39):19.4 (8.5) **12 months:** Group1(n=44): 17.2 (8.4) Group 2(n=42): 18.4 (8.4); p=0.66	
			Mean (SD) PVR	**Baseline:** Group1 (n=57): 205 (197) Group 2 (n=52): 215 (208) **1 month:** Group1(n=54): 47.4 (93) Group 2(n=48): 56.2 (79.5) **3 months:** Group1(n=44): 57.2 (104) Group 2(n=39):73.7 (96) **6 months:** Group1(n=40): 55 (100) Group 2(n=39):67.5 (90) **12 months:** Group1(n=44):68.9 (90) Group 2(n=42):66 (101); p=0.92	
			Mean (SD) laser time, minutes	**Group1:** 69.8 (31.6) **Group 2:** 55.5 (21) **P=0.008**	
			Mean (SD) catheterisation, days	**Group1:** 2.1 (2.7) **Group 2:** 1.65 (1.6) **P=0.29**	
			Mean (SD) hospital stay, days	**Group1:** 0.87 (0.3) **Group 2:** 0.96 (0.27) **P=0.15**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Number (%) complications	**Intraoperative bleeding** Group1: 0 Group 2: 3 (5.7) **Blood transfusions** Group1: 0 Group 2: 0 **Hematuria** Group1: 1 (1.7) Group 2: 1 (1.9) **Irritative symptoms** Group1: 13 (22.8) Group 2: 10 (19.2) **Re-catheterisation** Group1: 7 (12.2) Group 2: 6 (11.5) **Clot retention** Group1: 1 (1.7) Group 2: 1 (1.9) **Stress incontinence** Group1: 1 (1.7) Group 2: 2 (3.8) **Urge incontinence** Group1: 4 (7) Group 2: 3 (5.7) **Urinary tract infection** Group1: 3 (5.3) Group 2: 2 (3.8)	
			Number (%) late postoperative complications	**Urethral stricture** Group1: 1 (1.7) Group 2: 3 (5.7) **BNC** Group1: 2 (3.5) Group 2: 4 (7.7) **Reoperation** Group1: 2 (3.5) Group 2: 1 (1.9)	
			Mean prostate volume	Group1: 19.8	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			(cc) at 6 months	Group 2: 24.4; p=NS	

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1 **Evidence Table 34: Transurethral microwave thermotherapy (TUMT) vs. no treatment**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Abbou et al., 1995[3] **Study design:** Randomised controlled trial **Setting:** France **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Men recruited from 7 urological departments with symptomatic prostatism that had voiding disorders for at least 3 months. **Inclusion criteria:** Men >50 years, peak flow rate <15mL/s for a voided volume of ≥150mL; and residual urine <300mL/s. No suspicion of prostate cancer, prostate weight between 30 and 80g; PSA level < 10ng/mL for a prostatic weight <60g or a PSA level <15ng/mL for a prostatic weight ≥60g; serum creatinine level <160mol/L; no infection. **Exclusion criteria:** undergone previous surgery on the prostate or bladder; mental incapacity; any chronic disease potentially hindering follow-up; diabetes; participation in any clinical protocol within at least 3 months; any other urological disease; any medical treatment of voiding disorders within 15 days of inclusion; taken diuretics in the previous 3 months; anticoagulant therapy; allergy to lidocaine or colorectal disease. **<u>All patients</u>** **N:** 200 (includes transrectal arms) **<u>Group 1</u>** **N:** 66 Mean (±SD) Age: 65 (8) Mean (±SD) prostate weight: 45g (15) Dropouts: 17% (complementary medical or surgical treatment for worsening obstructive	**Group 1: Transurethral hyperthermia (TUMT)** Three devices used for transurethral treatment (Thermex II, Technorex, Israel; Prostcare, Brucker Spectrospin, France; BSD-50, BSD medical Corp, USA). Prostate temperature was monitored by an integrated microwave generator and controlled each device through a fibre-optic temperature monitor. One session given that lasted between1-3 hours depending on the device used. Deliver a temperature compatible with hyperthermia treatment (45˚C). **Group 2: SHAM** Single session with the temperature maintained at 37˚C.	**Number (%) of complications during treatment**	**Urethral bleeding:** Group1: 2 (3) Group 2: 0 **Urethral pain** Group1: 1 (1.5) Group 2: 0 **Acute retention:** Group1: 1 (1.5) Group 2: 0	**Funding:** Grant from Comite d'Evaluation et de Diffusion des Innovations Technologiques (CEDIT). Assitance Publique – Hopitaux de Paris. Devices were lent by the following companies: Biodan, Brucker, BSD, Direc and Tecnomatrix. **Limitations:** Unclear if allocation concealment used. All withdrawals included in the analysis as non-responders, except for two patients who excluded for reasons unrelated to treatment. **Additional outcomes:** Study randomised patients to transrectal hyperthermia and transrectal sham arm but results not reported. **Notes:** * responder defined as patients showing excellent, good or moderate responses according to each of the criteria analysed separately
			Number (%) of early post-treatment complications	**Urethral bleeding:** Group1: 18 (27) Group 2: 9 (29) **Cystitis** Group1: 12 (18) Group 2: 6 (19) **Acute retention:** Group1: 0 Group 2: 0 **Urinary tract infection:** Group1: 0 Group 2: 1 (3) **Prostatistis** Group1: 1 (1.5) Group 2: 1 (3) **Other:** Group 1: 4 (6) Group 2: 0	
			% Objective response rates (PFR)*	**Group1 (n=66) :** 14 **Group 2 (n=29):** 17	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	symptoms; one lost to follow-up and 1 withdrew during treatment) **<u>Group 2</u>** **N:** 31 Mean (±SD) Age: 66 (7) Mean (±SD) prostate weight: 44g (11) Dropouts:38% (complementary medical or surgical treatment for worsening obstructive symptoms; one lost to follow-up)		**% Subjective response (Madsen score)***	**Group1 (n=66):** 50 **Group 2 (n=29):** 17 P<0.05	(Madsen decrease >30%; a PFR>10mL/s with a PFR increase>30%) Non responders were patients who withdrew during treatment (because of complications complementary treatment or refusal to continue) and patients who had a Madsen score decrease <30%, PFR<10mL/s or a PFR>10mL/s but with an increase <30%.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Albala et al., 2002[12] **Study design:** Randomised controlled study **Setting:** US **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Male patients between 50-80 years old with a diagnosis of symptomatic BPH to a sufficient degree that treatment was warranted. **Inclusion criteria**: AUA symptom index > 13 and a bother score >11. Peak flow rates were <12mL/s and the post voiding residual volume was <125mL. Prostate volume between 30-100cc without a significant intravesical middle lobe. **All patients** **N:** 200 **Group 1** **N:** 125 Mean (±SD) Age: 65.2 (7.3) Mean (±SD) volume: 50.5 (18.6) cc Dropouts: NR Number reporting AUA scores indicates that was 6 drop outs at 12 months. Complications reported for 121 out of 125 randomised patients. **Group 2** **N:** 65 Mean (±SD) Age: 64.6 (7.1) Mean (±SD) volume: 47.1 (17.9) cc Dropouts: NR Complications reported for 62 of 65 patients.	Performed in urology offices or clinics. **Group 1: TUMT** TherMatrx TMx-2000 that directly heats the transition zone to greater than 50 degrees C. 60-90W. Toradol, narcotic analgesic and lorazepam were given orally 45 minutes before treatment. Prior to catheter insertion lidocaine jelly injected into the urethra and allowed to remain in place for 15 minutes. Treatment temperature delivered to peak tissue temperature of 50 to 55˚C. After temperature had increased to 50 degrees the treatment was continued for 40 minutes under computer control. Foley catheter inserted into bladder following treatment and left in place from 2 to 4 days. **Group 2: SHAM** Placement of the microwave catheter for the treatment period without energy delivery and received the same post treatment care as the active treatment patients.	**AUA symptom index (SI)**	**Baseline:** Group1 (n=125): 22.5 Group 2 (n=65): 22.8 **3 months:** Group1 (n=124): 12.4 Group 2 (n=NR): 17 **6 months:** Group1 (n=115): 12.1 Group 2 : NR **12 months:** Group1 (n=119): 11.9 Group 2: NR	**Funding:** NR **Limitations:** Symptom scores only reported fro TUMT arm for 6 and 12 months. **Additional outcomes:** Bother and quality of life scores reported but only for the treatment arm. **Notes:** Patients were unblended at 3 months and sham treated patients offered options of having active treatment. Results for treatment arm only includes patients randomised to active treatment and not those that crossed over at 3 months (intention to treat analysis used).
			AUASI Change (12 months)	Group1: -10.6 (-47.1%) Group 2: NR	
			PFR change, mL/sec (12months)	Group1: +5.0 (58.1%) Group 2: NR	
			Number of complications	**Recatheterisation** Group 1: 20/121 (16.8%) Group 2: 0/62 (0%) **Dysuria** Group 1: 8/121 (6.6%) Group 2: 3/62 (4.8%) **Urgency** Group 1: 0/121 (0%) Group 2: 0/62 (0%) **Gross haematuria** Group 1: 11/121 (9.1%) Group 2: 0/62 (0%) **Bladder spasm** Group 1: 5/121 (4.1%) Group 2: 0/62 (0%) **Urethral stricture** Group 1: 0/121 (0%) Group 2: 0/62 (0%) **Ejaculatory dysfunction pain** Group 1: 0/121 (0%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group 2: 0/62 (0%) **Rectal damage fistula** Group 1: 0/121 (0%) Group 2: 0/62 (0%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Bdesha et al., 1994[26] **Study design:** RCT **Setting:** UK **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** patients with significant symptoms of prostatism and unequivocally benign glands recruited. **Inclusion criteria:** symptoms of prostatism at least 6 months in duration, symptom score >10, peak flow rate of <15ml/s and/or residual urine volume of greater than 50ml. **Exclusion criteria:** upper tract dilatation, impaired renal function, acute urinary retention, residual urine volume >200ml, prostatic malignancy, significant middle lobe hypertrophy, large gland, coexisting urinary tract pathological condition or previous prostatic surgery. **<u>All patients</u>** **N:** 42 **<u>Group 1</u>** **N:** 22 Mean Age: 63.7 years Drop outs: 0 **<u>Group 2</u>** **N:** 18 Mean Age: 62.6 years Drop outs: 2 lost to follow-up	Dedicated day care unit. Anaesthetised with topical lidocaine gel and a catheter passed to empty the bladder. Balloon inflated and the catheter pulled back to position the microwave antenna accurately within the prostatic urethra. Rectal temperature monitoring probe was placed the microwave catheter was connected to the microwave device. LEO Microthermer used and delivers a maximum power output of 20W at 915MHz and automatic power cut-off when rectal temperature increases to greater than 42.5˚C. Heated pad placed across lower abdomen of all patients to minimise speculation of which treatment arm patients were in. **Group 1: TUMT** Single active 90 minute treatment **Group 2: SHAM** Sham treatment for the same time when no power was delivered.	**Mean [SD] (95% CI) AUA symptom scores at 3 months**	**Baseline:** Group1: 19.2 (16.3-22.1) Group 2: 18.8 (16.0-21.7) **3 months:** Group1: 7.1 [5.00] (5.0-9.2) Group 2: 16.2 [7.35] (12.8-19.6)	**Funding:** NR **Limitations:** Randomisation method unclear. **Additional outcomes:** Reported results of sham patients that went onto have active treatment. Scores for force of stream, hesitancy, intermittent voiding and incomplete voiding. **Notes:** SD reported from HTA report. Patients in the sham arm that showed no improvement after 3 months were offered the active treatment. One patient had sham treatment for 3 months and then retreated with active treatment and subsequently had urinary retention followed by reoperation of transurethral prostatectomy.
			Mean (95% CI) peak flow rate (ml/s)	**Baseline:** Group1: 12.3 (10.7-13.9) Group 2: 10.8 (9.2-12.4) **3 months:** Group1: 14.6 [5.98] (12.1-17.1 Group 2: 9.8 [2.81] (8.5-11.1)	
			Mean (95% CI) Residual volume, ml	**Baseline:** Group1: 104 (85-125) Group 2: 80 (57-103) **3 months:** Group1: 52 (34-70) Group 2: 94 (71-117)	
			Mean (95% CI) number of daytime voids (frequency)	**Baseline** Group1: 9.4 (7.3-11.4) Group 2: 7.4 (5.4-9.4) **3 months:** Group1: 5.5 (4.4-6.5) Group 2: 7.4 (5.9-8.9)	
			Mean (95% CI) number of voids (nocturia)	**Baseline** Group1: 3.5 (2.5-4.4) Group 2: 3.5 (2.5-4.6) **3 months:** Group1: 1.6 (0.9-2.3) Group 2: 3.3 (2.9-3.7)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Mean (95% CI) urgency	**Baseline** Group1: 3.5 (2.8-4.2) Group 2: 2.8 (1.6-3.1) **3 months:** Group1: 1.1 (0.5-1.8) Group 2: 1.6 (0.9-2.5)	
			Retrograde ejaculation (new cases) * number with antegrade ejaculation preoperatively not reported	**Group 1:** 0/NR **Group 2:** 0/NR	
			% correctly guesses which treatment arm they were in	**Group 1: 86%** **Group 2: 50%**	
			Successful outcomes (defined as a decrease in symptom scores with greater than a 50% decrease) at 3 months	**Group 1:** 18/22 **Group 2:** 2/20	
			Reoperation (at 3 months patients in sham arm offered active treatment)	**Group 1:** 0/22 **Group 2:** 16/20	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Blute et al., 1996[31] **Study design:** RCT **Setting:** US **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** patients with symptomatic BPH. **Inclusion criteria**: peak urine flow rate<10ml/s; residual volume 100-200ml; Madsen score>8; prostate length 35-50 mm from TRUS. **Exclusion criteria:** Prostate cancer; transurethral or rectal surgery ; urinary retention; any medications that affect prostate symptoms; antiandrogen therapy; upper UT pathology shown by ultrasound; metallic implants; symptoms suggesting neuropathological bladder; serum creatinine>2mg/dl; bladder stones; uncontrolled dysrhythmias or cardiac pacemaker; asymmetric median lobe enlargement; patients at high risk from prostatic disease. **<u>All patients</u>** **N:** 115 **Drop outs:** NR **<u>Group 1</u>** **N:** 78 Mean (±SD) Age: 66.9 (7.8) **<u>Group 2</u>** **N:** 37 Mean (±SD) Age: 66.9 (7.1)	Outpatient procedure. Antibodies and nonsteroidal anti-inflammatory agent given before therapy. **Group 1: TUMT** – Prostatron (Prostasoft) Rectal thermometry probe inserted and treatment catheter with Foley balloon located by transabdominal ultrasound and TURS; anaesthesia: 89% had only local anaesthetic (lidocaine), 11% had midaxolam-fentanyl intravenously; blood pressure, pulse and temperature monitored every 15 minutes during treatment; observation for 2 hours. **Group 2: SHAM** No sedation; urethral coolant circulated; NSAIDs given before therapy. Treatment ran for 60 minutes.	**Mean (SD) AUA scores**	**Baseline** Group1 (n=64): 19.7 (7.2) Group 2 (n=31): 21.9 (6.3) **6 weeks:** Group1 (n=59): 12.8 (6.6) Group 2 (n=28): 17.1 (6.9) **3 months:** Group1 (n=64): 11.3 (6.3) Group 2 (n=31): 16.3 (7.6)	**Funding:** NR **Limitations:** Drop outs and reasons not reported. **Additional outcomes:** PSA levels at baseline and at 6 months. Madsen symptom scores reported. **Notes:** Sham group offered active treatment at 3 months. Reported that no sexual dysfunction following procedure but no indication of patients that previously had dysfunction.
			Mean (SD) peak flow rates (mL/s)	**Baseline** Group1 (n=74): 7.2 (1.6) Group 2 (n=34): 7.4 (1.6) **6 weeks:** Group1 (n=72): 10.7 (4.1) Group 2 (n=32): 8.5 (3.7) **3 months:** Group1 (n=74): 11.5 (4.0) Group 2 (n=34):9.4 (3.7)	
			Mean (SD) residual urine by catheter, mL	**Baseline** Group1 (n=71): 140.9 (35.9) Group 2 (n=33): 142.1 (35.5) **3 months:** Group1 (n=71): 145.5 (126.1) Group 2 (n=33):147.2 (107.7)	
			Number (%) of improved symptoms assessed by the patient at 3 months	**Any positive change** Group1: 60/75 (80%) Group 2: 11/37 (29.7%) **No change** Group 1:12/75 (16.0%) Group 2: 23/37 (62.2%) **Uncertain** Group 1: 3/75 (4.0%) Group 2: 3/37 (8.1%)	
			Number (%) of improved symptoms assessed by the	**Any positive change** Group1: 63/75 (84%) Group 2: 13/37 (35.1%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			physician at 3 months	**No change** Group 1:8/75 (10.7%) Group 2: 23/37 (62.2%) **Uncertain** Group 1: 4/75 (5.3%) Group 2: 1/37 (2.7%)	
			Number (%) complications at 3 months	**Haematuria:** Group 1: 54/78 (69.2%) Group 2: 19/37 (51.3%) **Urethral bleeding** Group 1:16/78 (20.5%) Group 2: 5/37 (13.5%) **Urethral discharge** Group 1:2/78 (2.6%) Group 2:0 **Urinary retention** Group 1:20/78 (25.6%) Group 2:0 **Other urinary tract** Group 1:11/78 (14.1%) Group 2: 4/37 (10.8%) **Reproductive** (including genital dermatology) Group 1: 8/78 (10.3%) Group 2: 0 **Rectal** (including proctoscopy findings) Group 1: 4/78 (5.1%) Group 2: 4/37 (10.8%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Brehmer et al., 1999[34] **Study design:** RCT **Setting:** Sweden **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Men with LUTS dominated by hesitancy, slow urination and an enlarged prostate. **Inclusion criteria**: maximum flow rate of <12mL/s **Exclusion criteria:** indwelling catheter, median prostatic lobe, a prostate gland estimated as >50g, suspected prostatic malignancy, neurological disease and previous surgery for prostatic disease. **<u>All patients</u>** **N:** 44 Mean age (range): 70.4 (53-83) **Drop outs:** 2 **<u>Group 1</u>** **N:** 14 Dropouts: 1 (withdrew as had repeated transient ischaemic attacks and developed early dementia **<u>Group 2</u>** **N:** 16 Dropouts: 0 **<u>Group 3</u>** **N:** 14	An ECP system (Comair, Sweden) equipped with a 22F catheter with a microwave antenna (915MHz), a fibre-optic system for measuring the temperature in the urethra and, by a rectal probe in the rectum. The two-way urethral catheter has a circulation cooling system that reduces the heat delivered to the urethral wall. Maximum heating is achieved within 30s and the temperature limit is 46 degrees in the urethral and 43 in the rectum. If unable to void a urethral catheter inserted and left in place for 3 days. All patients received antibiotics for 5 days. **Group 1:** TUMT for 30 minutes **Group 2:** TUMT for 60 minutes **Group 3:** SHAM Only water at 20˚ was circulated in the treatment catheter and a computer monitor, visible to the patient, showed a simulated heat treatment curve, similar to that	**Qmax, mL/s**	**Baseline:** Group1: 8.7 Group 2: 7.0 Group 3: 7.9 **4 months:** Group1: 12.3 Group 2: 9.9 Group 3: 8.3	**Funding:** NR **Limitations:** Method of randomisation, allocation concealment unclear. Baseline urodynamic scores similar between groups but A scores were significantly higher in the 30 minute TUMT group (Group 1). Complications reported as whole rather than by group. **Additional outcomes:** Frequency and timed void before and after treatment. % improved in different variables reported (but actual figures reported in full). **Notes:** ICS score defined as a Questionnaire with 32 questions (A questions about symptoms and B question about the bother related to the symptom. Maximum A and B scores are 124 and 92 respectively. High score
			Treatment failure	**Group1& 2:** 5/30 (17%) **Group 3:** 7/14	
			Reoperation	**Group1:** 0/14 **Group 2:** 3/16 **Group 3:** 7/14	
			ICS A score (with % decrease) * See notes for definition of score	**Before** Group1: 58 Group 2: 49 Group 3:46 **4 months:** Group1: 44 (25) Group 2: 41 (16) Group 3: 44 (4)	
			ICS B score (with % decrease) * See notes for definition of score	**Before** Group1: 40 Group 2: 36 Group 3: 36 **4 months:** Group1: 30 (34) Group 2: 30 (17) Group 3: 31 (14)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Dropouts: 1 (prostatic carcinoma)	produced during TUMT.	% **improvement using quality of life score** (from ICS questionnaire last question - with 7 points indicating worst situation possible)	**Group 1: 25%** **Group 2: 4%** **Group 3: 0%**	indicates worse symptoms.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Dewildt et al., 1996[67] Links with Delarosette 1994[64] and Francisca 1997[95] **Study design:** Randomised controlled trial **Setting:** 2 centres – London and Nijmegen, Netherlands **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** From June 1991 to December 1992 patients recruited. **Inclusion criteria:** >45 years; complaining of symptoms of bladder outlet obstruction for >3 months, have a Madsen symptom score of >8 and urinary free-flow rate estimates of <15 mL/s during two voids of >150mL. **Exclusion criteria:** prostate caner, prostatitis, urethral stricture, intravesical pathology, neurogenic bladder dysfunction UTI, isolated enlargement of the middle lobe, a residual urine volume of ≥300mL, use of drugs influencing bladder or prostate function, previous transurethral resection of the prostate or transurethral incision, a metallic pelvic implant, disorders of blood flow or coagulation, diabetes, mental incapacity or inability to give informed consent. **All patients N:** 93 **Group 1** **N:** 47 Mean (±SD) Age: 66.3 (8.1) Dropouts: 2 (had TURP) At 12 months: 14 (TURP=4, Lost to follow-up5, second TUMT=4, death (not related to treatment)=1) **Group 2** **N:** 46 Mean (±SD) Age: 63.9 (6.0) Drop outs: 3 (lost to follow up=2, technical failure=1) At 12 months: 33 (5 lost to follow up, technical failure=1 and 27 had TUMT at 3 months)	**Group 1: TUMT** Transurethral thermotherapy Prostatron, Prostasoft 2.0 **Group 2: SHAM** Procedure simulated but without applying microwave energy. Real time treatment profile displayed on the computer screen as done in active treatment and explained to the patient. Sequence of temperature, calibration and checks were identical in both groups.	**Mean (95% CI) of Madsen symptom score**	**Baseline** Group1: 13.7 (12.7-14.7) Group 2: 12.9 (11.9-13.9) **3 months** Group1: 4.7 (3.6-5.9) Group 2: 10.4 (8.9-11.8) **12 months** Group1: 4.2 (3.0-5.3) Group 2: 8.2 (5.5-11.0)	**Funding:** NR **Limitations:** Method of randomisation and use of allocation concealment are unclear. Some significant baseline differences between the two centre. London centre had significantly older patients, more obstructive symptoms and greater residual volume. **Additional outcomes:** Reports results for SHAM group when they have had an active treatment as 3 months following no improvement. Voided fraction reported. **Notes:** When patients had no improvement after 3 months, whether he had received sham or active treatment, a second genuine TUMT was performed on request.
			Mean (95% CI) of peak flow rate, mL./s	**Baseline** Group1: 9.2 (8.4-9.9) Group 2: 9.6 (8.8-10.4) **3 months** Group1: 13.4 [6.16] (11.7-15.3) Group 2: 9.7 [3.30] (11.7-15.3) **12 months** Group1: 13.4 [5.13] (11.6-15.1) Group 2: 10.5 [4.79] (7.9-13.1)	
			Mean (95% CI) of post void residual urine, mL	**Baseline** Group1: 93.9 (71.8-116.0) Group 2: 84.7 (64-105.1) **3 months** Group1: 34.2 (19.4-46.8) Group 2: 104.1 (74.7-133.4) **12 months** Group1: 49.72 (33-66.3) Group 2: 56.3 (16.9-95.7)	
			Mortality	**Group1:** 1/47 **Group 2:** 0/46	
			Retention	**Group 1:** 10/47 **Group 2:** 1/46	
			Reoperation	**Group 1:** 8/47 **Group 2:** 27/46	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Larson et al., 1998[159] **Study design:** RCT **Setting:** 5 centres in US. **Evidence level:** 1+ **Duration of follow-up:** 6 months.	**Patient group:** symptomatic BPH patients enrolled between September 1994 and June 1996 **Inclusion criteria:** Qmax ≤12mL/s with voided volume ≥12mL/s with voided volume ≥25mL., AUA symptom score ≥9, 3-5cm preprostatic urethral length as determined by cystocscopy or TURS, No disproportionally enlarged or prominent prostatic median lobe on cystoscopy, life expectancy ≥1year. **Exclusion criteria:** UTI within 1 week of study enrolment, gross hematuria, acute urinary retention, prostate weight>100g, concomitant medications, use of alpha antagonists or antiandrogens, coexisting disease that could mimic obstructive bladder neck syndrome, coexisting illness or specific obstructive symptoms caused by neurogenic bladder; bladder stones, renal failure, cardiac failure, prostate cancer, urethral stricture, sever bladder neck contracture, bladder cancer, urinary sphincter abnormalities, prostatitis or hepatic failure. Continuous or intermittent urinary catheterisation within 2 weeks or study, previous prostate surgery	**Group 1:TUMT** Urologix Targis system used. Microwave energy for one hour. Outpatient setting without anaesthesiologist or anaesthetist. The catheter provides urethral cooling via circumferential cooking compartments and monitors temperatures. The thermoablation system automatically interrupts microwave power if urethral temperatures reach 44.5˚C or higher or rectal temperatures over 42.5. Topical ligocaine anaesthesia used for catheterisation. Microwave power applied in increments to achieve target temperature of 40 degrees. Treatment administered for one hour. Given 3 day prescription of prophylactic oral antibiotics and catheterisation for 36 to 60 hours. **Group 2: SHAM** Underwent procedures identical to those in active arm but the microwave energy not applied. Coolant temperature was increased in increments from 8 to 20˚ over the same time period as microwave power was increased in active group. Given 3 day prescription of	**Mean (SD) / [range] symptom score (AUA)**	**Baseline:** Group1 (n=124): 20.8 [19.8-21.9] Group 2 (n=42): 21.3 [19.3-23.3] **3 months:** Group1 (n=123): 9.60 (5.94) Group 2 (n=40): 14.50 (6.77) **6 months:** Group1 (n=120): 10.50 (7.26) Group 2 (n=35): 14.30 (6.34)	**Funding:** Supported by a grant from Urologix, Inc. **Limitations:** Method of randomisation and whether allocation concealment used were not reported. One enrolee who had been assigned to the sham group was inadvertently made aware of his group assignment and consequently this patient's schedule study treatment was cancelled. Prostate volume 17% greater in sham group at baseline. **Additional outcomes:** PSA levels before and after treatment. 6 week results for symptom score and Qmax. Prostate volume reported but only for active group. **Notes:**
			Mean (SD) / [range] Qmax	**Baseline:** Group1 (n=106): 7.8 [7.4-8.2] Group 2 (n=39): 7.8 [7.00-8.6] **3 months:** Group1 (n=102): 11.70 (5.41) Group 2 (n=37): 9.20 (3.72) **6 months:** Group1 (n=101): 11.80 (5.89) Group 2 (n=31): 9.80 (4.00)	
			Mean [range] post void residual, mL	**Baseline:** Group1 (n=105): 99.1 [82.0-116.1] Group 2 (n=39): 103.6 [79.4-127.8] **3 months:** Group1 (n=103): 68.4 [52.9-83.8] Group 2 (n=37): 93.0 [57.6-128.4] **6 months:** Group1 (n=101): 84.5 [67.8-101.2] Group 2 (n=31): 84.4 [58.3-110.6]	
			Quality of life score (SD) evaluated by patient responses to the question of how they would feel if their current urinary symptoms were to continue indefinitely	**Baseline:** Group1 (n=120): 4.2 (95% CI: 4.0-4.4) Group 2 (n=35): 4.0 (95% CI: 3.6-4.3) **6 months:** Group1 (n=120): 2.20 (1.40) Group 2 (n=35): 2.90 (1.20)	
			Complications	**Blood transfusions**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	or non medical treatment for BPH , penile implant or artificial urinary sphincter, previous pelvic or rectal surgery, metallic implants in the pelvic area, cardiac pacemaker, desire for future offspring, likely non compliance. **<u>All patients</u>** **N:** 169 Mean age: 45-85 years **Drop outs:** **<u>Group 1</u>** **N:** 125 Mean (range) Age: 66.0 (64.7-67.4) Dropouts: 5 (prostate cancer=2, need for further treatment for BPH=2, died of unrelated causes=1) **<u>Group 2</u>** **N:** 44 Mean (range) Age: 65.9 (63.4-68.3) Dropouts: 9 (study procedure cancelled=1, missed prostatitis at screening=1, need for further treatment for BPH=7)	prophylactic oral antibiotics and catheterisation for 36 to 60 hours.		Group1: 0/125 Group 2: 0/44 **Urinary retention** Group1: 10/125 Group 2: 1/44 **Urinary tract infection** Group1: 11/125 Group 2: 2/44 **Stricture** Group1: 3/125 Group 2: 0/44 **Urinary incontinence** Group1: 5/125 Group 2: 0/44 **Reoperation** Group1: 2/125 Group 2: 27/44 **Ejaculatory disorders:** Group 1: 5/125 Group 2: 0/44 **Mortality:** Group 1: 1/125 Group 2: 0/44	SD for Qmax and symptom scores was calculated in HTA report. After 6 months follow up continued on unblinded basis, with follow up to one year by mail in questionnaire only. After 6 months evaluation sham group patients could elect to undergo microwave or other treatment for BPH.
			Number (%) that correctly identified intervention received	**Group1:** 100/112 (90%) **Group 2:** 21/37 (50%)	
			Number of patients experiencing discomfort during the procedure	**None or mild:** Group 1: 65/125 (52.0%) Group 2: 37/42 (88.1%) **Moderate:** Group 1: 57/125 (45.6%) Group 2: 5/42 (11.9%) **Severe** Group 1: 3/125 (2.4%) Group 2: 0/42 (0%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Nawrocki et al., 1997[218] **Study design:** Randomised controlled trial. **Setting:** UK **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** men with symptoms associated with bladder outlet obstruction and BPH. **Inclusion criteria:** symptoms of lower urinary tract dysfunction thought to e due to benign enlargement of the prostate meriting surgical treatment, Qmax<15mL/s and voided volume 150mL or more, Pdet max of 70cmH2O or more. **Exclusion criteria:** Complications of bladder outlet obstruction (retention, residual urine volume >350mL, renal failure, recurrent urinary tract infection, bladder calculus, bladder diverticulum); suspicion of malignancy, short prostate, presence of a prominent middle lobe projecting asymmetrically into the bladder, presence of a urethral stricture, previous prostate or pelvic surgery or radiotherapy, presence of metal within the lower trunk or upper legs, uncontrolled cardiac dysrythmias or presence of a cardiac pacemaker, neurological disorders, inability to understand treatment procedure, presence of other treatment which may affect LUT function. **All patients** **N:** 120 Median age: 70 (56-80) years **Drop outs:** NR (only that urodynamic data incomplete in 4 patients). **Group 1** **N:** 38 **Group 2** **N:** 40 **Group 3** **N:** 42	**Group 1: TUMT** Prostasoft v 2.0. 1 hour treatment with microwaves performed with the patient under local anaesthesia and as an out-patient. **Group 2: SHAM** Simulated TUMT with identical procedure as active treatment but treatment device emitted no microwaves during the procedure. The machine noise, treatment duration and graphical computer display were all simulated by placebo software on disk. Heat simulated using a heat pad. **Group 3:** No treatment	**Median (range) AUA symptom score:**	**Baseline:** Group1: 19 (7-31) Group 2: 17.5 (7-28) Group 3: 18 (10-29) **6 months:** Group1: 9.5 (1-27) Group 2: 9.5 (0-30) Group 3: 17 (4-28)	**Funding:** Research was in part supported by a LORS grant from the South East Thames Regional Research Committee. This work in part contributed to the award of an MS thesis from University of London. **Limitations:** Allocation concealment use was unclear and drop outs not reported. **Additional outcomes:** Minimum urethral opening pressure, maximum detrusor pressure, voided volume, detrusor instability, functional bladder capacity. **Notes:** Active and sham arms included in the meta-analysis. 37% judged that they knew which treatment that they had. Of which 59% were correct. Operators judged correctly 68% of time.
			Mean (SD) Qmax, mL/s	**Baseline:** Group1: 8.83 (2.32) Group 2: 9.44 (2.78) Group 3: 8.79(2.66) **6 months:** Group1: 9.94 (3.08) Group 2: 9.49 (2.88) Group 3: 8.47 (1.92)	
			Mean (SD) residual urine volume, mL	**Baseline:** Group1: 85.7 (56.6) Group 2: 96.5 (56.3) Group 3: 86.0 (62.7) **6 months:** Group1: 85.8 (51.2) Group 2: 106.3 (84.5) Group 3: 82.7 (52.7)	
			Mean (SD) prostate volume, mL	**Baseline:** Group1: 41.2 (14.6) Group 2: 46.7 (16.8) Group 3: 46.4 (19.9) **6 months:** Group1: 45.6 (17.6) Group 2: 48.9 (19.7) Group 3: 45.2 (17.9)	
			Urinary retention	Group 1: 4/38 (10.5%) Group 2: 0/40	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Ogden et al., 1993[232] (abstract only but data extracted in HTA systematic review) **Study design:** Randomised controlled trial. **Setting:** UK **Evidence level:** Abstract only **Duration of follow-up:** 3 months	**Patient group:** Recruitment dates from September 1991. **Inclusion criteria:** peak urine flow rate <15ml/s on two occasions; residual volume ≤350ml. Madsen score>8 for 6 months, prostate urethral length 35-50mm. **Exclusion criteria:** prostate cancer from DRE; heat to prostate or pelvic surgery/radiotherapy; urinary retention; alpha blockers within 4 weeks; antiandrogens within 1 year; anything affecting prostate of bladder; prostatitis or UTI; renal dysfunction; peripheral arterial disease; diabetic neuropathy; UT disease; bladder disease; mental incapacity; dementia, inability to give informed consent; neurological disorders affecting bladder function; disorders of blood flow or coagulation; history or uncontrolled cardiac arrhythmias or cardiac pacemaker; metallic pelvic implant; prominent isolated median lobe; intravesical pathology; renal impairment due to chronic retention; urethral stricture inhibiting catheterisation. **<u>All patients</u>** **N:** 43 **<u>Group 1</u>** **N:** 22 Mean (±SD) Age: 68.3 (64.1-72.5) **<u>Group 2</u>** **N:** 21 Mean (±SD) Age: 67.1 (63.7-70.3)	**Group 1: TUMT** Catheter protocol – inserted for retention for one week. **Group 2: SHAM** Catheter protocol – inserted for retention for one week.	**Mean (95% CI) Madsen score**	**Group1:** 14.5 (12.9-16.1) **Group 2:** 14.2 (12.7-15.7)	**Funding:** Unknown **Limitations:** HTA appraisal of study reports unclear method of randomisation and no allocation concealment. Patients blinded but assessors were not. **Additional outcomes:** Voided volume and residual volume reported in the HTA report. **Notes:** If patient saw no improvement in 3 months after sham or TUMT a second TUMT was performed on request.
			Mean (95% CI) Qmax, ml/s	**Baseline:** Group1: 8.5 (7.5-9.5) Group 2: 8.6 (7.6-9.6) **3 months:** Group 1: (n=21) 13.0 (5.84) Group 2: (n=19) 9.2 (4.45)	
			Mean (95% CI) Quality of life score	**Group1:** 13.4 (10.7-16.1) **Group 2:** 13.3 (9.2-17.4)	
			Urinary tract infection	Group 1: 5/22 Group 2: 1/21	
			Urinary retention	Group 1: 5/22 Group 2: 0/21	
			Reoperation	Group 1: 1/22 Group 2: 1/21	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Trachtenberg et al., 1998[296] Linked to Tan 2005 **Study design:** Randomised controlled trial. **Setting:** multicentre, US and Canada **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** Men over 55 years **Inclusion criteria:** AUA >13; peak urinary flow rate <12 ml/s and voided volume >125ml. serum PSA <10ng/ml; prostate volume between 25-100ml; bladder neck to verumontanum distance <30mm. **All patients** **N:** 220 **Group 1** **N:** 147 Mean (rang)) Age: 66.2 (54.4-82.7) Dropouts: between 2-5 **Group 2** **N:** 73 Mean (range) Age: 66.0 (55.1-78.1) Dropouts: 3	**Group 1: TUMT** Dornier Urowave used which operates at 915MHz. Generator capable of delivering up to 90W of power. Safety threshold set at 50˚C in the urethra and 42.5˚C in the rectum. Outpatient procedure without general anaesthesia. Peri-treatment antibiotic prophylaxis at the investigators choice. Following treatment a Foley catheter was inserted and left indwelling for 2-5 days. **Group 2: SHAM** 60minute pre-programmed treatment cycle without the application of power.	**Mean (range) AUA symptom score**	**Baseline:** Group1: 23.6 [5.6] (12-35) Group 2: 23.9 [5.6] (13-35) **3 months:** Group1: 11.6 Group 2: 16.4 **6 months:** Group1: 12.6 Group 2: 17.9	**Funding:** NR **Limitations:** Randomisation method unclear and reason for dropouts not reported. Results report one stricture in the active treatment compared to none in the sham arm. Conversely, the conclusion reports no strictures in the study so have excluded this outcome. **Additional outcomes:** Prostate volume and PSA baseline scores. Quality of life question (0-6) but only reported figures for baseline scores. **Notes:** At 6 months follow-up patients on sham treatments were offered active treatment.
			Mean (range) AUA bother score	**Baseline:** Group1: 18.5 (0-28) Group 2: 18.6 (0-28) **6 months:** Group1: 8.7 Group 2: 12.6	
			Mean peak flow, ml/s	**Baseline:** Group1: 7.7 (3.5-11.5) Group 2: 8.1 (4.0-11.9) **3 months:** Group1: 11.0 Group 2: 9.7 **6 months:** Group1: 10.6 Group 2: 9.6	
			Complications	**Pain** Group 1: 80% Group 2:56% **Occurrences ejaculatory dysfunction** Group 1: 30/147 Group 2: 1/73 **Irritative voiding:** Group 1: 21/147 Group 2: 4/73 **haematuria** Group 1: 19/147 Group 2: 1/73	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				UTI Group 1: 11/147 Group 2: 2/73 **Urinary retention:** Group 1: 8/147 Group 2: 0/73 **Scrotal abscess** Group 1: 6/147 Group 2: 1/73 **Rectal disorder:** Group 1: 8/147 Group 2: 2/73 **Pelvic pain:** Group 1: 5/147 Group 2: 1/73 **Penile disorder:** Group 1: 5/147 Group 2: 0/73 **Urinary incontinence** Group 1:0/147 Group 2: 0/73 **Bladder spasm:** Group 1: 1/147 Group 2: 1/73 **Split urinary stream:** Group 1: 0/147 Group 2: 1/73	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Zerbib et al., 1994[331] **Study design:** Randomised controlled study **Setting:** France **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** symptomatic BPH patients. **Inclusion criteria:** candidates for prostatectomy. All had failed one conservative treatment (e.g. alpha-blockers) and the symptoms were of sufficient severity such that prostatectomy was indicated. **Exclusion criteria:** anterior rectal wall thickness>10mm or <2mm; anterior to posterior thickness of prostate >55mm. **<u>All patients</u>** **N:** 68 Mean age: 69.5±10.44 (53-88) **Drop outs:** NR **<u>Group 1</u>** **N:** 38 **<u>Group 2</u>** **N:** 30	**Group 1: TUMT** Prostatic hyperthermia treatments were performed using Prostathermer. Intraprostatic temperature maintained at 43±0.5˚C. 1 hour session per week for 5 consecutive weeks. Outpatient without anaesthesia. **Group 2: SHAM** Intraprostatic temperature maintained at 37±0.5˚C by radiofrequency power. One hour session per week for 5 consecutive weeks.	**Mean (SD) peak flow, ml/s**	**Baseline** Group1: 7.6 (3.8) Group 2: 10.6 (5.8) **3 Months:** Group1: 9.60 (5.80) Group 2: 10.8 (5.4)	**Funding:** NR. **Limitations:** Randomisation method and allocation concealment unclear. Baseline peak flow significantly different between arms. Inclusion and exclusion criteria not defined. No complications reported. **Additional outcomes:** Siroky S.D. and adjusted flow scores. Response rate (objective criteria) reported. **Notes:** 3 month result for peak flow for TUMT group not reported in study – result obtained from HTA report.
			Mean (SD) voided volume, ml	**Baseline** Group1: 151 (92.0) Group 2: 145 (86.3) **3 Months:** Group1: 154 (90) Group 2: 166 (91.3)	
			Mean (SD) Residual volume, ml	**Baseline** Group1: 110 (88.8) Group 2: 84.2 (76.6) **3 Months:** Group1: 67 (101.6) Group 2: 81.2 (66.8)	
			Objective score (simplified version of the Siroky nomogram, lower scores indicates a higher degree of urinary obstruction)	**Baseline** Group1: 17.8 (8.5) Group 2: 24.8 10.3) **3 Months:** Group1: 25.8 (12.0) Group 2: 24.3 (11.8)	
			Subjective score, ranging from 6 (sever disturbance) to 38 (no disturbance)	**Baseline** Group1: 16.7 (7.8) Group 2: 19.4 (8.2) **3 Months:** Group1: 23.0 (10.8) Group 2: 23.6 (7.0)	

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1 **Evidence Table 35: Transurethral microwave thermotherapy (TUMT) vs. transurethral resection of the prostate (TURP)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Ahmed et al., 1997[9] Reported in systematic review HTA 2008 **Study design:** RCT **Setting:** Single centre, UK **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** Patients presenting with symptomatic, uncomplicated BPH. **Inclusion criteria**: residual urine volume ≤300 ml; AUA score ≥ 12; urine flow rate< 15ml/s, prostate volume 25-100ml by TRUS; symptomatic uncomplicated BPH > 1 year; pdet max>70cm H2O; informed consent; obstructed on Abrams-Griffith nomogram; suitable for either treatment. **Exclusion criteria:** <55years; prostate cancer; previous prostatic surgery; acute or chronic retention; mental incapacity; severe cardiovascular disease; rectal surgery or disease; pelvic mass surgery; cardiac pace marker; metallic implants; uncontrolled coagulation disorder; meatal stricture; upper tract dilation; obstructive uropathy; bladder calculi; bladder diverticuli; recurrent prostatic haematuria; active drugs; previous medication for BPH; prostatic abscess; active UTI; recurrent UTI; prominent middle lobe. **<u>Group 1</u>** **N:** 30 Mean (range) age: 69.36 (56-88) Mean AUA score (95% CI): 18.5 (17.1-20.1) Dropouts: 0 **<u>Group 2</u>** **N:** 30 Mean (range) age: 69.45 (58-82) Mean AUA score (95% CI): 18.4 (16.7-20.1) Dropouts: 0	**Group 1: TUMT** With urethral cooling in a high energy protocol (Prostratron version 2.5). Temperature 43.5 degrees, power at 70W. 60 minute session under topical anaesthesia with instillagel. 3 required parenteral pethidine. Antibiotics: gentamycin (80mg) before treatment and oral trimethoprim, 200mg, 2 times day for 5 days. **Group 2: TURP** No post operative irrigation was used. Urethral catheter was removed 3 or 4 days after surgery.	**Mean (range) [SD] AUA symptom scores:**	**Baseline:** Group1: 18.5 (17.1-20.1) Group 2: 18.4 (16.7-20.1) **6 months:** Group1: 5.3 (3.9-6.4) [3.5] Group 2: 5.2 (3.9-6.5) [3.6]	**Funding:** NR **Limitations:** 3 drop outs after randomisation were substituted. One emigrated to Australia; one developed severe UTI requiring hospital admission and one patient could not be catheterised with the treatment catheter. Method of randomisation and use of blinding unclear. **Additional outcomes:** None **Notes:** Urodynamic outcomes improved in TURP group but not after TUMT.
			AUA symptom score decreased > 50%	**Group 1**: 18/30 (60%) **Group 2:** 30/30 (100%)	
			Qmax (mL/s):	**Baseline:** Group1: 10.1 (9.2-10.9) Group 2: 9.5 (8.9-10.1) **6 months:** Group1: 9.1 (8.0-10.2) Group 2: 14.6 (13.4-15.8)	
			Pdet max (cmH20):	**Baseline:** Group1: 98.5 (70.1-116.9) Group 2: 96.7 (85.5-103.9) **6 months:** Group1: 105.6 (73.7-117.5) Group 2: 48.8 (44.3-52.7)	
			PVR (mL):	**Baseline:** Group1: 94.4 (70.0-112.8) Group 2: 109.1 (88.2-130.0) **6 months:** Group1: 104.9 (78.9-130.9) Group 2: 32.5 (22.5-40.5)	
			Prostate volume (mL):	**Baseline:** Group1: 36.6 (31.8-41.4) Group 2: 46.1 (38.1-54.1) **6 months:** Group1: 34.5 (29.7-39.3) Group 2: 25.4 (19.4-31.4)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Blood transfusion:	Group 1: 0/30 Group 2: 4/30	
			Urinary tract infection:	Group 1: 1/30 Group 2: 3/30	
			Strictures:	Group 1: 0/30 Group 2: 1/30	
			Retrograde ejaculation (sexually active men only):	Group 1: 4/18 Group 2: 12/19	
			Hematuria:	Group 1: 1/30 Group 2: 0/30	
			Erectile dysfunction:	Group 1: 0/18 Group 2: 4/19	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Delarosette et al., 2003[65] Reported in systematic review HTA 2008 **Study design:** RCT **Setting:** Netherlands **Evidence level:** 1+ **Duration of follow-up:** Median 33 months.	**Patient group:** From January 1996 to March 1997 patients with LUTS suggestive of BPH were recruited. **Inclusion criteria**: age ≥ 45 years; duration of LUTS ≥ 3 months, prostate volume ≥ 30 mL; urethral length ≥ 25mm; peak urine flow rate ≤ 15ml/s; Residual urine volume ≤ 350 ml; and severe co morbidity. E**xclusion criteria:** acute prostatitis or urinary tract infection; prostate carcinoma; previous prostatic surgery; heart pacemaker; neurological disorders affecting lower urinary tract function; isolate prostate middle lobe protruding in bladder; urethral stricture. **<u>All patients</u>** **N:** 155 **Group 1:** 82 **Group 2**: 73 **Drop outs:** 11 (10 refused and 1 died) – 4 from Group 1 and 7 in Group 2. Not included in the ITT analysis as no follow-up data. **<u>Group 1</u>**	**Group 1: TUMT** Prostatron device and Prostasoft 2.5 software. Administered under local anaesthesia. Outpatient procedure. **Group 2: TURP** Under spinal anaesthesia. Mean in-hospital stay of 5.3 days.	**Mean (SD) symptom score IPSS**	**Baseline:** Group1 (n=78): 20 (6.7) Group 2 (n=66): 20 (6.2) **3months:** Group 1: (n=57): 10.5 (7.9) Group 2 (n=55): 5.3 (5.2) **1 year:** Group1 (n=58): 8.1 (6.0) Group 2 (n=48): 3.2 (3.0) **2 years:** Group1 (n=46): 9.3 (7.3) Group 2 (n=38): 3.7 (4.9) **3 years:** Group1 (n=35): 11.5 (6.4) Group 2 (n=33): 2.6 (2.2)	**Funding:** NR **Limitations:** Method of randomisation, allocation concealment and blinding unclear. **Additional outcomes:** Cost analysis was performed. **Notes:** Links with Francisca 1999, Francisca 2000, Floratos 2001.
			Mean (SD) IPSS Quality of life question	**Baseline:** Group1 (n=78): 4 (0.9) Group 2 (n=66): 4(1.1) **1 year:** Group1 (n=58): 1.9 (1.3) Group 2 (n=48): 0.6 (0.7) **2 years:** Group1 (n=46): 1.9 (1.0) Group 2 (n=38): 0.9 (1.1) **3 years:** Group1 (n=35): 2.3 (1.2) Group 2 (n=33): 0.6 (0.8)	
			Mean (SD) Maximum urinary flow (Qmax, mL/s)	**Baseline:** Group1: 9.2 (3.1) Group 2: 7.8 (2.8) **3 months:** Group1 (n=54): 15.5 (12.1) Group 2 (n=47): 25.0 (7.5) **1 year:** Group1: 14.9 (7.2) Group 2: 23.8 (10.4) **2 years:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 78 Mean (±SD) Age: 67(±8.3) Mean (±SD) IPSS: 20 (±6.7) Dropouts: 23 (5 lost to follow up and 2 died unrelated causes, 16 re-treated by TURP=8, laser prostatectomy=1, cystolithotripsy=2, internal optical urethrotomy=1, TUMT=1, alpha blockers=3). **Group 2** **N:** 66 Mean (±SD) Age: 66 (±8.2) Mean (±SD) IPSS: 20 (±6.3) Dropouts: 21 (11 lost to follow up and 2 died of unrelated causes, 8 retreated by bladder neck incisions=3, internal optical urethrotomy=2, physiotherapy=1, medication=2).			Group1: 13.7 (6.4) Group 2: 22.5 (11.4) **3 years:** Group1: 11.7 (5.8) Group 2: 22.8 (11.6)	
			Mean (SD) post void residual (PVR, mL)	**Baseline:** Group1: 68 (85) Group 2: 97 (99) **I year:** Group1: 55 (69) Group 2: 20 (49) **2 years:** Group1: 91 (116) Group 2: 29 (39) **3 years:** Group1: 94 (114) Group 2: 35 (56)	
			Patients with re-treatment:	**Group1:** 16/78 22.9% (12.5-33.2) **Group 2:** 8/66 13.2 (4.5-21.9), P=0.215	
			Kaplan-Meier risk of retreatment (36 months)	**Group 1:** 22.9 (12.5-33.2)% **Group 2:** 13.2 (4.5-21.9)%, P=0.215	
			Urinary retention:	**Group 1:** 2/78 (3%) **Group 2:** 0/66 (0%)	
			Urinary incontinence:	**Group 1:** 0/78 (0%) **Group 2:** 1/66 (2%)	
			Stricture:	**Group 1:** 1/78 (1%) **Group 2:** 2/66 (3%)	
			Mortality (unrelated causes)	**Group 1:** 2/78 (3%) **Group 2:** 2/66 (3%)	
			Retrograde ejaculation (reported in HTA 2008)	**Group 1:** 24/36 (67%) **Group 2:** 5/42 (12%)	
			Erectile dysfunction	**Group 1:** 7/35 (20%) **Group 2:** 9/53 (17%)	
			Reoperation	**Group 1:** 13/78 (17%) **Group 2:** 5/66 (8%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Mattiasson et al., 2007[186] and Wagrell et al., 2002[312] Reported in systematic review HTA 2008 **Study design:** RCT **Setting:** Sweden, Denmark and USA **Evidence level:** 1+ **Duration of follow-up:** 60 months	**Patient group:** Patients from ten centres in Scandinavia and the United States recruited between October 1998 and November 1999. **Inclusion criteria**: symptomatic BPH, peak urine flow rate ≤ 13ml/s; ml; IPSS score ≥13; prostate volume 30-100ml. **<u>All patients</u>** **N:** 154 eligible Drop outs: 8 withdrawn before treatment **<u>Group 1</u>** **N:** 100 **Mean** (±SD) **Age**: 67 (8) **Mean** (±SD) **IPSS**: 21 (5.4 **Dropouts before intervention**: 3 (screening failures and not treated) **Withdrawn at 12m**: 9 **Withdrawn at 60m**: 38 (adverse events=5, treatment failure=10, patient request=22, other =1) **<u>Group 2</u>** **N:** 46 **Mean** (±SD) **Age**: 69 (8) **Mean** (±SD) **IPSS**: 20.4 (5.9) **Dropouts before intervention**: 5 (screening failures and not treated) **Withdrawn**: 4 Withdrawn at 60m: 12 (reasons: adverse events=4, treatment	**Group 1: TUMT** PLFT technique. Given as outpatient procedure requiring sedo-analgesic with or without local anaesthetic. Diazepam, ketorolac, or ketobemidone or combinations of these. Mean duration of treatment 57 (27-80) minutes. Catheter after treatment: 14±8 days before removal. **Group 2: TURP** Urethral catheter usually removed after 3±4 days.	**Mean (SD) IPSS**	**Baseline:** Group1 (n=99): 21.0 (5.4) Group 2 (=46): 20.4 (5.9) **3 months:** Group1 (n=85): 8.4 (5.5) Group 2 (n=41): 6.7 (4.3) **6 months:** Group1 (n=95): 7.4 (6.2) Group 2 (n=43): 5.9 (5.0) **12 months:** Group1 (n=93): 7.2 (6.2) Group 2 (n=43): 7.1 (6.6) P=0.603 **24 months:** Group1 (n=77): 7.2 (5.9) Group 2 (n=38): 4.6 (4.4) **36 months:** Group 1 (n=68): 8.2 (6.9) Group 2 (n=35): 5.0 (3.9) **48 months:** Group 1: (n=56): 7.1 (5.4) Group 2: (n=30):6.4 (6.6) **60 months:** Group 1 (n=63): 7.4 (4.8) Group 2 (n=34): 6.0 (5.8)	**Funding:** ProstaLund. Authors (Wagrell, Schelin, Larson, Mattiasson) are paid consultants to the sponsor of this study. **Limitations:** Method of randomisation, allocation concealment and blinding not reported. **Additional outcomes:** Detrusor pressure Qmax at 3 and 6 months. **Notes:** % of responders at 12 months defined as those with an IPSS of 7 or less or > 50% gain compared with baseline and/or a Qmax of 15mL/s or greater and/or > 50% gain. Links with Wagrell 2004[313]
			Mean (SD) IPSS Quality of life:	**Baseline:** Group1 (n=99): 4.3 (1.0) Group 2 (n=46): 4.2 (1.1) **3 months:** Group1 (n=84): 1.5 (1.4) Group 2 (n=41): 1.1 (1.6) **6 months:** Group1 (n=93): 1.3 (1.4) Group 2 (n=42): 1.0 (1.5) **12 months:** Group1 (n=93): 1.4 (1.3)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	failure=2, patient request=5 and other=1)			Group 2 (n=43): 1.5 (1.7) **24 months:** Group 1 (n=77): 1.3 (1.2) Group 2 (n=38): 0.9 (1.3) **36 months:** Group 1 (n=68): 1.3 (1.2) Group 2 (n=35): 1.0 (1.4) **48 months:** Group 1: (n=56): 1.2 (1.0) Group 2: (n=30): 1.0 (1.3) **60 months:** Group 1 (n=63): 1.1 (0.9) Group 2 (n=34): 1.1 (1.2)	
			Urinary flow rate (Qmax mL/s):	**Baseline:** Group1 (n=79): 7.6 ± 2.7 Group 2 (n=35): 7.9 ± 2.7 **3 months:** Group1 (n=81): 12.8 ± 6.1 Group 2 (n=41): 14.6 ± 9.0 **6 months:** Group1 (n=91): 13.5 ± 6.1 Group 2 (n=43): 13.8 ± 6.8 **12 months:** Group1 (n=73): 13.3 ± 6.0 Group 2 n=31): 15.2 ± 7.8 **24 months:** Group 1 (n=77): 12.4 ±5.3 Group 2 (n=37): 15.6 ±9.6 **36 months:** Group 1 (n=66): 11.9± 4.9 Group 2 (n=34): 13.5± 7.4 **48 months:** Group1 (n=49): 12.3 ± 5.7 Group 2 (n=30: 14.7 ± 7.57 **60 months:** Group 1 (n=61): 11.4 (4.9) Group 2 (n=32): 13.6 (7.8)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Mean (SD) residual urine in mL	**Baseline:** Group1 (n=99): 106 ± 77 Group 2 (n=45): 94 ± 82 **12 months:** Group1 (n=86): 49 ± 70 Group 2 (n=38): 54 ± 77 **24 months:** Group1 (n=75): 56 (63) Group 2 (n=38): 40 (48) **36 months:** Group1 (n=68): 47 (62) Group 2 (n=34): 54 (118) **48 months:** Group1 (n=55): 60 (59) Group 2 (n=29): 55 (53) **60 months:** Group 1 (n=63): 70 (90) Group 2 (n=32): 51 (45)	
			Reduction in prostate volume (after 12 months):	Group1 (n=16): 30% Group 2 (n=13): 51%	
			Additional BPH treatment (5 year follow-up)	Group 1: 10/100 (10%) Group 2: 2/46 (4.3%)	
			Mortality (27 days after treatment)	Group 1: 0/100 Group 2: 1/46	
			Complications	**Micturition urgency at 12months:** Group 1: 37/100 (37%) Group 2: 6/46 (13%) **Urinary retention:** **0-12 months:** Group 1: 19/100 (19%) Group 2: 6/46 (13%) **12-60 months** Group 1: 2/80 (2.5%) Group 2: 0/39 **Urinary tract infection:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				12 months: Group 1: 18/100 (18%) Group 2: 9/46 (20%) **12-60 months:** Group 1: 0/80 Group 2: 1/39 (2.6%) **Haematuria:** **12 months** Group 1: 13/100 (13%) Group 2: 18/46 (39%) **12-60 months** Group 1: 5/80 (6.3%) Group 2:0 **Erectile dysfunction:** **12 months:** Group 1: 6/100 (6%) Group 2: 5/46 (11%) **12-60 months:** Group 1: 6/80 (7.5%) Group 2: 6/39 (15.4%) **Transient incontinence** **12 months:** Group 1: 3/100 (3%) Group 2: 6/46 (13%) **12-60 months:** Group 1: 1/80 (1.3%) Group 2: 2/39 (5.1%) **TUR syndrome:** Group 1: 0/100 Group 2: 1/46 **Reoperation (up to 60 months):** Group 1: 8/100 Group 2: 1/46	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Dahlstrand et al., 1993[62] Reported in systematic review HTA 2008 **Study design:** RCT **Setting:** Sweden **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Inclusion criteria**: residual urine volume ≤ 350ml; Madsen score ≥ 8; prostate length 35-50mm from TRUS. Qmax <15m/s (twice); BPH; anaesthetic risk group 1-3; obstructive symptoms > 3 months. **Exclusion criteria:** <45 years; suspicion or known prostate cancer or bladder cancer; previous surgery for cancer of prostate or radiotherapy; rectal surgery; prior surgery or heat treatment of BPH; large median lobe; neurogenic bladder disorder; mental incapacity, dementia or inability to give informed consent; neurological disorders that may affect bladder function; peripheral arterial disease; disorder of haemostasis or serum creatinine >2mg/dl; uncontrolled cardiac dysrhythmias, or cardiac pacemaker; total hip replacement or other metallic implants; indwelling or condom catheter; post void residual urine >350ml; urethral stricture; bladder stones; adrenergic blockers antiandrogen medication or other medication that might affect prostate or bladder; bacterial prostatitis or UTI at time of treatment ; prostatic urethral length of >50mm or <35mm by transrectal US; anaesthesia risk category 4 or 5.	**Group 1: TUMT** Prostatron, Power: 60W; Temperature: urethral: 44.5 degrees and rectal 42.5 degrees. If no voiding use indwelling catheter for 3-5 days. No general anaesthesia but intraurethral topical lidocaine HCl jelly 2% and NSAID. Postoperative oral norfloxacin 400mg twice per day for 5 days. Treatment time 60 minutes. **Group 2: TURP** performed by urologists were senior registrar or above. Mean operative time: 60.9 minutes. Hospital stay: 5 ±1.9 days	**Mean (SD) Madsen symptom score**	**Baseline:** Group1 (n=39): 11.2±3.1 Group 2(n=39): 13.3±4.2 **3 months:** Group1(n=37): 2.3±2.7 Group 2(n=39): 1.6±2.5 **6 months:** Group1(n=28): 3.1±3.0 Group 2(n=23): 0.9±1.6 **12 months:** Group1(n=25): 2.7±2.9 Group 2(n=22): 0.9±2.2	**Funding:** NR **Limitations:** Method of randomisation, allocation concealment and blinding not reported. **Additional outcomes:** Maximum capacity change. Additional follow-up 6-8 weeks after surgery. **Notes:** * Catheterisation required but removed within 3-5 days.
			Mean (SD) residual urine volume (ml)	**Baseline:** Group1 (n=39): 105±88 Group 2 (n=40): 116±97 **3 months:** Group1(n=37): 55±51 Group 2(n=39): 31±25 **6 months:** Group1(n=28): 68±69 Group 2(n=24): 17±10 **12 months:** Group1 (n=24): 47±51 Group 2 (n=22): 22±16	
			Mean (SD) maximum flow rate (ml/s)	**Baseline:** Group1 (n=39): 8.0±2.8 Group 2 (n=40): 7.9±3.2 **3 months:** Group1 (n=35): 12.2±4.9 Group 2 (n=37): 18.7±6.0 **6 months:** Group1 (n=32):12.0±4.5 Group 2 (n=24):18.8±5.9 **12 months:** Group1 (n=24): 12.3±4.7 Group 2 (n=22): 17.7±6.5	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	All patients **N:** 79 **Drop outs:** 4 **Group 1** **N:** 39 Mean Age: 68 Prostate volume: 33ml Mean Madsen ±SD: 11.2± 3.1 Dropouts: 0 **Group 2** **N:** 40 **Mean Age**:70 Prostate volume: 37ml Mean Madsen ± SD: 13.3± 4.2 **Dropouts**: 4 (sever hepatitis=1, cancer discovered=2, refusal for TURP=1).		**Reoperation:**	**Group1:** 4/39 (10.2%) **Group 2:** 0/40	
			Re-catheterisation due to unable to void:	**Group1:** 8/39* **Group 2:** 2/40	
			Transient urgency after surgery	**Group 1:** 7/39 **Group 2:** 4/40	
			Transient urinary leakage	**Group 1**: 0/39 **Group 2**: 1/40 (2.5%)	
			Bleeding and rehospitalisation	**Group 1** 0/39 **Group 2:** 3/40	
			Internal urethrotomy due to stricture	**Group 1:** 0/39 **Group 2:** 3/40	
			Urinary tract infections	**Group 1:** 3/39 **Group 2:** 0/40	
			Men with retrograde ejaculation following surgery (previously with antegrade ejaculations)	**Group 1:** 0 **Group 2:** 4/16	
			% Reduction in prostate size (6m)	**Group 1:** 0 **Group 2:** 47	
			Unstable detrusor contractions	**Baseline** Group 1: 6/21 Group 2: 5/13 **After surgery:** Group 1: 8/21 Group 2: 2/13	
			Sexually active men	All men who were sexually active before treatment remained so after.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Dahlstrand et al., 1995[63] Reported in systematic review HTA 2008 **Study design:** RCT **Setting:** Sweden **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Inclusion criteria**: residual urine volume ≤ 350ml; Madsen score ≥ 8; prostate length 35-50mm from TRUS. **Exclusion criteria:** prostate cancer or bladder cancer; previous surgery for cancer of prostate; prior treatment for BPH; indwelling catheter, urethral stricture; large median lobe; neurogenic bladder disorder, metallic hip implant. **<u>All patients</u>** **N:** 72 eligible – 69 randomised **Drop outs:** 10 **<u>Group 1</u>** **N:** 37 Mean Age: 67.9±9 Mean Madsen ± SD: 12.1± 3 Dropouts: 2 (died=1, hernia operation=1) **<u>Group 2</u>** **N:** 32 Mean Age:70±6 Mean Madsen ± SD: 13.6± 3.9 Dropouts: 8 (TURP=2, abroad=1, refused=1, severe pancreatitis=1, neurological disease=1, reoperation with TUMT and then TURP=2)	**Group 1:** TUMT Prostatron (Prostasoft 2.0 software) – 60W. Treatment in single session as outpatient. Intra-urethrally applied lidocaine hydrochloride jelly used. Before treatment patients given indomethacin 50mg and norfloxacin 400mg was given; after treatment indomethacin given twice for one day and norfloxacin 400mg twice daily for 5 days. **Group 2:** TURP by senior registrar grade or above. Mean operation time=48±17 minutes. Mean hospital stay=3.9±1.3 days.	**Madsen symptom score**	**Baseline:** Group1 (n=37): 12.1±3.0 Group 2 (n=32): 13.6±3.9 **3 months:** Group1 (n=36): 2.9±3.0 Group 2 (n=32): 1.7±2.6 **6 months:** Group1 (n=37): 2.6±2.6 Group 2 (n=32): 1.1±1.8 **12 months:** Group1 (n=33): 2.2±2.4 Group 2 (n=31): 0.6±1.4 **24 months:** Group1 (n=31): 2.3±3.0 Group 2 (n=30): 1.2±1.9	**Funding:** NR **Limitations:** Method of randomisation, use of allocation concealment and blinding were not reported. Unsure if same study as Dahlstrand 1993 – HTA attempted to contact authors. **Additional outcomes:** Volume at first sensation to void after 6 months. Detrusor contractions and urethral resistance factor. **Notes:** Reoperation: TUMT group=4: 2 retreated by TURP, 2 by TUMT; the TUMT reoperations had TURP at 1 year due to unsatisfactory improvement. TURP group: reoperation from early complication=3 due to bleeding or to remove clots; 1 retreatment
			Reduction in symptom score > 50%	**Group1:** 26/31 **Group 2:** 29/30	
			Maximum flow rate (mL/s)	**Baseline:** Group1 (n=37): 8.6±2.5 Group 2 (n=32): 8.6±3.0 **3 months:** Group1 (n=36): 11.6±4.2 Group 2 (n=32): 18.1±7.1 **6 months:** Group1 (n=37): 11.8±3.9 Group 2 (n=31): 18.6±5.2 **12 months:** Group1 (n=33): 12.6±3.9 Group 2 (n=31): 18.9±6.0 **24 months:** Group1 (n=30): 12.3±4.4 Group 2 (n=29): 17.6±5.9	
			Residual urine volume (mL)	**Baseline:** Group1 (n=37): 194±78 Group 2 (n=32): 1104±95 **3 months:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				Group1 (n=36): 147±45 Group 2 (n=32): 134±32 **6 months:** Group1 (n=37): 166±64 Group 2 (n=32): 134±30 **12 months:** Group1 (n=33):152±64 Group 2 (n=31): 123±18 **24 months:** Group1 (n=31):148±44 Group 2 (n=30):127±2	after 1 year due to bladder neck sclerosis.
			Prostate volume	**Baseline:** Group1: 33.9±11.9 Group 2: 36.8 ±16 **2 years:** Group1: 30.3 ±9.6 Group 2: 22.5±10.9	
			Reoperation:	**Group1:** 4/37 **Group 2:** 1/32	
			Catheterisation due to failure to void	**Group1:** 5/37 **Group 2:** 0/32	
			Transient rectal pain in perineum	**Group1:** 1/37 **Group 2:** 0/32	
			Urethral stricture	**Group1:** 0/37 **Group 2:** 2/32	
			Meatal stenosis	**Group1:** 0/37 **Group 2:** 2/32	
			Urinary tract infection	**Group1:** 5/37 **Group 2:** 4/32	
			Mortality (brain tumour)	**Group 1:** 0/37 **Group 2:** 1/32	
			Erectile dysfunction	**Group 1:** 0/37 **Group 2:** 0/32	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
D'Ancona et al., 1998[61] Reported in systematic review HTA 2008 **Study design:** RCT **Setting:** Netherlands **Evidence level:** 1+ **Duration of follow-up:** 2.5 years	**Patient group:** Between January 1994 and August 1995 patients recruited. **Inclusion criteria**: unequivocal BPH candidates for TURP. Qmax 15ml/s; residual volume <350ml; Madsen score ≥ 8; prostate length 25-50mm, Prostate Volume 30-100ml; 45 years plus. **Exclusion criteria:** prostate cancer; prior prostate surgery; urinary retention requiring catheterisation; medications prescribed for prostate/bladder treatment; neurogenic disorders affecting bladder function; diabetic neuropathy; possible microwave sensitive implants (pacemaker, hip prosthesis); renal impairment or obstructed bladder neck due to enlarged median lobe of prostate **All patients** **N:** 52 **Group 1** **N:** 31 Mean Age ± SD: 69.6 ± 8.5 Mean IPSS ± SD: 18.3 ± 6.3 Dropouts: 14 (6 TURP, 1 died, 5 refused or lost to follow up, 2 medication) **Group 2** **N:** 21	**Group 1:** TUMT – Prostatron software version 2.5. Total mean energy applied 151.8kJ. 100mg suppository of diclofenac administered and 2mg of medazolam injected. No additional anaesthesia during treatment. Out patient. Prolonged catheterisation: 12.7 days. **Group 2:** TURP by 2 urologists and resection performed under spinal anaesthesia. Mean length of hospital stay 4.1. Mean catheterisation 4.1 days.	**Mean (SD) IPSS score:**	**Baseline:** Group1 (n=31): 18.3 (6.3) Group 2 (n=21): 16.7 (5.6) **3months:** Group1 (n=31): 15.1 (8.2) Group 2 (n=21): 5.1 (3.1) **6 months:** Group1 (n=28): 6.7 (5.5) Group 2 (n=20): 4.0 (2.1) **12 months:** Group1 (n=27): 5.0 (2.7) Group 2 (n=17): 3.4 (2.2) **30 months:** Group1 (n=17): 7.9 (6.3) Group 2 (n=12): 6.3 (4.8)	**Funding:** NR **Limitations:** Method of randomisation, allocation concealment and blinding unclear. **Additional outcomes:** Madsen score, voided volumes, URA and LPURR. **Notes:** Links with D'Ancona 1997[60]
			Qmax (mL/s)	**Baseline:** **Group1 (n=31):** 9.3 (3.9) **Group 2 (n=21):** 9.3 (3.4) **3months:** **Group1 (n=31):** 15.5 (8.0) **Group 2 (n=21):** 19.6 (11.2) 6 months: **Group1 (n=38):** 17.0 (7.5) **Group 2 (n=20):** 15.3 (5.9) 12 months: **Group1 (n=27):** 17.1 (7.8) **Group 2 (n=17):** 19.3 (29.8) 30 months: **Group1 (n=17):** 15.1 (9.6) **Group 2 (n=12):** 19.1 (8.2)	
			PVR (mL)	**Baseline:** Group1 (n=31): 49.5 (69.9) Group 2 (n=21): 91.1 (104.7) **3months:** Group1 (n=31): 25.5 (58.1) Group 2 (n=21): 10.5 (24.5)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean Age ± SD: 69.3 ± 5.9 Mean IPSS ± SD: 16.7± 5.6 Drop outs: 9 (4 refused or lost to follow up, 1 bladder neck incision, 1 bladder carcinoma, 1 at own request, 2 dementia)			**6 months:** Group1 (n=28): 30.6 (41.0) Group 2 (n=20): 52.7 (70.7) **12 months:** Group1 (n=27): 70.4 (81.3) Group 2 (n=17): 23.6 (29.8) **30 months:** Group1 (n=17): 27.4 (49.1) Group 2 (n=12): 9.3 (14.6)	
			Pdet Qmax (cmH20)	**Baseline** Group1: 77.7 (40.0) Group 2: 65.4 (24.9) **6 months:** Group1: 54.0 (15.9) Group 2: 38.5 (24.5)	
			Prostate volume (mL)	**Baseline** Group1: 43.4 (11.8) Group 2: 44.9 (15.3) **3 months:** Group1: 36.6 (10.0) Group 2: 23.0 (8.8)	
			Reoperation:	**Group 1: 2/31 (6.4%)** **Group 2: 1/21 (4.8%)**	
			Blood transfusions	**Group 1: 0/31** **Group 2: 0/21**	
			UTI	**Group 1: 5/31 (16%)** **Group 2: 1/21 (4%)**	
			Irritative voiding symptom	**Group 1: 9 (29%)** **Group 2: 4 (19%)**	
			Hematuria	**Group 1: 0** **Group 2: 3 (14%)**	
			Mortality	**Group 1: 1** **Group 2: 0**	

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Evidence Table 36: Transurethral vaporisation of the prostate (TUVP) vs. transurethral resection of the prostate (TURP)

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Çetinkaya et al.,1996[47] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 3 months after surgery	**Patient group:** moderate or severe symptoms of prostatism **Setting:** single centre, urology clinic, Ankara Nummune Hospital, Turkey **Inclusion criteria:** • Peak urine flow rate <15 • AUA moderate to severe **Exclusion criteria:** • Patients who had previously undergone a prostate operation or who had any abnormality of kidney and liver function, urethral strictures, neurogenic deficits, bladder stones • Those with confirmed or suspected prostate cancer. **<u>All patients</u>** **N:** 46 **Drop outs:** NR **<u>Group 1:</u>** **N:** 23 **Age (mean ± SD):** 68.4 ± 8.3 **Mean prostate size ± SD:** 48.4 ± 9.7 ml (TRUS) **Operative duration ± SD:** 41.6 ± 22.1 min **Solution volume used ± SD:** 16.0 ± 10.2 ml **Catheterisation time (days):** 1.4 ± 0.8 days **Length of stay (days):** NR **Drop outs:** NR **<u>Group 2:</u>**	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Storz Spike 5mm 2-system electrode. cutting mode: 240-300 W & coagulation mode: 40-70 W TUVP continued until capsule was visible **Group 2: Transurethral resection of the prostate (TURP)** Conventional electroresection **All patients:** Glycine was used as irrigant. Indwelling catheter placed after surgery and removed when urine was clear. **Examination Methods** **Preoperative:** Baseline prostate volume (TRUS), digital rectal examination, uroflowmetry, haemocrit & Na^+ levels, AUA symptom score, post void residual (PVR) **Postoperative** PVR, symptom score and uroflowmetry taken 3 months after catheter removed. Haemocrit & Na^+ levels taken 24 h after surgery	**Mean change in AUA symptom score from baseline at 3 months** **Mean change in Qmax from baseline at 3 months** **Mean change in PVR from baseline at 3 months** **Complications: transfusion** **Complications: re-catheterisation required (retention)** **Complications: urethral or meatal stricture:**	**Group 1:** -20.89 **Group 2:** -21.31 **p value:** NR **Group 1:** 16.37 **Group 2:** 17.49 **p value:** NR **Group 1:** -211.52 **Group 2:** -199.05 **p value:** NR **Group 1:** 0/23 **Group 2:** 2/23 **Group 1:** 4/23 **Group 2:** 0/23 **Group 1:** 1/23 **Group 2:** 0/23	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Masking of outcome assessment not reported • Symptom score and Qmax were not reported at 3 months or at baseline • Standard deviations not reported for changes from baseline • Not clear whether ITT analysis performed • Drop outs not reported **Additional outcomes:** Irritative symptoms after catheter removal more in TUVP group. **Notes:** None.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 23 **Age (mean ± SD):** 62.5 ± 10.1 **Mean prostate size ± SD**: 48.8 ± 15.4 ml (TRUS) **Operative duration ± SD**: 52.4 ± 20 min **Solution volume used ± SD**: 19.8 ± 8.6 ml **Catheterisation time (days)**: 1.9 ± 0.8 days **Length of stay (days):** NR **Drop outs:** NR				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Ekengren et al., 2000[77] **Study design:** RCT Unmasked **Evidence level:** 1+ **Duration of follow-up:** 12 months after surgery	**Patient group:** men scheduled for surgery for obstruction **Setting:** single centre, department of surgery and urology, Söder Hospital, Stockholm, Sweden **Inclusion criteria:** NR **Exclusion criteria:** NR **All patients** **N:** 54 **Drop outs:** 3 died (TUVP) **Group 1:** **N:** 26 **Median age (range):** 71 (49-82) **Median IPSS (range):** 22 (1-100) **Median QoL score (range):** 4.5 (2-6) **Mean QoL score ± SD:** 4.6 ± 1.2* **Median PSA (range):** 4 (2-23) ng/mL **Median PVR (range):** 55 (0-3000) mL **Median Qmax (range):** 4 (0-8) mL/s **Mean Qmax ± SD:** 3.7 ± 2.4 mL/s* **Median prostate vol. (range):** 50 (25-90) mL (TRUS) **Median operative duration (range):** 30 (15-80) min **Median blood loss (range):** 75 (8-400) mL **Drop outs:** 3 (1 died from myocardial infarction, 1 died (catheter) and 1 with urethral stricture lost to follow up)	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Roller-ball 27050 electrode (Stortz) Cutting mode: 240 W **Group 2: Transurethral resection of the prostate (TURP)** Conventional electroresection **All patients:** Operations performed using 26F resectoscope. Ringer's solution with heparin used to replace blood lost measured using a photometer. Irrigating fluid of mannitol & ethanol and fluid absorption using ethanol method. **Preoperative:** Baseline prostate volume & PVR (TRUS), IPSS, uroflowmetry (Flo-LabII), serum PSA, Quality of Life Score (QoL) score, **Postoperative** prostate volume & PVR (TRUS), IPSS, uroflowmetry (Flo-LabII), serum PSA, Quality of Life Score (QoL) score	**Median IPSS score (range) at 12 months**	**Group 1:** 4.5 (0-24) **Group 2:** 4.0 (0-100) **p value:** Not	**Funding:** Supported by the Board of Research and Education of Stockholm County Council **Limitations:** • Patients and investigators were unmasked to treatment allocation • Not clear whether ITT analysis performed • **Values for mean IPSS given by author were very different to the median reported in the study values at baseline were >35 **Additional outcomes:** Significantly higher blood loss during the operation for TURP. Unable to check p value. **Notes:** *Requested Mean IPSS, Qmax, QoL and follow up data from author. Author reports that data were skewed hence presented as
			Mean ± SD IPSS at 12 months*	**Group 1:** 7.0 ± 6.5 ** **Group 2:** 9.3 ± 19.8 ** **p value:** NR	
			Median Qmax mL/s (range) at 12 months	**Group 1:** 10 (4-19) **Group 2:** 11 (0-19) **p value:** Not sig.	
			Mean Qmax ± SD mL/s at 12 months*	**Group 1:** 10.7 ± 4.1(n=23) **Group 2:** 11.1 ± 4.4 (n=28) **p value:** NR	
			Median QoL score (range) at 12 months	**Group 1:** 1.5 (0-6) **Group 2:** 1.0 (0-6) **p value:** Not sig.	
			Mean ± SD QoL at 12 months*	**Group 1:** 1.8 ± 1.6 (n=23) **Group 2:** 1.8 ± 2.0 (n=28) **p value:** NR	
			Complications: mortality	**Group 1:** 2/26 **Group 2:** 0/28	
			Complications: transfusion	**Group 1:** 0/26 **Group 2:** 0/28	
			Complications: urethral stricture	**Group 1:** 2/26 **Group 2:** 0/28	
			Complications: urinary retention	**Group 1:** 0/26 **Group 2:** 1/28	
			Complications: reoperation rate	**Group 1:** 2/26 **Group 2:** 1/28	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2: **N:** 28 **Median age (range):** 70 (48-83) **Median IPSS (range):** 25 (13-100) **Median QoL score (range):** 5.5 (3-6) **Mean QoL score ± SD:** 5.2 ± 1.0* **Median PSA (range):** 6 (1-82) ng/mL **Median PVR (range):** 100 (0-3000) mL **Median Qmax (range):** 2 (0-10) mL/s **Mean Qmax ± SD:** 2.8 ± 3.0 mL/s* **Median prostate vol. (range):** 39 (20-80) mL (TRUS) **Median operative duration (range):** 33 (10-90) min **Median blood loss (range):** 150 (10-726) mL **Drop outs:** 0				median and range. Author reported randomisation performed by drawing of sealed envelopes from a box prior to surgery

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Erdagi et al., 1999[83] **Study design:** RCT Unmasked **Evidence level:** 1+ **Duration of follow-up:** 6 months after surgery	**Patient group:** men with symptomatic BPH **Setting:** single centre, Turkish High Specialisation Hospital, Ankara, Turkey **Inclusion criteria:** NR **Exclusion criteria:** NR **<u>All patients</u>** **N:** 40 **Drop outs:** NR **<u>Group 1:</u>** **N:** 20 **Mean age (range):** 64.2 (56-82) **Mean IPSS (range):** 20.6 (12-27) (n=15*) **Mean Qmax ml/s (range):** 5.1 (0-11.27) (n=15*) **Mean PVR ml (range):** 68 (20-150) **Mean prostate weight. (range):** 32.5 (20-48) (TRUS) **Mean operative duration (range):** 61.5 min **Mean operative blood loss ml:** 117.6 **Catheterisation time (days):** 1.1 **Drop outs:** NR **<u>Group 2:</u>** **N:** 20 **Mean age (range):** 66.1 (58-75) **Mean IPSS (range):** 21.5 (11-30) (n=15*)	**Group 1: Transurethral vaporisation of the prostate (TUVP)** VaporTrode® rollerball electrode (Storz) at 240W for cutting and 40W for coagulation. **Group 2: Transurethral resection of the prostate (TURP)** Standard 0.012 inch loop **All patients:** Operations performed using 26F resectoscope under continuous 1.5% mannitol solution. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, PSA, uroflowmetry using Synectics Urodynamics Polygraph System, PVR by ultrasonography and prostate volume by TRUS. Assessed at 1, 3 & 6 months postoperatively	**Mean IPSS score (range) at 3 months**	**Group 1:** 0.9 ± NR (0-4) **Group 2:** 5.3 ± NR (1-12) **p value:** Not sig.	**Funding:** NR **Limitations:** • Mean and standard deviations not reported for outcomes at baseline or end point. • Randomisation method and allocation concealment not reported • Masking of patients or outcome assessment not reported • Dropouts not reported • Small sample size **Notes:** Mann Whitney test was used for statistical analysis
			Mean IPSS score (range) at 6 months	**Group 1:** 0.6 ± NR (0-3) **Group 2:** 3.9 ± NR (1-9) **p value:** 0.92 (Mann Whitney-U)	
			Mean Qmax mL/s (range) at 3 months	**Group 1:** 21.0 ± NR **Group 2:** 17.0 ± NR **p value:** NR	
			Mean Qmax mL/s (range) at 6 months	**Group 1:** 21.4 ± NR **Group 2:** 17.7 ± NR **p value:** 0.04 (Mann Whitney-U)	
			Catheterisation time (days)	**Group 1:** 1.1 ± NR **Group 2:** 3.4 ± NR **p value:** <0.001	
			Complications: transfusion	**Group 1:** 0/20 **Group 2:** 9/20 **p value:** NR NCC_AC calculate p=0.01 Fishers exact test	
			Complications: retrograde ejaculation	**Group 1:** 2/20 **Group 2:** 12/20	
			Complications: UTI	**Group 1:** 1/20 **Group 2:** 5/20 **p value:** NR NCC_AC calculate p=0. 18 Fishers exact test	
			Complications: Urethral Stricture	**Group 1:** 0/20 **Group 2:** 1/20 **p value:** NR NCC_AC calculate p=1.00 Fishers exact test	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean Qmax ml/s (range): 4.6 (0-9.6) (n=15*) **Mean PVR ml (range):** 123 (0-600) **Mean prostate weight. (range):** 37 (15-60) (TRUS) **Mean operative duration (range):** 67.7 min **Mean operative blood loss ml:** 491 **Catheterisation time (days):** 3.4 **Drop outs:** NR *10 patients with chronic retention with indwelling catheter also included did not have baseline IPSS or Qmax data				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Fowler et al., 2005[94] **Study design:** RCT Single masked (though patients on regional anaesthetic may have known which operation they had) **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient group:** men considering surgery for BPH **Setting:** multi-centre, UK **Inclusion criteria:** • Must have completed pre-treatment evaluation with current criteria for prostate surgery. • Able to give written informed consent to randomisation and treatment **Exclusion criteria:** • Previous bladder outlet surgery clinical evidence of prostate cancer • Physical status >ASA 3 • Medications that (in investigators opinion) would preclude entry into trial • Clinically significant acute illness • Known disease of central or peripheral nervous system. • Prostate cancer. **<u>All patients</u>** **N:** 235 45/235 patients in acute retention **Drop outs:** Number of patients completing study NR **<u>Group 1:</u>** **N:** 115 **Mean age (± SD):** 70.2 ± NR **Mean IPSS (± SD):** 20.7 ± 7.2 (n=107) **Mean EuroQoL score:** 0.78 ± 0.23 (n=112) **Mean IPSS QoL:** 4.6 ± 1.7 (n=109) **Mean PSA (± SD):** 4.7 ± NR ng/mL (n=101)	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Circon-ACMI 24.5 Fr continuous flow rectoscope with new Circon- ACMI Fluted VaporTrode® electrode for each patient. 180W for cut and 55W for coagulation **Group 2: Transurethral resection of the prostate (TURP)** Circon-ACMI 24.5 Fr continuous flow rectoscope with new wire loop for each patient. Cutting mode: 120-140 W. Coagulation mode: 50-60 W **All patients:** Irrigating fluids varied between glycine and glycine & ethanol depending on the centre.. 3-way catheters were removed when degree of haematuria was permitted. **Preoperative:** Baseline blood tests (FBC, urea, PSA), Uroflow using Dantec Urodyn 1000 (2	**Mean change in IPSS Score from baseline ± SD at 2 mths**	**Group 1:** 9.8 ± 7.2 (n=105) **Group 2:** 11.8 ± 7.7 (n=110) **p value NR**	**Funding:** Supported the INAHTA Health Technology Assessment programme **Limitations:** • Baseline data was not available for all outcomes • Drop outs reported for primary outcome rather than those completing study • Investigators were not masked to treatment allocation **Additional outcomes:** Change in General Health related EuroQoL score from baseline Erectile dysfunction, failed ejaculation, change in ejaculatory function, change in PVR and prostate volume. Additional procedures **Notes:** Randomisation method was computer generated by study organisers and allocation concealment by sequentially
			Mean change in IPSS Score from baseline ± SD at 6 mths	**Group 1:** 8.5 ± 7.4 (n=106) **Group 2:** 6.9 ± 5.5 (n=108) **p value NR**	
			Mean change in IPSS Score from baseline ± SD at 2 years	**Group 1:** 8.6 ± 7.2 (n=90) **Group 2:** 7.5 ± 5.8 (n=77) **p value NR**	
			Mean change in IPSS QoL Score from baseline ± SD at 2 mths	**Group 1:** 2.6 ± 1.82 (n=105) **Group 2:** 2.3 ± 1.73 (n=109) **p value NR**	
			Mean change in IPSS QoL Score from baseline ± SD at 6 mths	**Group 1:** 2.0 ± 1.63 (n=107) **Group 2:** 1.6 ± 1.34 (n=108) **p value NR**	
			Mean change in IPSS QoL Score from baseline ± SD at 2 years	**Group 1:** 1.9 ± 1.62 (n=89) **Group 2:** 1.8 ± 1.34 (n=80) **p value NR**	
			Mean change in Qmax from baseline ± SD at 2 mths	**Group 1:** 19.12 ± 11.76 (n=108) **Group 2:** 21.23 ± 10.20 (n=111) **p value NR**	
			Mean change in Qmax from baseline ± SD at 6 mths	**Group 1:** 19.60 ± 11.04 (n=109) **Group 2:** 22.29 ± 10.25 (n=109) **p value NR**	
			Duration of catheterisation (days)	**Group 1:** 4.9 ± 11.6* (CI95% 2.7-7.1) n=107 **Group 2:** 3.1 ± 4.4* (CI95% 2.3-3.9) n=116 **p value:** 0.93	
			Length of hospital stay (days)	**Group 1:** 4.4 ± 3.6* (CI95% 3.8-5.1) n=115 **Group 2:** 4.6 ± 4.2* (CI95% 3.9-	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean PVR (± SD): 181 ± NR mL (n=91) **Mean Qmax (SD):** 10.1 ± 4.35 mL/s (n=94) **Mean prostate vol. (SD):** 54.3 ± NR mL (TRUS) (n=100) **Serum creatinine (mmol/L):** 105 ± NR (n=100) **Number of patients with ED:** 34/109 **Drop outs:** 6/115 violated protocol. Number of patients completing study NR **Group 2:** **N:** 120 **Mean age (± SD):** 69.7 ± NR **Mean IPSS (± SD):** 20.7 ± 6.9 (n=114) **Mean EuroQoL score:** 0.74 ± 0.25 (n=116) **Mean IPSS QoL:** 4.9 ± 0.98 (n=114) **Mean PSA (± SD):** 4.6 ± NR ng/mL (n=99) **Mean PVR (± SD):** 171 ± NR mL (n=94) **Mean Qmax (SD):** 10.52 ± 5.04 mL/s (n=97) **Mean prostate vol. (SD):** 51.1 ± NR mL (TRUS) (n=103) **Serum creatinine (mmol/L):** 104 ± NR (n=106) **Number of patients with ED:** 48/110 **Drop outs:** 6/120 violated protocol Number of patients completing study NR	flow rates >150mL if possible), PVR using TRUS 7.5 MHz, Cystometrography and questionnaires: IPSS, EuroQoL, Sexual Function from ICS-BPH questionnaire. **Postoperative** Assessment at 2 months, 6 months: Blood tests (FBC & urea only) Uroflow using Dantec Urodyn 1000 (2 flow rates >150mL if possible), PVR using TRUS 7.5 MHz, cystometrography and questionnaires: IPSS, EuroQoL, Sexual Function from ICS-BPH questionnaire. IPSS Score, ICS-BPH & EuroQoL repeated 2 years as well.		5.4) n=120 **p value:** 0.47	numbered opaque envelopes. *SD calculated from confidence intervals and sample size according to section 7.7.3.2 of the Cochrane Handbook Number of patients in each group was not reported for length of stay data but states that data collected for all but 3 patients. Use numbers randomised for calculation.
			Complications: transfusion	**Group 1:** 2/115 **Group 2:** 9/120 **P value:** 0.04 (Chi-squared)	
			Complications: reoperation rate (TUIP)	**Group 1:** 5/115 **Group 2:** 17/120 **P value:** NR	
			Complications: urethral or meatal stricture. Reported as number of meatotomies, otis urethrotomies and urethral dilatations	**Group 1:** 64/115 **Group 2:** 66/120	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Gallucci et al., 1998[99] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men symptomatic men with BPH who were urodynamically obstructed **Setting:** multi-centre, 9 centres, Italy **Inclusion criteria:** NR **Exclusion criteria:** • Complete urinary retention • Bladder calculi • Neurogenic bladder • Prostate weight >70g • Bladder cancer • Mental illness • Prostate cancer or suspect **<u>All patients</u>** **N:** 150 **Drop outs:** 0 **<u>Group 1:</u>** **N:** 70 **Mean age (range):** NR **Mean IPSS ± SD**: 18.84 ± 5.69 **Mean Qmax ml/s ± SD**: 7.26 ± 3.1 **Mean PVR ml ± SD**: 84.7 ± 95.3 **Mean prostate weight ± SD (g)**: 36.61 ± 12.72 **Drop outs:** 0 **<u>Group 2:</u>** **N:** 80 **Mean age (range):** NR	**Group 1: Transurethral vaporisation of the prostate (TUVP)** VaporTrode® rollerball electrode (Circon ACMI) at 200-250W for cutting. **Group 2: Transurethral resection of the prostate (TURP)** Standard diathermic loop **All patients:** Operations performed using 22.5F resectoscope under continuous 5% mannitol solution. 3-way catheter inserted. Prophylactic antibiotics were used. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, PSA, Blood, TRUS, uroflowmetry (opening pressure, detrusor pressure, Qmax and PVR using <6f catheters). Flow rate at months 1 & 6 and pressure flow at 3 months. IPSS assessed at 1, 3, 6 & 12 months postoperatively	**Mean IPSS score ± SD at 3 months**	**Group 1:** 5.50 ± 4.77 **Group 2:** 5.52 ± 4.11 **p value:** Not sig.	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Masking of outcome assessment not reported **Additional outcomes:** Detrusor and opening pressure at 3 months. Transient stress incontinence. **Notes:** No patients were lost to follow up SD calculated from standard error and and sample size according to section 7.7.3.2 of the Cochrane Handbook numbers randomised for calculation.
			Mean IPSS score ± SD at 6 months	**Group 1:** 4.94 ± 4.69 **Group 2:** 3.77 ± 3.31 **p value:** Not sig.	
			Mean IPSS score ± SD at 12 months	**Group 1:** 4.04 ± 4.27 **Group 2:** 3.52 ± 3.04 **p value:** Not sig.	
			Mean Qmax mL/s ± SD at 3 months	**Group 1:** 18.18 ± 7.7 **Group 2:** 19.21 ± 8.14 **p value:** Not sig.	
			Mean Qmax mL/s ± SD at 6 months	**Group 1:** 20.13 ± 9.62 **Group 2:** 20.77 ± 8.5 **p value:** Not sig.	
			Mean Qmax mL/s ± SD at 12 months	**Group 1:** 20.31 ± 6.02 **Group 2:** 20.30 ± 6.35 **p value:** Not sig.	
			Catheterisation time (days)	**Group 1:** 1.96 ± 1.09 **Group 2:** 2.71 ± 1.07 **p value:** <0.0001	
			Length of hospital stay (days)	**Group 1:** 3.9 ± 2.01 **Group 2:** 4.69 ± 1.97 **p value:** <0.0001	
			Complications: incontinence (at 12 mths)	**Group 1:** 4/70 **Group 2:** 3/80 **p value:** NR	
			Complications: Urethral Stricture	**Group 1:** 3/70 **Group 2:** 3/80 **p value:** NR	
			Complications: transfusion	**Group 1:** 0/70 **Group 2:** 0/80 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean IPSS ± SD: 18.19 ± 5.90 **Mean Qmax ml/s ± SD**: 8.78 ± 10.38 **Mean PVR ml ± SD**: 64.61 ± 77.37 **Mean prostate weight ± SD (g)**: 36.59 ± 12.25 **Drop outs:** 0		**Complications: transient urinary retention**	**Group 1:** 12/70 **Group 2:** 3/80 **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hammadeh et al., 2003[110] linked to Hammadeh et al., 2000[111] & Hammadeh et al., 19980[109] **Study design:** RCT Investigator masked **Evidence level:** 1+ **Duration of follow-up:** 5 years	**Patient group:** men with bladder outflow obstruction due to BPH considering surgery **Setting:** single-centre, Whipps Cross Hospital, UK **Inclusion criteria:** • IPSS ≥ 13 • QoL index ≥ 3 • Qmax ≤ 15 mL/s **Exclusion criteria:** • Complete urinary retention • Neurogenic bladder • Previous prostatic or urethral surgery • Bladder calculi • Prostate cancer or suspect • Receiving anticoagulant therapy **<u>All patients</u>** **N:** 104 (109 randomised but 5 excluded for medical problems or social circumstances) **Drop outs:** *51 at 5 years: 6 TURP and 3 TUVP died from cardiopulmonary disease, 12 TURP and 16 TUVP lost to follow up. Remaining 14 patients unaccounted for. **<u>Group 1:</u>** **N:** 52 **Mean age (± SD):** 67.5 ± 6.7 (52-	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Circon VaporTrode® roller-ball at 240W for cutting & 60W coagulation. **Group 2: Transurethral resection of the prostate (TURP)** Standard loop with 145W cutting & 60W coagulation **All patients:** Operations performed using 27F resectoscope using continuous glycine. 3-way catheter inserted. TURP patients were irrigated postoperatively until bleeding stopped. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up visits at 6 weeks, 3, 6 & 12 months, 2, 3 5 years postoperatively	**Mean IPSS score ± SD at 1 year**	**Group 1:** 4.4 ± 3.8 (n=51) **Group 2:** 5.9 ± 5.2 (n=51) **p value:** 0.3	**Funding:** NR **Limitations:** • Dropouts were only partially reported. **Additional outcomes:** **Notes:** Patients allocated by nurse drawing a sealed opaque envelope prior to surgery.
			Mean IPSS score ± SD at 2 years	**Group 1:** 4.3 ± 3.5 (n=47) **Group 2:** 6.3 ± 4.6 (n=47) **p value:** 0.02	
			Mean IPSS score ± SD at 3 years	**Group 1:** 4.1 ± 3.3 (n=40) **Group 2:** 7.1 ± 6.2 (n=40) **p value:** 0.01	
			Mean IPSS score ± SD at 5 years	**Group 1:** 5.9 ± 6.3 (n=26) **Group 2:** 8.6 ± 7.1 (n=27) **p value:** 0.16	
			Mean Qmax mL/s ± SD at 1 year	**Group 1:** 22.5 ± 9.0 (n=51) **Group 2:** 20.8 ± 7.7 (n=51) **p value:** 0.4	
			Mean Qmax mL/s ± SD at 2 years	**Group 1:** 22.4 ± 7.7 (n=47) **Group 2:** 21.2 ± 8.5 (n=47) **p value:** 0.5.	
			Mean Qmax mL/s ± SD at 3 years	**Group 1:** 22.2 ± 8.5 (n=40) **Group 2:** 18.0 ± 7.1 (n=40) **p value:** 0.02	
			Mean Qmax mL/s ± SD at 5 years	**Group 1:** 21.0 ± 9 (n=26) **Group 2:** 17.9 ± 13.1 (n=27) **p value:** 0.17	
			Mean IPSS QoL ± SD at 1 year	**Group 1:** 1.2 ± 1.0 (n=51) **Group 2:** 1.5 ± 1.0 (n=51) **p value:** 0.3	
			Mean IPSS QoL ± SD at 2 years	**Group 1:** 1.1 ± 1.0 (n=47) **Group 2:** 1.7 ± 1.1 (n=47) **p value:** 0.004	
			Mean IPSS QoL ± SD at 3 years	**Group 1:** 1.0 ± 0.9 (n=40) **Group 2:** 1.6 ± 1.4 (n=40) **p value:** 0.04	
			Mean IPSS QoL ± SD at 5 years	**Group 1:** 1.1 ± 1.2 (n=26) **Group 2:** 1.7 ± 1.4 (n=27) **p value:** 0.09	
			Catheterisation time (days) hours reported converted to days	**Group 1:** 0.87 ± 0.29 **Group 2:** 1.94 ± 0.52 **p value:** <0.001	
			Length of hospital stay (days)	**Group 1:** 2.2 ± 0.59 **Group 2:** 3.19 ± 0.76 **p value:** <0.001	
			Complications: transfusion (early)	**Group 1:** 0/52 **Group 2:** 1/52 **p value:** 0.3	
			Complications: urinary	**Group 1:** 12/52	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	82) **Mean IPSS ± SD**: 26.5 ± 4.5 **IPSS QoL ± SD:** 4.9 ± 0.9 **Mean Qmax ml/s ± SD**: 8.9 ± 3.2 **Mean PVR ml ± SD**: 131.0 ± 78.5 **Mean prostate weight ± SD (g)**: 32.0 ± 9.1 **Drop outs:** * **<u>Group 2:</u>** **N:** 52 **Mean age (± SD):** 70.2 ± 7.2 (52-87) **Mean IPSS ± SD**: 26.6 ± 4.8 **IPSS QoL ± SD:** 5.0 ± 0.7 **Mean Qmax ml/s ± SD**: 8.6 ± 3.2 **Mean PVR ml ± SD**: 101.0 ± 87.93 **Mean prostate weight ± SD (g)**: 27.0 ± 12.2 **Drop outs:** *		**retention (early)**	**Group 2:** 4/52 **p value:** 0.04	
			Complications: UTI (early)	**Group 1:** 3/52 **Group 2:** 2/52 **p value:** 0.7	
			Complications: TUR (early)	**Group 1:** 0/52 **Group 2:** 0/52 **p value:** 0.7	
			Complications: urethral stricture (long term)	**Group 1:** 2/52 **Group 2:** 2/52 **p value:** NR	
			Complications: incontinence (long term)	**Group 1:** 0/52 **Group 2:** 0/52 **p value:** NR	
			Complications: Retrograde ejaculation	**Group 1:** 21/52 **Group 2:** 28/52 **p value:** NR	
			Reoperation rate	**Group 1:** 2/52 **Group 2:** 2/52 **p value:** NR	
			Mortality at 5 years (cardiopulmonary)	**Group 1:** 3/52 **Group 2:** 6/52 **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kaplan et al., 1998[133] **Study design:** RCT Examiner masked **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men with moderate to severe LUTS **Setting:** single-centre, department of urology, Columbia University, New York, USA **Inclusion criteria:** • AUA symptom score ≥ 10 • Qmax ≤ 15 mL/s • Prostate volume 15-60g (TRUS) **Exclusion criteria:** • < 50 years old • Neurogenic bladder • Previous prostatic or urethral surgery • On medications know to affect voiding function • Prostate or bladder cancer **<u>All patients</u>** **N:** 64 **Drop outs:** 3 at 1 year **<u>Group 1:</u>** **N:** 32 **Mean age (± SD):** 68.9 ± 8.7 **Mean AUA ± SD:** 19.4 ± 3.5 **Mean Qmax ml/s ± SD:** 7.2 ± 2.8 **Mean PVR ml ± SD:** 77.8 ± 20.3 **Mean prostate volume ± SD:** 47.8 ± 22.3 **Operative time ± SD:** 47.6 ± 17.6 mins **Drop outs:** 2	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Fluted roller-ball electrode at 240-270W for cutting **Group 2: Transurethral resection of the prostate (TURP)** Standard loop **All patients:** Operations performed using 27F continuous flow resectoscope. **Examination methods** **Preoperative:** Baseline AUA symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry (Dantec Urodyn). Follow up visits at 1, 3, 6 and 12 months postoperatively	**Mean AUA score ± SD at 3 months**	**Group 1:** 9.2 ± 2.7 (n=32) **Group 2:** 8.6 ± 2.5 (n=32) **p value:** Not sig.	**Funding:** Partial funding: Grant RR-0045 from National Institutes of Health **Limitations:** • Randomisation method and allocation concealment not reported • Masked outcome assessment was not reported **Additional outcomes:** PVR at follow up **Notes:** Statistical analysis was performed by third party who was masked to treatment allocation
			Mean AUA score ± SD at 6 months	**Group 1:** 7.4 ± 2.9 (n=32) **Group 2:** 7.9 ± 3.1 (n=32) **p value:** Not sig.	
			Mean AUA score ± SD at 12 months	**Group 1:** 6.6 ± 2.4 (n=30) **Group 2:** 6.1 ± 1.9 (n=31) **p value:** Not sig.	
			Mean Qmax mL/s ± SD at 3 months	**Group 1:** 14.8 ± 3.9 (n=32) **Group 2:** 16.8 ± 3.6 (n=32) **p value:** 0.03 (NCGC calculate as t-test with equal variance)..	
			Mean Qmax mL/s ± SD at 6 months	**Group 1:** 15.6 ± 3.2 (n=32) **Group 2:** 18.1 ± 4.2 (n=32) **p value:** 0.01 (NCGC calculate as t-test with equal variance)..	
			Mean Qmax mL/s ± SD at 12 months	**Group 1:** 16.9 ± 4.1 (n=30) **Group 2:** 19.6 ± 4.9 (n=31) **p value:** 0.02 (NCGC calculate as t-test with equal variance).	
			Catheterisation time (days) hours reported converted to days	**Group 1:** 0.54 ± 0.19 **Group 2:** 2.81 ± 0.57 **p value:** <0.01	
			Length of hospital stay (days)	**Group 1:** 1.3 ± 0.5 **Group 2:** 2.6 ± 0.9 **p value:** <0.03	
			Complications: transfusion	**Group 1:** 0/32 **Group 2:** 1/32 **p value:** NR	
			Complications: UTI	**Group 1:** 5/32 **Group 2:** 4/32 **p value:** NR	
			Complications: TUR	**Group 1:** 0/32	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	<u>Group 2:</u> **N:** 32 **Mean age (± SD):** 72.8 ± 6.9 **Mean AUA ± SD:** 18.3 ± 4.7 **Mean Qmax ml/s ± SD:** 8.3 ± 3.6 **Mean PVR ml ± SD:** 66.9 ± 15.7 **Mean prostate volume ± SD:** 41.5 ± 19.7 **Operative time ± SD:** 34.6 ± 11.2 mins **Drop outs:** 1			**Group 2:** 1/32 **p value:** NR	
			Complications: urethral stricture	**Group 1:** 1/32 **Group 2:** 1/32 **p value:** NR	
			Complications: incontinence	**Group 1:** 0/32 **Group 2:** 0/32 **p value:** NR	
			Retrograde ejaculation	**Group 1:** 17/32 **Group 2:** 13/32 **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kupeli et al., 1998[153] KUPELI A 1998 (forest plot) **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men with symptomatic BPH **Setting:** single-centre, department of urology, Ankara Hospital, Turkey **Inclusion criteria:** • AUA symptom score ≥ 7 • Qmax ≤ 15 mL/s **Exclusion criteria:** • Prostate volume ≥ 60g (TRUS) • < 50 years old • Neurogenic bladder • Previous prostatic or urethral surgery • On medications know to affect voiding function • Prostate or bladder cancer **<u>All patients</u>** **N:** 66 **Drop outs:** 6 at 6 months and 10 at 1 year. **<u>Group 1:</u>** **N:** 30 **Mean age (range):** 65.7 (52-72) **Mean AUA (range):** 13.7 (7-29) **Mean Qmax ml/s (range):** 8.3 (2.7 -11.8) **Mean prostate volume ± SD:** 43.57 ± 12.01	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Storz spike electrode: cutting 180-250W (mean 220W) and coagulation 40-70W (mean 60W) **Group 2: Transurethral resection of the prostate (TURP)** Standard loop **All patients:** Operations performed using 24F continuous flow resectoscope with 1.5% glycine as an irrigant **Examination methods** **Preoperative:** Baseline AUA symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up visits to collect AUA symptom score and Qmax collected at 6 and 12 months postoperatively	**Mean AUA score (range) at 6 months**	**Group 1:** 7.9 ± NR (0-12) (n=27) **Group 2:** 7.3 ± NR (1-12) (n=33) **p value:** NR	**Funding:** NR **Limitations:** • Allocation concealment not reported • Masked outcome assessment was not reported • Standard deviations were missing from primary outcome measures (AUA symptom score and Qmax) and p values not reported **Notes:** Randomisation by flipping a coin
			Mean AUA score (range) at 12 months	**Group 1:** 6.1 ± NR (0-11) (n=26) **Group 2:** 7.0 ± NR (1-14) (n=30) **p value:** NR	
			Mean Qmax (range) at 6 months	**Group 1:** 13.8 ± NR (8.2-16.4) (n=27) **Group 2:** 14.3 ± NR (7.2-17.5) (n=33) **p value:** NR	
			Mean Qmax (range) at 12 months	**Group 1:** 17.3 ± NR (11.5-23.8) (n=26) **Group 2:** 19.6 ± NR (9.4-24.5) (n=30) **p value:** NR	
			Catheterisation time (days)	**Group 1:** 1.61 ± 0.8 **Group 2:** 3.83 ± 1.39 **p value:** <0.0001	
			Length of hospital stay (days)	**Group 1:** 1.92 ± 0.89 **Group 2:** 4.16 ± 1.46 **p value:** <0.0001	
			Complications: transfusion	**Group 1:** 0/30 **Group 2:** 2/36 **p value:** NR	
			Complications: UTI	**Group 1:** 4/30 **Group 2:** 3/36 **p value:** NR	
			Complications: urinary retention	**Group 1:** 1/30 **Group 2:** 0/36 **p value:** NR	
			Complications: reoperation rate	**Group 1:** 1/30 **Group 2:** 0/36 **p value:** NR	
			Complications: urethral stricture	**Group 1:** 0/30 **Group 2:** 0/36 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Operative time ± SD: 38.61 ± 7.32 mins **Drop outs:** 3 at 6 months and 4 at 1 year **<u>Group 2:</u>** **N:** 36 **Mean age (range):** 62.4 (56-70) **Mean AUA (range):** 14.6 (8-32) **Mean Qmax ml/s (range):** 8.8 (3.0 -12.4) **Mean prostate volume ± SD:** 41.46 ± 10.7 **Operative time ± SD:** 41.40 ± 7.95 mins **Drop outs:** 3 at 6 months and 6 at 1 year		**Complications: incontinence**	**Group 1:** 1/30 **Group 2:** 1/36 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kupeli et al., 1998[154] KUPELI B 1998 (forest plot) **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 3 months (mean 4.2 months)	**Patient group:** men with moderate to severe symptoms of BPH **Setting:** single-centre, department of urology, Ankara Hospital, Turkey **Inclusion criteria:** • IPSS symptom score ≥ 8 • Qmax < 15 mL/s **Exclusion criteria:** • Neurogenic bladder • Previous prostatic surgery • Prostate cancer **<u>All patients</u>** **N:** 60 **Drop outs:** 0 **<u>Group 1:</u>** **N:** 30 **Mean age (± SD):** 62.4 ± 3.2 **Mean IPSS score:** 19.4 ± NR **Mean Qmax ml/s (± SD):** 7.9 ± 2.1 **Mean prostate size (g) ± SD:** 48.9 ± 8.7 **Operative time ± SD:** 47.3 ± NR mins **Drop outs:** 0 **<u>Group 2:</u>** **N:** 30 **Mean age (± SD):** 59.8 ± 2.6 **Mean IPSS score:** 21.6 ± NR **Mean Qmax ml/s (± SD):** 9.2 ± 2.6 **Mean prostate size (g) ± SD:** 51.7 ± 9.1 **Operative time ± SD:** 41.6 ± NR mins Drop outs: 0	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Storz spike electrode: cutting mean 250-300W **Group 2: Transurethral resection of the prostate (TURP)** Standard loop (80-120W) **All patients:** Operations performed using 24F continuous flow resectoscope **Examination methods** **Preoperative:** Baseline AUA symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up visits to collect AUA symptom score and Qmax collected at 6 and 12 months postoperatively	**Mean IPSS score at 3 months**	**Group 1:** 4.1 ± 22.25* **Group 2:** 5.2 ± 23.85* **p value:** Not sig.	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Masked outcome assessment was not reported • Standard deviations were missing from primary outcome measure IPSS symptom score • Dropouts were not mentioned. Assume all patients completed study at 3 months **Notes:** *SD for change from baseline estimated using Cochrane methods with p ≈ 0.01
			Mean Qmax (± SD) at 3 months	**Group 1:** 17.7 ± 4.1 **Group 2:** 19.7 ± 3.2 **p value:** 0.05 (NCGC calculated using *t* test with equal variances)	
			Catheterisation time (days) hours reported converted to days	**Group 1:** 2 ± NR **Group 2:** 4 ± NR **p value:** <0.05	
			Length of hospital stay (days)	**Group 1:** 2.5 ± NR **Group 2:** 4.5 ± NR **p value:** <0.05	
			Complications: transfusion	**Group 1:** 0/30 **Group 2:** 0/30 **p value:** NR	
			Complications: TUR	**Group 1:** 0/30 **Group 2:** 0/30 **p value:** NR	
			Complications: UTI	**Group 1:** 4/30 **Group 2:** 3/36 **p value:** NR	
			Complications: urinary retention	**Group 1:** 0/30 **Group 2:** 0/30 **p value:** NR	
			Complications: urethral stricture	**Group 1:** 0/30 **Group 2:** 0/30 **p value:** NR	
			Complications: retrograde ejaculation	**Group 1:** 23/30 **Group 2:** 13/30 **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Nathan & Wickham 1996[211] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** men requiring TURP **Setting:** single-centre, department of minimally invasive therapy, Guy's Hospital, UK **Inclusion criteria:** NR **Exclusion criteria:** • Patients with indwelling catheters • Patients on anticoagulant therapy • Neurogenic bladder • Previous prostatic surgery **<u>All patients</u>** **N:** 40 **Drop outs:** NR **<u>Group 1:</u>** **N:** 20 **Mean age (range):** 65.4 (57-77) **Mean IPSS score:** 21.9 ± 4.2 **Mean IPSS QoL ± SD:** 4.9 ± 0.7 **Mean Qmax ml/s (± SD):** 10.2 ± 4.4 **PVR mL (range):** 130 (0-300) **Mean prostate size (g) ± SD:** 53.5 ± 28 **Operative time ± SD:** 39.2 ± NR mins **Drop outs:** 0 **<u>Group 2:</u>**	**Group 1: Transurethral vaporisation of the prostate (TUVP)** VaporTrode® electrode: cutting 200W and 40W **Group 2: Transurethral resection of the prostate (TURP)** Standard loop: cutting 120W and coagulation 60W **All patients:** Operations performed using 24Ch continuous flow resectoscope. A 3-way catheter was inserted. **Examination methods** **Preoperative:** Baseline IPSS symptom score and IPSS QoL, , TRUS, uroflowmetry. Follow up visits at 4, 8, 12 weeks for IPSS and uroflowmetry	**Mean IPSS score at 3 months** (follow up interval not clear) **Mean IPSS QoL score at 3 months** (follow up interval not clear) **Mean Qmax ± SD mL/s at 3 months** (follow up interval not clear) **Catheterisation time (days)** hours reported converted to days **Length of hospital stay (days)** **Complications: transfusion** **Complications: UTI at 3 months** **Complications: TUR** **Complications: incontinence (urgency & frequency) at 3 months** **Complications: reoperation rate**	**Group 1:** 2.86 ± 2.8 **Group 2:** 3.1 ± 2.3 **p value:** NR. **Group 1:** 0.5 ± 7 **Group 2:** 0.9 ± 0.9 **p value:** NR **Group 1:** 21.3 ± 5.9 **Group 2:** 20.6 ± 2.6 **p value:** NR **Group 1:** 0.58 **Group 2:** 1.9 **p value:** NR **Group 1:** 1.85 **Group 2:** 3.45 **p value:** <0.0001 **Group 1:** 0/20 **Group 2:** 2/20 **p value:** NR **Group 1:** 0/20 **Group 2:** 0/20 **p value:** NR **Group 1:** 0/20 **Group 2:** 0/20 **p value:** NR **Group 1:** 0/30 **Group 2:** 0/30 **p value:** NR **Group 1:** 1/20 **Group 2:** 3/20 **p value:** NR	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Masked outcome assessment was not reported • Follow up interval for postoperative measurements not clear • There were significant baseline differences in IPSS score and Qmax. • Dropouts were not mentioned. Assume all patients completed study at 3 months **Notes:** None.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 30 **Mean age (range):** 69.2 (57-81) **Mean IPSS score:** 17.0 ± 4.3 **Mean IPSS QoL ± SD:** 4.9 ± 0.7 **Mean Qmax ml/s (± SD):** 7.2 ± 3.5 **PVR mL (range):** 120 (0-380) **Mean prostate size (g) ± SD:** 53.4 ± 21 **Operative time ± SD:** 37.4 ± NR mins **Drop outs:** 0				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Nuhoglu et al., 2005[227] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 5 years	**Patient group:** men with LUTS association with BPH **Setting:** single-centre, Ankara, Turkey **Inclusion criteria:** • IPSS >15 • Qmax < 10 mL/s **Exclusion criteria:** • Suspected prostate cancer • Neurogenic bladder • Previous prostatic or urethral surgery **<u>All patients</u>** **N:** 77 **Drop outs:** 33 at 5 years (5 died, 5 dropped out and 19 could not be contacted. 4 patients are unaccounted for in the study report) **<u>Group 1:</u>** **N:** 37 **Mean age (± SD):** 64.5 ± 8.7 **Mean IPSS score:** 17.3 ± 6.8 **Mean Qmax ml/s (± SD):** 6.3 ± 2.1 **PVR mL (range):** 88 ± 20 **Mean prostate volume mL ± SD:** 39 ± 8.1 **Operative time ± SD:** 45 ± 13.2 mins **Drop outs:** 16 at 5 years.	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Storz spike loop: cutting 250W and 100W coagulation **Group 2: Transurethral resection of the prostate (TURP)** Standard loop: **All patients:** Operations performed using 24F continuous flow resectoscope using glycine as irrigant. A 3-way catheter was inserted. Antibiotic prophylaxis applied to surgeon's discretion **Examination methods** **Preoperative:** Baseline DRE, IPSS symptom score, urinalysis, PSA, TRUS, uroflowmetry. Follow up visits at 1 & 3 months and >5 years thereafter	**Mean IPSS score ± SD at 3 months**	**Group 1:** 4.7 ± 3.1 (n=35) **Group 2:** 4.8 ± 4.2 (n=38) **P value:** Not sig.	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Masked outcome assessment was not reported • Dropouts were not reported completely **Additional outcomes:** PVR and average flow at 3 months and ≥ 5 years. Serum electrolytes **Notes:** None.
			Mean IPSS score ± SD at ≥5 years	**Group 1:** 6.5 ± 3.2 (n=21) **Group 2:** 6.1 ± 3.5 (n=23) **P value:** Not sig.	
			Mean Qmax ± SD mL/s at 3 months	**Group 1:** 17.7 ± 2.3 **Group 2:** 17.5 ± 3.3 **P value:** Not sig.	
			Mean Qmax ± SD mL/s at ≥5 years	**Group 1:** 12.9 ± 3.1 **Group 2:** 13.8 ± 2.9 **P value:** Not sig.	
			Catheterisation time (days) hours reported converted to days	**Group 1:** 0.92 ± 0.24 **Group 2:** 3.15 ± 0.52 **p value:** <0.001	
			Complications: transfusion	**Group 1:** 0/37 **Group 2:** 2/40 **p value:** NR	
			Complications: urinary retention	**Group 1:** 1/37 **Group 2:** 0/40 **p value:** NR	
			Complications: retrograde ejaculation	**Group 1:** 5/37 **Group 2:** 4/40 **p value:** NR	
			Complications: reoperation rate	**Group 1:** 1/37 **Group 2:** 0/40 **p value:** NR	
			Complications: urethral stricture	**Group 1:** 1/37 **Group 2:** 0/40 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean follow up time yrs: 5.7 ± 0.6 **<u>Group 2:</u>** **N:** 40 **Mean age (± SD):** 65.1 ± 9.4 **Mean IPSS score:** 17.6 ± 7.2 **Mean Qmax ml/s (± SD):** 5.9 ± 2.6 **PVR mL (range):** 95 ± 26 **Mean prostate volume mL ± SD:** 39 ± 7.7 **Operative time ± SD:** 42 ± 9.5 mins **Drop outs:** 17 at 5 years **Mean follow up time yrs:** 5.7 ± 0.9				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Patel et al., 1997[235] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** men with symptomatic BOO **Setting:** single-centre, department of urology, UCLA, USA **Inclusion criteria:** • IPSS moderate or severe (n=6) • Qmax < 15 mL/s • Acute urinary retention (n=6) **Exclusion criteria:** • UTI • Neurogenic bladder **<u>All patients</u>** **N:** 12 **Drop outs:** **<u>Group 1:</u>** **N:** 6 **Mean age (range):** 67 (60-85) **Mean IPSS score (range):** 29.6 (28-31)* **Mean Qmax ml/s (range):** 10 (7.3-13.1) **Mean prostate volume mL (range):** 54 (25-90) TRUS **Operative time (range):** 64.3 (40-120) mins **Median energy used:** 1657.5 (1286-2010) kJ **Drop outs:** NR **<u>Group 2:</u>** **N:** 6	**Group 1: Transurethral vaporisation of the prostate (TUVP)** VaporTrode® grooved bar electrode (Circon ACMI) cutting 130-190W and 40W coagulation **Group 2: Transurethral resection of the prostate (TURP)** Standard loop resection. cutting 120-170W and 40W coagulation **All patients:** Operations performed using 25F continuous flow resectoscope using water as irrigant. **Examination methods** **Preoperative:** Baseline IPSS symptom score, urinalysis, TRUS, uroflowmetry. Follow up visits at 3 months	**Mean IPSS score (range) at 3 months***	**Group 1:** 3.5 (2-4) **Group 2:** 3.2 (1-5) **P value:** NR	**Funding:** Equipment loaned from Circon ACMI **Limitations:** • Randomisation method and allocation concealment not reported • Masked outcome assessment was not reported • Dropouts were not reported • Small sample size pilot study • Adverse events poorly reported **Additional outcomes:** PVR and average flow at 3 months and ≥ 5 years. Serum electrolytes **Notes:** Randomised after stratification for prostate volume (TRUS) *IPSS score for patients without retention for baseline but unclear whether IPSS postoperative results were for all patients
			Mean Qmax (range) mL/s at 3 months	**Group 1:** 21.4 (17.2-25.3) **Group 2:** 22.6 (19.3-25.2) **P value:** NR	
			Catheterisation time (days)	**Group 1:** 2 (1-3) **Group 2:** 2.6 (1-5) **p value:** NR	
			Length of hospital stay (days)	**Group 1:** 1.8 (1-2) **Group 2:** 2.6 (2-4) **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean age (range): 65.8 (59-71) **Mean IPSS score (range):** 23.3 (17-29)* **Mean Qmax ml/s (range):** 7.5 (5.1-11) **Mean prostate volume mL (range):** 64.6 (31.5-119) TRUS **Operative time (range):** 66 (27-95) mins **Median energy used:** 753 (555-977) kJ **Drop outs:** NR				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Shokeir et al., 1997[278] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months Mean 14.4 months (12-17)	**Patient group:** men symptomatic LUTS **Setting:** multi-centre, department of urology, New Jeddah and King Hafd Madina Hospitals, Saudi Arabia **Inclusion criteria:** • AUA-7 Symptom score >15 • Qmax < 12 mL/s • Prostate size < 60g measured by TRUS **Exclusion criteria:** • Neurogenic bladder • Prostate cancer • Bladder stone • Previous prostatic surgery • Prostate size > 60g measured by TRUS • Patients with acute urinary retention • Patients with indwelling catheter **<u>All patients</u>** **N:** 70 **Drop outs:** NR **<u>Group 1:</u>** **N:** 35 **Mean age (± SD):** 68.4 ± 9.5 **Mean AUA-7 score:** 26.3 ± 5.2 **Mean Qmax ml/s (± SD):** 7.8 ± 2.1 **PVR mL (range):** 75.2 ± 21.2 **Mean prostate size (g) ± SD:**	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Storz grooved roller electrode: cutting mean 240W (200-300) and mean 70W (50-80W) coagulation **Group 2: Transurethral resection of the prostate (TURP)** Standard loop: **All patients:** Operations performed using 26F continuous flow resectoscope using glycine as irrigant. A 3-way catheter was inserted. **Examination methods** **Preoperative:** Baseline serum electrolytes, AUA-7 symptom score, urinalysis, PSA, TRUS, uroflowmetry (Qmax from 3 voids >150mL, Urodyn Dantec). Follow up visits at 1, 3, 6 and 12 months	**Mean AUA-7 score ± SD at 3 months**	**Group 1:** 4.5 ± 1.9 **Group 2:** 4.8 ± 2.2 **P value:** Not sig.	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Masked outcome assessment was not reported • Dropouts were not reported **Additional outcomes:** PVR at each follow up and serum electrolytes **Notes:** None.
			Mean AUA-7 score ± SD at 6 months	**Group 1:** 4.6 ± 1.2 **Group 2:** 4.5 ± 1.3 **P value:** Not sig.	
			Mean AUA-7 score ± SD at 12 months	**Group 1:** 5.2 ± 1.4 **Group 2:** 4.7 ± 1.5 **P value:** Not sig.	
			Mean Qmax ± SD mL/s at 3 months	**Group 1:** 19.4 ± 2.2 **Group 2:** 19.4 ± 2.1 **P value:** Not sig.	
			Mean Qmax ± SD mL/s at 6 months	**Group 1:** 19.2 ± 2.0 **Group 2:** 19.3 ± 2.0 **P value:** Not sig.	
			Mean Qmax ± SD mL/s at 12 months	**Group 1:** 20.1 ± 3.2 **Group 2:** 18.2 ± 3.0 **P value:** Not sig.	
			Catheterisation time (days)	**Group 1:** 1.1 ± 0.4 **Group 2:** 2.0 ± 0.8 **p value:** <0.001	
			Length of hospital stay (days)	**Group 1:** 1.5 ± 0.7 **Group 2:** 2.5 ± 1.0 **p value:** <0.001	
			Complications: transfusion	**Group 1:** 0/35 **Group 2:** 0/35 **p value:** NR	
			Complications: TUR	**Group 1:** 0/35 **Group 2:** 0/35 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	44.6 ± 10.1 **Operative time ± SD:** 52 ± 12.5 mins **Mean follow up time mths:** 14.3 ± 2.1 **Drop outs:**. NR **<u>Group 2:</u>** **N:** 35 **Mean age (± SD):** 68.4 ± 9.6 **Mean AUA-7 score:** 25.1 ± 5.5 **Mean Qmax ml/s (± SD):** 6.9 ± 1.7 **PVR mL (range):** 77.1 ± 20.3 **Mean prostate volume mL ± SD:** 39 ± 7.7 **Operative time ± SD:** 39.7 ± 8.8 mins **Mean follow up time mths:** 14.5 ± 1.8 **Drop outs:** NR				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Van Melick et al., 2003[309] Links with Van Melick et al., 2002[307] (up to 6 months) and Van Melick et al., 2003[308] (up to 12 months) **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** Up to 7 years	**Patient group:** men over 45 years with LUTS associated with BPH that were recruited from their clinic from1996 to 2001 **Setting:** single-centre, University Medical Centre Utrect, Netherlands **Inclusion Criteria:** • met ISC criteria for BPH • Schafer obstruction score≥ 2 • prostate size between 20-65ml. **Exclusion Criteria:** age ≤45 yrs **<u>All patients</u>** **N:** 96 **<u>Group 1</u>** **N:** 46 **Age (mean) ± SD:** 64 ± 10 **IPSS (mean) ± SD:** 20.2 ± 6.6 **Mean prostate size, ml:** 35 ± 11 **Mean (SD) Global quality of life score:** 4.1 ± 1.4 **Mean Qmax ± SD ml/s:** 11 ± 4 Follow-up 1to 4 years = 12 Follow-up 4 to 7 years=12 **Drop outs:** 12 at one year post-operatively (procedure during surgery changed for medical reasons=2, surgery cancelled=1, equipment failure resulting in TURP)=1, surgery incorrectly performed=4, morbidity=1, reoperation –TURP=2, reoperation – due to stricture =1)	**Group 1: Laser vaporisation** VaporTrode® (Circon ACMI) power settings were not reported **Group 2: TURP** Standard resection. Suprapubic catheter if required perioperatively. **All patients:** Standard 24FR resectoscope using glycine for irrigation. Pre-procedural antibiotics and transurethral 20F catheter postoperatively. **Examination methods:** Urodynamic studies (cystometry and pressure flow) at baseline and 1-6 weeks, 3, 6, 12 months after treatment	**Mean (± SD) symptom score (IPSS) at 6 months** **Mean (± SD) symptom score (IPSS) at 12 months** **Mean (± SD) symptom score (IPSS) at 1-4 years*** **Mean (± SD) symptom score (IPSS) at 4-7 years*** **Mean (SD) Global quality of life score at 6 months** **Mean (SD) Global quality of life score at 12 months** **Mean (SD) Global quality of life score at 1-4 years*** **Mean (SD) Global quality of life score at 4-7 years*** **Qmax mean ± SD at 3 months** **Qmax mean ± SD at 6 months** **Qmax mean ± SD at 12 months** **Qmax mean ± SD at 1-4* years** **Qmax mean ± SD at 4-7* years** **Catheterisation time (days)** **Length of hospital stay (days)**	**Group 1:** 7.2 ± 6.7 (n=33) **Group 2:** 5.3 ± 5.1 (n=37) **Group 1:** 6.7 ± 6.4 (n=34) **Group 2:** 4.6 ± 4.8 (n=41) **Group 1:** 8.4 ± 8.7 (n=12) **Group 2:** 5.8 ± 7.5 (n=15) **Group 1:** 7.0 ± 5.6 (n=12) **Group 2:** 7.3 ± 7.1 (n=15) **Group 1:** 1.6 ± 1.6 **Group 2:** 0.9 ± 1.2 **Group 1:** 1.4 ± 1.4 **Group 2:** 0.9 ± 1.2 **Group1:** 1.0 ± 1.2 **Group 2:** 1.1 ± 1.2 **Group 1:**1.4 ± 0.8 **Group 2:** 1.3 ± 1.3 **Group 1:** 20 ± 10 (n=19) **Group 2:** 25 ± 11 (n=15) **Group 1:** 23 ± 10 (n=33) **Group 2:** 24 ± 7 (n=37) **Group1:** 28 ± 6 (n=34) **Group 2:** 23 ± 10 (n=41) **Group1:** 23 ± 6 **Group 2:** 20 ± 5 **Group1:** 16 ± 11 **Group 2:** 17 ± 8 **Group 1:** 1.9 ± 0.6 **Group 2:** 2.1 ± 0.7 **p value:** NR **Group 1:** 3.4 ± 0.9 **Group 2:** 3.9 ± 0.9	**Funding:** NR **Limitations:** • Randomisation method was not described and masking of outcome assessment was not reported. • Significant baseline difference in IPSS score • Not all patients were evaluated with urodynamics during the follow up period • Numbers of patients completing IPSS score not clear at 6 & 12 mths **Additional outcomes:** Frequency during day, frequency during night, symptom problem index and BPH impact index. Uroflowmetry also reported. **Notes:** Follow up time varied individually as all patients were analysed within a 2 month period. Depending on the

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2 **N:** 50 **Age (mean) ± SD:** 66 ± 8 **IPSS (mean) ± SD:** 16.8 ± 6.0 **Mean prostate size, ml ± SD:** 37 ± 11 **Mean ± SD Global quality of life score:** 3.8 ± 1.5 **Mean Qmax ± SD ml/s:** 11 ± 4 Follow-up 1to 4 years = 10 Follow-up 4 to 7 years=17 **Drop outs:** 9 at one year post-operatively (surgery cancelled=1, mortality=2, morbidity=2, emigrated=1, reoperation (TURP) =2, reoperation (stricture)=1)			**p value:** NR	individual follow-up time, patient divided into two groups: those with a follow-up time between 1 and 4 years and those with follow up time between 4 and 7 years. * follow up = 2.8 yrs for TUVP 1-4 yrs and 5.4 yrs for category 4-7 years. For TURP mean follow up = 2.7 yrs for category 1-4 yrs and 5.7 yrs for category 4-7 yrs.
			Post-op complications: urethral stricture (within 12 mths)	**Group1:** 1/46 **Group 2:** 2/50	
			Post-op complications: mortality (within 12 mths)	**Group 1:** 0/46 **Group 2:** 2/50	
			Post-op complications: transfusion required (within 12 mths)	**Group 1:** 0/46 **Group 2:** 1/50	
			Post-op complications: urinary retention (within 12 mths)	**Group 1:** 0/46 **Group 2:** 0/50	
			Reoperation rate (TURP) within 12 mths	**Group 1:** 2/46 **Group 2:** 2/50	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Wang et al., 2002[315] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 24 months	**Patient group:** NR **Setting:** China **Inclusion criteria:** NR **Exclusion criteria:** • Prostate cancer or suspect • Neurogenic bladder • Urethral stricture **All patients** **N:** 206 **Drop outs:** **Group 1:** **N:** 97 **Mean age (range):** 72 (62-85) **Mean IPSS score (range):** 20 (8-30) **Mean Qmax ml/s (range):** 7 (2-13) **Mean PVR ml (range):** 120 (60-400) **Mean prostate volume mL (range):** NR **Operation time (range) mins:** 35 (25–70) **Drop outs:** 1 (death due to cardiovascular event) **Group 2:** **N:** 109 **Mean age (range):** 71 (61-84) **Mean IPSS score (range):** 20 (9-31) **Mean Qmax ml/s (range):** 7 (3-12) **Mean PVR ml (range):** 131 (60–380) **Operation time (range) mins:** 35 (25–70) **Mean prostate volume mL (range):** NR **Drop outs:** NR	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Electrode not specified. Power 240-260W **Group 2: Transurethral resection of the prostate (TURP)** Power 100-140W **Examination methods** **Preoperative:** Not reported in HTA report	**Mean IPSS score (range) at 12 months**	**Group 1:** 4 (4–20) n=109 **Group 2:** 3 (1–17) n=96 **P value:** NR	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Masked outcome assessment was not reported • Unable to obtain copy of reference to check figures **Notes:** Data taken from HTA report.
			Mean IPSS score (range) at 24 months	**Group 1:** 5 (4-23) n=38 **Group 2:** 4 (2-21) n=43 **P value:** Not sig.	
			Complications: TUR syndrome	**Group 1:** 3/97 **Group 2:** 5/109	
			Complications: mortality	**Group 1:** 1/97 **Group 2:** 0/109	
			Complications: incontinence	**Group 1:** 5/97 **Group 2:** 1/109	
			Complications: strictures	**Group 1:** 5/97 **Group 2:** 2/109	

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1 **Evidence Table 37: Bipolar transurethral vaporisation of the prostate (TUVP) vs. transurethral resection of the prostate (TURP)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Dunsmuir et al., 2003[76] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months (mean 9 months)	**Patient group:** men with LUTS secondary to BPH being considered for surgery **Setting:** single-centre: Department of Urology, Monash Medical Centre, Melbourne, Australia. **Inclusion criteria:** • <80 years **Exclusion criteria:** • Acute urinary retention • Anticoagulant therapy • Prostate volume >80mL • Prostate cancer or suspect • Previous prostate surgery **<u>All patients</u>** **N:** 51 **Drop outs:** 0 **<u>Group 1:</u>** **N:** 30 **Mean age ± SD:** 63 ± 7.1 **Mean AUA ± SD:** 24.0 ± 6.9 **Mean Qmax ± SD, mL/s:** 9.6 ± 3.0 **Mean PVR± SD, mL:** 112 ± 13.3 **Mean prostate volume ± SD, mL:** 36 ± 19 **QoL ± SD:** 12 ± 3.4 **Operative time ± SD, min:** 33 ± NR **Drop outs:** 0 **<u>Group 2:</u>** **N:** 35 **Mean age ± SD:** 60 ± 6.5 **Mean AUA ± SD:** 17.0 ± 6.2 **Mean Qmax ± SD, mL/s:** 10.4 ± 3.1	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ system. **Group 2: Transurethral resection of the prostate (TURP)** Standard loop **All patients:** **Examination methods** **Preoperative:** Baseline IPSS Symptom score, QoL, Qmax, PVR assessed and follow up of IPSS, QoL, PVR and Qmax at 3, 6 12 months	**Mean ± SD IPSS at 3 months**	**Group 1:** 5.7 ± NR (n=30) **Group 2:** 8.2 ± NR (n=21) **P value:** NR	**Funding:** NR **Limitations:** • Masking of outcome assessment was not reported • Mean ± SD were not reported for IPSS and Qmax. Data were estimated from graph. • Intermediate report, not all patients randomised have received surgery or been followed up for 12 mths. **Notes:** Randomisation by drawing tickets from previously sealed box containing equal numbers of tickets for each type of surgery. QoL score was based on AUA symptom scoring section C with a maximum score of 19
			Mean ± SD IPSS at 6 months	**Group 1:** 7.1 ± NR (n=24) **Group 2:** 5.7 ± NR (n=20) **P value:** NR	
			Mean ± SD IPSS at 12 months	**Group 1:** 5.0 ± NR (n=20) **Group 2:** 6.4 ± NR (n=20) **P value:** NR	
			Mean ± SD Qmax at 3 months	**Group 1:** 18.0 ± NR (n=30) **Group 2:** 20.0± NR (n=21) **P value:** NR	
			Mean ± SD Qmax at 6 months	**Group 1:** 18.5 ± NR (n=24) **Group 2:** 17.0 ± NR (n=20) **P value:** NR	
			Mean ± SD Qmax at 12 months	**Group 1:** 17.0 ± NR (n=20) **Group 2:** 15.0 ± NR (n=20) **P value:** NR	
			Catheterisation time (days) converted into days	**Group 1:** 0.8 ± NR **Group 2:** 0.7 ± NR **P value:** 0.92	
			Length of stay (days) reported as time to discharge	**Group 1:** 1.45 ± NR **Group 2:** 1.55 ± NR **P value:** 0.88	
			Complications: urinary retention (re-catheterisation)	**Group 1:** 10/30 **Group 2:** 1/21 **P value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean PVR± SD, mL: 96 ± 11.4 **Mean prostate volume ± SD, mL:** 42 ± 21 **QoL ± SD:** 11 ± 3.2 **Operative time ± SD, min:** 26 ± NR **Drop outs:** 0				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hon et al., 2006[121] **Study design:** RCT Observer masked **Evidence level:** 1+ **Duration of follow-up:** Mean 9 months	**Patient Group:** Men with BOO undergoing surgery **Setting:** single centre: Shrewsbury & Telford Hospital, UK **Inclusion criteria:** • NR **Exclusion criteria:** • Previous myocardial infarction • Prostate cancer or suspect • Previous history of prostatic surgery • Serum creatinine >200 mmol/L • Prostate volume > 80 mL • Neurogenic bladder • Urethral stricture **<u>All patients</u>** **N:** 160 **Dropouts:** NR **<u>Group 1</u>** **N:** 81 **Mean age ± SD:** 66.1 ± 8.5 **Mean IPSS ± SD:** 21.3 ± 6.2 **Mean Qmax ± SD, mL/s:** 12.0 ± 6.4 **Mean PVR± SD, mL:** 147 ± 156 **Mean prostate volume ± SD, mL:** 38.0 ± 17.5 **IPSS QoL ± SD:** 4.2 ± 1.1 **History of urinary retention:** 17/81 **Catheter in situ:** 8/81 9.9% **Operative time ± SD, min:** 32.6 ± 13.4 **Drop outs:** 0	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ system with Plasma V™ bar (320-450kHz) at 160W cutting and 80W coagulation. Isotonic saline as irrigant **Group 2: Transurethral resection of the prostate (TURP)** Standard loop and irrigation with mannitol/sorbitol. **All patients** Underwent Otis urethrotomy before prostatectomy and received continuous irrigation with saline. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up for IPSS, QoL, PVR and Qmax	**Mean ± SD IPSS at 9 months**	**Group 1:** 7.7 ± 6.8 (n=73) **Group 2:** 6.9 ± 5.8 (n=76) **P value:** 0.44	**Funding:** NR **Limitations:** • Reasons for missing data at follow up were not reported • Data presented for mean overall follow up **Additional outcomes:** Irrigation volumes. **Notes:** Randomisation using sequentially numbered opaque envelopes containing computer generated numbers.
			Mean ± SD Qmax at 9 months	**Group 1:** 25.6 ± 15.6 (n=73) **Group 2:** 23.5 ± 15.2 (n=76) **P value:** 0.41	
			Mean ± SD QoL at 9 months	**Group 1:** 1.7 ± 1.5 (n=73) **Group 2:** 1.5 ± 1.5 (n=76) **P value:** 0.64	
			Length of Stay ± SD, days reported as mean postoperative stay	**Group 1:** 3.0 ± 0.9 (n=81) **Group 2:** 3.4 ± 1.1 (n=79) **P value:** 0.04	
			Complications: Transfusion	**Group 1:** 0/81 **Group 2:** 4/79 **P value:** 0.02	
			Complications: urinary retention (re-hospitalisation)	**Group 1:** 1/81 **Group 2:** 2/79 **P value:** NR	
			Complications: urethral stricture	**Group 1:** 0/81 **Group 2:** 1/79 **P value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2 **N:** 79 **Mean age ± SD:** 68.1 ± 7.5 **Mean IPSS ± SD:** 20.6 ± 7.0 **Mean Qmax ± SD, mL/s:** 11.9 ± 6.0 **Mean PVR± SD, mL:** 182 ± 180 **Mean prostate volume ± SD, mL:** 40.0 ± 17.1 **IPSS QoL ± SD:** 4.3 ± 1.3 **History of urinary retention:** 18/79 **Catheter in situ:** 13/79 16% **Operative time ± SD, min:** 28.5 ± 15.2 **Drop outs:** 0				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Karaman et al., 2005[137] and Kaya et al., 2007[139] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months.	**Patient Group:** men with BOO secondary to BPH **Setting:** single centre: Department of Urology, Haydarparsa Numune Training & Research Hospital, Istanbul, Turkey **Inclusion criteria:** • Severe LUTS on IPSS score requiring treatment • Qmax < 15 mL/s or obstructive pressure flow study • Prostatic volume <60 mL **Exclusion criteria:** • Prostate cancer or suspect after biopsy for DRE or PSA >4 ng/mL • Untreated UTI • Previous history of prostatic surgery • Neurogenic bladder • Urethral stricture **<u>All patients</u>** **N:** 75 **Dropouts:** NR **<u>Group 1</u>** **N:** 38 **Median Age (range), yrs:** 66 (49-80) **IPSS ± SD:** 21.0 ± 3.8 **Mean ± SD Qmax, mL/s:** 6.0 ± 2.1 **Mean prostate volume ± SD, mL:** 50.0 ± 2.0 **Operation time ± SD, min:** 40.3 ± 15 **Dropouts:** NR	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ tissue management system (160Ω, 320-450kHz, 254-350V) using saline irrigant/ 80-100 V coagulation **Group 2: TURP** Standard loop through 26F continuous flow resectoscope with glycine irrigant. **All patients** 3-way catheter inserted and irrigation continued until urine was clear. Catheter was before the patient was discharged All operations performed by the same surgeons **Examination methods** **Preoperative:** Baseline IPSS, Qmax and PVR, PSA, blood, urinalysis, TRUS **Postoperative:** IPSS and Qmax repeated at follow up of 3, 6 & 12 mths	**Mean ± SD IPSS at 3 months**	**Group 1:** 5.0 ± 3.4 (n=38) **Group 2:** 9.0 ± 2.9 (n=37) **P value:** <0.001	**Funding:** NR **Limitations:** • Randomisation method, allocation concealment and masking of outcome assessment were not reported • Dropouts NR. Unclear whether all patients completed follow up **Notes:** Long term follow up for 2 and 3 years was available for 25 Group1 patients and 15 group 2 patients reported in Kaya et al., 2007[139]
			Mean ± SD IPSS at 6 months	**Group 1:** 6.0 ± 2.7 (n=38) **Group 2:** 10.0 ± 2.6 (n=37) **P value:** <0.001	
			Mean ± SD IPSS at 12 months	**Group 1:** 7.0 ± 8.7 (n=38) **Group 2:** 12.0 ± 2.6 (n=37) **P value:** <0.001	
			Mean ± SD IPSS at 2 years	**Group 1:** 7.1 ± 1.5 (n=25) **Group 2:** 5.2 ± 1.1 (n=15) **P value:** <0.05	
			Mean ± SD IPSS at 3 years	**Group 1:** 7.6 ± 1.4 (n=25) **Group 2:** 5.7 ± 1.2 (n=15) **P value:** <0.05	
			Mean ± SD Qmax at 3 months	**Group 1:** 17.0 ± 2.3 (n=38) **Group 2:** 18.0 ± 2.0 (n=37) **P value:** NS	
			Mean ± SD Qmax at 6 months	**Group 1:** 17.0 ± 1.3 (n=38) **Group 2:** 17.0 ± 3.3 (n=37) **P value:** NS	
			Mean ± SD Qmax at 12 months	**Group 1:** 16.0 ± 1.3 (n=38) **Group 2:** 15.0 ± 0.7 (n=37) **P value:** NS	
			Mean ± SD Qmax at 2 years	**Group 1:** 12.5 ± 2.1 (n=25) **Group 2:** 20.8 ± 2.4 (n=15) **P value:** <0.05	
			Mean ± SD Qmax at 3 years	**Group 1:** 14.4 ± 2.6 (n=25) **Group 2:** 21.8 ± 3.1 (n=15) **P value:** <0.05	
			Catheterisation time (days) converted into	**Group 1:** 1.5 ± 0.4 **Group 2:** 2.8 ± 1.1	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2 **N:** 37 **Median Age (range), yrs:** 65 (54-78) **IPSS ± SD:** 22.0 ± 4.6 **Mean ± SD Qmax, mL/s:** 6.0 ± 3.1 **Mean prostate volume ± SD, mL:** 51.1 ± 1.0 **Operation time ± SD, min:** 55.0 ± 11.0 **Dropouts:** NR		days	**P value:** <0.001	
			Length of stay (days) equal to catheterisation time	**Group 1:** 1.5 ± 0.4 **Group 2:** 2.8 ± 1.1 **P value:** <0.001	
			Complications: Transfusion	**Group 1:** 0/38 **Group 2:** 2/37 **P value:** NR	
			Complications: TUR	**Group 1:** 0/38 **Group 2:** 0/37 **P value:** NR	
			Complications: urethral stricture	**Group 1:** 2/38 **Group 2:** 2/37 **P value:** NR	
			Complications: retrograde ejaculation	**Group 1:** 31/38 (82%) **Group 2:** 32/37 (86%) **P value:** NR	
			Complications: erectile dysfunction	**Group 1:** 13% **Group 2:** 12% **P value:** NR	

1 **Evidence Table 38: Transurethral needle ablation (TUNA) vs. transurethral resection of the prostate (TURP)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Cimentepe et al., 2003[54] **Study design:** RCT **Setting:** May1999 to 2000, Turkey **Evidence level:** 1+ **Duration of follow-up:** 18 months	**Patient group:** ▪ Patients with lower urinary tract symptoms attributable to BPH. **Inclusion criteria:** ▪ Lower urinary tract symptoms due to BPH ▪ Age > 40 ▪ Qmax<15mL/sec ▪ IPSS > 13 ▪ Prostate weight 20-70 g ▪ No suspicion of prostate malignancy (according to DRE and PSA) **Exclusion criteria:** ▪ Urethral stricture ▪ Bladder neck contracture ▪ Previous prostate surgery ▪ Bladder stones or tumours ▪ Neurogenic bladder ▪ Prominent median lobe **<u>All patients</u>** **N:** 59 patients enrolled **Drop outs:** 0 **<u>Group 1-TUNA</u>** **N:** 26 Dropouts: 0 **Age,** years, mean (±SD): 60.1± 7.3 **IPSS,** mean (±SD): 22.9±3.8 **IPSS-QoL,** mean (±SD): 4.8±0.75	**Group 1: TUNA** TEAP system (Vidamed Inc.) Radiofrequency (RF)-powered generator that delivers a dual 465-kHz RF signal. The TEAP procedure was performed with the patient in the lithotomy position under spinal or epidural anaesthesia. The number of treatments for each lateral lobe was determined according the length of the prostatic urethra. The procedure was performed at 1-cm intervals starting 1 cm from the bladder neck to 1 cm proximal to the verumontanum. The RF energy was delivered continuously and slowly increased to achieve a minimum of 50°C on the shields after 4 minutes of treatment. At the same time, it has been shown that the temperature at the tips of the needles is increased to aprox. 100°C. This temperature should be	**IPSS,** mean ± SD	<u>Baseline:</u> **Group 1:** 22.9 ± 3.8 **Group 2:** 24.1 ± 3.8 **p value:** 0.41 <u>3 months</u>: **Group 1:** 9.7 ± 2.8 **Group 2:** 8.3 ± 2.9 **p value:** 0.25 <u>18 months</u>: **Group 1:** 8.5 ± 3.2 **Group 2:** 8.6 ± 1.8 **p value:** 0.90	**Funding:** Not reported. Authors from Department of Urology Faith University, School of Medicine, Ankara, Turkey. **Limitations:** ▪ Method of randomisation, allocation concealment, ITT and sample size calculation was not reported ▪ It was unclear how patients were recruited and screened, and how many of those screened were enrolled ▪ Unequal number of patients in both arms, 27% more patient sin the TURP arm **Additional outcomes:** ▪ 1 patient in TUNA group had acute urinary
			IPSS-QOL , mean ± SD	<u>Baseline:</u> **Group 1:** 4.8 ± 0.75 **Group 2:** 5.2 ± 0.65 **p value:** 0.11 <u>3 months</u> **Group 1:** 2.1 ± 0.5 **Group 2:** 1.9 ± 0.5 **p value:** 0.30 <u>18 months</u>: **Group 1:** 1.8 ± 1.3 **Group 2:** 1.7 ± 0.5 **p value:** 0.35	
			Q_{max} , mean ± SD (ml/s)	<u>Baseline:</u> **Group 1:** 9.8 ± 3.6 **Group 2:** 9.2 ± 3.4 **p value:** 0.66 <u>3 months</u>: **Group 1:** 16.7 ± 4.5 **Group 2:** 23.1 ± 5.3 **p value:** 0.002 <u>18 months</u>: **Group 1:** 17.7 ± 4.2 **Group 2:** 23.3 ± 4.9 **p value:** 0.004	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Qmax, ml/s, mean(±SD):9.8±3.6 **Prostate size**, g, mean(±SD):46.1±11.2 **PVR**, ml, mean(±SD):67.4±29.4 **<u>Group 2-TURP</u>** **N:** 33 Dropouts: 0 **Age**, years, mean (±SD): 63.3 ±5.9 **IPSS**, mean (±SD): 24.1 ±3.8 **IPSS-QoL**, mean (±SD): 5.2±0.65 **Qmax**, ml/s, mean(±SD):9.2±3.4 **Prostate size**, g, mean(±SD):49.1±17.7 **PVR**, ml, mean(±SD):76.1±50.1 (all parameters not stat sig between two groups)	maintained for 1.5 minutes to create lesions. Therefore the device tip was kept firmly pressed against the prostate, and the RF power was applied for 5.5 minutes for each lesion. **Catheter protocol:** catheter was left indwelling for 12-24 hours. **Discharge:** discharged home on the same day. **Group 2: TURP** Performed under spinal or epidural anaesthesia. **Catheter protocol:** catheter was left indwelling for 48- 72 hours. **Discharge:** hospitalised for a minimum of 48 hours. **All patients** received analgesics and antibiotics	**Complications:** **Blood transfusion**, (2 patients in TEAP and all patients in TURP group had transient bleeding-haematuria after operation)	**Group 1:** 0/26 (7.7%) **Group 2:** 0/33 (100) **P value:** Not stat sig	retention requiring recatheterisation, unclear how many in the TURP group ▪ Prostate size at <u>18 months</u>: g), mean ± SD: TEAP: 41.9 ± 10.9, TURP: 34.3 ± 10.4, p value: 0.08 ▪ **Post void residual volume (mL)**, mean ± SD <u>3 months</u>: **Group 1:** 45.3 ± 16.7 **Group 2:** 32.4± 17.4 **p value:** 0.07 <u>18 months</u>: **Group 1:** 46.4 ± 17.5 **Group 2:** 30.3 ± 18.7 **p value:** 0.03 **Notes:** None.
			Complications: **Retrograde ejaculation** (all patients were sexually active pre-operatively)	<u>18 months follow-up</u> **Group 1:** 0/26 (0) **Group 2:** 16/33 (48.5) **RR:** 0.0 (95% CI: 0.0 to 0.25) **P value:** <0.01	
			Complications: **Urethral stricture**	<u>18 months follow-up</u> **Group 1:** 0/26 (0) **Group 2:** 2/33 (6.0) **P value:** Not stat sig	
			Complications: **Reoperation**, 18 months follow-up) n/N (%)	<u>18 months follow-up</u> **Group 1:** 2/26 (7) **Group 2:** 0/33 (0) **P value:** Not stat sig	
			Complications: **Slight stress incontinence:** (definition not provided)	<u>18 months follow-up</u> **Group 1:** 0/26 (0) **Group 2:** 1/33 (0.3) **P value:** Not stat sig	
			Complications: **Erectile impairment** (deterioration in achieving and maintaining erection)	<u>18 months follow-up</u> **Group 1:** 0/26 (0) **Group 2:** 4/33 (12) **P value:** Not stat sig	
			Duration of operation, minutes, mean±SD	**Group 1:** 44.3±7.8 **Group 2:** 55.9±12.4 **P value:** 0.06	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hill2004[116] **Study design:** RCT **Setting:** 7 medical centres across the US **Evidence level:** 1+ **Duration of follow-up:** 5-years Links with: BRUSKEWITZ 1998[36] – 1 year study ROEHRBORN 1999B[259] – 6 months data	**Patient group:** Men with LUTS secondary to BPH **Inclusion criteria:** ▪ Men 50 years or older who have LUTS secondary to BPH a minimum of three months in duration. ▪ I-PSS of greater than 13, a PFR of 12 ml per second or less with a minimum voided volume of at least 125 ml and a prostate size of between 20 and 75 gm, as determined by TRUS. **Exclusion criteria:** ▪ Active urinary tract infection ▪ urinary retention or PVR greater than 350 cc ▪ abnormal renal function, ▪ PSA greater than 10 ng/ml (If serum PSA between 4 to 10 ng/ml, TRUS guided prostate biopsies were performed to exclude prostate cancer), biopsy proven prostate cancer ▪ an enlarged median lobe ▪ neurogenic bladder and/or sphincter abnormalities ▪ previous non-pharmacological prostate treatment ▪ Prostate gland size < 34 or greater than 64 mm in transverse diameter, ▪ Current therapy affecting	**Group 1: TUNA** TEAP device consisted of a hand piece similar to a rigid 18 Fr cytoscope with a 0-degree optical lens, light source and irrigation system, an RF generator that operated a frequency of 460 kHz and 2, 18 gauge needle electrodes to deliver RF energy to the prostate. Temperatures at the centre of the lesion reached 90C to 110C with a gradient decreased of 5C to 15C for 2 to 3 mm such that peripheral temperatures attained 50C to 54C. **Group 2: TURP** Each TURP was done at one of the reporting centres. The patient received general or spinal anaesthesia. Resection was performed using standard techniques and a urethral catheter was left indwelling for 24 to	**IPSS**, mean ±SEM	Baseline **Group 1:** 24.0 ± 0.8 (n=65) **Group 2:** 24.1 ± 0.8 (n=55) **P value:** NR 1 year follow up **Group 1:** 11.7 ± 1.0 (n=56) **Group 2:** 7.8 ± 0.9 (n=44) **P value:** 0.0049 2 year follow up **Group 1:** 15.0 ± 1.3 (n=43) **Group 2:** 9.5 ± 1.1 (n=35) **P value:** 0.0028 3 year follow up **Group 1:** 15.2 ± 1.3 (n=38) **Group 2:** 10.1 ± 1.4 (n=31) **P value:** 0.0079 4 year follow up **Group 1:** 13.2 ± 1.5 (n=24) **Group 2:** 7.6 ± 1.6 (n=21) **P value:** 0.0137 5 year follow up **Group 1:** 10.7 ± 1.4 (n=18) **Group 2:** 10.8 ± 1.6 (n=22) **P value:** 0.9813	**Funding:** Authors report financial interest and/or other relationship with Glaxo, Merek, Medtronic and Celsion. Funding for trial not reported. **Limitations:** ▪ Randomisation well described but concealment of allocation is not described. ▪ Number of withdrawals and drop-outs is described for 1-year follow up but not for the 5-year period. ▪ Sample size calculation was mentioned, but assumptions used were not described ▪ There were discrepancies in the baseline and follow up values of 3 papers reporting the study. ▪ Quality of life scale – it was unclear how this was calculated in Bruskewitz1998 and Hill2004. The mean score was more the maximum of IPSS-QoL Scale. Only Roehborn1999B
			Qmax (ml/s), mean±SEM	Baseline **Group 1:** 8.8 ± 0.3 (n=65) **Group 2:** 8.8 ± 0.3 (n=56) **P value:** NR 1 year follow up **Group 1:** 14.6 ± 1.0 (n=53) **Group 2:** 21.1± 1.3 (n=43) **P value:** <0.0001 2 year follow up **Group 1:** 12.5 ± 0.7 (n=40) **Group 2:** 21.3± 1.4 (n=33) **P value:** 0.0001 3 year follow up	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	prostate physiology or other medical conditions that would pose an unacceptable patient risk. **<u>All patients</u>** **N:** 121 patients **Drop outs:** 15 lost to follow-up at 1 year **<u>Group 1-TUNA</u>** **N:** 65 **Age**, years, mean (±SE): 66 ± 1.0 **IPSS**, mean (±SD): 24±0.8 **Dropouts:** 6 lost to follow up at 1 year **PVR**, ml, mean ±SEM : 91.8 ± 10.0 (n=65) **<u>Group 2- TURP</u>** **N:** 56 **Age**, years, mean (±SE): 66 ± 1.0 **IPSS**, mean ±SD: 24.1± 0.8 **Dropouts**: 9 lost to follow up at 1 year **PVR**, ml, mean ±SEM : 81.9 ± 9.3 (n=56)	48 hours postoperatively.		**Group 1:** 13.0 ± 1.3 (n=33) **Group 2:** 19.1 ± 2.0 (n=26) **P value:** 0.0106 <u>4 year follow up</u> **Group 1:** 11.7 ± 1.4 (n=18) **Group 2:** 18.9± 2.5 (n=17) **P value:** 0.0142 <u>5 year follow up</u> **Group 1:** 11.4 ± 1.2 (n=13) **Group 2:** 18.6 ± 2.3 (n=15) **P value:** 0.0143	reported used of IPSS-QOL. **Additional outcomes:** Percent improvement over baseline for AUA, QOL, PFR and PVR (table 3) Procedure related mortality: 0 in both arms
			QoL score, mean ±SEM (Unclear what scales were used)	<u>Baseline</u> **Group 1:** 11.8 ± 0.5 (n=64) **Group 2:** 12.6 ± 0.5 (n=56) **P value:** NR <u>1 year follow up</u> **Group 1:** 4.3 ± 0.5 (n=55) **Group 2:** 3.7 ± 0.7 (n=45) **P value:** 0.4814 <u>2 year follow up</u> **Group 1:** 6.0 ± 0.7 (n=43) **Group 2:** 3.7 ± 0.7 (n=33) **P value:** 0.0309 <u>3 year follow up</u> **Group 1:** 5.4 ± 0.7 (n=40) **Group 2:** 4.7 ± 1.0 (n=32) **P value:** 0.5275 <u>4 year follow up</u> **Group 1:** 5.2 ± 0.9 (n=22) **Group 2:** 3.7 ± 1.0 (n=21) **P value:** 0.2316 <u>5 year follow up</u> **Group 1:** 3.8 ± 0.7 (n=18) **Group 2:** 4.0 ± 0.8 (n=22) **P value:** 0.719	**PVR**, ml, mean ±SEM: <u>1 year follow up</u> **Group 1:** 80.3 ± 11.0 (n=52) **Group 2:** 47.1± 7.0 (n=43) **P value:** 0.0173 <u>2 year follow up</u> **Group 1:** 74.1 ± 12.6 (n=40) **Group 2:** 34.6± 5.6 (n=31) <u>3 year follow up</u> **Group 1:** 78.2 ± 13.7 (n=32) **Group 2:** 50.7 ± 10.4 (n=26) **P value:** 0.1285 <u>4 year follow up</u> **Group 1:** 138.2 ± 45.7 (n=19) **Group 2:** 39.5 ± 13.1 (n=17) **P value:** 0.0564 <u>5 year follow up</u> **Group 1:** 60.4 ± 21.8 (n=13) **Group 2:** 27.4 ± 7.9 (n=17)
			QoL- IPSS Scale, mean ±SD (only reported in Roehborn1999B)	<u>Baseline</u> **Group 1:** 4.6±1.1 **Group 2:** 4.8±1.1	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				6 months follow up: **TEAP**: 2.0 (sd not provided) **Group 2:** 1.5 P<0.001	**P value:** 0.128
			Stricture formation/scar tissue	Five-year follow up **Group 1:** 1/65(1.5) **Group 2:** 4/56(7.1)	**Notes:** Where there were discrepancies, values from Hill2004 were used.
			Retrograde ejaculation:	Five-year follow up **Group 1:** 0/65 **Group 2:** 23/56 (41.1)	
			Urinary incontinence:	Five-year follow up **Group 1:** 2/65(3.1) **Group 2:** 12/56 (21.4)	
			Reoperation: (The 9 men in TEAP group received TURP, the TURP patient received TUIP). One additional patient received radical prostatectomy for prostate cancer.	Five-year follow up **Group 1:** 9/65(13.8) **Group 2:** 1/56(1.8)	
			Erectile dysfunction:	Five-year follow up **Group 1:** 2/65(3.1) **Group 2:** 12/56(21.4)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hindley2001[118] **Study design:** RCT **Setting:** UK **Evidence level:** 1+ **Duration of follow-up:** 2-year Links with MOSTAFID1997[205]	**Inclusion criteria:** ▪ Men > 50 years referred to an integrated prostate-assessment unit for cystometry. ▪ Urodynamically confirmed bladder outlet obstruction (BOO) due to BPH, defined as Pdet Q_{max} value within the obstructed area of the Abrams Griffith pressure/flow nomogram. ▪ Bothersome LUTS, defined as an IPSS>=13 and an IPSS QOLscore ≥3 ▪ Written informed consent. **Exclusion criteria:** ▪ History of any illness or surgery that might confound the results of the study, and that produce symptoms which might be confused with those produced by BPH, or that pose additional risk to the patient. ▪ Confirmed or suspected malignancy of the prostate by DRE or biopsy. ▪ PSA level >4 ng/mL unless T1 carcinoma of the prostate excluded by TRUS-guided biopsy. ▪ Previous prostatic surgery or thermotherapy ▪ Pharmacological treatment of symptomatic BPH within the last 6 months. ▪ Confirmed or suspected bladder cancer. ▪ Previous rectal surgery other than haemorrhoidectomy. ▪ Previous pelvic irradiation. ▪ History of cystolithiasis, haematuria or bladder pathology, urethral strictures, bladder neck contracture, active urinary tract infection or prostatitis.	**Group 1: TUNA** A simple disposable 7 F RF needle-electrode was inserted into the lateral lobes of the prostate and, where appropriate, the median lobe of the prostate, using a catheterising endoscope. A standard surgical diathermy generator was used to produce the 10 W of coagulation for 3 min. After treatment, patients were catheterised and allowed home on first-operative day. The catheter was removed and a trial of voiding carried out 7 days after treatment. **Group 2: TURP** Patients undergoing TURP were operated on by an experienced surgeon according	**Mortality**	There were no deaths during the 2-year follow-up.	**Funding:** NR **Limitations:** ▪ Small sample size ▪ Drop outs accounted for but intention to treat analyses not conducted. Patients (2 in TEAP 1 in TURP) who refused cystometry at 6 months were also excluded **Additional outcomes:** ▪ **Post void residual volume** (mL), mean ±SD: 6-months: **Group 1:** 50 (44) (n=20) **Group 2:** 87 (74)(n=22) 1 year: **Group 1:** 104 (109) (n=19) **Group 2:** 21 936) (n=19) 2 years: **Group 1:** 89 (81) (n=19) **Group 2:** 32
			IPSS, median (interquartile range)	Baseline **Group 1:** 20 (15-23) (n=25) **Group 2:** 22 (18-15) (n=25) 6-months: **Group 1:** 9 (6-23) (n=20) **Group 2:** 3 (2-6) (n=22) 1 year: **Group 1:** 6 (4-10) (n=19) **Group 2:** 3 (2-6) (n=19) 2 years: **Group 1:** 8 (5-13) (n=19) **Group 2:** 3 (1-5) (n=19) **P value:** NR for all time points	
			QoL score, median (inter-quartile range)	Baseline **Group 1:** 4 (3-5) (n=25) **Group 2:** 5 (4-5) (n=25) 6-months: **Group 1:** 2 (1-3) (n=20) **Group 2:** 1 (0-2) (n=22) 1 year: **Group 1:** 1 (1-3) (n=19) **Group 2:** 1 (0-2) (n=19) 2 years: **Group 1:** 2 (1-3) (n=19) **Group 2:** 1 (0-2) (n=19) **P value:** NR for all time points	
			Q_{max} (mL/s), mean ±SD	Baseline **Group 1:** 8.5 (3.7) (n=25) **Group 2:** 9.0 (3.6) (n=25) 6-months: **Group 1:** 9.8 (4.0) (n=20) **Group 2:** 18.4 (7.7) (n=22)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	▪ Previous history of neurogenic disorder including Parkinson's disease, multiple sclerosis, stroke and diabetic neuropathy. ▪ Patients wishing to maintain potential fertility. ▪ PVR >250 mL (measured by ultrasonography) ▪ Compromised renal function with a serum creatinine >180 mg/L or radiological evidence of upper tract dilatation. ▪ Unable to provide at least one voided volume of >150 mL. ▪ Unable to give informed consent. **<u>All patients</u>** **N:** 50 **Drop outs:** 12 **<u>Group 1-TUNA</u>** **N:** 25 Dropouts: 5 **Age**, years, mean (range): 66 (56-82) **IPSS**, mean (IQ range): 20 (15-23) **Post void residual volume** (mL), mean ±SD: 55 (44) **PdetQ$_{max}$**(cmH_2O), mean ±SD: 92 (12) **<u>Group 2-TURP</u>** **N:** 25 Dropouts: 3 **Age**, years, mean (range): 71 (56-88) **IPSS**, mean (IQ range): 22 (18-25) **Post void residual volume** (mL): 74 (53) **PdetQ$_{max}$**(cmH_2O), mean ±SD: 99 (10)	to the normal principles of prostatic resection. At the end of the procedure a 22 F three-way urethral catheter was inserted to allow bladder irrigation; after a successful trial of voiding the patient was allowed home. Prophylactic antibiotic cover with 120 mg IV gentamicin was given preoperatively in both groups.		<u>1 year</u>: **Group 1:** 9.7 (5.0) (n=19) **Group 2:** 22 (10.3) (n=19) <u>2 years:</u> **Group 1:** 8.6 (3.5) (n=19) **Group 2:** 18.1 (7.1) (n=19) **P value:** NR for all time points	(42) (n=19) **P value:** NR ▪ **PdetQ$_{max}$**(cmH_2O), mean ±SD **<u>6-months</u>:** **Group 1:** 70 (12) (n=20) **Group 2:** 44 (11) (n=22) **P value:** NR **<u>2 years:</u>** **Group 1:** 71 (36) (n=12) **Group 2:** 36 (8) (n=9) **P value:** NR **Notes:** The methodology stated in MOSTAFID1997[205]. The PdetQmax was the primary outcomes variable in the study design
			Blood transfusion: (2 units each)	**Group 1:** 0/20 **Group 2:** 3/22	
			Incontinence (all were urge incontinence, with detrusor instability)	**Group 1:** 2/20 **Group 2:** 2/22	
			Urinary retention (post-op) (Failed trial of voiding)	**Group 1:** 1/20 **Group 2:** 0/22	
			Clot retention:	**Group 1:** 0/20 **Group 2:** 1/22	
			Urinary tract infection:	**Group 1:** 4/20 **Group 2:** 4/22	
			Persistent dysuria:	**Group 1:** 4/20 **Group 2:** 0/22	
			Treatment failure: Defined as patient dissatisfaction with treatment or the development of complications from persisting BOO, including evidence of detrusor dysfunction, incomplete bladder emptying, urinary retention, infection or upper tract obstruction.	<u>2-year follow-up:</u> **Group 1:** 2/25 **Group 2:** 0/25 One patient was dissatisfied with the outcome at 8 months. Another patient was dissatisfied at 2 years. Both patients were found to have persistent BOO at urodynamic assessment and underwent TURP.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kim et al., 2006 [146] (data obtained from HTA report) **Study design:** RCT **Setting:** Korea, recruitment from January 1998–December 2002 **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** Patients with symptomatic BPE **Inclusion criteria:** NR **Exclusion criteria:** NR **All patients** **N:** 94/110/89/110 204 randomised, from 223 eligible for TEAP vs. TURP 199 randomised from 212 eligible for Laser coagulation vs. TURP 220 randomised out of 235 eligible for TUNA vs. TURP **Drop outs:** overall drop out not reported **Group 1-TEAP** **N:** 94 **Dropouts:** Unknown **Age**, years, mean or median (range) : 66.2 (49–88) **QoL score**, mean: 4.4 **Qmax** (ml/s), mean or median: 7.2 **Residual volume**, (ml), mean or median: 126.1 **Prostate size**, (ml), mean or median: 36.4 **Group 2- TUNA** **N:** 110 **Dropouts:** Unknown **Age**, years, mean or median(range): 66.4 (48–80) **IPSS QoL score**, mean: 4.3 **Qmax** (ml/s), mean or median: 7.0 **Residual volume**, (ml), mean or median:	**Group 1-TEAP** Prostajec device (American Medical Systems, Minnetonka, MN, USA) **Group 2 - TUNA** VidaMed TUNA system (VidaMed Inc.)4 **Group 3 - Laser Coagulation:** Other: procedure: Indigo 830e laser optic system (Ethicon Endosurgery) **Group 4 - TURP**	**IPSS**, mean:	Baseline **TEAP:** 19.5 **TUNA**: 20.8 **Coag**; 21.1 **TURP**: 24.0 3 months **TEAP:** 9.6 **TUNA:** 10.8 **TURP:** 10.6 12 months **TEAP**: 7.5 **TUNA**: 11.6 **TURP**: 8.8	**Funding:** Unknown **Limitations:** ▪ Uncertain whether the data reported was mean or median ▪ Randomisation allocation, concealment and blinding had been rated as "unclear" ▪ Baseline severity of TEAP vs. TURP patient may diffrer: 1. "medium sized" prostates in TEAP vs. large prostate sizes in TURP 2. Mean IPSS at baseline level was numerically higher in TURP compared to TEAP. ▪ Uncertain length of follow up for complications **Additional outcomes:** (values not reported in HTA reported) Duration of operation, Recatheterisation, Retrograde ejaculation, Erectile dysfunction Reoperation, IPSS-QoL,
			Blood transfusion	**TEAP**: 0/94 **TUNA:** 0/100 **TURP**: 19/101 TEAP vs. TURP **RR (95% CI)**: 0.03(0.00 to 0.45) **P value:** 0.01 TUNA vs. TURP: **RR (95% CI)**: 0.03(0.00 to 0.42) **P value:** Sig	
			Urinary retention	**TEAP**: 2/94 **TUNA:** 4/100 **TURP**: 4/101 TEAP vs. TURP **RR (95% CI)**: 0.54 (0.10 to 2.87) **P value:** 0.47 TUNA vs. TURP: **RR (95% CI)**: 1.01 (0.26 to 3.93) **P value:** Not sig	
			Urinary tract infection	**TEAP**: 5/94 **TUNA:**10/100 **TURP**: 7/101 TEAP vs. TURP **RR (95% CI)**: 0.77(0.25 to 2.34)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	257 **Prostate size,** (ml), mean or median: 40.6 **<u>Group 3 - Laser Coagulation</u>** **N:** 89 **Dropouts:** Unknown **Age,** years, mean or median(range): 68.7 (50–89) **IPSS QoL score,** mean: 4.7 **Qmax** (ml/s), mean or median: 8.6 **Residual volume,** (ml), mean or median: 219 **Prostate size,** (ml), mean or median: 42.7 **<u>Group 4 -TURP</u>** **N:** 110 **Dropouts:** Unknown, 9/110? **Age,** years, mean or median(range): 7.4 (60–87) **QoL score,** mean: 4.7 **Qmax** (ml/s), mean or median:11.9 **Residual volume,** (ml), mean or median: 187 **Prostate size,** (ml), mean or median: 44.2			**P value:** 0.64 <u>TUNA vs. TURP</u>: **RR (95% CI):** 1.44(0.57 to 3.64) **P value:** Not sig	Length of hospital stay Qmax, Residual volume , Prostate size **Notes:** Evidence Table produced with data from Evidence Table of the HTA report. Values for complications obtained from Figure 11 of HTA report (page 49).
			Stricture (in the TURP arm, this was recorded as 7 in TEAP vs. TURP and 5 in TUNA vs. TURP- 5 urethral + 2 bladder neck)	**TEAP:** 0/94 **TUNA:** 0/100 **TURP:** 7/101 <u>TEAP vs. TURP</u> **RR (95% CI):** 0.07(0.00 to 1.24) **P value:** 0.07 <u>TUNA vs. TURP</u>: **RR (95% CI):** **P value:**	
			Retrograde ejaculation	**TEAP:** NR **TUNA:**5/100 **TURP:** 39/101 <u>TUNA vs. TURP</u>: **RR (95% CI):**0.13(0.05 to 0.32) **P value:** Not sig	
			Urinary incontinence	**TEAP:** 0/94 **TUNA:** 4/100 **TURP:** 4/101 <u>TEAP vs. TURP</u> **RR (95% CI):** 0.12(0.01 to 2.19) **P value:** 0.15 <u>TUNA vs. TURP</u>: **RR (95% CI):** 1.01 (0.26 to 3.93) **P value:** Not sig	
			Reoperation	**TEAP:** NR **TUNA:** 0/100 **TURP:** 0/101 <u>TUNA vs. TURP</u>: **RR (95% CI):** **P value:**	
			Duration of operation, minutes, mean (range)	**TEAP:** NR **TUNA:** 37(25-60) **TURP:** 51(20-85)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Length of hospitalisation, days, mean (range)	**TEAP:** NR **TUNA:** 1.3(1-3) **TURP:** 6.5(6-8)	

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1 **Evidence Table 39: Transurethral incision of the prostate (TUIP) vs. transurethral resection of the prostate (TURP)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Dorflinger et al., 1992[75] **Study design:** RCT **Setting:** Denmark **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Inclusion criteria:** ▪ bladder neck to seminal crest < 2 cm **Exclusion criteria:** ▪ Prostatic cancer ▪ previous prostatic or major pelvic ▪ surgery; high operative risk or overt ▪ neurological or psychiatric disease; ▪ patients with urethral stricture; prostate size > 20 g **All patients** **N:** 60 Sexually/not sexually active: 44/8 **Drop outs:** **Group 1-TUIP** **N:** 29 **Age**, years, median: 69 **Symptom score, Madsen Iversen** (median) : 15 **Qmax (ml/s)**, median:10 **Urinary retention**:9/29 (31%); **Group 2 -TURP** **N:** 31 **Age**, years, median: 71 **Symptom score, Madsen Iversen** (median) : 15	**Group 1-TUIP** 24Fr resectoscope and Collings knife used. An incision to the depth of the surgical capsule was made at the 7 o clock position **Catheter protocol:** A balloon catheter was inserted into the bladder and left in until urine was clear **Group 2-TURP** 24Fr resectoscope used and prostatic tissue resected in a standard fashion	**Symptom score, Madsen Iversen** (range of 1-27) , median. Only included data from "successfully treated patients"	At baseline **Group 1:** 14.5, n=22 **Group 2:** 16, n=29 **p value:** Not sig At 3 month follow up **Group 1:** 2.5, n=22 **Group 2:** 1, n=29 **p value:** Not sig At12 months follow up **Group 1:** 2, n=21 **Group 2:** 2, n=26 **p value:** Not sig	**Funding:** NR **Limitations:** ▪ Methods of randomisation and concealment and whether subjects were blinded to treatment received were not reported ▪ Only median values were reported for most outcomes **Additional outcomes:** ▪ Median values for Obstructive and Irritative components of Madsen Iversen score at baseline, 3 months and 6 months follow up. ▪ Total voided volume ▪ 1/44 patient was made sexually inactive by the operations ▪ No bladder neck
			Qmax, ml/s, mean± SD:	At baseline **Group 1:** 10.0, n=22 **Group 2:** 8.0, n=29 **p value:** Not sig At 3 month follow up **Group 1:** 15.2, n=22 **Group 2:** 18.8, n=29 **p value:** Not sig At12 months follow up **Group 1:** 14.5, n=21 **Group 2:** 20.2, n=26 **p value:** 0.025 (Mann Whitney signed rank test)	
			Blood transfusion	**Group 1:** 0/29 **Group 2:** 4/31 **p value:** 0.11	
			Retrograde ejaculation (among patients who were sexually active before and after the operations)	**Group 1:** 1/19 **Group 2:** 12/24 **Relative risk:** 0.11(95% CI: 0.02 to 0.51) **p value:** 0.002 [RR calculated by NCGC team]	
			Erectile dysfunction	**Group 1:** 1/19 **Group 2:** 4/24	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Qmax (ml/s), median:8 **Urinary retention**:5/31 (16%)			**p value:** Not sig	contracture **Notes:** Appropriate statistical tests were used Preliminary results reported in Dorflinger1987
			Urethral stricture	**Group 1:** 0/29 **Group 2:** 1/31 **p value:** Not sig	
			Reoperation (data from study abstract)	At12 months follow up **Group 1:** 8/29 **Group 2:** 4/31 **P value:** Not sig	
			Length of hospitalisation, days, median	**Group 1:** 3 **Group 2:** 3 **p value:** Not sig	
			Length of indwelling catheterisation, min, median	**Group 1:** 2 **Group 2:** 2 **p value:** Not sig	
			Length of operation, min, median	**Group 1:** 15 **Group 2:** 30 **p value:** <0.001	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hellstrom1986[114] **Study design:** RCT **Setting:** Finland **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** Patients with symptomatic bladder outlet obstruction **Inclusion criteria:** ▪ Prostate size < 30 g ▪ Symptoms of infravesicle obstruction, including hesitancy, weakened stream, urgency and a feeling of inadequate emptying. **<u>All patients</u>** **N:** 24 **<u>Group 1-TUIP</u>** **N:** 11 **Age (mean):** 63 (54-77) **Drop outs:** Not reported **<u>Group 2 -TURP</u>** **N:** 13 **Age (mean):** 59 (54-63) **Drop outs:** Not reported	**Group 1** TUIP – bladder neck incision using a vertical knife electrode to make a deep diathermy incision from the right ureteral orifice to the verumontanum though the bladder neck and prostatis tissue. **Group 2** TURP Using 26F continuous flow resectoscope by cutting from the bladder neck to the verumontanum and step by step to the prostatic capsule. After both operations a 22F 3-way indwelling catheter was left in position for 3 days and prophylactic sulphatrimethoprim medication used for about 2 weeks.	**All cause mortality** (myocardial infarction in TURP and colon cancer in TUIP)	**Group 1:** 1/24 **Group 2:** 1/25 **p value:** Not sig	**Funding:** Not reported **Limitations:** ▪ No symptom scores were collected ▪ Randomisation method reported but concealment method unclear **Additional outcomes:** None **Notes:** None
			Mean (SD) Qmax	**Group 1:** 12.9 (6) **Group 2:** 16.5 (6)	
			Transfusion	**Group 1:** 0/11 **Group 2:** 0/13	
			Acute urinary retention	**Group 1:** 0/11 **Group 2:** 0/13	
			UTI	**Group 1:** 0/11 **Group 2:** 0/13	
			Stricture	**Group 1:** 1/11 **Group 2:** 0/13	
			Retrograde ejaculation	**Group 1:** 0/11 **Group 2:** 8/12	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Johnson et al., 1998[129] **Study design:** RCT, open **Setting:** Sweden. Feb to Sept 1991 **Evidence level:** 1+ **Duration of follow-up:** 60 months	**Patient group:** small to medium BPH **Inclusion criteria:** ▪ Admitted from the waiting list for surgical treatment of BPH ▪ No previous treatment for BPH ▪ Estimated prostate weight at DRE 20-40g, or 20-40mL by TRUS ▪ Distance from verumontanum to bladder neck < 4.0cm1 **Exclusion criteria:** ▪ Bladder stone or cancer ▪ Cystitis ▪ Clinical prostatic cancer ▪ Prominent median lobe of the prostate ▪ Adequate follow up difficult for geographical, psychological or social reasons **All patients** **N:** **Age**, years, mean (±SD): **Drop outs:** **Group 1** **N:** 43 **Drop outs:** 2 (reoperated after failing to void post catheter removal) **Age**, years, mean (range): 70.2 (52–87)	**Group 1-TUIP** **Catheter protocol:** overnight **Others:** Perioperative heparin :13 Antibiotics:17 **Group 2-TURP** Resected in a standard manner from bladder neck to verumontanum out to the prostate capsule **Catheter protocol:** overnight **Others:** Perioperative heparin:17 Antibiotics: 14 Resection weight, g, mean (range): 18.8 (8–45) **For both groups:** Anti provided to those who had indwelling catheter preoperatively, diabetes mellitus or with positive urine culture	**All cause mortality** (due to cerebrovascular lesion at 8 weeks)	**Group 1:** 0/43 **Group 2:** 1/42 **p value:** Not sig	**Funding:** NR **Limitations:** ▪ Methods of randomisation and concealment and whether subjects were blinded to treatment received were not reported ▪ Patients who were reoperated not included in analysis **Additional outcomes:** ▪ Cystoscopy at 24 and 60 months to investigate healing and incision ▪ Post void residual volume, blood loss in volume, number of preoperative positive cultures. ▪ 3 patients in TURP group was detected with cancer **Notes:** None.
			Symptom score (Madsen Iversen, total score), mean (95% CI)	At baseline **Group 1:** 15.4 (6–27), n=43 **Group 2:** 15.8 (5–28), n=42 At 3 months: **Group 1:** 3.5(0-21), n=41 **Group 2:** 3.8(0-16), n=39 At 6 months: **Group 1:** 4.3(0-21),n=36 **Group 2:** 3.5(0-18),n=34 At 12 months: **Group 1:** 3.6(0-15),n=31 **Group 2:** 2.8(0-11),n=32 At 24 months: **Group 1:** 4.5(0-14),n=33 **Group 2:** 4.7(0-17),n=31 At 60 months: **Group 1:** 4.5(0-14),n=22 **Group 2:** 4.7(0-17),n=24 **p value:** Not sig between groups; Sig compared to baseline
			Qmax, ml/s, mean (95% CI) estimated from graph for follow ups:	At baseline **Group 1:** 9 (7.5–11) ,n=34 **Group 2:** 8.5 (7.5–9.5), n=36 At 3 months: **Group 1:** 20, n=41 **Group 2:** 15, n=39 At 60 months: **Group 1:** 15, n=22 **Group 2:** 12, n=24 **p value:** Reported sig difference between groups at 3, 6, 12 and 24 months. Not sig diff between groups at 60 months. All sig better than baseline except at 60 months

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Madsen Iversen, mean (95% CI):15.4 (6–27) **Prostate size,** ml, mean (range): 26.2(20.0-37.6) **Residual volume,** ml, mean (range): 139 (0–650) **Indwelling catheter:** 7/43 **<u>Group 2</u>** **N:** 42 **Drop outs:** 2 (1lost to follow up at 8 weeks, 1 died) **Age,** years, mean (±SD): 70.8 (56–85) **Madsen Iversen,** mean (95% CI): 15.8 (5–28) **Prostate size,** ml, mean (range): 25.4(20.0-39.8) **Residual volume** ml, mean (range): 109 (0–400) **Indwelling catheter:** 8/42		**Blood transfusion**	**Group 1:** 0/43 **Group 2:** 1/42 **p value:** Not sig	
			Urinary retention, 2 cases from TUIP group failed to void after catheter removal. 1 from TURP group had urinary retention 3 weeks post surgery and a bladder neck stricture was incised 3 weeks later	**Group 1:** 2/43 **Group 2:** 1/42 **p value:** Not sig	
			Reoperation rate (repeated when it was impossible to remove the indwelling catheter or symptoms scores deteriorated, combined with a maximum urinary flow rate of ≥150ml)	**Group 1:** 10/43 (within 1-38 months) **Group 2:** 3/42 (within 2-25 months) **Relative risk:** 3.26 (95% CI: 1.06 to 10.65) **p value:** 0.04	
			Catheter duration, days, mean (range)	**Group 1:** 2.8 (1-15) **Group 2:** 1.4(1-5) **P value:** Sig	
			Duration of operation, min, mean (range)	**Group 1:** 15 (5-40) **Group 2:** 32 (15-60) **P value:** Sig	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Larsen et al., 1987[158] **Study design:** RCT, open **Setting:** US, Veteran Affairs **Evidence level:** 1+ **Duration of follow-up:** 1 year	**Patient group:** ▪ Men with symptoms of prostatism due to BPH **Inclusion criteria:** ▪ Estimated prostate weight at cystoscopy to be ≤20g **Exclusion criteria:** ▪ Severe neurologic and or psychiatric disease ▪ Previous TURP ▪ Urethral stricture ▪ Urinary retention ▪ Clinical suspicion of cancer of the prostate ▪ Previous major intrapelvic surgical procedures **All patients** **N:** 40 **Drop outs:** 3 (2 lost to follow up- 1 had operation cancelled) **Group 1 –TUIP** **N:** 19 **Age**, years, median (range): 63(51-73) **Estimated prostate weight**, g, median(range): 20(10-20) **Duration of symptoms**, months, median(range): 24(6-240) **Group 2 –TURP** **N:** 18 **Age**, years, median (range):	**Group 1- TUIP** Performed using Colling's knife at the 6 pm position extending form the internal urethral orifice to the verumontanum down through the prostate and the capsule. A 3-way Foley catheter with continuous irrigation was used for bladder drainage. **Group 2 – TURP** performed using method described by Blandy JP 1978. **All** patients received antibiotic prophylaxis	**Symptom score** (Madsen Iversen, Total score), median (range)	Baseline **Group 1:** 17(9-23), n=19 **Group 2:** 17(9-23), n=18 At 3-month follow up **Group 1:** 2(0-19), n=19 **Group 2:** 2(0-12), n=18 At 12-month follow up **Group 1:** 2(0-19), n=12 **Group 2:** 2(0-7), n=11 **p value:** Not sig between groups; <0.05, compared to baseline values using Mann Whitney signed rank test	**Funding:** US Veterans Administration and Danish Medical Research Council grant **Limitations:** ▪ Methods of randomisation and concealment and whether subjects were blinded to treatment received were not reported ▪ Relevance of study – published in 1987 **Additional outcomes:** Voided volume, post void residual volume **Notes:** None.
			Symptom score (Madsen Iversen, Irritative score), median (range)	Baseline **Group 1:** 13(5-16), n=19 **Group 2:** 12(4-16)18 At 3-month follow up **Group 1:** 0(0-15), n=19 **Group 2:** 1(0-7), n=18 At 12-month follow up **Group 1:** 0(0-8), n=12 **Group 2:** 0(0-5), n=11 **p value:** Not sig between groups; <0.05, compared to baseline values using Mann Whitney signed rank test	
			Symptom score (Madsen Iversen, Obstructive score), median (range)	Baseline **Group 1:** 5(2-8), n=19 **Group 2:** 5(2-8), n=18 At 3-month follow up **Group 1:** 1(0-5), n=19 **Group 2:** 1(0-6), n=18 At 12-month follow up **Group 1:** 1(0-3), n=12 **Group 2:** 1(0-6), n=11 **p value:** <0.05, compared to baseline values using Mann Whitney signed rank test	
			Qmax, ml/s, median (range)	Baseline	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	61(43-74) **Estimated prostate weight,** g, median(range): 20(15-20) **Duration of symptoms,** months, median(range): 24(0.5-72)			**Group 1:** 7.4(2.7-27.3), n=15 **Group 2:** 8.6(1.7-15.5), n=16 At 3-month follow up **Group 1:** 14.4(2.6-34.6), n=15 **Group 2:** 18.5(5.3-45.3), n=16 At 12-month follow up **Group 1:** 16.3(6.4-34.7), n=11 **Group 2:** 20.6(9.0-41.3), n=11 **p value:** Not sig between groups; <0.05, compared to baseline values using Mann Whitney signed rank test	
			Urinary tract infections (within 1 month of surgery)	**Group 1:** 2/19 **Group 2:** 3/18 **P value:** Not sig	
			Post operative bleeding (definition not provided)	**Group 1:** 1/19 **Group 2:** 2/18 **P value:** Not sig	
			Recatheterisation (2 cases due to bleeding and clot retention in TURP, and 1 case due to haematuria on 10th day for TUIP)	**Group 1:** 1/19 **Group 2:** 2/18 **P value:** Not sig	
			Retrograde ejaculation (based on number of patients who were potent and had antegrade ejaculation preoperatively)	**Group 1:** 2/10 **Group 2:** 8/10 **Relative risk:** 0.25 (95% CI: 0.09 to 0.71) **p value:** 0.02 [*calculated by NCGC using Fisher's exact test*]	
			Catheterisation, hours median (range)	**Group 1**: 1(1-2) **Group 2:** 2(2-7) **p value:** Not sig between groups; **<**0.01 (Mann Whitney signed rank test)	
			Hospital stay, days, median (range)	**Group 1:** 2.5(1-4) **Group 2:** 4.5(3-10) **p value:** Not sig between groups; <0.01 (Mann Whitney signed rank test)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Li et al., 1987[165] **Study design:** RCT, open **Setting:** Hong Kong **Evidence level:** 1+ **Duration of follow-up:** Up to 3 months	**Patient group:** Patient with prostatism presented with acute urinary retention **Inclusion criteria:** ▪ Acute urinary retention ▪ Ambulatory ▪ Diagnosis confirmed with urethroscopy with use of local anaesthesia before operation **Exclusion criteria:** ▪ medical diseases such as ischaemic heart disease, stroke, diabetes mellitus. **All patients** **N:** 59 **Group 1 –TUIP** **N:** 29 **Dropouts:** 0 **Age**, years, mean (±SD): 65±1.4 **Prostate size**, g, mean(±SD): NR **Group 2** -TURP **N:** 30 **Dropouts:** 0 **Age**, years, mean (±SD): 70±1.7 **Prostate size**, g, mean(±SD): NR	**Group 1-TUIP** Bladder neck resection was performed with diathermy loops. A 24 or 26F continuous irrigation Wolf resectoscope was used. The prostate was resected at the 4 and 8 o'clock positions until the capsule was reached. Homeostasis was secured before the capsule of the prostate was incised. Incisions were made with the same diathermy loop until extracapsular fat was reached. The incision extended from the verumontanum to the level below the trigone. The prostatic chips, which weighted approximately 5 g were sent for pathological examination **Group 2-TURP** The usual complete resection of the prostatic adenoma to the capsule was performed. A 22F 3-way Foley catheter was used with traction on a 40 to 50 ml balloon and irrigation with normal saline in both situations.	**Mortality (at operation)**	**Group 1:** 0/29 **Group 2:** 0/30 **p value:** Not sig	**Funding:** NR **Limitations:** ▪ Baseline parameters, except age, not reported (patients were in acute urinary retention). ▪ Method of concealment not reported. ▪ No symptom scores were collected **Additional outcomes:** Bleeding or extravasation requiring further operation=0 **Notes:** All the surgeries were only performed by 2 "experienced urologists"
			Qmax (ml/s), mean ±se [baseline values not reported]	At 3 months **Group 1:** 22.8±2.9 **Group 2:** 18.5±2.7 **p value:** Not sig	
			Perioperative complications: Blood transfusions determined by anaesthetist based on blood pressure , pulse rate, and general condition or observation on the return of irrigation fluid	**Group 1:** 2/29 **Group 2:** 13/30 **Relative risk:** **95% CI:** **p value:** 0.004	
			Perioperative complications: UTI	**Group 1:** 5/29 **Group 2:** 13/30 **Relative risk:** **95% CI:** **p value:** 0.05	
			Perioperative complications: TUR syndrome	**Group 1:** 0/29 **Group 2:** 0/30 **p value:** Not sig	
			Post operative complications: Acute urinary retention	**Group 1:** 0/29 **Group 2:** 0/30 **p value:** Not sig	
			Recatheterisation (due to secondary haemorrhage)	**Group 1:** 0/29 **Group 2:** 2/30 **p value:** Not sig	
			Urinary incontinence (transient, 2 weeks for the TURP group)	**Group 1:** 1/29 **Group 2:** 2/30 **p value:** Not sig	
			Urethral stricture (at bulbous urethra asymptomatic, detected using cystoscopy)	At 3 months **Group 1:** 0/29 **Group 2:** 1/30 **p value:** Not sig	
			Bladder neck stenosis	At 3 months	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			(asymptomatic, detected using cystoscopy)	**Group 1:** 0/29 **Group 2:** 1/30 **p value:** Not sig	
			Length of operation, min, mean±se	**Group 1:** 19±2.9 **Group 2:** 36±3.6 **p value:** 0.0002	
			Length of hospitalisation, days, mean ± se	**Group 1:** 5.6±0.6 **Group 2:** 8.0±1.3 **p value:** Not sig	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Nielsen1988[221] **Study design:** RCT **Setting:** Odense University Hospital, Denmark **Evidence level:** 1+ **Duration of follow-up:** Up to 1 year	**Patient group:** Consecutive patients with symptomatic benign BPH **Inclusion criteria:** ▪ patients with symptomatic bladder outlet obstruction cause by prostate hypertrophy ▪ Age >60 **All patients** **N:** 49 **Drop outs:** 4 at 12 months (2 deaths, 2 refused to attend follow up) **Group 1-TUIP** **N:** 24 **Age**, years, median: 69(60-85) **Qmax (ml/s)**, median; 5(5-10) **Prostate weight**, g, estimated: <30: 3 30-50:14 >50: 7 **Group 2 -TURP** **N:** 25 **Age**, years, median: 73(61-83) **Qmax (ml/s)**, median; 5(5-13) **Prostate weight**, g, estimated: <30: 7 30-50:14 >50: 4	**Group 1-TUIP** After cytoscopy, a resectoscope was inserted and a cut was made along the sulcus, using the Stortz diathermy knife, either at 5 or 7 o'clock from the left or right ureteric orifice to the level of the verumontanum, and deepened along its whole length until reaching the fat layer. **Group 2-TURP** The whole of the prostatic gland resected using a cutting loop. **For both groups:** Haemostasis was achieved using electrocoagulation. Prophylactic antibiotics not used **Anaesthesia:** spinal or general **Catheter protocol:** A catheter (18 to 22 F) was inserted and withdrawn as soon as urine became clear.	**All cause mortality** (myocardial infarction in TURP and colon cancer in TUIP)	**Group 1:** 1/24 **Group 2:** 1/25 **p value:** Not sig	**Funding:** NR **Limitations:** ▪ No symptom scores were collected ▪ Randomisation method reported but concealment method unclear **Additional outcomes:** **Notes:** Sample size calculation provided for this study – assumption that TURP was 30% better (not stated which outcome) that TUIP, at the 90% power and Type I error or 0.05. Authors reported statistical significance based on fisher's exact test or Mann Whitney test (appropriate) Sexual function, eg retrograde ejaculation not reported
			Qmax, ml/s, mean	At baseline **Group 1:** 5(5-10), n=24 **Group 2:** 5(5-13), n=25 **p value:** Not sig At 2 month follow up **Group 1:** 10(7-18), n=24 **Group 2:** 17(6-32) n=25 **p value:** <0.02 At12 months follow up **Group 1:** 9(5-25), n=22 **Group 2:** 12(5-28), n=23 **p value:** Not sig	
			Perioperative complication; Blood transfusion	**Group 1:** 1/24 **Group 2:** 20/25 **Relative risk:** **p value:** <0.02	
			Septicaemia	**Group 1:** 1/24 **Group 2:** 2/25 **p value:** >0.1	
			Acute urinary retention (required reoperation, TURP)	**Group 1:** 3/24 **Group 2:** 0/25 **p value:** Not sig	
			Clot retention (reoperation required)	**Group 1:** 1/24 **Group 2:** 1/25 **p value:** Not sig	
			Incontinence	**Group 1:** 0/24 **Group 2:** 1/25 **p value:** Not sig	
			Successful (incontinence or increased frequency of micturation was not considered not successful results)	At 2 month follow up **Group 1:** 24/24, n=24 **Group 2:** 20/25 n=25 **p value:** Not sig	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				At12 months follow up **Group 1:** 21/22, n=22 **Group 2:** 18/23, n=23 **p value:** Not sig	
			Reoperation rate (At 2 months, 3 patients in the TUIP group had urinary retention group had required TURP. 1 patient from each group had clot retention and had to be operated again)	At 2 month follow up **Group 1:** 4/24 **Group 2:** 1/25 At 12 month follow up This was not clearly reported	
			Stricture (4 patients in TURP group had stricture, 2 had internal urethratomy and 2 by dilatation)	At 2 month follow up **Group 1:** 0/24 **Group 2:** 4/25	
			Length of catheterisation days, median (range)	**Group 1:** 1(1-2) **Group 2:** 1(1-4) **p value :** >0.1	
			Length of operation, minutes, median (range)	**Group 1:** 18 (10-35) **Group 2:** 45(20-80) **p value:** <0.01	
			Length of hospitalisation, days, median, (range)	**Group 1:** 3(2-13) **Group 2:** 3(2-18) **p value:** >0.1	

See Evidence Table 26 Laser coagulation vs. transurethral resection of the prostate (TURP)

for Rodrigo et al., 1998[253]

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Riehmann et al., 1995[250] **Study design:** RCT **Setting:** Jan 1985 to Aug 1990, Madison, Wisconsin, US **Evidence level:** 1+ **Duration of follow-up:** Mean 34 months (range 7 to 82 months)	**Inclusion criteria:** patients with bladder outlet obstruction symptoms **Exclusion criteria:** ▪ prostatic urethra > 3 cm or median lobe > 2g ▪ previous prostatic or major pelvic surgery ▪ high operative risk or overt neurological or psychiatric disease **<u>All patients</u>** **Number of eligible patients:** 120 **Number of patients randomised:** 117 **Drop outs:** 5 (1 received radical prostatectomy after TURP specimen revealed cancer of the prostate, 1 had bladder perforation during the surgery and 1 patient who had TUIP initially had a TURP before the one month follow up) Mean age: **<u>Group 1-TUIP</u>** **N:** 61 **Drop outs:** **Age,** years, mean (range):65(51–77) **Madsen Iversen score,** mean: 15.5	**Group 1-TUIP** Performed using a Coling's knife at the 6 o'clock position from the bladder neck distally to the verumontanum. The incision extended through the posterior prostatic capsule **Group 2-TURP** The prostate was resected completely and circumferentially to the anatomic capsule from the bladder neck to the verumontanum. Mean weight of tissue resected : 15 g (range from 1 to 37 g) **For both groups** Procedures were performed by staff members or residents supervised for staff	**All cause mortality** (one death in the TURP group was due to saddle pulmonary embolism, classified as operative death) **Madsen Iversen,** (range of 1-27), mean±se *[Values estimated from graph]*	**Group 1:** 14/61 **Group 2:** 8/56 **p value:** Not sig <u>At baseline</u> **Group 1:** 15.5, n=61 **Group 2:** 15.5, n=56 **p value:** Not sig <u>At 3 month follow up</u> **Group 1:** 6 SE1 n=51 **Group 2:** 6, SE1 n=52 **p value:** Not sig <u>At12 months follow up</u> **Group 1:** 6 SE 0.5, n=50 **Group 2:** 5.5 SE 0.5, n=46 **p value:** Not sig <u>A24 months follow up</u> **Group 1:** 7 SE 1, n=41 **Group 2:** 5 SE 1.5, n=40 **p value:** Not sig <u>At 36 months follow up</u> **Group 1:** 8 SE 1, n=22 **Group 2:** 6.5 SE 1.5, n=19 **p value:** Not sig <u>At 48 months follow up</u> **Group 1:** 10.5 SE 1, n=17 **Group 2:** 9.5 SE 1.5, n=17 **p value:** Not sig <u>At 60 months follow up</u> **Group 1:** 9.5 SE 1, n=8 **Group 2:** 9.5 SE 1.5, n=15 **p value:** Not sig <u>At 72 months follow up</u> **Group 1:** 10 SE 1, n=6 **Group 2:** 9.5 SE 1.5, n=11 **p value:** Not sig All stat sig compared to	**Funding:** Not stated **Limitations:** ▪ Methods of randomisation and concealment and whether subjects were blinded to treatment received were not reported ▪ Results reported graphically-actual values not stated ▪ Qmax significantly higher in TURP group preoperatively **Additional outcomes:** ▪ Madsen Iversen symptom score – results reported in graph, no statistical difference between two groups' pre and post operatively. The scores were significantly lower compared to baseline for both procedures. ▪ Overall subjective assessment of surgical outcomes ▪ Perforation during surgery- 1 case (did not state which arm) **Notes:** Christensen1990[52] reported the preliminary results

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Qmax , ml/s mean: 9 (n = 52) **Group 2-TURP** **N:** 56 **Drop outs:** **Age,** years, mean (range):64 (42–78) **Madsen Iversen score,** mean: 15 **Qmax** , ml/s mean:11 (n = 50)			baseline	
			Qmax, ml/s, mean± SD: *[Values estimated from graph]*	At baseline **Group 1:** 9, n=52 **Group 2:** 11, n=50 **p value:** Stat sig, p<0.015 At 3 month follow up **Group 1:** 15 SE2 n=42 **Group 2:** 20, SE2 n=44 **p value:** Stat sig, p<0.015 At12 months follow up **Group 1:** 16 SE 2 , n=42 **Group 2:** 19 SE 2, n=37 **p value:** Not sig A24 months follow up **Group 1:** 12.5 SE 1, n=32 **Group 2:** 17 SE 2, n=31 **p value:** Stat sig, p<0.015 At 72 months follow up **Group 1:** 13 SE 4, n=4 **Group 2:** 19 SE 5, n=8 **p value:** Not sig Not sig compared to baseline for 72 month follow up	
			Reoperation (TURP group – 8 TUIP or resection of bladder neck contracture, 1 further TURP, TUIP group- 12 received TURP, 1 received another TUIP)	**Group 1:** 13/61 **Group 2:** 9/56 **p value:** Not sig	
			Retrograde ejaculation (among patients who were sexually active before an after surgery)	**Group 1:** 8/23 **Group 2:** 15/22 **Relative risk:** **95% CI:** **p value:** 0.02	
			Duration of operation time, mean, (range)	**Group 1:** 23 (7 to 95) **Group 2:** 55 (5 to 135) **P value:** 0.001	
			Catheter duration, day,	**Group 1:** 1.4 (1-3)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			mean,(range)	**Group 2:** 2.5(1-12) **P value:** 0.001	
			Length of hospital stay day, mean,(range)	**Group 1:** 3.0 (1-8) **Group 2:** 4.3 (2-14) **P value:** 0.001	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Saporta et al., 1996[268] **Study design:** RCT **Setting:** Not stated (Israel/Turkey) **Evidence level:** 1+ **Duration of follow-up:** 72 months	**Inclusion criteria:** ▪ patients with obstructive BPH symptoms ▪ prostate weight at DRE ≤ 40g **Exclusion criteria:** ▪ chronic urinary retention ▪ urethral stricture, bladder cancer, prostatitis; clinical and suspicion of prostatic cancer; ▪ prominent median lobe of prostate ▪ neurogenic bladder **<u>All patients</u>** **N:** 40 **Age**, years, mean (±SD): **Drop outs:** 4 **<u>Group 1</u>** **N:** 20 **Drop outs:** 3 **Age**, yea , mean (±SE): 66.85 ± 2.28 **Prostate size** , g, mean(±SE): 29.55±.0.94(20-37) **Sexually active with antegrade ejaculation:** 16/20† **<u>Group 2</u>** **N:** 20 **Drop outs:** 1 at 3rd year **Age**, years, mean (±SE): 71.45 ± 1.15 **Prostate size** , g, mean(±SE): 30.0±1.51(19-40) **Sexually active with antegrade ejaculation:** 10/20†	**Group 1-TUIP** Incision with Collings knife from interureteric ridge from 6 o'clock to verumontanum as deep as fat layer **Catheter protocol:** 20Fr Foley for 18–24 hours **Group 2-TURP** Low pressure continuous flow with trocar cystostomy **Catheter protocol:** 14Fr Foley through trocar cystostomy channel and 20Fr Foley through urethra; irrigated for 18–24 hours; 14Fr Foley removed next day, 20Fr 48 hours after procedure **For both groups:** spinal, epidural or general were used	**Symptom score, Madsen Iversen** (range of 1-27) , mean ± se (range)	<u>At baseline</u> **Group 1:** 14.7±0.96 (7-21) **Group 2:** 14.3±0.93 (6-22) **p value:** Not sig <u>At 1st year</u> **Group 1:** 5.29±0.62 (2-13), n=17 **Group 2:** 4.95±0.74 (1-14), n=20 **p value:** Not sig <u>At 3rd year</u> **Group 1:** 7.0±0.64 (3-14), n=17 **Group 2:** 5.79±0.85 (1-18), n=19 **p value:** Not sig	**Funding:** Not stated **Limitations:** ▪ Baseline slightly different ▪ Methods of randomisation and concealment and whether subjects were blinded to treatment received were not reported ▪ Patients who were reoperated not included in analysis **Additional outcomes:** There was a third arm of balloon dilatation. **Notes:** Appropriate non-parametric tests used for this study † Unequal number of patients with retrograde ejaculation at baseline
			Global assessment of symptoms (marked/moderate or slight improvement/no improvement or worse, %) Patients who required additional treatment were recorded as no improvement	<u>At 1st year</u> **Group 1:** 80/5/15 **Group 2:** 85/10/5 **p value:** Not sig <u>At 3rd year</u> **Group 1:** 50/30/20 **Group 2:** 60/35/5 **p value:** Not sig	
			Qmax, ml/s, mean ± se(range)	<u>At baseline</u> **Group 1:** 7.35±0.56 (3.7-12) **Group 2:** 6.5±0.43(3.2-11.9) **p value:** Not sig <u>At 1st year</u> **Group 1:** 14.58±1.05(5.3-5.7), n=17 **Group 2:** 17.29±1.16(8.2 -7.1), n=20 **p value:** Not sig <u>At 3rd year</u> **Group 1:** 12.65±1.04(4.1-23.3), n=17 **Group 2:** 14.36±1.14(5.5-25.5), n=19 **p value:** Not sig	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Retrograde ejaculation †	At 3rd year **Group 1:** 3/16 **Group 2:** 9/10 **RR:** 0.21 (0.14-0.49) **P value:** 0.001 [calculated by NCGC team using Fisher's exact test]	
			Reoperation rate For TURP patient- 1 internal urethrotomy in 3rd year. For TUIP patients, 2 had TURP and 1 had another TUIP at 1 year	At 1st year **Group 1:** 3/20 **Group 2:** 0/20 **P value:** NR At 3rd year **Group 1:** 3/20 **Group 2:** 1/20 **P value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Soonawalla and Pardanani1992 [285] **Study design:** RCT **Setting:** India **Evidence level:** 1+ **Duration of follow-up:** 24 months	**Inclusion criteria:** ▪ patients with prostate hypertrophy **Exclusion criteria:** ▪ prostatic cancer or suspicion of malignancy ▪ prostate size >30g **All patients** **N:** 220 **Age:** 45-87 years **Group 1-TUIP** **N:** 110 **Age**, years, mean: 62.2 **Qmax (ml/s)**, mean; 7.91 **Prostate weight**, g, mean: 14.8 **Sexually active:** 60/110 **Group 2 -TURP** **N:** 110 **Age**, years, mean: 65.0 **Qmax (ml/s)**, mean; 8.04 **Prostate weight**, g, mean: 15.6 **Sexually active:** 49/110	**Group 1-TUIP** A single incision at the 5 or 7 o clock position extending from below the ureteric orifice up to the verumontanum was made the Coling's knife and deepened up to the perivesicle and periprostatic fat along its entire length **Anaesthesia:** general Anaesthesia (69) and spinal (24), local (17 cases) **Catheter protocol:** 24Fr Foley; 24–48hours **Group 2-TURP** **Catheter protocol:** 24Fr Foley; ≤ 48hours **For both groups:** **Anaesthesia:** general Anaesthesia (88) and spinal (20) and epidural (2 cases)	**All cause mortality** (myocardial infarction- 1 each in TUIP and TURP, 1 septicaemia in TURP	**Group 1:** 1/110 **Group 2:** 2/110 **p value:** Not sig[#]	**Funding:** NR **Limitations:** ▪ Methods of randomisation and concealment and whether subjects were blinded to treatment received were not reported ▪ No symptom scores were collected **Additional outcomes:** ▪ 4/7 of the patients with retention after TUIP had repeat TUIP, and 3 had resection. All 4 TURP patients with urinary retention had reoperation. ▪ % of patients satisfied (excellent/fair) vs. not satisfied (no change/worse)- determined "subjectively", methods not reported **Notes:** [#] Relative risk (RR) and/or P value
			Qmax, ml/s, mean	At baseline **Group 1:** 7.91, n=110 **Group 2:** 8.04, n=110 At 3 month follow up **Group 1:** 19.38, n=110 **Group 2:** 20.69 n=110 At12 months follow up **Group 1:** 19.45, n=70 **Group 2:** 20.10, n=67 At 24 months follow up **Group 1:** 18.91, n=70 **Group 2:** 19.86, n=67 **p value:** Not sig for all time points	
			Perioperative complication; Blood transfusion (mean number of units transfused per patient was 0.44)	**Group 1:** 0/110 **Group 2:** 38/110 **Relative risk:** 0.0(95% CI: 0.00 to 1.00)[#] **p value:** <0.001[#]	
			TUR Syndrome	**Group 1:** 0/110 **Group 2:** 7/110 **RR:** 0.00 (95%CI: 0.00 to 0.53)[#] **p value:** 0.01[#] [RR and P value calculated by NCGC team]	
			Haemorrhage, 3 intraoperative, requiring open surgery, 2 post-operative haemorrhage	**Group 1:** 0/110 **Group 2:** 5/110 **p value:** Not sig[#]	
			Perforation requiring open surgery	**Group 1:** 2/110 **Group 2:** 3/110 **p value:** Not sig[#]	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Acute urinary retention (failure to void upon catheter removal)	**Group 1:** 7/110 **Group 2:** 4/110 **p value:** Not sig#	calculated by NCGC team using Fisher's exact test
			Acute renal failure	**Group 1:** 0/110 **Group 2:** 1/110 **p value:** Not sig #	
			Retrograde ejaculation (among sexually active patients before and after the operations)	**Group 1:** 14/60 **Group 2:** 13/49 **p value:** Not sig #	
			Erectile dysfunction	**Group 1:** 0/60 **Group 2:** 0/49 **p value:** Not sig#	
			Epididymo-orchitis	**Group 1:** 5/110 **Group 2:** 2/110 **p value:** Not sig#	
			Urethral stricture	**Group 1:** 5/110 **Group 2:** 3/110 **p value:** Not sig#	
			Incontinence	**Group 1:** 2/110 **Group 2:** 4/110 **p value:** Not sig#	
			Length of hospitalisation, days, mean	**Group 1:** 6.03 **Group 2:** 7.16 **p value:** NR	
			Length of indwelling catheterisation, min, mean	**Group 1:** 2.62 **Group 2:** 3.01 **p value:** NR	
			Length of operation, min, mean	**Group 1:** 20.4(10-40) **Group 2:**59.2(30-95) **p value:** NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Tkocz and Prajsner 2002[295] **Study design:** RCT **Setting:** Poland **Evidence level:** 1+ **Duration of follow-up:** 24 months	**Patient group:** Men with moderate symptoms of BPH caused by a small prostate **Inclusion criteria:** ▪ prostate size<30g **Exclusion criteria:** ▪ presence of median lobe **All patients** **N:** 100 **Mean age:** 68±6.7(51 to 78) years **Drop outs:** 0 (no drop outs reported) **Group 1** **N:** 50 **Dropouts:** 0 **Age,** years, mean (±SD): Not reported separately for each group **IPSS,** mean (±SD): 17.1±2.2 **IPSS-QoL,** mean (±SD): 4.6±0.5 **Prostate size** (incised adenoma), g, mean(±SD): 27±2 **Residual volume,** mean ± SD (ml): 75 ± 22 Pdetmax, cmH2O, mean ± SD: 84 ± 10 **Group 2** **N:** 50 **Dropouts:** 0 **Age,** years, mean (±SD): Not	**Group 1-TUIP** Incisions with a Collins blade, from the urethral orifice to the level of the urethral colliculus, deeply reaching the perivesicle fat. All incisions were performed bilaterally, thus resulting in the full opening of the neck and prostatic urethra. **Catheter protocol:** Foley 18-French catheter left in the urethra for 24 hours **Group 2-TURP** Performed using the resectoscope, calibre 24-French. **All:** subarachnoid anaesthesia with hyperbaric lidocaine	**Symptom score, IPSS** (range of 1-35), mean±sd	At baseline **Group 1:** 17.1±2.2 **Group 2:** 17.1±1.9 **P value:** Not sig At 24 months: **Group 1:** 4.1±1.8 **Group 2:** 5.1±1.9 **p value:** Not sig between groups; <0.01 compared to baseline	**Funding:** NR **Limitations:** ▪ Methods of randomisation and concealment not reported ▪ Patient diary- no mention of content, validation and duration of method of data collection and analysis **Additional outcomes:** Urodynamic parameters such as Pdetop, PdetQmax, CysCapF etc **Notes:** No patient reported to have dropped out from study
			IPSS-QoL(range of 1-6) mean±sd	At baseline **Group 1:** 4.6±0.5 **Group 2:** 4.4±0.3 At 24 months: **Group 1:** 2.1±0.3 **Group 2:** 1.9±0.6 **p value:** Not sig between groups; <0.01 compared to baseline	
			Qmax, ml/s, mean± SD:	At baseline **Group 1:** 7.6±1.8 **Group 2:** 6.9 ±1.5 At 24 months: **Group 1:** 16.9±1.9 **Group 2:** 17.6±1.7 **p value:** Not sig between groups; <0.01 compared to baseline	
			Blood transfusion	**Group 1:** 0/50 **Group 2:** 1/50 **p value:** Not sig	
			Retrograde ejaculation	**Group 1:** 6/50 **Group 2:** 16/50 **Relative risk:** 0.38(95% CI: 0.16 to 0.84 **P value:** 0.03	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	reported separately for each group **IPSS**, mean (±SD): 17.1±1.9 **IPSS-QoL**, mean (±SD): 4.4±0.3 **Prostate size** (resected adenoma), g, mean(±SD); 28.2±2 **Residual volume**, ml, mean ±SD : 68 ±21 **$Pdet_{max}$**, cmH2O, mean, ±SD : 85 ±8		**Detrusor instability**	Baseline; **Group 1:** 31/50 **Group 2:** 30/50 At 24 months **Group 1:** 15/50 **Group 2:** 11/50 **P value:** Not sig	
			Weakening of detrusor post operation ("lazy" and incomplete voiding, returned to normal by 24 months)	Post-op (time not provided) **Group 1:** 4/50 **Group 2:** 11/50 P value: Not sig At 24 months **Group 1:** 0/50 **Group 2:** 0/50	
			Urinary frequency, diurnal (recorded through diary. Diary kept for 7 days after preliminary examination (baseline. No mention of how many days data were collected for follow up)	Baseline; **Group 1:** 7.8±0.9 **Group 2:** 7.2±1.2 At 24 months **Group 1:** 4.9±1.1 **Group 2:** 5.2±1.0 **P value:** Not sig between groups; <0.001 compared to baseline	
			Urinary frequency, noctural (recorded through diary. Diary kept for 7 days after preliminary examination (baseline. No mention of how many days data were collected for follow up)	Baseline; **Group 1:** 2.8±0.9 **Group 2:** 2.4±0.8 At 24 months **Group 1:** 1.1±0.5 **Group 2:** 0.9±0.5 **P value:** Not sig between groups; <0.001 compared to baseline	

Evidence Table 40: Botulinium toxin vs. placebo

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Maria et al., 2003[182] **Study design:** RCT, double blinded **Setting:** Jan to Dec 2000 Department of Surgery, University Hospital of Agostino Gemelli, Rome **Evidence level:** 1+ **Duration of follow-up:** 2 months for blinded study, 12 months for open label on the active arm	**Patient group:** Men with symptomatic BPH **Inclusion criteria:** ▪ Age 50 to 80 years with symptomatic BPH ▪ Moderate to severe symptoms of urinary obstruction as determined by the AUA score ▪ Qmax ≤ 15 ml/s with a voided volume of ≥150mL ▪ An enlarged prostate gland on digital rectal examination **Exclusion criteria:** ▪ Neurogenic voiding disorders ▪ Prostate or bladder cancer or a serum PSA level of 10 ng/ml or more ▪ Previously had surgery or treated with botulinum toxin **<u>All patients</u>** **N:** 30 (out of 42 assessed for eligibility, 8 did not meet inclusion criteria, 4 refused) **Drop outs:** 0 **<u>Group 1</u>** **N:** 15 **Age**, years, mean (±SD): 69.4±4.9 **Prostate vol** ml, mean ± (SD): 52.6±10.6 **Residual vol**, ml, mean±(SD): 126.3±38.3 **<u>Group 2</u>** **N:** 15 **Age**, years, mean (±SD): 68.2±3.9 **Prostate volume** ml, mean ± (SD): 52.3±10.0 **Residual volume**, ml, mean±(SD): 118.0±39.7	**Group 1 Botulinum toxin** Received 200U of botulinum toxin **Group 2 – Placebo** Received saline solution **For both groups:** 4 ml of solution injected in to the prostate, divided into 2 injections of equal volume (2 mL) into each lobe of the gland. With patient lying on the left side, a 22-gauge spinal needle (0.7 X 90-mm Yale spinal needle, Becton Dickinson, Spain) was inserted in the perineum in the anterior midline approximately 1.5 to 2.0 cm from the anus. The injection sites were visualised using transrectal ultrasonography. No sedation or anaesthesia was used during the procedure	**AUA symptom score**, mean±sd: (No data reported for group 2 after 2nd month)	<u>Baseline</u> **Group 1**: 23.2±4.1 **Group 2**: 23.3±3.9 <u>1 month</u> **Group 1**: 10.6±1.7 **Group 2**: 23.4±3.5 <u>2 month</u> **Group 1**: 8.0±1.6 **Group 2**: 23.3±3.3 <u>6 month (open label)</u> **Group 1**: 9.1±3 <u>12 month (open label)</u> **Group 1**: 8.9±3.2 **P values**: Sig *	**Funding:** Not stated **Limitations:** ▪ Small sample size – no calculation provided ▪ Uncertain whether all outcomes/side effects relevant to the patient had been reported (eg pain) **Additional outcomes:** Prostate volume, serum PSA, and residual volume at 1 and 2-months follow up. Also reported the 6 and 12 months follow up results for the botulinum toxin group Prostate size reduction at 1 and 2 months were significant for the botulinum toxin arm **Notes:** * **P values** <0.001 for Group 1 compared to baseline, and between Group 1 and 2 at 1 and 2 months
			Qmax, ml/s, mean±sd (No data reported for group 2 after 2nd month)	<u>Baseline</u> **Group 1**: 8.1±2.2 **Group 2**: 8.8±2.5 <u>1 month</u> **Group 1**: 14.9±2.1 **Group 2**: 8.8±2.3 <u>2 month</u> **Group 1**: 15.4±1.7 **Group 2**: 8.7±2.3 <u>6 month (open label)</u> **Group 1**: 14.6±4.1 <u>12 month (open label)</u> **Group 1**: 15±2.9 **P values**: Sig *	
			Urinary incontinence (at <u>1 and 2 months</u>	**Group 1**: 0/15 **Group 2**: 0/15	

Evidence Table 41: Transurethral vaporesection of the prostate (TUVRP) vs. transurethral resection of the prostate (TURP)

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Gotoh et al., 1999[106] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** men with moderate to severe LUTS **Setting:** multi-centre, Department of Urology, Nagoya University School of Medicine, Japan **Inclusion criteria:** • IPSS ≥10 • Qmax < 15mL/s • Prostate volume ≥ 30 ml or higher than normal PSA **Exclusion criteria:** NR **<u>All patients</u>** **N:** 53 **Drop outs:** 2 **<u>Group 1:</u>** **N:** 25 **Mean age (± SD):** 69.7 ± 6.3 **Mean IPSS ± SD:** 19.6 ± 7.5 **Mean Qmax ml/s ± SD:** 7.3 ± 2.8 **Mean PVR ml ± SD:** 56.7 ± 51.4 **Mean prostate volume ± SD (mL):** 47.8 ± 16.4 **Operative time ± SD mins:** 60 ± 28 **Resected weight (g):** 29.4 ± 15.1 **Drop outs:** 2 excluded because cancer found **<u>Group 2:</u>** **N:** 28 **Mean age (± SD):** 66.5 ± 15.7 **Mean IPSS ± SD:** 18.9 ± 7.3	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Bandloop cutting 230–250W **Group 2: Transurethral resection of the prostate (TURP)** Standard loop cutting 120W **All patients:** Same surgeon performed all procedures at each different hospital **Examination methods** **Preoperative:** Baseline IPSS Symptom score, PSA, Blood, TRUS, uroflowmetry. Flow rate at months 1 & 6 and pressure flow at 3 months. IPSS assessed at 3 months postoperatively	**Mean IPSS score ± SD at 3 months**	**Group 1:** 3.7 ± 2.4 (n=23) **Group 2:** 3.8 ± 2.3 (n=28) **p value:** Not sig.	**Funding:** NR **Limitations:** • Author confirmed no masking of outcome assessment and no allocation concealment • Significant differences at baseline for Qmax **Additional outcomes:** Urinalysis **Notes:** Author reports randomisation by drawing envelopes
			Mean Qmax mL/s ± SD at 3 months	**Group 1:** 23.6 ± 13.9 **Group 2:** 21.2 ± 9.4 **p value:** Not sig.	
			Catheterisation time (days)	**Group 1:** 3.4 ± 1.3 **Group 2:** 3.3 ± 1.3 **p value:** Not sig.	
			Complications: transfusion	**Group 1:** 0/25 **Group 2:** 0/28 **p value:** NR	
			Complications: TUR	**Group 1:** 0/25 **Group 2:** 0/28 **p value:** NR	
			Complications: Urethral Stricture	**Group 1:** 0/25 **Group 2:** 0/28 **p value:** NR	
			Complications: UTI	**Group 1:** 0/25 **Group 2:** 0/28 **p value:** NR	
			Complications: incontinence	**Group 1:** 0/25 **Group 2:** 0/28 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean Qmax ml/s ± SD: 9.4 ± 2.8 **Mean PVR ml ± SD**: 41.9 ± 25.5 **Mean prostate volume ± SD (mL)**: 44.7 ± 15.2 **Operative time ± SD mins**: 61.1 ± 29 **Resected weight (g)**: 36.5 ± 17.6 **Drop outs**: 0				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Gupta et al., 2006[108] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months.	**Patient Group**: Patients with BPH who were candidates for TURP were selected from July 2002 to December 2003. **Setting:** single centre: All India Institute of Medical Sciences, New Delhi, India **Inclusion criteria**: glands of >40g **Exclusion criteria:** • Previous history of prostatic and urethral surgery • Neurovesical dysfunction • Carcinoma of the prostate **<u>All patients</u>** **N:** 100 **Dropouts:** NR **<u>Group 1</u>** **N:** 50 **Mean ± SD Age**: 67.68 ± 9.8 **IPSS ± SD:** 24.9 ± 3.9 **Mean SD Qmax:** 4.65 ± 3.6 **Mean SD PVR, mL:** 103 ± 174.1 **Mean prostate size ± SD, g:** 62.6 ± 14.8 **Resectate ± SD g:** 24.8 ± 12.7 **Operation duration ±SD min:** 55.9 ± 18.1 **Patients with catheter:** 19/50 **Dropouts:** NR **<u>Group 2</u>** **N:** 50 **Mean ±SD Age:** 65.67 ± 7.5 **IPSS ± SD:** 23.3 ± 3.9 **Mean SD Qmax:** 4.5 ± 3.9	**Group 1: TUVRP** Wing (Wolf) loop: 180W cutting and 80W coagulation **Group 2: TURP** Standard tungsten wire loop 80W cutting and 50W coagulation **All patients** 27F continuous-flow resectoscope. 22 F Foley catheter inserted and irrigation with saline. Catheter removed when urine clear. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up at 1, 3, 6, 12 months for complications and IPSS, PVR, Qmax reassessed at 6 & 12 months	**Mean (SD) IPSS at 6 months**	**Group 1**: 5.9 ± 0.25 **Group 2**: 6.1 ± 0.42 **P value**: NS	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment were not reported. • Outcome assessment was not masked • Drop outs NR so patient numbers at follow up unclear **Additional outcomes:** Irrigation, haemoglobin decrease, serum sodium decrease. **Notes:** HOLEP arm of study not reported. *ANOVA analysis used to compare 3 groups
			Mean (SD) IPSS at 12 months	**Group 1**: 5.4 ± 0.28 **Group 2**: 5.6 ± 0.32 **P value**: NS	
			Mean (SD) Qmax at 6 months	**Group 1**: 22.5 ± 0.95 **Group 2**: 20.7 ± 1.32 **P value**: NS	
			Mean (SD) Qmax at 12 months	**Group 1**: 23.6 ± 0.96 **Group 2**: 23.7 ± 1.58 **P value**: NS	
			Mean (SD) catheter duration, days (converted from hours)	**Group 1**: 1.51 ± 0.35 **Group 2**: 1.90 ± 0.53 **P value**: Significant*	
			Complications: urinary retention (re-catheterisation)	**Group 1**: 3/50 **Group 2**: 3/50	
			Complications: TUR Syndrome	**Group 1**: 1/50 **Group 2**: 1/50	
			Complications: Transfusion	**Group 1**: 0/50 **Group 2**: 1/50	
			Complications: Mortality (pneumonia)	**Group 1**: 1/50 **Group 2**: 0/50	
			Complications: urethral stricture	**Group 1**: 1/50 **Group 2**: 2/50	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean SD PVR, mL: 84.0 ± 129.7 **Resectate ±SD g:** 18.9 ± 12.9 **Mean prostate size ± SD, g:** 59.8 ± 16.5 **Operation duration ±SD min:** 64.1 ± 13.1 **Patients with catheter:** 16/50 **Dropouts:** NR				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Helke et al., 2001[113] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months.	**Patient Group**: Patients moderate or severe voiding dysfunction and BPE. **Setting:** single centre: University Hospital Carl Gustav Carus, Dresden, Germany **Inclusion criteria**: • Enlarged prostate on DRE • At least moderate LUTS • IPSS > 10 and/or PVR >60 mL • Patients with recent urinary retention and indwelling catheters < 6 weeks duration **Exclusion criteria:** • Previous prostatic surgery • Neurogenic bladder disorders • Known urethral strictures • Prostate cancer • Indwelling catheter > 6 weeks duration • Severe neurological disease • Psychiatric abnormalities • Reduced patient compliance **All patients** **N:** 185 **Dropouts:** 37 **Group 1** **N:** 93 **Mean ± SD Age**: 67.3 ± 7.73 (47-85) **IPSS ± SD:** 17.29 ± 6.06 **Mean SD Qmax:** 10.8 ± 4.76 **Mean SD PVR, mL:** 76.0 ± 60.5 **Mean prostate volume ± SD, mL**: 48.8 ±	**Group 1: TUVRP** Vaporising loop 1mm: 250W cutting **Group 2: TURP** Standard loop 0.3 mm: 150W cutting **All patients** 26F intermittent flow resectoscope. Irrigation with Purisole 0.96% alcohol. Antibiotic prophylaxis was given and catheter removed 2-3 days after surgery. TUVRP performed by 5 urologists with experience of at least 5 TUVRP patients each **Examination methods** **Preoperative:** Baseline ASA, New York Heart Association scores, IPSS Symptom score, AUA bother score, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up at 3, 6, 12 months for PVR and flow rates at 12 months. Symptom score follow up by postal questionnaire	**Mean (SD) IPSS at 12 months**	**Group 1**: 4.66 ± 4.3 (n=79) **Group 2**: 5.21 ± 5.1 (n=69) **P value**: NS	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment were not reported. • Outcome assessment was not masked • Significant difference reported between baseline Qmax p = 0.02 • Significant difference found between baseline PVR p =0.02 which was not reported as significant. **Additional outcomes:** IPSS & Bother score were reported graphically at 3, 6 and 12mths **Notes:** None.
			Mean (SD) Qmax at 12 months	**Group 1**: 22.19 ± 12.3 **Group 2**: 22.12 ± 10.6 **P value**: NS	
			Complications: incontinence	**Group 1**: 0/93 **Group 2**: 0/92	
			Complications: Transfusion	**Group 1**: 6/93 **Group 2**: 9/92	
			Complications: urethral stricture	**Group 1**: 5/93 **Group 2**: 7/92	
			Complications: reoperation	**Group 1**: 9/93 **Group 2**: 5/92	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	21.21 **Resectate ± SD g:** 21.98 ± 13.47 **Operation duration ±SD min:** 71.02 ± 27.5 **Indwelling catheter:** 28/93 **Dropouts:** 14 (2 patients underwent radical prostatectomy and were excluded, 11 lost to follow up and incomplete outcome data for 1) **Group 2** **N:** 92 **Mean ±SD Age:** 68.7 ± 8.38 (53-89) **IPSS ± SD:** 18.29 ± 7.49 **Mean SD Qmax:** 8.5 ± 5.19 **Mean SD PVR, mL:** 101.8 ± 84.1 **Resectate ±SD g:** 18.9 ± 12.9 **Mean prostate volume ± SD, mL:** 49.9 ± 22.1 **Operation duration ±SD min:** 65.68 ± 25.8 **Indwelling catheter:** 32/93 **Dropouts:** 23 (4 patients underwent radical prostatectomy and were excluded, 14 lost to follow up and incomplete outcome data for 5)				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kupeli et al., 2001[155] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient Group:** Moderate to severe symptoms of prostatism **Setting:** single centre: Ankara University, Turkey **Inclusion criteria:** • IPSS ≥ 8 • Qmax < 15 mL/s **Exclusion criteria:** • Neurogenic bladder • Carcinoma of the prostate • History of prostate surgery **All patients** **N:** 100 **Dropouts:** NR **Group 1** **N:** 50 **Mean ± SD Age:** 61.4 ± 3.2 **IPSS ± SD:** 19.4 ± NR **Mean SD Qmax:** 7.9 ± 2.1 **Mean prostate size ± SD, g:** 57.8 ± 4.1 **Resectate ± SD g:** NR **Operation duration ±SD min:** 48.2 ± NR **Previous medical treatment:** 32/50 **Preoperative retrograde ejaculation:** 50/50 **Preoperative erectile dysfunction:** 14/50 **Dropouts:** NR **Group 2** **N:** 50 **Mean ±SD Age:** 58.9 ± 3.6	**Group 1: TUVRP** Wing (Wolf) loop: 205-300W cutting **Group 2: TURP** Storz 24F loop: 80-120W cutting **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up at 6 months	**Mean (SD) IPSS at 6 months**	**Group 1:** 4.0 ± NR **Group 2:** 5.0 ± NR* **P value:** NS	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment were not reported. • Outcome assessment was not masked • No mention of drop outs in the study • Standard deviations for IPSS NR • Significance difference in baseline Qmax p=0.007 • Almost all patients had retrograde ejaculation prior to surgery **Additional outcomes:** Haemocrit and sodium **Notes:** None.
			Mean (SD) Qmax at 6 months	**Group 1:** 26.7 ± 3.7 **Group 2:** 24.6 ± 3.4 **P value:** NR	
			Mean (SD) catheter duration, days (converted from hours)	**Group 1:** 2 ± NR **Group 2:** 4 ± NR **P value:** <0.05	
			Mean (SD) length of stay, days	**Group 1:** 2.5 ± NR **Group 2:** 4.5 ± NR **P value:** <0.05	
			Complications: urinary retention (re-catheterisation)	**Group 1:** 0/50 **Group 2:** 0/50	
			Complications: TUR Syndrome	**Group 1:** 0/50 **Group 2:** 0/50	
			Complications: Transfusion	**Group 1:** 0/50 **Group 2:** 0/50	
			Complications: Incontinence	**Group 1:** 0/50 **Group 2:** 0/50	
			Complications: Retrograde ejaculation	**Group 1:** 26/50 **Group 2:** 27/50	
			Complications: urethral stricture	**Group 1:** 0/50 **Group 2:** 0/50	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	IPSS ± SD: 21.6 ± NR **Mean SD Qmax:** 9.2 ± 2.6 **Mean prostate size ± SD, g:** 56.7 ± 6.3 **Resectate ± SD g:** NR **Operation duration ±SD min:** 42.7 ± NR **Previous medical treatment:** 31/50 **Preoperative retrograde ejaculation:** 44/50 **Preoperative erectile dysfunction:** 19/50 **Dropouts:** NR				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Liu et al., 2006[168] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 2 years	**Patient Group:** Patients with BOO due to BPH on waiting list for surgery **Setting:** single centre: Taipei City Hospital, Taiwan **Inclusion criteria:** • IPSS ≥ 15 • IPSS QoL ≥ 3 • Qmax ≤ 12 mL/s **Exclusion criteria:** • PSA ≥ 4 ng/mL • Neurogenic bladder • Carcinoma of the prostate • History of prostate or urethral surgery • Bladder stones • Patients on anticoagulant therapy **<u>All patients</u>** **N:** 76 **Dropouts:** NR **<u>Group 1</u>** **N:** 44 **Mean ± SD Age:** 66.0 ± 6.6 **IPSS ± SD:** 26.8 ± 4.7 **IPSS QoL ± SD:** 4.1 ± 0.6 **Mean SD Qmax:** 6.9 ± 2.1 **Mean SD PVR, mL:** 142 ± 48 **Mean prostate volume ± SD, mL:** 60.5 ± 10.9 **Resectate ± SD g:** 32.2 ± 7.1	**Group 1: TUVRP** Wedge resection loop: 200W cutting and 60W coagulation **Group 2: TURP** Standard wire loop 110W cutting and 60W coagulation. **All patients** 27F continuous-flow resectoscope. 22 F Foley catheters inserted. TUVRP performed by 3 urologists with experience of at least 10 TUVRP patients each **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up at 3, 6, 12 months and 2 years Sexual function was assessed by face to face or telephone questionnaire	**Mean (SD) IPSS at 3 months**	**Group 1:** 8.2 ± 2.2 (n=42) **Group 2:** 7.9 ± 1.8 (n=30) **P value:** 0.53	**Funding:** NR **Limitations:** • Unbalanced baseline numbers • Allocation concealment unclear • Outcome assessment was not masked • Number of patients remaining at 2 years was unclear and reasons for incomplete outcome data not given. **Notes:** Randomisation by drawing envelopes
			Mean (SD) IPSS at 2 years	**Group 1:** 9.0 ± 3.1 **Group 2:** 8.4 ± 2.6 **P value:** 0.45	
			Mean (SD) IPSS QoL at 3 months	**Group 1:** 1.7 ± 0.5 (n=36) **Group 2:** 1.5 ± 0.7 (n=26) **P value:** 0.57	
			Mean (SD) IPSS QoL at 2 years	**Group 1:** 1.6 ± 0.6 **Group 2:** 1.4 ± 0.7 **P value:** 0.48	
			Mean (SD) Qmax at 3 months	**Group 1:** 20.7 ± 2.8 (n=29) **Group 2:** 21.6 ± 2.0 (n=21) **P value:** 0.2	
			Mean (SD) Qmax at 2 years	**Group 1:** 19.6 ± 3.7 **Group 2:** 21.2 ± 2.7 **P value:** 0.12	
			Mean (SD) catheter duration, days (converted from hours)	**Group 1:** 1.06 ± 0.18 **Group 2:** 1.66 ± 0.38 **P value:** <0.0001	
			Mean (SD) length of stay, days	**Group 1:** 1.65 ± 0.2 **Group 2:** 2.06 ± 0.35 **P value:** <0.0001	
			Complications: urinary retention (re-catheterisation)	**Group 1:** 3/44 **Group 2:** 4/32	
			Complications: TUR Syndrome	**Group 1:** 0/44 **Group 2:** 2/32	
			Complications: Transfusion	**Group 1:** 1/44 **Group 2:** 2/32	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Operation duration ± SD min: 49.4 ± 8.0 **Dropouts:** NR **<u>Group 2</u>** **N:** 32 **Mean ±SD Age:** 64.7 ± 6.3 **IPSS ± SD:** 25.6 ± 3.5 **IPSS QoL ± SD:** 4.0 ± 0.7 **Mean SD Qmax:** 6.9 ± 1.9 **Mean SD PVR, mL:** 131 ± 41 **Resectate ±SD g:** 35.5 ± 4.3 **Mean prostate volume ± SD, mL:** 58.4 ± 8.4 **Operation duration ± SD min:** 52.9 ± 6.0 **Dropouts:** NR		**Complications: Incontinence**	**Group 1:** 2/44 **Group 2:** 1/32	
			Complications: Reoperation rate	**Group 1:** 2/44 **Group 2:** 3/32	
			Complications: urethral stricture	**Group 1:** 3/44 **Group 2:** 2/32	
			Complications: retrograde ejaculation * answered by those men who were sexually active preoperatively in each group	**Group 1:** 10/17 **Group 2:** 7/13	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Netto et al., 1999[219] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** mean 17 months (11-23)	**Patient group:** moderate to severe symptomatic BPH **Setting:** single-centre, division of urology, Unicamp & Hospital Benefcencia Portuguesa, São Paulo, Brazil **Inclusion criteria:** • Patients with >1 symptomatic and uncomplicated BPH • IPSS >12 • Qmax < 15 mL/s • Voided volume ≥150mL • PVR <250 mL • Prostate volume 25-90 mL **Exclusion criteria:** • Exposure to α-antagonists, anticholinergics, cholinergics, diuretics, estrogens, androgens, antihypertensive medications or other agents within the previous 2 weeks • Prostate cancer • Urethral stricture • Urinary tract stone disease • Neurogenic bladder • Hydronephrosis • UTI within 3 months prior to surgery • Pelvic irradiation • Previous prostatic surgery **<u>All patients</u>** **N:** 78 **Drop outs:** NR	**Group 1: Transurethral vaporisation of the prostate (TUVP)** Standard loop: cutting 250-300 without haemostasis **Group 2: Transurethral resection of the prostate (TURP)** Standard loop: cutting 50-80 and haemostasis mode 50W **All patients:** Operations performed using 24F continuous flow resectoscope using a 3% mannitol as irrigant. A 22F Foley catheter was inserted. Oral antibiotics for 1 week. **Examination methods Preoperative:** Baseline IPSS symptom score, urinalysis, PSA, TRUS, uroflowmetry. Follow up visits at 3, 6, 12 months and annually thereafter	**Mean IPSS score at mean follow up 17 months** (follow up interval not clear for each group)	**Group 1:** 3.83 ± 4.62 **Group 2:** 8.68 ± 2.30 **p value:** <0.00001 (calculated by NCGC as *t* test with unequal variances) **conflicts with study finding p=0.88**	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Masked outcome assessment was not reported • Follow up interval for each group not clear only overall mean follow up reported. • There were significant baseline differences in IPSS score • Dropouts were not reported. • P values reported conflicted with outcome measures. **Notes:** None.
			Mean Qmax ± SD mL/s at mean follow up 17 months (follow up interval not clear for each group)	**Group 1:** 15.43 ± 3.4 **Group 2:** 16.16 ± 2.48 **p value:** 0.28 (calculated by NCGC as *t* test with equal variances) **conflicts with study finding p=0.02**	
			Catheterisation time (days) hours reported converted to days	**Group 1:** 0.77 ± 0.29 **Group 2:** 1.68 ± 0.36 **p value:** <0.00001 (calculated by NCGC as *t* test with equal variances)	
			Length of hospital stay (days)	**Group 1:** 1.55 ± 0.75 **Group 2:** 2.63 ± 0.63 **p value:** <0.0001	
			Complications: retrograde ejaculation	**Group 1:** 26/40 (65%) **Group 2:** 12/38 (32%) **p value:** NR	
			Complications: TUR	**Group 1:** 0/40 **Group 2:** 0/38 **p value:** NR	
			Complications: urethral stricture	**Group 1:** 0/40 **Group 2:** 0/38 **p value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1: **N:** 40 **Mean age (range):** 66.8 (52-80) **Mean IPSS score:** 19.65 ± 6.14 **Mean Qmax ml/s (± SD):** 7.88 ± 2.51 **PVR mL (range):** 73.0 ± 5.81 **Mean prostate volume mL ± SD:** 46.88 ± 17.1 **Operative time ± SD:** 29.78 ± 11.78 mins **Resectate ± SD, g:** 21.6 ± NR **Drop outs:** NR **Group 2:** **N:** 38 **Mean age (range):** 65 (51-82) **Mean IPSS score:** 24.29 ± 6.48 **Mean Qmax ml/s (± SD):** 6.77 ± 3.08 **PVR mL (range):** 88.64 ± 8.43 **Mean prostate volume mL ± SD:** 53.4 ± 21 **Operative time ± SD:** 56.32 ± 8.36 mins **Resectate ± SD, g:** 22.3 ± NR **Drop outs:** NR				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Talic et al., 2000[291] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 months (Mean follow up 9.2 mths for TUVRP and 8.8 mths for TURP)	**Patient Group:** Patients with BOO due to BPH on waiting list for surgery **Setting:** single centre: King Khalid University Hospital, Saudi Arabia **Inclusion criteria:** • Men with urinary retention • IPSS > 15 • Qmax < 15 mL/s **Exclusion criteria:** • Neurogenic bladder • Carcinoma of the prostate • History of prostate or urethral surgery **<u>All patients</u>** **N:** 68 **Dropouts:** NR **<u>Group 1</u>** **N:** 34 **Mean ± SD Age:** 70.9 ± 9.3 **IPSS ± SD:** 24.9 ± 6 **Mean SD Qmax:** 7.5 ± 3.5 **Mean prostate size ± SD, g:** 52.4 ± 18.7 **Resectate ± SD g:** 22.4 ± 10.5 **Men with urinary retention:** 15/34 **Operation duration ± SD min:** 42.4 ± 15 **Urinary retention:** 15/34 **Dropouts:** NR **<u>Group 2</u>** **N:** 34 **Mean ±SD Age:** 70.4 ± 8.8 **IPSS ± SD:** 20.1 ± 6.8	**Group 1: TUVRP** Wing resection loop: 250W cutting and 80W coagulation **Group 2: TURP** Standard wire loop 150W cutting and 50W coagulation. **All patients** 27F continuous-flow resectoscope. Foley catheters inserted with saline irrigation TUVRP performed by 3 urologists with experience of at least 10 TUVRP patients each **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, blood, uroflowmetry. Follow up every 3 months Sexual history questionnaire was answered by those men that were sexually active	**Mean (SD) IPSS at 6 months** **Mean (SD) Qmax at 6 months** **Mean (SD) catheter duration, days** (converted from hours) **Complications: TUR Syndrome** **Complications: Transfusion** **Complications: urethral stricture**	**Group 1**: 4.0 ± 3.4 **Group 2**: 5.6 ± 3.1 **P value**: 0.03 **Group 1**: 19.0 ± 6.5 **Group 2**: 15.2 ± 10.0 **P value**: 0.01 **Group 1**: 0.96 ± 0.43 **Group 2**: 1.5 ± 0.72 **P value**: <0.0001 **Group 1:** 0/34 **Group 2**: 0/34 **Group 1:** 0/34 **Group 2**: 0/34 **Group 1:** 3/34 **Group 2**: 4/34	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment not reported • Outcome assessment was not masked • Significant baseline differences in Qmax p=0.02 & IPSS p<0.0001 • Dropouts were not reported **Additional outcomes:** Haematocrit, haemoglobin, serum sodium **Notes:** None.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean SD Qmax: 9.1 ± 6.3 **Resectate ±SD g:** 20.2 ± 9.5 **Men with urinary retention:** 18/34 **Mean prostate size ± SD, g:** 57.2 ± 22.5 **Operation duration ± SD min:** 35.9 ± 12.8 **Urinary retention:** 18/34 **Dropouts:** NR				

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1 **Evidence Table 42: Bipolar TUVRP vs. transurethral resection of the prostate (TURP)**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Fung et al., 2005[98] **Study design:** RCT Observer and patient masked **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient group:** men on waiting list for surgery for BPH with acute or chronic retention, failure to remove catheter and **Setting:** single-centre: Division of Urology, Pamela Youde Nethersole Eastern Hospital, Hong Kong, China **Inclusion criteria:** • IPSS >20 • Qmax <10 mL/s **Exclusion criteria:** • Neurogenic bladder • Urethral stricture • Anticoagulant therapy • Bladder stone • Prostate cancer or suspect • Previous prostate surgery **<u>All patients</u>** **N:** 60 **Drop outs:** 9 **<u>Group 1:</u>** **N:** 29 (n=21) **Mean age (range):** 72.5 (59-91) **Mean IPSS ± SD:** 15.82 ± NR **Mean IPSS QoL ± SD:** 3.55 ± NR **Mean PVR± SD, mL:** NR **Mean prostate volume ± SD, mL:** NR **Resection time (range), min:** 36.6 (12-76) **Resected weight (range), g:** 18.6 (1-57) **Patients with urinary retention:** 17 **Drop outs:** 8 for machine failure	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ system through 27F resectoscope at 240W for vaporisation and 60W for coagulation. **Group 2: Transurethral resection of the prostate (TURP)** Standard loop through 27F continuous flow resectoscope. Cutting 120W and coagulation 60W **All patients:** Surgery performed by a consultant, senior medical officer or senior registrar with experience of performing TURP. A 22F 3-way catheter was inserted with saline irrigant until effluent was clear. Catheter removed the following morning **Examination methods** **Preoperative:** Baseline IPSS Symptom score, QoL, assessed and follow up of IPSS, QoL and Qmax at 3 months	**Mean ± SD IPSS change from baseline at 3 months**	**Group 1:** 8.81 ± NR (n=21) **Group 2:** 9.63 ± NR (n=30) **P value:** 0.86	**Funding:** NR **Limitations:** • 8 dropouts in Group 1 due to machine failure • Allocation concealment was not reported **Additional outcomes:** reduction in serum sodium and haemoglobin **Notes:** Randomisation using computer generated numbers
			Mean ± SD change in Qmax from baseline at 3 months	**Group 1:** 16.57 ± NR (n=21) **Group 2:** 14.71 ± NR (n=30) **P value:** 0.96	
			Mean ± SD IPSS QoL change from baseline at 3 months	**Group 1:** 0.55 ± NR (n=21) **Group 2:** 1.54 ± NR (n=30) **P value:** 0.17	
			Mean ± SD Qmax at 12 months	**Group 1:** 17.0 ± NR (n=20) **Group 2:** 15.0 ± NR (n=20) **P value:** NR	
			Catheterisation time (days)	**Group 1:** 1.14 ± NR **Group 2:** 1.21 ± NR **P value:** 0.59	
			Complications: urinary retention (re-catheterisation)	**Group 1:** 4/21 **Group 2:** 3/30 **P value:** NR	
			Complications: urinary retention UTI	**Group 1:** 4/21 **Group 2:** 4/30 **P value:** NR	
			Complications: TUR	**Group 1:** 0/21 **Group 2:** 0/30 **P value:** NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2: **N:** 31 (n=30) **Mean age (range):** 73 (59-88) **Mean IPSS ± SD:** 19.36 ± NR **Mean IPSS QoL ± SD:** 3.64 ± NR **Mean PVR± SD, mL:** NR **Mean prostate volume ± SD, mL:** NR **Resection time (range), min:** 32.9 (12-105) **Resected weight (range), g:** 25.1 (4-100) **Patients with urinary retention:** 25 **Drop outs:** 1 (patient contracted sepsis)				

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Evidence Table 43: Transurethral ethanol ablation of the prostate (TEAP) vs. transurethral resection of the prostate (TURP)

See Evidence Table 38: Transurethral needle ablation (TUNA) vs. transurethral resection of the prostate (TURP) for Kim et al. 2006 [146]

1 **Evidence Table 44: Transurethral resection of the prostate (TURP) vs. watchful waiting**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Wasson et al., 1995[316] & Anon1993[1] **Study design:** RCT **Setting:** US, July 1986 to 1989. **Evidence level:** 1+ **Duration of follow-up:** 3 years (average of 2,8 years)	**Patient group:** Consecutive male veterans referred to urology clinics because of BPH symptoms **Inclusion criteria:** Score of 10-20 on the Madsen Iverson symptom score (moderate or somewhat severe) **Exclusion criteria:** ▪ <55 years old ▪ History of prostate surgery or radiation treatment ▪ Unable to walk ▪ Had active urinary tract infection not responding to treatment ▪ Received diagnosis of prostate or bladder cancer ▪ Residual volume > 350 ml ▪ Low total score on a scale that rates BPH on a the basis of cystoscopy, the symptom interview and bladder ultrasonography ▪ Serious medical conditions that would have made surgery inappropriate for follow-up unlikely (e.g: uncontrolled diabetes, neurogenic bladder, cirrhosis, active alcoholism, bleeding diathesis, psychosis, and late stage cardiac or respiratory disease) ▪ Serum creatinine concentration	**Group 1: TURP** Performed by the chief surgical resident or staff surgeon. No description of the procedure was provided **Group 2: Watchful waiting** No specific description **All patients:** All participants were told to avoid ingesting coffee, alcohol, and other liquids after dinner and were informed about medications that might make their symptoms worse. Physicians were asked to avoid prescribing medications such as alpha-adrenergic antagonists that might confound the results of the trial. A referral to a urologist was considered if there was an indication of treatment failure or a patient requested such referral. All participants were followed in general	**All cause mortality** (no deaths associated with surgery)	<u>At 3 year follow up</u> **Group1:** 13/280 **Group 2:** 10/276 **Relative risk:**1.28 (95% CI: 0.57 to 2.87) **P value:** Not sig	**Funding:** Cooperative Studies Programme of the Department of Veteran Affairs Medical Research Service **Limitations:** Randomisation allocation and concealment **Additional outcomes:** ▪ Residual volume ▪ Perioperative complications: 5 perforation of capsule, 1 thrombophlebitis. 10 men found to have prostate cancer ▪ Factors predicting improvement, and influence of patient reported bother from urinary symptoms on outcomes of surgery and watchful waiting (see outcomes measure)
			Symptom scores, mean (±SD) : Range: 0 to 27, (Madsen Iversen questionnaire) higher values more severe	<u>At baseline</u> **Group 1:** 146±3.0 **Group 2:** 14.6±2.8 **p value:** Not sig <u>At 3 year follow up</u> **Group 1:** 4.9±4.0 **Group 2:** 9.1±4.7 **p value:** <u>Change from baseline</u> **Group 1:** -9.6±5.0 **Group 2:** -5.5±5.2 **p value:** <0.001	
			Qmax, mean (±SD) :	<u>At baseline</u> **Group 1:** 11.6±6.4 **Group 2:** 12.5±7.5 **p value:** Not sig <u>At 3 year follow up</u> **Group 1:** 17.8±9.1 **Group 2:** 12.7±7.6 **p value:** <0.001 <u>Change from baseline</u> **Group 1:** 6.3±9.7 **Group 2:** 0.4±9.2 **p value:** <0.001	
			Perioperative complications: Recatheterisation	**Group 1:** 9/280 **Group 2:** 0/276 **p value:** <0.05*	
			Perioperative complications: transfusion	**Group1:** 3/280 **Group 2:** 0/276	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	>3.0 mg /dl or had doubled in the previous year **<u>All patients</u>** A total of 800 patients screened 591 eligible for randomisations 30 did not provide informed consent, and 5 were found to be ineligible. **N:** 556 **Drop outs:** 71/556 [41/556 withdrew consent, 30 lost to follow up] **Age, years, mean (±SD):** 66±5 **<u>Group 1</u>** **N:** 280 **Dropouts:** 38/280, [24/280 withdrew consent, 14/280 lost to follow up] Age, years, mean (±SD): 65.6±5.2 White race, %: 91.4 **QoL scores, mean (±SD) : ▪ Bother from urinary difficulties: 43.8±29.3 ▪ Sexual performance: 43.3±32.7 ▪ Activities of daily living: 66.5±27.2 ▪ General well being: 72.8±27.9 ▪ Social activities: 75.6±23.5 Problems with dripping urine or wetting of plans: 46.0 Erective dysfunction: 60.7 **<u>Group 2</u>** N=276 **Dropouts:** 33/276 [17/276 withdrew consent, 16/276 lost to follow up]	medical clinic six to eight weeks after randomisation and followed-up twice a year		**p value:** Not sig	**Notes:** Related publication: Anon1993 published the patient reported outcomes aspects Intention to treat analyses used. Data for all men, including those who had dropped out were analysed based on the group assigned. *Calculated by NCGC team using Fisher's exact test ** Score on a scale ranging from 0 (greatest impairment) to 100 (least impairment) Average period of follow up; 2.8 years
			Perioperative complications: Urinary tract infection	**Group1:** 2/280 **Group 2:** 0/276 **p value:** Not sig	
			Incontinence (new persistent urinary incontinence requiring use of pads, clamps or condom)	<u>At 3 year follow up</u> **Group 1:** 4/280 **Group 2:** 4/276 **Relative risk:** 0.99(95% CI: 0.25-3.90) **P value:** Not sig	
			Treatment failure (Any of these events: death, repeated or intractable UTI, a residual volume of >350ml, development of bladder calculus, new urinary incontinence; a symptom score of ≥24 at one visit of a symptom score of ≥21 at 2 consecutive visits, doubling of baseline serum creatinine concentration)	<u>At 3 year follow up</u> **Group 1:** 23/280 **Group 2:** 47/276 **Relative risk:** 0.47 (95% CI: 0.29 to 0.72) **p value:** <0.05	
			Reoperation/received surgery (in the watchful waiting arm) Reason: 9 bladder neck contracture, 9 urethral strictures, 8 received second TURP (4 due to adenoma). In the watchful waiting group: 20 treatment failure (11 high volume residual urine, 8 urinary symptoms, 5 intractable urinary retention)	<u>At 3 year follow up</u> **Group 1:** 26/280 **Group 2:** 65/276 **Relative risk:** 0.39 (95% CI: 0.26 to 0.60) **p value:** <0.05	
			QoL scores - Bother from urinary difficulties, mean (±SD) :	<u>At baseline</u> **Group 1:** 43.8±29.3 **Group 2:** 46.3±29.3 **p value:** Not sig <u>At 3 year follow up</u> **Group 1:** 75.7±23.9 **Group 2:** 57.6±28.3 **p value:** <u>Change from baseline</u>	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Age, years, mean (±SD):66.2±5.3 White race, %: 93.1 **QoL scores, mean (±SD) : ▪ Bother from urinary difficulties: 46.3±29.3 ▪ Sexual performance: 42.5±30.3 ▪ Activities of daily living: 69.0±26.6 ▪ General well being: 71.2±28.8 ▪ Social activities: 74.2±23.1 Problems with dripping urine or wetting of plans: 44.4 Erective dysfunction: 63.7			**Group 1:** 29.6±29.4 **Group 2:** 9.6±29.7 **p value:** <0.001	
			QoL scores - Sexual performance: mean (±SD) :	At baseline **Group 1:** 43.3±32.7 **Group 2:** 42.5±30.3 At 3 year follow up **Group 1:** 36.0±26.0 **Group 2:** 35.6±25.6 Change from baseline **Group 1:** -3.0±27.9 **Group 2:** -3.2±26.6 **p values:** Not sig	
			QoL scores - Activities of daily living: mean (±SD) :	At baseline **Group 1:** 66.5±27.2 **Group 2:** 69.0±26.6 **p value:** Not sig At 3 year follow up **Group 1:** 86.4±20.1 **Group 2:** 75.6±27.1 **p value:** Change from baseline **Group 1:** 19.6±26.5 **Group 2:** 6.4±30.3 **p value:** <0.001	
			QoL scores - General well being: mean (±SD) :	At baseline **Group 1:** 72.8±27.9 **Group 2:** 71.2±28.8 At 3 year follow up **Group 1:** 76.2±27.8 **Group 2:** 71.4±31.0 Change from baseline **Group 1**: 3.0±25.5 **Group 2:** 0.1±28.3 **p values:** Not sig	
			QoL scores - Social activities: mean	At baseline	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			(±SD) :	**Group 1:** 75.6±23.5 **Group 2:** 74.2±23.1 At 3 year follow up **Group 1:** 75.5±25.3 **Group 2:** 73.1±25.5 Change from baseline **Group 1:** -1.6±24.3 **Group 2:** -1.7±23.5 **p values:** Not sig	
			Factors predicting improvement from bother from urinary difficulties at follow up (logistic regression, "improvement" not defined. Factors in model were baseline variables of bother from urinary difficulties, treatment assignment, age, symptom score, residual urinary volume, urinary volume after voiding, bladder trabeculation, Qmax)	2 factors were significant: **Treatment assigned:** odds ratio 5.7 (95% CI: 1.9 to 17.3) **High bother score (>55) at baseline** (for surgery group only, odds ration of 6.6(95% CI: 3.0 to 14.3) for surgery group, odds ratio of 1.4 (95% CI: 0.8 to 2.5) for watchful waiting group. In the TURP group, % improved High bother: 134/148 (91%) Less bother: 45/73 (62%) In the watchful waiting group, % receiving surgery High bother: 48/155 (31%) Low bother: 16/97(16%)	
			Association of symptom severity with QoL aspects (Perception of urinary difficulty(UD), sexual function (SF), Activities of daily living (ADL), general well being (GWB), Social activities(SA))	Nocturia: UD, ADL, GWB, Dribbling: UD Urgency: Sig for all Hesistancy: SF Frequency: UD, ADL, GWB, SA	

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1 **Evidence Table 45: Bipolar transurethral resection of the prostate (TURP) vs. TURP**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Autorino et al., 2009[20] De Sio et al., 2006[66] reported 12 month outcomes. **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 48 months	**Patient group:** men with LUTS including those with urinary retention from failed medical therapy **Setting:** Seconda Università di Napoli, Università magna Graecia, Catanzaro & Università Federico, Naples, Italy. **Inclusion criteria:** • >50 years • AUR if catheter failed after medical therapy and CUR after unresponsiveness to medical therapy • IPSS >18 • Qmax < 15mL/s • Prostate volume > 30 ml or higher than normal PSA **Exclusion criteria:** • Prostate cancer or suspect • Neurogenic bladder • Bladder stone and/or diverticula • Urethral stricture • Maximum bladder capacity >500mL • Previous prostate surgery • Warfarin therapy **<u>All patients</u>** **N:** 70 **Drop outs:** 7 (refused follow-up=3; moved away=2; death, other causes=2) **<u>Group 1:</u>** **N:** 35 **Mean age ± SD:** 59.0 ± 5.9 **Mean IPSS ± SD:** 24.8 ± 4.0	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ system. **Group 2: Transurethral resection of the prostate (TURP)** Standard loop **All patients:** 26F resectoscope. Insertion of 22F 3-way Dufour catheter and irrigation with saline until urine was clear **Examination methods** **Preoperative:** Baseline IPSS Symptom score, QoL, Qmax, PVR, PSA assessed and follow up of IPSS, QoL, PVR and Qmax at 3, 6 12 months	**Mean ± SD IPSS at 3 months**	**Group 1**: 8.0 ± NR (n=35) **Group 2**: 8.0 ± NR (n=35) **P value**: NR	**Funding:** NR **Limitations:** • Allocation concealment not reported. • Masking of IPSS and Qmax were not reported but catheterisation time was masked as primary outcome. • 3 and 6 month outcomes estimated from graphs **Additional outcomes:** Bladder irrigation time PVR at longer follow up periods. **Notes:** Randomisation sequence was computer generated NCC calculated average SD per arm from P values and means reported [from Cochrane
			Mean ± SD IPSS at 6 months	**Group 1**: 5.0 ± NR (n=35) **Group 2**: 5.5 ± NR (n=35) **P value**: NR	
			Mean ± SD IPSS at 12 months	**Group 1**: 3.9 ± 3.32 (n=35) **Group 2**: 3.8 ± 3.32 (n=35) **P value**: 0.9	
			Mean ± SD IPSS at 24 months	**Group 1**: 4.5 ± 3.84 (n=33) **Group 2**: 4.8 ± 3.84 (n=34) **P value**: 0.75	
			Mean ± SD IPSS at 36 months	**Group 1**: 6.8 ± 5.19 (n=33) **Group 2**: 6.2 ± 5.19 (n=33) **P value**: 0.64	
			Mean ± SD IPSS at 48 months	**Group 1**: 6.9 ± 3.57 (n=32) **Group 2**: 6.4 ± 3.57 (n=31) **P value**: 0.58	
			Mean ± SD IPSS QoL at 3 months	**Group 1**: 2.1 ± NR (n=35) **Group 2**: 1.4 ± NR (n=35) **P value**: NR	
			Mean ± SD IPSS QoL at 6 months	**Group 1**: 1.1 ± NR (n=35) **Group 2**: 1.0 ± NR (n=35) **P value**: NR	
			Mean ± SD IPSS QoL at 12 months	**Group 1**: 1.0 ± 2.16 (n=35) **Group 2**: 0.8 ± 2.16 (n=35) **P value**: 0.7	
			Mean ± SD IPSS QoL at 24 months	**Group 1**: 1.1 ± 2.49 (n=33) **Group 2**: 1.2 ± 2.49 (n=34) **P value**: 0.87	
			Mean ± SD IPSS QoL at 36 months	**Group 1**: 1.2 ± 1.27 (n=33) **Group 2**: 1.3 ± 1.27 (n=33) **P value**: 0.75	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean Qmax ± SD, mL/s: 7.1 ± 2.0 **Mean PVR± SD, mL:** 80.0 ± 22.5 **Mean prostate volume ± SD, mL:** 51.6 ± 3.9 **IPSS QoL ± SD:** 4.2 ± 1.0 **Operative time ± SD, min:** 49 ± NR **Resection time ± SD, min:** 33 ± NR **Resected weight (g):** 20 ± NR **Drop outs:** 3 **<u>Group 2:</u>** **N:** 35 **Mean age ± SD:** 61.0 ± 5.9 **Mean IPSS ± SD:** 24.38 ± 5.0 **Mean Qmax ± SD, mL/s:** 6.3 ± 3.0 **Mean PVR± SD, mL:** 75.5 ± 35.5 **Mean prostate volume ± SD, mL:** 47.5 ± 5.1 **IPSS QoL ± SD:** 3.9 ± 1.0 **Operative time ± SD, min:** 53 ± NR **Resection time ± SD, min:** 39 ± NR **Resected weight (g):** 24 ± NR **Drop outs:** 4		**Mean ± SD IPSS QoL at 48 months**	**Group 1:** 1.3 ± 1.74 (n=32) **Group 2:** 1.4 ± 1.74 (n=31) **P value:** 0.82	handbook].
			Mean ± SD Qmax at 3 months	**Group 1:** 21.5 ± NR (n=35) **Group 2:** 20.5 ± NR (n=35) **P value:** NR	
			Mean ± SD Qmax at 6 months	**Group 1:** 20.5 ± NR (n=35) **Group 2:** 20.0 ± NR (n=35) **P value:** NR	
			Mean ± SD Qmax at 12 months	**Group 1:** 20.8 ± 7.73 (n=35) **Group 2:** 22.3 ± 7.73 (n=35) **P value:** 0.42	
			Mean ± SD Qmax at 24 months	**Group 1:** 20.2 ± 14.37 (n=33) **Group 2:** 22.0 ± 14.37 (n=34) **P value:** 0.61	
			Mean ± SD Qmax at 36 months	**Group 1:** 20.5 ± 7.3 (n=33) **Group 2:** 21.5 ± 7.3 (n=33) **P value:** 0.58	
			Mean ± SD Qmax at 48 months	**Group 1:** 19.8 ± 7.15 (n=32) **Group 2:** 21.2 ± 7.15 (n=31) **P value:** 0.44	
			Catheterisation time (days) converted into days	**Group 1:** 3.0 ± NR **Group 2:** 4.2 ± NR **P value:** <0.05	
			Length of stay (days) converted into days reported at time to discharge	**Group 1:** 3.3 ± NR **Group 2:** 4.5 ± NR **P value:** <0.05.	
			Complications: transfusion	**Group 1:** 1/35 **Group 2:** 0/35 **P value:** NS	
			Complications: TUR	**Group 1:** 0/35 **Group 2:** 0/35 **P value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Complications: urinary retention	**Group 1:** 0/35 **Group 2:** 0/35 **P value:** NS	
			Late complications at 48 months	**Stricture** **Group 1:** 1/32 **Group 2:** 2/31; p=0.6 **Bladder neck contracture** **Group 1:** 1/32 **Group 2:** 1/31; p=0.8 **BPH recurrence** **Group 1:** 1/32 **Group 2:** 1/31; p=0.8 **Reoperation** **Group 1:** 2/32 **Group 2:** 3/31; p=0.15	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Bhansali et al., 2009[30] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 1 year	**Patient group:** Men with BPH related LUTS that necessitated surgical intervention between May 2004 and December 2005. **Setting:** Institute of Urology in Pune, India **Inclusion criteria:** • >45 years **Exclusion criteria:** • AUA <18 • Qmax >12 • Gland size < 60g • Neurologic illness • Renal insufficiency, bladder stone • Urethral stricture, prostate carcinoma • Receiving 5AR inhibitors **<u>All patients</u>** **N:** 70 **Drop outs:** 3 **<u>Group 1:</u>** **N:** 35 **Preop Qmax: 4.367** **Gland size: 82.38** **Mean age ± SD:** NR **<u>Group 2:</u>** **N:** 35 **Preop Qmax: 4.194** **Gland size: 82.61** **Mean age ± SD**: NR	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** PK superpulse using 26F Gyrus Superpulse PK resectoscope and physiologic saline with 1% ethanol as irrigation fluid. Generator settings were 160 and 80 for cutting and coagulation, respectively. **Group 2: Transurethral resection of the prostate (TURP)** Standard loop 26F resectoscope and an electrosurgical generator with glycine as irrigation fluid. Generator settings were 110 for cutting and 70 for coagulation. **All patients:** 500mg ciprofloxacin and 80mg gentamicin 1 hour preoperatively. All patients catheterised with 20F triple lumen Foley catheter at end of surgery, and irrigation started.	**Mean (SD) Qmax at 3 months**	Group 1 (n=34): 19.85 (3.939) Group 2 (n=33): 19.23 (5.176) P=0.582	**Funding:** NR **Limitations:** • Dropouts not explained • Allocation concealment method unclear **Notes:** None.
			Mean (SD) Qmax at 9 months	Group 1 (n=34): 17.41 (2.840) Group 2 (n=33): 17.76 (3.269) P=0.645	
			Mean (SD) Qmax at 12 months	Group 1 (n=34): 16.6 (2.640) Group 2 (n=33): 15.9 (3.126) P=0.715	
			Mean (SD) Blood loss	Group 1 (n=34): 195.97 (50.079) Group 2 (n=33): 361.52 (97.599) P=0.000	
			Mean (SD) Time catheterised	Group 1 (n=34): 19.05 (3.920) Group 2 (n=33): 39.25 (10.223) P=0.000	
			Mean (SD) Hospital stay	Group 1 (n=34): 79.21 (14.251) Group 2 (n=33): 81.09 (15.438) P=0.605	
			Average tissue resected, g	Group 1: 42.8 Group 2: 45.0	
			Mean AUASS at baseline	Group 1: 26.3 Group 2: 24.6	
			Mean AUASS at 3 months	Group 1: 6.5 Group 2: 6.8	
			Mean AUASS at 9 months	Group 1: 8.2 Group 2: 8.0	
			Mean AUASS at 12 months	Group 1: 8.8 Group 2: 9.1	
			TUR	Group 1: 0% Group 2: 12.2%	
			Strictures	Group 1: 5 Group 2: 4	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Bladder neck contracture	Group 1: 1 Group 2: 0	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Erturhan et al., 2007[84] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months.	**Patient Group:** Patients with BPH and moderate to severed LUTS **Setting:** single centre: Sahinbey Medical Center, Univerity of Gaziantep, Turkey **Inclusion criteria:** • IPSS ≥ 18 or PVR > 50 mL **Exclusion criteria:** • Prostate cancer or suspect • Previous history of prostatic surgery • Neurogenic bladder • Urethral stricture **<u>All patients</u>** **N:** 240 **Dropouts:** NR **<u>Group 1</u>** **N:** 120 **Mean age (range):** 68.5 (52-90) **Mean IPSS ± SD:** 25.0 ± 5.0 **Mean Qmax ± SD, mL/s:** 10.9 ± 1.2 **Mean PVR± SD, mL:** 114 ± 19 **Mean prostate volume ± SD, mL:** 43 ± 9 **IPSS QoL ± SD:** 2.0 ± 1.0 **Operative time ± SD, min:** 36 ± 19 **Drop outs:** 0 **<u>Group 2</u>** **N:** 120 **Mean age (range):** 67.4 (68-74) **Mean IPSS ± SD:** 24.0 ± 6.0	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ system with Plasma Sect electrode (200W, 160Ω, 320-450kHz, 254-350V) 27F continuous flow resectoscope with isotonic saline as irrigant **Group 2: Transurethral resection of the prostate (TURP)** Standard loop: 120W cutting and 80W coagulation. 26F continuous flow resectoscope with glycine 5% irrigant **All patients** 22 F Foley catheter inserted and irrigation with saline. Catheter removed when urine clear. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up at 1 and 12 months for IPSS, QoL, PVR and Qmax	**Mean ± SD IPSS at 1 months**	**Group 1:** 5.0 ± 2.0 (n=120) **Group 2:** 5.0 ± 2.0 (n=120) **P value:** NS	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment were not reported. • Outcome assessment was not masked **Additional outcomes:** Irrigation volumes. **Notes:** None.
			Mean ± SD IPSS at 12 months	**Group 1:** 4.0 ± 2.0 (n=120) **Group 2:** 4.0 ± 2.0 (n=120) **P value:** NS	
			Mean ± SD Qmax at 1 months	**Group 1:** 17.4 ± 2.5 (n=120) **Group 2:** 16.4 ± 3.5 (n=120) **P value:** <0.001 P=0.01 calculated by NCGC using t-test with unequal variances	
			Mean ± SD Qmax at 12 months	**Group 1:** 19.5 ± 3.5 (n=120) **Group 2:** 18.5 ± 3.0 (n=120) **P value:** <0.001 P=0.02 calculated by NCGC using t-test with unequal variances	
			Mean ± SD QoL at 1 months	**Group 1:** 2.1 ± 1.0 (n=120) **Group 2:** 2.1 ± 1.0 (n=120) **P value:** NS	
			Mean ± SD QoL at 12 months	**Group 1:** 2.1 ± 1.0 (n=120) **Group 2:** 2.1 ± 1.0 (n=120) **P value:** NS	
			Mean ± SD catheter duration, days	**Group 1:** 3.0 ± 1.1 (n=120) **Group 2:** 4.5 ± 1.1 (n=120) **P value:** <0.001	
			Length of Stay ± SD, days reported as time to discharge	**Group 1:** 3.0 ± 1.2 (n=120) **Group 2:** 5.0 ± 1.2 (n=120) **P value:** <0.001	
			Complications: Transfusion	**Group 1:** 1/120 **Group 2:** 7/120 **P value:** <0.0001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean Qmax ± SD, mL/s: 9.29 ± 1.7 **Mean PVR± SD, mL:** 135 ± 25 **Mean prostate volume ± SD, mL:** 42 ± 11 **IPSS QoL ± SD:** 3.0 ± 1.0 **Operative time ± SD, min:** 57 ± 24 **Drop outs:** 0		**Complications: urinary retention** (re-catheterisation)	**Group 1:** 2/120 **Group 2:** 5/120 **P value:** 0.083	
			Complications: TUR Syndrome	**Group 1:** 0/120 **Group 2:** 2/120 **P value:** 0.15	
			Complications: Reoperation rate	**Group 1:** 0/120 **Group 2:** 5/120 **P value:** 0.025	
			Complications: Incontinence	**Group 1:** 0/120 **Group 2:** 0/120	
			Complications: Mortality	**Group 1:** 0/120 **Group 2:** 0/120	
			Complications: urethral & meatal stricture	**Group 1:** 5/120 **Group 2:** 4/120	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Ho et al., 2007[120] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months.	**Patient Group:** Patients awaiting TURP for failed medical therapy (alpha-blockers or 5-alpha reductase inhibitors), UTI or haematuria **Setting:** single centre: Department of Urology, Singapore General Hospital, Singapore **Inclusion criteria:** • >50 years • Fit for anaesthesia • IPSS > 18 • Qmax < 15 mL/s • Patients with acute urinary retention and failed trial of voiding without catheter also included **Exclusion criteria:** • Previous prostatic surgery • Neurogenic bladder disorders • Bladder stones • Renal impairment • Hydronephrosis • Prostate cancer or suspect • Urethral strictures **<u>All patients</u>** **N:** 100 **Dropouts:** 0 **<u>Group 1</u>** **N:** 48 **Mean ± SD Age, yrs:** 66.6 ± 6.8 **IPSS ± SD:** 22.6 ± 5.5	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Olympus TURIS system with 180W cutting and 100W coagulation **Group 2: TURP** Standard loop: 100W cutting and 50W coagulation with glycine 5% as irrigant. **All patients** 26F Olympus continuous flow resectoscope. 20F Foley 3-way catheter inserted for bladder irrigation and removed after 1 or 2 days. All operations performed by 2 senior consultants **Examination methods** **Preoperative:** Baseline IPSS, QoL, Qmax and PVR, PSA, Na^+, creatinine and Hb. **Postoperative:** Na^+, Hb repeated after 6 hours and IPSS and Qmax assessed at 1, 3, 6, 12 months follow up visits	**Mean ± SD IPSS at 3 months**	**Group 1:** 9.0 ± NR (n=48) **Group 2:** 7.5 ± NR (n=52) **P value:** NS	**Funding:** NR **Limitations:** • Allocation concealment not reported • Outcome assessment was not masked • Mean values are estimated from graph for IPSS and Qmax. P values were not provided for change from baseline so SDs could not be estimated **Additional outcomes:** Decline in post op serum Na^+ and Hb **Notes:** Computer randomisation
			Mean ± SD IPSS at 6 months	**Group 1:** 7.0 ± NR (n=48) **Group 2:** 7.0 ± NR (n=52) **P value:** NS	
			Mean ± SD IPSS at 12 months	**Group 1:** 6.0 ± NR (n=48) **Group 2:** 6.0 ± NR (n=52) **P value:** NS	
			Mean ± SD Qmax at 3 months	**Group 1:** 19.5 ± NR (n=48) **Group 2:** 16.5 ± NR (n=52) **P value:** NS	
			Mean ± SD Qmax at 6 months	**Group 1:** 17.5 ± NR (n=48) **Group 2:** 18.0 ± NR (n=52) **P value:** NS	
			Mean ± SD Qmax at 12 months	**Group 1:** 17.0 ± NR (n=48) **Group 2:** 17.5 ± NR (n=52) **P value:** NS	
			Complications: Transfusion	**Group 1:** 1/48 **Group 2:** 1/52 **P value:** NS	
			Complications: TUR	**Group 1:** 0/48 **Group 2:** 2/52 **P value:** <0.05	
			Complications: urethral stricture	**Group 1:** 3/48 **Group 2:** 1/52 **P value:** NS	
			Complications: urinary retention (re-catheterisation)	**Group 1:** 5/48 **Group 2:** 4/52 **P value:** NS	
			Complications: UTI	**Group 1:** 2/48 **Group 2:** 2/52 **P value:** NS	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	PSA ± SD, ng/mL: 2.8 ± 1.0 **Mean ± SD Qmax, mL/s:** 6.8 ± 4.8 **Mean prostate volume ± SD, mL:** 56.5 ± 17.9 **Resectate ± SD, g:** 29.8 ± 11.2 **Resection time ± SD, min:** 59 ± 18 **Number with AUR:** 24/48 **Number with failed medical therapy:** 20/48 **Number with UTI/Haematuria:** 4/48 **Dropouts:** 0 **Group 2** **N:** 52 **Mean ± SD Age, yrs:** 66.5 ± 7.2 **IPSS ± SD:** 24.6 ± 6.0 **PSA ± SD, ng/mL:** 2.2 ± 0.5 **Mean ± SD Qmax, mL/s:** 6.5 ± 3.2 **Mean prostate volume ± SD, mL:** 54.8 ± 19.2 **Resectate ± SD, g:** 30.6 ± 9.8 **Resection time ± SD, min:** 58 ± 16 **Number with AUR:** 21/52 **Number with failed medical therapy:** 25/52 **Number with UTI/Haematuria:** 6/52 **Dropouts:** 0				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Iori et al., 2008[124] **Study design:** RCT Observer masked **Evidence level:** 1+ **Duration of follow-up:** 12 months.	**Patient Group:** Patients scheduled for surgery for obstruction **Setting:** single centre: Department of Urology, University of Rome, Italy **Inclusion criteria:** • Obstruction class 2-5 on Schaefer nomogram **Exclusion criteria:** • Neurogenic bladder • Bladder stones • Urethral stricture • Renal insufficiency • Current finasteride medical therapy **<u>All patients</u>** **N:** 51 **Dropouts:** 0 **<u>Group 1</u>** **N:** 25 **Mean age (range):** 65.0 ± 5.0 **Mean IPSS ± SD:** 21.0 ± 2.0 **Mean Qmax ± SD, mL/s:** 7.0 ± 1.0 **Mean PVR± SD, mL:** 99 ± 58 **Mean prostate volume ± SD, mL:** 49 ± 11 **IPSS QoL ± SD:** 3.0 ± 1.0 **Resection time ± SD, min:** 39 ± 19 **Drop outs:** 0 **<u>Group 2</u>** **N:** 26 **Mean age (range):** 63.0 ± 5.0 **Mean IPSS ± SD:** 20.0 ± 4.0	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ system with Plasma Sect electrode (200W, 160Ω, 320-450kHz, 254-350V) 27F continuous flow resectoscope with isotonic 0.9% saline as irrigant **Group 2: Transurethral resection of the prostate (TURP)** Standard loop. 26F continuous flow resectoscope with mannitol as irrigant **All patients** 22 F Foley catheter inserted and irrigation with saline. Catheter removed when urine clear and patient had passed a stool. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, QoL DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up at 12 months for IPSS, QoL, PVR and Qmax	**Mean ± SD IPSS at 12 months**	**Group 1:** 7.0 ± 1.7 (n=25) **Group 2:** 6.7 ± 4.0 (n=26) **P value:** NR	**Funding:** NR **Limitations:** None. **Additional outcomes:** Irrigation time, postoperative Schaefer obstruction class **Notes:** Randomisation by drawing opaque sealed envelopes.
			Mean ± SD Qmax at 12 months	**Group 1:** 24.2 ± 5.0 (n=25) **Group 2:** 23.2 ± 9.0 (n=26) **P value:** NR	
			Mean ± SD QoL at 12 months	**Group 1:** 1.1 ± 1.0 (n=25) **Group 2:** 1.1 ± 1.0 (n=26) **P value:** NR	
			Mean ± SD catheter duration, days (converted from hours)	**Group 1:** 0.96 ± 0.2 (n=25) **Group 2:** 1.33 ± 0.2 (n=26) **P value:** <0.0001	
			Length of Stay ± SD, days (converted from hours)	**Group 1:** 2.0 ± 0.04 (n=25) **Group 2:** 2.1 ± 0.13 (n=26) **P value:** 0.9	
			Complications: Transfusion	**Group 1:** 0/25 **Group 2:** 0/26	
			Complications: urinary retention (re-catheterisation)	**Group 1:** 1/25 **Group 2:** 0/26	
			Complications: TUR Syndrome	**Group 1:** 0/25 **Group 2:** 0/26	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean Qmax ± SD, mL/s: 8.7 ± 2.0 **Mean PVR± SD, mL:** 96 ± 97 **Mean prostate volume ± SD, mL:** 48 ± 91 **IPSS QoL ± SD:** 3.6 ± 1.0 **Resection time ± SD, min:** 39 ± 19 **Drop outs:** 0				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Michielsen et al., 2007[200] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 1 month	**Patient Group:** Men with obstruction due to BPH **Setting:** single centre: Department of Urology, Virije Universiteit, Brussels, Belgium **Inclusion criteria:** • IPSS ≥ 13 • Qmax < 15 mL/s • QoL ≥ 3 **Exclusion criteria:** • Neurogenic bladder • Carcinoma of the prostate • History of prostate or urethral surgery • Bladder stones • Patients on anticoagulant therapy **<u>All patients</u>** **N:** 238 **Dropouts:** 0 **<u>Group 1</u>** **N:** 118 **Mean ± SD Age:** 73.8 ± 8.1 (53-92) **IPSS ± SD:** NR **Mean SD Qmax:** NR **Mean prostate size ± SD, g:** NR **Resectate ± SD g:** 21.0 ± NR **Operation duration ±SD min:** 56 ± 25 **Dropouts:** 0 **<u>Group 2</u>** **N:** 50 **Mean ± SD Age:** 73.1± 8.6 (52-92)	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Olympus TURIS system with 270W cutting and 75W coagulation **Group 2: TURP** Standard loop with 26F resectoscope: 175W cutting and 75W coagulation **All patients** 22 F Foley catheter inserted and irrigation with saline until bleeding ended. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. **Postoperative:** Full blood count was performed	**Mean ± SD catheter duration, days** **Mean ± SD length of stay, days** **Complications: urinary retention** (re-catheterisation) **Complications: TUR Syndrome** **Complications: Transfusion** **Complications: reoperation (transurethral revision)**	**Group 1**: 4.0 ± 3.0 **Group 2**: 4.5 ± 3.5 **P value**: 0.2 **Group 1**: 4.9 ± NR **Group 2**: 5.1 ± NR **P value**: 0.6 **Group 1**: 3/118 **Group 2**: 5/120 **Group 1**: 0/118 **Group 2**: 1/120 **Group 1**: 4/118 **Group 2**: 1/120 **Group 1**: 0/118 **Group 2**: 2/120	**Funding:** NR **Limitations:** • Unclear whether sealed envelopes were opaque. • Primary outcome in study is not IPSS or Qmax • Follow up very short to capture early complications only **Additional outcomes:** Haemoglobin, sodium, potassium, chloride. Differences in operative times for staff v trainees **Notes:** None.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	IPSS ± SD: NR **Mean SD Qmax:** NR **Mean prostate size ± SD, g:** NR **Resectate ± SD g:** 21.3 ± NR **Operation duration ± SD min:** 44 ± 20 **Dropouts:** 0				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Nuhoglu et al., 2006[228] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient Group:** Patients with LUTS **Setting:** single centre: Ministry of Health Ankara Training & Teaching Hospital, Turkey **Inclusion criteria:** • IPSS > 15 • Qmax < 10 mL/s **Exclusion criteria:** • Neurogenic bladder • Carcinoma of the prostate • History of prostate or urethral surgery • Bladder stones • Patients on anticoagulant therapy **<u>All patients</u>** **N:** *57* **Dropouts:** 7 (5 patients could not be contacted, 1 died and 1 left study) **<u>Group 1</u>** **N:** 27 **Mean ± SD Age, years:** 64.6 ± 8.8 **IPSS ± SD:** 17.6 ± 6.1 **Mean SD Qmax:** 6.9 ± 2.8 **Mean SD PVR, mL:** 96 ± 27 **Mean prostate volume ± SD, mL:** *47 ± 7.7* **Operation duration ± SD min:** *55 ± 9.7* **Number of patients on alpha-blockers:** 18/27 **Dropouts:** 3 **<u>Group 2</u>**	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ system with Plasma Sect electrode (200W, 160Ω, 320-450kHz, 254-350V) Resection performed on PK3 mode with 340V. Saline irrigant **Group 2: TURP** 25F Storz resectoscope with glycine as irrigant. **All patients** All patients received antibiotic prophylaxis. 22 F Foley catheters inserted and continuous irrigation with saline for 1 postoperative day. Catheters removed when urine clear and discharge after free micturation. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, DRE, urinalysis, PSA, Blood, TRUS, uroflowmetry. Follow up at 1 and 12 months for IPSS, Qmax, PVR, and prostate volume. Complications were assessed at end of the first year.	**Mean ± SD IPSS at 1 months**	**Group 1**: 4.8 ± 3.4 (n=27) **Group 2**: 4.7 ± 3.1 (n=30) **P value**: NS	**Funding:** NR **Limitations:** • Randomisation method and allocation concealment were not reported • Outcome assessment was not masked **Additional outcomes:** Sodium, Haemocrit, Haemoglobin **Notes:** None.
			Mean ± SD IPSS at 12 months	**Group 1**: 5.4 ± 3.7 (n=24) **Group 2**: 5.2 ± 3.2 (n=26) **P value**: NS	
			Mean ± SD Qmax at 1 months	**Group 1**: 17.6 ± 4.3 (n=27) **Group 2**: 17.7 ± 2.3 (n=30) **P value**: NS	
			Mean ± SD Qmax at 12 months	**Group 1**: 17.1 ± 2.7 (n=24) **Group 2**: 17.9 ± 3.1 (n=26) **P value**: NS	
			Mean ± SD catheter duration, days (converted from hours)	**Group 1**: 1.96 ± 0.23 (n=27) **Group 2**: 3.15 ± 0.52 (n=30) **P value**: 0.009	
			Complications: Transfusion	**Group 1:** 1/27 **Group 2**: 2/30	
			Complications: urinary retention (re-catheterisation)	**Group 1:** 1/27 **Group 2**: 0/30	
			Complications: TUR Syndrome	**Group 1:** 0/27 **Group 2**: 0/30	
			Complications: Incontinence	**Group 1:** 0/27 **Group 2**: 0/30	
			Complications: Reoperation rate	**Group 1:** 0/27 **Group 2**: 0/30	
			Complications: urethral stricture	**Group 1:** 1/27 **Group 2**: 0/30	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	N: 30 **Mean ± SD Age, years:** 65.2 ± 9.3 **IPSS ± SD:** 17.3 ± 5.8 **Mean SD Qmax:** 7.3 ± 2.1 **Mean SD PVR, mL:** 88 ± 20 **Mean prostate volume ± SD, mL:** 49 ± 8.1 **Operation duration ± SD min:** 52 ± 13.2 **Number of patients on alpha-blockers:** 21/30 **Dropouts:** 4				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Patankar et al., 2006[234] **Study design:** RCT Double blind (patients and observer) **Evidence level:** 1+ **Duration of follow-up:** 3 weeks	**Patient group:** men with LUTS associated with BPH **Setting:** single-centre. Institute of urology & BJ Medical College, Pune, India **Inclusion criteria:** • >45 years • AUA score ≥ 18 • Qmax < 10 mL/s • Prostate volume 35-70 mL **Exclusion criteria:** • Prostate cancer • Previous prostatic surgery **<u>All patients</u>** **N:** 104 **Drop outs:** 1 **<u>Group 1:</u>** **N:** 53 **Mean age:** 64 **Mean AUA score ± SD:** 23.3 ± 4.85 **Mean Qmax ± SD, mL/s:** 5.9 ± 1.98 **Mean PVR ± SD, mL:** NR **Mean prostate volume± SD, mL:** 51.3 ± 12.44 **Operative time ± SD, mins:** 49.99 ± 12.35 **Resectate ± SD, g:** NR **Drop outs:** 1 **<u>Group 2:</u>** **N:** 51 **Mean age:** 62	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PK Superpulse system: Cutting 150V and 120V coagulation with saline irrigant. **Group 2: Transurethral resection of the prostate (TURP)** Standard loop through 24F resectoscope with glycine as irrigant **All patients:** Preoperative antibiotics. One consultant performed all the operations. A 20 3-way catheter was inserted and irrigation continued until returning fluid was clear for a minimum of 6 hours. Post irrigation catheter was removed if urine remained clear. **Examination methods Preoperative:** Baseline AUA score, urinalysis, PSA, TRUS, uroflowmetry. Uroflowmetry and AUA score repeated 21 days	**Mean AUA score at 3 weeks** **Mean Qmax ± SD mL/s at 3 weeks** **Catheterisation time (days)** hours reported converted to days **Complications: transfusion** **Complications: UTI**	**Group 1:** 6.11 ± 1.02 **Group 2:** 7.7 ± 1.86 **P value:** NS **Group 1:** 19.16 ± 1.9 **Group 2:** 20.67 ± 1.63 **P value:** NS **Group 1:** 0.77 ± 0.11 **Group 2:** 1.77 ± 0.63 **P value:** <0.05 **Group 1:** 0/53 **Group 2:** 1/51 **p value:** 0.5 **Group 1:** 6/53 **Group 2:** 7/51 **p value:** 0.74	**Funding:** NR **Limitations:** • Short follow up interval **Notes:** Randomisation via drawing opaque envelopes

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Mean AUA score ± SD: 23.73 ± 4.6 **Mean Qmax ± SD, mL/s:** 6.4 ± 1.77 **Mean PVR ± SD, mL:** NR **Mean prostate volume± SD, mL:** 52.26 ± 10.71 **Operative time ± SD, mins:** 49.99 ± 12.35 **Resectate ± SD, g:** NR **Drop outs:** 0				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Seckiner et al., 2006[270] **Study design:** RCT Observer masked **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient Group:** Not specified **Setting:** single centre: Department of Urology, Zonguldak Karaelmas University School of Medicine, Turkey **Inclusion criteria:** • IPSS ≥ 8 • Qmax < 15 mL/s • Prostate volume 30-70g on TRUS **Exclusion criteria:** • < 50 years • Neurogenic bladder • Carcinoma of the prostate or bladder • History of prostate or urethral surgery • On current medication known to affect voiding function **<u>All patients</u>** **N:** 48 **Dropouts:** 4 **<u>Group 1</u>** **N:** 24 **Mean ± SD Age:** 61.2 ± 9.3 **IPSS ± SD:** 24.1 ± 5.2 **IPSS QoL ± SD:** 4.4 ± 0.6 **Mean ± SD Qmax, mL/s:** 8.5 ± 2.9 **Mean PVR ± SD, mL:** 88 ± 74 **Mean prostate size ± SD, mL:** 49.4 ± 18.9 **Resectate ± SD, g:** 36.6 ± 14.4	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** Gyrus PlasmaKinetic™ system with Plasma Sect electrode (200W, 160Ω, 320-450kHz, 254-350V) set to 160W cutting and 80W. Resection performed through 27F resectoscope with saline as irrigant. **Group 2: TURP** Standard wire loop 120W cutting and 80W coagulation through 26F resectoscope with glycine 5% as irrigant **All patients** All operations were performed by the same surgeon. Bladder irrigation carried out for not more than 12 hours **Examination methods** **Preoperative:** Baseline IPSS Symptom score, QoL, DRE, urinalysis, blood, TRUS, uroflowmetry. IPSS and Qmax were recorded at 1, 3, 6 & 12 months, PVR at 3, 6 & 12 months and TRUS at 6 months.	**Mean ± SD IPSS at 3 months**	**Group 1:** 9.3 ± 3.9 (n=24) **Group 2:** 10.6 ± 6.3 (n=24) **P value:** NS	**Funding:** NR **Limitations:** • Allocation concealment with opaque sealed envelopes was not used **Additional outcomes:** Bleeding score, serum haemoglobin and sodium **Notes:** Randomisation using random number tables
			Mean ± SD IPSS at 6 months	**Group 1:** 7.4 ± 2.2 (n=24) **Group 2:** 6.0 ± 6.7 (n=23) **P value:** NS	
			Mean ± SD IPSS at 12 months	**Group 1:** 8.7 ± 4.1 (n=23) **Group 2:** 8.3 ± 2.9 (n=21) **P value:** NS	
			Mean ± SD Qmax at 3 months	**Group 1:** 17.7 ± 9.1 (n=24) **Group 2:** 18.6 ± 9.1 (n=24) **P value:** NS	
			Mean ± SD Qmax at 6 months	**Group 1:** 23.4 ± 10.6 (n=24) **Group 2:** 16.2 ± 12.0 (n=23) **P value:** NS	
			Mean ± SD Qmax at 12 months	**Group 1:** 18.8 ± 6.9 (n=23) **Group 2:** 15.7 ± 6.3 (n=21) **P value:** NS	
			Mean ± SD IPSS QoL at 3 months	**Group 1:** 1.8 ± 1.0 (n=24) **Group 2:** 2.1 ± 1.2 (n=24) **P value:** NS	
			Mean ± SD IPSS QoL at 6 months	**Group 1:** 1.6 ± 0.7 (n=24) **Group 2:** 1.6 ± 1.3 (n=23) **P value:** NS	
			Mean ± SD IPSS QoL at 12 months	**Group 1:** 1.8 ± 0.8 (n=23) **Group 2:** 2.0 ± 0.8 (n=21) **P value:** NS	
			Mean ± SD catheter duration, days	**Group 1:** 3.1 ± 0.6 **Group 2:** 3.1 ± 1.4 **P value:** 0.98	
			Complications: urethral stricture	**Group 1:** 2/24 **Group 2:** 1/24	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Operation duration ± SD, min: 52.9 ± 12.8 **Dropouts:** 1 patient where measurements were not obtained **<u>Group 2</u>** **N:** 24 **Mean ± SD Age:** 63.9 ± 10.9 **IPSS ± SD:** 23.2 ± 4.9 **IPSS QoL ± SD:** 4.7 ± 0.9 **Mean ± SD Qmax, mL/s:** 8.3 ± 3.1 **Mean PVR ± SD, mL:** 138 ± 115 **Mean prostate size ± SD, mL:** 41.4 ± 14.5 **Resectate ± SD, g:** 31.9 ± 13.2 **Operation duration ± SD, min:** 52.9 ± 16.3 **Dropouts:** 3 patients where measurements were not obtained				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Singh et al., 2005[280] **Study design:** RCT Observer masked **Evidence level:** 1+ **Duration of follow-up:** 3 months	**Patient Group:** Patients with symptomatic BPH requiring surgical intervention **Setting:** single centre: Department of Urology, Muljibhai Patel Urological Hospital, Gujarat, India **Inclusion criteria:** • >50 • IPSS > 7 • Qmax < 12 mL/s • PCAR (from TRUS) >0.75 **Exclusion criteria:** • Neurogenic bladder • Renal insufficiency • Bladder stone • Urethral stricture • Current finasteride therapy **<u>All patients</u>** **N:** 60 **Dropouts:** NR **<u>Group 1</u>** **N:** 30 **Mean ± SD Age:** 68.9 ± 7.6 **IPSS ± SD:** 20.5 ± 4.8 **IPSS QoL ± SD:** 4.6 ± 0.9 **Mean ± SD Qmax, mL/s:** 5.8 ± 3.0 **Mean PVR ± SD, mL:** 124 ± 58 **Resectate ± SD, g:** 24.0 ± 18.2 **Operation duration ± SD, min:** 39.3 ± 17.8 **Number of patients with retention:**	**Group 1: Bipolar transurethral resection of the prostate (B-TURP)** ACMI Vista CTR Controlled Tissue Resection system through 25.6F resectoscope and cautery setting of 6-8 for cutting and 7 for coagulation with saline as irrigant. **Group 2: TURP** Standard wire loop through 25.5F resectoscope. **All patients** All operations were performed by the same surgeon. A 20F 3-way catheter was placed and saline irrigation continued as required. **Examination methods** **Preoperative:** Baseline IPSS Symptom score, QoL, PCAR (TRUS), PSA, Blood, uroflowmetry. IPSS, QoL, Qmax at 1 and 3 months. Patients were given a questionnaire on postoperative complications on haematuria, dysuria, urgency, incontinence and pain weekly after surgery	**Mean ± SD IPSS at 3 months** **Mean ± SD Qmax at 3 months** **Mean ± SD IPSS QoL at 3 months** **Mean ± SD catheter duration, days** **Mean ± SD length of stay, days** **Complications: TUR** **Complications: UTI** **Complications: urethral stricture**	**Group 1**: 5.3 ± NR **Group 2**: 6.2 ± NR **P value**: NR **Group 1**: 19.0 ± NR **Group 2**: 17.8 ± NR **P value**: NR **Group 1**: 1.1± NR **Group 2**: 1.0 ± NR **P value**: NR **Group 1**: 2.52 ± 0.5 **Group 2**: 3.41 ± 0.53 **P value**: 0.02 **Group 1**: 3.02 ± 0.55 **Group 2**: 3.88 ± 0.58 **P value**: 0.02 **Group 1**: 0/30 **Group 2**: 0/30 **Group 1**: 3/30 **Group 2**: 4/30 **Group 1**: 2/30 **Group 2**: 1/30	**Funding:** NR **Limitations:** • Allocation concealment with opaque envelopes not clear. • Unclear if all the patients completed study • Standard deviations not reported for IPSS, Qmax or QoL and could not be estimated because there were p values for change from baseline **Additional outcomes:** Haematuria, dysuria, urgency, incontinence and pain results from questionnaire. **Notes:** Randomised by drawing envelopes

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	10/30 **Dropouts:** NR **<u>Group 2</u>** **N:** 30 **Mean ± SD Age:** 67.9 ± 9.8 **IPSS ± SD:** 21.6 ± 6.3 **IPSS QoL ± SD:** 4.47 ± 1.0 **Mean ± SD Qmax, mL/s:** 5.1 ± 2.0 **Mean PVR ± SD, mL:** 136 ± 52 **Resectate ± SD, g:** 27.6 ± 13.4 **Operation duration ± SD, min:** 36.9 ± 14.6 **Number of patients with retention:** 11/30 **Dropouts:** NR	up to 4 weeks.			

Evidence Table 46 Conservative vs. surgery

Bladder training vs. TURP

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Donovan et al., 2000[74] **CLasP** study **Study design:** RCT, multicentre, open label **Evidence level:** 1+ **Duration of follow-up:** 7.5 months	**Patient group:** men with uncomplicated LUTS symptoms **Setting:** 3 centres in UK **Inclusion criteria:** • IPSS score of≥8, with physician and patient agreement that the symptoms require intervention • Qmax <15ml.s when voided volume>200ml, <13ml/s when voided volume between 150-200ml and <10ml/s when voided volume between 100 to 149ml measured on two occasions, with the higher value between these two used for analysis • >300ml post void volume urine on ultrasound **Exclusion criteria:** • Prostate cancer or previous prostatic surgery; • prostate size > 120ml; • Life expectancy < 6 months; • Urinary retention associated with recent operation, constipation or drugs which could cause acute urinary	**Group 1- Laser coagulation** **Procedure**: Nd:YAG/ Non-contact VLAP, side-firing fibre (Bard Urolase), using standard fixed spot technique **Power:** 60W ND: YAG for 60s, depends on prostate size. For prostate size with urethral length of >25 mm, additional set of laser was used. If median lobe was present, 60W for 30s was applied for each side of lobe. **Energy:** 28684J **Catheter protocol:** Suprapubic catheter, removed when clinically appropriate. **Other:** All patients received antibiotic prophylaxis and anti-inflammatory suppository. **Group 2 –TURP** **Procedure:** Standard electroresection	**IPSS, mean change from baseline** (95%CI)**:** Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -10.8 ± 8.64* (95% CI: -12.5,-9.0), n=96 **Group 2:** -12.3 ± 7.36* (95% CI: -13.8,-10.7), n=89 **Group 3:** -1.3 ± 5.29* (95% CI: -2.8,0.2), n=85 **p value:** Group 2 v Group 3 - NR Statistically significant for surgical procedures vs. conservative	**Funding:** Laser machines provided by Bard Diagnostics, Redmond, Washington. **Limitations:** • Open label study, with main outcomes using patient reported measures • The clinician following up patients was different to the surgeon although it was not stated whether the clinician was masked to treatment allocation **Additional outcomes:** Composite outcomes categories, and categorical outcomes for IPSS and Qmax **Notes:** Randomisation using computer generated numbers in blocks of 6
			IPSS-QoL, mean (95%CI)**:** Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -1.9 ± 1.7* (95% CI: -2.3, -1.6), n=93 **Group 2:** -2.2 ± 1.62* (95% CI: -2.5, -1.8), n=85 **Group 3:** -0.4 ± 1.39* (95% CI: -0.7, -0.1), n=85 **p value:** Group 2 v Group 3 - NR	
			Qmax, mean(95%CI)**:** Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** 5.8 ± 6.87* (95% CI: 4.5, 7.2), n=102 **Group 2:** 9.7 ± 9.73* (95% CI: 7.7, 11.6), n=98 **Group 3:** 0.2 ± 2.9* (95% CI: -0.4, 0.8), n=92 **p value:** Group 2 v Group 3 - NR	
			Post void residual volume, mean(95%CI)**:** Adjusted for centre and baseline symptom score, ANCOVA	**Group 1:** -73.4(95% CI:-91.3, -55.5), n=100 **Group 2:** -74.0 (95% CI:-89.2, -58.8), n=98 **Group 3:** 2.19 (95% CI:-23.1, -27.5, n=90 **p value:** Group 2 v Group 3 - NR	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	dysfunction, • Neurogenic bladder dysfunction; • Serum creatinine >250 µmol/L. **<u>All patients</u>** **N:** 340 **Drop outs:** **<u>Group 1-Laser coagulation</u>** **N:** 117 **Dropouts:**1/117 **Age,** mean ± SD: 67.4 ± 8.1 **IPSS,** mean ± SD: 19.1 ± 6.6 **IPSS-QoL,** median(range)**:** 4(2-6) **Qmax,** mean, ± SD: 10.4 ± 2.9 **Post void residual urine,** mean, ± SD: 123.7 ± 91.8 **Prostate volume,** mean, ± SD: 40.7 ± 21.4 **No obstructed** (%): 90/117 (78.3) **No equivocal and/or unobstructed** (%): 25/117 (21.7) **<u>Group 2 - TURP</u>** **N:** 117 **Dropouts:**2/117 **Age,** mean ± SD: 66.4 ± 7.9 **IPSS,** mean ± SD: 19.2 ± 6.7 **IPSS-QoL,** median(range)**:** 4(0-6) **Qmax,** mean, ± SD: 10.3 ± 2.7 **Post void residual urine,** mean, ± SD: 104.2 ± 69.5 **Prostate volume,** mean, ± SD: 38.1 ± 19.1 **No obstructed** (%): 91/117(78.4) **No equivocal and/or unobstructed**	**Catheter protocol:** Suprapubic catheter. **Group 3 – Conservative management** **Procedure:** Men were given general advice and bladder training as deemed clinically appropriate	**All cause mortality** Not treatment related	**Group 1:** 5/117 **Group 2:** 0/117 **Group 3:** 1/106 **p value:** NS for all groups	Allocation concealed using consecutive opaque sealed envelopes. Sample size calculation performed Please see Chacko et al., 2001[48] for the acute urinary retention population of CLASP trial and Gujral et al., 2000[107] for the chronic urinary retention population. * SD estimated using methods detailed in the Cochrane handbook for change from baseline with confidence intervals
			Post-op complications: Blood transfusion (units and criteria not stated)	**Group 1:** 1/117 **Group 2:** 1/117 **p value:** NS	
			Post-op complications: Perforation	**Group 1:** 0/117 **Group 2:** 2/117 **p value:** NS	
			Post-op complications: Septicaemia	**Group 1:** 0/117 **Group 2:** 2/117 **p value:** NS	
			Post-op complications: Urinary tract infection (symptomatic)	**Group 1:** 3/117 **Group 2:** 2/117 **p value:** NS	
			Time to catheter removal geometric mean, days	**Group 1:** 2.2 (95%CI 1.9 to 2.4) **Group 2:** 3.9 (95%CI 3.7 to 4.2) **Relative risk: 1.83** **95% CI:** 1.58 to 2.11 **P value:** <0.0001	
			LOS, geometric mean (95% CI) days	**Group 1:** 11.8(95%CI: 10.2 to 13.7) **Group 2:** 2.4 (95%CI: 2.1 to 2.9) **Relative risk:** 4.79 **95% CI:** 3.88 to 5.91 **p value:** <0.0001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	(%): 25/117(21.6) **<u>Group 3 – Conservative management</u>** **N:** 106 **Dropouts:** 5/106 **Age,** mean ± SD: 67.2 ± 7.8 **IPSS,** mean ± SD: 18.8 ± 6.5 **IPSS-QoL,** median(range)**:** 4(1-6) **Qmax,** mean, ± SD: 9.9 ± 2.7 **Post void residual urine,** mean, ± SD: 119.1 ± 90.4 **Prostate volume,** mean, ± SD: 36.8±17.2 **No obstructed** (%): 82/106(77.4) **No equivocal and/or unobstructed** (%): 24/106(22.6)				

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1 **Catheters vs. TURP**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Ghalayini et al., 2005[100] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** men with chronic urinary retention (CUR) **Setting:** 2 centres in Jordan and UK **Inclusion criteria:** • IPSS >7 • CUR defined by PVR > 300mL measured by ultrasonography on 2 occasions **Exclusion criteria:** • Prostate cancer • Previous prostatic surgery • Uncontrolled renal impairment • Life expectancy <6 months • Neurogenic bladder dysfunction • Inability to perform clean intermittent self catheterisation. **<u>All patients</u>** **N:** 51 **Drop outs:** 10 **<u>Group 1 – CISC</u>** **N:** 29 (baseline variables for only 24 patients who completed the study) **Age, mean (± SD):** 69 ± 7.3 **IPSS, mean (± SD):** 23.2 ± 6.1 **IPSS-QoL, mean (± SD):** 4.2 ± 1.1 **Qmax, mean (± SD), mL/s:** 5.5 ± 4.2 **PVR, mean (± SD), mL:** 963 ± 503	**Group 2 – Clean intermittent self catheterisation (CISC)** Patients were taught how to use a 12 or 14 F catheter every 6 hours. **Group 1 – TURP** **Procedure:** Standard electroresection **Examination methods:** Prior to start men had cystometry and PFS. Men were reviewed at 3 and 6 months after TURP or start of CISC for IPSS, serum creatinine, urine culture and PFS at 6 months. Men in the CISC group with urodynamic evidence of BOO at 6 months were advised to have TURP at the end of the study.	**IPSS, mean change from baseline at 6 months** (95%CI)**:** **IPSS QoL, mean change from baseline at 6 months** (95%CI)**:**	**Group 1:** -12.25 ± 7.77* (95% CI: -15.53,-8.97), n=24 **Group 2:** -20.29 ± 8.86* (95% CI: -24.85,-15.74), n=17 **p value:** NR **Group 1:** -2.54 ± 1.35* (95% CI: -3.11,-1.97), n=24 **Group 2:** -3.00 ± 1.46* (95% CI: -3.75,-2.25), n=17 **p value:** NR	**Funding:** NR **Limitations:** • Randomisation method, allocation concealment and masking of outcome assessment were not reported. • Complications were listed but not by group **Additional outcomes:** At 6 months, PVR, voiding, end-filling and end-void pressures **Notes:** * SD estimated using methods detailed in the Cochrane handbook for change from baseline with confidence intervals

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Dropouts: 5 (3 withdrawn and 2 lost to follow up) **<u>Group 2 - TURP</u>** **N:** 22 (baseline variables for only 17 patients who completed the study) **Age, mean (± SD):** 67 ± 8 **IPSS, mean (± SD):** 25.8 ± 4.2 **IPSS-QoL, mean (± SD):** 4.4 ± 0.9 **Qmax, mean (± SD), mL/s:** 5.2 ± 3.4 **PVR, mean (± SD), mL:** 954 ± 531 **Dropouts:** 5 lost to follow up				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Kadow et al., 1988[130] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** men with prostatism and proven BOO **Setting:** single-centre, UK **Inclusion criteria:** • Men with prostatism **Exclusion criteria:** • Haematuria • Prostate cancer • Normal peak flow rate and pattern after urodynamics **<u>All patients</u>** **N:** 38 **Drop outs:** 0 **<u>Group 1 – Conservative</u>** **N:** 17 **Age, mean (± SD):** 64.5 ± NR **Qmax, mean (± SD), mL/s:** 9.8 ± 2.1 **PVR, mean (± SD), mL:** 115 ± 305 **Day-time frequency, mean ± SD:** 8.25 ± 11.34 **Nocturia, voids ± SD:** 1.7 ± 4.6 **Dropouts:** 0 **<u>Group 2 - TURP</u>** **N:** 21 **Age, mean (± SD):** 66.5 ± NR **Qmax, mean (± SD), mL/s:** 8.5 ± 9.53 **PVR, mean (± SD), mL:** 86.2 ± 369 **Day-time frequency, mean ± SD:** 7.76 ± 16.59 **Nocturia, voids ± SD:** 2.6 ± 5.6 **Dropouts:** 0	**Group 2 – Conservative treatment** Instruction on bladder training for 1 month consisting of weekly visits of encouragement to increase interval between day-time voids and reduce fluid intake < 1 litre/day. Advice on timing was given to those with nocturia. Frequency/volume charts were analysed at each visit. Those with bladder instability after a cystometrogram at the end of training were given Pro-Banthine for urgency symptoms (10 patients). All patients were encouraged to continue bladder training throughout 6 month period **Group 1 – TURP** **Procedure:** Standard electroresection with histological conformation of BPH **Examination methods:** Prior to start men completed a frequency/volume chart for 7 days then voiding water cystometry. Reassessment after 6 months	**Q max ± SD at 6 months**	**Group 1:** 11.2 ± 3.42, n=17 **Group 2:** 19.0 ± 4.08, n=21 **p value:** NR	**Funding:** NR **Limitations:** **Additional outcomes:** Voiding patterns, day time frequency, nocturia, Max voided volume, average voided volume, maximum intervals between voids, P det max, PVR after treatment. **Notes:** Marked cards in identical envelopes were used for randomisation

Evidence Table 47: What is the effectiveness of alpha-blockers in treating men after acute urinary retention?

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Lucas et al., 2005[176] **Study design:** Randomised controlled study **Setting:** 8 hospitals and one in Ireland. **Evidence level:** 1+ **Duration of follow-up:** 3-8 days depending on normal practice of hospital.	**Patient group:** Men with acute urinary retention (AUR) secondary to benign prostatic hyperplasia recruited from March 1997 to December 2000 from an Accident and Emergency department. . **Inclusion criteria:** Men with acute urinary retention, who had been catheterised in the previous 72 hours. **Exclusion criteria:** Men with initial catheterisation volumes of >1500mL or <500mL ; evidence of renal or hepatic dysfunction; previous surgery on the urinary tract; other diseases of the bladder; any malignancy; retention-enhancing medications; allergies; and sever cardiac disease. **All patients** **N:** 149 **Mean age:** 69.4 (range: 51-91) years **Drop outs:** 8 not evaluable and not included in ITT analysis. **Group 1** **N:** 71 Mean (±SD) Age: NR Dropouts: NR **Group 2** **N:** 70 Mean (±SD) Age: NR Dropouts: NR	**Group 1: Alpha-blocker** Tamsulosin hydrochloride 0.4mg in a modified-release capsule once daily. Medication given after breakfast or lunch on the first dose, then after each day's breakfast. Duration of treatment was decided by each site to be either three or 8 doses, according to their normal practice. **Group 2: placebo**	**Successful trial without catheter** (defined as a flow rate of >5mL/s, >100mL voided volume, and a residual volume of≤200mL)	**Group1:** 24/71 (34%) **Group 2:** 17/70 (24%) **p value:** 0.193	**Funding:** Sponsored by a grant from Yamanouchi Pharma Ltd. **Limitations:** None **Notes:** Definition of success in treatment of AUR has yet to be universally agreed. The initial definition was not significant but the authors conducted secondary analysis using revised criteria of success. This was completed before breaking randomisation code. Some patients were catheterised for 3 day and others for 8; to allow for variations in practice across the sites. Differences in outcome between the two were not statistically significant.
			Secondary analysis: (success defined as any of two free-flow criteria described above)	**Group1:** 41/71 (58%) **Group 2:** 28/70 (40%) **p value:** 0.02	
			Secondary analysis: Success defined as flow rate >5mL/s, voided volume>100mL	**Group1:** 37/71 (52%) **Group 2:** 24/70 (34%) **p value:** 0.019	
			Secondary analysis: (defined as a flow rate of >5mL/s, >100mL voided volume, and a residual volume of≤250mL)	**Group1:** 43/71 (61%) **Group 2:** 29/70 (41%) **p value:** 0.013	
			Patients not re-catheterised	**Group1:** 34/71 (48%) **Group 2:** 18/70 (26%) **p value:** 0.011 OR: 2.47, 95% CI: 1.23-4.97	
			Patients re-catheterised	**Group1:** 37/71 (52%) **Group 2:** 52/70 (74%)	
			Adverse events	**Dizziness** Group 1: 7/71 (10%) Group 2: 2/70 (3%) **Somnolence** Group 1: 4/71 (6%) Group 2: 2/70 (3%) **Mortality** (carcinomatosis; not due to intervention) Group 1: 1/71 (1%) Group 2: 0/70 (0%)	
			Patients withdrew due to adverse events	Group 1: 7 (9%) Group 2: 1 (1%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
McNeill et al., 1999[193] **Study design:** Randomised controlled trial **Setting:** Scotland (4 centres) **Evidence level:** 1+ **Duration of follow-up:** Treatment for 48 hours. Follow-up of successful patients for mean 7.2 months	**Patient group:** patients with a first episode of acute urinary retention related to benign prostatic obstruction were recruited between September 1996 and March 1998 from 4 centres in Scotland. **Inclusion criteria:** 55 years or over; residual volume of 0.5-1.5L on catheterisation. **Exclusion criteria:** patients unwilling or unable to give informed consent; significant renal and/or hepatic disease; depressive illness on medication; extra-pyramidal disorders; neurological disease; confirmed or suspected urethral stricture; dipstick detected UTI, acute or chronic prostatitis. History of unstable angina pectoris, myocardial infarction, transient ischaemic attacks, cerebrovascular accident of congestive cardiac failure during the previous 6 months, current or previous orthostatic hypotension. Patient taking monoamine oxidase inhibitors, cholinergic or anticholinergic drugs, calcium-channel blockers, or alpha blocking drugs. Other antihypertensive drugs were not altered whilst the patient was receiving the trail medication. Phytotherapy or finasteride use did not exclude patients from study but	**Group 1: alpha-blocker** Sustained-release alfuzosin, an alpha1-selective blocker, (5mg twice daily, with no dose titration) for 48 hours. Catheter removed after 24 hour of treatment and final dose was given on the afternoon after catheter removal. **Group 2: placebo** Identical procedure as intervention but with placebo (twice daily for 48 hours).	**Number (%) of patients successful:** (defined as able to void successfully after removal of catheter and not re-catheterised within 24h)	**Group1**: 22/40 (55%) **Group 2**: 12/41 (29%), P=0.034 **Odds Ratio (OR)**: 2.95 (95% CI 1.08-8.21)	**Funding:** Financial support for the study was received from Lorex Synthelabo UK & Ireland; authors received financial support from Lorex Synthelabo to attend and present their work at scientific meetings. **Limitations:** The mean age was 5 years lower in the intervention group (significant difference). Following power calculation the authors planned to recruit 100 per arm to detect a 20% difference in outcome with 95% power. Unable to reach this number before the trial medication expired. The difference in outcome between the groups was >20% and power of the study is reflected in statistical significance of the results. **Additional outcomes:** Comparison of variables
			Number (%) of patient successful using per-protocol analysis (excluding patient that withdrew and ailed to complete medication)	**Group1**: 22/39 (56%) **Group 2**: 12/41 (29%), P=0.026 **Odds Ratio (OR)**: 3.13 (95% CI 1.13-8.76)	
			Mean (SD) age for all patients:	**Successful: 68.4 (7.8)** **Unsuccessful: 72.9 (8.1)** **P=0.02**	
			Mean (SD) age by success in each group:	**Group 1:** Successful: 69.1 (8.7) Unsuccessful: 69.6 (7.3), p=0.81 **Group 2:** Successful: 67.2 (6.1) Unsuccessful: 75.0 (8.1), p=0.005	
			Logistic regression analysis of treatment versus outcome adjusted for age	P=0.052 **OR**: 2.55, 95% CI 0.99-6.58	
			Logistic regression using per-protocol analysis:	P=0.039 **OR**: 2.72, 95% CI 1.05-7.08	
			All reported adverse events	**Faint:** Group 1: 1/40 Group 2: 0/41 **Dizziness:** Group 1: 1/40 Group 2: 0/41	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	their use was recorded. Known hypersensitivity to afluzosin or alpha blockers. Patients requiring suprapubic catheterisation where urethral catheterisation was unsuccessful; patients who had a suprapubic catheter as a primary procedure were not excluded. Postoperative retention after major abdominal/pelvic surgery. Large residual volume, clot retention secondary to haematuria of any cause. **<u>All patients</u>** **N:** 81 **<u>Group 1</u>** **N:** 40 Mean (±SD) Age: 67.7 (13.6) Dropouts: 1 (withdrew following a faint after the first dose of the trial medication) **<u>Group 2</u>** **N:** 41 Mean (±SD) Age: 72.7 (8.33) Dropouts: 0			**Headache**: Group 2: 1/40 Group 2: 0/41 **Atrial fibrillation*** Group 1: 1/40 Group 2: 0/41	between successful and unsuccessful patients. Non significant results for mean residual volume on catheterisation, mean duration of catheterisation and prostate size. Additional follow-up of 11/34 (32%) successful patients experiencing a further episode of AUR and/or requiring a prostatectomy (mean follow-up of 7.2 months). **Notes:** Atrial fibrillation 8 hours after last dose, which was later resolved. A subsequent 24-h ECG revealed previously undiagnosed asymptomatic paroxysmal atrial trachycardia, which was treated with sotalol.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
McNeill et al., 2004[194] **Study design:** Randomised controlled trial. **Setting:** 71 centres across Europe and South Africa. **Evidence level:** 1+ **Duration of follow-up:** Treatment for 3 days.	**Patient group:** patients presenting with a first episode of spontaneous AUR related to BPH between January 2000 and March 2002. **Inclusion criteria**: Minimum age of 51 yrs; urine retention volume 500-1500ml at catheterisation **Exclusion criteria:** Patients with mental disorders, in a trial within last 3 months, patients with neurogenic bladder dysfunction, isolated bladder neck disease, prostatitis, carcinoma of prostate, history of prostatic and urethral surgery, urethral stricture, bladder stones, clot retention secondary to hematuria; residual volume <500ml or >1500ml, AUR not related to BPH; Parkinson's disease, insulin dependent diabetes, multiple sclerosis, stroke or myocardial infarction within last 6 months, hepatic abnormalities, unstable or severe heart failure, history of postural hypotension or syncope, hypersensitivity to a-blockers, evolutive neoplastic disease; patients who received sympathomimetics within the previous week, received 5a-reductase inhibitors within previous 3 months or a-blocker in previous month, received tricyclic antidepressants, anticholinergics, sympathomimetics or first generation antihistamines within previous months, patients receiving disopyramide. **<u>All patients:</u> N:** 363 **Drop outs:** 3 (results missing) **<u>Group 1:</u> N:** 238 Mean (±SD) Age: 69.3 (8.5) Dropouts: 4 (postural hypotension=2,	**All patients:** urethral bladder catheterisation was performed. Catheter removed after minimum of two doses of study drug and each patient received one additional tablet the day after catheter removal. **Group 1: Alpha-blocker** 10mg alfuzosin once daily for three days **Group 2: Placebo** Once daily for three days.	**Success** (defined as patient returned to satisfactory voiding within the first 24 hours following removal of the urethral catheter without re-catheterisation)	**Group1:** 146/236 (61.9%) **Group 2:** 58/121 (47.9%) **p value:** 0.012	**Funding:** NR. **Limitations:** Breakdown of adverse events not listed. **Additional outcomes:** Logistic regression analysis of successful trial without catheter. Age 65 years plus and drained volume 1000ml or greater adversely influenced the successful voiding rate. Backward multiple logistic regression. **Notes:** Randomisation in a 2:1 ratio for intervention: placebo. Extension study carried out following patients that had a successful trial without catheter.
			Number of patients experiencing at least one adverse event	**Group1:** 20/238 (8.4%) **Group 2:** 16/122 (13.1%)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	catheter related infection=1 and treatment unrelated haemorrhoids=1) **Group 2: N:** 122 Mean (±SD) Age: 69.4 (8.0) Dropouts: 1 (catheter related infection)				

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Shah et al., 2002[272] **Study design:** Randomised controlled trial **Setting:** St Lukes Hospital and Bradford Royal infirmary, UK **Evidence level:** 1+ **Duration of follow-up:** 2 weeks for primary study and follow up of successful patients at 2 years.	**Patient group:** patients presenting with acute urinary retention at the hospital between March 1998 and December 1999. **Exclusion criteria:** patients with cardiac disease contra-indicating the use of alpha blockers, receiving medical therapy for bladder outflow obstruction, patients with bladder calculi, prostate cancer, renal impairment, urethral stricture, urinary infection, neurogenic bladder dysfunction, bladder tumour and clot retention. **<u>All patients</u>** **N:** 81 Mean age: 68.6 (46-88) years **Drop outs:** 19 (urethral stricture=1, patient request for removal=9, adverse events=1, other reasons including suprapubic catheter, aortic aneurysm and other severe co-morbidity=8) **<u>Group 1</u>** **N:** 34 Mean (±SD) Age: 69.5 (56-88) Dropouts: 0 **<u>Group 2</u>** **N:** 28 Mean (±SD) Age: 67.7 (46-84) Dropouts: 0	**Group 1: Alpha-Blocker** Alfuzosin SR 5mg twice a day. Catheter removed after a minimum of three doses or 36 hours of admission. **Group 2: Placebo** Catheter removed after a minimum of three doses or 36 hours of admission. **All patients:** if trial without catheter was unsuccessful a second trial was given 2 weeks later. During this period patients continued their trial medication. If unsuccessful again patients were offered alternative treatment options.	**Successful voiding** (defined as being able to void with a residual volume of < 200ml)	**Group1:** 17/34 (50%) **Group 2:** 16/28 (57%) **OR: 0.86 (95% CI: 0.38, 1.98; p=0.72)**	**Funding:** Lorex Synthelabo Pharma **Limitations:** Method of randomisation and allocation concealment not reported. Baseline characteristics not addressed except for age. **Additional outcomes:** Additional outcomes for patients that had an unsuccessful trial without catheter and were given alfuzosin. **Notes:** The mean age and range at baseline was lower in the placebo group.
			Unsuccessful voiding and re-catheterised	**Group 1:** 17/34 (50%) **Group 2:** 12/28 (43%)	
			TURP following successful trial without catheter (open labelled study where all patients on alfuzosin)	**Year 1**: 13/30 (43%) **Year 2**: 6/15 (40%)	

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Evidence Table 48 Phytotherapy vs. placebo

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Bent et al., 2006[29] **Study design:** Randomised controlled trial **Setting:** Northern California, US **Evidence level:** 1+ **Duration of follow-up:** 1 year	**Patient group:** Men who had moderate to severe symptoms of benign prostatic hyperplasia. Recruited from San Francisco Veterans Affairs Medical Center and the surrounding area by direct mailings, letters to primary care providers, posters and newspapers and local radio adverts between July 2001 and May 2004. **Inclusion criteria**: Over 49 years, AUA of 8 or more, peak urinary flow rate <15ml/s. Eligible if had stopped taking alpha-blocker at least one month before randomisation or discontinued taking saw palmetto or a 5 alpha-reductase inhibitor 6 months before randomisation. **Exclusion criteria:** high risk for urinary retention; history of prostate cancer; surgery for BPH; urethral stricture or neurogenic bladder; had a creatinine level >2.0mg per decilitre; PSA >4ng; using medications known to affect urination; severe concomitant disease. **All patients** **N:** 225 **Group 1** **N:** 112 Mean (±SD) Age: 62.9 (8.0) Dropouts: 5 Discontinued medication: 5 (outcomes assessments completed)	**All patients:** One month placebo run in period – excluded if rate of adherence was <75%. **Group 1: Saw palmetto extract** (160mg twice a day with meals) Carbon dioxide extract in a soft gelatine capsule – manufactured in one batch for product consistency. **Group 2: Placebo** Similar appearing placebo in soft brown gelatine capsules. Twice a day with meals.	**Mean (SE) change in AUA symptom index score**	Group1 (n=112): -0.68 (0.35) [95% CI: -0.37 to 0.01] Group 2 (n=113): -0.72 (0.35) [95% CI: -1.40 to -0.04] **Difference=0.04 [-0.93 to1.01]**	**Funding:** Grant from the national institute of diabetes and digestive and kidney diseases and by a grant from the National Centre for Complementary and Alternative medicine. **Limitations:** BPH impact score significantly different at baseline. **Additional outcomes:** Prostate transitional zone volume, BPH impact index score reported. Subgroup analyses of AUASI outcome when stratified by varying baseline levels. **Notes:** Most commonly reported nonserious adverse events also reported – no significance difference between the groups.
			Mean (SE) difference maximum urinary flow rate, ml/min	Group1: 0.42 (0.34) Group 2: -0.01 (0.34) **Difference=-1.22 [-3.90 to 1.47]**	
			Mean (SE) Prostate volume (ml)	Group1: 3.76 (0.98) Group 2: 4.98 (0.96) **Difference=0.43 [-0.52 to 1.38]**	
			Mean (SE) residual volume, ml	Group1: 14.10 (7.24) Group 2: 18.62 (7.14) **Difference=-4.51 [-24.44 to 15.42]**	
			SF-36 score (scores range from 0-100; higher scores indicate better quality of life)	Mental subscale: Group1: -0.72 (0.72) Group 2: 0.47 (0.71) **Difference=-1.18 [-3.16 to 0.79]** Physical subscale: Group1: 0.10 (0.67) Group 2: -0.51 (0.66) **Difference=0.61 [-1.24 to 2.45]**	
			Sexual function (O'Leary scale) range from 0-4; with higher scores indicating better function	Group1: -0.06 (0.10) Group 2: 0.07 (0.10) **Difference=-0.13 [-0.40 to 0.14]**	
			Serious adverse events	**cardiovascular** Group1: 2 Group 2: 7 **Elective orthopaedic surgery** Group1: 3 Group 2: 3	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 2 **N:** 113 Mean (±SD) Age: 63.0 (7.4) Dropouts: 4 Discontinued medication: 5 (outcomes assessment completed)			**Gastrointestinal bleeding** Group1: 2 Group 2: 1 **Bladder cancer** Group1: 0 Group 2: 1 **Colon cancer:** Group1: 0 Group 2: 1 **Elective hernia repair** Group1: 0 Group 2: 1 **Hematoma** Group1: 0 Group 2: 1 **Melanoma** Group1: 1 Group 2: 0 **Prostate cancer** Group1: 0 Group 2: 1 **Shortness of breath** Group1: 0 Group 2: 1 **Rhabdomyolysis** Group1: 0 Group 2: 1 **Total** Group 1: 8/112 (n=6) Group 2: 18/113 (n=11)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Safarinejad et al., 2005[265] **Study design:** Randomised controlled trial **Setting:** Iran **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** men with LUTS due to BPH, 1-3 years in duration presenting to the outpatient urology clinic. **Inclusion criteria:** no cancer laboratory findings were normal; and patient had no lower urinary tract problem other than BPH. **Exclusion criteria:** loss to follow-up, surgical intervention for BPH, discontinuation of study medication; alpha blocker, 5-alpha reductase inhibitor or other drug therapy during trial and follow-up, any combination of Urtica dioica with other phototherapeutic agent and insufficient follow-up. **All patients: N:** 620 **Group 1** **N:** 305 Completed by: 287 Mean (range) Age: 64 (57-71) Dropouts: 36; follow-up=25, surgical intervention =5, medication discontinued=2, other pharmacological treatment=4 **Group 2** **N:** 315 Completed by: 271 Mean (range) Age: 62 (53-73) Dropouts: follow-up=36, surgical intervention =14, medication discontinued=10, other pharmacological treatment=9	**Group 1: Urtica dioica** 120mg three times daily Herbal blend contained a standard preparation of 100mg of urtica dioica root extract in 1ml. Ingested three times daily with meals. **Group 2: placebo** three times daily placebo.	**Mean (SD) IPSS**	**Baseline** Group1: 19.8 (4.9) Group 2: 19.2 (4.6) **6 months** Group1: 11.8 (4) Group 2: 17.7 (3.1)	**Funding:** NR **Limitations:** Number completed trial was used for analysis. Reasons for drop-outs gives different total number of dropouts but this may have included the extension study. **Additional outcomes:** Serum PSA and serum testosterone also reported. **Notes:** After the 6 month randomised trial placebo patients were switched to the active treatment until 18 months.
			Mean (SD) Qmax (mL/s)	**Baseline** Group1: 10.7 (2.4) Group 2: 10.8 (2.8) **6 months** Group1: 18.9 (4.7) Group 2: 14.2 (3.7)	
			Mean (SD) PVR, mL	**Baseline** Group1: 73 (32.6) Group 2: 74 (29.6) **6 months** Group1: 36 (25.5) Group 2: 71 (24.4)	
			Mean (SD) Prostate volume, cc	**Baseline** Group1: 40.1 (6.8) Group 2: 40.8 (6.2) **6 months** Group1: 36.3 (4.2) Group 2: 40.6 (5.1)	
			Patients reporting improved LUTS	Group 1: 232/287 (86%) Group 2: 43/271 (16%) P<0.001	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Shi et al., 2008[274] **Study design:** Randomised controlled trial **Setting:** China **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** men between 49-75 years old with newly diagnosed LTS associated with BPH based on urological symptoms, including nocturia, incomplete emptying, urinary frequency, intermittence, weak urine stream, straining and urgency. **Inclusion criteria**: digital rectal examination showing an enlarged prostate but no signs of prostate cancer, serum creatinine >160umol/l, bacterial count less than 1000,000/ml, serum PSA 4ng/ml or less, IPSS greater than 12, uroflowmentry with MFR no more than 15ml per second and voiding volume greater than 150ml. Urinalysis by dipstick and microscopic examination of the spun urine specimen were performed to rule out urinary tract infection or hematuria. All patients had refused conventional therapy or elected watchful waiting. **Exclusion criteria:** history of prostate cancer and the use of any drugs, herbs or other non-prescription preparations for LUTS associated with BPH within 4 weeks of screening, including finasteride, alpha or beta blockers, diuretics, calcium channel blockers and anticholinergic drugs. Abnormal lab parameters, including PSA>4, serum	**Group 1:** 2 Prostataplex soft gels daily **Group 2:** 2 placebo soft gels daily	**Mean (SD) IPSS**	**Baseline** Group1: 16.85 (6.48) Group 2: 14.46 (4.32) **12 weeks:** Group1: 14.83 (6.42) Group 2: 14.13 (4.25)	**Funding:** NR. **Limitations:** Significant baseline difference in IPSS scores (lower in placebo group) Baseline IPSS for control was reported differently in the text as 14.46 and 14.27. **Additional outcomes:** Compliance rates reported as > 95% for both groups at each time point. **Notes:** Prostataplex, contains mainly saw palmetto.
			Number of patients with an IPSS improvement (defined as decrease of 3 points or greater)	Group1: 18/46 (39.1%) Group 2: 1/46 (2.2%) **P<0.001**	
			Mean (SD) Qmax, ml/s	**Baseline** Group1: 12.40; 95%CI:11.90-12.89 Group 2: 12.89; 95% CI: 2.22-13.56 **12 weeks:** Group1: 14.07 (2.56) Group 2: 11.74 (1.23) **P<0.001**	
			Mean (SD) Relative urinary resistance	**Baseline** Group 1: 2.97; 95% CI: 2.60-3.35 Group 2: 2.88; 95%CI: 2.57-3.19 **12 weeks:** Group1: 2.35 (0.83) Group 2: 3.02 (1.18) **P=0.002**	
			Mean (95%CI) Blood urea nitrogen at 12 weeks mg/dl	**Group 1:** 3.872 (3.426-4.318) **Group 2:** 3.809 (3.414-4.203) P=0.832	
			Mean (95% CI) Prostate size, cm3	**Group 1:** 45.62 (43.85-47.39) **Group 2:** 45.90 (44.04-47.76) P=0.826	
			Mean (95% CI) PSA, ng/ml	**Group 1:** 1.845 (1.617-2.073) **Group 2:** 1.694 (1.505-1.882)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	creatinine >160umol/l, urine bacterial count>100,000/ml, BUN more than 8mg/dl, MFR >15ml/s and voiding volume <150ml, previous bladder or prostate surgery, micturition problems associated with identified bladder pathology, urethral stricture, recurrent urinary tract infections, known renal or hepatic or cardiac insufficiency, diabetes mellitus, recent myocardial infarction, known alcohol abuse, known sensitivity to the ingredients in the product, significant depression or other psychiatric disease, any other cancer in the last 5 years except skin cancer and being on anticoagulation therapy. **<u>All patients</u>** **N:** 94 Mean age: 49-75 **Drop outs:** 2 **<u>Group 1</u>** **N:** 46 Dropouts: 0 **<u>Group 2</u>** **N:** 48 Dropouts: 2 lost to follow-up		**Mean (95% CI)** **Creatinine, mg/dl**	**Group 1:** 1.107.80 (100.24-115.36) **Group 2:** 115.43 (109.13-121.73)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Willetts et al., 2003[322] **Study design:** Randomised controlled trial **Setting:** Australia **Evidence level:** 1+ **Duration of follow-up:** 12 weeks	**Patient group:** men with symptoms of benign prostatic hyperplasia screened between January 1999 and March 2000. **Inclusion criteria**: Men with at least three symptoms of prostatism, (increased frequency of urination, nocturia, hesitancy, dribbling and poor stream); Under 80 years, with a maximum urinary flow rate of 5-15mL/s for a voiding volume of 150mL and a normal PSA level (<4ng/mL) within previous 3 months. **Exclusion criteria:** insulin-dependent diabetes, severe cardiopulmonary disease or significant CNS disease. Men who had used androgens, 5alpha reductase inhibitors, alpha blocker or herbal preparations in the last 4 weeks. Men with a history of prostate cancer, adenomas, urethral bladder, uretric or renal abnormalities, urogenital surgery ,renal stones, strictures or scarring , acute urinary	**Group 1: Serenoa repens** 320mg (2X160mg of CO2 extract) **Group 2: Placebo** Paraffin oil (2 capsules a day)	**Mean IPSS**	**Group1:** 12 **Group 2:** 13 1.74 (-0.54 to 4.03; p=0.131	**Funding:** Blackmores Ltd. **Limitations:** At baseline the men in the placebo arm had significantly higher IPSS scores and more had symptoms of incontinence than in the intervention arm. Qmax reported for 62 men who attended initial and final visits and who voided >150mL but number in each group not provided. Therefore, further analysis can not be conducted. **Additional outcomes:** Multivariate regression analysis.
			Mean (95% CI) [SD] Quality of life score (IPSS question)	**Baseline:** Group1: 3.66 (3.35-3.97) Group 2: 4.0 (3.58-4.42) **12 weeks:** Group1: 3.17 (2.76-3.58) [1.38] Group 2: 3.31 (2.85-3.77) [1.57] **Treatment effect:** 0.18 (-0.16 to 0.53); p=0.292	
			Mean Qmax, mL/s	**Baseline (n=62):** Group 1: 11.1 (10.3-11.8) Group 2: 11.2 (10.5-11.9) **12 Weeks (n=62):** Group1: 12.6 (11.0-14.2) Group 2: 15.6 (13.2-18.1)	
			IIEF scores (reported for 74 sexually active men)	**Baseline** Group 1: 51.5 (43.9-59.1) Group 2: 49.4 (43.3-55.4) **12 weeks:** Group 1:55.11 (48.4-61.8) Group 2: 48.7 (41.9-55.4)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	retention or allergy to study treatment. **All patients N:** 100 **Group 1** **N:** 50 Mean (SEM) Age: 62.1 (1.2) Dropouts: 4 (discontinued due to acute bladder retention, abdominal pain, high PSA, arthralgia) **Group 2** **N:** 50 Mean (SEM) Age: 63.9 (1.3) Dropouts: 3 (atrial fibrillation, dysuria, urinary incontinence)		**Serious adverse events leading to withdrawal**	**Acute urinary retention** Group 1: 1 Group 2: 0 **Atrial fibrillation** Group 1: 0 Group 2: 1 **Abdominal pain** Group 1: 1 Group 2: 0	**Notes:** Mean IPSS scores estimated from a graph as exact figures not given.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Wilt et al., 1999[328] Reports on four studies. **Study design:** Systematic review – Cochrane review **Setting:** Germany (3 studies) and UK (one study) **Evidence level:** 1++ **Duration of follow-up:** 4-26 weeks	**Patient group:** Men with mild to moderate symptomatic benign prostatic hyperplasia. **Inclusion criteria:** Treatment duration of at least 30 days. **Exclusion criteria:** None reported **<u>All patients</u>** **N:** 519 Mean age: 65.4 (34-85) yrs Mean IPSS score=15.2 points (n=377) Mean peak urine flow=10.2mL/s (n=519) Mean prostate size=49.1 cc (n=262) Drop outs: 41 (7.9%) **<u>Group 1</u>** Dropouts: 7.8% **<u>Group 2</u>** Dropouts: 8.0%	**Group 1: Phytotherapy** Beta-sitosterols derived from South African star grass, Hypoxis rooperi or from species of Pinus and Picea. Three studies contained non-glucosidic B-sitosterol, but dosages ranged form 60mg/day to 195mg/day. Two studies utilised a preparation that contains at least 70% non-glucosidic B-sitosterol and one utilised a preparation with a non-glucosidic B-sitosterol concerntartion of 50%. One study utilised a preparation that contained 100% B-sitosteryl-B-D-glucoside. The other 3 trials had a quantitiy of the b-sitosterol derivative, B-sitosterol-b-D-glucoside was leess than 5% of the daily B-sitosterol. **Group 2: placebo**	**Mean difference Symptom score (IPSS)**	-4.91 (95% CI: -6.29 to -3.53); 2 studies (n=342)	**Funding:** Internal support from: Department of Veterans Affairs Health Services Research and Development Program, USA and Minneapolis/VISN-13 Center for chronic Diseases Outcomes Research, USA. **Limitations:** Allocation concealment and method of randomisation was unclear in 2 of the 4 studies. Different studies used varying doses and preparations of B-sitosterols. **Additional outcomes:** - Boyarsky quality of life score in one study. - Physician overall evaluation of efficacy. - Sensitivity analysis of peak and residual volume without study Kadow 1986. Increases significance for intervention. **Notes:** IPSS symptom scores from 0 to 35.
			Mean difference Nocturia; times per evening	-1.00 (95% CI: -1.75 to -0.25); one study (n=80)	
			Mean difference Peak urine flow, mL/s	3.91 (95% CI: 0.91 to 6.90); 4 studies (n=474)	
			Mean difference urine flow	2.60 (95% CI: 1.30 to 3.90)	
			Mean difference Residual volume, mL ; 4 studies	-28.62 (95% CI: -41.42 to -15.83); 4 studies (n=475)	
			Mean difference in reduction in prostate size	-6.19 (95% CI: -15.29 to 2.91); 2studies (n=216)	
			% of patients with adverse events	**Gastrointestinal:** Group 1: 1.6 Group 2: 0 **Impotence:** Group 1: 0.5 Group 2: 0	
			Mean difference of Boyarsky quality of life scale	-4.50 [-6.05, -2.95]; one study (n=200)	
			Patient overall evaluation of efficacy (rated very good or good)	8.25 [3.22, 21.13]; one study (n=80)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Wilt et al., 2002a[326] **Study design:** Cochrane systematic review 21 RCTS included but 17 included that were compared to placebo. **Setting:** Europe and USA **Evidence level:** **1++** **Duration of follow-up:** Mean study duration 13 weeks (4 -48 weeks range).	**Patient group:** Men with lower urinary tract symptoms consistent with benign prostatic hyperplasia. **Inclusion criteria:** Treatment duration of at least 30 days **<u>All patients</u>** **N:** 3139 (1408 in this comparison) Mean age: 65 years (40-88) **Drop outs:** 319 (10%) [0-18% range]	**Group 1: Serenoa repens (SR)** - alone or in combination) **Group 2: placebo** Also compares against other interventions.	**Mean difference symptom score (0-19)**	-1.41 [-2.52, -0.30]; one study (n=205) P=0.013	**Funding:** Internal sources of support: • Management decision and research center- department of veterans affairs, USA • Minneapolis/VISN-13 Center for Chronic Diseases Outcomes Research, USA. **Limitations:** Studies utilised different doses of serenoa repens but most frequently reported dose was 160mg twice per day. **Additional outcomes:** Also reported: • SR/urtica vs. finasteride. • SR vs. pygeum africanum • SR vs. gestonorone **Notes:** Results did not substantially change when restricted analysis to studies that had adequate allocation concealment or were double blinded. Meta-analysis used randoms effect model for all comparisons.
			Mean change in IPSS score (score from 0-35)	-2.20 [-4.70, 0.30]; one study (n=79) P=0.084	
			Patient reported self rating from improved symptoms (men rating very good to good)	RR=1.76 [1.21, 2.56]; 6 studies (n=659) P=0.0029	
			Physician assessed improvement of symptoms	RR=1.72 [1.11, 2.66]; 3 studies (n=524) P=0.015	
			Mean difference Nocturia (times/evening)	-0.76 [-1.21, -0.31]; 10 studies (n=634) P=0.00084	
			Weighted mean difference Qmax, mL/s	1.86 [0.60, 3.12]; 9 studies (n=723) P=0.0038	
			Mean urine flow, ml/s	2.23 [1.18, 3.27]; 4 studies (n=382) P=0.000028	
			Residual volume, mL	-22.95 [-42.33, -3.56]; 6 studies (n=450) P=0.020	
			Prostate size	-2.14 [-10.93, 6.65]; 2 studies (n=243) P=0.63	
			Study withdrawals	0.72 [0.39, 1.32]; 7 studies (n=595) P=0.29	
			IPSS total score, mean change (serenoa repens/sabal urtica)	-3.50 [-6.75, -0.25]; one study (n=40) P=0.035	
			Qmax (serenoa repens/sabal urtica)	1.60 [-1.67, 4.87]; one study (n=40) P=0.34	

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Evidence Table 49 Phytotherapy combinations vs. placebo

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Lopatkin et al., 2005[171] **Study design:** Randomised controlled trial **Setting:** Multi centre, **Evidence level:** 1+ **Duration of follow-up:** 24 weeks	**Patient group:** Male outpatients≥ 50 years suffering from LUTS caused by BPH. **Inclusion criteria**: maximum urinary flow rate<15ml/s; change in maximum urinary flow between screening and end of run-in period 3ml/s or less; urinary output>100ml at baseline; IPSS total score 14 or greater; IPSS quality of life 4 or greater. Written informed consent. **Exclusion criteria: Inability to** give informed consent or to complete self-ratings; previous or scheduled surgery involving pelvis or urinary tract; urethral stricture disease or a history of pelvic radiation therapy; PSA>10ng/ml; large residual urine >350ml; symptomatic urinary tract infection; chronic bacterial prostatitis; patients with diabetes mellitus, diabetic neuropathy or prostate carcinoma; serious general and specific risks; concomitant medication affecting the micturition pattern. **All patients: N:** 257 **Group 1** **N:** 129 Mean (±SD) Age: 68 (7) Dropouts: 4 (informed consent revoked=1; adverse events=3) **Group 2** **N:** 128 Mean (±SD) Age: 67 (7) Dropouts: 3 (lost to follow-up=1, non-compliance=1; informed consent revoked=1)	**Group 1: Phytotherapy combination of sabal/urtica** 2 X 1capsule daily of 160mg sabal fruit extract WS1473 and 120mg urtica root extract WS 1031 per capsule (PRO 160/120). **Group 2: Placebo** 2X1 capsule day (capsule identical in appearance to intervention). **All patients:** Placebo run in phase 2 weeks.	**Mean (SD) total changes IPSS**	**Baseline** Group1 (n=127): 18 (4) Group 2 (n=126): 18 (3) **Week 16** Group1 (n=127): -4 (4) Group 2 (n=126): -3 (5) **Week 24** Group1 (n=127): -6 (4) Group 2 (n=126): -5 (5) P=0.03	**Funding:** NR **Limitations:** Baseline assessments: Initial diagnosis of BPH was systematically longer in patients randomised to intervention. **Additional outcomes:** Per protocol analysis also completed to assess robustness of results. Sub-analysis of IPSS score by irritative and obstructive components and by individual question. Sub-analysis of moderate and severe baseline IPSS scores and number in mild, moderate and severe IPSS category after 24 weeks. **Notes:** This trial was followed by an open label extension period were all patients received the intervention. 2 patients from each group terminated trial early without any data for the primary outcome measure, and were excluded from the analysis.
			Mean (SD) changes in Qmax, ml/s	**Baseline** Group1: 10.4 (2.4) Group 2: 10.5 (2.6) **Week 24** Group1: +1.8 (4.6) Group 2: +1.9 (4.5) P=0.59	
			Adverse events	Group1: 23/129 (17.8%) Group 2: 24/128 (18.8%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Melo et al., 2002[199] **Study design:** Randomised controlled trial. **Setting:** NR **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** Men with urinary symptoms. **Inclusion criteria:** ≥50 years, urinary symptoms assessed by IPSS with minimal score of 12, quality of life index of at least 3 points, rectal examination consistent with BPH and Maximum urinary flow rate between 5 and 15mL/s. **Exclusion criteria:** NR **All patients** **N:** 49 **Drop outs:** NR **Group 1** **N:** 27 Mean (range) Age: 65.3 (52-86) Dropouts: NR **Group 2** **N:** 22 Mean (range) Age: 65 (50-79) Dropouts: NR	**Group 1: PHYTOTHERAPY COMBINATION** 25mg Pygeum africanum and 300mg stinging nettle (1 PO bid). **Group 2: PLACEBO** Placebo (bid)	**Mean (SD) IPSS score**	**Baseline** Group1: 19.3 (5.2) Group 2: 20.0 (5.9) **6 months** Group1: 14.6 (7.3) Group 2: 15.6 (7.9); P=0.658	**Funding:** NR. **Limitations:** No dropouts were reported in the study and method of randomisation was unclear. **Additional outcomes:** Comparison of ≥30% and 50% drop in IPSS, QoL and increase in Qmax. **Notes:** Baseline Qmax was better in the intervention group but Not sig.ly different.
			Mean (SD) quality of life index	**Baseline** Group1: 3.81 (0.83) Group 2: 3.95 (1.09) **6 months** Group1: 3.33 (1.27) Group 2: 3.73 (1.52)	
			Mean (SD) Qmax	**Baseline** Group1: 11.4 (3.1) Group 2: 10.2 (2.4); P=0.066 **6 months** Group1: 12.5 (6.1) Group 2: 11.4 (3.8); P=0.770	
			Adverse events	**Headache** Group 1: 1/27 (3.7%) Group 2: 1/22 (4.5%) **Chest pain** Group 1: 0/27 Group 2: 1/22 (4.5%) **Epigastric pain** Group 1: 4/27 (14.8%) Group 2: 0/22 **Drowsiness** Group 1: 1/27 (3.7%) Group 2: 1/22 (4.5%) **Vertigo** Group 1: 0/27 Group 2: 1/22 (4.5%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Preuss et al., 2001[242] **Study design:** Randomised controlled trial **Setting:** 3 sites, US **Evidence level:** 1+ **Duration of follow-up:** 90 days	**Patient group:** Men with diagnosis of BPH. **Inclusion criteria:** no evidence of cancer by digital rectal and/or PSA examinations; maximal urinary flow rates were to be between 5-15ml/s for a voided volume in excess of 100ml. Read, speaks and understand English and written informed consent obtained. **Exclusion criteria:** Age over 80 years, presence of any tumour, malformation, or infection of the genitourinary tract; sever concomitant medical condition, severe laboratory abnormalities at baseline; finasteride within the last 4 weeks; patients being treated with antibiotics for genitourinary tract infections. **<u>All patients:</u> N:** 144 **Drop outs:** 17 **<u>Group 1</u>** **N:** 75 Mean (±SD) Age: Dropouts:5 (withdrew consent=1, lost to follow-up=1) **<u>Group 2</u>** **N:** 69 Mean (±SD) Age: Dropouts:12 (adverse events=3, withdrew=5, lost to follow-up=3;	**Group 1: phytotherapy** 2 pills of combined natural products Cernitin 378mg, saw palmetto complex and phytosterol (saw palmetto fruit standardised to 40-50% free fatty acids and B-sitosterol standardised to 43%) 286g, and Vitamin E 100 IU. **Group 2: Control** 2 pills of placebo	**Mean AUA scores**	**Baseline** Group1 (n=70): 18.9 Group 2 (n=57): 17.7 **Day 45** Group1 (n=70): 14.6 Group 2 (n=57): 15.0 **Day 90** Group1 (n=70): 12.7 Group 2 (n=57): 14.5 ANOVA p=0.014	**Funding:** Rexall/Sundown, Inc, Boca Raton, FL through the National Research Council for Health, Washington DC and Meridian ID. **Limitations:** Baseline levels not reported. **Additional outcomes:** AUA scores for each of 7 questions reported. Comparison of PSA changes. **Notes:** SD calculated by NCC.
			Mean (SEM) [SD] change in AUA symptom index	Group1 (n=70): -6.171 (0.766) [6.41] Group 2 (n=57): -3.241 (0.774) [5.84] P=0.009	
			Mean (SEM) [SD] maximum flow rate, ml/min	**Baseline** Group1 (n=70): 11.2 (0.8) Group 2 (n=57): 12.1 (0.9) **Day 90** Group1 (n=70): 11.8 (0.7) [5.86] Group 2 (n=57): 13.1 (1.0) [7.55]	
			Mean (SEM) Average flow rate, ml/min	**Baseline** Group1 (n=70): 6.0 (0.4) Group 2 (n=57): 6.1 (0.5) **Day 90** Group1 (n=70): 6.0 (0.5) Group 2 (n=57): 6.8 (0.5)	
			Mean (SEM) Bladder volume, ml	**Baseline** Group1 (n=70): 58.9 (11.4) Group 2 (n=57): 59.6 (12.8) **Day 90** Group1 (n=70): 57.5 (12.8) Group 2 (n=57): 40.7 (10.4)	
			Adverse events	**Flatulence:** Group 1: 3 Group 2: 0 **Lower abdominal rash:** Group 1: 0	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	protocol violation=1)			Group 2: 1 **Dizziness** Group 1: 0 Group 2: 1 **Headache** Group 1: 1 Group 2: 1 **Nausea**/GI distress Group 1: 0 Group 2: 2 **Urinary tract infection:** Group 1: 1 Group 2: 0 **Ear infection:** Group 1: 0 Group 2: 1 **Lumbar spine surgery** Group 1: 0 Group 2: 1 **Herpes Zoster** Group 1: 1 Group 2: 0 **Elevated BP:** Group 1: 0 Group 2: 1 **Chest pain:** Group 1: 0 Group 2: 1 **Right arm laceration** Group 1: 1 Group 2: 0	

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1 Evidence Table 50 Phytotherapy vs. Alpha-blockers

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Debruyne et al., 2002[68] **Study design:** RCT Patients masked to treatment **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men with BPH **Setting:** multicentre, 98 centres across 9 European countries. **Inclusion criteria:** • IPSS >10 • Qmax between 5-15 mL/sec with a urine volume of ≥ 150 mL and PVR <150mL • Prostate volume ≥25 mL • Serum PSA <4ng/mL • Men with serum PSA 4-10 ng/mL required to have free/total PSA ratio of ≥15% to be enrolled • 50 - 85 years • 90% compliance after a 4 week placebo run in. **Exclusion criteria:** • Prostate cancer • Known history of bladder disease (cancer, bladder neck surgery, neurogenic) • Urethral strictures • Pelvic radiotherapy • Lower urinary tract infection • Chronic bacterial prostatitis • Any disease affecting micturation • Patients with clinically significant cardiovascular disease, haematuria, type II diabetes, history of hepatic failure or abnormal liver function tests.	**Group 1:** Serenoa repens (saw palmetto), Permixon® 320 mg/day **Group 2** Tamsulosin 0.4 mg/day **Examination methods:** Each patient evaluated at baseline then at 6, 13, 26, 39 and 52 weeks for IPSS and uroflowmetry. At weeks 26 and 52 TRUS was performed and blood and serum PSA taken at week 52. **Patient completed the validated male sexual function (MSF-4) questionnaire of 4 questions (0-5 points each): • interest in sex • quality of erection • achieving orgasm • achieving ejaculation	**IPSS ± SD at 12 mths**	**Group 1:** 10.8 ± 5.5, n=269 **Group 2:** 11.0 ± 6.0, n=273 **p value:** 0.99	**Funding:** Grant from Pierre Fabre Médicament, Castres, France, manufacturer of Permixon®. Authors have served as consultants or speakers for, or have received research grants from Pierre Fabre Médicament. **Limitations:** • Randomisation method was not clear • Allocation concealment was not clear • Masking of outcome assessment was not clear. • Only the per protocol data was available at follow up. **Additional outcomes:** **Notes:** Masking of treatments to patients was achieved by providing tamsulosin in a green coloured size 0 capsule similar to Permixon®
			Qmax ± SD at 12 mths	**Group 1:** 12.7 ± 5.2, n=267 **Group 2:** 13.0 ± 4.9, n=265 **p value:** 0.79	
			MSF-4 ± SD at 12 mths	**Group 1:** 8.8 ± 5.4, n=267 **Group 2:** 8.2 ± 5.0, n=266 **p value:** 0.69	
			Serum PSA ± SD at 12 mths	**Group 1:** 2.8 ± 2.3, n=266 **Group 2:** 2.9 ± 2.5, n=268 **p value:** 0.50	
			Prostate Volume ± SD at 6 mths	**Group 1:** 47.0 ± 20.9, n=269 **Group 2:** 48.2 ± 22.7, n=270 **p value:** 0.27	
			Incidence of Adverse Events N Decreased Libido Ejaculation Disorders Asthenia Fatigue Dizziness Rhinitis Hypotension postural Headache Dry Mouth	**Group 1: (%)** **349** 1 (0.3) 2 (0.6) 4 (1.1) 6 (1.7) 10 (2.9) 30 (8.6) 4 (1.1) 28 (8.0) 3 (0.9)	**Group 2: (%)** **354** 4 (1.1) 15 (4.2) 5 (1.4) 5 (1.4) 6 (1.7) 43 (12.1) 3 (0.8) 37 (10.5) 2 (0.64)
			Reasons for withdrawal* Serious Adverse Events Non-serious adverse events Acute urinary retention Lack of efficacy Sexual dysfunction	**Group 1: n=54** **n=56** 3 10 4 15 1	**Group 2:** 8 13 3 8 2

Study details	Patients	Interventions	Outcome measures	Effect size		Comments
	• Patients on concomitant medication likely to interfere with study medication. • Hypersensitivity to study drugs • Participation in another trial within previous 3 mths **<u>All patients</u>** **N:** 704 randomised but only 685 included in ITT analysis **Mean age:** 65.2 yrs **Drop outs:** 110 (16.1%)* **<u>Group 1</u>** **N:** 340 **Mean (± SD) Age:** 65.6 ± 7.4 **BMI (± SD):** 26.7 ± 3.6 **IPSS (± SD):** 15.5 ± 4.8 **MSF-4 (± SD):** 8.3 ± 5.3** **Qmax (± SD), mL/s:** 10.9 ± 3.9 **Prostate volume (± SD), mL:** 48.0 ± 18.2 **Serum PSA (± SD), ng/mL:** 2.8 ± 2.0 **Dropouts:** 54* **<u>Group 2</u>** **N:** 345 **Mean (± SD) Age:** 64.9 ± 7.6 **BMI (± SD):** 26.7 ± 3.7 **IPSS (± SD):** 15.2 ± 5.2 **MSF-4 (± SD):** 7.7 ± 5.0** **Qmax (± SD), mL/s:** 11.3 ± 4.3 **Prostate volume (± SD), mL:** 47.7 ± 18.6 **Serum PSA (± SD), ng/mL:** 2.8 ± 2.2 **Dropouts:** 56*		Other events Patient decision Lost to follow up Other	2 14 2 3	1 15 2 4	Serious advent events defined as fatal, life threatening, disabling resulting in hospitalisation or associated with cancer

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Engelmann U et al., 2006[82] **Study design:** RCT **Setting:** 23 private urological practices in Germany. **Evidence level:** 1+ **Duration of follow-up:** 60 weeks	**Patient group:** Outpatients suffering from BPH that did not require surgery. **Inclusion criteria:** A maximum urinary flow rate ≤12ml/s at a urinary volume ≥150ml was required. Aged 50 years old and above. Initial IPSS score of ≥13 points and an IPSS QoL assessment score ≥3. **Exclusion criteria:** Patients whose peak urinary flow rate changed by more than 3ml/s during a 2-week placebo run-in phase were excluded. Patients with a residual urinary volume > 150ml, congested urinary tract passages, an indication for BPH surgery, urinary tract infection, prostate carcinoma, diabetes, neurogenic or bladder dysfunction as well as patients previously treated with 5α-reductase inhibitors. **<u>All patients</u>** **N:** 140 **Drop outs:** 9/140 **<u>Group 1</u>** **N:** 71 **Age ± SD, years:** 65 ± 8 **Time since diagnosis of BPH (years):** 3.1±4 **Dropouts:** 11 **<u>Group 2</u>** **N:** 69 **Age ± SD, years:** 65 ± 8 **Time since diagnosis of BPH (years):** 3.61±4.5 **Dropouts:** 8	**Group 1: PRO 160/120** 160mg Sabal fruit extract and 120mg Urtica root per capsule. **Group 2: Tamsulosin** Slow-release capsules containing 0.4mg active ingredient. For both drugs placebo capsules were available which were indistinguishable from their pharmacologically active counterparts in all aspects of their outer appearance. (After screening patients entered a single blind placebo run in phase of two weeks.) **Examination methods:** Visits scheduled after 8, 16, 24,	**Median IPSS total score**	**Baseline** **Group 1:** 20 **Group 2:** 20 **24 weeks** **Group 1:** 13 **Group 2:** 12 **60 weeks** **Group 1:** 10 **Group 2:** 9	**Funding:** NR **Limitations:** Median scores reported. Details of adverse events not reported. **Additional outcomes:** Subgroup analysis of patients with IPSS baseline score of ≤19 and IPSS baseline score ≥20 Erectile function score – median score change for both groups = 0. **Notes:** Randomization was performed in balanced blocks, by means of a validated EDP random number generator program.
			Median improvement from baseline in LUTS-associated QoL (single item, range 0 [very good] -6 [very bad].	**Group 1:** 2 **Group 2:** 1	
			Adverse events (details not reported)	**Group 1**:15 patients (21.1%) reported 18 events **Group 2**: 19 patients (27.5%) reported 23 events.	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	<u>Exclusions after randomization</u> **Revoked informed consent:** 2 **Adverse event during placebo run-in:** 2 **Not meeting selection criteria:** 5	36, 48 and 60weekk of double blind treatment.			

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hizli & Uygar, 2007[119] **Study design:** RCT open label **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** men with symptomatic BPH **Setting:** Department of Urology, Oncology, Education and research, Ankara Hospital, Turkey. **Inclusion criteria:** • IPSS ≥ 10 • Qmax 5-15 mL/s • PVR ≤ 150 mL • Prostate volume ≥ 25 mL • PSA ≤ 4 ng/mL **Exclusion criteria:** • History of bladder disease affecting micturation • Urethral stenosis • Pelvic radiotherapy • Prostate cancer • Infections of urinary tract or chronic bacterial prostatitis • Clinically significant cardiovascular disease • Haematuria • Type II diabetes • Severe hepatic failure or abnormal liver function tests • Known hypersensitivity to study drugs • Participation in another trial within previous 3 months **<u>All patients</u>** **N:** 60 **Age (range):** 43-73 years **Drop outs:**	**Group 1:** Serenoa repens (Prostagood®) 320 mg/day **Group 2** Tamsulosin 0.4 mg/day **Group 3** Serenoa repens (Prostagood®) 320 mg/day + Tamsulosin 0.4 mg/day **Examination methods:** IPSS, Qol, Qmax by uroflowmetry recorded at baseline and months 2, 4, 6	**IPSS ± SD reduction from baseline at 6 mths**	**Group 1:** -6.1 ± 2.7 **Group 2:** -4.6 ± 3.3 **Group 3:** -4.9 ± 2.3 **p value:** 0.16 (Kruskal-Wallis)	**Funding:** NR **Limitations:** • Randomisation method not reported • Allocation concealment not reported • Masking of outcome assessment not reported • Open label • Small study **Additional outcomes:** No patients withdrew from the study due to adverse events. **Notes:** Notes
			IPSS QoL ± SD reduction from baseline at 6 mths	**Group 1:** -2.6 ± 0.9 **Group 2:** -2.1 ± 0.8 **Group 3:** -2.2 ± 1.0 **p value:** 0.14 (Kruskal-Wallis)	
			Qmax ± SD increase from baseline at 6 mths	**Group 1:** 3.2 ± 2.2 **Group 2:** 3.7 ± 2.6 **Group 3:** 4.2 ± 2.5 **p value:** 0.38 (Kruskal-Wallis)	
			Prostate volume ± SD decrease from baseline at 6 mths	**Group 1:** -0.7 ± 2.2 **Group 2:** -1.0 ± 2.2 **Group 3:** -0.8 ± 2.0 **p value:** 0.61 (Kruskal-Wallis)	
			PSA ± SD decrease from baseline at 6 mths	**Group 1:** -2.0 ± 0.3 **Group 2:** -0.1 ± 0.2 **Group 3:** -3.5 ± 0.2 **p value:** 0.07 (Kruskal-Wallis)	
			Incidence of Adverse Events	**Group 1:** (%) **Group 2:** (%) **Group 3:** (%)	
			N	**20** **20** **20**	
			Decreased Libido	- 4 (20) 1 (5)	
			Ejaculation Disorders	- 7 (35) 3 (15)	
			Asthenia	- - 1 (5)	
			Fatigue	- 2 (10) -	
			Dizziness	- 2 (10) -	
			Rhinitis	- 2 (10) -	
			Hypotension postural	- 3 (15) -	
			Dry Mouth	- 5 (25) 1 (5)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1 **N:** 20 **Age ± SD, years:** 56.8 ± 7.8 **IPSS ± SD:** 18.0 ± 4.9 **IPSS QoL ± SD:** 4.2 ± 1.1 **Qmax ± SD, mL/s:** 9.4 ± 2.9 **Prostate volume ± SD, mL:** 35.2 ± 10.3 **PVR ± SD, mL:** 67.4 ± 27.7 **PSA ± SD, ng/mL:** 1.9 ± 0.9 **BMI ± SD, kg/m²:** 26.7 ± 2.5 **Dropouts:** 0 **Group 2** **N:** 20 **Age ± SD, years:** 58.9 ± 5.7 **IPSS ± SD:** 16.2 ± 4.7 **IPSS QoL ± SD:** 3.5 ± 1.1 **Qmax ± SD, mL/s:** 10.5 ± 2.8 **Prostate volume ± SD, mL:** 38.6 ± 11.6 **PVR ± SD, mL:** 65.5 ± 33.3 **PSA ± SD, ng/mL:** 2.1 ± 0.9 **BMI ± SD, kg/m²:** 28.0 ± 3.4 **Dropouts:** 0 **Group 3** **N:** 20 **Age ± SD, years:** 60.2 ± 6.3 **IPSS ± SD:** 15.6 ± 3.2 **IPSS QoL ± SD:** 3.5 ± 1.1 **Qmax ± SD, mL/s:** 9.9 ± 2.4 **Prostate volume ± SD, mL:** 31.2 ± 4.2 **PVR ± SD, mL:** 63.7 ± 23.7 **PSA ± SD, ng/mL:** 1.7 ± 0.7 **BMI ± SD, kg/m²:** 27.8 ± 2.3 **Dropouts:** 0				

Evidence Table 51 Phytotherapy vs. 5-Alpha Reductase inhibitors

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Carraro et al., 1996[43] **Study design:** RCT Placebo controlled **Evidence level:** 1+ **Duration of follow-up:** 6 months	**Patient group:** men with BPH and symptoms of BOO **Setting:** multicentre, 87 centres across 9 European countries. **Inclusion criteria:** • BPH diagnosed by DRE • IPSS >6 • Qmax between 4-15 mL/sec with a urine volume of ≥ 150 mL and PVR <200mL • Prostate volume >25 mL • Serum PSA <10 ng/mL for prostates ≤60ml • Serum PSA < 15 ng/mL for prostates > 60mL (measured before or 3 days after DRE & TRUS) • > 50 years • 2 week washout period after previous alpha-blockers or Pygeum • Good physical and mental condition **Exclusion criteria:** • Prostate cancer • Known history of bladder disease (cancer, bladder neck surgery, neurogenic) • Lower urinary tract infection • Any disease affecting micturation • Abnormal liver function (twice upper normal limit of serum aminotransferases and/or bilirubin, creatinine >160 μmol/L • Diuretics or drugs with antiandrogen	**Group 1:** Serenoa repens (saw palmetto), Permixon® 160 mg + placebo 2/day morning and evening for 26 weeks. **Group 2** Finasteride (Proscar®) 5mg + placebo 1/day in the morning then 2 x placebo in the evening **Examination methods:** Each patient was examined prior to baseline and at 6, 13 and 26 weeks by the same investigator. At each visit Qmax (at 200 mL voided volume), IPSS, IPSS QoL and sexual function score (0-20 points) were determined. At weeks 13 & 26 TRUS and PSA were performed.	**IPSS ± SD at 6 mths**	**Group 1:** 9.9 ± 5.4, n=467 **Group 2:** 9.5 ± 5.5, n=484 **p value:** 0.17 (CI 95%: -0.17, 0.96)	**Funding:** NR **Limitations:** • Masking of outcome assessment was not clear. • Allocation concealment by packaging of drugs was not clear. **Additional outcomes:** % patients with Qmax <10 mL/s or Qmax ≥ 10 mL/s at baseline and at 6 mths against % patients with IPSS <18 or IPSS ≥18 at baseline and at 6 mths. **Notes:** Computer generated randomisation sequence **Sexual function comprised 4 questions in the male sexual function questionnaire MSF-4 (0-5 points each) on interest in sex, quality of erection, achieving orgasm & ejaculation
			IPSS QoL score ± SD at 6 mths	**Group 1:** 2.25 ± 1.29, n=467 **Group 2:** 2.15 ± 1.26, n=484 **p value:** 0.14 (CI 95%: -0.04, 0.24)	
			Sexual Function Score ± SD at 6 mths	**Group 1:** 7.9 ± 5.4, n=467 **Group 2:** 9.3 ± 5.7, n=484 **p value:** <0.0001 (CI 95%: -1.52, 0.96)	
			Qmax ± SD at 6 mths	**Group 1:** 13.3 ± 6.7, n=467 **Group 2:** 14.0 ± 7.4, n=484 **p value:** 0.035 (CI 95%: -1.46, -0.054)	
			Prostate Volume ± SD at 6 mths	**Group 1:** 41.5 ± 20.5 n=467 **Group 2:** 36.7 ± 17.2 n=484 **p value:** <0.001 (CI 95%: 1.11, 1.18)	
			Serum PSA at 6 mths	**Group 1:** 3.22 ± 4.00, n=467 **Group 2:** 1.99 ± 1.98, n=484 **p value:** <0.001 (CI 95%: 1.33, 1.45)	
			Inter current clinical events	**Group 1: (%)** **Group 2: (%)** 17 (3.1) 12 (2.2) Hypertension 12 (2.2) 16 (3.0) Decreased Libido 10 (1.8) 15 (2.8) Abdominal pain 8 (1.5) 15 (2.8) Impotence 9 (1.6) 3 (0.6) Back pain 5 (0.9) 6 (1.1) Diarrhoea 5 (0.9) 6 (1.1) Influenza-type symptoms 7 (1.3) 3 (0.6) Urinary retention 7 (1.3) 3 (0.4) Headache 3 (0.5) 6 (1.1)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	or alpha receptor properties administered over previous 3 months for hypertension, cerebrovascular insufficiency. • Prior treatment with Permixon® or Finasteride **<u>All patients</u>** **N:** 1098 **Mean age:** 64.5 yrs **Drop outs:** 147 (13.4%) **<u>Group 1</u>** **N:** 553 **Mean (range) Age:** 64.3 (49-87) **BMI (range):** 26 (17-38) **IPSS (± SD):** 15.7 ± 5.8 **IPSS QoL (± SD):** 3.63 ± 1.28 **MSF-4 (± SD):** 8.4 ± 5.5** **Qmax (± SD), mL/s:** 10.6 ± 2.8 **PVR (± SD), mL:** 52 ± 44 **Prostate volume (± SD), mL:** 43.0 ± 19.6 **Serum PSA (± SD), ng/mL:** 3.26 ± 3.41 **Dropouts:** 86* **<u>Group 2</u>** **N:** 545 **Mean (range) Age:** 64.7 (49-88) **BMI (range):** 25.9 (18-36) **IPSS (± SD):** 15.7 ± 5.7 **IPSS QoL (± SD):** 3.66 ± 1.17 **MSF-4 (± SD):** 8.5 ± 5.5** **Qmax (± SD), mL/s:** 10.8 ± 3.1 **PVR (± SD), mL:** 52 ± 44 **Prostate volume (± SD), mL:** 44.0 ± 20.6 **Serum PSA (± SD), ng/mL:** 3.23 ± 3.34 **Dropouts:** 61*		Nausea Constipation Dysuria	2 (0.4) 6 (1.1) 2 (0.4) 6 (1.1)	
			Reasons for withdrawal*	**Group 1: n=86** **Group 2: n=61**	
			Side effects		
			Lack of efficacy	28 14	
			Patient decision	0 2	
			Lost to follow up	28 20	
			Mortality (non drug related)	5 7 1 (heart attack) 1 (fatal MI)	
			Other	24 17	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Sökeland, 2000[282] **Study design:** RCT Placebo controlled **Evidence level:** 1+ **Duration of follow-up:** 1 year	**Patient group:** men with BPH (Aiken stages I to II) **Setting:** multicentre, University of Münster, Germany. **Inclusion criteria:** • NR **Exclusion criteria:** • < 50 years • BPH III or above (Aiken) • PSA > 10 ng/mL • Prostate cancer • Use of other prostate medications • Infections • Severe concomitant disease requiring therapy **<u>All patients</u>** **N:** 516 **Age (range):** 50 - 88 **Drop outs:** 27 (5%) 489 available for efficacy analysis **<u>Group 1</u>** **N:** 261 **IPSS (± SD):** 11.3 ± 6.5 (n=258) **Qmax (± SD), mL/s:** 12.4 ± 4.5 (n=245) **Prostate volume (± SD), mL:** 42.7 ± 27.8 (n=215) **Dropouts:** 16 **<u>Group 2</u>** **N:** 255	**Group 1:** Combination phytotherapy PRO 160/120 (serenoa repens (saw palmetto) extract 160 mg and Urtica (nettle) extract 120 mg) 2/day + 1 placebo 1/day **Group 2** Finasteride (Proscar®) 5mg 1/day + 1 placebo 2/day **Examination methods:** Qmax, average flow and IPSS measured.	**IPSS ± SD at 6 mths**	**Group 1:** 8.2 ± 5.8, n=233 **Group 2:** 8.0 ± 5.7, n=230 **p value:** 0.66	**Funding:** NR **Limitations:** • Safety information was not reported in the 2000 study and not available from the Wilt et al., 2002[326] Cochrane Review. • Neither standard deviations or p values **Notes:** Additional methods information is available from first publication, Sökeland & Albrecht, 1997[283], translated from German in the Wilt et al., 2002[326] Cochrane Review. Randomisation was computer generated and allocation concealment was reported as being adequate in the Cochrane Review
			IPSS ± SD at 12 mths	**Group 1:** 6.5 ± 5.8, n=230 **Group 2:** 6.2 ± 5.2, n=223 **p value:** 0.54	
			Qmax ± SD at 3 mths	**Group 1:** 14.2 ± 6.0, n=240 **Group 2:** 14.6 ± 6.6, n=242 **p value:** 0.46	
			Qmax ± SD at 6 mths	**Group 1:** 14.6 ± 6.2, n=245 **Group 2:** 15.1 ± 7.1, n=244 **p value:** 0.34	
			Qmax ± SD at 12 mths	**Group 1:** 14.6 ± 6.4, n=233 **Group 2:** 15.4 ± 6.8, n=232 **p value:** 0.19	
			Prostate volume ± SD at 12 mths	**Group 1:** 42.4 ± NR **Group 2:** 37.2 ± NR **p value:** NR	
			Number of adverse events (details not reported in Cochrane review or Sökeland, 2000) but the	**Group 1:** 74 in 52 patients **Group 2:** 96 in 54 patients Note: the abstract for Sökeland & Albrecht, 1997[283] states that there were less cases of diminished ejaculation volume, erectile dysfunction and headache for those patients on PRO160/120	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Dropouts: 11 **IPSS (± SD):** 11.8 ± 6.6 (n=255) **Qmax (± SD), mL/s:** 12.8 ± 4.0 (n=241) **Prostate volume (± SD), mL:** 44.0 ± 26.6 (n=216)				

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1 **Evidence Table 52 Provision of information**

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Barry et al., 1997[23] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 1 Year	**Patient group:** Men with clinical diagnosis of BPH. **Setting:** Urologic practices of Group Health Cooperative of Puget Sound (staff model health maintenance organisation) in Washington; 2 practices were located in Seattle and Tacoma. **Exclusion criteria:** Evidence of prostate cancer, obstructive nephropathy, post void residual >350mL, recurrent or refractory urinary infection, acute retention, previous prostate surgery, repeated gross hematuria, clot retention, bladder stones, comorbid conditions, inability to understand English. **<u>All patients</u>** **N:** 227 **<u>Group 1</u>** **N:** 104 **Age (mean):** 66.4 (SD: 8.6) **AUA score (mean):** 16.6 (SD: 6.7) **Drop outs:** 1 **<u>Group 2</u>** **N:** 123 **Age (mean):** 66.2 (SD: 8.2) **AUA score (mean):** 15.9 (SD: 7.0) **Drop outs:** 7	**Group 1:** Computer and interactive video-based **shared decision-making program (SDP)** to educate men about their condition and its treatments. - short questionnaire before viewing; so a subset of items entered into computer to tailor programme to viewer. - 30 minute segment explaining importance of participation in the treatment decision and outlines the choices of watchful waiting, medical or surgical treatment. Estimates of outcome probabilities given. - then there is an interactive segment that allows for review of old material and inspection of 30 minutes of new material in optional modules on acute retention, sexual dysfunction, incontinence, new treatments, BPH and prostate cancer, blood transfusion, symptom response to surgery. **Group 2:** Brochure to provide basic information about the prostate gland and disease that can affect it, including BPH. No quantitative information about treatment outcomes provided.	**Treatment selection at 3 months:**	**<u>Prostatectomy:</u>** **Group1:** 5/104 (4.8%) **Group 2:** 8/123 (6.5%) **<u>Medication</u>:** **Group1:** 14/104 (13.5%) **Group 2:** 14/123 (11.4%) **<u>Watchful waiting:</u>** **Group1:** 85/104 (81.7%) **Group 2:** 101/123 (82.1%) **P=0.8**	**Funding:** Grant Nos. HS 06540 and 08397 from the Agency for Health Care Policy and Research. The development of the first edition of the SDP for BPH was funded by a grant from the John A. Hartford Foundation. **Limitations:** 2 phases of recruitment (pre-consent randomisation phase and post consent randomisation phase). **Additional outcomes:** Mean change in autonomy preference scores. **Notes:** * p values from a repeated measures analysis of covariance over all assessment points, controlling for age, practice site, marital status, education, income and race.
			Men undergone prostatectomy at 1 year:	**Group1:** 8/104 (7.7%) **Group 2:** 16/123 (13.0%) **p value:** 0.28 **Absolute diff:** 5.3% (CI: -2.5%, +13.0%)	
			Mean BPH knowledge score: at 2 weeks	**Group1:** 11.5 (SEM 0.5) **Group 2:** 6.7 (SEM 0.4) **p value:** <0.001	
			Mean (SE) satisfaction scores for decision process: 12 months	**Group1:** 74.77 (1.72) **Group 2:** 69.26 (1.89) **p value*:** 0.03	
			Mean (SE) satisfaction scores for decision made: 12 months	**Group1:** 75.16 (1.80) **Group 2:** 71.74 (1.75) **p value:** 0.21	
			Mean (SE) changes of AUA symptom score: 12 months	**Group1:** -0.88 (0.74) **Group 2:** -1.45 (0.58) **p value:** 0.58	
			Mean (SE) change in BPH impact score: 12 months	**Group1:** -1.05 (0.25) **Group 2:** -0.59 (0.25) **p value:** 0.12	
			Mean (SE) changes in general health score at 12 months:	**Group1:** 0.61 (1.58) **Group 2:** -4.99 (1.44) **p value:** 0.02	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
			Mean (SE) changes in physical functioning score at 12 months:	**Group1:** 0.15 (1.40) **Group 2:** -3.74 (1.18) **p value:** 0.02	
			Mean (SE) changes in social functioning score at 12 months:	**Group1:** -1.46 (1.85) **Group 2:** -3.52 (1.71) **p value:** 0.17	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Brown et al., 2007[35] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 12 months	**Patient group:** men over 40 with uncomplicated lower urinary tract symptoms who were referred for the first time by their GP (from January 2003 and April 2004). **Setting:** Outpatient departments of 2 urological centres in London, a teaching hospital and a district general hospital. **Exclusion criteria:** medical treatment in the previous three months, recent surgery, complications potentially related to their symptoms or severe comorbidity. **<u>All patients</u>** **N:** 140 **Drop outs:** 25 **<u>Group1:</u>** **N:** 73 **Age (mean):** 63.3 (11.1) **Drop outs:** 14 at 12M **Mean (SD) duration of symptoms** (years): 3.9 (4.0) **Mean (SD) IPSS:** 16.9 (5.1) **Mean (SD) AUA-QoL score:**	**Group 1: Self management and standard care group** Small group sessions (5-8 men), each lasting between 1.5 and 2 hours, which were scheduled one, two and six weeks after randomisation. The aim of these sessions was to bring about modification of lifestyle (fluid management, avoidance of caffeine, and use of alcohol) and specific changes in behaviour (bladder training, double voiding, and urethral milking). Facilitated by urology nurses trained to enhance self management skills and provided support by brainstorming and group discussion. This intervention group also received standard care (as described below). **Group 2: Standard care** Standard care began with watchful waiting. Escalation to medical treatment and surgery was left to the discretion of the clinician and patient. All patients, irrespective of treatment allocation, received standard written information about lower urinary tract symptoms.	**Number (%)of men with treatment failure:** Failure defined as a rise of 3 points or more on the international prostate symptom score, use of drugs to control lower urinary tract symptoms, acute urinary retention, or surgical intervention) during follow-up.	**3-month outcome:** **Group 1:** 7/71 (10%) **Group 2:** 27/65 (42%) **Difference (95% CI):** 32 (18 to 46) **p value:** <0.001 **6-month outcome:** **Group 1:** 13/69 (19%) **Group 2:** 39/64 (61%) **Difference (95% CI):** 42 (27 to 57) **p value:** <0.001 **12-month outcome:** **Group 1:** 18/59 (31%) **Group 2:** 44/56 (79%) **Difference (95% CI):** 48 (32 to 64) **p value:** <0.001	**Funding:** BUPA Foundation Project Grant. Author CTB received a research fellowship from the Royal College of Surgeons of England, funded by Cazenove & Co. Author JvdM is funded by a national public health career scientist award from the Department of Health and NHS R&D Programme. **Limitations:** The study was underpowered as according to their calculations 84 men in each group were necessary to have a 90% chance to detect a 3 point reduction in mean international prostate symptom score at 5% level of significance with SD of 6. **Additional outcomes:** Reasons for treatment failure at 3, 6 and 12 months. BPH index score.
			Mean (SD) International Prostate Symptom Score (IPSS) (Score: 0-35; the higher the score the worse the symptoms)	**3-month outcome:** **Group 1:**(n= 71): 10.7 (5.9) **Group 2:** (n=64): 16.4 (5.8) **Difference (95% CI):** 5.7 (3.7 to 7.7), **p value:** <0.001 **6-month outcome:** **Group 1**(n= 67): 10.4 (6.1) **Group 2**(n=61): 16.9 (6.4) **Difference (95% CI):** 6.5 (4.3 to 8.7), **p value:** <0.001 **12-month outcome:** **Group 1:** (n=53): 10.2 (6.1) **Group 2:**(n=51): 15.4 (6.6) **Difference (95% CI):** 5.1 (2.7 to 7.6), **p value:** <0.001	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	4.0 (1.0) **<u>Group 2:</u>** **N:** 67 **Age (mean):** 63.4 (10.4) **Drop outs:** 11 at 12M **Mean (SD) duration of symptoms** (years): 4.3 (6.7) **Mean (SD) IPSS:** 15.9 (6.5) **Mean (SD) AUA-QoL score:** 3.3 (1.1)		**Mean (SD) AUA-QoL score:** (lower score the better quality of life)	**3-month outcome:** **Group 1:**(n= 71): 2.8 (1.2) **Group 2:**(n=64): 3.4 (1.1) **Difference (95% CI):** 0.6 (0.2 to 1.0), **p value:** < 0.001 **6-month outcome:** **Group 1:**(n= 67): 2.6 (1.3) **Group 2:**(n=61): 3.3 (1.4) **Difference (95% CI):** 0.7 (0.2 to 1.2), **p value:** 0.008 **12-month outcome:** **Group 1:** (n=54): 2.6 (1.3) **Group 2:** (n=52): 3.1 (1.2) **Difference (95% CI):** 0.5 (0 to 1.0) **p value:** 0.03	**Notes:** Compliance with self management programme was high; 68 (93%) patients attended all three sessions. The five patients who did not attend were included in the self management group for analysis. Self management group included more men with university degree and fewer men with no qualification.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Murray et al., 2001[207] **Study design:** RCT **Evidence level:** 1+ **Duration of follow-up:** 9 months	**Patient group:** Men with benign prostatic hypertrophy **Setting:** Primary care **Inclusion criteria:** Men with benign prostatic hypertrophy. No more details provided. **Exclusion:** Men with any clinical suggestion of carcinoma of the prostate or if they had chronic retention of the urine, recent urinary tract infection, a history of acute urinary retention or prostate surgery, severe visual or hearing impairment, or severe learning difficulties or mental illness. **<u>All patients</u>** **N:** 112 **Drop outs:** 10 **<u>Intervention group</u>** **N:** *57* **Age (mean +/- SD):** 63.7 +/- 8.4 **Drop outs:** 3 **Mean (SD) American Urological Association score:** 15.64 (6.57) **Up to secondary education; n (%):** 25 (44) **Beyond secondary education; n (%):** 32 (56) **Mean (SD) Spielberg state trait**	**<u>Group 1:</u>** Interactive multimedia programme with booklet and printed summary. Treatment options discussed were surgery, balloon dilatation of the prostate, drugs, and watchful waiting. Information comprised probabilities of the risks and benefits of each treatment, calculated on the basis of information on age, severity of symptoms, and general health entered by the patient at the beginning of the session. All patients saw the core interactive video disc, lasting about 45 minutes; viewing optional sections for further information took up to 60 min. more. A research nurse started the programme, taught the patient how to use it, and then withdrew. **<u>Group 2:</u>** Normal care from GP practitioner.	**Mean (SD) decisional conflict score at three months:** Higher scores indicated increased uncertainty.	Group 1: 2.3 (0.4) Group 2: 2.6 (0.5) Mean difference (95% CI): -0.3 (-0.5 to -0.1), p <0.01	**Funding:** NHS national research and development programme, the BUPA Foundation, and the King's Fund. **Limitations:** The initial aim of the study was to detect a difference in anxiety, however, recruitment rate was low and it was not possible to recruit the 210 patients needed from the sample size calculation. **Additional outcomes:** Cost per patient for a number of item. Only total costs are reported in this table. Authors found no difference between the two groups in the trends over time in the EQ-5D responses nor in the SF-36 scores. Data not provided. Anxiety scores: the Spielberger scores were similar at the final assessment in the two groups (Mann-Whitney U test). No data provided. Resource volumes per patient over nine months of trial.
			Mean (SD) decisional conflict score at nine months:	Group 1: 2.23 (0.38) Group 2: 2.55 (0.50) Mean difference (95% CI): -0.33 (-0.51 to -0.14)	
			GPs perceptions of decision making at three months. Values are numbers and (%). **Question:** ***Who do you think made the treatment decision?***	**Mainly or only GP:** Group 1 (n=48): 1(2) Group 2 (n=49): 5 (10) % difference (95% CI): -8 (-17.5 to 1.3) **GP and patient together:** Group 1: 25 (52) Group 2: 32 (65) % difference (95% CI): -13 (-32.6 to 6.2) **Mainly or only patient:** Group 1: 22 (46) Group 2: 12 (25) % difference (95% CI): 21 (2.8 to 39.9) X^2= 6.458, df=2; p=0.04	
			Patients' perceptions of decision making at three months. ***Question: Who do you think made the treatment decision?***	**Mainly or only GP:** Group 1 (n=57): 5(9) Group 2 (n=48): 4 (8) % difference (95% CI): 1 (-10.3 to 11.2) **GP and patient together:** Group 1: 34 (60) Group 2: 42 (88) % difference (95% CI): -28 (-43.7 to 12.0) **Mainly or only patient:**	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	anxiety inventory: 33.93 (13.09) **<u>Control group</u>** **N:** 55 **Age (mean +/- SD):** 63.9 +/- 8.4 **Drop outs:** 7 **Mean (SD) American Urological Association score:** 14.85 (7.10) **Up to secondary education; n (%):** 28 (51) **Beyond secondary education; n (%):** 27(49) **Mean (SD) Spielberg state trait anxiety inventory:** 32.01 (10.49)			Group 1: 18 (32) Group 2: 2 (4) % difference (95% CI): 28 (14.1 to 40.7) X^2= 13.078, df=2; p=0.001	**Notes:** Decisional conflict score contains three subscales that elicit uncertainty about choosing between alternatives, awareness of modifiable factors contributing to the uncertainty, and perceived effectiveness of decision making process. Higher scores indicated increased uncertainty in each subscale. Subscales combined to give a total decisional conflict score.
			American Urological Association scores	**Scores improved in both groups over the study period.** **Median change in score:** Group 1: -1 Group 2: -2 Mann-Whitney U test, p=0.8	
			Total costs in pounds sterling (at 1999 prices) per patient: Mean (SD)	**Excluding intervention:** Group 1 (n=57): 310.3 (602.0) Group 2 (n=48): 188.8 (300.4) Mean difference (95% CI): 121.5 (-58.9 to 302.0) **including intervention:** Group 1: 594.1 (602.0) Group 2: 188.8 (300.4) Mean difference (95% CI): 405.4 (224.9 to 585.8) P<0.001	

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Evidence Table 53 Economic evidence

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Annemans 2005[17] UK **Economic analysis:** cost-effectiveness analysis **Study design** Decision analysis* **Time horizon:** 6 months **Discount rates:** Costs: NA Effects: NA	**Patient group:** patients hospitalised for acute urinary retention	**Intervention 1:** Alfuzosin 10mg once daily used for 3 days during the initial hospitalization followed by TWOC (mean duration 55hours). If TWOC is successful treatment with Alfuzosin for 6 months. **Intervention 2:** Immediate inpatient prostatectomy **Intervention 3:** Placebo followed by TWOC (mean duration 55hours) and placebo if TWOC is successful.	Successful TWOC*	**Int 1:** 62% **Int 2:** NA **Int 3:** 48% **p value:** 0.012	**Funding:** Sanofi-Aventis **Limitations:** Short follow-up. **Additional outcomes:** After successful TWOC, 17% of patients treated with Alfuzosin for 6 months require prostatectomy compared to 24% of patients treated with placebo. **Notes:** * based on the ALFAUR Study[195] **based on 2002 Reference Costs inflated to 2003 (inflator 1.035)
			Mean cost per patient over 6 months** 2002 GBP cost of hospitalisation, prostatectomy and TURP, drugs, unsuccessful TWOC (prostatectomy), tests.	**Int 1:** 2,029 **Int 2:** 2,378 **Int 3:** 2,921 **p value:** NR	
			Incremental costs over 6 months (based on 1,000 Monte Carlo simulations)	Int 3 vs. Int 1: 349 (95% CI 64-624) Int 2 vs. Int 1: 892 (95% CI 644-1121) Int 2 vs. Int 3 : 543 (95% CI 228 - 776) p value : Sig	
			Cost-effectiveness cost per successful TWOC	Int 1 dominates Int 2 and 3	
			Sensitivity analysis Monte Carlo simulation	If the proportion of patients having an immediate prostatectomy after a failed TWOC is higher, Alfuzosin is more cost-saving. If surgery after successful TWOC is done in an elective setting, Alfuzosin is more cost saving.	

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Study details	Patients	Interventions*	Outcome measures	Effect size	Comments
DiSantostefano 2006 [71] USA **Economic analysis:** Cost-utility analysis **Study design** Decision analysis **Time horizon:** 20 years **Discount rates:** Costs: 3% Effects: 3%	**Patient group:** men aged 65 years with moderate to severe LUTS and uncomplicated BPH, with no contraindications to any of the drugs. **Group A:** moderate symptoms (IPSS 8-19) **Group B:** severe symptoms (IPSS 20-35)	**Intervention 1:** Watchful waiting (WW) **Intervention 2:** Alpha-blockers (AB) **Intervention 3:** 5-Alpha reductase inhibitors (5-ARI) **Intervention 4:** High-energy transurethral microwave thermotherapy (TUMT) **Intervention 5:** Transurethral resection of the prostate (TURP)	QALYs – Group A	**Intervention 1:** 10.68 **Intervention 2:** 10.76 **Intervention 3:** 10.71 **Intervention 4:** 10.69 **Intervention 5:** 10.63 **p value:** NR	**Funding:** National Research Service Award Institutional Training Grant from the Institute of Aging; grant from the Agency for Healthcare Research and Quality. Conflict of Interest: the author is an employee of GlaxoSmithKline. **Limitations:** Partial applicability. The lack of long-term studies and differences between patient populations might have biased the results in favour of pharmaceuticals. **Notes:** * Combination of AB and 5-ARI was an additional intervention compared in the study but it was excluded because its effectiveness was based only on experts opinion. ** GBP calculated by using the 2008 PPP
			QALYs – Group B	**Intervention 1:** 9.79 **Intervention 2:** 9.88 **Intervention 3:** 9.83 **Intervention 4:** 10.30 **Intervention 5:** 10.47 **p value:** NR	
			Mean cost per patient – Group A** 2004 USD, cost of GP visits, tests, drugs, surgery, complications (strictures, incontinence)	**Intervention 1:** $ 4,419 (£ 2,793) **Intervention 2:** $ 6,666 (£ 4,213) **Intervention 3:** $ 8,891 (£ 5,619) **Intervention 4:** $ 7,982 (£ 5,045) **Intervention 5:** $ 8,599 (£ 5,435) **p value:** NR	
			Mean cost per patient – Group B** 2004 USD, cost of GP visits, tests, drugs, surgery, complications (strictures, incontinence)	**Intervention 1:** $ 4,403 (£ 2,783) **Intervention 2:** $ 6,664 (£ 4,212) **Intervention 3:** $ 8,888 (£ 5,617) **Intervention 4:** $ 7,983 (£ 5,045) **Intervention 5:** $ 8,558 (£ 5,409) **p value:** NR	
			Cost-effectiveness –** incremental cost per QALY	**Group A** Int 2 vs. Int 1: $ 28,088 (£17,752) Int 3, 4 and 5 are dominated by Int 2. Int 6 is dominated by Int 5. **Group B** Int 2 vs. Int 1: $ 25,122 (£ 15,877) Int 3 is dominated by Int 2. Int 4 vs. Int 2: $ 3,140 (£ 1,984) Int 5 vs. Int 2: $ 3,210 (£ 2,029) Int 5 vs. Int 1: $ 6,110 (£ 3,861) Int 5 vs. Int 4: $ 3,382 (£ 2,137)	

Study details	Patients	Interventions*	Outcome measures	Effect size	Comments
			Sensitivity analysis One-way sensitivity analysis	If switching between treatments was not permitted, TURP would cost $30,204 (£ 19,090) more than AB for each QALY gained for moderate symptoms patients. The overall results did not change with the age of the patient. If effectiveness of TUMT is set equal to TURP, TUMT dominates TURP.	
			Probabilistic sensitivity analysis	For a willingness to pay equal to $50,000 alpha-blockers have about a 70% probability of being cost-effective for patients with moderate symptoms. For the same willingness to pay, TURP had almost a 90% probability of being cost-effective for patients with severe symptoms.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Fader 2008[86] UK **Economic analysis:** Cost-effectiveness analysis **Study design** RCT (cross-over)* **Duration of follow-up:** One month **Discount rates:** Costs: NA Effects: NA	**Patient group:** moderate/heavily incontinent adults (urinary or urinary/faecal) living in the community **<u>All patients</u>** **N:** 85 **IPSS:** NR **Age (mean):** 52.8 **M/F:** 49/36 **Drop outs:** 0	**Intervention 1:** Insert **Intervention 2:** Diaper **Intervention 3:** Pull-up **Intervention 4:** T-shaped **Intervention 5:** Washables	Proportion of patients willing to buy a product used during the day if they had to bear the cost	**Int 1:** 39% **Int 2:** 50% **Int 3:** 43% **Int 4:** 39% **Int 5:** 38% **p value:** NR	**Funding:** commissioned by the Health Technology Assessment Programme. Some of the authors have received research grant money and travel grant money from SCA AB (absorbent pad manufacturing company) **Limitations:** The study included women and faecal incontinence as well. Not a full economic evaluation. Effectiveness was not measured in terms of any of the clinical outcomes included in our Guideline. **Notes:** *crossover design in which each participant tested all products within their group in random order. Only trial 2a is included and reported. ** scale from 0 – 100 to assess patients' preference for a product. *** Visual Analogue Scale score is not a clinical outcome of interest and an incremental cost-effectiveness analysis based on this outcome would not be useful.
			Proportion of patients willing to buy a product used during the night if they had to bear the cost	**Int 1:** 33% **Int 2:** 52% **Int 3:** 39% **Int 4:** 33% **Int 5:** 53% **p value:** NR	
			Mean Visual Analogue Scale score** (day use – night use)	**Int 1:** 48 – 53 **Int 2:** 66 – 64 **Int 3:** 73 – 62 **Int 4:** 60 – 54 **Int 5:** 34 – 43 **p value:** NR	
			Mean monthly cost per patient (day – night) 2005 GBP, cost of supplying the product, assuming three products per day and one per night are used. Cost of laundering washable products is not included.	**Int 1:** £44 - £23 **Int 2:** £47 - £15 **Int 3:** £79 - £25 **Int 4:** £75 - £25 **Int 5:** £9 - £6 **p value:** NR	
			Cost-effectiveness	NA***	
			Sensitivity analysis	Different types of products within the same category have different costs and performance. The results are very sensitive to these variations.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Fehrling2007[90] Sweden **Economic analysis:** Cost consequences analysis **Study design** Within group comparison **Duration of follow-up:** 3 months **Discount rates:** Costs: NA Effects: NA	**Patient group:** patients with an overactive bladder with or without incontinence **<u>All patients</u>** **N:** 60 **IPSS:** **Age:** the majority was 70 or older **M/F:** 31/29 **Drop outs:** 0	**Treatment:** 10 session (twice weekly for 5 weeks) of Maximal Functional Electrical Stimulation (MFES) at the highest tolerable amplitude	Number of patients with: up to 8 voids per day > 8voids per day - NR	**Before treatment:** 11 – 44 – 5 **After treatment:** 11 – 30 – 19 **p value:** NR	**Funding:** Swedish Research Council, Sahlgrenska university Hospital, and the Martha and Gustaf Agrens research Foundation. **Limitations:** Within group study. The outcomes are not clear-cut. Only the cost of the intervention is considered. Mixed male and female population. **Notes:** * the total sum is 61 while N=60 **Cost of treatment for each successfully treated patient is reported (€17,000) but success is not defined. *** calculated by using the 2008 PPP for Germany
			Number of patients with the following degree of leakage: No leakage - Minor - Moderate - Severe- NR	**Before treatment*:** 17 – 11 – 16 – 13 – 4 **After treatment:** 21 – 12 – 10 – 11 – 6 **p value:** NR	
			Mean cost per patient 2007 Euro, cost of 10 sessions.	**Before treatment:** NR **After treatment:** €3,500 (£2,640***) **p value:**	
			Cost-effectiveness	NR**	
			Sensitivity analysis)	NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Fraundorfer2001[97] New Zealand **Economic analysis:** Cost consequences **Study design** RCT* [104] **Duration of follow-up:** 1 year **Discount rates:** Costs: NA Effects: NA	**Patient group:** men with urodynamically proved outflow obstruction due to BPH, AUA score of 8 or greater, independent peak urinary flow rate (Qmax) of 15 mL/s or less, and bladder outflow obstruction confirmed by pressure flow urodynamic studies (Schafer grade 2 or more). **<u>All patients</u>** **N:** 120 **<u>Group 1</u>** **N:** 61 **Mean (±SD) Age:** 66.9±6.5 **<u>Group 2</u>** **N:** 59 **Mean (±SD) Age**: 66.8±7.4	**Group 1** Holmium laser resection (HoLRP) **Group 2** TURP	Qmax (mL/s) ± SD	**Group 1:** 25.2 ± 11.9 **Group 2:** 20.4 ± 8.5 **p value:** <0.05	**Funding:** partially funded by Coherent Medical Group. Clinical study authors have financial interest and/or other relationship with Lumenis, Inc. **Limitations:** Not a full economic evaluation. Partially applicable. In real practice HoLEP might be less successful as it requires high level of skills and experience. **Additional outcomes:** Group 1 had a shorter LOS and lower complication rate. **Notes:** * The two year follow-up study [318] was reviewed for clinical effectiveness **calculated by using the 2008 PPP
			AUA score	**Group 1:** 4.2 ± 6.0 **Group 2:** 4.3 ± 4.1 **p value:** Not Sig	
			Mean cost per patient 2001 NZD cost of consumables, hospital facility use, operations, clinic visits, capital equipment, and unplanned events.	**Group 1:** 2,012 (£857**) **Group 2:** 2,663 (£1,134**) **p value:** NR	
			Cost-effectiveness	NA	
			Sensitivity analysis	NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Hillman 1996[117] USA **Economic analysis:** Cost consequences and cost-effectiveness **Study design** Multicentre RCT[262] **Duration of follow-up:** 12 months **Discount rates:** Costs: NA Effects: NA	**Patient group:** men 55 years or older with a clinical diagnosis of BPH and at least moderate IPSS. **<u>All patients</u>** **N:** 2084 **IPSS:** 20.1 **Age (mean and range):** 65.7 (46 – 94) **Drop outs*:** 867 **<u>Group 1</u>** **N:** 1053 (1010 in economic analysis) **IPSS:** 20.1 **Age (mean):** 65.7 **Drop outs*:** 396 **<u>Group 2</u>** **N:** 1031 (983 in economic analysis) **IPSS:** 20.1 **Age (mean):** 65.7 **Drop outs*:** 471	**Group 1:** Alpha-blockers (Terazosin). 1mg daily for 3days followed by 2mg daily for the remainder of the first 4 weeks. The medication dose was titrated upward at the investigator's discretion until a satisfactory response was achieved (improvement of 35% or more of IPPS). **Group 2:** Placebo	Mean change in IPSS ± SE	**Group 1:** -7.6 ±0.2 **Group 2:** -3.7 ±0.2 **p value:** <0.001	**Funding:** Abbott Laboratories, Abbott Park, Illinois. **Limitations:** Partial applicability. Placebo was used instead of watchful waiting. Short follow up. **Notes:** *Patients withdrawn because of adverse events and lack of efficacy were respectively 168 and 93 in group 1, and 114 and 220 in group 2 (p<0.001). **Calculated by using the 2008 PPP *** calculated by NCGC
			Mean change in IPSS – Quality of Life ± SE	**Group 1:** -3.6 ±0.1 **Group 2:** -1.8 ±0.1 **p value:** <0.001	
			Mean cost per patient 1992 USD, cost of visits (home, GP and urologist), inpatient care, medication.	**Group 1:** $2,932 (£1,865**) **Group 2:** $3,404 (£2,165**) **p value:** NR	
			Cost-effectiveness*** incremental cost per IPSS point change	Group 1 dominates Group 2	
			Sensitivity analysis one-way SA	Overall results were not sensitive to outlier costs, costs assigned by patient-reported events, regional vs. satellite patients, costs of patients completing a full year of therapy, costs of improperly randomised patients.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Johansen 2007[127] Norway **Economic analysis:** cost analysis **Study design** decision analysis* **Time horizon:** 4 years **Discount rates:** Costs: 5% Effects: NA	**Patient group:** men with BPH	**Intervention 1:** Alpha-blockers (Tamsulosin) **Intervention 2:** 5-Alpha-reductase inhibitors (Dutasteride and Finasteride) **Intervention 3:** TURP	**Mean cost per patient over 4 years** 2006 NOK, cost of drugs, tests, visits to GP, pre-TURP visits to urologist, TURP, surgical follow-up, prostate cancer evaluation following TURP, post-TURP antibiotics, cost of AUR.	**Int 1:** 16,933 (£1,219**) **Int 2*****:** 13,946 (£ 1,004**) **Int 3:** 46,109 (£ 3,320**) **p value:** NR	**Funding:** NR. One of the authors was an employee of GlaxoSmithKline. **Limitations:** Risk of AUR and TURP for Tamsulosin was assumed to be equal to the placebo arm of the trials. **Notes:** *improvement rates, risk of AUR and TURP were taken from Phase-III trials[1] for Dutasteride, assumed to be equal for Finasteride. Risk of AUR and TURP of Tamsulosin was assumed to be equal to the placebo arm of those trials. Improvement rate of Tamsulosin was obtained from Phase-III trials and improvement rate of TURP was based on clinical opinion. ** Calculated by using the 2008 PPP ***cost of Dutasteride. Finasteride was more costly than Dutasteride but less costly than Tamsulosin.
			Cost-effectiveness	NA	
			Sensitivity analysis One-way and multi-way SA	The overall results were not sensitive to the following changes in one-way, two-way and multi-way SA: - Time-horizon increased to lifetime. - Decrease or increase costs of TURP and AUR by 10%. - Inclusion of indirect costs. - Probability of AUR decreased by 10% after TURP/any intervention. - Probability of TURP after AUR reduced by 25%. - Decrease symptoms improvement by 10%. - Change in discount rate (0-8%).	

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[1] http://www.gsk-clinicalstudyregister.com/files/pdf/883.pdf, http://www.gsk-clinicalstudyregister.com/files/pdf/895.pdf , http://www.gsk-clinicalstudyregister.com/files/pdf/3241.pdf

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Study details	Patients	Interventions*	Outcome measures	Effect size	Comments
Johnson 1999[128] UK **Economic analysis:** cost-consequences analysis **Study design** decision analysis **Time horizon:** 5 years **Discount rates:** Costs: 6% Effects: 6%	**Patient group:** 60 years old patients with uncomplicated moderate to severe benign prostatic hyperplasia	**Intervention 1:** Watchful waiting. If ineffective it will be followed by second line (Doxazosin or Finasteride) and if necessary surgery. **Intervention 2:** Alpha-blockers (Doxazosin). If ineffective or have side effects it will be followed by second line (Finasteride or watchful waiting) and if necessary surgery. **Intervention 3:** 5-alpha-reductase inhibitors (Finasteride). If ineffective or have side effects it will be followed by second line (Doxazosin or watchful waiting) and if necessary surgery.	Patients discontinuing treatment over 5 years	**Int 1:** 46.0% **Int 2:** 39.1% **Int 3:** 42.0% **p value:** NR	**Funding:** Pfizer International **Limitations:** It was not clear how the response-years gained were calculated. **Notes:** * Surgery was excluded from the interventions compared as this was a mix of TURP and open prostatectomy. ** Obtained from the meta-analysis described by the American Agency for Health Care Policy and Research
			Patients with improved symptoms**	**Int 1:** 42% **Int 2:** 74% **Int 3:** 67% **p value:** NR	
			Improvement in symptom score from baseline**	**Int 1:** 32% **Int 2:** 48% **Int 3:** 31% **p value:** NR	
			Response-years gained	**Int 1:** 0.57 **Int 2:** 0.81 **Int 3:** 0.60 **p value:** NR	
			Mean cost per patient over 5 years 1999 GBP; cost of GP and urologist consultations, laboratory procedures, examinations, medications, surgical procedures, complications.	**Int 1:** £791 **Int 2:** £1427 **Int 3:** £1720 **p value:** NR	
			Cost-effectiveness	NR	
			Sensitivity analysis One-way SA	Results not sensitive to cost of surgery, response rates, discontinuation rates, response degree, and time horizon	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Keoghane2000[142] UK **Economic analysis:** cost-effectiveness analysis **Study design** RCT **Duration of follow-up:** 36 months (costs only 24 months) **Discount rates:** Costs: NR Effects: NR	**Patient group:** all patients presenting for TURP who had not undergone previous surgery. **<u>All patients</u>** **N:** 152 (100 for cost analysis) **Drop outs:** NR **<u>Group 1</u>** **N:** 47 for cost analysis **AUA score (SD):** 19.9 (7.7) **<u>Group 2</u>** **N:** 53 for cost analysis **AUA score (SD):** 19.4 (6.5)	**Group 1** Vaporisation using MD60 Nd:YAG (Selected Laser Technologies) with 600 μm fibre incorporating sapphire-tipped probe. Irrigation using saline. **Group 2** TURP in standard manner using Storz equipment and irrigation with glycine	Mean change in AUA 7 symptom score from baseline at 12 months (±SD)	**Group1:** 10.9 ± 8.4 (n=44) **Group 2:** 13.3 ± 7.8 (n=53) **p value:** not Sig (NCGC-ACC t-test)	**Funding:** Oxford Regional Health Authority **Limitations:** Surgeons had limited experience with the laser technique which may have caused the high failure rate with this treatment. **Additional outcomes:** Duration of catheterisation and complications favour Contact Laser. Reoperation rate was 18% in Group 1 and 9% in Group 2. Inpatient stay was 3.5 days in Group 1 and 3.9 days in Group 2. **Notes:** * In the study prices were up-rated using the NHS hospital and community price index.
			Mean change in AUA 7 symptom score from baseline at 24 months (±SD)	**Group1:** 11.7 ± 9.7 (n=35) **Group 2:** 13.7 ± 7.7 (n=47) **p value:** not Sig (NCGC-ACC t-test)	
			Mean change in AUA 7 symptom score from baseline at 36 months (±SD)	**Group1:** 11.0 ± 9.7 (n=37) **Group 2:** 12.9 ± 7.9 (n=41) **p value:** not Sig (NCGC-ACC t-test)	
			Change in flow rate (Qmax) from baseline at 3 years	**Group1:** 1.8 ± 6.2 (n=24) **Group 2:** 2.1 ± 6.9 (n=24) **p value:** Not Sig (NCGC-ACC t-test)	
			Mean cost per patient at 2 years 1997 GBP*, cost of operation, hospitalisation, outpatient visits, GP and nurse visits, re-operation, capital costs and overheads.	**Group 1:** £1,252 **Group 2:** £971 **p value:** Sig	
			Cost-effectiveness cost per change in AUA score	TURP is dominant	
			Sensitivity analysis One way	If inpatient stay in Group 1 is reduced to 1.5 days laser becomes less costly by £50.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Lourenco 2008[174] UK **Economic analysis:** Cost-utility analysis **Study design** Decision analysis **Time horizon:** 10 years **Discount rates:** Costs: 3.5% Effects: 3.5%	**Patient group:** Men at the age of 70 years with BPE, presence of LUTS with a measure of IPSS>7, no complications and TURP indicated (medical treatment either contraindicated or failed). Mean start age 70 years.	**Intervention 1:** TUVP **Intervention 2:** TUMT **Intervention 3:** HoLEP **Intervention 4:** TURP **Intervention 5:** KTP **Intervention 6:** TUVP followed by HoLEP if it fails **Intervention 7:** TUVP followed by TURP if it fails **Intervention 8:** TUVP followed by repeated TURP if it fails	QALYs*	**Int 1:** 0.3668 **Int 2:** 0.3625 **Int 3:** 0.3679 **Int 4:** 0.3673 **Int 5:** 0.3631 **Int 6:** 0.3684 **Int 7:** 0.3684 **Int 8:** 0.3684 **p value:** NR	**Funding:** NHS R&D Health Technology Assessment Programme **Limitations:** Cost of equipment was included only for some strategies. Duration and cost of operations were equal in all the strategies. Training costs not included. Some interventions (TURP) are used to identify prostate cancer. Additional diagnostic tests would be necessary of another strategy is adopted. **Additional outcomes:** Other sequences of treatments starting with TURP or TUMT were dominated. When compared to TURP alone, only TUVP, KTP and all the strategies involving a second operation starting with TUMT are not cost-effective. Expected value of partial perfect
			Mean cost per patient* 2006 GBP, cost of procedure, short-term complications (acute urinary retention, bladder neck contracture or urethral stricture, blood transfusion, transurethral syndrome, urinary tract infections), long-term complications (incontinence: 95% oxybutinin, 5% artificial sphincter), equipment for KTP, HoLEP and TUMT only.	**Int 1:** £152 **Int 2:** £155 **Int 3:** £160 **Int 4:** £174 **Int 5:** £223 **Int 6:** £166 **Int 7:** £167 **Int 8:** £167 **p value:** NR	
			Cost-effectiveness incremental cost per QALY	Int 3 vs. Int 1: £7,273 Int 6 vs. Int 3: £12,000 Int 2 dominated by Int 1. Int 3 vs. Int 2: £833. Int 4 dominated by Int 3, 6, 7, 8. Int 5 dominated by any interventions. Int 7 and 8 dominated by Int 6**.	
			Sensitivity analysis Probabilistic sensitivity analysis One way sensitivity analysis	At the threshold of £20,000/QALY, Int 6 has a probability of being cost-effective of about 80%. If LOS TURP is 2 days instead of 3 days, Int 8 is cost-effective. Results not sensitive to start age, utility of 'incontinence no remission'	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
				state = utility of 'incontinence remission' state, utility of IPSS<8 is 0.97 instead of 1, risk data from all studies instead of UK studies only, test for obstruction after TUVP.	information was £4,187,062 for TUVP epidemiology and £1,652,886 for HoLEP epidemiology. **Notes:** * results per patient of Monte Carlo simulation with 10,000 samples where 25,000 new individuals enter the model each year. ** Int 8 vs. 6 ICER=£90,576/QALY when results are calculated per population

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
McDonald 2004[192] Canada **Economic analysis:** Cost-utility analysis **Study design** Decision analysis* **Time horizon:** 15 years **Discount rates:** Costs: 5% Effects: 5%	**Patient group:** men 65 years old with moderate to severe symptoms of BPH and an enlarged prostate as determined by digital rectal examination who choose not to undergo immediate surgical treatment.	**Intervention 1:** Watchful waiting (WW) **Intervention 2:** Alpha-blockers (Doxazosin) **Intervention 3:** 5-alpha-reducatse inhibitors (Finasteride) **Intervention 4:** Combination therapy with Doxazosin and Finasteride.	QALYs gained	**Int 1:** 8.608 **Int 2:** 8.787 **Int 3:** 8.709 **Int 4:** 8.930 **p value:** NR	**Funding:** Merck Frosst Canada Ltd. **Limitations:** Partially applicable. **Additional outcomes:** Incremental cost per AUR averted and incremental cost per TURP averted. **Notes:** * based mainly on the PLESS[256] and MTOPS studies[191] ** GBP calculated by using the 2008 PPP *** calculated by NCGC
			Mean cost per patient** 2003 CAD, cost of drugs (including 10% pharmacy mark-up charge and dispensing fee), visits (one full and one partial per year plus two partial for Group 1), hospitalisation, surgery, surgical complications, tests.	**Int 1:** $2,254 (£ 1,181) **Int 2:** $4,615 (£ 2,418) **Int 3:** $6,167 (£ 3,231) **Int 4:** $9,477 (£ 4,966) **p value:** NR	
			Cost-effectiveness ** incremental cost per QALY gained	Int 2 vs. Int 1***: $13,190 (£ 6,912) Int 3 dominated by Int 2. Int 4 vs. Int 2: $34,000 (£ 17,816)	
			Sensitivity analysis One way SA.	Considering only patients with PSA>1.3 ng/ml or PSA >3.2 ng/ml the results were similar. Results were not sensitive to discounting, probability of TURP following AUR, cost of TURP, cost of AUR. Combination is no longer cost-effective when AUR rates are obtained from MTOPS instead of PLESS, treatment effect is decreased by 50%, or QALY weights from Baladi1996[21] are used. Finasteride is more cost-effective than Doxazosin if it improves IPSS past year 4 by 2 points.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Medicare Services Advisory Committee[198] Australia **Economic analysis:** cost-utility analysis **Study design** Decision analysis **Time horizon:** 20 years **Discount rates:** Costs: 5% Effects: 5%	**Patient group:** Patients with symptomatic benign prostatic hyperplasia.	**Intervention 1:** TUNA **Intervention 2:** TURP	QALY	**Int 1:** 12.2869 **Int 2:** 12.3082 **p value:** NR	**Funding:** Report prepared from the National Health and Medical Research Council Clinical Trials Centre, University of Sydney for the Medical Services Advisory Committee. **Limitations:** Utilities were obtained from expert opinion and not elicited with recognised methods. **Notes:** * Calculated by using the 2008 PPP
			Mean cost per patient 1999 AUD, cost of procedures, cost of side effects, cost of treatment failure (GP visits, surgery, hospitalisation, medical treatment).	**Int 1:** $8,296 (£4,165*) **Int 2:** $6,910 (£3,469*) **p value:** NR	
			Cost-effectiveness cost per QALY gained	TURP dominates TUNA	
			Sensitivity analysis One-way SA	TUNA is cost-effective when either: probability that TURP fails within 6 months ≥20%; time horizon = 5 years; annual failure rate of TUNA ≤ 2.4%; probability of having TURP after TUNA fails =100%	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Murray2001[207] UK **Economic analysis:** cost consequences analysis **Study design** RCT **Duration of follow-up:** 9 months **Discount rates:** Costs: NA Effects: NA	**Patient group:** Men with benign prostatic hypertrophy in 33 general practices in the UK. **<u>All patients</u>** **N:** 112 **Drop outs:** 10 **<u>Group 1</u>** **N:** 57 **Age (mean +/- SD):** 63.7 +/- 8.4 **Drop outs:** 3 **Mean (SD) American Urological Association score:** 15.64 (6.57) **<u>Group 2</u>** **N:** 55* **Age (mean +/- SD):** 63.9 +/- 8.4 **Drop outs:** 7 **Mean (SD) American Urological Association score:** 14.85 (7.10)	**<u>Group 1:</u>** Interactive multimedia programme with booklet and printed summary. Treatment options discussed were surgery, balloon dilatation of the prostate, drugs, and watchful waiting. Information comprised probabilities of the risks and benefits of each treatment, calculated on the basis of information on age, severity of symptoms, and general health entered by the patient at the beginning of the session. All patients saw the core interactive video disc, lasting about 45 minutes; viewing optional sections for further information took up to 60 min. more. A research nurse started the programme, taught the patient how to use it, and then withdrew. **<u>Group 2:</u>** Normal care from GP practitioner.	**Mean (SD) decisional conflict score at nine months**	**Group 1**: 2.23 (0.38) **Group 2**: 2.55 (0.50) **p value:** sig	**Funding:** NHS national research and development programme, the BUPA Foundation, and the King's Fund. **Limitations:** Results on EQ-5D scores were not reported. The intervention might be different to the clinical practice with a consequent overestimation of costs. **Additional outcomes:** No difference in health utility scores (EQ-5D) and anxiety scores (data not provided). Mean decisional conflict score at 3 months (-0.3). GPs and patients' perception of decision making at 3months was significantly different between the two groups with higher proportion of GPs and patients perceiving that the treatment decision had been mainly or only by the patients in Group 1. **Notes:** *Only 48 included in the economic analysis
			Median change in American Urological Association scores	**Group 1**: -1 **Group 2:** -2 **p value:** 0.8	
			Mean cost per patient 1999 GBP, Cost of equipment and staff time, consultations with GPs, referrals to urologists, other referrals, drugs, tests, diagnostic and surgical procedures.	**Group 1:** 594 **Group 2:** 188 **p value:** <0.001	
			Cost-effectiveness	NR	
			Sensitivity analysis	NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Nathan 1996[211] UK **Economic analysis:** cost consequence **Study design** (e.g. RCT, Decision analysis, etc) **Duration of follow-up:** 3 months **Discount rates:** Costs: Effects:	**Patient group:** men requiring TURP **<u>All patients</u>** **N:** 40 **Drop outs:** 0 **<u>Group 1</u>** **N:** 20 **Mean age (range):** 65.4 (57-77) **Mean IPSS score:** 21.9 ± 4.2 **Mean IPSS QoL ± SD:** 4.9 ± 0.7 **Mean Qmax ml/s (± SD):** 10.2 ± 4.4 **Drop outs:** 0 **<u>Group 2:</u>** **N:** 30 **Mean age (range):** 69.2 (57-81) **Mean IPSS score:** 17.0 ± 4.3 **Mean IPSS QoL ± SD:** 4.9 ± 0.7 **Mean Qmax ml/s (± SD):** 7.2 ± 3.5 **Drop outs:** 0	**Group 1:** Transurethral electrovaporisation of the prostate (TVP) **Group 2:** TURP	Mean IPSS score at 3 months (follow up interval not clear)	**Group 1:** 2.86 ± 2.8 **Group 2:** 3.1 ± 2.3 **p value:** NR	**Funding:** NR **Limitations:** Cost components included in the analysis were only those that significantly differed between interventions. **Additional outcomes:** There were more complications in the TURP group. There was no statistically significant or appreciable difference in the success rates among the two groups.
			Mean IPSS QoL score at 3 months (follow up interval not clear)	**Group 1:** 0.5 ± 7 **Group 2:** 0.9 ± 0.9 **p value:** NR	
			Mean Qmax ± SD mL/s at 3 months (follow up interval not clear)	**Group 1:** 21.3 ± 5.9 **Group 2:** 20.6 ± 2.6 **p value:** NR	
			Mean cost per patient 1996 GBP, cost of fibres and consumables, transfusions, and hospital stay.	**Group 1:** £1,730 **Group 2:** £2,373 **p value:** NR	
			Cost-effectiveness	NR	
			Sensitivity analysis	NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Noble 2002[222] UK **Economic analysis:** Cost-consequences analysis **Study design** RCT[74] **Duration of follow-up:** 7.5 months **Discount rates:** Costs: NA Effects: NA	**Patient group:** men with uncomplicated lower urinary tract symptoms (no acute or chronic urinary retention) **<u>All patients</u>** **N:** 340 **Drop outs:** **<u>Group 1</u>** **N:** 117 **Dropouts:**1/117 **Age**, mean (±SD): 67.4±8.1 **IPSS**, mean (±SD): 19.1±6.6 **IPSS-QoL**, median(range): 4(2-6) **<u>Group 2</u>** **N:** 117 **Dropouts:**2/117 **Age**, mean (±SD): 66.4±7.9 **IPSS**, mean (±SD): 19.2±6.7 **IPSS-QoL**, median(range): 4(0-6) **<u>Group 3</u>** **N:** 106 **Dropouts:** 5/106 **Age**, mean (±SD): 67.2±7.8 **IPSS**, mean (±SD): 18.8±6.5 **IPSS-QoL**, median(range): 4(1-6)	**Group 1:** Laser therapy with a noncontact side firing neodymium:YAG probe **Group 2:** Standard transurethral prostate resection **Group 3:** conservative management	Mean difference in IPSS from baseline	**Group 1:** -10.8 **Group 2:** -12.3 **Group 3:** -1.3 **p value:** NR	**Funding:** Bard UK provided the laser fibres. South West and Northern Regional National Health Service Research and Development Directorates. **Limitations:** Resource use data were available only for 30% of the patients population. The conclusions of the study were incorrect. **Additional outcomes:** Patient costs were higher for noncontact laser. **Notes:** * calculated by NCGC using mean cost and mean change in health-related quality of life utility
			Mean difference in IPSS quality of life from baseline	**Group 1:** -1.9 **Group 2:** -2.2 **Group 3:** -1.3 **p value:** NR	
			Mean change in QALY from baseline	**Group 1:** 0.044 **Group 2:** 0.016 **Group 3:** - 0.001 **p value:** NR	
			Mean cost per patient 1998 GBP, cost of resources used in investigations, staff time, equipment, medication, hospital stay, rehospitalisation for catheter-free trial, other rehospitalisation, outpatient visits, GP and nursing visits, consumables (catheter bags, pads and other aids)	**Group 1:** £1,223 **Group 2:** £928 **Group 3:** £45 **p value:** NR	
			Cost-effectiveness* cost per QALY gained	Group 1 vs. Group 2: £10,536 Group 1 vs. Group 3: £26,178	
			Sensitivity analysis one-way	Cost of probes, their multiple use, and machinery lifetime were varied with no considerable difference in results.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Norby2002[223] Denmark **Economic analysis:** CEA **Study design** RCT[224] **Duration of follow-up:** 6 months **Discount rates:** Costs: NA Effects: NA	**Patient group:** Men ≥ 50 years between May 1996 and November 1999. **<u>All patients</u>*** **N:** 113 **<u>Group 1</u>** **N:** 45 **IPSS (±SD):** 21.4 ±5.8 **<u>Group 2</u>** **N:** 46 **IPSS (±SD):** 20.5 ±5.7	**Group 1:** Interstitial laser coagulation (ILC). **Group 2:** Transurethral microwave thermotherapy (TUMT).	Mean difference in IPSS at 6 months from baseline (±SD)	**Group 1:** 12.0 ±7.5 **Group 2:** 11.2 ±9.2 **p value:** Not sig	**Funding:** Vejle County, Denmark. **Limitations:** Small sample size for economic analysis. Short follow-up. Limited applicability. **Notes:** * 22 patients were randomised to a mix of TUIP and TURP and therefore excluded. In the results this group dominates Group 1. **ITT analysis was used for clinical outcomes but not for costs **Data collected in 20 patients only. *** Calculated by using the 2008 PPP ****Incremental analysis done by NCGC
			Mean cost per patient** 1999 DKK, cost of hospitalisation, medications, examinations, follow-up visits, GP visits, nurse visits, and re-operations.	**Group 1:** 14,398 (£1,152***) **Group 2:** 10,508 (£841***) **p value:** NR	
			Cost-effectiveness** cost per 1-point of reduction in IPSS	Group 1 vs. Group 2: DKK 4,862 (£ 388***) per point	
			Sensitivity analysis One way	If TUMT catheters were reused once, Group 1 vs. Group 2 ICER = DKK 7,981 (£ 638***) If ITT analysis is applied, Group 1 vs. Group 2 ICER = DKK 4,161 (£ 332***)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Salonia 2006[267] Italy **Economic analysis:** cost analysis **Study design** RCT **Duration of follow-up:** NR **Discount rates:** Costs: NR Effects: NR	**Patient group:** consecutive patients with symptomatic benign prostatic hyperplasia in a large prostate (70 to 220 g) and documented bladder outlet obstruction. **<u>All patients</u>** **N:** 63 **<u>Group 1</u>** **N:** 29 **IPSS:** 21.6 **Age (mean):** 68.0 **Drop outs:** **<u>Group 2</u>** **N:** 34 **IPSS:** 19.6 **Age (mean):** 67.4 **Drop outs:**	**Group 1:** Open prostatectomy **Group 2:** HoLEP	Operative time (minutes)	**Group 1:** 57.5 **Group 2:** 73.4 **p value:** 0.002	**Funding:** Scientific Institute San Raffaele Hospital, Milan **Limitations:** Partial applicability. **Additional outcomes:** The amount of unplanned events was not significantly different. Notes: *calculated byvusing the 2008 PPP
			Catheterisation time (hours)	**Group 1:** 106.3 **Group 2:** 35.3 **p value:** 0.0001	
			Hospital stay (hours)	**Group 1:** 131.0 **Group 2:** 64.6 **p value:** <0.0001	
			Mean cost per patient 2004 Euro, costs associated with the procedures (operating room time, disposables, blood transfusion) and hospital stay. Medical salaries were not included. Capital cost for HoLEP was 85% of actual capital cost. Holmium fibres were used at least 10 times.	**Group 1:** 2,869 (£2,079*) **Group 2:** 2,356 (£1,708*) **p value:** NR	
			Cost-effectiveness	NR	
			Sensitivity analysis	NR	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Stovsky2006[288] USA **Economic analysis:** Cost consequences analysis **Study design** Decision analysis **Time horizon:** 2 years **Discount rates:** Costs: NR Effects: NR	**Patient group:** patients with lower urinary tract symptoms indicative of BOH requiring procedural management with of the interventions indicated.	**Intervention 1:** Photoselective vaporisation **Intervention 2:** TURP **Intervention 3:** TUNA **Intervention 4:** TUMT Targis **Intervention 5:** TUMT Prostatron 2.5	% change from baseline IPSS at 2 years	**Int 1:** 76 **Int 2:** 66 **Int 3:** 44 **Int 4:** 46 **Int 5**: 39 **p value:** NR	**Funding:** All the authors had financial interest and/or relationship with Laserscope **Limitations:** Discount rate NR. Partially applicable: cost of inpatient stay in the USA is higher than in the UK, which favours laser. **Additional outcomes:** Qmax and QoL were also reported. The cost-effectiveness results did not change if those outcomes were used. **Notes:** * based on the assumption that PVP was performed in a hospital outpatient setting, TUNA and TUMT at a physician office site of service, TURP in a hospital inpatient setting, ILC at a physician office site of service (86%), ambulatory surgery centre (9%) and hospital outpatient setting (5%) ** converted into GBP by using the 2008 PPP ***incontinence, UTI, impotence, dysuria/irritative voiding, bladder neck stenoisis/stricture, urinary retention, hematuria **** calculated by NCGC-ACC
			% change from baseline Quality of Life score at 2 years	**Int 1:** 83 **Int 2:** 73 **Int 3:** 61 **Int 4:** 52 **Int 5:** 24 **p value:** NR	
			% Qmax at 2 years from baseline	**Int 1:** 221 **Int 2:** 117 **Int 3:** 28 **Int 4:** 45 **Int 5:** 45 **p value:** NR	
			Mean cost per patient* 2005 USD**, cost of intervention, follow-up care, adverse events***, re-treatment. Cost of pharmacological therapy not included.	**Int 1:** $ 3,589 (£ 2,315) **Int 2:** $ 4,927 (£ 3,178) **Int 3:** $ 6,179 (£ 3,985) **Int 4: $** 5,699 (£ 3,676) **Int 5: $** 5,488 (£ 3,562) **p value:** NR	
			Cost-effectiveness** cost per 1-point of %reduction in IPSS	Intervention 2 dominates Interventions 3, 4 and 5. Intervention 1 dominates all the other interventions, including 2.	
			Sensitivity analysis One way Threshold SA	If ILC performed in a less costly setting, it is still dominated by PVP. When retreatment rate of PVP = 17%, PVP and TURP are cost equivalent.	

Appendix E – Forest Plots

1 Diagnostic Tests

1.1 Free Uroflowmetry (Peak Urinary Flow)

Figure E-1: Sensitivity and specificity of free uroflowmetry (Qmax) in the diagnosis of bladder outlet obstruction

Figure E-2: Summary receiver operating characteristic (SROC) curve for uroflowmetry Qmax in the diagnosis of bladder outlet obstructions

2 Conservative Interventions

2.1 Pelvic Floor Muscle Training (PFMT)

2.1.1 PFMT vs. Control

Figure E-3: PFMT vs. Control: Number of post-prostatectomy men who were incontinent

Figure E-4: PFMT vs. Control: Mean urine lost (g) per 24 hours (pad test) in post-prostatectomy men

Figure E-5: PFMT vs. Control: Number of post-TURP men who were incontinent

2.2 Biofeedback

2.2.1 Biofeedback + PFMT vs. Control

Figure E-6: PFMT + Biofeedback vs. no intervention: Number of men who were incontinent at follow up

2.3 Electrical Stimulation (ES)

2.3.1 ES + PFMT vs. Control

Figure E-7: ES + PFMT vs. no intervention: Number of men who were incontinent at follow up

3 Pharmacological Interventions

3.1 Alpha-blockers

3.1.1 Alpha-blockers vs. placebo

Figure E-8: Alpha-blockers vs. Placebo: Symptom score (random effects analysis)

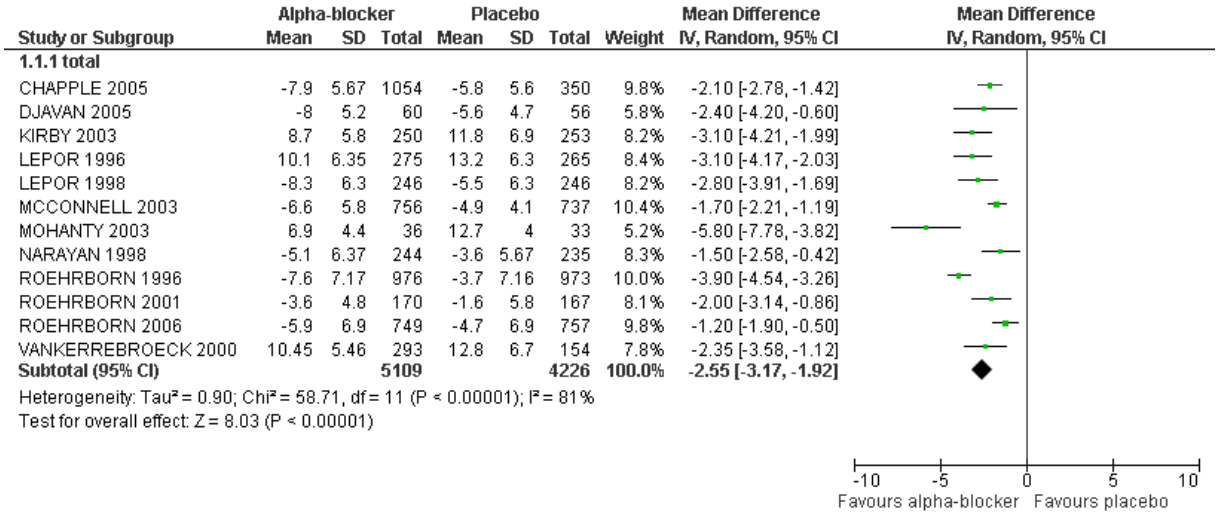


Figure E-9: Alpha-blockers vs. Placebo: Qmax (ml/s) (random effects analysis)

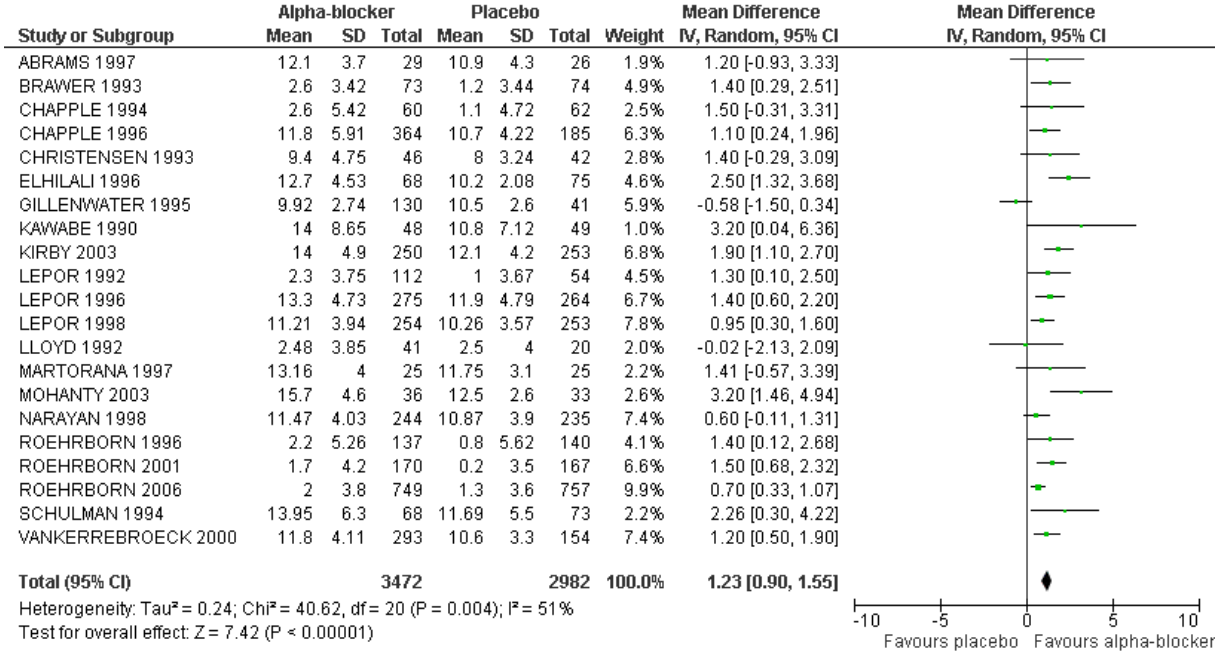


Figure E-10: Alpha-blockers vs. Placebo: Quality of life – IPSS question (random effects analysis)

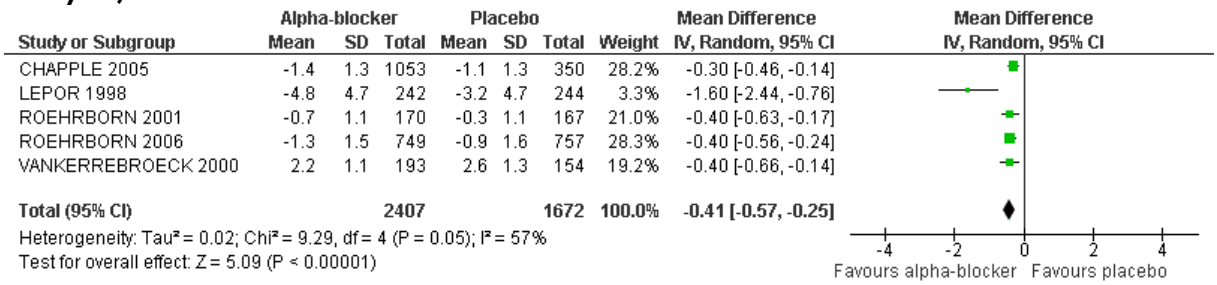


Figure E-11: Alpha-blockers vs. Placebo: Adverse events (cardiovascular and neurological) - asthenia (fatigue) and headache

Figure E-12: Alpha-blockers vs. Placebo: Adverse events (cardiovascular and neurological) - postural hypotension and rhinitis

Figure E-13: Alpha-blockers vs. Placebo: Adverse events - erectile dysfunction /impotence

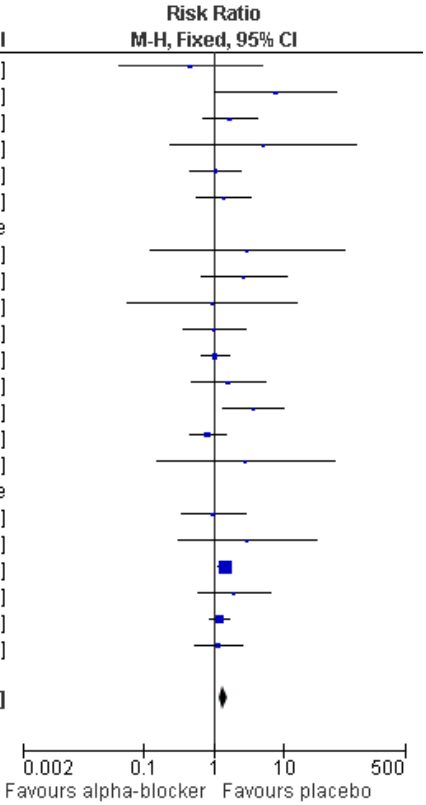
Figure E-14: Alpha-blockers vs. Placebo: Adverse events - dizziness and retrograde ejaculation (random effects analysis)

Figure E-15: Alpha-blockers vs. Placebo: Withdrawal from study due to adverse events

Study or Subgroup	Alpha-blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ABRAMS 1997	1	30	2	28	0.7%	0.47 [0.04, 4.87]
ANDERSEN 2000	31	639	1	156	0.5%	7.57 [1.04, 55.01]
BRAWER 1993	12	81	7	79	2.4%	1.67 [0.69, 4.03]
CHAPPLE 1994	2	67	0	68	0.2%	5.07 [0.25, 103.74]
CHAPPLE 1996	17	382	8	193	3.5%	1.07 [0.47, 2.44]
CHAPPLE 2005	25	1069	6	356	3.0%	1.39 [0.57, 3.36]
DJAVAN 2005	0	61	0	56		Not estimable
FAWZY 1995	1	50	0	50	0.2%	3.00 [0.13, 71.92]
GILLENWATER 1995	22	199	2	49	1.1%	2.71 [0.66, 11.13]
HANSEN 1994	1	104	1	101	0.3%	0.97 [0.06, 15.32]
KAPLAN 2006	7	215	7	220	2.3%	1.02 [0.37, 2.87]
KIRBY 2003	32	275	30	269	10.1%	1.04 [0.65, 1.67]
LEPOR 1992	15	216	3	69	1.5%	1.60 [0.48, 5.35]
LEPOR 1996	18	305	5	305	1.7%	3.60 [1.35, 9.57]
LEPOR 1998	18	254	22	254	7.3%	0.82 [0.45, 1.49]
LLOYD 1992	4	66	0	20	0.3%	2.82 [0.16, 50.27]
MOHANTY 2003	0	38	0	34		Not estimable
NORDLING 2005	10	312	5	154	2.2%	0.99 [0.34, 2.84]
RESNICK 2007	3	185	1	185	0.3%	3.00 [0.31, 28.58]
ROEHRBORN 1996	168	1053	114	1031	38.3%	1.44 [1.16, 1.80]
ROEHRBORN 2001	8	176	4	172	1.3%	1.95 [0.60, 6.37]
ROEHRBORN 2006	69	749	58	757	19.2%	1.20 [0.86, 1.68]
SOLOWAY 1992	12	96	11	103	3.5%	1.17 [0.54, 2.53]
Total (95% CI)		**6622**		**4709**	**100.0%**	**1.37 [1.19, 1.58]**
Total events	476		287			

Heterogeneity: Chi² = 16.77, df = 20 (P = 0.67); I² = 0%

Test for overall effect: Z = 4.34 (P < 0.0001)



3.1.2 Alpha-blockers vs. 5-Alpha reductase inhibitors (5-ARI)

Figure E-16: Alpha-blockers vs. 5-ARI: Symptom score

Figure E-17: Alpha-blockers vs. 5-ARI: Quality of life (IPSS-question)

Figure E-18: Alpha-blockers vs. 5-ARI: Qmax (ml/s)

Figure E-19: Alpha-blockers vs. 5-ARI: Prostate volume (ml)

Figure E-20 Alpha-blockers vs. 5-ARI: PSA (ng/ml)

Figure E-21: Alpha-blockers vs. 5-ARI: Adverse events (cardiovascular or neurological)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998 and Rigatti2003, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

Figure E-22: Alpha-blockers vs. 5-ARI: Adverse events (sexual or urological)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998 and Rigatti2003, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

Figure E-23: Alpha-blockers vs. 5-ARI: Adverse events - postural hypotension and ejaculatory abnormality (random effects analysis)

Figure E-24: Alpha-blockers vs. 5-ARI: Ejaculatory abnormality – subgroup analysis of tamsulosin and other alpha-blockers

Figure E-25: Alpha-blockers vs. 5-ARI: Withdrawal from study due to adverse events (random effects analysis)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998 and Rigatti2003, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

3.1.3 Alpha-blockers vs. Anticholinergics

See section 3.3.2 Anticholinergics vs. Alpha-blockers

3.1.4 Alpha-blockers vs. Phosphodiesterase 5-inhibitors (PDE5-I)

See section 3.4.2 PDE5-I vs. Alpha-blockers

3.2 5-alpha reductase inhibitors (5-ARI)

3.2.1 5-ARI vs. placebo

Figure E-26: 5-ARI vs. Placebo: Symptom score at 3 months, 6 months 2 years and 4 years or longer (random effects analysis)

Figure E-27: 5-ARI vs. Placebo: Symptom score at 2 years- subgroup analysis

Figure E-28: 5-ARI vs. Placebo: Symptom score at 12 months and 3 years

Figure E-29: 5-ARI vs. Placebo: Qmax (ml/s) at 3 months, 6 months, 2 years, 3 years and 4 years or longer

Figure E-30: 5-ARI vs. Placebo: Qmax (ml/s) at 12 months (random effects analysis)

Figure E-31: 5-ARI vs. Placebo: Prostate volume(ml) at 1 year follow up

Figure E-32: 5-ARI vs. Placebo: Prostate volume (ml) at 2 years follow up (random effects analysis)

Figure E-33: 5-ARI vs. Placebo: PSA (ng/ml) level at 2 year follow up

Figure E-34: 5-ARI vs. Placebo: Adverse events (cardiovascular and neurological)

Figure E-35: 5-ARI vs. Placebo: Adverse events (sexual and urological)

Figure E-36: 5-ARI vs. Placebo: Withdrawal from study due to adverse events

3.2.2 5-Alpha reductase inhibitors (5-ARI) vs. Alpha-blockers

See section 3.1.2: Alpha-blockers vs. 5-Alpha reductase inhibitors (5-ARI)

3.3 Anticholinergics

3.3.1 Anticholinergics vs. placebo

Figure E-37: Anticholinergics vs. Placebo: Adverse events

Figure E-38: Anticholinergics vs. Placebo: Withdrawal from study due to adverse events

3.3.2 Anticholinergics vs. Alpha-blockers

Figure E-39: Anticholinergics vs. Alpha-blockers: Adverse events

3.4 Phosphodiesterase-5-inhibitors (PDE5-I)

3.4.1 PDE5-I vs. placebo

Figure E-40: PDE5-I vs. Placebo: Symptom score

Figure E-41: PDE5-I vs. Placebo: Quality of life (IPSS question)

Figure E-42: PDE5-I vs. Placebo: Qmax(ml/s)

Figure E-43: PDE5-I vs. Placebo: Adverse events

3.4.2 PDE5-I vs. Alpha-blockers

Figure E-44: PDE5-I vs. Alpha-blockers: Symptom score

Figure E-45: PDE5-I vs. Alpha-blockers: Qmax (ml/s)

Figure E-46: PDE5-I vs. Alpha-blockers: Voiding frequency

Figure E-47: PDE5-I vs. Alpha-blockers: Nocturia

Figure E-48: PDE5-I vs. Alpha-blockers: Adverse events

3.5 Diuretics

3.5.1 Diuretics vs. placebo

Forest plots were not prepared for this comparison. Please see Evidence Table 16 in Appendix D for details.

3.6 Desmopressin

3.6.1 Desmopressin vs. placebo

Forest plots were not prepared for the efficacy outcomes of this cross over trial. Please see Evidence Table 17 in Appendix D for details.

Figure E-49: Desmopressin vs. Placebo: Adverse events

This is a cross over trial and a paired test would be more appropriate. Forest plots prepared for illustration purpose.

3.7 NSAIDS

3.7.1 NSAIDS vs. placebo

Figure E-50: NSAIDs vs. Placebo: Symptom score at 1 month

Figure E-51: NSAIDs vs. Placebo: Qmax (ml/s) at 1 month

Figure E-52: NSAIDs vs. Placebo: Nocturia frequency at 1month

Figure E-53: NSAIDs vs. Placebo: Adverse events (1 month follow up)

Only one type of adverse event was reported.

3.8 Combination therapy: Alpha-blockers plus 5-alpha reductase inhibitors(5-ARI)

3.8.1 Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers

Figure E-54: Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers: Symptom score

Figure E-55: Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers: Qmax (ml/s)

Figure E-56: Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers: Prostate volume(ml)

Figure E-57: Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers: PSA (ng/ml)

Figure E-58: Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers: Adverse events (cardiovascular or neurological)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

Continued Figure E-58: Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers: Adverse events (cardiovascular or neurological

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

Figure E-59: Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers: Adverse events (sexual or urological)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

Figure E-60: Combination (Alpha-blockers + 5-ARI) vs. Alpha-blockers: Withdrawal from study due to adverse events

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

3.8.2 Combination (Alpha-blockers + 5-ARI) vs. 5-ARI

Figure E-61: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Symptom score

Figure E-62: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Qmax(ml/s)

Figure E-63: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Prostate volume (ml)

Figure E-64: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: PSA (ng/ml)

Figure E-65: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Adverse events (Cardiovascular or neurological)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

Continued Figure E-65: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Adverse events (cardiovascular or neurological)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

Figure E-66: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Adverse events (sexual or urological)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998, 1 year for Lepor1996 and Kirby2003, 2 years for Roehrborn2008 and 4 years for McConnell2003)

Figure E-67: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Ejaculatory abnormality (random effects analysis)

Figure E-68: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Ejaculatory abnormality subgroup analysis

Figure E-69: Combination (Alpha-blockers + 5-ARI) vs. 5-ARI: Withdrawal from study due to adverse events (random effects analysis)

The studies were arranged in the forest plots based on duration of follow up (6 months for Debruyne1998, 1 year for Lepor1996 and Kirby2003 and 2 years for Roehrborn2008)

3.8.3 Combination (Alpha-blockers + 5-ARI) vs. placebo

Figure E-70: Combination (Alpha-blockers + 5-ARI) vs. Placebo: Symptom score

Figure E-71: Combination (Alpha-blockers + 5-ARI) vs. Placebo: Qmax (ml/s)

Figure E-72: Combination (Alpha-blockers + 5-ARI) vs. Placebo: Prostate volume (ml)

Figure E-73: Combination (Alpha-blockers + 5-ARI) vs. Placebo: Change in PSA (ng/ml)

Figure E-74: Combination (Alpha-blockers + 5-ARI) vs. Placebo: Adverse events (cardiovascular and neurological)

The studies were arranged in the forest plots based on duration of follow up (1 year for Lepor1996 and Kirby2003 and 4 years for McConnell2003)

Figure E-75: Combination (Alpha-blockers + 5-ARI) vs. Placebo: Adverse events – postural hypotension (random effects analysis)

Figure E-76: Combination (Alpha-blockers + 5-ARI) vs. Placebo: Adverse events (sexual or urological)

Figure E-77: Combination (Alpha-blockers + 5-ARI) vs. Placebo: Withdrawal from study due to adverse events (random effects analysis)

The studies were arranged in the forest plots based on duration of follow up (1 year for Lepor1996 and Kirby2003 and 4 years for McConnell2003)

3.9 Combination Therapy : Anti-cholinergic plus Alpha-blockers

3.9.1 Combination (Anti-cholinergic + Alpha-blockers) vs. Alpha-blockers

Figure E-78: Combination (Anti-cholinergic + Alpha-blockers) vs. Alpha-blockers: Adverse events

3.9.2 Anti-cholinergic added on to Alpha-blockers vs. Alpha-blockers

Figure E-79: Anti-Ch added on to Alpha-blockers vs. Alpha-blockers: Symptom score at 3 months

Study or Subgroup	Anticholinergic add on Mean	SD	Total	Alpha blockers Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Macdiarmid2008	-6.9	6.5	209	-5.2	6.2	209	-1.70 [-2.92, -0.48]

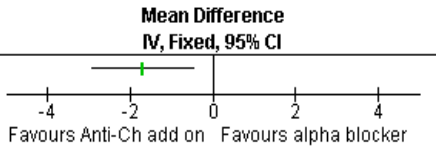


Figure E-80: Anti-Ch added on to Alpha-blockers vs. Alpha-blockers: Quality of life (IPSS question)at 3 months

Study or Subgroup	Anticholinergic add on Mean	SD	Total	Alpha blockers Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Macdiarmid2008	-1.3	1.5	209	-0.8	1.4	209	-0.50 [-0.78, -0.22]

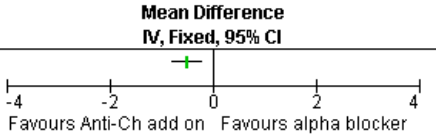


Figure E-81: Anti-Ch added on to Alpha-blockers vs. Alpha-blockers: Qmax (ml/s) at 3 months

Study or Subgroup	Anti-Ch add on Mean	SD	Total	Alpha blockers Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Macdiarmid2008	-0.2	7.8	209	0.1	7.6	209	-0.30 [-1.78, 1.18]

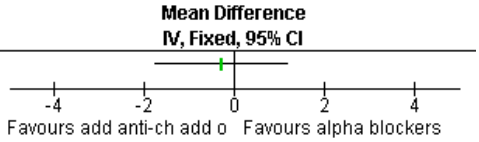
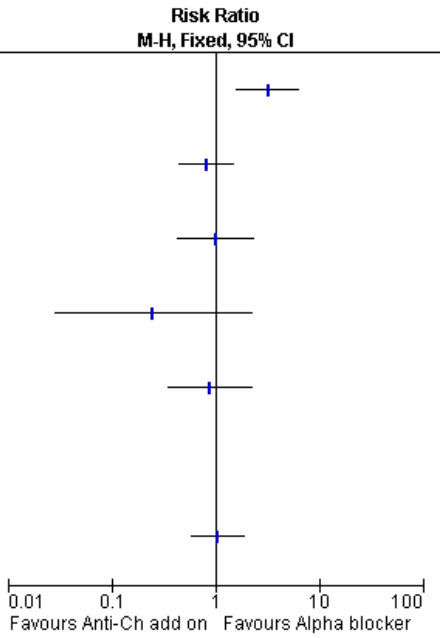


Figure E-82: Anti-Ch added on to Alpha-blockers vs. Alpha-blockers: Adverse events (3-months follow up)

Study or Subgroup	Anticholinergic add on Events	Total	Alpha blockers Events	Total	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Dry mouth					
Macdiarmid2008	32	209	10	209	3.20 [1.62, 6.34]
1.4.2 Infections and infestations					
Macdiarmid2008	18	209	22	209	0.82 [0.45, 1.48]
1.4.3 Renal and urinary adverse events					
Macdiarmid2008	10	209	10	209	1.00 [0.43, 2.35]
1.4.4 Constipations					
Macdiarmid2008	1	209	4	209	0.25 [0.03, 2.22]
1.4.5 Nervous system disorders					
Macdiarmid2008	8	209	9	209	0.89 [0.35, 2.26]
1.4.6 Acute urinary retention					
Macdiarmid2008	0	209	0	209	Not estimable
1.4.7 Adverse events leading to withdrawals					
Macdiarmid2008	21	209	20	209	1.05 [0.59, 1.88]



3.9.3 Combination (Anti-cholinergic + Alpha-blockers) vs. Anticholinergics

Figure E-83: Combination (Anti-cholinergic + Alpha-blockers) vs. Anticholinergics: Adverse events

3.9.4 Combination (Anti-cholinergic + Alpha-blockers) vs. Placebo

Figure E-84: Combination (Anti-cholinergic + Alpha-blockers) vs. Placebo: adverse events

3.10 Combination (PDE5-I + Alpha-blockers)

3.10.1 Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers

Figure E-85: Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers: Symptom score

Figure E-86: Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers: Quality of life (IPSS question)

Figure E-87: Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers: Qmax(ml/s)

Figure E-88: Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers: Frequency at 3-month

Figure E-89: Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers: Nocturia at 3 months

Figure E-90: Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers: Adverse events

Continued Figure E-90: Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers: Adverse events

Figure E-*91*: Combination (PDE5-I + Alpha-blockers) vs. Alpha-blockers: Adverse events resulting in withdrawal at 3-month

3.10.2 Combination (PDE5-I + Alpha-blockers) vs. PDE5-I

Figure E-92: Combination (PDE5-I + Alpha-blockers) vs. PDE5-I: symptom score (random effects analysis)

Figure E-93: Combination (PDE5-I + Alpha-blockers) vs. PDE5-I: Quality of life (IPSS-QoL) up to 3-month

Figure E-94: Combination (PDE5-I + Alpha-blockers) vs. PDE5-I: Qmax (ml/s) at 3-month

Figure E-95: Combination (PDE5-I + Alpha-blockers) vs. PDE5-I: Frequency at 3-month

Figure E-96: Combination (PDE5-I + Alpha-blockers) vs. PDE5-I: Nocturia at 3-month

Figure E-97: Combination (PDE5-I + Alpha-blockers) vs. PDE5-I: Adverse events (only those resulting in withdrawals reported)

Figure E-98: Combination (PDE5-I + Alpha-blockers) vs. PDE5-I: Withdrawal from study due to adverse events

4 Surgery

4.1 Holmium Laser Enucleation of the Prostate (HoLEP

4.1.1 HoLEP vs. Transurethral resection of the prostate (TURP)

Figure E-99: HoLEP vs. TURP: Symptom score at 3 months, 36 months and 48 months

Figure E-100: HoLEP vs. TURP: Symptom score at 6, 12 and 24 months (random effects analysis)

Figure E-101: HoLEP vs. TURP: Quality of life (IPSS question) – 3, 24 and 48 months

Figure E-102: HoLEP vs. TURP: Quality of life (IPSS question) – 6 to 12 months (random effects analysis)

Figure E-103: HoLEP vs. TURP: Qmax(ml/s) at 3 months and longest available follow up

Figure E-104: HoLEP vs. TURP: All cause mortality and complications

Continued Figure E-104: HoLEP vs. TURP: All cause mortality and complications

4.1.2 Thulium laser resection vs. TURP

Figure E-105: Thulium laser resection vs. TURP: Symptom score – 6 months postoperatively

Figure E-106: Thulium laser resection vs. TURP: Symptom score – 12 months postoperatively

Figure E-107: Thulium laser resection vs. TURP: Qmax(ml/s) – 12 months postoperatively

Figure E-108: Thulium laser resection vs. TURP: Quality of life (IPSS question) – 6 and 12 months

Figure E-109: Thulium laser resection vs. TURP: Complications

4.1.3 HoLEP vs. Transurethral Incision of the Prostate (TUIP)

Figure E-110: HoLEP vs. TUIP: Symptom score

* Only one study using holmium laser for bladder neck incision (HoBNI) was found.

Figure E-111: HoLEP vs. TUIP: quality of life (IPSS question)

Figure E-112: HoLEP vs. TUIP: Qmax(ml/s)

Figure E-113: HoLEP vs. TUIP: All cause mortality and complications

4.1.4 HOLEP vs. Open prostatectomy (OP)

Figure E-114: 1 HoLEP vs. OP: Symptom score

Figure E-115: 1 HoLEP vs. OP: quality of life (IPSS question

Figure E-116: 1 HoLEP vs. OP: Qmax(ml/s) at 3 months (random effects analysis) and longest available follow up (fixed effects analysis)

Figure E-117: 1 HoLEP vs. OP: All cause mortality and complications

4.2 Laser treatments

4.2.1 Laser Coagulation Techniques vs. TURP

Figure E-118: 1 Laser Coagulation Techniques vs. TURP: Symptom score at 3 and 6 months (random effects analysis), 12 months and 24 months (change and endpoints)

Figure E-119: Laser Coagulation Techniques vs. TURP: Quality of life (IPSS question), change and endpoints.

Figure E-120: Laser Coagulation Techniques vs. TURP: Qmax (ml/s)

Figure 121: Laser Coagulation Techniques vs. TURP: All cause mortality and complications

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Continued Figure 121 Laser Coagulation Techniques vs. TURP: All cause mortality and complications

Figure E-122: Laser Coagulation Techniques vs. TURP: Complications – retrograde ejaculation (random effects analysis)

4.2.2 Laser Coagulation Techniques vs. TURP in AUR patients

Figure E-123: Laser Coagulation Techniques vs. TURP in AUR patients: Symptom score change

Figure E-124: Laser Coagulation Techniques vs. TURP in AUR patients: Quality of life (IPSS question), change

Figure E-125: Laser Coagulation Techniques vs. TURP in AUR patients: Complications

4.2.3 Laser Vaporisation Techniques vs. TURP

Figure E-126: Laser Vaporisation Techniques vs. TURP: Symptom score at 3 months and 6 months (random effects analysis)

Figure E-127: Laser Vaporisation Techniques vs. TURP: Symptom score at 1, 2, 3 and 5 years (fixed effects analysis)

Figure E-128: Laser Vaporisation Techniques vs. TURP: quality of life (IPSS question)

Figure E-129: Laser Vaporisation Techniques vs. TURP: Qmax(ml/s) – 3 months(fixed effect analysis) and longest available follow up(random effects analysis)

Figure E-130: Laser Vaporisation Techniques vs. TURP: All cause mortality and complications

Continued Figure E-130: Laser Vaporisation Techniques vs. TURP : Complications

Figure E-131: Laser Vaporisation Techniques vs. TURP: Complications – retrograde ejaculation (random effects analysis)

4.2.4 Laser (photoselective vaporisation) vs. Open prostatectomy(OP)

Figure E-132: Laser (photoselective vaporisation) vs. OP: Complications

4.2.5 Laser coagulation vs. TUMT (Transurethral Microwave Thermotherapy)

Figure E-133: Laser coagulation vs. TUMT –Symptom score at 6 months

Figure E-134: Laser coagulation vs. TUMT – Qmax(ml/s) at 6 months

Figure E-135: Laser coagulation vs. TUMT: Complications

4.2.6 Laser vs. TUVP (Transurethral Vaporisation of the Prostate)

Figure E-136: Laser vs. TUVP: Symptom score (random effects analysis)

Figure E-137: Laser vs. TUVP – Quality of life (IPSS question)

Figure E-138: Laser vs. TUVP – Qmax(ml/s) at 6 month, 12 month(fixed effect analysis) and longest available follow up (random effects analysis)

No 3 month data was available for this comparison.

Figure E-139: Laser vs. TUVP – All cause mortality and complications

4.2.7 Laser vs. laser

4.2.7.1 Laser Vaporisation Techniques vs. Laser Coagulation Techniques

Figure E-140: Laser Vaporization Techniques vs. Laser Coagulation Techniques: Symptom score at 3 months (random effects analysis)

Figure E-140b: Laser Vaporisation Techniques vs. Laser Coagulation Techniques: Symptom score at 6, 12 and 24 months (fixed effect analysis)

Figure E-141: Laser Vaporisation Techniques vs. Laser Coagulation Techniques: Qmax (ml/s) at 3 months and longest available follow up

Figure E-142: Laser Vaporisation Techniques vs. Laser Coagulation Techniques: Complications

4.2.7.2 Holmium laser resection of the prostate(HoLRP) vs. Laser coagulation

Figure E-143: HoLRP vs. Laser coagulation: Complications

4.2.7.3 Holmium Laser Ablation of the Prostate(HoLAP) vs. Laser Vaporisation

Figure E-144: HoLAP vs. Laser vaporisation: Symptom score

Only one study was using photoselective laser vaporisation (PVP) method was found

Figure E-145: HoLAP vs. Laser vaporisation: quality of life (IPSS question)

Figure E-146: HoLAP vs. laser vaporisation: Qmax(ml/s) at 3 and longest available follow up(12 months)

Figure E-147: HoLAP vs. laser vaporisation: All cause mortality and complications

4.3 Transurethral Microwave Thermotherapy (TUMT)

4.3.1 TUMT vs. Sham procedure

Figure E-148: TUMT vs. SHAM: Symptom score at 3 and 6 months

Figure E-149: TUMT vs. SHAM: Qmax(ml/s)and 3 months and at long term follow up

Figure E-150: TUMT vs. SHAM: All cause mortality and complications

Figure E-151: TUMT vs. SHAM: Complications – reoperatoions (random effects analysis)

4.3.2 TUMT vs. TURP

Figure E-152: TUMT vs. TURP: Symptom score at 3, 12 and 36 months (random effects analysis)

Figure E-153: TUMT vs. TURP: Symptom score at 6, 24, 48 and 60 months postoperatively

Figure E-154: TUMT vs. TURP: Qmax(ml/s) at 3 months and longest available follow up (random effects analysis)

Figure E-155: TUMT vs. TURP: Quality of life (IPSS question) at 3 and 6 months postoperatively

Figure E-156: TUMT vs. TURP: quality of life (IPSS question) at 12 months postoperatively (random effects analysis)

Figure E-157: TUMT vs. TURP: quality of life (IPSS question) at 48 and 60 months postoperatively

Figure E-158: TUMT vs. TURP: All cause mortality and complications

Continued Figure E-158: TUMT vs. TURP: Complications

Figure E-159: TUMT vs. TURP: Complications - Incontinence and retrograde ejaculation (random effects analysis)

4.3.3 TUMT vs. Laser

See section 4.2.5 Laser coagulation vs. TUMT (Transurethral Microwave Thermotherapy)

4.4 TUVP

4.4.1 TUVP vs. TURP

Figure E-160: TUVP vs. TURP: Symptom score at 3, 6 and 12 months and 5 years or more postoperatively (fixed effects model)

Figure E-161: TUVP vs. TURP: Symptom score at 2 and 3 years postoperatively (random effects analysis)

Figure E-162: TUVP vs. TURP: Quality of life (IPSS question)

Figure E-163: TUVP vs. TURP: Quality of life (IPSS question) – 1 year and 2 year postoperatively (random effects analysis)

Figure E-164: TUVP vs. TURP: Qmax(ml/s) at 3 months (fixed effect analysis) and longest available follow up(random effects analysis)

Figure E-165: TUVP vs. TURP: All cause mortality and complications

Continued Figure E-165: TUVP vs. TURP: All cause mortality and complications

Figure E-166: TUVP vs. TURP: Complications – retrograde ejaculation (random effects analysis)

4.4.2 Bipolar TUVP vs. TURP

Figure E-167: Bipolar TUVP vs. TURP: Symptom score

Figure E-168: Bipolar TUVP vs. TURP: Qmax(ml/s) at 3 months and longest available follow up

Figure E-169: Bipolar TUVP vs. TURP: All cause mortality and complications

4.4.3 TUVP vs. Laser

See section 4.2.6 Laser vs. TUVP (Transurethral Vaporisation of the Prostate)

4.5 Transurethral Needle Ablation of the Prostate (TUNA)

4.5.1 TUNA vs. TURP

Figure E-170: TUNA vs. TURP: Symptom score

Figure E-171: TUNA vs. TURP: Quality of life (IPSS question)

Figure E-172: TUNA vs. TURP: Qmax(ml/s)

Figure E-173: TUNA vs. TURP: All cause mortality and complications

4.6 Transurethral Incision of the Prostate (TUIP)

4.6.1 TUIP vs. TURP

Figure E-174: TUIP vs. TURP: Symptom score

Figure E-175: TUIP vs. TURP: Quality of life (IPSS question)

Figure E-176: TUIP vs. TURP: Qmax (ml/s)

Figure E-177: TUIP vs. TURP: All cause mortality and complications

Figure E-178: TUIP vs. TURP: Complications – retrograde ejaculation (random effects analysis)

4.6.2 TUIP vs. TURP in AUR patients

Figure E-179: TUIP vs. TURP in AUR patients: All cause mortality and complications

4.6.3 TUIP vs. HOLEP

See 4.1.3HoLEP vs. Transurethral Incision of the Prostate (TUIP)

4.7 Botulinum toxin in the prostate

4.7.1 Botulinum toxin vs. placebo

Figure E-180: Botulinum toxin vs. placebo: Symptom score at 1- and 2-month follow up

Figure E-181: Botulinum toxin vs. placebo: Qmax (ml/s) at-2 month follow up

Figure E-182: Botulinum toxin vs. placebo: Complications (urinary incontinence) – 2 month follow up

4.8 Transurethral Vapouresection of the Prostate (TUVRP)

4.8.1 TUVRP vs. TURP

Figure E-183: TUVRP vs. TURP: Symptom score at 3 months, 1 year and 2 years follow up

Figure E-184: TUVRP vs. TURP: Symptom score at 6 months follow up (random effects analysis)

Figure E-185: TUVRP vs. TURP: Quality of life (IPSS question)

Figure E-186: TUVRP vs. TURP: Qmax (ml/s)

Figure E-187: TUVRP vs. TURP: All cause mortality and complications

Figure E-188: TUVRP vs. TURP: Complications – retrograde ejaculation (random analysis)

4.8.2 Bipolar TUVRP vs. TURP

Figure E-189: Bipolar TUVRP vs. TURP: Symptom score at 3-month follow up

Figure E-190: Bipolar TUVRP vs. TURP: Quality of life (IPSS question) at 3-month follow up

Figure E-191: Bipolar TUVRP vs. TURP: Qmax(ml/s) at 3-month follow up

Figure E-192: Bipolar TUVRP vs. TURP: Complications

4.9 Transurethral Ethanol Ablation of the Prostate (TEAP)

4.9.1 TEAP vs. TURP

Figure E-193: TEAP vs. TURP: Complications

4.10 Open Prostatectomy (OP)

4.10.1 Open prostatectomy vs. HOLEP

See section 4.1.4 on HOLEP vs. Open prostatectomy (OP)

4.10.2 Open prostatectomy vs. laser vaporisation

See section 4.2.4 on Laser (photoselective vaporisation) vs. Open prostatectomy(OP)

4.11 Transurethral Resection of the Prostate TURP

4.11.1 TURP vs. Watchful Waiting

Figure E-194: TURP vs. Watchful waiting: Qmax (ml/s)

Figure E-195: TURP vs. Watchful waiting: All cause mortality and complications

4.11.2 Bipolar TURP vs. TURP

Figure E-196: Bipolar TURP vs. TURP: Symptom score

Figure E-197: Bipolar TURP vs. TURP: Quality of life (IPSS question)

Figure E-198: Bipolar TURP vs. TURP: Qmax (ml/s) at 3 months or longest available follow up

Figure E-199: Bipolar TURP vs. TURP: All cause mortality and complications

Continued Figure E-199b: Bipolar TURP vs. TURP: All cause mortality and complications

4.11.3 TURP vs. TUVP

See section 4.4.1 TUVP vs. TURP

4.11.4 TURP vs. TUNA

See section 4.5.1TUNA vs. TURP

4.11.5 TURP vs. Laser

See sections 4.2.1Laser Coagulation Techniques vs. TURP, 4.2.2 Laser Coagulation Techniques vs. TURP in AUR patients, 4.2.3 Laser Vaporisation Techniques vs. TURP

4.11.6 TURP vs. TUMT

See section 4.3.2 TUMT vs. TURP

4.11.7 TURP vs. TUIP

See section 4.6.1 TUIP vs. TURP

4.11.8 TURP vs. HoLEP

See section 4.1.1 HoLEP vs. TURP

4.11.9 TURP vs. TUVP

See section 4.4.1 TUVP vs. TURP

4.11.10 TURP vs. Bipolar TUVP

See section 4.4.2 Bipolar TUVP vs. TURP

4.11.11 TURP vs. TUVRP

See section 4.8.1 TUVRP vs. TURP

4.11.12 TURP vs. Bipolar TUVRP

See section 4.8.2 Bipolar TUVRP vs. TURP

4.11.13 TURP vs. TEAP

See section 4.9.1 TEAP vs. TURP

5 Surgical vs. Medical Interventions

There are no forest plots for this section

6 Medical vs. Conservative Interventions

No results found – no forest plots

7 Surgical vs. Conservative Interventions

7.1.1 Bladder training vs. TURP

Figure E-200: Bladder training vs. TURP: Symptom score change at 6 months follow up

Figure E-201: Bladder training vs. TURP: Symptom score change at 6 months follow up

Figure E-202: Bladder training vs. TURP: Qmax (ml/s) change at 6 months follow up

7.1.2 Self-catheterisation vs. TURP

Figure E-203: Self catheterisation vs. TURP in men with chronic urinary retention: Symptom score change at 6 months follow up

Figure E-204: Self catheterisation vs. TURP in men with chronic urinary retention: quality of life (IPSS question) change at 6 months follow up

8 Urinary retention

8.1.1 Acute urinary retention

Figure E-205: Alpha-blockers vs. placebo in men with acute urinary retention: Able to void

Figure E-206: Alpha-blockers vs. placebo in men with acute urinary retention: Re-catheterisation

8.2 Chronic retention

See forest plots in section surgery vs. conservative and conservative

9 Alternative and complementary therapies

9.1 Phytotherapy vs. placebo

9.1.1 Beta-sitosterol

Figure E-207: Beta-sitosterol vs. placebo: Symptom score

Figure E-208: Beta-sitosterol vs. placebo: Qmax (ml/s)

9.1.2 Serenoa repens

Figure E-209: Serenoa repens vs. placebo: Symptom score

Figure E-210: Serenoa repens vs. placebo: Qmax (ml/s)

Figure E-211: Serenoa repens vs. placebo: Quality of life (IPSS question)

9.1.3 Urtica diocia

Figure E-212: Urtica diocia vs. placebo: Symptom score

Figure E-213: Urtica diocia vs. placebo: Qmax (ml/s)

9.1.4 Pygeum

Figure E-214: Urtica diocia vs. placebo: Qmax(ml/s)

9.1.5 Cernilton

Figure E-215: Cernilton vs. placebo: Qmax (ml/s)

9.1.6 Phytotherapy combinations

Figure E-216: Combination of serenoa repens and uritca diocia vs. placebo: Symptom score

Figure E-217: Combination of serenoa repens and uritca diocia vs. placebo: Qmax (ml/s)

Figure E-218: Combination of pygeum and uritca diocia vs. placebo: Symptom score

Figure E-219: Combination of pygeum and uritca diocia vs. placebo: Qmax (ml/s)

Figure E-220: Combination of pygeum and uritca diocia vs. placebo: Quality of life (IPSS question)

Figure E-221: Combination of cernitin, serona repens, phytosterol and Vitamin E vs. placebo: Symptom score

Figure E-222: Combination of cernitin, serona repens, phytosterol and Vitamin E vs. placebo: Qmax (ml/s)

9.2 Phytothearpy vs. Alpha-blockers

9.2.1 Serenoa repens vs. Alpha-blockers

Figure E-223: Phytotherapy vs. Alpha-blockers: Symptom score

Figure E-224: Phytotherapy vs. Alpha-blockers: Quality of life (IPSS question)

Figure E-225: Phytotherapy vs. Alpha-blockers: Qmax (ml/s)

Figure E-226: Phytotherapy vs. Alpha-blockers: Urinary retention

9.3 Phytotherapy vs. 5-ARI

9.3.1 Serenoa repens vs. 5-ARI

Figure E-227: Serenoa repens vs. 5-alpha-reductase inhibitors: Symptom score

Figure E-228: Serenoa repens vs. 5-alpha-reductase inhibitors: quality of life (IPSS question)

Figure E-229: Serenoa repens vs. 5-alpha-reductase inhibitors: Qmax (ml/s) at longest available follow up

Figure E-230: Serenoa repens vs. 5-alpha-reductase inhibitors: Urinary retention

9.3.2 Serenoa repens and urtica diocia vs. 5-ARI

Figure E-231: Serenoa repens and urtica diocia vs. 5-alpha-reductase inhibitors: Symptom score

Figure E-232: Serenoa repens and urtica diocia vs. 5-alpha-reductase inhibitors: Qmax (ml/s) at 3 months and 12 months

10 Provision of information

10.1 Educational intervention vs. no intervention

Figure E-233: Interactive video vs. no intervention: Decisional conflict score

10.2 Self management vs. standard care

Figure E-234: Self management vs. standard care: symptom score

Figure E-235: Self management vs. standard care: Treatment failure

Appendix F - Cost-effectiveness analysis

10.1 Introduction

Two original cost-effectiveness analyses were carried out to answer the clinical questions on transurethral resection of the prostate (TURP) vs. laser (Chapter 8), and the clinical question on Alpha-blockers (AB) alone or in combination with 5-Alpha Reductase-Inhibitors (5-ARI) (Chapter 6). Throughout the guideline we refer to these two analyses respectively as 'NCGC Surgery Model' and 'NCGC Combination model'.

10.2 Methods

A review of the literature was conducted followed by economic modelling of the cost-effectiveness of the listed interventions in England and Wales. The literature search and review methods can be found in Chapter 2.

Our aim in constructing the models was to determine the most cost-effective strategy in men considering respectively surgery and medical treatment. Those would be mainly men with moderate to severe lower urinary tract symptoms (LUTS).

We found a number of economic evaluations in the published literature (Chapters 6 and 8), among which a Health Technology Assessment (HTA) model of good quality[172]. However the Guideline Development Group (GDG) felt that they needed an original model with slightly different assumptions and data in order to make a recommendation with confidence.

The following general principles were adhered to:

- The GDG was consulted during the construction and interpretation of the model.
- When published data was not available we used expert opinion to populate the model.
- Model assumptions were reported fully and transparently.
- The results were subject to sensitivity analysis and limitations were discussed.
- We followed the methods of the NICE reference case[215]. Therefore costs were calculated from a health services perspective. Health gain was measured in terms of quality-adjusted life-years (QALYs) gained. Both future costs and QALYs were discounted at 3.5%.
- The model employed a cost-effectiveness threshold of £20,000 per QALY gained.
- The model was peer-reviewed by another health economist at the NCGC.

10.2.1 Software

The cost-effectiveness analyses were conducted using TreeAge Pro 2008.

10.3 NCGC Surgery model

10.3.1 General method

We based the model on two of the main outcomes considered in our systematic review of the clinical evidence (Chapter 2.4): mean IPSS change from baseline and adverse events. We chose IPSS change because it better expresses the change in quality of life as felt by the patient compared to other clinical measures such as Qmax. Consequently, it was easier to find data linking utility values to levels of symptoms.

Since LUTS are a lifelong condition, we built a Markov model with a life time horizon and we changed this in a sensitivity analysis. The cycle length is three months, as this was deemed the minimum clinically meaningful time interval to detect differences in patients undergoing surgery.

All the probabilities, costs and health utilities were converted in order to reflect the three-month values.

The treatments compared in our analysis are TURP and Holmium Laser Enucleation of Prostate (HoLEP). TURP is the current standard practice and HoLEP was one of the alternative treatments that were significantly effective as compared to TURP. Transurethral electrovaporisation of prostate (TUVP) was another effective treatment as compared to TURP but the available economic evidence was considered sufficient to prove it cost-effective.

Patients in the studies included in our clinical review had a moderate-to-severe level of symptoms. Therefore patients in our model were defined as men with moderate-to-severe LUTS who are suitable for either TURP of HoLEP.

Both arms of the model have the same structure (Figure 236): after the intervention, the patient can either have a significant remission of symptoms (success) or no remission/minor remission (failure).

Short-term complications identified in the clinical review (see Appendix E) were assumed to be resolved within 3 months (the cycle length) and could occur with a probability independent from the success. Incontinence is the only long-term adverse event and in some cases it requires an artificial urinary sphincter (AUS). If the man still has storage LUTS together with incontinence, he will not undergo further de-obstructive surgery, therefore he will remain in this health state throughout the model.

Men who initially had a successful outcome can have deterioration in symptoms and end up with residual LUTS state. Some of them will undergo further de-obstructive surgery if incontinence is not present, and some will be medically treated. The second surgery is always TURP, even in the HoLEP arm, as the experts in the GDG believe that HoLEP is unlikely to be performed twice. We

varied the structure between the two arms in a structural sensitivity analysis where we assumed TURP was not possible after HoLEP either.

The list of the health states that are part of the model is reported in Table 1.

Table 1 - Health states

HEALTH STATES
(Moderate-to-Severe) LUTS
Remission
LUTS + Incontinence
LUTS + Incontinence AUS
Incontinence
Incontinence AUS

The experts of the GDG members have defined a significant remission of symptoms after surgery as a change in IPSS greater than five. This was agreed after considering that the minimally important difference is estimated as 3 points[24] but a more consistent improvement is expected after an invasive intervention. It was agreed that a change by 5 points would constitute a treatment success.

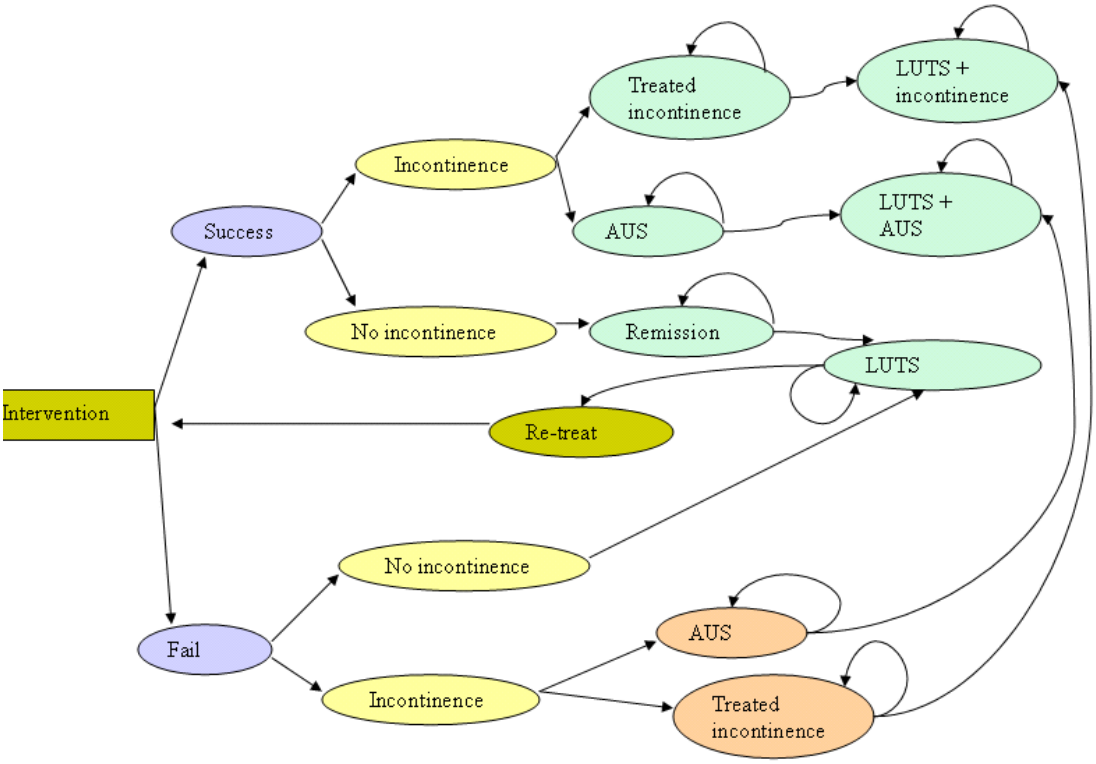

Figure 236 - Model structure. The health states are represented by the six blue circles on the top right corner. The arrows represent the possible transitions from a state to another or to the same state.

For each strategy the expected healthcare costs and expected QALYs were calculated by estimating the costs and QALYs for each state and then multiplying them by the proportion of patients who would be in that state as determined by the strategy taken.

We performed a probabilistic sensitivity analysis (SA) to test the robustness of the results against the imprecision of these estimates and the other model parameters, and to obtain more accurate estimates of expected costs and QALYs.

We identified sensitive parameters with a threshold analysis and then conducted multi-way sensitivity analyses on those parameters at decision point.

10.3.2 Key assumptions

The experts in the GDG were consulted in order to make the following assumptions:

a) After a relapse in symptoms, only 5% of patients will undergo a second TURP. The remaining 95% are treated medically.

b) The probability of success of the same intervention when performed a second time is 75% the probability of success when performed for the first time.

c) The proportion of men with incontinence after surgery/laser requiring an AUS is 5%. The remaining 95% are treated medically or with incontinence products (catheters, pads, etc).

10.3.3 Probability of success - TURP

We searched for an RCT which reported the probability of success of either TURP or HoLEP as defined in our model (change in IPSS≥5). We found only one large multicentre RCT[94] where 120 of the randomised patients received TURP while the other 115 received TUVP. Data from this study[94] that were used in the model are reported in Table 2.

Table 2 - Data on TURP used in the model (a)

	Data used in the model
IPSS at baseline (IPSS pre)	20.7 (SD 6.9)
IPSS at 6 months (IPSS post)	6.9 (SD 5.5)
Probability of success of TURP at 6 months	85.4%
Probability of success of TURP at 24 months	84.0%

(a) From Fowler et al. (2005)[94]

10.3.4 Probability of success - HoLEP

We could not find similar data for HoLEP so we adopted an alternative approach, linking the probability of success of the two interventions using the IPSS change data from our clinical review.

Table 3 - Effectiveness from meta-analysis

	HoLEP vs. TURP
Weighted Mean Difference (WMD) from baseline IPSS at 6 months	- 0.52
WMD from baseline IPSS at 24 months	- 0.80

10.3.4.1 Setting up the precondition

IPSSpost is the mean IPSS after the intervention and it is equal to:

I IPSSpost = Psuccess * IPSSsuccess + (1-Psuccess) * IPSSfail

Where IPSSfail and IPSSsuccess are respectively the mean IPSS in the group of patients whose treatment has failed and the mean IPSS in the group of patients whose treatment was successful.

By assuming that IPSSfail is the same for both TURP and HoLEP and also that IPSSsucess is the same for both, we can estimate the success rate for HoLEP.

10.3.4.2 Deriving IPSS after a TURP failure

II IPSSfail = IPSSpre - ΔIPSSfail

Where ΔIPSSfail is the change in IPSS in patients for whom the intervention has failed. By definition this must be ≤4. Assuming in some patients the symptoms might have deteriorated, we can consider the range -1 to 4, and use the central value 1.5, which is then varied in a sensitivity analysis. Substituting this value in II and using the data from TURP we get IPSSfail = 20.7 – 1.5 = 19.2

10.3.4.3 Deriving IPSS after a successful TURP

We can rearrange equation **I** as

III IPSSsuccess = (IPSSpost- (1-Psuccess)xIPSSfail)/P(success)

Using data from Table 2 and our result for IPSSfail from 10.3.4.2 we get:

IV IPSSsuccess = (6.9 –14.6%*19.2)/85.4% = 4.8

10.3.4.4 Deriving IPSS after HoLEP

The mean difference in change in IPSS from baseline to 6 months was -0.52 compared with TURP (Chapter 8.3.1). The IPSS 6 months after HoLEP is simply the IPSS at 6 months for TURP plus this difference:

V IPSSpost=6.9-0.52=6.4

10.3.4.5 Calculating the probability of HoLEP success at 6 months

We rearranged equation **I** to give us:

VI Psuccess= (IPSSpost-IPSSfail)/(IPSSsuccess-IPSSfail)

Substituting the values derived above (10.3.4.2, 10.3.4.3, 10.3.4.4) we get:

VII Psuccess = (6.4-19.2)/(4.8-19.2) = 88.9%

10.3.5 Probability of relapse

According to the data reported in Fowler et al (2005)[94], TURP was more effective after 6 months than after 24 months, as only 84% of patients had an improvement in symptoms by at least 5 points at 24 months compared to 85.4% of patients at 6 months Table 2. To mimic what happens in real practice, where a relapse in symptoms sometimes follows an initial improvement, it was necessary to incorporate a time-dependant probability of relapse after an initial success.

The probability of relapse between these two intervals (6 months and 24 months) is calculated as follows:

VIII (P success 6 months – P success 24 months)/P success 6 months

Which in case of TURP is equal to (85.4% - 84%)/85.4% = 1.6%

We converted the probability of relapse of TURP over 18 months into a 3-month rate, which is the cycle length of the model, by using the formula:

IX 1 - exp((ln(1- relapse18months))/6)

We used the same probability of relapse for HoLEP (a conservative assumption).

10.3.6 Probability of complications

Several complications of HoLEP and TURP were identified in the systematic review (Appendix E). In our economic model we only included those that would require additional treatment and generate additional costs.

To calculate the probability of complications following TURP (Table 4), we aggregated data from the TURP arm in every study included in our review, excluding the duplicates. We then compared the incidences of adverse events after TURP with those reported in the AUA[14] and we found no considerable difference.

The incidence of complications following HoLEP (Table 4) was estimated by multiplying their probability after TURP by the risk ratio (RR) of HoLEP compared to TURP.

Table 4 - Probability of complications

	TURP	**HoLEP**	
	Probability	RR vs. TURP	Probability
Incontinence	4.0%	1.19	4.8%
Blood transfusion	6.2%	0.27	1.8%
Acute urinary retention (AUR)	3.9%	0.71	2.8%
Urinary tract infections	6.9%	0.45	3.1%
Transurethral syndrome	2.0%	0.31	0.6%
Strictures	7.2%	0.69	5.0%

All the adverse events were assumed to occur within three months after the intervention, and so within the same cycle in the model. All of them have associated one-off costs (see 10.3.11) and no detriment in quality of life with the exception of incontinence which has a lifetime cost and disutility (10.3.8).

10.3.7 Life expectancy

The mean age of the men when entering the model was 71 as this was the mean age of men in the diagnosis-related group 'Hyperplasia of prostate' in the Hospital Episode Statistics 2006/07.

Life expectancy in patients with LUTS was assumed to be the same as the general population in England and Wales. The remaining life expectancy for men aged 71 is 12.99 years, as reported in the Life Tables for the general

population of England and Wales in the year 2005-2007 from the Government Actuary Department (http://www.gad.gov.uk/Documents/Demography/EOL/ILT%202005-07/wltewm0507.xls).

10.3.8 Quality of life

The utility scores in Table 5 are a measure of the quality of life associated with LUTS and incontinence. A systematic search for quality of life in men with LUTS and with incontinence was performed (Appendix C). Studies were included if they reported utility values for the states of LUTS or incontinence.

Studies reporting utilities specific to non-compared interventions were excluded.

Two studies[21,198] were excluded because the values were obtained from consensus rather than from patients or general public.

Kok et al (2002)[149] reported utility values according to the obstructive and irritative dimension of IPSS. However, using this study to estimate an average utility score for LUTS would have required further assumptions on the nature of the symptoms.

Ackerman et al (2000)[8] assessed the preference of 13 patients to health states with the standard gamble technique. We excluded this study due to the small sample size but we used it as an alternative source of data in the sensitivity analysis.

Trueman et al (1999)[297] designed a survey to collect EQ-5D scores by symptoms severity in 1115 men in the UK. The results of this study[297] were used in our model and are reported in Table 5. Although the population in the model is made of men with moderate-to-severe LUTS we used the utility value for severe LUTS as 20.7 was the average IPSS of this population.

We found a UK study[58] reporting the deterioration in quality of life caused by incontinence. A multivariate analysis of EQ-5D scores, found that after controlling for age, gender and body mass index, incontinence was associated with a reduction in the EQ-5D score by 0.11 (SE 0.026). This value was subtracted from the remission and LUTS utility scores for the health states respectively characterised by symptoms remission and Incontinence and LUTS and Incontinence. The values thus obtained are reported in Table 5.

Among patients with incontinence, 5% require an artificial urinary sphincter while the remaining 95% are treated pharmacologically or with incontinence products. The utility score does not differ for these two subgroups.

Other adverse events were assumed to be negligible in terms of quality of life because they could be promptly treated.

Table 5 - Utility values

	Utility score
Remission (a)	0.91
LUTS (a)	0.71
Remission + Incontinence (a, b)	0.80
LUTS + Incontinence (a, b)	0.60

(a) *Source: Trueman at al (1999)*[297]
(b) *Source: Currie et al (2006)*[58]

10.3.9 Calculating QALYs gained

For each strategy, the expected QALYs in each cycle are calculated as follows:

X **Expected QALYs = Σ (U_i x P_i)**

where

U_i = the utility score for health state i

P_i = the proportion of patients in health state i

and where health state i could be any of the health states reported in Table 1.

The proportion of patients in each health state depends on the effectiveness of the treatment, in terms of symptoms improvement and incontinence, and on the proportion of patients still alive, which falls as the number of cycles and therefore age increases.

The overall *lifetime expected QALYs* are given by the sum of QALYs calculated for each cycle. The *incremental QALYs gained* associated with a treatment strategy are calculated as the difference between the expected QALYs with that strategy and the expected QALYs with the comparator.

10.3.10 Cost of interventions

We adopted a bottom-up approach to calculate the intervention cost as differentiating the total costs for the two intervention was not possible by using national sources (NHS Reference Costs or Tariffs) or published evidence. In fact, no UK study could be found which reported the cost of HoLEP as this is performed only in a few UK centres only while TURP is a widespread technique. For this reason we decided to include only the capital cost of the HoLEP equipment as the TURP equipment is already present in every Urology centre. Only disposables used in TURP were included in the calculation.

We contacted the UK supplier of HoLEP equipment (SIGMACON) to obtain precise data on the cost of the machine and the cost and number of uses of disposables. We assumed the life span of the machine is 10 years. As we want

to estimate the cost of the machine per patient, the GDG had to estimate the number of patients per centre undergoing surgery for LUTS in a year.

We found the cost of TURP disposables in a study[94] and the GDG estimated the number of uses. The data thus collected are reported in Table 6.

In addition to the cost of equipment, other factors influencing the total costs are the operating theatre cost, the length of stay after the intervention, and the complications. The costs of operating theatre and hospital stay are reported in Table 6 while the costs of complications are described in 10.3.11.

Table 6 – Resources used and costs

	HoLEP	Source
Cost of HoLEP machine	£150,000	UK supplier (SIGMACON)
Lifespan of HoLEP	10 years	Assumption
Number of patients per year per HoLEP machine	280	Expert opinion
Cost of morcellator blades (HoLEP)	£595 each	UK supplier (SIGMACON)
Number of uses per blade	10	UK supplier (SIGMACON)
Cost of fibres (HoLEP)	£550 each	UK supplier (SIGMACON)
Number of uses per fibre	20	UK supplier (SIGMACON)
Cost of loops (TURP)	£47	Expert opinion
Number of uses per loop	10	Expert opinion
Operating time TURP	60 minutes	Systematic review (Appendix E) (a)
Operating time HoLEP	75 minutes	Systematic review (Appendix E) (a)
Cost of urology operating theatre	£9 per minute	Local cost estimate
Median length of hospital stay after TURP (b)	3 days	Hospital Episode Statistics 2006/07
Median length of hospital stay after HoLEP (b)	2 days	Hospital Episode Statistics 2006/07
Mean cost per bed day	£204	National Schedule of Reference Costs 2006-07 for NHS Trust & PCT Combined – HRG LB25C

(a) *Mean number of times reported in Gupta et al (2006)[108] and Montorsi et al (2004)[202].*
(b) *The median was used as an estimate of the mean to exclude outliers probably due to complications.*

The annual cost of the HoLEP machine is a function of the capital cost of the machine, its life span and the discount rate according to the formula:

XI $E = K*r/[1-(1+r)^{-n}]$

where E = annual cost of the machine

K = capital outlay (cost of purchasing the machine)

r = discount rate / interest rate = 3.5%

n = lifespan

The total cost of a single intervention can be represented by the formula:

XII $TCi = E/np + cDisp_i + opT_i*cTheatre + cComp * pComp_{A-i}$

Where TC_i = total cost of the intervention i

E = annual cost of machine (only HoLEP)

np = number of patients using the machine per year

$cDisp_i$ = cost of disposables of intervention i

opT_i = operating time of intervention i

cTheatre = cost of theatre per minute

$cComp_A$ = cost of treating complication A (Table 7)

$pComp_{A-i}$ = probability of complication A after intervention i (Table 4)

where i is either TURP or HoLEP and A is any complication described in Table 7.

10.3.11 Cost of complications

The complications included in the model and their probabilities are reported in 10.3.6. The GDG estimated the resources used to treat each complication as shown in Table 7 with the exception of acute urinary retention for which we used a UK economic study[17]. When a procedure could be performed as a daycase or inpatient, we checked this proportion in the Hospital Episode Statistics 2006/07 [2].

Table 7 - Cost of complications

	COST	SOURCE
Blood transfusion	£635 (a)	Varney et al (2003)[310]
Stricture	£706 (b)	National Schedule of Reference Costs 2006-07 – HRG code LB30B
Acute urinary retention	£2,029 (c)	Annemans et al (2005)[17]
Trans-urethral syndrome	£1,710 (d)	National Schedule of Reference Costs 2006-07: 1) High Dependency Unit – 0 organs supported XC07ZHDU; plus 2) Excess bed day - HRG LB25C

Urinary tract infections	£742 (e)	National Schedule of Reference Costs 2006-07– HRG code LA04C

(a) cost of a transfusion of red blood cells
(b) weighted cost - £509 x 54%(daycase) + £938 x 46%(inpatient)
(c) cost of the most cost-effective intervention to treat AUR in the study
(d) cost of two days in HDU and two days in normal ward
(e) weighted cost - £376 x 10%(daycase) + £783 x 90%(inpatient)

Incontinence is a complication but it is also a health state in the model so its cost is calculated separately in 10.3.12.

10.3.12 Cost of health states

The possible health states in which a patient could be in the model are listed in Table 1. By collecting information on the resources used while in these states from the GDG experts, we calculated the costs reported in Table 8.

When the patient has a remission of symptoms, we assumed no further treatment would be necessary and this state has no cost associated.

If after the intervention a patient still has LUTS, he would undergo urodynamic studies to investigate the cause of the intervention failure. He would then be treated with either anticholinergics or alpha-blockers and be recalled for a visit every six months. We assumed that 50% would be treated with anticholinergics and 50% with alpha-blockers. The details of the cost calculations are reported in Table 8.

Table 8 - Cost of residual LUTS state

Resources used	Proportion of patients using the resource	Unit cost of resource	Total cost per month per patient
Alpha-blockers	50%	£0.35 (a)	£5.32
5mg Oxybutynin twice daily	25%	£0.39 (b)	£5.93
Other Anticholinergics	25%	£1.05 (c)	£15.97
One visit every 6 months	100%	£75 (d)	12.50
TOTAL			**£39.72**
Urodynamic studies (one-off)	100%	£165 (e)	**-**

(a) Average cost per day of Alfuzosin, Tamsulosin, Doxazosin, and Prazosin (BNF 57)
(b) Cost of treatment per day (BNF 57)
(c) Average cost per day of Darifenacin, Solifenacin, Tolterodine, Trospium, Propiverine and Fesoterodine (BNF 57)
(d) From National Schedule of Reference Costs 2006-07– Consultant led follow-up attendance – outpatient face-to-face – Urology
(e) From National Schedule of Reference Costs 2006-07 - Outpatient procedure LB42Z

To estimate the cost of incontinence in men treated with drugs or products we searched for UK cost-of-illness studies excluding those studies conducted in women. We did not find any so we estimated the resources and their costs with the help of experts from the GDG (Table 9).

Table 9 - Cost of incontinence in men treated with products or drugs

Resources used	Proportion of patients using the resource	Unit cost of resource	Total cost per month per patient (f)
3 ISC catheters per day	25%	£1.30	£29.66
1 indwelling catheter every 6 weeks	25%	£6.00	£1.08
5mg Oxybutynin twice daily	50%	£0.39 (a)	£5.93
Other anticholinergics	50%	£1.05 (b)	£15.97
1 pad a day	25%	£0.34	£2.58
1 leg bag per week	25%	£2.50	£2.71
1 overnight bag per night	25%	£0.10	£0.76
1 bag support, leg sleeve and Stalock Bard per week	25%	£6.00	£6.50
Sheath appliances	25%	£40.00 (c)	£10.00
1 district nurse visit per week	100%	£21.00 (d)	£91.00
1 specialist nurse visit every 6 months	100%	£66.00 (e)	£11.00
TOTAL			**£177.19**

(a) Cost of treatment per day (BNF 57)
(b) Average cost per day of Darifenacin, Solifenacin, Tolterodine, Trospium, Propiverine and Fesoterodine (BNF 57)
(c) Estimate on cost per month rather than number of items.
(d) From Curtis (2008)[59] – cost of district nurse per home visit including travel, excluding qualification
(e) From Curtis (2008)[59] – cost of specialist nurse per hour of client contact, excluding qualification
(f) These figures account for the proportion of patients who use that resource

In the model, 5% of the men with incontinence have an AUS implanted. The costs associated with this intervention are the one-off cost of urodynamic studies, the cost of implanting the AUS and the recurrent visits. The AUS needs to be re-implanted on average every ten years and this is taken into account in the model with a recurrent cost of the operation (Table 10).

Table 10 - Cost of artificial urinary sphincter (AUS)

Resources used	Frequency	Unit cost of resource	Source of cost
AUS implant	10 years	£4,137	National Schedule of Reference Costs 2006-07– HRG code LB21Z
Urology visit	6 months	£75	National Schedule of Reference Costs 2006-07– Consultant led follow-up attendance – outpatient face-to-face – Urology
Urodynamic studies	One-off	£165	National Schedule of Reference Costs 2006-07 - Outpatient procedure LB42Z

The costs associated with the 'LUTS + Incontinence' state are similar to the costs of the Incontinence state, while the 'LUTS + Incontinence AUS' state generates the same costs as the 'LUTS+Incontinence AUS' state with the addition of the anticholinergics (in 50% of the men) and alpha-blockers (in the other 50%).

For each strategy, the expected cost per cohort of patients is calculated as follows:

XIII Expected cost = $C_s + \sum_{j=1}^{40} \sum_{i=1}^{6} C_i P_{ij}$

where

C_s = cost of the initial strategy (TURP or HoLEP)

C_i = cost of health state i

P_{ij} = proportion of patients in health state i in cycle j

and where health state i could be any stage in Table 1.

The proportion of patients in a health state depends on the magnitude of the improvement in symptoms specific to each treatment, its probability of causing incontinence, and on the proportion of patients still alive according to the mortality rate for the general population of England and Wales.

The overall lifetime expected costs are given by the sum of costs calculated for each cycle. The incremental cost associated with a treatment strategy is calculated as the difference between the expected cost with that strategy and the expected cost with the comparator.

10.3.13 Probabilistic sensitivity analysis

A probabilistic sensitivity analysis was performed to assess the robustness of the model results to plausible variations in the model parameters.

Probability distributions were assigned to each model parameter, where there was some measure of parameter variability (Table 11). We then re-calculated the main results 10000 times, and each time all the model parameters were set simultaneously, selecting from the respective parameter distribution at random.

Table 11 - Parameters and distributions used in the probabilistic sensitivity analysis

Description of variable	Mean value	Probability distribution	Parameters	Source
IPSS post treatment with TURP after 6 months	6.9	Normal	SD = 0.5102	Fowler et al (2005)[94]
IPSS post treatment with TURP after 2 years	7.5	Normal	SD = 0.6633	Fowler et al (2005)[94]
Initial IPSS	20.7	Normal	SD=0.6633	Fowler et al (2005)[94]

IPSS change when treatment fails	1.5	Triangular	Min=0 Likeliest=1.5 Max=3	Assumption
Weighted mean difference of IPSS at 6 months	0.52	Normal	SD=0.4235	Systematic review of clinical effectiveness
Weighted mean difference of IPSS at 2 years	0.8	Normal	SD=0.9847	Systematic review of clinical effectiveness
Capital cost of HoLEP	£150,000	None		UK Supplier SIGMACON
Lifespan of HoLEP machine (years)	10	Gamma (a)	$\alpha = 61.46$ $\lambda = 6.146$	Assumption
Number of patients per year	280	Gamma (a)	$\alpha = 61.46$ $\lambda = 0.2195$	Assumption
Cost of each blade	£595	None		UK Supplier SIGMACON
Cost of each fibre	£550	None		UK Supplier SIGMACON
Cost of each loop	£47	None		Experts opinion
Number of uses of a blade	10	Triangular (b)	Min=5 Likeliest=10 Max=15	UK Supplier SIGMACON
Number of uses of a fibre	20	Triangular (b)	Min=15 Likeliest=20 Max=25	UK Supplier SIGMACON
Number of uses of a loop	10	Triangular	Min=5 Likeliest=10 Max=15	Experts opinion
Cost of operating theatre per minute	£9	Gamma (a)	$\alpha = 61.46$ $\lambda = 6.829$	Local cost estimate
Operating time – HoLEP (minutes)	75	Triangular	Min=55 Likeliest=75 Max=95	Gupta at al (2006)[108] and Montorsi at el (2004)[202]
Operating time – TURP (minutes)	60	Triangular	Min=45 Likeliest=60 Max=75	Gupta at al (2006)[108] and Montorsi at el (2004)[202]
Cost bed day	£204	Gamma (c)	$\alpha = 4.925$ $\lambda = 0.0241$	National Schedule of Reference Costs 2006-07 Excess Bed Day HRG code LB25C
Hospital stay after HoLEP (days)	2	Triangular (d)	Min=1 Likeliest=2 Max=3	Hospital Episode Statistics 2006/07

Hospital stay after TURP (days)	3	Triangular (d)	Min=2 Likeliest=3 Max=4	Hospital Episode Statistics 2006/07
Cost of residual LUTS state	see 10.3.12	None		NCGC calculations
Cost of incontinence per three months (see 10.3.12)	£510	Gamma (a)	$\alpha = 61.46$ $\lambda = 0.1205$	NCGC calculation of cost of health states
Cost of AUS	£4,137	Gamma (c)	$\alpha = 7.089$ $\lambda = 0.0017$	National Schedule of Reference Costs 2006-07 HRG code L25 – LB21Z
Cost of treating AUR	£2,029	Gamma (a)	$\alpha = 61.46$ $\lambda = 0.0303$	Annemans2005[17]
Cost of treating TUR	See Table 7			
Cost of HDU per day	£651	Gamma (c)	$\alpha = 5.096$ $\lambda = 0.0078$	National Schedule of Reference Costs 2006-07 HDU – 0 organs supported XC07ZHDU
Cost of multichannel cystometry	£165	Gamma (c)	$\alpha = 4.094$ $\lambda = 0.0248$	National Schedule of Reference Costs 2006-07 Outpatient procedure LB42Z
Cost of treating strictures – daycase	£509	Gamma (c)	$\alpha = 4.055$ $\lambda = 0.008$	National Schedule of Reference Costs 2006-07 non elective LB30B
Cost of treating strictures – inpatient	£938	Gamma (c)	$\alpha = 3.344$ $\lambda = 0.0036$	National Schedule of Reference Costs 2006-07 non elective LB30B
Cost of blood transfusion	£635	Gamma (a)	$\alpha = 61.46$ $\lambda = 0.0968$	Varney et al (2003)[310]
Cost of treating UTI – daycase	£376	Gamma (c)	$\alpha = 3.926$ $\lambda = 0.0104$	National Schedule of Reference Costs 2006-07 LA04C
Cost of treating UTI - inpatient	£783	Gamma (c)	$\alpha = 3.079$ $\lambda = 0.0039$	National Schedule of Reference Costs 2006-07 LA04C
Cost of urology visit	£75	Gamma (c)	$\alpha = 7.898$ $\lambda = 0.1053$	National Schedule of Reference Costs 2006-07 Consultant led follow-up attendance, face-to-face - Urology
Number of visits every 3 months	0.5	Triangular	Min=0.25 Likeliest=0.5 Max=1	Experts opinion
Probability of AUR after TURP (see 10.3.6)	3.9%	Beta	$\alpha = 88$ $\beta = 2184$	Systematic review of clinical effectiveness

Proportion of patients with incontinence requiring an AUS	5%	Triangular	Min=2.5% Likeliest=5% Max=7.5%	Experts opinion
Probability of incontinence after TURP (see 10.3.6)	4.0%	Beta	α = 84 β = 2036	Systematic review of clinical effectiveness
Probability of strictures after TURP (see 10.3.6)	7.2%	Beta	α = 180 β = 2316	Systematic review of clinical effectiveness
Proportion of treating strictures - inpatient: daycase	0.46 : 0.54	None		Hospital Episodes Statistics 2006-07
Probability of success at 6 months after TURP	85%	Beta	α = 88 β = 15	Fowler et al (2005)[94]
Probability of success at 2 years after TURP	84%	Beta	α = 63 β = 12	Fowler et al (2005)[94]
Probability of blood transfusion after TURP (see 10.3.6)	6.2%	Beta	α = 197 β = 2977	Systematic review of clinical effectiveness
Probability of TUR after TURP (see 10.3.6)	2.0%	Beta	α = 29 β = 1454	Systematic review of clinical effectiveness
Probability of UTI after TURP (see 10.3.6)	6.9%	Beta	α = 111 β = 1488	Systematic review of clinical effectiveness
Proportion of treating UTI - inpatient: daycase	0.9 : 0.1	None		Hospital Episodes Statistics 2006-07
Proportion of patients being re-operated after a first failure	5%	Triangular	Min=0% Likeliest=5% Max=10%	Experts opinion
Relative Risk of AUR – HoLEP vs. TURP	0.72	Log-normal	SD=0.313	Systematic review of clinical effectiveness
Relative Risk of incontinence – HoLEP vs. TURP	1.26	Log-normal	SD=0.213	Systematic review of clinical effectiveness
Relative Risk of strictures – HoLEP vs. TURP	0.69	Log-normal	SD=0.356	Systematic review of clinical effectiveness
Relative Risk of blood transfusion – HoLEP vs. TURP	0.27	Log-normal	SD=0.615	Systematic review of clinical effectiveness
Relative Risk of TUR – HoLEP vs. TURP	0.31	Log-normal	SD=1.685	Systematic review of clinical effectiveness
Relative Risk of UTI – HoLEP vs. TURP	0.45	Log-normal	SD=0.636	Systematic review of clinical effectiveness
Utility of severe LUTS	0.71	Beta	α = 80.23 β = 32.77	Trueman et al (1999)[297]

Utility of Remission	0.91	Beta	α = 33.67 β = 3.33	Trueman et al (1999)[297]
Disutility from incontinence	0.11	Normal	SD = 0.026	Currie et al (2006)[58]
Effectiveness when procedure is performed the second time compared to first time	75%	Triangular	Min=50% Likeliest=75% Max=100%	Experts opinion
Discount rate (cost and QALYs)	3.5%	None		

(a) We approximated the standard error (SE) of the mean by assuming the width of the 95% CI was 50% of the mean using the following equation: SE=0.25 x mean / $Z_{0.0975}$

(b) Based on experts opinion

(c) We used the interquartile range (IQR) to approximately estimate the SE of the mean using the following equation: SE=0.5 x IQR / $Z_{0.75}$

(d) Based on the range from HES 2006/07

10.3.14 Results of the cost-effectiveness analysis

We analysed the data deterministically (Table 12) and probabilistically (Table 13). We found that the results of the model were sensitive to various parameters and this is reflected in the extreme confidence intervals obtained with the probabilistic SA.

In the base case analysis HoLEP is more cost-effective than TURP but this result is overthrown by minimal changes in variables (Table 12).

Table 12 - HoLEP vs. TURP - Results of base case analysis

	Mean cost (£)	QALYs	Incremental cost per QALY gained (HOLEP vs. TURP)	Sensitivity analysis
TURP	2,938	8.5761	-	TURP is cost-effective if: - probability that TURP fails <12% - probability that HoLEP fails >13.5% - RR of Incontince (Holep vs TURP) >1.51 - WMD in IPSS change <0.17 - TURP is not possible after HoLEP - probability of incontinence after TURP and RR incontinence (HoLEP/TURP) are varied together (Figure 237).
HoLEP	2,920	8.6019	HoLEP dominates (a)	

(a) HoLEP dominates means that HoLEP is both more effective and less costly. Hence the ICER cannot be calculated.

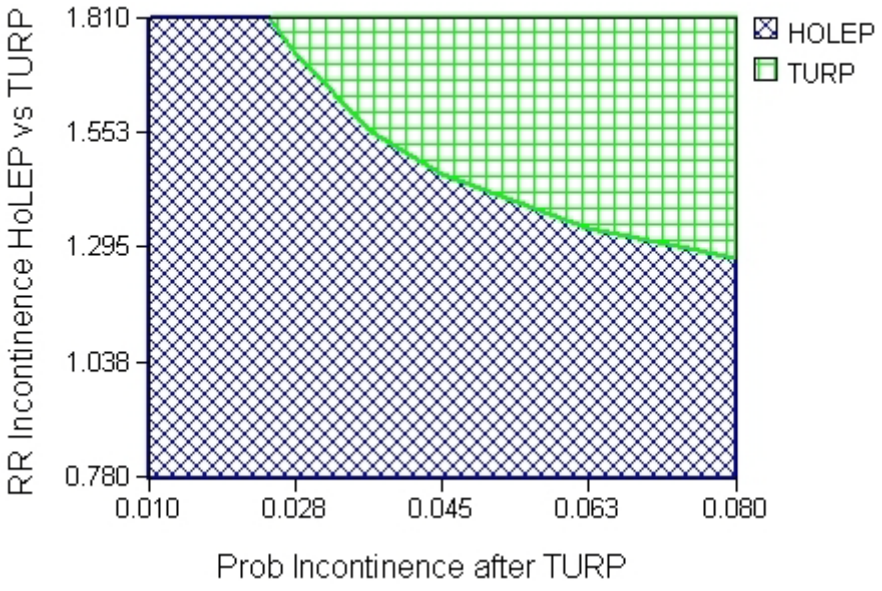

Figure 237 - Two-way sensitivity analysis of probability of incontinence after TURP and RR of Incontinence HoLEP vs TURP. The green and blue areas of the graph represent respectively the combinations of the two parameters where TURP or HoLEP is cost-effective.

The instability of this conclusion is even more evident from the results of the probabilistic SA (Table 13).

Table 13 - Probabilistic SA results - HoLEP vs. TURP

Mean incremental cost/mean QALYs gained	95% CI – lower limit (£/QALY)	95% CI – upper limit (£/QALY)	Probability of being cost-effective at £20,000/QALY
TURP dominates (a)	HoLEP dominates	TURP dominates	HoLEP 48% TURP 52%

(a) TURP dominates means that TURP is both more effective and less costly. Hence the ICER cannot be calculated.

The probability of HoLEP being cost-effective (48%) is very close to the probability of TURP being cost-effective (52%) at a willingness to pay of £20,000/QALY (the NICE threshold). The probabilities are very similar for other willingness to pay thresholds (Figure 238).

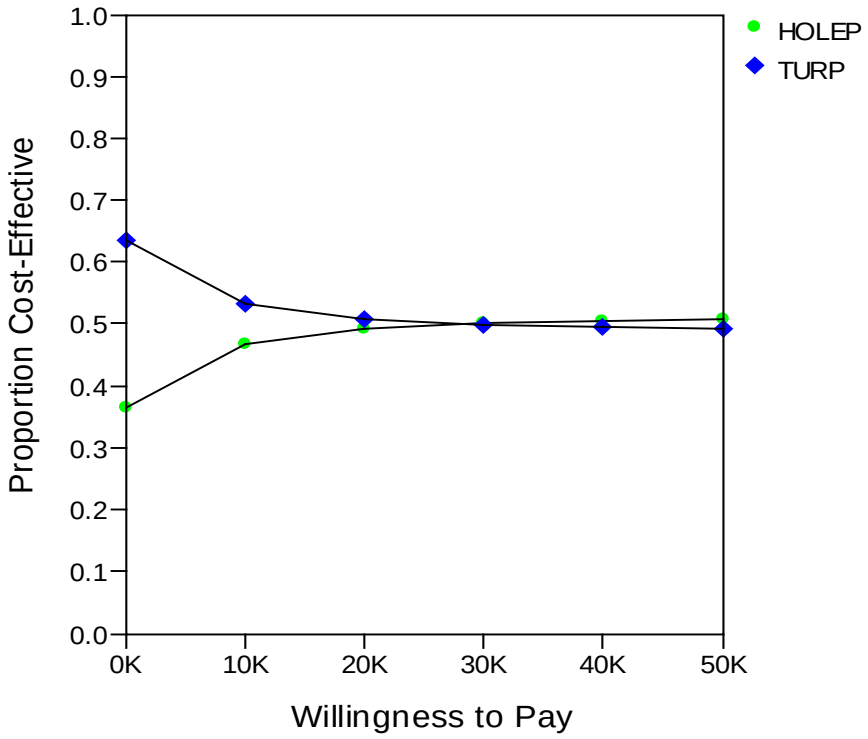

Figure 238 - Acceptability curve of HoLEP and TURP

The uncertainty can also be graphically represented by plotting the results of the incremental analysis for all the 10,000 simulations into a cost-effectiveness plane (Figure 239). Each point represents the ICER of TURP vs. HoLEP for each simulation. The dotted line represents the £20,000/QALY threshold while the ellipse delimits the 95% confidence interval.

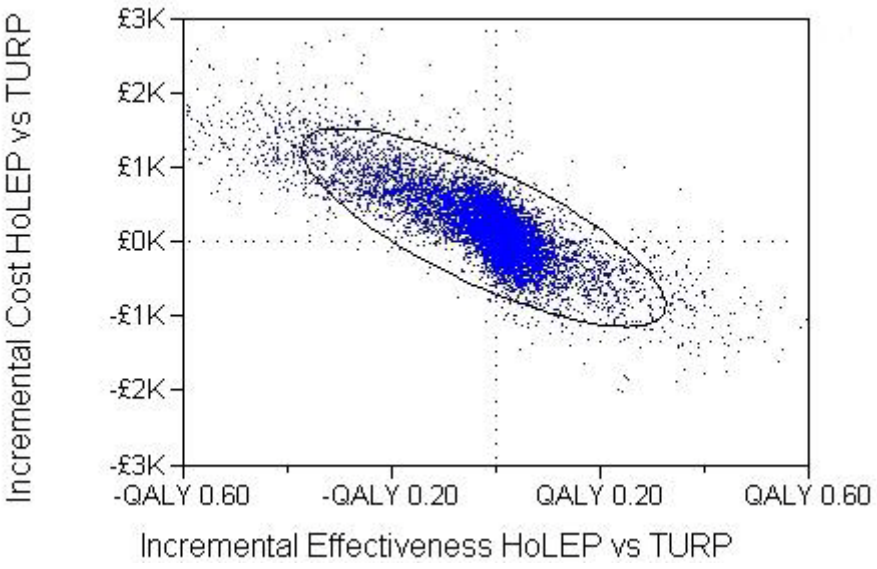

Figure 239 - Incremental cost-effectiveness scatterplot - HoLEP vs TURP

10.3.15 Discussion

HoLEP and TURP could be equally cost-effective.

TURP is the current standard of care in the UK while HoLEP is a relatively new technique practiced in a small number of UK centres. Although our analysis shows that HoLEP is at least as cost-effective as TURP, careful considerations should be given to recommending its widespread use.

The cost-effectiveness of HoLEP seems to be associated with the skills of the surgeons as the probabilities of complications depend on the expertise of the surgeon performing the operation. The probabilities as reported in the studies included in our clinical review, where HoLEP was performed by specialised surgeons, might be largely different from the actual events following an operation performed by a trainee surgeon. Therefore we might have overestimated the effectiveness of HoLEP.

Another overestimation might be due to the blood transfusion rate after TURP as estimated from our review of clinical studies. Some of the included studies[145] reported a blood transfusion rate after TURP higher than the average.

The major limitation of our model is the arbitrary definition of success (IPSS change of at least 5 points). Although other authors[94] have adopted this definition, it is still debatable whether a change of 5 points could be considered a remission in symptoms. Other authors[172] have used an improvement by 10% in IPSS as a proxy for success but this was judged to be even more optimistic by our experts, as this would equate to 2 points of improvement when the baseline score is 20.

The results of our study are based on trial data for men with moderate-to-severe symptoms with a mean baseline IPSS of 20.7. For men with less severe symptoms, TURP might be more cost-effective as it is less costly, while for men with more severe symptoms HoLEP might be more cost-effective as it is more effective than TURP at improving symptoms.

We compared the results of our study with the economic analysis from the HTA[172] included in our review and we found similar results and conclusions. In this study[172], HoLEP was more effective and less costly than TURP but the results were highly sensitive to several parameters. Unlike this study[172] our model takes into account the capital cost of HoLEP which might explain the higher cost of HoLEP compared to TURP in the mean results of the probabilistic analysis.

From an NHS perspective, the results of our study would suggest training new surgeons in HoLEP could improve outcomes and save costs if performed correctly. However, a shift from TURP to HoLEP would have to be gradual for it to be cost-effective since purchasing the new equipment might not warrant the improved outcomes which were marginal. It is important to note that there is still inadequate long-term data for HoLEP. However, if a centre has to replace old equipment and surgeons trained in HoLEP are available, HoLEP could be an efficient option.

In conclusion, given the learning curve associated with the new technique and the cost of purchasing the new equipment, the GDG felt it was reasonable to recommend HoLEP only in centres specialised in the technique.

10.3.16 Conclusions

- HoLEP and TURP are similarly cost-effective
- In settings where HoLEP is not currently performed, TURP is more cost-effective because of the capital cost and the learning curve

10.4 NCGC Combination model

An economic model comparing Alpha-Blockers (AB) with a combination of AB and 5-Alpha-Reductase Inhibitors (Comb) was developed further to the exclusion of any economic evidence focusing on this comparison. The main outcomes considered were the change in IPSS from baseline and the treatment adverse events which were expressed in quality of life measures. Patients in this model are men who have moderate lower urinary tract symptoms and are selected for medical treatment. Studies specifically conducted on patients with a prostate size larger than the average[191,263] were not used to estimate IPSS change as it was the GDG opinion that this would have favoured the Combination intervention.

We built a Markov model with a lifetime horizon (Figure 240) and we chose a cycle length of six months as it was the shortest follow up period in our clinical review of effectiveness (Chapter 6.10.1). All the probabilities, costs and health utilities were converted in order to reflect the six-month values. The time horizon was shortened to 5 years in a sensitivity analysis.

After a treatment period of six months, men can have either a meaningful improvement in IPSS (treatment success) or a negligible/no improvement (treatment failure). During this period they can also experience various adverse events which are independent from the treatment success. However, a proportion of those men experiencing adverse events will discontinue treatment, going back to the LUTS state. Men who had a treatment failure to start with will go to the LUTS state (with or without adverse events) but they can still have an improvement in the following six month cycle. Some men in the LUTS state will undergo TURP and they will feed into the TURP model (10.3).

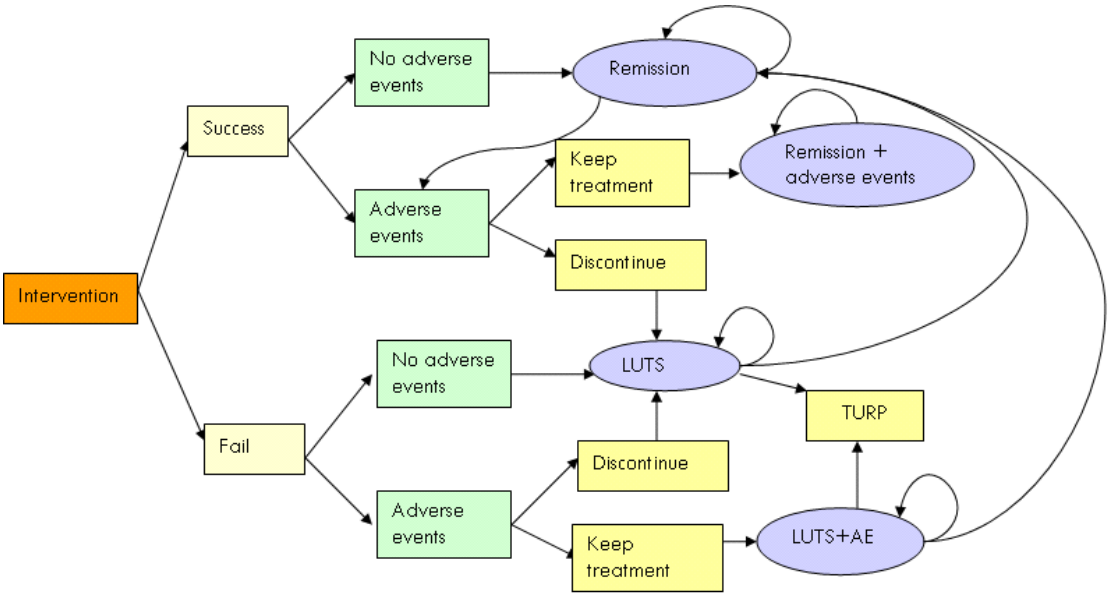

Figure 240 - Structure of the combination model. The squared boxes represent the chance nodes in the model while the circles are the possible health states.

The list of the health states that are part of the combination model is reported in Table 14.

Table 14 - Health states of combination model

HEALTH STATES
(Moderate) LUTS
Remission
LUTS +adverse events
Remission + adverse events
TURP

While in the Surgery model a significant remission of symptoms was a change in IPSS greater than five, in the Combination model we used the 3 point estimate by Barry et al (1995)[24].

For each strategy the expected healthcare costs and expected QALYs were calculated by estimating the costs and QALYs for each state and then multiplying them by the proportion of patients who would be in that state as determined by the strategy taken.

We performed a probabilistic sensitivity analysis (PSA) to test the robustness of the results against the imprecision of these estimates and the other model parameters, and to obtain more accurate estimates of expected costs and QALYs.

10.4.1 Key assumptions

The experts in the GDG were consulted in order to make the following assumptions:

a) Patients are kept on treatment for all their life if the treatment is effective and there are no adverse events.

b) If the treatment does not work (i.e. IPSS improves by less than 3 points) the treatment is kept for one year then it is discontinued.

c) 50% of the patients who discontinue the treatment after one year undergo TURP.

d) If adverse events have not occurred during the first two years, they will never occur.

The following assumption was based on the conclusions of our clinical review:

a) After the first year the treatment effectiveness is stable (no improvement or deterioration in IPSS are possible).

10.4.2 Probability of success

We could not find any studies reporting the proportion of successful treatment where success was defined as an improvement of at least 3 points of IPSS. We assumed that the IPSS change was normally distributed and we used the standard deviation (SD) from the mean to obtain the proportion of cases within the 3-point cut-off (Table 15). This was calculated as:

Success rate=1- $\Phi_{\mu\sigma^2}$(IPSS) where IPSS=3,

where μ=mean IPSS, σ^2=IPSS variance= IPSS SD squared (Table 15), 3 is the IPSS cut-off for success and where $\Phi_{\mu\sigma^2}$(IPSS) gives the cumulative distribution function for a normal distribution with mean μ and variance σ^2.

Table 15 - Probability of treatment success when the cut-off is 3 points

	Mean IPSS change (a)	SD of IPSS change (a)	Proportion of treatment success
AB – 6 months	6.3	5.8	72%
Comb – 6 months	6.1	7.4	66%
AB – 12 months	7.1	5.7	76%
Comb – 12 months	7.3	5.8	77%

a) *Source: clinical review.*

As the figures in Table 15 suggest, treatment success is more likely achieved at 12 months than 6 months. Therefore men in the model for whom treatment has failed in the first six months can still experience a remission in the following 6 months. The probability of remission is simply the difference between the probability of success at 12 months and the probability of success at 6 months (Table 16).

Table 16 - Probability of symptoms remission at 12 months

	P success 6 months	P success 12 months	P remission between 6 and 12 months (a)
AB	72%	76%	14.3%
Comb	66%	77%	16.6%

a) *(P success 12 months – P success 6 months)/(1- P success 6 months)*

We changed the definition of success in sensitivity analyses where we defined success as an improvement by at least 5 or at least 8 points.

10.4.3 Probability of adverse events and withdrawals

We looked for RCT data on adverse events and withdrawals due to adverse events. We realised it was not feasible to estimate the incidence of specific adverse events and their specific probability of causing withdrawals from treatment. Consequently we adopted a three-step approach:

1. estimate the overall probability of a man experiencing a drug-related adverse event with AB and with combinations
2. estimate the probability of an adverse event leading to treatment discontinuation with AB and with combination
3. once an adverse event occurs, estimate the probability of specific adverse events

We found a large RCT[263] reporting both drug related adverse events and drug-related adverse events leading to study withdrawals. With these data (Table 17) we were able to perform step 1 and 2 (Table 17).

Table 17 - Probability of discontinuation in patients with adverse events*

	Number of drug-related adverse events x	Number of drug-related adverse events leading to withdrawal y	Probability of drug-related adverse events	Probability of discontinuation in patients with adverse events z=y/x

AB	258	48	16%	18.6%
Comb	386	80	24%	20.7%

** From Roehrborn et al (2008)[263]*

Figure 241 and Figure 242 illustrate how these values were used in the model.

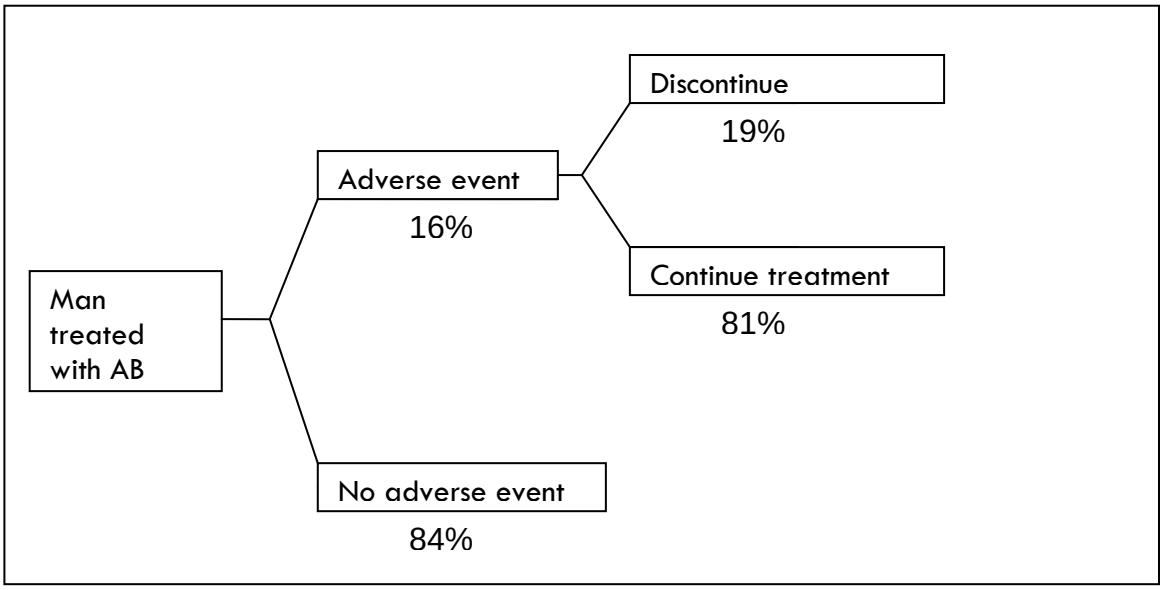

Figure 241 - Adverse events in the AB arm of the model

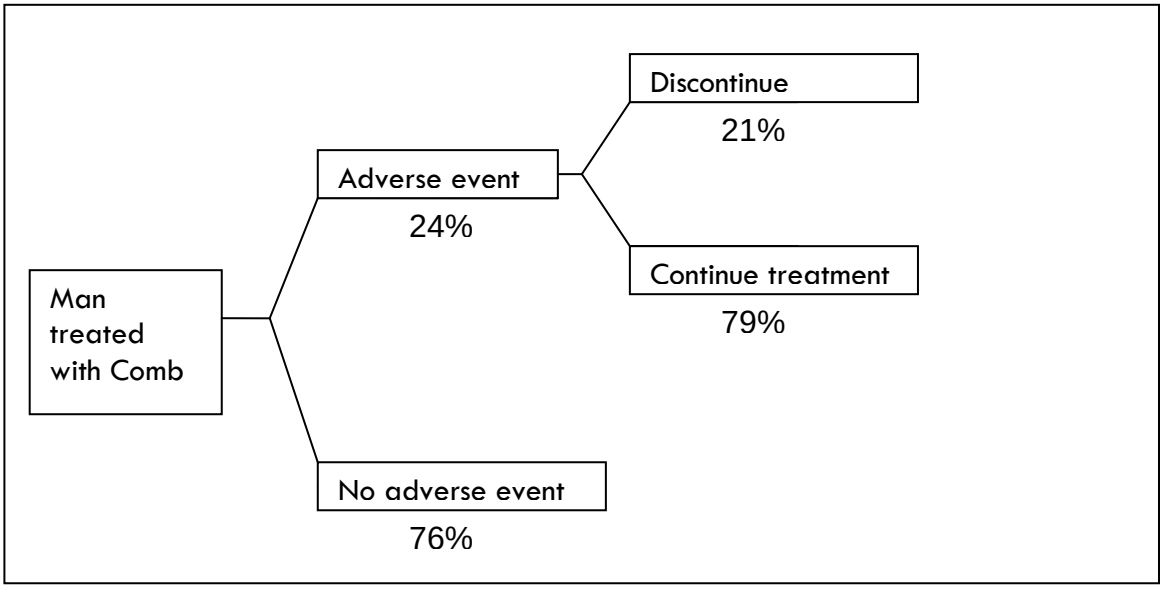

Figure 242 - Adverse events in the combination arm of the model

For step 3 we used the evidence from the review of clinical effectiveness (Chapter 6.10.1). Various adverse events were reported in the included studies and in order to avoid double-counting we grouped those adverse events that could be similar in symptoms. The most common adverse event was used to represent the group (Table 18). Therefore whilst in the clinical review postural

hypotension, headache, syncope and dizziness are all reported, it is likely to be an overlap of those symptoms and just dizziness (the most frequent one) is reported as part of that group. Similarly decreased libido was grouped together with impotence or erectile dysfunction.

In our model we did not use the incidences reported in the included studies (Chapter 6.10.1) but these were used to calculate the probability of each type being the adverse event occurring (Table 18).

Table 18 - Incidence and proportion of adverse events

	Incidence		Proportion of adverse events	
	AB X_i	Comb Y_i	AB $X_i/\sum X_i$	Comb $Y_i/\sum Y_i$
Dizziness	4.8%	4.3%	22%	16%
Fatigue	3.6%	4.2%	17%	16%
Rhinitis	6.6%	7.8%	31%	29%
Ejaculatory abnormality	0.6%	3.0%	3%	11%
Impotence/erectile dysfunction	3.0%	5.9%	14%	22%
Breast enlargement	1.8%	1.4%	8%	5%
Acute urinary retention (AUR)	1.0%	0.4%	5%	1%
TOTAL	*21.4%*	*27.0%*	*100%*	*100%*

The probability of each adverse event group was used in the model to estimate the detriment in quality of life and additional costs due to adverse events (see 10.4.5 and 10.4.7).

10.4.4 Life expectancy

Men in the Combination Model were assumed to be on average 60 years old.

Life expectancy in patients with LUTS was assumed to be the same as the general population in England and Wales. The remaining life expectancy for men aged 60 is 21.22 years, as reported in the Life Tables for the general population of England and Wales in the year 2005-2007 from the Government Actuary Department (http://www.gad.gov.uk/Documents/Demography/EOL/ILT%202005-07/wltewm0507.xls).

10.4.5 Quality of life

The same sources used in the Surgery Model for quality of life estimates of the residual LUTS and remission states (10.3.8) were used in the Combination Model.

However, while men in the Surgery Model had on average severe symptoms, in the Combination Model men have moderate symptoms.

The health states 'Remission + Adverse events' and 'LUTS + Adverse events' are made of the Remission or LUTS utility value and the disutility (decrease in utility) due to adverse events.

Being the spectrum of adverse events in the AB arm different from that in the combination arm (10.4.3), the adverse events health states will also have different utility values in the different arms.

The utility value of the LUTS + adverse events state for intervention y will be calculated as:

XIV $uLUTS\text{-}AEy = uLUTS + \sum(disutilityAEi * pAEiy)$

where uLUTS is the utility values of Moderate LUTS reported in Table 19,

disutilityAEi is the disutility of the adverse event i where i is any of the adverse events reported in Table 18,

and pAEi,y is the proportion of the adverse event i for the intervention y, where y could be either AB or combination.

From equation **XIV** it can be deduced that the utility of these health states depend on the intervention being the proportion of adverse events the variable parameter.

We conducted a search in the CEA Registry (https://research.tufts-nemc.org/cear/default.aspx) to find quality of life values associated with the adverse events reported in Table 18.

Two studies[289,311] were found which reported the one-day disutilites deriving from dizziness, fatigue and rhinitis. We assumed that those symptoms were experienced half the time; therefore the original value was halved in our analysis (Table 19) but this assumption was varied in sensitivity analyses.

One study[238] reported the disutility due to breast enlargement.

In a study by Dedhia et al (2008)[70] patients with LUTS were interviewed and their time-trade off scores for various adverse events collected. The utility values reported in this study were 0.71 for ejaculatory abnormality and 0.73 for erectile dysfunction in men with LUTS. If we assume that the utility decrements are additive, we can calculate the disutility due to these adverse events as the difference of the utility of LUTS and the utility of adverse event in presence of LUTS:

XV $disutilityAE = uLUTS - uLUTS{+}AE$

By substituting the values from the study[70] in formula **XV** we obtain the disutilities reported in Table 19.

Table 19 - Utility values used in the Combination Model

	Utility score	Source
Remission	0.91	Trueman et al (1999)[297]
Moderate LUTS	0.78	Trueman et al (1999)[297]
Disutility breast enlargement	- 0.05	Penson et al (2005)[238]
Disutility dizziness (a)	- 0.11	Vera-Llonch et al (2008)[311]
Disutility ejaculatory abnormality	-0.07	Dedhia et al (2008)[70]
Disutility fatigue (a)	-0.125	Vera-Llonch et al (2008)[311]
Disutility impotence	-0.05	Dedhia et al (2008)[70]
Disutility rhinitis (a)	-0.095	Sullivanet al (2004)[289]
Disutility AB adverse events	- 0.088	Weighted average of above disutilities
Disutility Comb adverse events	- 0.086	Weighted average of above disutilities

(a) Assuming symptoms are experienced half the time.

The disutility due to Acute Urinary Retention (AUR) was not included in the model as this complication was assumed to be treated and resolved within six months. The cost associated with this adverse event is already explained in the Surgery Model (see 10.3.11).

10.4.6 Calculating QALYs gained

See 10.3.9.

10.4.7 Cost of interventions and health states

The cost components of the health states in the model are made of the continuous cost of drug therapy and the cost of visits (Table 20). During the first six-month cycle men are treated with either AB or Combination and have a follow-up visit. The cost of the initial treatment is kept for at least another cycle unless there is a discontinuation due to adverse events. If the treatment is discontinued only the cost of a visit is included in the cost of a cycle.

Table 20 - Resources used in the health states of the model

HEALTH STATE	RESOURCES USED
Moderate LUTS - initial	Drugs (AB or Comb) + 1follow-up visit
Moderate LUTS - residual	1 follow-up visit

Remission	Drugs (AB or Comb)
LUTS +adverse events	1 follow-up visit
Remission + adverse events	Drugs (AB or Comb)

The cost details of the resources used in the health states are reported in Table 21.

Table 21 - Cost of resources used

Resource	Total cost per patient over six months	Source
Alpha-blockers	£65	BNF 57 (a)
Combination (5-ARI+AB)	£186	BNF 57 (b)
Follow-up visit	£75	National Schedule of Reference Costs 2006-07– Consultant led follow-up attendance – outpatient face-to-face – Urology

a) Based on the average cost per day of Alfuzosin, Tamsulosin, Doxazosin, and Prazosin =£ 0.35

b) Based on the cost of AB and on the average cost per day of Dutasteride and Finasteride = £0.66

In addition, some costs are associated with particular events in the model: the cost of treating AUR when adverse events occur (adjusted by the proportion of AUR in the adverse events) and the cost of TURP if the therapy fails and the man considers surgery. In this event the model feeds directly into the Surgery Model described in 10.3 where the cost components are the same ones described in 10.3.10 and 10.3.11 for the TURP strategy.

10.4.8 Probabilistic sensitivity analysis

A probabilistic sensitivity analysis was performed to assess the robustness of the model results to plausible variations in the model parameters.

The same method described for the Surgery Model (10.3.13) was used for the Combination Model. The same parameters used in the TURP arm of the Surgery Model were used in the Combination Model when men undergo TURP after a treatment failure. All the other parameters and their distributions are listed in Table 22.

Table 22 - Parameters and distributions used in the probabilistic sensitivity analysis

Description of variable	Mean value	Probability distribution	Parameters	Source
Mean IPSS change at 6 months – AB	6.3	Normal	SD= 5.8	Systematic review of clinical effectiveness
Mean IPSS change at 6 months – Comb	6.1	Normal	SD=5.6	Systematic review of clinical effectiveness

Mean IPSS change at 12 months – AB	7.1	Normal	SD=5.7	Systematic review of clinical effectiveness
Mean IPSS change at 12 months – Comb	7.3	Normal	SD=5.8	Systematic review of clinical effectiveness
Probability of success at 6 months – AB	72%	None (function of IPSS change)		See 10.4.2
Probability of success at 6 months - Comb	66%	None (function of IPSS change)		See 10.4.2
Probability of success at 12 months – AB	76%	None (function of IPSS change)		See 10.4.2
Probability of success at 12 months - Comb	77%	None (function of IPSS change)		See 10.4.2
Probability of remission at 12 months – AB	14.3%	None (function of probability of success)		See 10.4.2
Probability of remission at 12 months - Comb	16.6%	None (function of probability of success)		See 10.4.2
Cost of Alpha-blockers treatment over 6 months	£65	None		BNF 57
Cost of combination treatment over 6 months	£186	None		BNF 57
Cost of urology visit	£75	Gamma (a)	$\alpha = 7.898$ $\lambda = 0.1053$	National Schedule of Reference Costs 2006-07 Consultant led follow-up attendance, face-to-face - Urology
Cost of treating AUR	£2,029	Gamma (b)	$\alpha = 61.46$ $\lambda = 0.0303$	Annemans et al (2005)[17]
Probability of adverse events - AB	16%	Beta	$\alpha = 258$ $\beta = 1353$	Roehrborn et al (2008)[263]
Probability of adverse events - Comb	24%	Beta	$\alpha = 386$ $\beta = 1224$	Roehrborn et al (2008)[263]
Probability of discontinuing in men with adverse events - AB	18.6%	Beta	$\alpha = 48$ $\beta = 210$	Roehrborn et al (2008)[263]
Probability of discontinuing in men with adverse events - Comb	20.7%	Beta	$\alpha = 80$ $\beta = 306$	Roehrborn et al (2008)[263]

Proportion of breast enlargement/adverse events AB	8%	Dirichlet	0.08, 0.22, 0.17, 0.03, 0.14, 0.31, 0.05 where each parameter refers to proportion of each type of adverse event	Systematic review of clinical effectiveness
Proportion of dizziness/adverse events AB	22%	Dirichlet		Systematic review of clinical effectiveness
Proportion of fatigue/adverse events AB	17%	Dirichlet		Systematic review of clinical effectiveness
Proportion of ejaculatory abnormality/adverse events AB	3%	Dirichlet		Systematic review of clinical effectiveness
Proportion of impotence/adverse events AB	14%	Dirichlet		Systematic review of clinical effectiveness
Proportion of rhinitis/adverse events AB	31%	Dirichlet		Systematic review of clinical effectiveness
Proportion of AUR/adverse events AB	5%	Dirichlet		Systematic review of clinical effectiveness
Proportion of breast enlargement/adverse events - Comb	5%	Dirichlet	0.05, 0.16, 0.16, 0.11, 0.22, 0.29, 0.01 where each parameter refers to proportion of each type of adverse event	Systematic review of clinical effectiveness
Proportion of dizziness/adverse events - Comb	16%	Dirichlet		Systematic review of clinical effectiveness
Proportion of fatigue/adverse events – Comb	16%	Dirichlet		Systematic review of clinical effectiveness
Proportion of ejaculatory abnormality/adverse events AB	11%	Dirichlet		Systematic review of clinical effectiveness
Proportion of impotence/adverse events – Comb	22%	Dirichlet		Systematic review of clinical effectiveness
Proportion of rhinitis/adverse events – Comb	29%	Dirichlet		Systematic review of clinical effectiveness
Proportion of AUR/adverse events – Comb	1%	Dirichlet		Systematic review of clinical effectiveness
Proportion of men undergoing TURP after treatment failure	50%	Triangular	Min=0% Likeliest=50% Max=100%	Experts opinion
Utility of Moderate LUTS	0.78	Beta	$\alpha = 80.23$ $\beta = 32.77$	Trueman et al (1999([297]
Utility of Remission	0.91	Beta	$\alpha = 33.67$ $\beta = 3.33$	Trueman et al (1999([297]

Disutility from breast enlargement	0.05	Beta	α = 23.7 β = 450.3	Penson et al (2005)[238]
Disutility from dizziness	0.11	Beta	α = 6.22 β = 50.32	Vera-Llonch et al (2008)[311]
Disutility from fatigue	0.125	Beta	α = 6.097 β = 42.681	Vera-Llonch et al (2008)[311]
Disutility from ejaculatory abnormality	0.07	Beta	α = 14.81 β = 196.76	Dedhia et al (2008)[70]
Disutility from impotence/erectile dysfunction	0.05	Beta	α = 6.706 β = 127.406	Dedhia et al (2008)[70]
Disutility from rhinitis	0.19	Beta	α = 20.604 β = 87.836	Dedhia et al (2008)[70]
Discount rate (cost and QALYs)	3.5%	None		NICE Reference Case

(a) We used the interquartile range (IQR) to approximately estimate the standard error (SE) of the mean using the following equation: se=0.5 x IQR / $Z_{0.75}$

(b) We approximated the SE of the mean by assuming the width of the 95% CI was 50% of the mean using the following equation: se=0.25 x mean / $Z_{0.975}$

10.4.9 Results

Alpha-blockers generate less cost and more QALYs compared to combinations (Table 23).

Table 23 - Results of base case analysis - Combination vs. Alpha-blockers

	Mean cost (£)	QALYs	Incremental cost (£) per QALY gained	Sensitivity analysis
Alpha-blockers	3,824	12.4347	-	One-way SA: Combination is cost-effective if probability of adverse events with AB>29% (16% in base case). Results were not sensitive to other changes in parameters or structure.
Combination	6,411	12.4276	Dominated	

In a set of one-way sensitivity analyses, where the low and high values were respectively half or double the base case value, we identified the parameters that might have changed the results. The only variable to which the model was sensitive was the probability of adverse events with AB. We explored this uncertainty further through a two-way SA where the probability of adverse events with AB was co-varied with the probability of adverse events with combination (Figure 243).

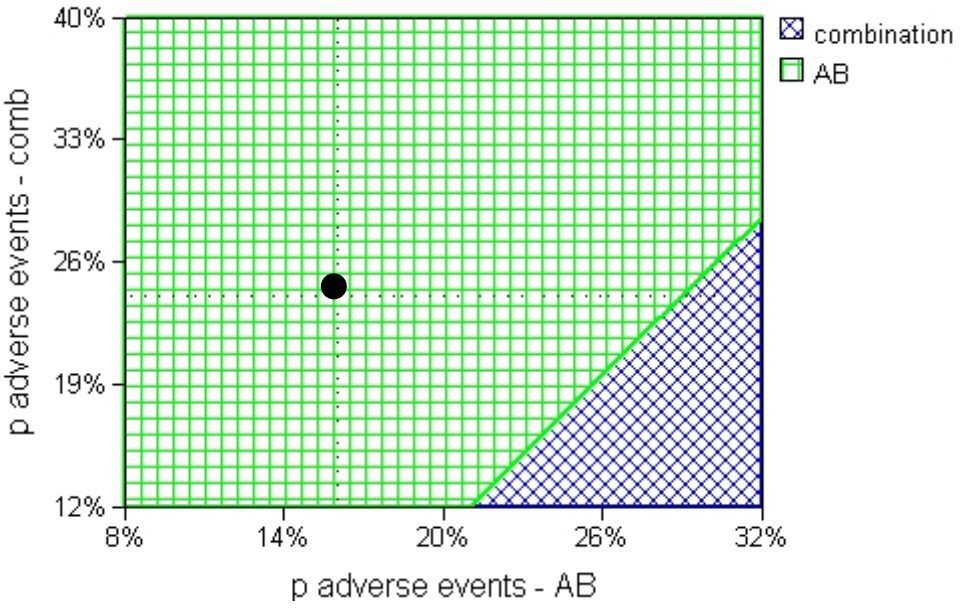

Figure 243 - Two-way SA on probability of adverse events with AB (x axis) and comb (y axis). The area in green is where AB is cost-effective, while the area in blue is where combination is cost-effective. The black dot represents the base case values.

If we consider a 95% confidence interval the base case results did not reach statistical significance (Table 24).

Table 24 - Results of probabilistic SA - Comb vs. AB

Mean ICER (£/QALY)	95% CI – lower limit (£/QALY)	95% CI – upper limit (£/QALY)	Probability of being cost-effective at £20,000/QALY
Comb dominated	3,850	Comb dominated	AB 90% Comb 10%

However, at a willingness to pay of £20,000/QALY alpha-blockers have a 90% probability of being cost-effective (Figure 244).

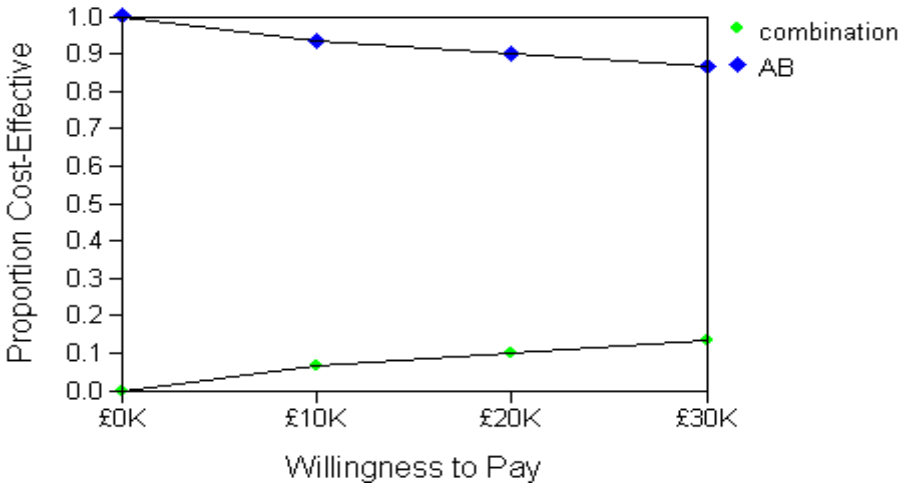

Figure 244 - Acceptability curve of AB and Comb

10.4.10 Discussion

5-ARI and AB have a different mechanism of action and the combination of the two could enhance the effectiveness on men with LUTS. Our review of clinical evidence (Chapter 6.10.1) has shown that the long-term (one year) improvement in IPSS is higher with combinations than with AB. However there are extra costs associated with the improvement and more side effects. The results of our model show that after weighting the advantages (improvement in IPSS) and disadvantages (costs and side effects) combinations are not cost-effective in a general population of men with LUTS.

We based our model on studies where men had a normal prostate size. We have deliberately excluded those studies conducted on men with large prostates as 5-ARI are believed to be more effective in this group of men. A specific model for that population could be built once good data are available.

We encountered some challenges when building our model: defining success of treatment according to an IPSS improvement by 3 points might have been arbitrary even if based on a previous study[24]; however, when we changed this definition to up to 10 points the overall results did not change.

Other assumptions were made while building the model but those did not have an impact on the conclusions.

Adverse events were a core component of the model and their incidence was the only parameter to which the results were sensitive. When we changed the probability of adverse events with AB and combinations simultaneously we noted that if the probability was lower with combination than with AB the former would have been more cost-effective than the latter. Nevertheless, as AB are part of the combination it would be very unlikely that their adverse events while used in combination would be less frequent than when they are used alone.

This is the only model which compares AB and combination using randomized data. A cost-utility analysis by McDonald et at (2004)[192] concluded that combinations were more cost-effective than Doxazosin but the clinical data were obtained from men with large prostate for one arm and men with normal prostate for the other arm. This explains the higher value-for-money of combination in this study compared to ours. Conversely the cost-utility analysis by DiSantostefano et al (2006)[71] reached our same conclusions, yet the effectiveness data on combinations were not based on RCTs but on assumptions.

10.4.11 Conclusions

- Combination of alpha-blockers with 5-ARI was not cost-effective in a general population of men with LUTS.

- Clinical data on men with large prostate might be useful to assess the cost-effectiveness in this group where combinations are presumed to be more effective.

Appendix G - Recommendations for research

10.1 Multichannel cystometry

PICO question Each research recommendation should be formulated as an answerable question or a set of closely related questions. This should use the PICO framework (patient, intervention, comparison and outcome).	Question: What is the clinical and cost effectiveness of multichannel csytometry in improving patient related outcomes in men being considered for bladder outlet surgery? Patients: Bothersome LUTS not responding to conservative therapy (catheterised patients excluded). Intervention: Pressure flow studies. Comparison: Two groups, awaiting bladder outlet surgery, randomised either to pre-operative pressure flow studies, or not Outcome: Primary outcome-patient-related outcome (IPSS, EQ5D), secondary outcomes-adverse events, flow rate, residual urine, pdetQmax.
Importance to patients or the population. What would be the impact of any new or altered guidance on the population? (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality).	This research would clarify whether this test could improve the outcome of surgery. If the result is positive, this could improve the chance of a good outcome from surgery.
Relevance to NICE guidance How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)?	As above, it would add to knowledge about the utility of pressure flow studies and allow them to be recommended or not recommended in future revisions of guidance.
Relevance to the NHS What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	It would allow the NHS to know whether resources should be committed to the test or not.
National priorities Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	NSF for older people, Integrated Continence Services.
Current evidence base What is the current evidence base? What are the problems with the current evidence	There are currently no randomised controlled trials comparing multichannel cystometry to no intervention in men

base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews. The date on which the final literature search was undertaken should be specified.	before surgery.
Equality Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	No specific consideration.
Study design It should also specify the most appropriate study design to address the proposed question(s). Primary research or secondary research (for example, systematic reviews) can be recommended.	*Design*: A randomised comparative trial of men awaiting bladder outlet surgery, to be randomised to either a pressure flow study or not, before their surgery. The results of the pressure flow study would be used in subsequent counselling of patients in a protocol-driven way, before the proposed surgery, and *might* result in surgery not being done. *Outcome*: As above.
Feasibility Can the proposed research be carried out in a realistic timescale and at an acceptable cost? As part of cost-effectiveness analysis, formal value-of-information methods may also sometimes be used to estimate the value for money of additional research. Are there any ethical or technical issues?	The research would be ethically and technically feasible.
Other comments Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue or methodological problems. However, this is not a research protocol.	The National Institute for Health Research (NIHR) would be an appropriate funding source. The normal service delivery cost to participants would be taken over by the research during the trial, thus relieving the service delivery budget. Since the NIHR is an NHS funded body the costs of care would simply be shifted from one NHS budget to another. Additional costs would be those associated with conducting the research itself.
Importance How important is the question to the overall guideline? The research	High. The research is essential to inform future updates of key recommendations in the guideline.

recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	

10.2 Catheterisation

PICO question Each research recommendation should be formulated as an answerable question or a set of closely related questions. This should use the PICO framework (patient, intervention, comparison and outcome)	What are the clinical and cost effectiveness and associated adverse events of intermittent catheterisation compared to indwelling suprapubic or urethral catheterisation for men with voiding difficulty and chronic retention of urine?
Importance to patients or the population. What would be the impact of any new or altered guidance on the population? (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality).	The number of men judged unfit to undergo de-obstructing surgery is steadily increasing given the increasing proportion of older men in the population. Current practice varies widely across the UK with no established standard for long term management and no systematic review of practice. The research could establish the best approach to management in these men in the longer term and so bring more effective treatment, better focused on each patient's need, and consequent cost-efficiency gains.
Relevance to NICE guidance How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)?	NICE currently cannot give clear guidance on this topic because of an inadequate evidence base.
Relevance to the NHS What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	Catheters are currently used variably across the UK with no systematic approach to management except for men with spinal cord injury. The aim of catheterisation, to drain the bladder so as to protect the upper renal tracts and maintain continence may not be achieved acceptably. Evidence-based guidance on the selection of the most suitable mode of catheterisation will benefit the quality of life of patients, ensure the efficient use of skilled staff and may reduce the costs of waste of unsuitable or sub-optimal product use.
National priorities Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	None currently relevant.
Current evidence base What is the current evidence base? What	There is no currently no evidence for these interventions.

are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews. The date on which the final literature search was undertaken should be specified.	
Equality Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	This treatment predominantly affects older people.
Study design It should also specify the most appropriate study design to address the proposed question(s). Primary research or secondary research (for example, systematic reviews) can be recommended.	A randomised controlled study of the interventions: a) intermittent catheterisation b) indwelling suprapubic catheterisation c) indwelling urethral catheterisation Outcomes of interest: quality of life, healthcare resource utilisation, adverse events (including leakage, skin breakdown, infection, erosion and death).
Feasibility Can the proposed research be carried out in a realistic timescale and at an acceptable cost? As part of cost-effectiveness analysis, formal value-of-information methods may also sometimes be used to estimate the value for money of additional research. Are there any ethical or technical issues?	The major issues with this trial would be the identification of cases and the studying of them in a primary care environment. An adequate population of men with this problem already exists precisely because of the absence of any consensus strategy for this group.
Other comments Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue or methodological problems. However, this is not a research protocol.	None.

Importance How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	High. Surgery is indicated as therapy for retention – but may not be appropriate in the presence of impaired bladder function (underactive) or where comorbidity precludes it.

10.3 Products for men with urinary incontinence

PICO question Each research recommendation should be formulated as an answerable question or a set of closely related questions. This should use the PICO framework (patient, intervention, comparison and outcome)	What is the clinical and cost effectiveness and associated adverse events of absorbent pads compared to sheath collectors for men with urinary incontinence?
Importance to patients or the population. What would be the impact of any new or altered guidance on the population? (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality).	The number of patients in this group is steadily increasing with more radical prostatectomies and an ageing demographic. Current practise varies widely across the UK with no established standards of good practice. The research could establish the best approach to continence management in these men and so bring more effective treatment, better focussed on each patient's needs, and consequently cost-efficiency gains.
Relevance to NICE guidance How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)?	NICE currently cannot give clear guidance on this topic because of an inadequate evidence base.
Relevance to the NHS What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	Containment products are currently used variably across the UK. It is rare that any element of bladder training or recognition and treatment of bladder dysfunction is recognised as part of the continence management problem. The aim, so often, is simply to keep the patient socially dry; and even that is not always achieved acceptably. Evidence-based guidance on the selection of the most suitable containment product and its subsequent management will benefit the quality of life of patients, use skilled nurse/career resources more efficiently and reduce the costs of waste of unsuitable or sub-optimal product use.
National priorities Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	There is currently no national service framework for men with LUTS and incontinence or difficulty with bladder emptying.
Current evidence base What is the current evidence base? What are the problems with the current	There is no currently no level 1 evidence for pads and sheaths.

evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews. The date on which the final literature search was undertaken should be specified.	
Equality Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	There are no equality issues.
Study design It should also specify the most appropriate study design to address the proposed question(s). Primary research or secondary research (for example, systematic reviews) can be recommended.	A randomised controlled trial to compare these interventions. Outcomes of interest would be symptom severity, quality of life, changes in measured leakage, and occurrence of adverse events.
Feasibility Can the proposed research be carried out in a realistic timescale and at an acceptable cost? As part of cost-effectiveness analysis, formal value-of-information methods may also sometimes be used to estimate the value for money of additional research. Are there any ethical or technical issues?	The major issues with this trial would be the identification of cases and the studying of them in a primary care environment. An adequate population of men with this problem already exists precisely because of the absence of any consensus strategy for this group.
Other comments Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue or methodological problems. However, this is not a research protocol.	In general, manufacturers have been reluctant to fund randomised controlled trials. Currently the D4D project is addressing unmet needs. Work with specialist and patient advocacy groups and manufacturers will be essential.
Importance How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the	High. This is a population of men who have been rendered incontinent by surgery. The impact on their quality of life is profound and there is currently only one realistic treatment option for more major incontinence namely surgery which many men find unacceptable. It is important that solutions are found for this growing number of men.

research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	

10.4 Laser vaporisation techniques

PICO question Each research recommendation should be formulated as an answerable question or a set of closely related questions. This should use the PICO framework (patient, intervention, comparison and outcome)	What is the clinical and cost effectiveness and associated adverse events of laser vaporisation techniques compared to TURP in men with moderate to severe bothersome LUTS considering surgery for bladder outlet obstruction? Assessed by symptom severity, quality of life, and adverse events.
Importance to patients or the population. What would be the impact of any new or altered guidance on the population? (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality).	The potential advantages of reduced blood loss, shorter hospital stay and earlier return to normal activities make laser vaporisation techniques attractive to patients and healthcare providers although there is uncertainty around degree of symptom improvement and improvement in quality of life in the short and longer term.
Relevance to NICE guidance How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)?	NICE cannot give clear guidance on this intervention because the evidence base is inadequate. The proposed research will add new knowledge.
Relevance to the NHS What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	Green Light laser use in the NHS is increasing at a rapid rate with approximately 70 units in the UK using it (~ 60% NHS and ~ 40% private sector) from personal communication with representatives of American Medical Systems Inc and clinical units. This is despite a lack of clinical and cost-effectiveness data to support this practice.
National priorities Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	None
Current evidence base What is the current evidence base? What are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews. The date on which the final literature search was undertaken should be specified.	A recent NCCHTA commissioned systematic review suggests that TURP should remain the standard of care and specifically that green Light Laser was unlikely to be cost-effective in the economic model and thereby arguing against its unrestricted use in the NHS until further evidence of effectiveness and cost-reduction is obtained [19,172-174].
Equality Does the research recommendation address equality issues? For example, does it focus	Not applicable

on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	
Study design It should also specify the most appropriate study design to address the proposed question(s). Primary research or secondary research (for example, systematic reviews) can be recommended.	Primary research (RCT). Comparator is TURP. Careful consideration must be given to treatment strategies within the trial design such as incorporating early versus delayed intervention.
Feasibility Can the proposed research be carried out in a realistic timescale and at an acceptable cost? As part of cost-effectiveness analysis, formal value-of-information methods may also sometimes be used to estimate the value for money of additional research. Are there any ethical or technical issues?	Proposed research can be carried out in a realistic timescale and at an acceptable cost. There are no ethical issues. A potential risk is that KTP laser vaporisation use may diminish without adequate assessment.
Other comments Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue or methodological problems. However, this is not a research protocol.	NCCHTA would be the obvious funder
Importance How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	High

10.5 Male slings

PICO question Each research recommendation should be formulated as an answerable question or a set of closely related questions. This should use the PICO framework (patient, intervention, comparison and outcome)	In men with mild to moderate post prostatectomy urinary incontinence (P), what is the clinical or cost effectiveness of a male sling or an extraurethral non circumferential compression device (IC), when assessed by symptom severity, quality of life, changes in measured leakage, and occurrence of adverse events (O). **Possible interventions include:** Non compression retrobulbar sling, compressive bulbar slings, adjustable bulbar slings, extraurethral compressive support and extraurethral non circumferential compression devices. Paraurethral injections have been used but are not recommended by the recent WHO International Consultation on Incontinence.
Importance to patients or the population. What would be the impact of any new or altered guidance on the population? (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality).	This increasingly prevalent group of men have, until recently, had no acceptable treatment option other than insertion of an artificial urinary sphincter but many men consider this treatment to be too invasive and too prone to complication or failure. A number of new interventions have been devised but there is no clarity on which of these offers the best outcomes. This research could lead to clear recommendations and effective treatment for the majority of these men.
Relevance to NICE guidance How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)?	NICE currently cannot give clear guidance on this topic because of an inadequate evidence base.
Relevance to the NHS What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	This group of men currently depend on containment alone for control of their incontinence – there are likely to be cost savings from effective incontinence treatment Insertion of an artificial urinary sphincter, whilst of recognised efficacy, carries a significant cost. Guidance is needed on the most suitable surgical options for this group of men.
National priorities Is the question relevant to a national priority	There is currently no national service framework for men with LUTS or

area (such as a national service framework or white paper)? The relevant document should be specified.	incontinence.
Current evidence base What is the current evidence base? What are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews. The date on which the final literature search was undertaken should be specified.	There is currently no level 1 evidence for these surgical interventions because they are relatively new and have not been subjected to randomised controlled trials. NICE Interventional Procedures Committee has reported on Male slings (mostly "Invance") and non circumferential extraurethral compression devices.
Equality Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	There are no equality issues.
Study design It should also specify the most appropriate study design to address the proposed question(s). Primary research or secondary research (for example, systematic reviews) can be recommended.	A randomised controlled trial comparing up to three current interventions; retrobulbar "non compressive" male sling (Advance) , adjustable compression sling (Argos), and extraurethral non circumferential compression device (Proact) is recommended. However other new devices are being introduced rapidly into the market place with little or no clinical data to underpin marketing.
Feasibility Can the proposed research be carried out in a realistic timescale and at an acceptable cost? As part of cost-effectiveness analysis, formal value-of-information methods may also sometimes be used to estimate the value for money of additional research. Are there any ethical or technical issues?	The major issues with this trial would be the centralisation of cases into centres able to offer the surgery and the training of participating surgeons since the procedures proposed are still relatively new. An adequate population of men with this problem already exists precisely because of the absence of any really effective treatment for this group.
Other comments Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue or methodological problems. However, this is not a research protocol.	In general, manufacturers have been reluctant to fund randomised controlled trials and prefer to sponsor the establishment of surgical registries. Whilst these facilitate the involvement of a greater number of surgeons and cases, the risk of bias is very high. It may be that independent registries are a better way to establish the associated risks of surgery because of the feasibility of including all patients, not just those eligible

	for inclusion in an RCT.
Importance How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	High. This is a population of men who have been rendered incontinent by surgery which may or may not cure their cancer. The impact on their quality of life is profound and there is currently only one realistic treatment option which many men find unacceptable. It is important that solutions are found for this growing number of men.

Appendix H –

International Prostate Symptom Score (IPSS)

INTERNATIONAL-PROSTATE SYMPTOM SCORE (I-PSS)							
	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	
1. Over the past 4 weeks, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5	
2. Over the past 4 weeks, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
3. Over the past 4 weeks, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Over the past 4 weeks, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5 Over the past 4 weeks, how often has your urinary stream been weaker than usual?	0	1	2	3	4	5	
6 Over the past 4 weeks, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	1 time	2 times	3 times	4 times	5 or more times	
7. Over the past 4 weeks, how many times, in general, did you get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5	
Total I-PSS Score S =							
QUALITY OF LIFE DUE TO URINARY SYMPTOMS							
	Delighted	Pleased	Mostly satisfied	Mixed - neither satisfied nor dissatisfied	Mostly dissatisfied	Unhappy	Terrible
1. If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6
Quality of life assessment index L =							

I-PSS contact information and permission to use:
MAPI Research Trust, Lyon, France.
E-mail: contact@mapi-trust.org
Website: www.mapi-trust.org

I-PSS 1_ Standard_UK English_Mapi Institute_ID2831

International Prostate Symptom Score – Acute version

INTERNATIONAL-PROSTATE SYMPTOM SCORE						
Question	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
1. Over the past week, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. Over the past week, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5
3. Over the past week, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5
4. Over the past week, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past week, how often has your urinary stream been weaker than usual?	0	1	2	3	4	5
6. Over the past week, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
	None	1 time	2 times	3 times	4 times	5 or more times
7. Over the past week, how many times, in general, did you get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5

INTERNATIONAL-PROSTATE SYMPTOM SCORE (cont'd)							
QUALITY OF LIFE DUE TO URINARY SYMPTOMS							
Question	Delighted	Pleased	Mostly satisfied	Mixed - neither satisfied nor dissatisfied	Mostly dissatisfied	Unhappy	Terrible
1. If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6

I-PSS contact information and permission to use:
MAPI Research Trust, Lyon, France.
E-mail: contact@mapi-trust.org
Website: www.mapi-trust.org

I-PSS1 Acute- UK English –ID3546_ 15/02/99

Note: formal permission is being obtained for the inclusion of IPSS in the appendix

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