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Fri 13th Sept 2019

NHS
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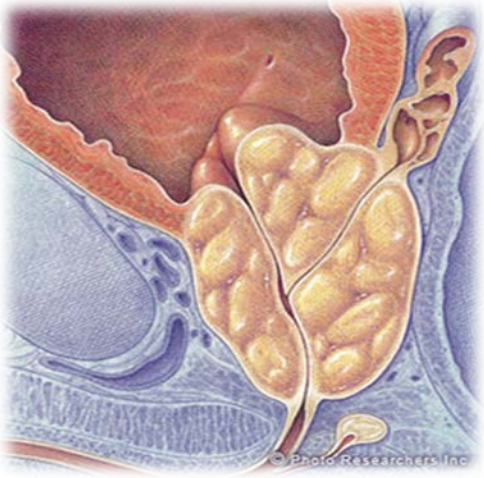

Prostate problems in older men
and OAB

Mark J Speakman MS(Lond) FRCS(Eng) FRCSEd(Hon)

Past President BAUS

Consultant Urological Surgeon

Taunton, UK

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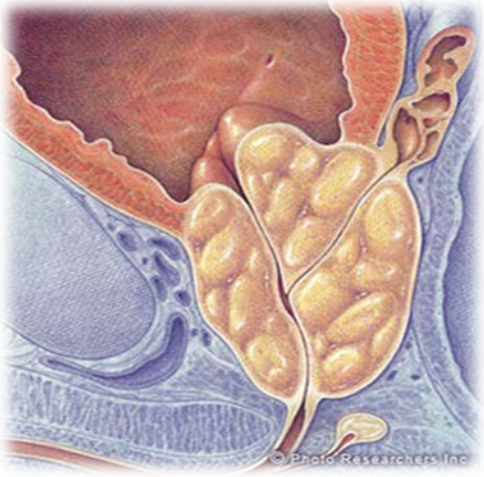

Lower Urinary Tract Symptoms (LUTS) in older men

Mark J Speakman MS(Lond) FRCS(Eng) FRCSEd(Hon)
Past President BAUS
Consultant Urological Surgeon
Taunton, UK

The British Association of Urological Surgeons

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Conflicts of interest

- Lecturer for Astellas at the EAU March 2017 (overactive bladder) and at the BAUS June 2018 (prostate cancer)

- Member of the European Association of Urology guideline group (LUTS/BPH)
- Advisor to NICE

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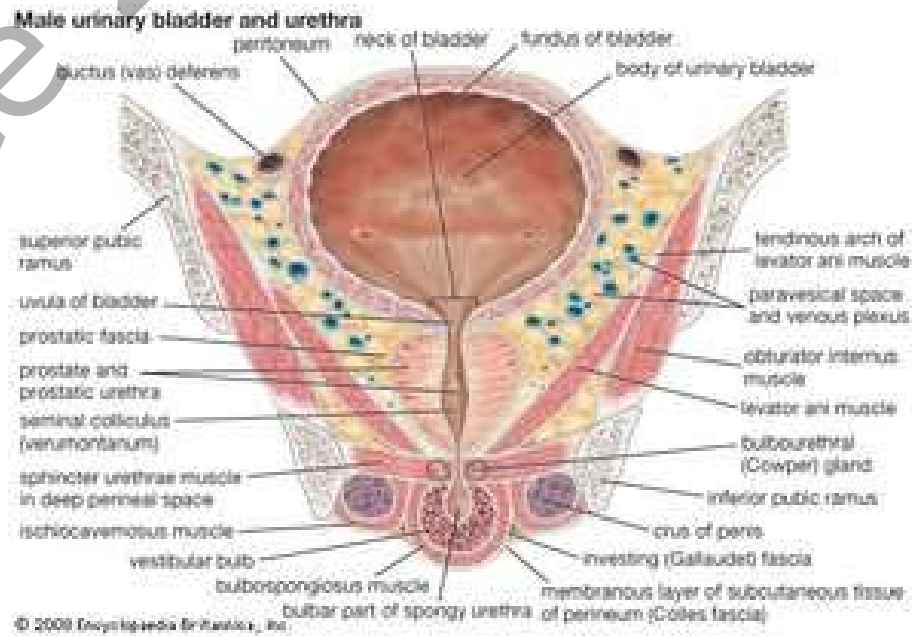
Basic knowledge

- Basic function of the bladder
- Basic anatomy
- Basic nerve supply
- ‘Basic’ terminology



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LUTS/BPH Terminology – Stop the Confusion!

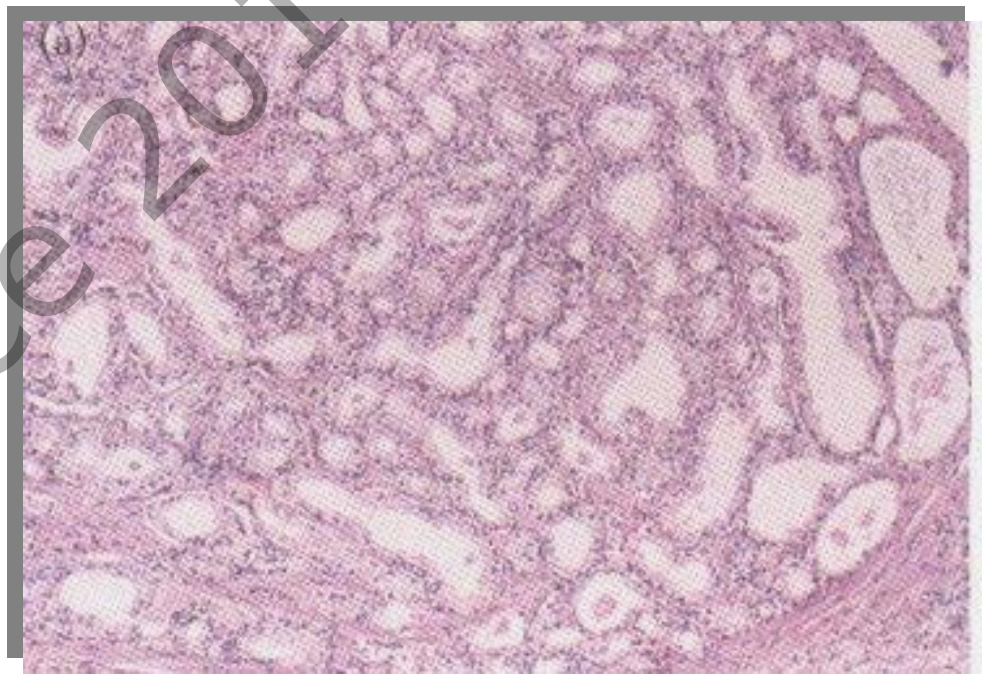
Paul Abrams, MD
Professor of Urology,
University of Bristol, UK

New words for old:

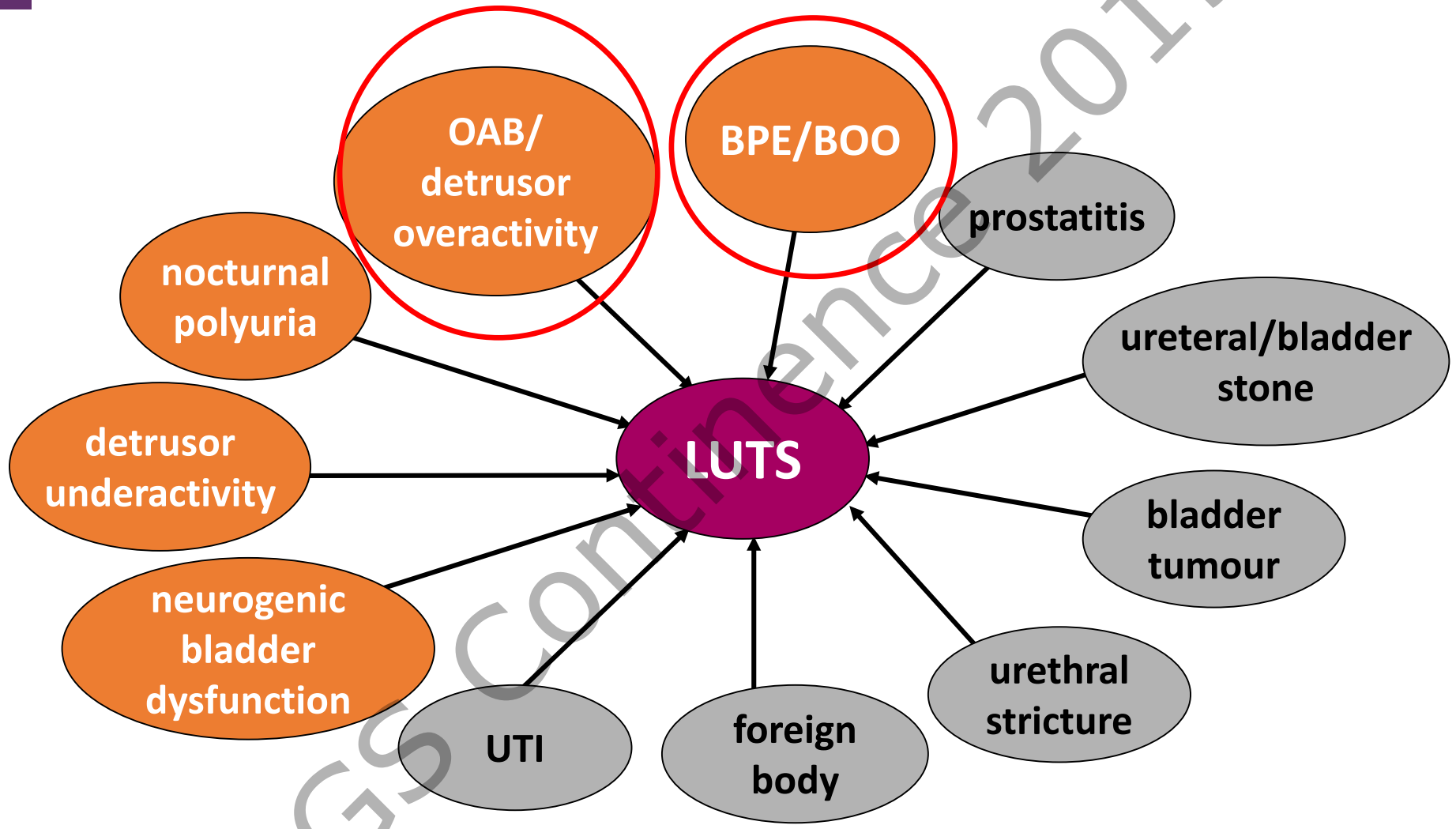
lower urinary tract symptoms *for*

"prostatism"

BMJ 1994;308:929



LUTS - a multitude of urological causes

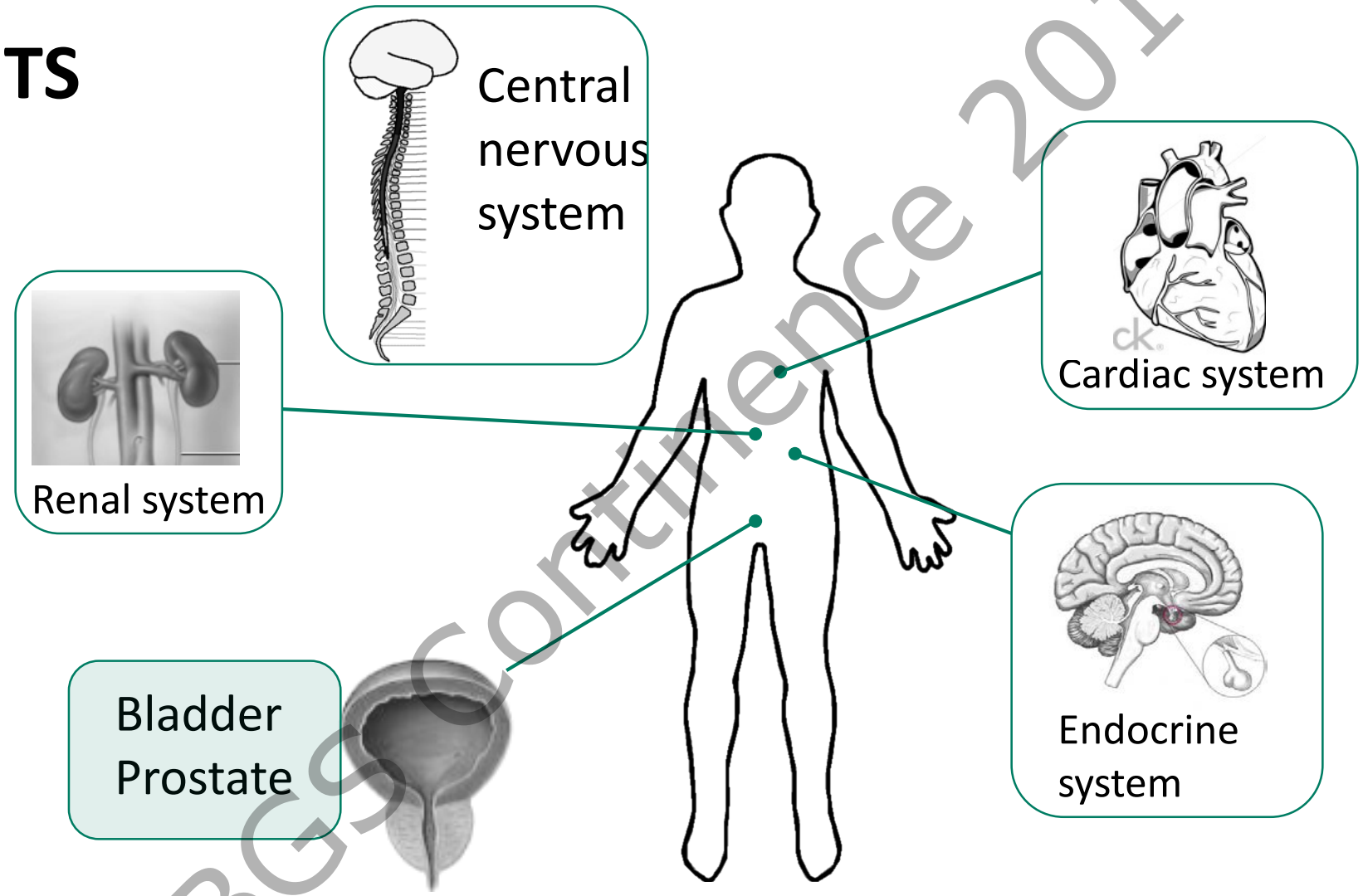


BOO: bladder outlet obstruction;
BPE: benign prostatic enlargement;
OAB: overactive bladder;
UTI: urinary tract infection

Adapted from Thorner DA et al. Urol Clin North Am 2009;36:417-29;
Speakman MJ. Eur Urol Suppl 2008;7:680-9

..and causes outside the lower urinary tract

LUTS



Speakman MJ. Eur Urol Suppl 2008;7:680-9

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LUTS present with a variety of symptoms

Storage symptoms	Voiding symptoms	Post micturition symptoms
• Altered bladder sensation • Increased daytime frequency • Nocturia • Urgency • Urinary incontinence	• Hesitancy • Intermittency • Slow stream • Splitting/spraying • Straining • Terminal dribble	• Feeling of incomplete bladder emptying • Post micturition dribble

2/3 of men with LUTS have symptoms from more than one symptom group

Abrams P et al. Urology 2003;61:37-49;
Sexton CC et al. BJU Int 2009;103(Suppl3):12-23

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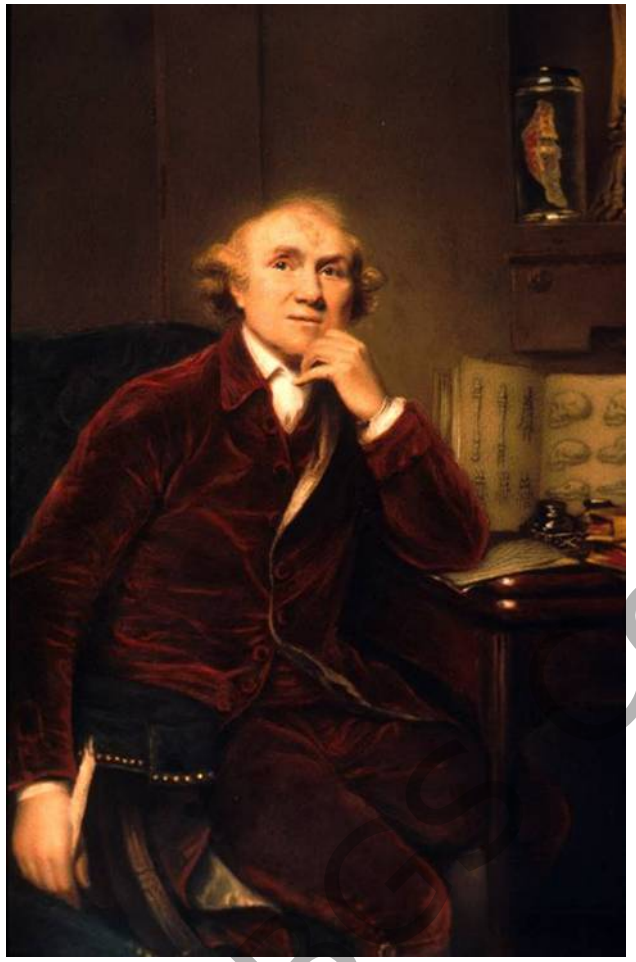
Voiding *v Obstructive* symptoms

- “On this point however, persons are always deceived. They never duly estimate the size of the stream they formerly made…
- it is only when great change has occurred that the sufferer is aware of the fact.”

Guthrie GJ 1843

On the anatomy and diseases of the urinary and sexual organs. London

Storage or *Irritative* Symptoms



- *"The disease of the bladder arising from obstruction alone, is increased irritability, and its consequences, by which the bladder admits of little distension, becomes quick in its action, and thick in its coats."*

Hunter J. 1786 A treatise on the venereal disease. 3rd Ed. 1810 London

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International Prostate Symptom Score (IPSS)

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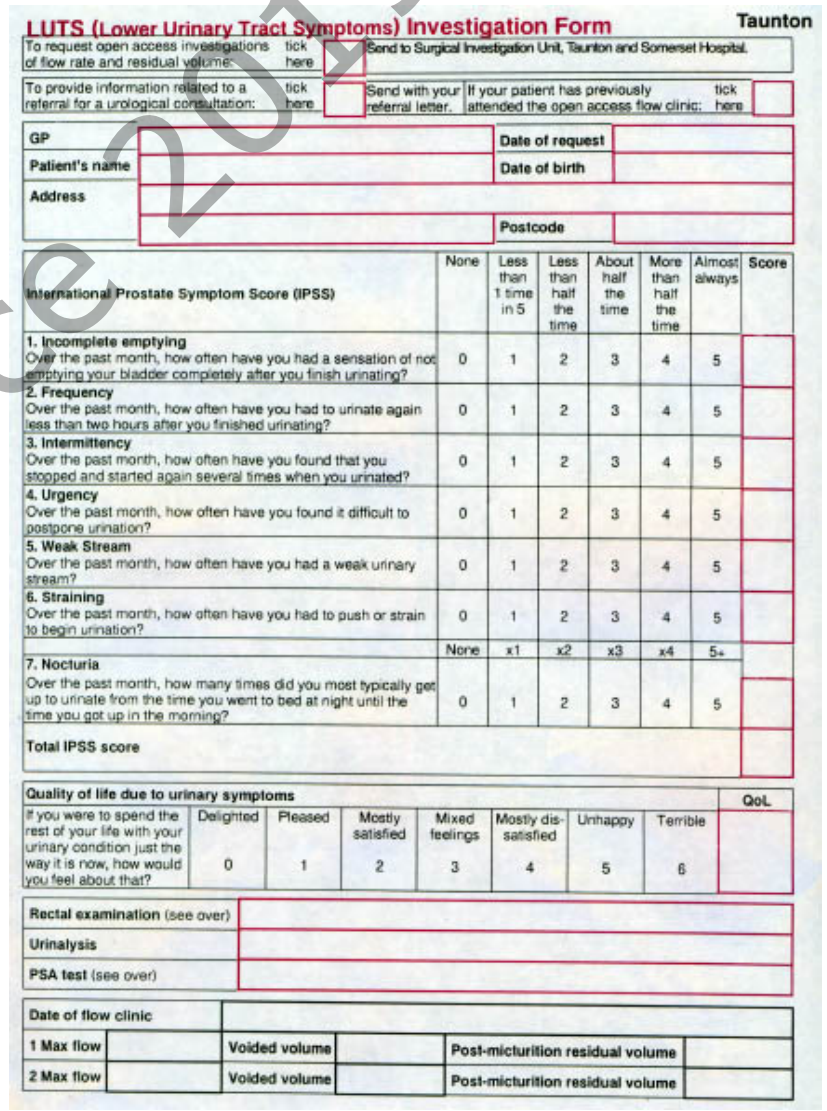
1. Incomplete Emptying
2. Frequency
3. Intermittency
4. Urgency
5. Weak Stream
6. Straining
7. Nocturia
8. If you were to spend …



LUTS (Lower Urinary Tract Symptoms) Investigation Form — Taunton

To request open access investigations of flow rate and residual volume: tick here ☐ — Send to Surgical Investigation Unit, Taunton and Somerset Hospital.

To provide information related to a referral for a urological consultation: tick here ☐ — Send with your referral letter. If your patient has previously attended the open access flow clinic: tick here ☐

GP		Date of request	
Patient's name		Date of birth	
Address			
		Postcode	

International Prostate Symptom Score (IPSS)	None	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Score
1. Incomplete emptying Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
2. Frequency Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
3. Intermittency Over the past month, how often have you found that you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	x1	x2	x3	x4	5+	
7. Nocturia Over the past month, how many times did you most typically 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 IPSS score							

Quality of life due to urinary symptoms								QoL
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?	Delighted	Pleased	Mostly satisfied	Mixed feelings	Mostly dis-satisfied	Unhappy	Terrible	
	0	1	2	3	4	5	6	

Rectal examination (see over)	
Urinalysis	
PSA test (see over)	

Date of flow clinic					
1 Max flow		Voided volume		Post-micturition residual volume	
2 Max flow		Voided volume		Post-micturition residual volume	

Is it a good questionnaire?

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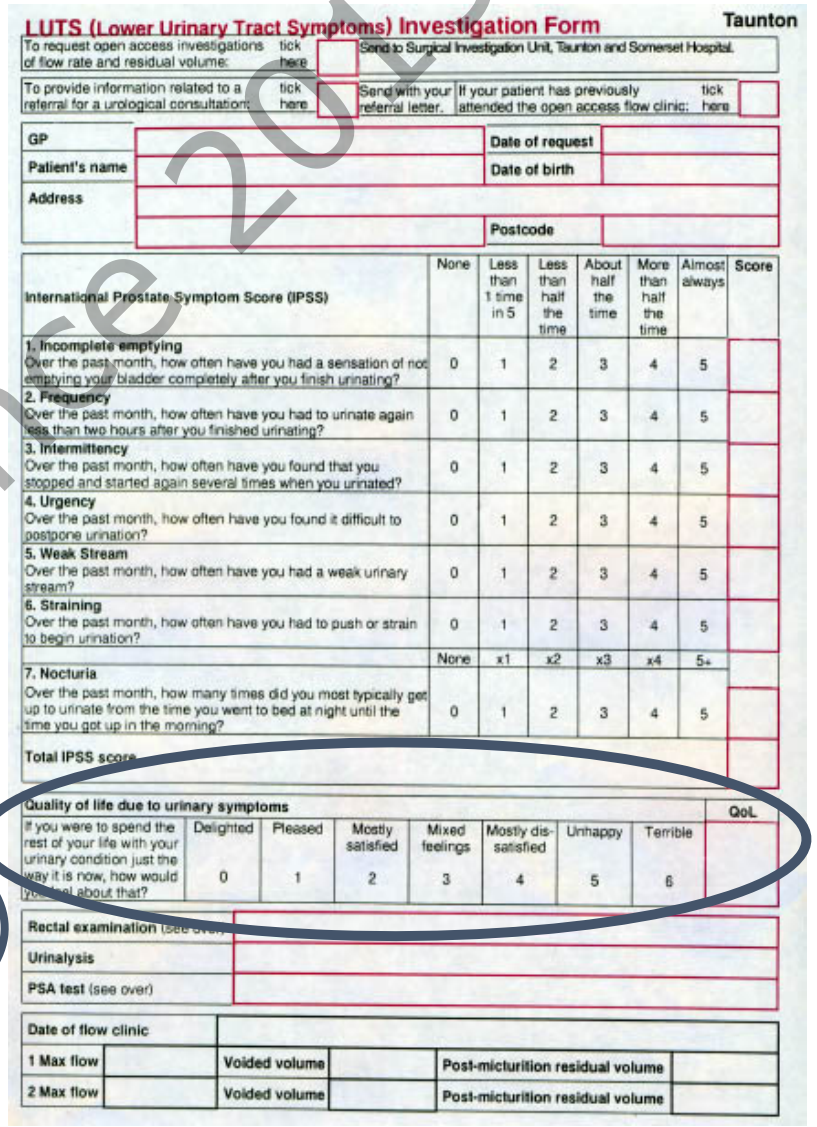
International Prostate Symptom Score (IPSS)
QoL Question

- 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 ?

“Delighted, Pleased, Satisfied, Mixed, Dissatisfied, Unhappy, Terrible”



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1. Incomplete emptying — Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
2. Frequency — Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
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4. Urgency — Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream — Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining — Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	x1	x2	x3	x4	5+	
7. Nocturia — Over the past month, how many times did you most typically 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 IPSS score							

Quality of life due to urinary symptoms	Delighted	Pleased	Mostly satisfied	Mixed feelings	Mostly dissatisfied	Unhappy	Terrible	QoL
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	

Rectal examination (see over)	
Urinalysis	
PSA test (see over)	

Date of flow clinic					
1 Max flow		Voided volume		Post-micturition residual volume	
2 Max flow		Voided volume		Post-micturition residual volume	

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BLADDER DIARY

Please complete your bladder diary each day for three continuous days.

Name: _____

URINE					DRINKS		
Date/time am/pm	Amount in mL	How strong was the urge to go? 0, +, ++	Did you experience accidental leakage?	Comments What were you doing?	Time	Amount in mL or cups	Type what kind?
This "sample" line shows you how to use the diary							
Tuesday 6.30 am	*150mL*	*0*	*No*	*Got out of bed*	*7am*	*500mL 2 cups*	*Tea*

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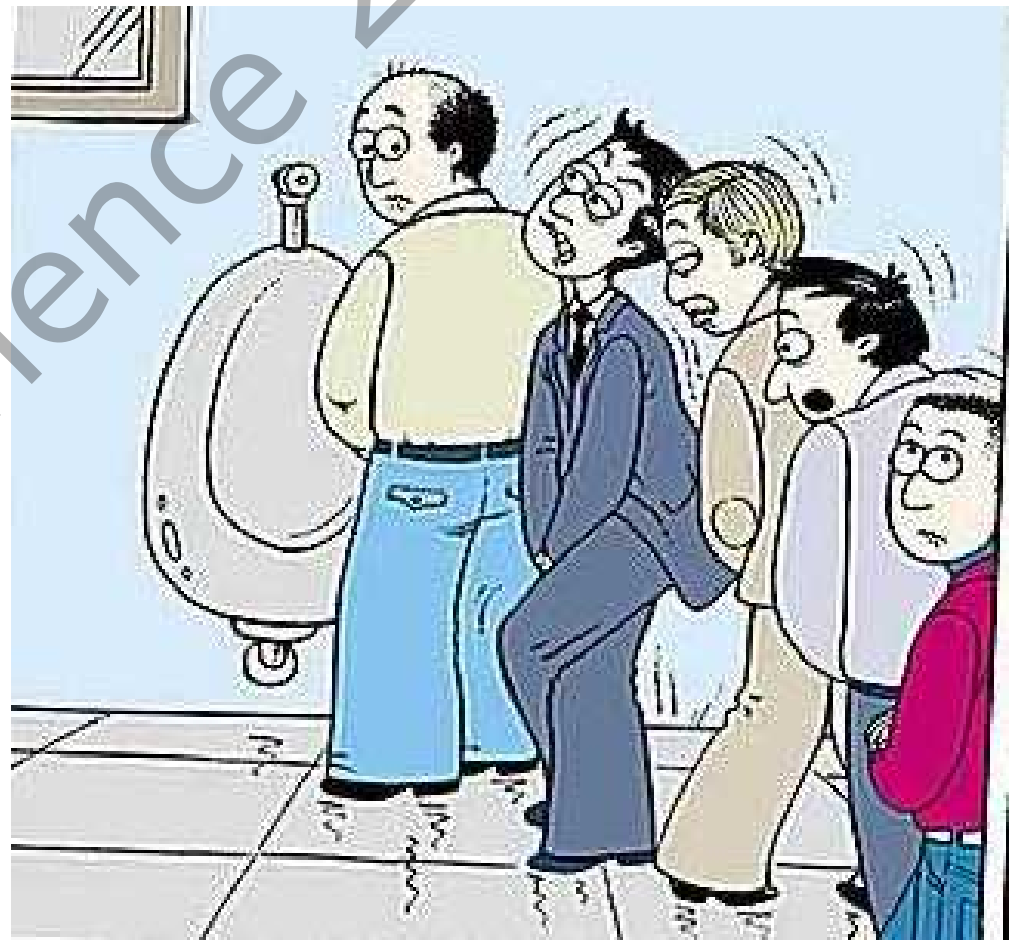
Overactive Bladder (OAB)

- Urgency, with or without urgency incontinence, often with frequency and nocturia in the absence of other pathologies
- E.g. UTIs, polyuria, bladder TCC, or neurologic abnormalities.

Overactive Bladder (OAB)

In Men too!



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Urgency: the most bothersome symptom?

Urgency is a sudden, compelling desire to pass urine, which is difficult to defer.

ICS 2004 Terminology Workshop
Abrams et al.

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Fratton Park – Portsmouth FC

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Portsmouth 1-2 Bolton
2009

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Urgency: changing the definition?

Urgency is a

sudden, compelling

desire to pass urine, which is

difficult to defer

ICS 2004 Terminology Workshop
Abrams et al.

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Urgency: changing the definition?

Urgency is a *abnormal, or inappropriate* sudden, compelling desire to pass urine, which is *very* difficult *or impossible* to defer *for fear of leakage*

ICS 2004 Terminology Workshop
Abrams et al 2006, NAU 25: 293

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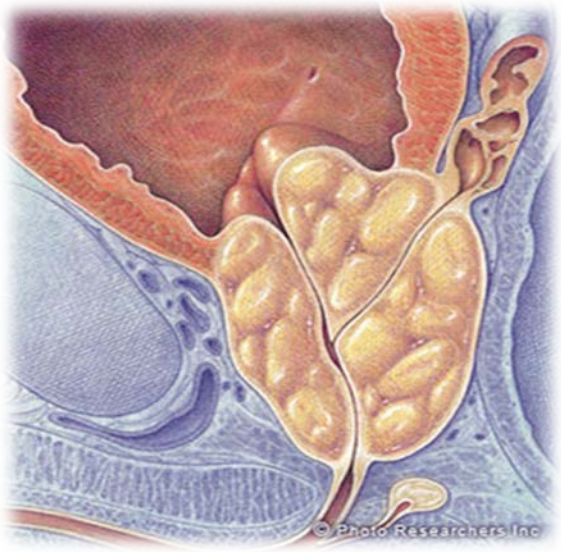
September 2019

Medical Treatment of LUTS/BPH



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Conservative measures in LUTS/BPH

An emerging paradigm in the contemporary study of LUTS is that obesity increases and physical activity decreases risk of progression

- Parsons JK, Sarma AV, McVary K, Wei JT. Obesity and BPH: clinical connections, emerging etiological paradigms and future directions. J Urol. 2012 189(1 Suppl):S102-6.

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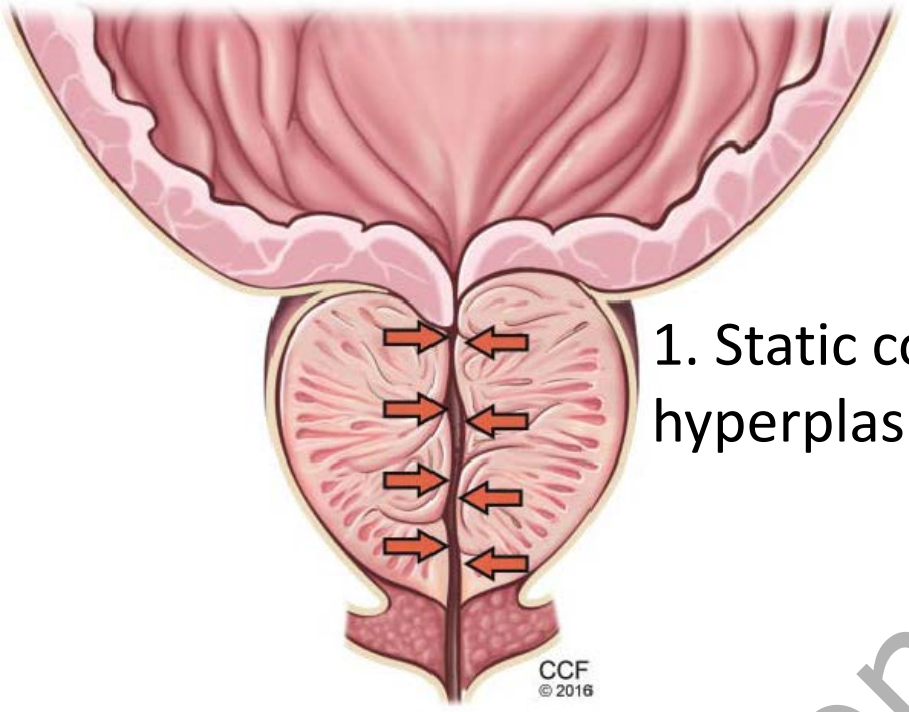
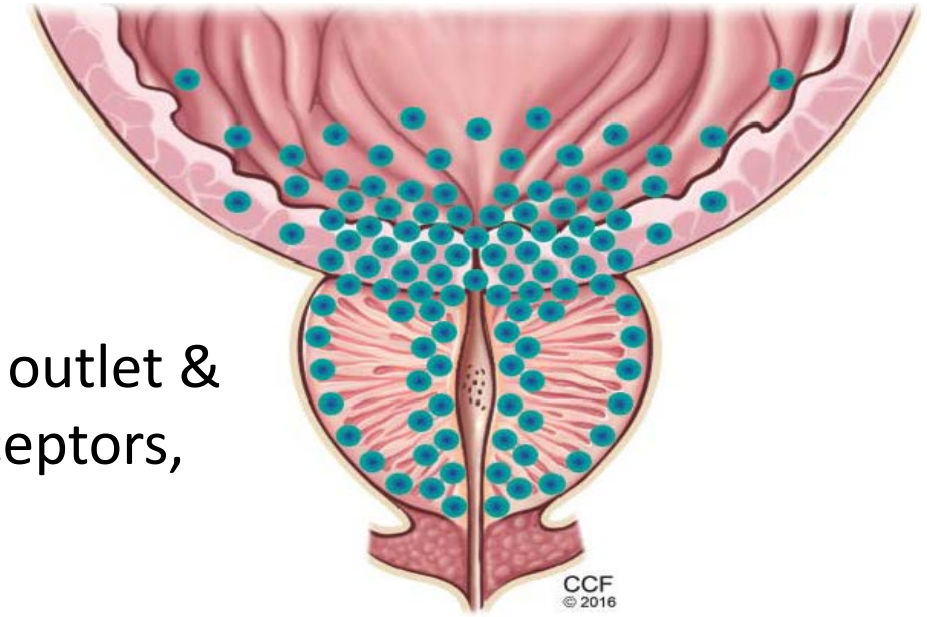
Medical Rx of LUTS



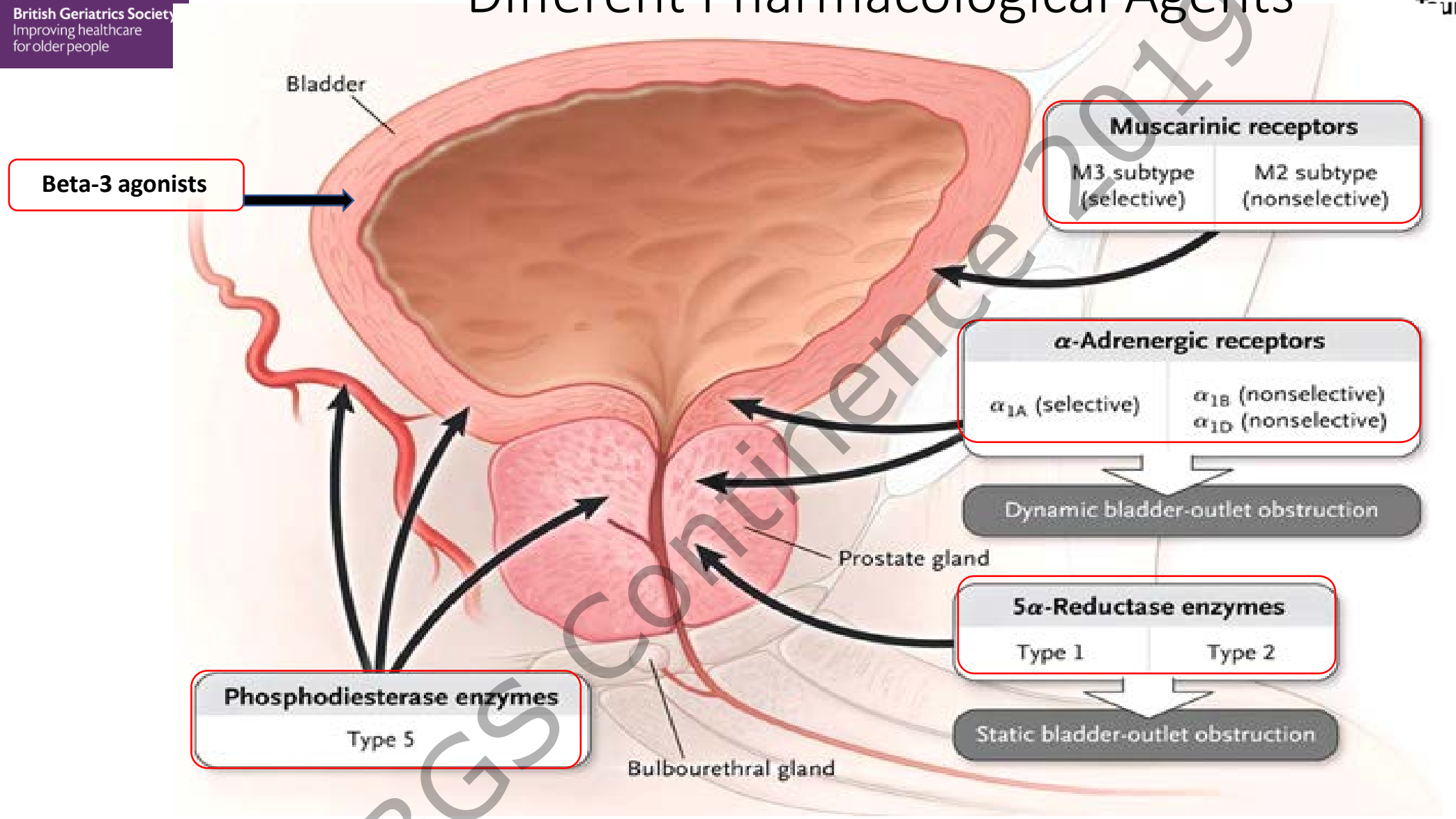
1. Static component of BPH & LUTS with hyperplasia leading to urethral compression



2. Dynamic component of BPH: Bladder outlet & prostate are richly supplied with α-1 receptors, which increase smooth muscle tone.

Unnikrishnan R, et al. Cleveland Clinic Journal of Medicine. 2017; 84(1): 53-64.

Different Pharmacological Agents



Sarma AV, et al. N Engl J Med. 2012; 367(3): 248-57.

Meta-analysis of efficacy & tolerability of alpha adrenergic agents

Djavan & Marberger Eur Urol 1999; 36:1-13

- "All alpha-blockers seen to have similar efficacy in improving symptoms and flow"

- "Alfuzosin and Tamsulosin *(and silodosin)* are better tolerated than doxazosin, terazosin & prazosin"

5-alpha reductase inhibitors - Finasteride, Dutasteride

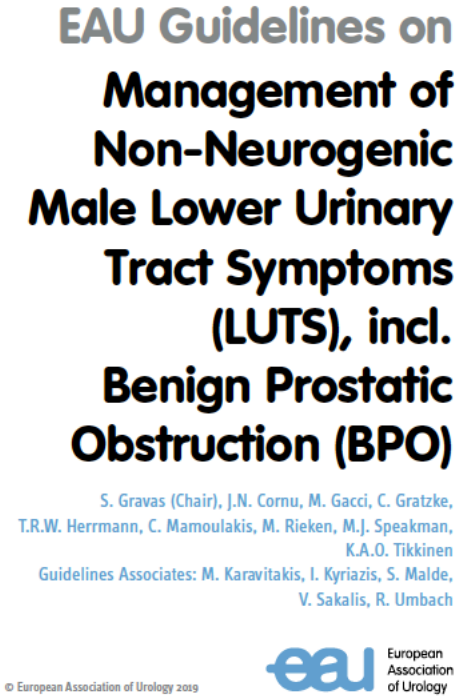
Which factors predict for Progression?

1.	Symptoms	Mod-Severe LUTS
2.	Bother	QoL >3
3.	Flow rate	<12mL/sec
4.	Age	>70yrs
5.	Prostatic volume	> 40cc
6.	PSA	> 1.4ng.mL
7.	Residual volume	>150mL
8.	Inflammation	+ve

5.2.3 Muscarinic receptor antagonists

Summary of evidence	LE
Antimuscarinic monotherapy can significantly improve urgency, UUI, and increased daytime frequency.	2
Antimuscarinic monotherapy can be associated with increased PVR after therapy, but acute retention is a rare event in men with a PVR volume of < 150 mL at baseline.	2

Recommendations	Strength rating
Use muscarinic receptor antagonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Strong
Do not use antimuscarinic overactive bladder medications in men with a post-void residual volume > 150 mL.	Weak



Anticholinergic cognitive burden (ACB)

thebmj

RESEARCH

Anticholinergic drugs and risk of dementia: case-control study

Kathryn Richardson,[1] Chris Fox,[2] Ian Maidment,[3] Nicholas Steel,[2] Yoon K Loke,[2] Antony Arthur,[1] Phyo K Myint,[4] Carlota M Grossi,[1] Katharina Mattishent,[2] Kathleen Bennett,[5] Noll L Campbell,[6] Malaz Boustani,[7] Louise Robinson,[8] Carol Brayne,[9] Fiona E Matthews,[10] George M Savva[1]

CONCLUSIONS A robust association between some classes of anticholinergic drugs and future dementia incidence was observed. This could be caused by a class specific effect, or by drugs being used for very early symptoms of dementia.

The Guardian

Tuesday 11 December 2018

Some antidepressants linked to dementia risk

Scientists say doctors should consider weaning patients with depression, Parkinsons or bladder problems off anticholinergic drugs

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Mirabegron

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EAU Guidelines on
Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO)

S. Gravas (Chair), J.N. Cornu, M. Gacci, C. Gratzke, T.R.W. Herrmann, C. Mamoulakis, M. Rieken, M.J. Speakman, K.A.O. Tikkinen
Guidelines Associates: M. Karavitakis, I. Kyriazis, S. Malde, V. Sakalis, R. Umbach

European Association of Urology

Int Urogynecol J (2018) 29:273–283
DOI 10.1007/s00192-017-3377-5

CrossMark

ORIGINAL ARTICLE

A prospective, double-blind, randomized, two-period crossover, multicenter study to evaluate tolerability and patient preference between mirabegron and tolterodine in patients with overactive bladder (PREFER study)

David Staskin[1] · Sender Herschorn[2] · Jonathan Fialkov[3] · Le Mai Tu[4] · Terry Walsh[5] · Carol R. Schermer[5]

4 arms; 358 patients

25-40% were men

Conclusions Tolerability of mirabegron was significantly higher than that of tolterodine, and patient preference and improvements in OAB symptoms were comparable. Both treatments were well tolerated; however, anticholinergic side effects were higher with tolterodine.

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Nocturnal Polyuria

- >33% of 24hr output in nighttime hours
- Desmopressin [Nocdurna]
- 25 and 50 micrograms

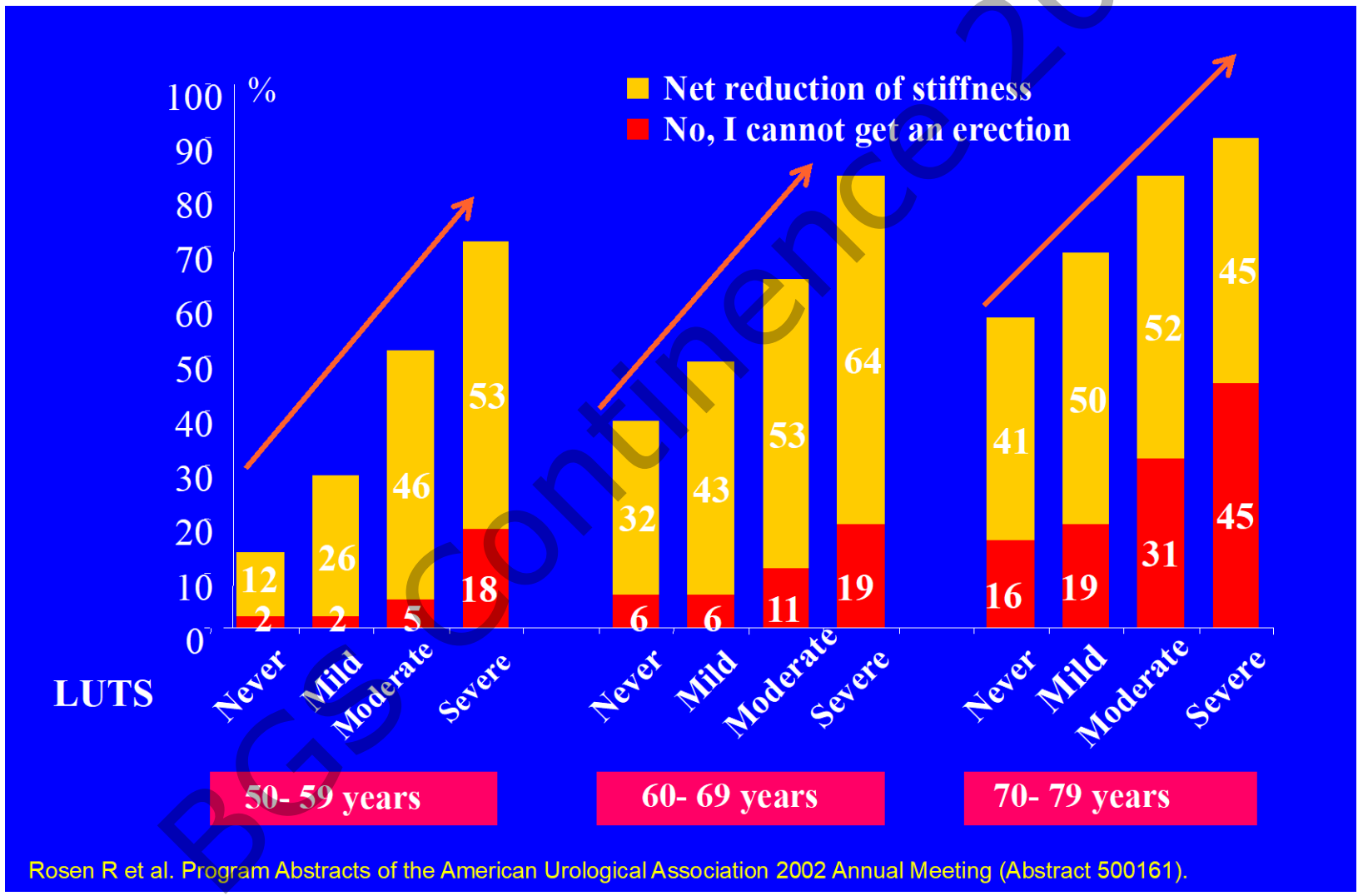
BLADDER DIARY

Please complete your bladder diary each day for three continuous days.

Name: _____

URINE					DRINKS		
Date/time am/pm	Amount in mL	How strong was the urge to go? 0, +, ++	Did you experience accidental leakage?	Comments What were you doing?	Time	Amount in mL or cups	Type what kind?
This "sample" line shows you how to use the diary							
Tuesday 6.30 am	*150mL*	*0*	*No*	*Got out of bed*	*7am*	*500mL 2 cups*	*Tea*

Erectile Dysfunction increases with Age and severity of LUTS



Rosen R et al. Program Abstracts of the American Urological Association 2002 Annual Meeting (Abstract 500161).

Conclusions (medical treatment)

- Patients with bothersome LUTS at low risk of progression: α_1-AR antagonist monotherapy
- Patients with bothersome LUTS at higher risk of progression: α_1-AR antagonist + 5α-RI
- Patients with LUTS and OAB: α_1-AR antagonist + antimuscarinic agent or beta-3 agonist
- Patients with LUTS and erectile dysfunction: α_1-AR antagonist + PDE-5 inhibitor

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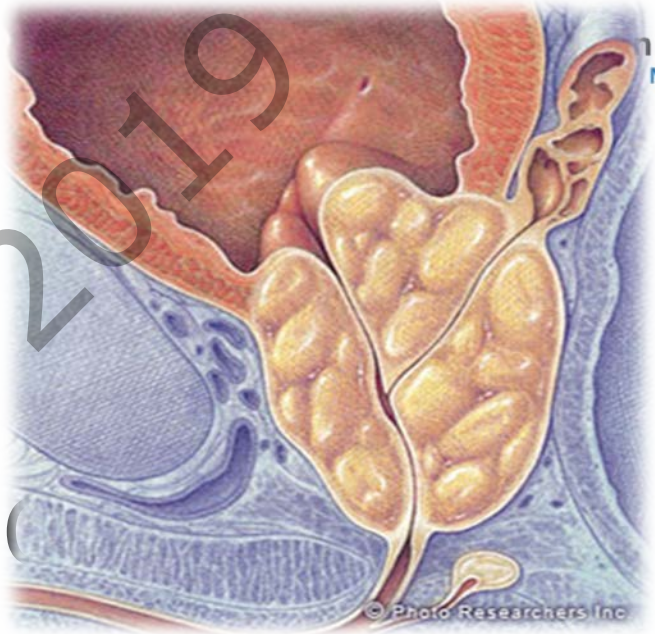

Surgical Treatment of LUTS/BPH

September 2019

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Established modalities

1. Bladder neck Incision / TUIP
2. Bipolar TURP
3. Open Prostatectomy
4. Holmium laser enucleation (HoLEP)
5. Greenlight laser ablation

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Newer modalities

1. Urolift
2. Prostate artery embolisation
3. Rezum
4. Aquablation
5. iTind
6. Newer forms of enucleation
7. Robotic assisted simple prostatectomy

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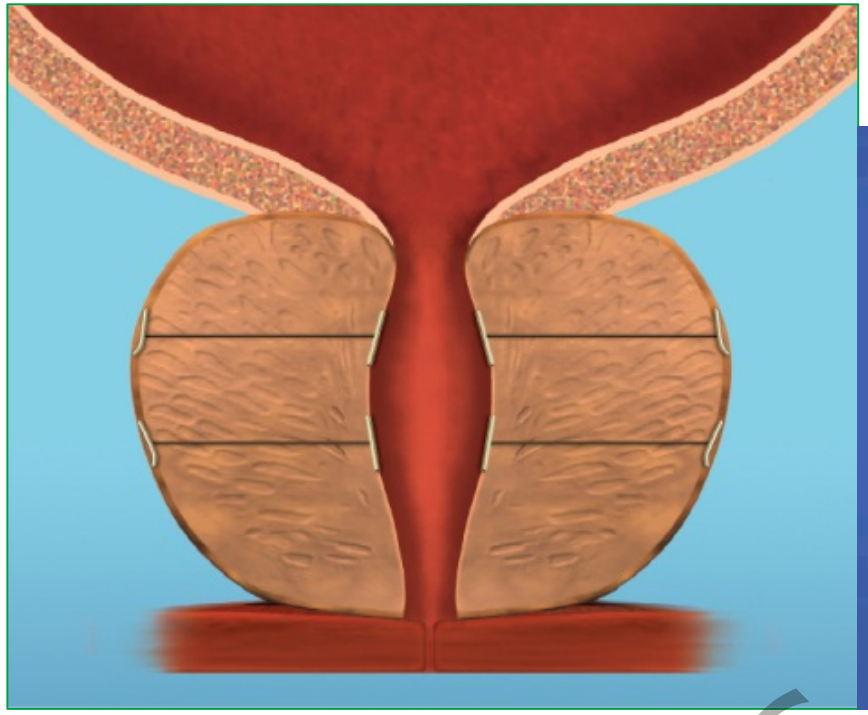
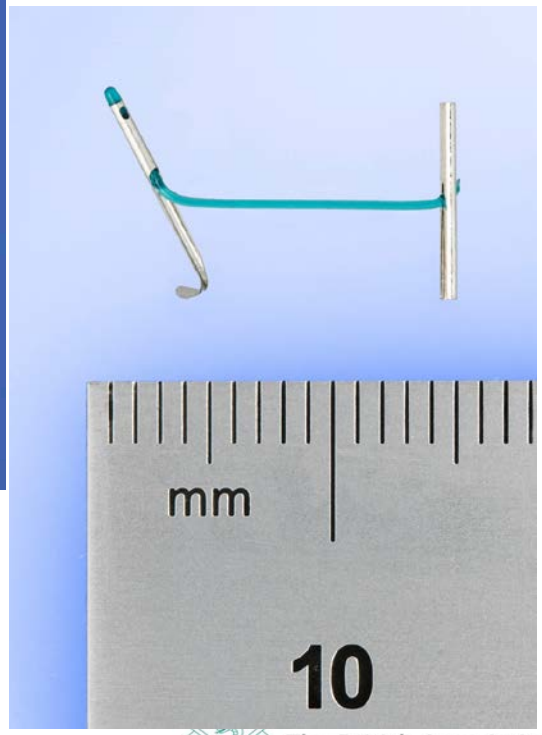
UROLIFT

Spot areas of prostate lobe retraction?





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Prostate artery embolisation

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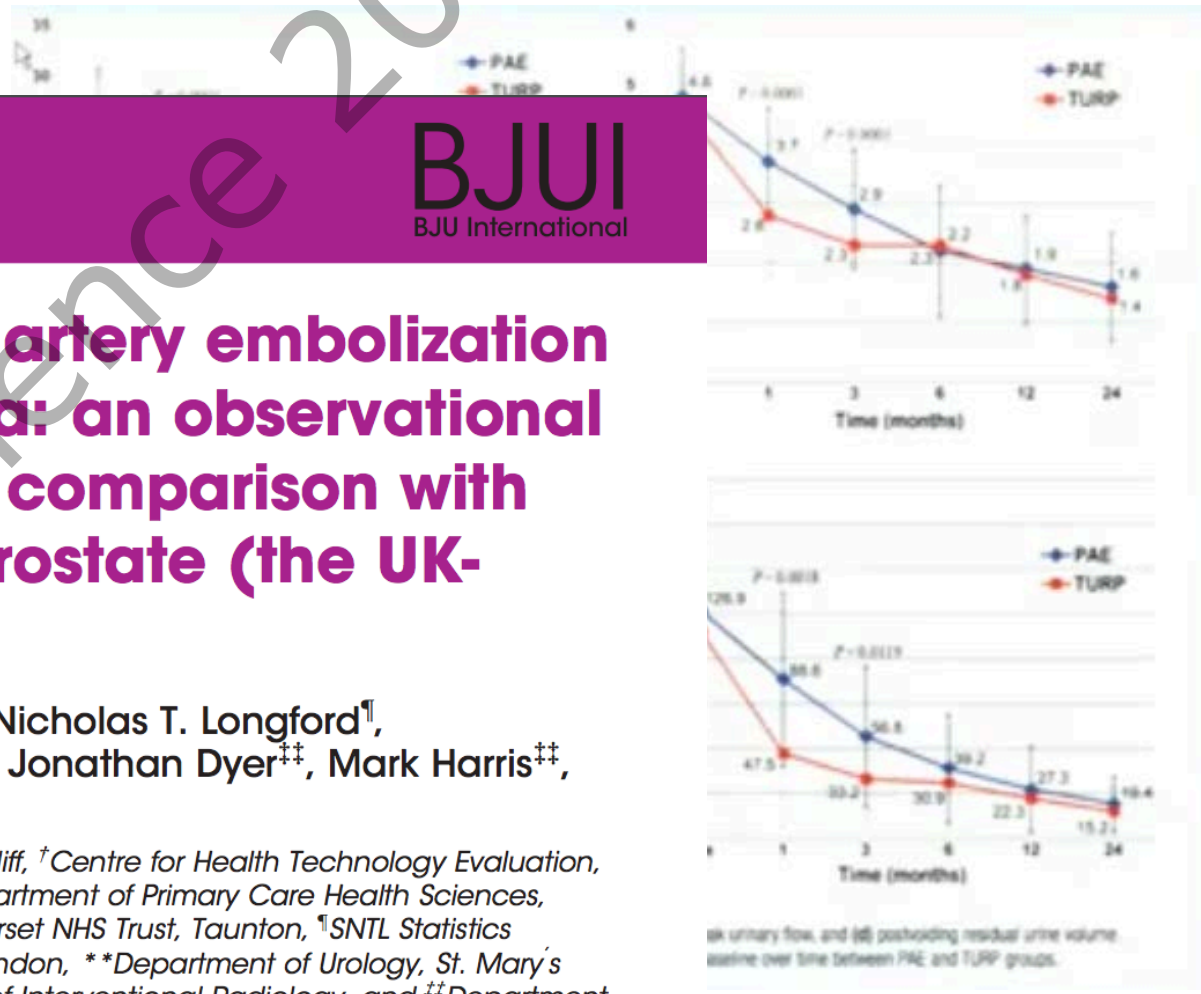

Trial

BJUI
BJU International

Efficacy and safety of prostate artery embolization for benign prostatic hyperplasia: an observational study and propensity-matched comparison with transurethral resection of the prostate (the UK-ROPE study)

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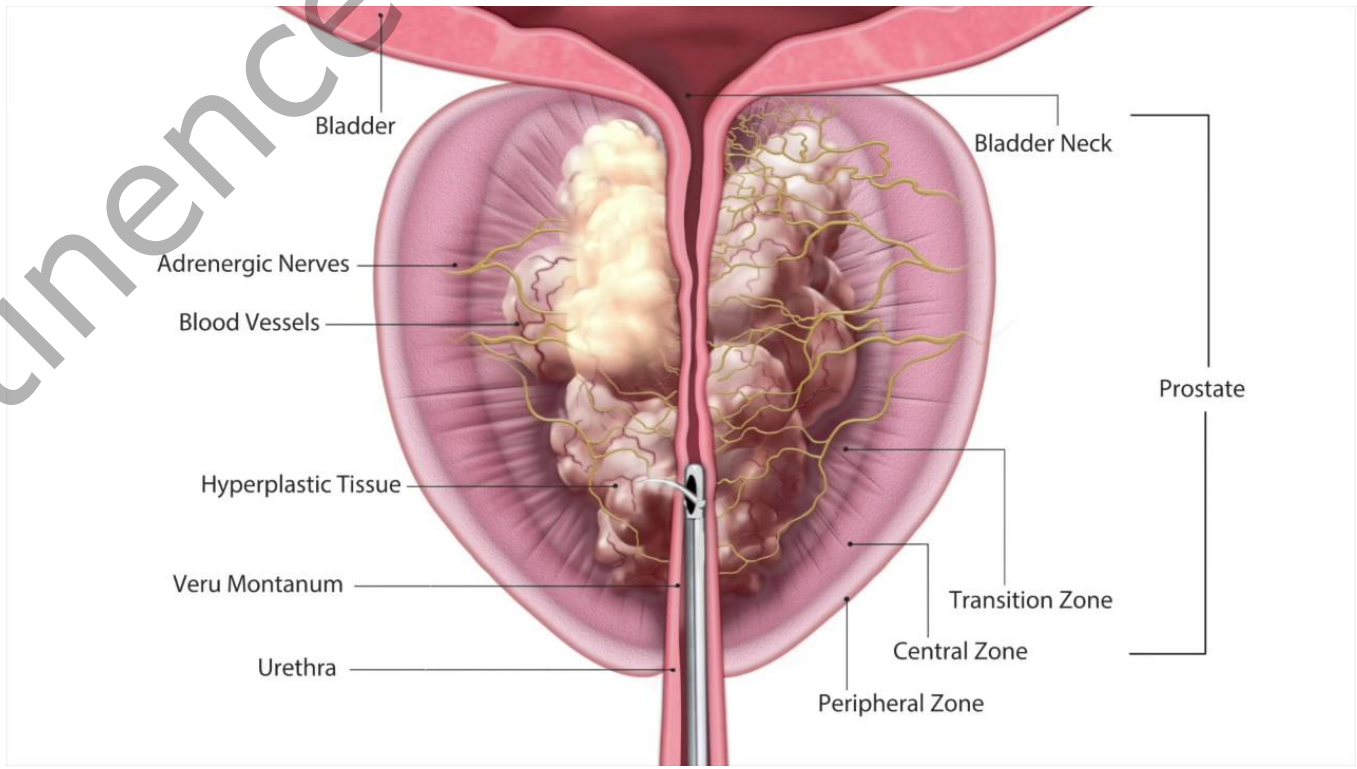
Rezum

FDA approved in 2015.

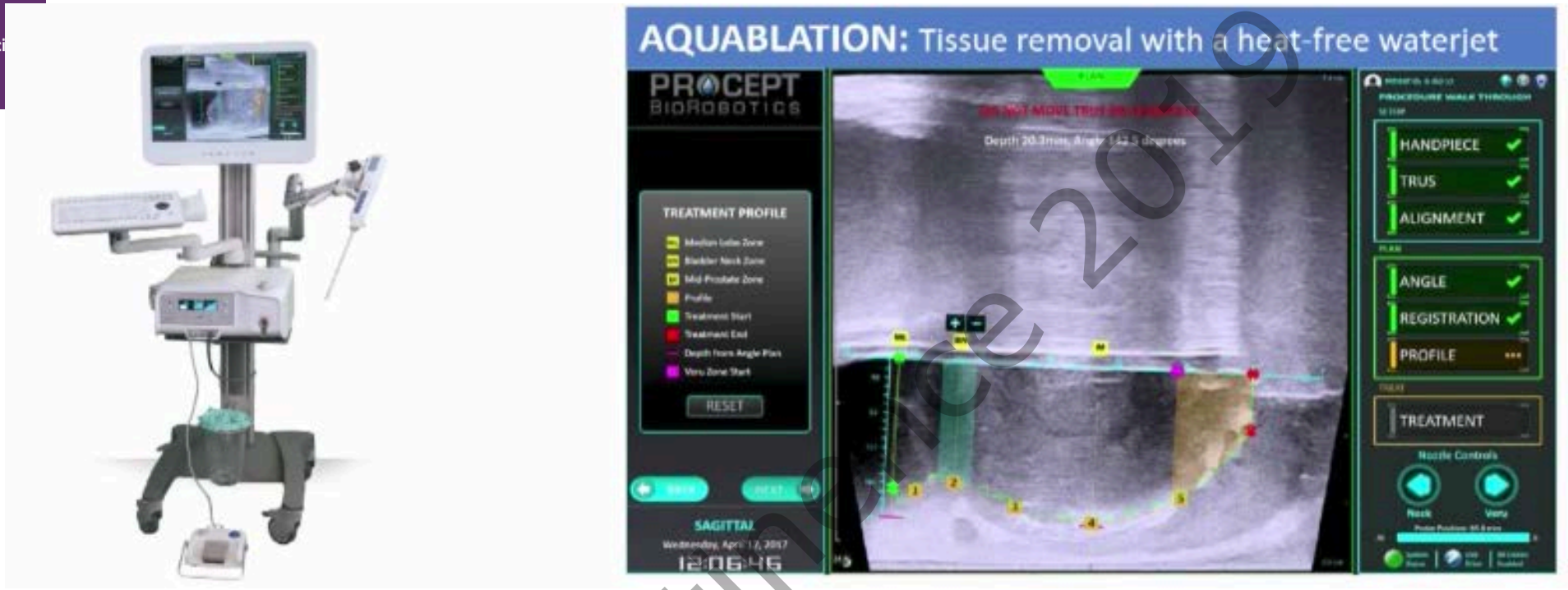
Transurethral convective water vapor treatment via a cystoscope.

Performed under local LA or light sedation- office based procedure.



Aquablation:-

Harnessing the power of water



<u>Real time image guidance</u>
Intra-procedural biplane TRUS
Imaging plus endoscopic evaluation

<u>Surgical Planning</u>
Surgeon defined treatment plan developed prior to Aquablation

<u>Robotic execution</u>
Robotically controlled tissue removal in ~4 mins independent of PV

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LUTS/BPH SURGERY SHOULD **and Medicines** BE MADE TO MEASURE

NHS
Taunton and Somerset
NHS Foundation Trust

Need to find the right **procedure** for the right **prostate** and for the right **patient**

SOME THINGS IN LIFE ARE JUST
BETTER WHEN THEY ARE MADE TO MEASURE

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What is the level of evidence needed to implement new operations ?

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Guidelines

What Is the Required Certainty of Evidence for the Implementation of Novel Techniques for the Treatment of Benign Prostatic Obstruction?

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Table 1 – Requirements for widespread implementation.

- Proof of concept study
- Placebo/sham comparison study
- Randomised controlled trial against accepted alternative treatment
- Cohort studies: to understand the generalisability and potential harm
- Systematic reviews and meta-analysis of high-quality primary studie

Speakman MJ, Cornu J-N, Gacci M et al., European Urology Focus 5 (2019) 351-356

"In God we trust.
All others must bring data."

- *Dr. W. Edwards Deming*

"Without data you're just another person with an opinion"

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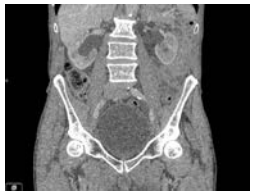
Urinary Retention - Questions?



- What is retention?
- What is acute, about acute retention?
- Why did AUR occur today?
- Which is the larger volume; acute or chronic retention?
- Who needs a catheter?
- Who doesn't get a trial without catheter?

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Urinary Retention

- Inability to pass urine ???
  - Acute – painful inability
  - Chronic – painless – usually voiding
    - Low pressure
    - High pressure

Kaplan et al Eur Urol 2008
Negro & Muir BJUI 2012

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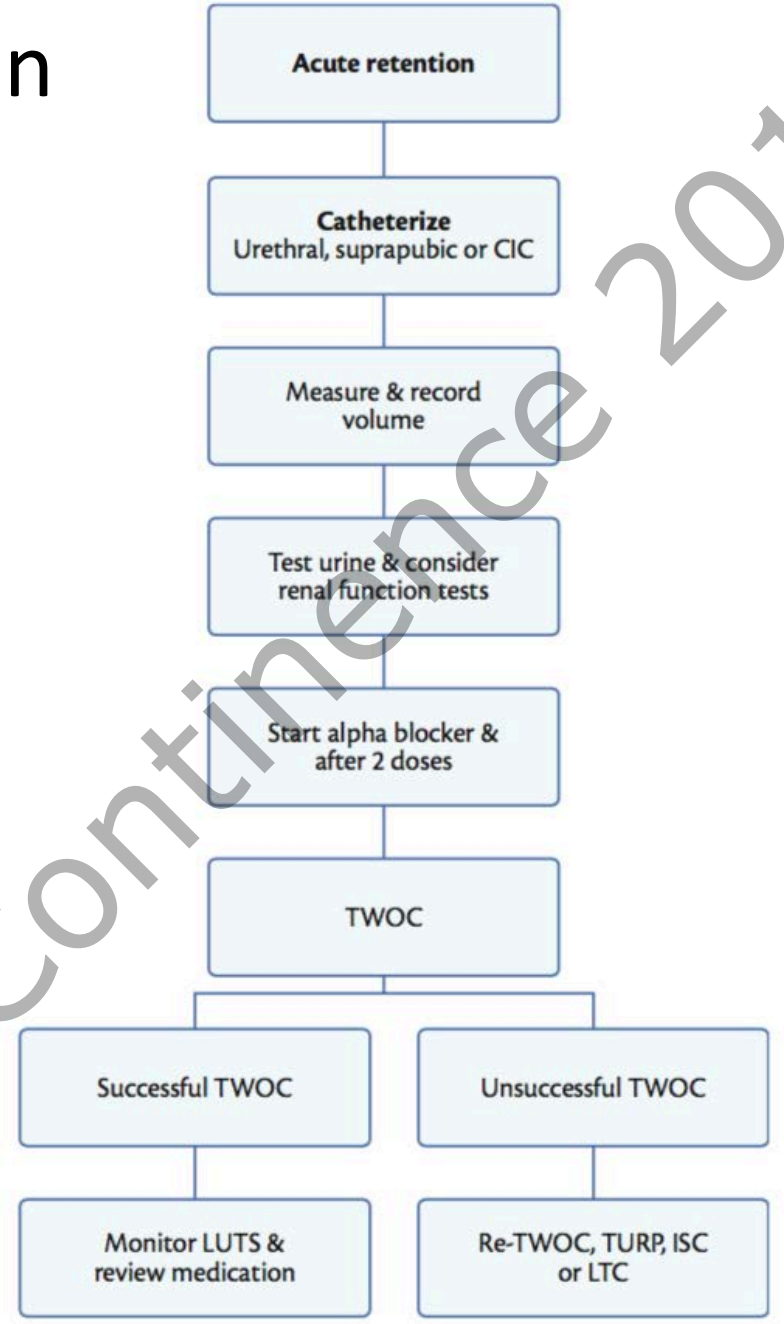
Acute Retention Management



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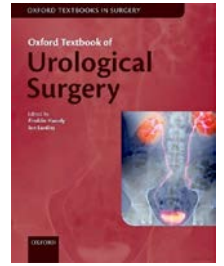

Speakman M J in Hamdy, Eardley. 2017

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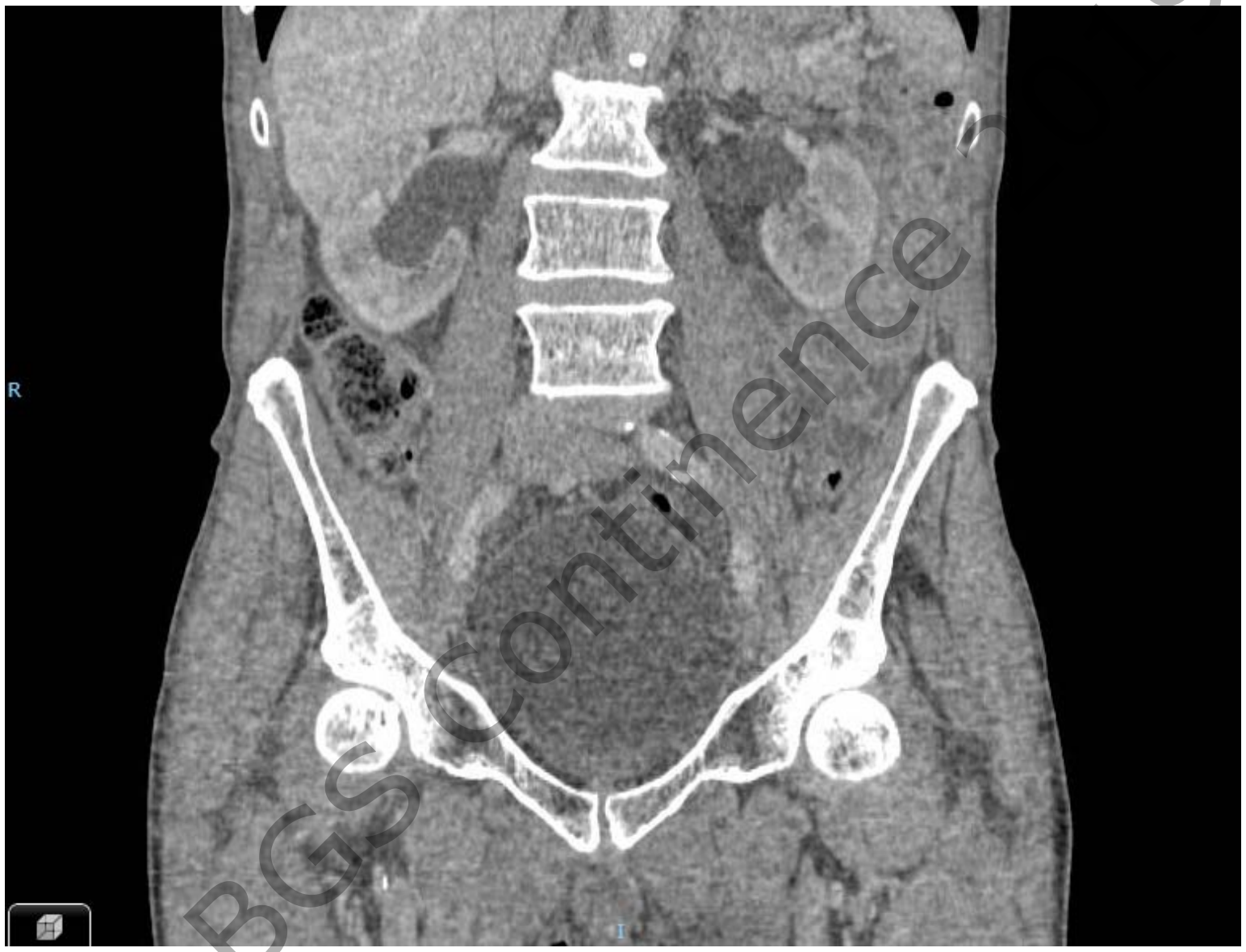
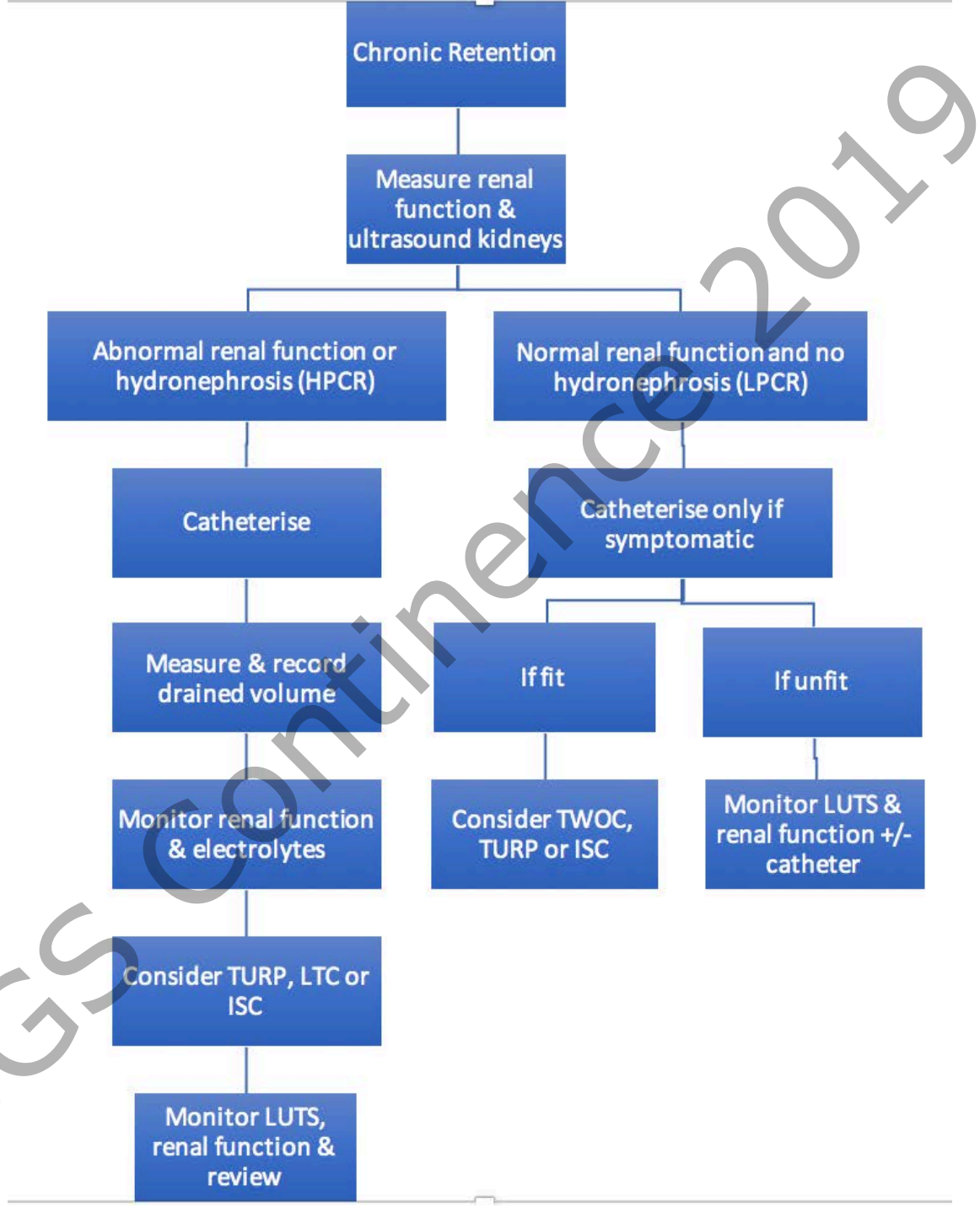
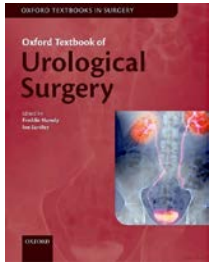


Chronic Urinary Retention

- Usually voiding
- Painless
- ‘Large’ post void residual urine
- > 300mls
- How is it managed?
  - LPCR – outpatient follow up – <u>don’t catheterise</u>
  - HPCR – in hospital management of diuresis and electrolytes
- Intravesical pressure at end of filling?

Management of chronic urinary retention





Speakman M J in Hamdy, Eardley. 2017

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What you need to know

- Patients with chronic retention are usually still voiding urine and it is not usually painful. Physical examination may reveal a painlessly distended urinary bladder
- Urine dipstick, blood tests for renal biochemistry, and ultrasound scanning can help differentiate low pressure chronic retention (LPCR) from the more serious but less common high pressure urinary retention (HPCR)
- Immediately refer patients with impaired renal function to secondary care for further management

thebmj

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PRACTICE

RATIONAL TESTING

Investigating chronic urinary retention

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