Is Urodynamics necessary when assessing a patient with Male LUTS?

Marcus Drake, *University of Bristol*

Urodynamics for **P**rostate **S**urgery **T**rial;
Randomised **E**valuation of **A**ssessment **M**ethods

UPSTREAM

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Heath Technology Appraisal; National Institute of Health Research. (HTA 12/140/01. £1.7M).
M. J. Drake, P. Abrams, P. S. Blair, C. Chapple, C. Glazener, J. Horwood, J. A. Lane, J. McGrath, S. Noble, R. Pickard, G. Taylor

5 year extension. (NIHR128478. 2018. £240k)
M. J. Drake, A. Lewis, P. Abrams, P. S. Blair, C. Chapple, J. A. Lane, S. Noble, G. Taylor

Men with voiding LUTS

- Hesitancy, slow stream, straining, …..
- Voiding problems may need prostate surgery (TURP) to relieve bladder outlet obstruction (BOO)
- Bladder underactivity gives similar symptoms and is unlikely to improve with TURP
- Usual assessment uses symptom scores and flow rate
- To decide if BOO/ underactivity is causing symptoms needs pressure measurement with Urodynamics
- Uncertainty due to limited evidence case

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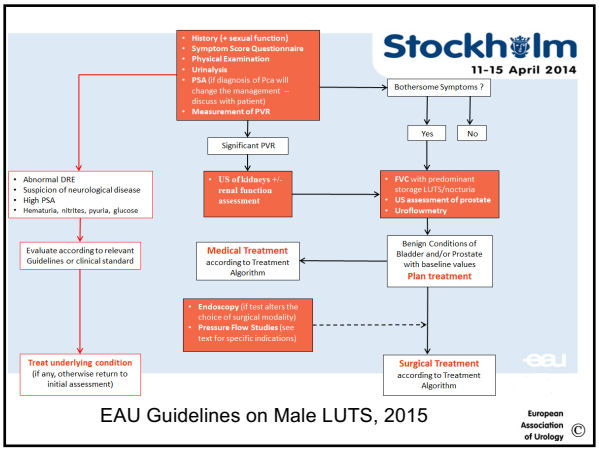

EAU Guidelines on Male LUTS, 2015

Stockholm
11-15 April 2014

	LE	GR
PFS should be performed only in individual patients for specific indications prior to surgery or when evaluation of the underlying pathophysiology of LUTS is warranted.	3	B
PFS should be performed in men who have had previous unsuccessful (invasive) treatment for LUTS.	3	B
When considering surgery, PFS may be used for patients who cannot void > 150 mL.	3	C
When considering surgery in men with bothersome, predominantly voiding LUTS, PFS may be performed in men with a PVR > 300 mL.	3	C
When considering surgery in men with bothersome, predominantly voiding LUTS, PFS may be performed in men aged > 80 years.	3	C
When considering surgery in men with bothersome, predominantly voiding LUTS, PFS should be performed in men aged < 50 years.	3	B

eau

PFS= Pressure Flow Study (voiding phase of urodynamics)

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UPSTREAM

- Does urodynamics reduce surgery use in male LUTS treatment, without impairing symptom outcomes?
- What is the contribution of each component of the assessment?
- How well are the tests done?
- Can we identify men at risk of bad outcome?

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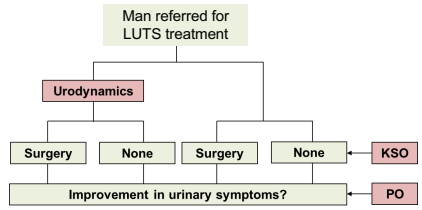

Main motivation: Urodynamics could reduce unnecessary surgery
Primary objective: Does it lead to symptoms that are non-inferior to routine care

Inclusion criteria

- Men considering undergoing surgery as a treatment option for bothersome urinary symptoms

Exclusion criteria

- Unable to pass urine without a catheter
- Relevant neurological disease
- Undergoing treatment for prostate or bladder cancer
- Previous prostate surgery
- Not medically fit for surgery
- Do not consent to be randomised

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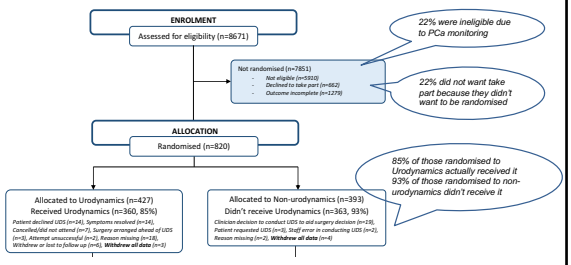
11 January 2019

CONSORT



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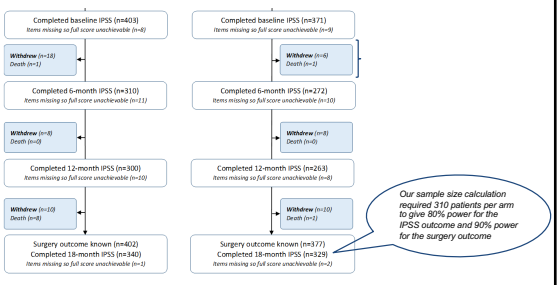
CONSORT



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Baseline clinical characteristics

		Urodynamics		Non-urodynamics
	n°	*Mean (SD)* or n (%)	n°	*Mean (SD)* or n (%)
Clinical baseline characteristics				
Comorbidities at baseline	420	281 (67%)	383	260 (68%)
DRE findings^				
No abnormality	288	108 (38%)	271	120 (44%)
Benign enlargement	352	312 (89%)	327	287 (88%)
Suspected prostate cancer	273	16 (6%)	241	8 (3%)
Other	210	22 (10%)	180	20 (11%)
Uroflowmetry				
Maximum flow rate – Qmax (ml/s)	402	*10.0 (7.7)*	372	*10.9 (7.4)*
Post void residual volume – PVR (ml)	401	*95.0 (136.0)*	373	*90.0 (132.0)*
Voided volume - Vvoid (ml)	404	*204.5 (175.0)*	375	*197.0 (161.0)*
Additional (discretionary) tests				
PSA test		57 (14%)		57 (15%)
Cystoscopy		43 (10%)		24 (6%)
Urinalysis		59 (14%)		59 (15%)
Urea & Electrolytes	413	14 (3%)	383	11 (3%)
Kidney Ultrasound		3 (1%)		2 (1%)
Cytology		15 (4%)		7 (2%)
Prostate volume measurement		18 (4%)		17 (4%)

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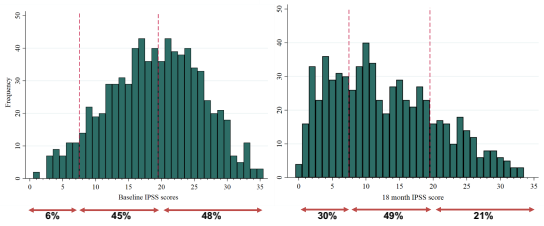
IPSS scores – the change



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Primary outcome: IPSS

Baseline IPSS in both arms: 19
At 18 months IPSS in both arms: 13
Non-inferiority confirmed

Table 3. Primary analysis results

Variable	N(U:R)	Urodynamics *Mean (SD)*	Routine care *Mean (SD)*	Crude difference in means (95% C.I.)	Adj. difference in means[a] (95% C.I.)
IPSS symptom questionnaire					
Total IPSS Score	340:329	*12.61 (7.92)*	*13.11 (7.86)*	-0.49 (-1.69, 0.70)	-0.33 (-1.47, 0.80)
QoL score	343:332	*2.72 (1.69)*	*2.74 (1.64)*	-0.02 (-0.28, 0.23)	-0.07 (-0.32, 0.18)

U=Urodynamics, R=Routine care, [a]Adjusted for centre and baseline IPSS score

- Upper confidence level for the total IPSS score is <1
- Minimally clinically important difference in the literature for QoL score is 0.5

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Key secondary: Surgery rates

Surgery rates 38% (UDS), 36% (Routine care)
Surgery rates not reduced by UDS

Table 4. Secondary Outcome: Proportion of men having surgery, difference between arms

Variable	Urodynamics [intervention] n (%)	Routine care [control] n (%)	OR[a] (95% C.I.)	P value[a]
Surgery outcome				
Surgery conducted	152 (38%)	136 (36%)	1.06 (0.78, 1.45)	0.694
No surgery	250 (62%)	241 (64%)		
Doctor's recommendation				
Surgery	196 (49%)	180 (47%)	1.06 (0.79, 1.43)	0.694
No surgery	201 (51%)	200 (53%)		
Surgery outcome (if matching the Doctor's recommendation)[b]				
Surgery conducted	142 (44%)	129 (40%)	1.16 (0.82, 1.62)	0.400
No surgery	181 (56%)	190 (60%)		

[a]Adjusted for centre, [b]Only those that followed their doctor's advice were included in this secondary analysis, e.g. if the doctor recommended surgery and the patient had it

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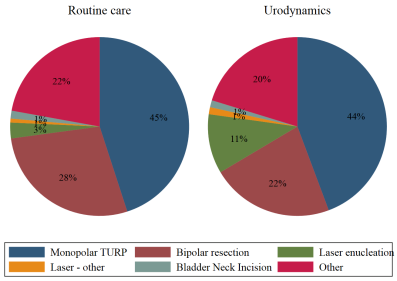

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Maximum flow rate (Qmax)

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Table 7. Secondary Outcome: Maximum urinary flow rate (Qmax) at 18 months, difference between arms

Variable	n(U:R)	Urodynamics [intervention] Mean (SD)	Routine care [control] Mean (SD)	Difference in means* (95% C.I.)	P value*
Qmax score					
Qmax at 18 months	268:271	*15.42 (8.33)*	*15.66 (9.10)*	0.29 (-1.19, 1.77)	0.700
Baseline Qmax	260:260	*11.85 (6.28)*	*12.39 (6.83)*		

* Adjusted for centre and baseline Qmax

Levels increased from a mean flow rate of 12 to a mean flow rate of 15.5ml/s. No evidence to suggest a difference between the arms in Qmax at 18 months.

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Secondary outcome: Adverse events

428 events, all reviewed by an independent clinician

Table 5a. Adverse events – relationship to a procedure

Variable	Urodynamics [intervention] n (%)	Routine care [control] n (%)	P value[a]
Was the event related to treatment?			
Probably	82 (35%)	71 (37%)	
Possibly	22 (9%)	12 (6%)	0.621
Unrelated	130 (56%)	111 (57%)	

[a]Ordinal logistic regression

Secondary outcome: ICIQ PROMS

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Table 6b. Secondary Outcome: ICIQ MLUTS analysis

Variable	n(U:R)	Urodynamics [intervention] n (%)/*Mean (SD)*	Routine care [control] n (%)/*Mean (SD)*	Difference in means* (95% C.I.)	P value*
ICIQ-MLUTS scores					
ICSmaleVS (voiding scale)[b]	296:278	*6.41 (4.40)*	*6.19 (4.23)*	0.09 (-0.59, 0.77)	0.791
ICSmaleIS (incontinence scale)[c]	295:282	*3.87 (3.07)*	*4.04 (2.81)*	-0.27 (-0.67, 0.13)	0.191
ICIQ-MLUTS bother scores					
Daytime frequency (>8 times)	297:284	84 (28%)	75 (26%)	1.00 (0.65, 1.52	0.987
Nocturia (>1 times per night)	299:282	176 (59%)	189 (67%)	0.56 (0.37, 0.87)	0.010

*Adjusted for centre and baseline scores, [b]Voiding scale, on a scale of 0-20 with larger scores indicating more severe symptoms, [c]Incontinence scale, on a scale of 0-24 with larger scores indicating more severe symptoms

Table 7b. Secondary Outcome: ICIQ-MLUTSsex analysis

Variable	n(U:R)	Urodynamics [intervention] n (%)	Routine care [control] n (%)	OR* (95% C.I.)	P value*
ICIQ-MLUTSsex					
Erections (reduced or none)	287:270	206 (72%)	196 (73%)	0.81 (0.55, 1.22)	0.315
Ejaculation (reduced or none)	286:264	244 (85%)	219 (83%)	1.07 (0.65, 1.76)	0.791
Painful ejaculation (Yes)	255:246	43 (17%)	39 (16%)	1.03 (0.62, 1.72)	0.901
Urinary symptoms affected sex life?	274:266	197 (72%)	179 (67%)	1.16 (0.78, 1.71)	0.470

*Adjusted for centre and baseline scores

Subgroup analysis

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Table 8. Subgroup Analyses: Primary outcome

Variable	n(U:R)[a]	IPSS score at 18 months[b] Subgroup specific difference in means (95% C.I)	Interaction effect Difference in means (95% C.I)	P value
Subgroup analyses				
Age				
≤Median	173:164	-0.16 (-1.88, 1.56)		
>Median	167:165	-0.47 (-2.00, 1.06)	-0.33 (-2.60, 1.94)	0.773
Flow rate				
≤12ml/s	205:194	-0.54 (-2.06, 0.98)		
>12ml/s	123:122	0.21 (-1.65, 2.08)	0.54 (-1.84, 2.92)	0.649
Maximum voided volume				
<200ml	144:144	-0.61 (-2.43, 1.20)		
≥200ml	187:177	-0.41 (-1.97, 1.15)	0.35 (-1.99, 2.69)	0.763
Storage dysfunction				
No nocturia	78:65	-0.30 (-2.56, 1.97)		
Nocturia	245:252	0.49 (-1.85, 0.88)	-0.60 (-3.33, 2.14)	0.661
Severity of storage LUTS[c]				
Less substantial	191:176	-0.14 (-1.49, 1.20)		
More substantial	140:143	-0.61 (-2.63, 1.42)	-0.70 (-2.99, 1.60)	0.542

U=Urodynamics, R=Routine care, [a]The numbers refer to the analysable sample for the IPSS score at 18 months, [b]Linear regression model adjusting for centre and baseline scores, [c]The summation of items 2, 4 and 7 in the IPSS questionnaire (split by the median)

Qualitative assessment

Bristol Medical School

- Most felt UD useful in decision making:
  - helped clarify what was happening to them
  - validated what they/clinician had suspected
  - helped realisation that had problem that needed treatment
  - helped understand treatment options- conservative or surgery
  - provided the conclusive answer that need to undergo surgery
- Some felt UD more helpful to clinicians than themselves
  - Not involved in decision making - clinician-led
  - Already decided on TURP- clinician seeking more justification

Selman LE, et al. *Neurourol Urodyn: 2018;Oct. doi: 10.1002/nau.23855* bristol.ac.uk

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- What is the contribution of each component of the assessment?
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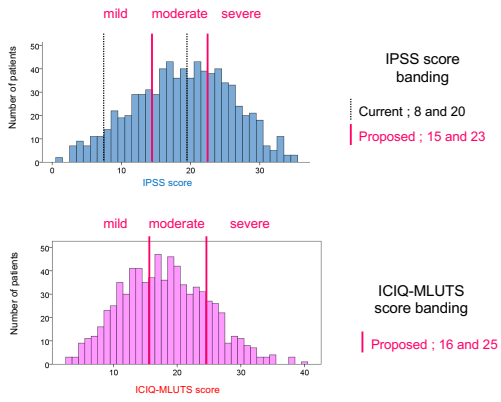
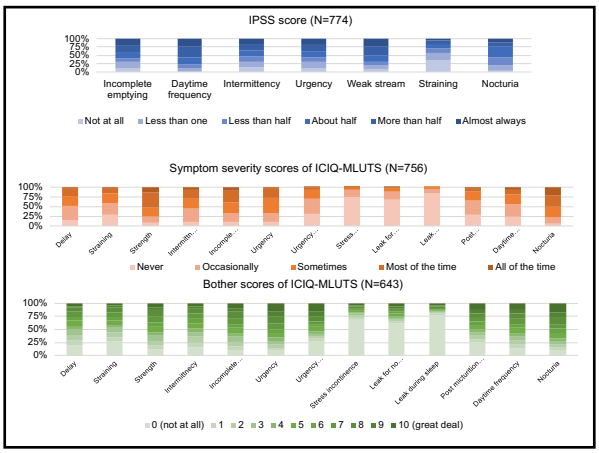


Minimum clinically important difference (MCID)

based on improving IPSS-QoL score by 1

	IPSS	ICIQ
OVERALL	**-4**	**-5**
Mild	-3 [1-14]	-2 [1-15]
Moderate	-4 [15-22]	-4 [16-24]
Severe	-8 [23-35]	-9 [25-52]



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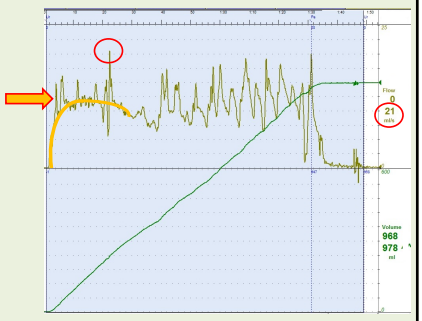
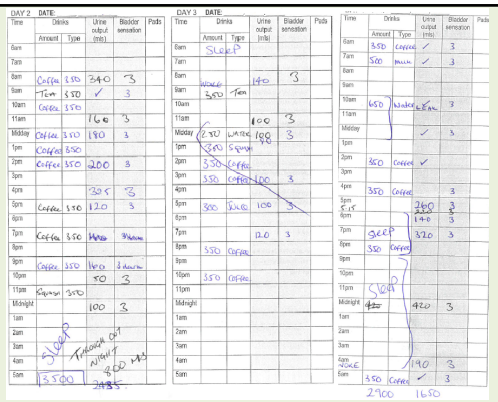
Flow rate

"UPSTREAM"

- Usual
- Pattern
- Shape
- Time
- Rate
- Emptying
- Artefact
- Meaningful





Bright E et al. Developing and validating the International Consultation on Incontinence Questionnaire bladder diary. Eur Urol 2014; 66: 294-300

"Can I have a taxi to go to Henleaze High Street, Bristol at 7pm please?"

29

Customer rating ★☆☆☆☆

- I will take you to Manchester
- You will travel very slowly, with no explanations
- I don't know how to drive
- We don't maintain our vehicles, so the brakes might be faulty
- I will pick up some strangers, and tell you to take off your clothes for the journey

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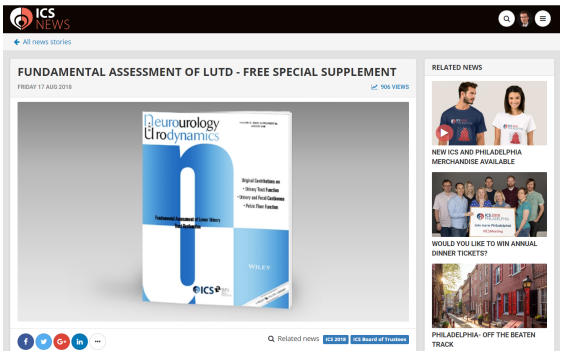

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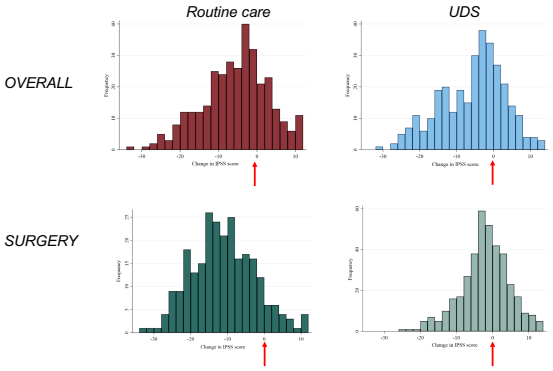
Change in IPSS



Synthesis

- History and examination
- Symptom score — *ICIQ-MLUTS*
  Individual item severity and bother
  Voiding/ Post voiding/ Storage
- Sexual function — *Sometimes profound influence*
- Urinalysis — *Exclude bladder tumour/ UTI/ inflammation*
- Bladder diary — *Intake, nocturia, increased daytime frequency, urgency*
- Free flow rate — *Pattern, corrected Qmax, PVR*
- Use of all information, explanatory dialogue, joint decision making
- Urodynamics — *Selective use not yet defined*

Urodynamics may be omitted if voiding LUTS are the dominant issue, all aspects of the pathway have been done to a suitable standard, and both doctor and patient have a clear insight into the individual case

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Conclusions

- Including Urodynamics in male LUTS assessment achieves equivalent symptomatic outcomes following treatment (non-inferiority)
- Surgery rates are unchanged
- Urodynamics is valued by patients; better understanding of their own condition, additional information for the doctor
- Severity bandings and MCID of IPSS and ICIQ-MLUTS
- Presenting symptoms are largely based on storage LUTS, yet therapy focusses on voiding LUTS
- The symptoms that bother the patient are best identified by ICIQ-MLUTS, due to inclusion of UUI, PMD and individual symptom bother
- A substantial proportion of men experience a deterioration in symptoms
- Many units do not maintain equipment or know how to interpret findings

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Publications

- BACKGROUND Drake MJ, et al. Urodynamic testing for men with voiding symptoms considering interventional therapy: the merits of a properly constructed randomised trial. Eur Urol (2016), 69(5):759-60
- PROTOCOL Bailey K, et al. Urodynamics for Prostate Surgery Trial; Randomised Evaluation of Assessment Methods (UPSTREAM) for diagnosis and management of bladder outlet obstruction in men; study protocol for a randomised controlled trial. *Trials; 2015 Dec 10;16:567. doi: 10.1186/s13063-015-1087-1*
- STATISTICAL ANALYSIS PLAN Young GJ, et al. Statistical analysis plan for the Urodynamics for Prostate Surgery Trial; Randomised Evaluation of Assessment Methods. *Trials. 2017 Oct 3;18(1):455. doi: 10.1186/s13063-017-2206-y.*
- QUALITATIVE RESULTS Selman LE, et al. Recommendations for conducting invasive urodynamics for men with lower urinary tract symptoms: Qualitative interview findings from a large randomised controlled trial (UPSTREAM). *Neurourology and Urodynamics: 2018 Oct 12. doi: 10.1002/nau.23855.*