The Prostate and Its Challenges
“LUTS in the Aging Male”

HJ Rayala, MD/PhD
Urologic Surgeon, Cambridge Health Alliance
Instructor, Harvard Medical School
Financial Disclosures

Spouse  Torque Pharma  Employee/Stock
Dr. Webber

- 60 yoM healthy
- 2010 presented to Urology with post-void residual of 500cc.
- Started on Tamsulosin (PVR 280cc)
- Added Finasteride (PVR 450cc)
- TURP recommended and declined
- Changed to Dutasteride
- Tamsulosin increased to 0.8mg -> nasal congestion. Then 0.4 BID.
- TURP again recommended, self-referred to my clinic.
• Urinates every 2hrs during day and 3 times per night. Has to Valsalva to void.
• Started self-treating for recurrent UTIs 2-3 times per year
• Very bothered by retrograde ejaculation on Tamsulosin
• I recommended TURP:
  – Significant PVR
  – Recurrent Infections
• He is concerned with TURP and risk of retrograde ejaculation or permanent ED
He asks to start Tadalafil

We discussed that Tadalafil improves SUBJECTIVE symptoms, but not OBJECTIVE symptoms.

Starts Tadalafil 5mg daily.

PVR remains ~300cc through 2015

2016 Preplace foleys before elective surgeries

2018 – hasn’t required surgery, remains on active duty.
Take Homes

- BPH is common in the aging male
- Primary Care Doctors can feel comfortable with initiating medical management:
  - Alpha-1-blocker (Floppy Iris Syndrome, Blood Pressure, Retrograde Ejaculation)
  - 5-alpha Reductase Inhibitors (Changes the PSA interpretation)
  - PDE-5 Inhibitors
  - Anticholinergics
  - Combination
- LUTS is not always due to BPH: Young Patient, Isolated nocturia
- When to see Urology: Recurrent UTIs, Hematuria, Episodes of Retention
- Prostate Cancer screening needs to be done with shared decision-making, documentation, and need not necessarily be done annually.
Prevalence of LUTS

• In 2003, the Multinational Survey of the Aging Male (MSAM-7) surveyed the prevalence of moderate-to-severe LUTS:

  Men aged 50–59 years  22%
  Men aged 70–80 years  45.3%

  (p < 0.0001)

Prior to 1990: TURP
(Transurethral Resection of the Prostate)
History of Medical Therapy for BPH

- In 1970’s non-selective $\alpha$-blockers were studied
  - phenoxybenzamine & prazosin
- 1980’s “selective $\alpha_1$-blockers” were introduced
  - Terazosin, doxazosin, and alfuzosin
- 1990’s 5-alpha reductase inhibitors & $\alpha_1a$-subtype-selective agents
  - Finasteride & dutasteride
  - Tamsulosin and silodosin

- In 1990 results of PRCT showed that COMBINATION of finasteride and terazosin significantly improved LUTS and increased flow rates.
TRANSURETHRAL RESECTION OF THE PROSTATE AMONG MEDICARE BENEFICIARIES: 1984 TO 1997


The Journal of Urology
Volume 164, Issue 4, Pages 1212-1215 (October 2000)
DOI: 10.1016/S0022-5347(05)67143-1
Pathophysiology of BPH
Pathophysiology of Aortic Stenosis

[Diagrams illustrating normal blood pressure and aortic stenosis]
Pathophysiology of BPH
“Normal”

- Generally urinates about 3-4x per day
- Wakes 0-1x per night
BPH

- **Daytime Frequency:**
  - Every 1-3 hrs

- **Nocturia:**
  - 1-4x per night

- **Urgency:**
  - Often accompanied by a detrusor contraction

- **Weakened Stream**

- **Post-void Dribble**
End-Stage BPH

• “I have no problems Doc”
• “I go 1 or 2 times a day”
• Recurrent UTIs
• Diapers may indicate overflow incontinence
• Hydronephrosis – renal failure
• Volume Overload – may mimic CHF
Presentation of BPH

• The severity of urinary symptoms do NOT correlate with the degree of obstruction

• The severity of urinary symptoms do NOT correlate with the size of prostate (either by DRE or on imaging)
Workup of BPH

- Relevant Medical History
- Assessment of LUTS
- Severity and Bother (i.e. AUA-SI)
- Physical Examination Including DRE
- Urinalysis
- Serum PSA
- Frequency/Volume Chart

- AUA Guidelines 2011
- AAFP Recommendations for Practice
- Canadian Urologic Guidelines
- European Association of Urology
Differential Diagnosis for LUTS

• Increased Urine Output

• Decreased Bladder Storage Capacity (myopathy or neuropathy)

• Bladder Irritation

• Bladder Outlet Obstruction
Increased Urine Output

- Diabetes – look for glucosuria
- New Diuretic Medicine
- CHF with LE edema

- Polyuria: >3L per 24 hours
  - Goal UOP for pts with urinary sx is <1L / 24 hrs
  - Consider fluid intake, SIADH

- Nocturnal Polyuria: >33% UOP during night
  - Normally produce <25% while sleeping
  - Lying Prone -> ADH release -> decreased UOP
    - Elderly have disruption in this endocrine loop
    - Pillows and La-Z-Boys

- Obstructive Sleep Apnea –
  - OSA -> ANP release -> increased UOP
# SIMPLE DAILY VOIDING DIARY

**NAME**

**DATE**

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Amount Voided CC or MLS (example 100 or 200)</th>
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<tbody>
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<td>11:00</td>
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<td>Noon</td>
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<td>Midnight</td>
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<td>3:00</td>
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<tr>
<td>4:00</td>
<td></td>
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<tr>
<td>5:00</td>
<td></td>
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</tbody>
</table>
Decreased Bladder Storage Capacity (myopathy or neuropathy)

- Diabetes
- Cerebrovascular Accident or Upper Motor Neuron compromise
- Multiple Sclerosis
- Parkinson’s Disease
- Spinal Cord
  - Degenerative Disk Disease
Bladder Irritation

- Bladder Infection
- Bladder Cancer
- Distal ureteral stone
- *Schistosomiasis haemotobium* (not *S. mansoni*)
Bladder Outlet Obstruction

• Urethral Stricture
  – Prior Urologic procedures, Gonorrhea
• Meatal Stenosis
• Significant Phimosis (especially in elderly)
• Penile Cancer

• BPH
**Intact Penis:** The foreskin protects the sensitive meatus from an irritating environment. The meatus is normally a wide slit. Finger applies pressure to show how wide the meatus opens.

**Circumcised Penis:** With no protective foreskin in infancy, the glans is exposed to urine and diapers that irritate the meatus, causing it to stenose (narrow) and restrict urine flow.
Medical History

- Medications – can account for 10% of LUTS\(^1\)
  - Antidepressants 4 %
  - Diuretics 3 %
  - Bronchodilators 2 %
  - Antihistamines 1%

Workup of BPH

**Recommended Tests:**

- Relevant Medical History
- Assessment of LUTS
- Severity and Bother (i.e. AUA-SI)
- Physical Examination Including DRE
- Urinalysis
- Serum PSA
- Frequency/Volume Chart

- AUA Guidelines 2011
- AAFP Recommendations for Practice
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Lower Urinary Tract Symptoms (LUTS) (formerly “Prostatism”)

• Urinary Frequency:
  – How many times do they wake to urinate
  – How frequently do they urinate during the day
• Urinary Urgency
• Strength of Flow
• Do they push (Valsalva)
• Double Voiding
• Post-void dribbling
• Sense of incomplete emptying
# International Prostate Symptom Score

(AUA Symptom Score)

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Over the past month, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>None</th>
<th>1 time</th>
<th>2 times</th>
<th>3 times</th>
<th>4 times</th>
<th>5 or more times</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. 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?</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Total Symptom Score</th>
<th>None</th>
<th>1 time</th>
<th>2 times</th>
<th>3 times</th>
<th>4 times</th>
<th>5 or more times</th>
</tr>
</thead>
</table>
Workup of BPH (AUA Guidelines 2011)

Score <8
Not Bothersome
Reassure & Follow

Score ≥8
Bothersome (+/- Further Tests)
Lifestyle Advice
Pharmacologic Therapy

Complicated:
- Recurrent Retention
- Recurrent UTI
- Recurrent Hematuria
- Bladder stones
- CRI

Surgery
(Option Chronic Foley)

Failure (~10%)
Exam and Labs

- **UA**
  - Glucosuria, UTI
  - Hematuria (Formal UA with 3 or more RBC/HPF)

- **PSA**
  - Most guidelines for PSA screening refer to “asymptomatic” patient
  - Men with a PSA level of ≥3 and LUTS were more likely to be diagnosed with benign disease than prostate cancer\(^1\)

- **DRE**
  - Low Sensitivity (59%) and PPV (28%) for prostate cancer

*Collin SM, et al. BJU Int. 2008*
Exam and Labs

- **UA**
  - Glucose, UTI
  - Hematuria (Formal UA with 3 or more RBC/HPF)

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- **DRE**
  - Low Sensitivity (59%) and PPV (28%) for prostate cancer

*Collin SM, et al. BJU Int. 2008*
Tests that Suggest Bladder Outlet Obstruction

• **Post-Void Residual**
  – Either by bladder scan or “Renal Ultrasound”
  – “Normal” PVR can be up to 100mls

• **Uroflow (In Urology Office)** – flow rate

• **Urodynamic study (UDS)** - determines not only the flow rate, but most importantly, whether the bladder is able to contract
Uroflow

RATE (cc/sec)

TIME

ml/s
Cystometry

2-Way Catheter

Balloon Catheter

Extension Set-2

Pressure Transducers 9022K0122

Infusion Line 9021O1173

1000 ml STERILE WATER BAG

Water Pump

P_abd P_ves

Urodynamics
Urodynamics
Therapies for BPH
Non-Invasive Therapies

Lifestyle Modifications

• Weight loss
• Change HTN med from diuretic to alternative if possible, limit diuretics to morning.
• Diet: Avoid caffeine, alcohol, spicy foods, acidic foods
• Decrease fluid intake in the evening (6pm)
• Avoid α-agonists (decongestants)
• Limit fluid intake to <1.5-2.0L per day
Non-Invasive Therapies
Phytotherapies

- Phytotherapies are not recommended as the standard for treatment of BPH at this time
  - *Saw Palmetto (Serenoa repens)*
  - *African Plum (Pygeum africanum)*
Non-Invasive Therapies
Medical Approach

• What medications work and why?
Benign Prostatic Hyperplasia

Obstruction Results from:

• Increase in Urethral Resistance due to:
  – Increase # of prostate smooth muscle cells
  – Increased number of \( \alpha \)-I adrenergic receptors on the SMC.

• Prostatic growth into the urethral lumen due to increased # of Epithelial and Stromal Cells
Medical Approach

• α -1 blockers
  – Relax the smooth muscle of prostate and bladder neck

• 5 α -Reductase Inhibitors
  – Shrink the Prostate Stroma

• PDE5-Inhibitor
  – Mechanism Unknown

• Combining α -1 blockers & 5 α -Reductase Inhibitors
• PDE5-Inhibitor (and Combinations)
• Addition of Anticholinergic
Medical Approach

• α-1 blockers
  – Relax the smooth muscle of prostate and bladder neck
# α-1A Receptor Subtypes

<table>
<thead>
<tr>
<th></th>
<th>Prostate α-1A</th>
<th>Bladder / Spinal Cord α-1D</th>
<th>Vasculature α-1B (1A)</th>
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</thead>
<tbody>
<tr>
<td>Terazosin</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>(Hytrin®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxazosin</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>(Cardura®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>(Uraxatral®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>(Flomax®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silodosin</td>
<td>X</td>
<td>X</td>
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<tr>
<td>(Rapaflo™)</td>
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</tr>
</tbody>
</table>
Nonselective $\alpha$-1 Blockers

Terazosin, Doxazosin, Alfuzosin

• Effects vasculature
• Side Effects: dizziness, orthostatic hypotension (uncommon), syncope (rare)
• Require titration, Take at Bedtime – REASSURE patient that symptoms subside
  Terazosin/Hytrin: 2mg -> 5mg -> 10mg
  Doxazosin/Cardura: 2mg -> 4mg -> 8mg
  (Start at 1mg if older, frail, low BP)
• 2-4 weeks for near maximal improvement
• Need to space at least 4 hours from Viagra. Cannot use with Cialis.
Selective α-1A Blockers
Tamsulosin, Silodosin

• Near maximal improvement within 8 hours
• Cause less (if any) dizziness

• Highest rate of retrograde ejaculation
• Nasal Congestion

• Do not need to space 4 hours from Viagra.
• OK to use with Cialis
• Sulfa allergy – minimal cross-reactivity
Efficacy of the $\alpha$-1A Blockers
Tamsulosin, Silodosin

- Efficacy of the following are comparable:
  - Doxazosin, Terazosin, Alfuzosin, Tamsulosin
  - No clinical comparisons with Silodosin

- Silodosin is the only one which has been shown to improve UDS outcomes
Meta-Analysis of Blood Pressure Effects for α-1 Blockers

- 25 Studies
- OR of developing:
  - Dizziness
  - Hypotension
  - Syncope

α-1 Blockers and Cardiovascular Effects

• Patients with HTN and CHF have chronic activation of sympathetic nervous system
• Thus at higher risk for increased cardiovascular side effects of blocking the α-1B receptors\(^1\)
  – Doxazosin, Terazosin, Alfuzosin all had higher adverse events in these patients (Doxazosin was withdrawn from ALLHAT due to increased risk of cardiovascular disease, esp CHF)
  – Tamsulosin has not been shown to adversely effect these patients compared to placebo

• Do not use these medicines for Blood Pressure control
• Use Tamsulosin or Silodosin preferentially in patients with HTN/CHF

*Barenderecht MM, et al. BJU International. 2005*
Intraoperative Floppy Iris Syndrome

- Severe complication during cataract surgery with patients on alpha-1 blocker
  - Intraoperative miosis causes iris prolapse toward incision, which can result in capsule rupture

- Incidence of IFIS on Tamsulosin is 43-90% (less on Doxazosin or Terazosin)

- Whether stopping medicine prior to surgery mitigates risk is unknown
Intraoperative Floppy Iris Syndrome

New Recommendations:

• Men with LUTS secondary to BPH for whom alpha-blocker therapy is offered should be asked about planned cataract surgery.

• Men with planned cataract surgery should avoid the initiation of alpha-blockers until their cataract surgery is completed.
5α-Reductase Inhibitors
(Finasteride and Dutasteride)

- Finasteride inhibits type II 5ARI
- Dutasteride inhibits type I&II 5ARI
- Reduces prostate volume by 20-25%
- Takes 6-9 months to achieve noticeable change in symptoms (improvement continues with time)
- Takes 12-18 mo to obtain same flow rate as α-blocker

- REDUCES PSA by HALF over the course of 1 year!
  (Includes Finasteride 1mg / Propecia)
  - Consider checking a PSA before starting
- Side effect: Impotence (5%), decreased libido (<4%)
5α-Reductase Inhibitors

**T**

5-ARI

Finasteride

Dutasteride

**T**

**DHT**

ANDROGEN RECEPTORS

**↑ Prostate Growth**

**↑ PSA**

**↓ Apoptosis**

(**↓ Hair Growth**)
5α-Reductase Variability

• ~25-30% of patients do no show improvement on 5α-Reductase Inhibitors
• 5-7% show worsening of symptoms

• 5α-Reductase Type II is variably expressed
• 30% of adult prostates do not express 5α-Reductase Type II

5α-Reductase Inhibitors

$\text{T} \xrightarrow{5-\text{AR} (1,2)} \text{DHT}$

$\uparrow \text{Prostate Growth}$
$\uparrow \text{PSA}$
$\downarrow \text{Apoptosis}$

(\text{Hair Growth})
5α-Reductase Variability “Non-Responders”

- Longitudinal studies have shown that 30% of men have prostate sizes that do not increase with time.

- Current research suggests that this is a somatic epigenetic event (rather than underlying chromosomal variability)

5α-Reductase Variability
“Non-Responders”

- Age and Obesity independently promote methylation and suppression of 5α-Reductase protein expression.
  - Obesity is a factory associated with decreased clinical benefit of 5α-Reductase inhibitors

5α-Reductase Inhibitors
Prostate Cancer Risk

• There is a proven benefit of using both Finasteride (PCPT) and Dutasteride (REDUCE Trial) for prostate cancer risk reductions.

• In the PCPT there was a slight INCREASE in HIGH GRADE prostate cancer with Finasteride.
  – Most experts believe this was statistical artifact due to reduced volume of Finasteride-treated gland

• In the REDUCE trial, there was NOT a difference in High Grade prostate cancer.
Combination – Alpha Blocker and 5α-Reductase Inhibitors
# Combination – MTOPS & ComBAT Trials

<table>
<thead>
<tr>
<th>Comparison</th>
<th>MTOPS (NIH Funded)</th>
<th>CombAT (GlaxoSmithKline Funded)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Placebo</strong></td>
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<td></td>
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<tr>
<td><strong>Doxazosin</strong></td>
<td>14%</td>
<td><strong>Tamsulosin</strong></td>
</tr>
<tr>
<td><strong>Finasteride</strong></td>
<td>9%</td>
<td><strong>Dutasteride</strong></td>
</tr>
<tr>
<td><strong>Combination</strong></td>
<td>5%</td>
<td><strong>Combination</strong></td>
</tr>
<tr>
<td><strong>Mean Prostate Size</strong></td>
<td>36g</td>
<td>55g</td>
</tr>
<tr>
<td><strong>Worsening Symptom Score</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
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<td></td>
</tr>
<tr>
<td><strong>Doxazosin</strong></td>
<td>7%</td>
<td><strong>Tamsulosin</strong></td>
</tr>
<tr>
<td><strong>Finasteride</strong></td>
<td>9%</td>
<td><strong>Dutasteride</strong></td>
</tr>
<tr>
<td><strong>Combination</strong></td>
<td>5%</td>
<td><strong>Combination</strong></td>
</tr>
<tr>
<td><strong>Risk of: Retention, Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td><strong>Doxazosin</strong></td>
<td>4%</td>
<td><strong>Tamsulosin</strong></td>
</tr>
<tr>
<td><strong>Finasteride</strong></td>
<td>3%</td>
<td><strong>Dutasteride</strong></td>
</tr>
<tr>
<td><strong>Combination</strong></td>
<td>2%</td>
<td><strong>Combination</strong></td>
</tr>
</tbody>
</table>

*MTOPS Trial, NEJM, 2003  3,047 men randomized and followed for average of 4.5 years*
*Table adapted from Lebor h. Reviews in Urology 2011.*
Combination

- MTOPS: In Glands <40g, $\alpha_1$-blocker outperformed 5-ARI with regards to LUTS

- CombAT: In Glands >50g, 5-ARI outperformed $\alpha$-blocker at reducing the risk of retention or need for surgery

In Practice, the $\alpha_1$-blocker are generally started before 5-ARI:

- $\alpha_1$-blocker reach effect much faster (2 weeks vs 1-1.5 years)
- $\alpha_1$-blocker are efficacious in all prostate sizes, whereas 5-ARI do not work as well in small glands
- 30% of patients won’t respond to 5-ARI (which you may not know for 1-1.5 years)

Combination
Withdrawing the $\alpha$-1 Blocker

- Studies suggest that the $\alpha$-1 blocker can be stopped after 6-12 months without worsening voiding symptoms

<table>
<thead>
<tr>
<th>Baseline Voiding Sxs</th>
<th>When can $\alpha$-blocker be withdrawn?</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS $&lt; 20$</td>
<td>$&gt; 6$ Months</td>
</tr>
<tr>
<td>IPSS $&gt; 20$</td>
<td>$&gt; 9$ Months</td>
</tr>
</tbody>
</table>

(Such that 80% will not have worse sxs)

(Remember: 12-18 months to get best 5ARI flow-rate)
PDE5-Inhibitor Tadalafil
FDA-approved for BPH

• 5mg Tadalafil improves the IPSS scores, the IPSS Quality of Life (QoL) and the BPH Impact Index (BII)
• Mechanism Unknown
• Onset of efficacy is ~1-4 weeks
• Its efficacy is irrelevant to the erectile function status of the patients.
• Effects are maintained with time

• In studies thus far, tadalafil is not associated with improvement in Flow Rate or PVR.
Combination

- Studies are beginning to look at
  - Tadalafil + Tamsulosin
  - Tadalafil + Finasteride
- Both combinations improve IPSS and Flow Rate compared to absence of Tadalafil
- Both combinations show improved sexual function
  - The decreased libido and ED with Finasteride is no longer seen
## Combination

<table>
<thead>
<tr>
<th>PDE5-I + 5ARI</th>
<th>Finasteride 5mg + Placebo</th>
<th>Finasteride 5mg + Tadalafil 5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate Size</td>
<td>&gt;30g</td>
<td></td>
</tr>
<tr>
<td>IPSS Change</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Wks</td>
<td>-2.3</td>
<td>-4</td>
</tr>
<tr>
<td>26wks</td>
<td>-4.5</td>
<td>-5</td>
</tr>
</tbody>
</table>

Adding an Anticholinergic
(Oxybutynin, Tolterodine, Darifenacin, Trospium, Solifenacin)

• Anticholinergics put bladder in the “storage” phase:
  – Relax detrusor
  – Contract Sphincter (increasing outlet obstruction)

• Helpful in relieving urgency/frequency associated with hypertrophic/overactive bladder.
  – Specifically in those patients already treated with α-blocker
Adding an Anticholinergic

- Theoretic concern that these could put patients into retention
- In patients with PVR<200 cc, risk of requiring catheter is <1%

- Perhaps best used temporarily while waiting for bladder hypertrophy to resolve
  - Can be used “prn” – when they need a good nights sleep or have a movie date.
Anticholinergic Warnings

• 25 studies have found significant association of anticholinergic use with:
  – Cognitive decline
  – Delirium
  – Dementia

• Avoid in patients with Narrow-angle Glaucoma.
Surgical Interventions

ZIGGY...
by Tom Wilson

...THE DOCTOR IS JUST SUITING UP FOR YOUR LASER SURGERY, MR. ZIGGY!!
Surgical Interventions

- TURP (Transurethral Resection of Prostate)
- Laser Ablation or Enucleation
- Suprapubic (Open)Prostatectomy
- TUMT (Transurethral Microwave Therapy)
- TUNA (Transurethral Needle Ablation)
- Prostatic Stent
- UroLift
TransUrethral Resection of Prostate
HoLAP (Holmium Laser Ablation Prostate)
PVP (Photoselective Vaporization – Greenlight)
HoLEP
(Holmium Laser Enucleation of Prostate)
Suprapubic “Open” Prostatectomy
TUMT and TUNA
(Microwave Therapy and Needle Ablation)
Prostatic Stent and UroLift

European Association for Urology Patient Website
Surgical Interventions

- **TURP (Transurethral Resection of Prostate)**
  - Remains Gold Standard

- **Laser Ablation or Enucleation**
  - Option which has more post-operative “bother” and less durability with time. Less bleeding.

- **Suprapubic Prostatectomy**
  - Best option for VERY large (>100g) glands

- **TUMT (Transurethral Microwave Therapy)**
- **TUNA (Transurethral Needle Ablation)**
  - Fallen out of favor

- **Prostatic Stent** - Fallen out of favor
- **UroLift** - ??
PROSTATE CANCER
**Archived: Prostate Cancer: Screening**

Original Release Date: May 2012

*This version of this topic is currently archived and inactive. It should be used for historical purposes only.*

### Archived: Recommendation Summary

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer.</td>
<td>D</td>
</tr>
</tbody>
</table>

**Read Full Recommendation Statement**

[PDF Version](#) (PDF Help)

View archived versions of this recommendation
# Final Recommendation Statement

## Prostate Cancer: Screening

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

For more information on the final recommendation on screening for prostate cancer, go to www.screeningforprostatecancer.org.

## Recommendation Summary

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men aged 55 to 69 years</td>
<td>For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)-based screening for prostate cancer should be an individual one. Before deciding whether to be screened, you should have an opportunity to discuss the potential benefits and harms of screening with your clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. However, some men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy, overstaging and overtreatment; and treatment complications, such as urinary incontinence and erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race, ethnicity, comorbid medical conditions, patient values about the harms and benefits of screening and treatment-specific outcomes, and other patient needs. Clinicians should not screen men who do not express a preference for screening.</td>
<td>C</td>
</tr>
<tr>
<td>Men 70 years and older</td>
<td>The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older.</td>
<td>D</td>
</tr>
</tbody>
</table>
Main Two PSA Prospective Randomized Studies

**PLCO (Prostate, Lung, Colorectal, Ovarian)**
- 46% of “control arm” received PSA screening
- No longer a RCT, rather “organized vs opportunistic screening”

**ERSPC (European Randomized Study for Screening of Prostate Cancer)**
- Compared with initial 9 and 11-year old date, the 13-year old data **DID** show reduction in prostate cancer mortality
- Prostate cancer mortality was 21 percent lower in the group offered screening (RR 0.79, 95% CI 0.69-0.91)
- The absolute rates of prostate cancer mortality were 0.43 versus 0.54 per 1000 person-years
  - 32% of screened men had “positive screen”
  - 27.7% of screened men received biopsies
  - 20-50% of cancers were “overdiagnosed”
ProtecT Study

Original Article

10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer


N Engl J Med
Volume 375(15):1415-1424
October 13, 2016
ProtecT Study

• In the ProtecT trial, over 1600 men with PSA-detected localized prostate cancer were assigned to:
  • Active monitoring
  • Prostatectomy
  • Radiotherapy

• Overall survival was similar in the three groups at 10 years

• However, more patients assigned to active monitoring had disease progression and metastasis

• Metastasis at 10 years:
  • Active monitoring 6.0%
  • Prostatectomy 2.3%
  • Radiotherapy 2.9%
CHA Multidisciplinary Task Force 2015-2016

- Internal Medicine
- Family Medicine
- Urology
- Community Health Improvement
- Oncology
- Nursing
- Pathology
- CRICO Representative
CRICO

• “Prostate cancer is the most common cancer diagnosed in American men

• Frequently cited in medical malpractice cases, alleging failure to diagnose, or delay in diagnose

• General medical MDs are named most frequently in such cases”
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Discussion initiation</td>
<td>“recommends that men….should have an opportunity to make an informed decision with their hcp”</td>
<td>“Clinicians inform men”</td>
<td>Unclear</td>
<td>“It is advisable to initiate a discussion…. and to revisit the topic with pt. periodically”</td>
<td>“All men should be informed about the availability of PSA screening and that there is uncertainty and controversy over its effectiveness….”</td>
<td>“If patient doesn’t raise issue, clinician not obligated to offer.”</td>
</tr>
<tr>
<td>Reason to screen</td>
<td>Shared decision-making with health professional; Provider and pt agree after informed discussion; “For men unable to decide, PCP can decide based on pts’ health preferences and values” Follow-up available.</td>
<td>Screen only when pt expresses clear preference for screening. Men can change mind at anytime Clinician bases decision on prostate ca risk, discussion of benefits + harms, pt gen health + life expectancy, + pt preferences.</td>
<td>Shared decision-making; precede based on man’s values and preferences</td>
<td>Patient has “clear preference for screening after shared decision making” - Testosterone replacement</td>
<td>Men interested after basic info, agrees to and receives SDM, then expresses clear preference for screening</td>
<td>Pt preference after being fully informed of benefits and harms</td>
</tr>
<tr>
<td>Age average risk</td>
<td>50</td>
<td>50</td>
<td>55</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Age increased risk</td>
<td>45; 40 if appreciably higher risk</td>
<td>45-50; 40 if significantly higher risk</td>
<td>&lt;55</td>
<td>45</td>
<td>40 or above, depends on individual risk</td>
<td>Not recommended</td>
</tr>
<tr>
<td>High risk definition</td>
<td>AA, 1st deg relative (fr/bro) dx’d &lt;65 Higher risk = multiple family members dx’d &lt;65</td>
<td>AA, 1st deg relative (fr/bro) dx’d &lt;65 Higher risk = multiple generations and dx’d &lt;55 yrs</td>
<td>AA, positive family hx Higher risk if multiple generations and dx’d &lt;55 yrs</td>
<td>AA, 1st deg relative(s), prior prostate bx showing high grade prostatic intraepithelial neoplasia or atypical acinar proliferation (refer to Urology)</td>
<td>AA, 1st degree relative (fr/bro) dx’d &lt;65</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Age end screening</td>
<td>&lt; 10 yr life expectancy</td>
<td>70+ or &lt; 10 yr life expectancy (LE)</td>
<td>70+ or &lt;10-15 yr LE</td>
<td>75+ or significant co-morbidities</td>
<td>70+</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Type of screening</td>
<td>PSA +/- DRE; Notes DRE unclear role – possible decision adjunct</td>
<td>PSA and DRE Cites ACS review of unclear role of DRE in screening</td>
<td>PSA: DRE can be used as an adjunct for decision-making</td>
<td>PSA with DRE; Document DRE as normal (including symmetrically enlarged) or abnormal</td>
<td>PSA</td>
<td>PSA not recommended; DRE not addressed</td>
</tr>
<tr>
<td>Screening Interval</td>
<td>No strong evidence to recommend interval Based on PSA: &gt;2.5 ng/mL – yearly &lt;2.5 – “can extend to 2 yrs” 2.5 – 4.0 – consider Indiv. risk assessment (AA, fam hx, age, abn DRE; prev neg bx lowers risk) 4.0 – refer for eval or bx</td>
<td>“No clear evidence guides frequency” “increased interval may reduce harm” “No clear evidence that screening more frequently than Q 4 yrs produces any additional benefit” “PSA levels 2.5 ng/mL or greater may warrant yearly screening”</td>
<td>Every 2 years For pts &gt;60yrs, if PSA &lt;1.0 ng/mL, consider longer interval (e.g. 4 yrs) “…no direct evidence to support a specific screening interval”</td>
<td>“Once testing initiated, MD obligated to continue to test periodically… and track results.” Frequency based on PSA: &lt;1.0ng/mL – q 5 yrs 1.0-2.0 – “periodic retesting” &gt;2.0 – 4.0 – yearly If increase &gt;2.0 ng/mL over 12 mos repeat within 3 mos. “For pts who decline PSA testing, discussion should be revisited periodically (not necessarily annually).”</td>
<td>Every 2 years</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
Documentation

• Recommend that the discussion and decision to forego screening be documented in the patients record starting at age 50.

• Document that an active decision was make to forego screening based on shared decision-making with the patient
  – Consider pertinent risk factors

• For patients who decline PSA testing, the topic should be revisited periodically (i.e., “no” is not necessarily “never”).
Screening Frequency

• There is no strong evidence to suggest specific intervals
• Overall trend in all guidelines is to be less frequent than “every year”

CRICO recommends:
• PSA <1.0  Every 4-5 yrs
• PSA 1.0-1.9 – “Periodic Retesting”
• PSA ≥ 2.0 – 4.0 – Annually
Questions?

 Death, Taxes & My Urologist, Dr. Heidi Rayala
Combination treatment with mirabegron and solifenacin in patients with overactive bladder: efficacy and safety results from a randomised, double-blind, dose-ranging, phase 2 study (Symphony).

Abrams P¹, Kelleher C², Staskin D³, Rechberger T⁴, Kay R⁵, Martina R⁶, Newgreen D⁶, Paireddy A⁶, van Maanen R⁶, Ridder A⁶.
Overall treatment outcomes after initial choice of anticholinergic agent at 24 months (N = 103,250).
Improvement in Mean Volume Voided (Improvement in Bladder Capacity)
Improvement in Urge Episodes during 24 hrs
Key Points:

• Understanding where your patient is in the pathophysiologic continuum of BPH in order to best direct medical management.

• Understanding the rationale for some of the newer pharmacologic interventions for BPH (such as tadalafil and silodosin) and how to integrate combination therapies into your practice.

• How to identify that small minority of patients who should be referred to Urology for evaluation, and providing a familiarity with surgical options for BPH.

• A thoughtful way to integrate PSA screening into your practice and brief review of 2018 USPTF rationale for changing recommendations on Prostate Cancer Screening.
Next Best Steps:

• If a patient has recurrent urinary tract infections, gross hematuria, or microscopic hematuria (defined as >RBC/HPF on formal urinalysis) they should be referred to Urology.

• If a patient has continued urinary complaints despite alpha-blocker, consider addition of 5alpha-reductase inhibitor, PDE5-inhibitor, or short-term anticholinergic.

• If a patient has ongoing urinary complaints despite best medical management, they should be referred to Urology for surgical consideration.

• After shared decision-making, make sure you have an easy method to document that an active decision was made on prostate cancer screening with your patient.