Update on the Prostate in Men's Health

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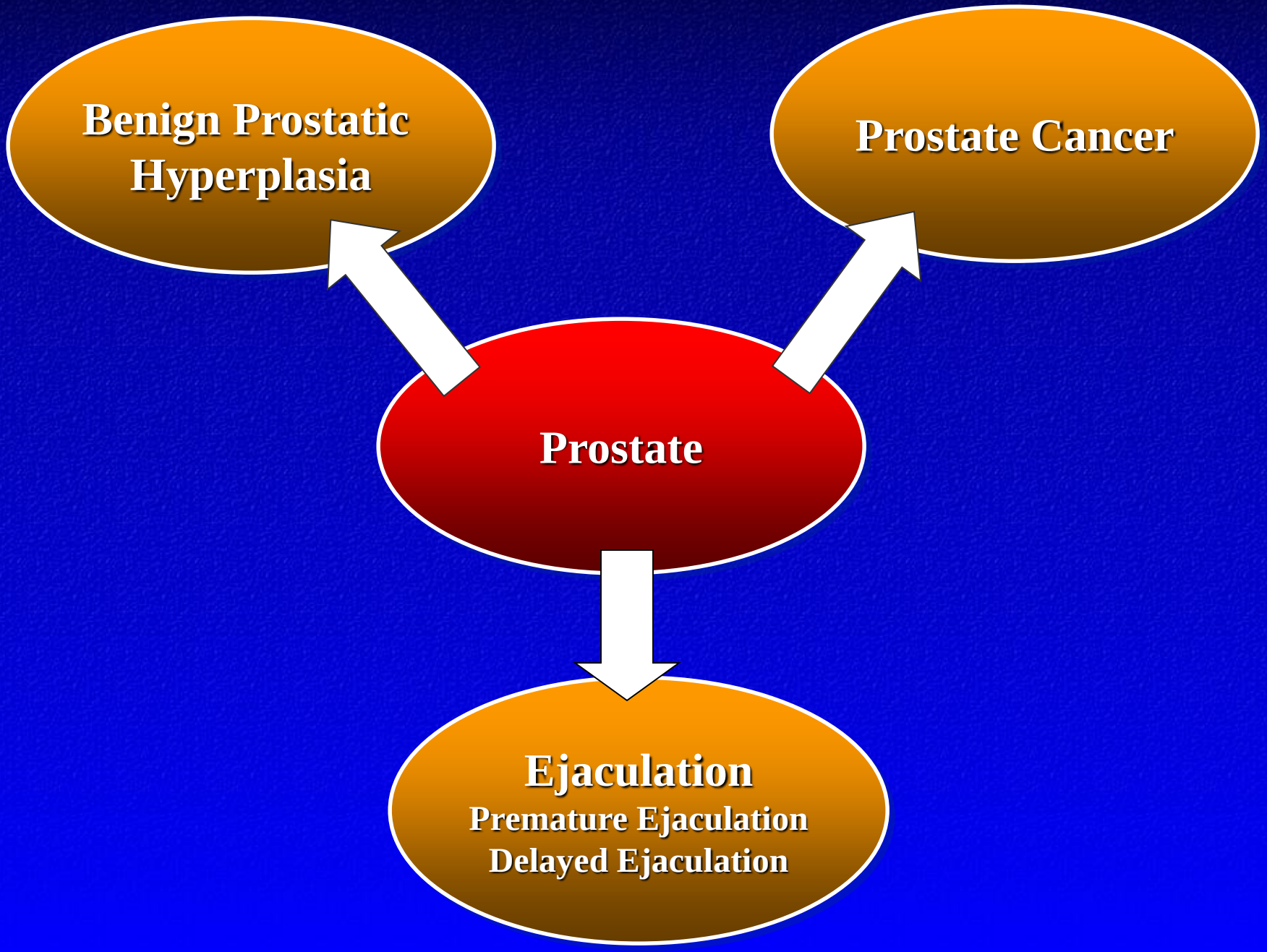
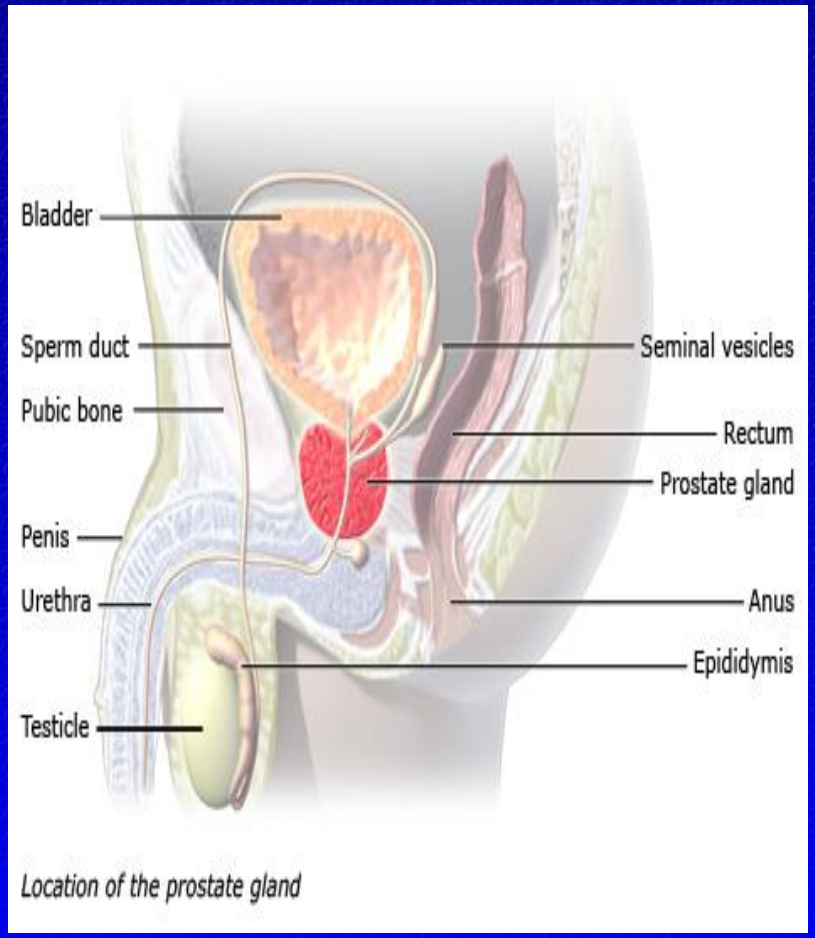
Disclosures

- Consultant- Abbvie, Boston Scientific, Coloplast, Endo


Benign Prostatic Hyperplasia
Prostate Cancer
Prostate
Ejaculation
Premature Ejaculation
Delayed Ejaculation

Prostate Physiology: The Most Diseased Organ in the Male Body

- "Prostate" = "one who stands before"
- 20- 30 grams (1ounce)
- Production of seminal fluid
- Propulsion of seminal fluid
- Production of PSA
- Conversion of T to DHT

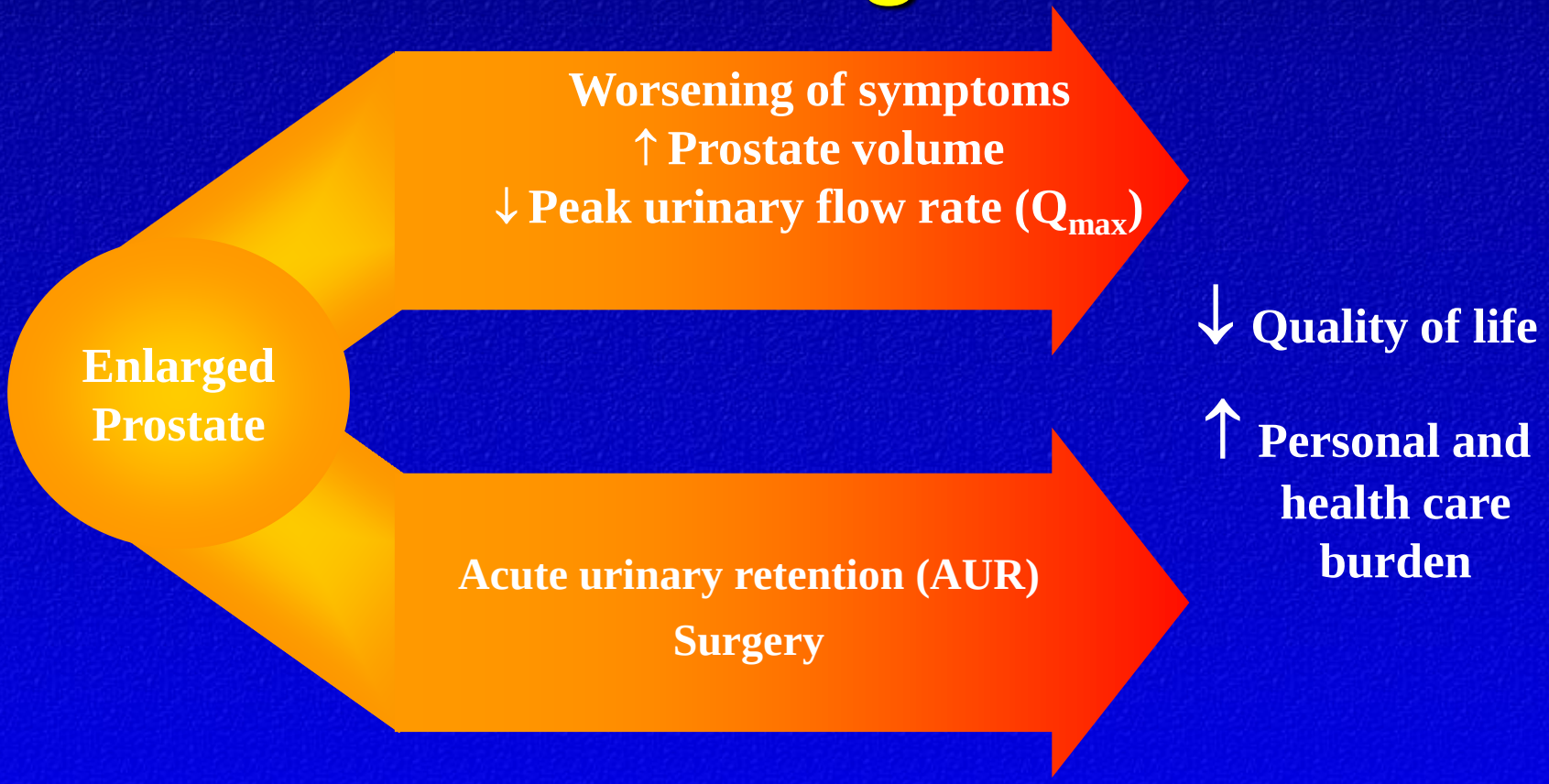


Location of the prostate gland

Pathophysiology of Clinical BPH: Predictive Risk Factors

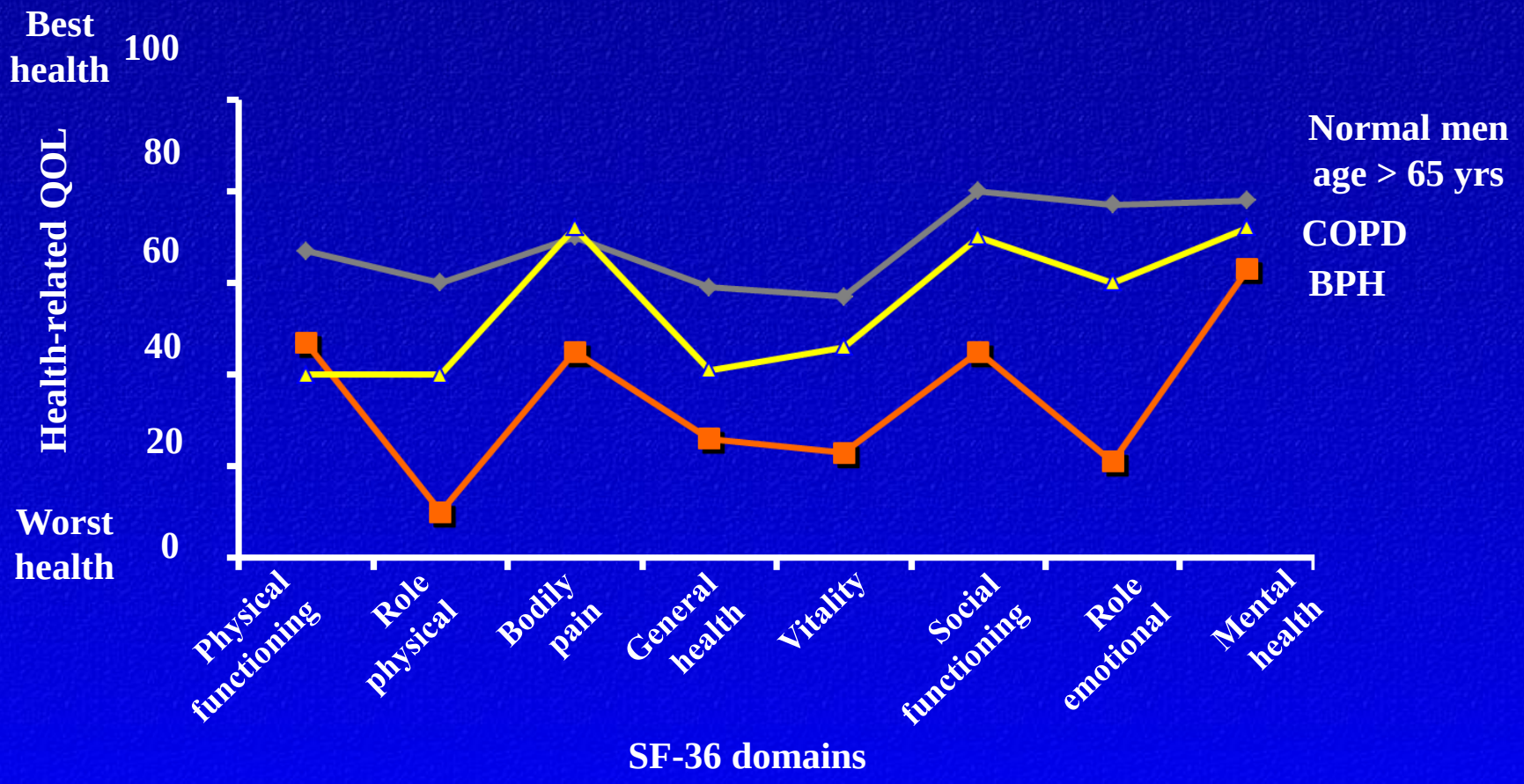
- Increasing age
- Prostatic enlargement
- Lower-urinary-tract symptoms (LUTS)
- Decreased urinary flow rate
- Elevated prostate-specific antigen (PSA)

Importance of Arresting Disease Progression



Rhodes T et al. *J Urol*. 1999;161:1174–1179. Kirby RS et. al. *Benign Prostatic Hyperplasia*. Oxford, UK: Health Press, 1995. Roehrborn CG et al. *Urology*. 1999;53:473–480. McConnell JD et al. *N Engl J Med*. 1998;338:557–563. Hong SJ et al. *BJU Int*. 2005;95:15–19. Fenter TC et al. *Am J Managed Care*. 2006;12:S90–S98.

Health-Related Quality of Life: BPH Compared with Another Chronic Disease (COPD)



COPD = chronic obstructive pulmonary disease; QOL = quality of life

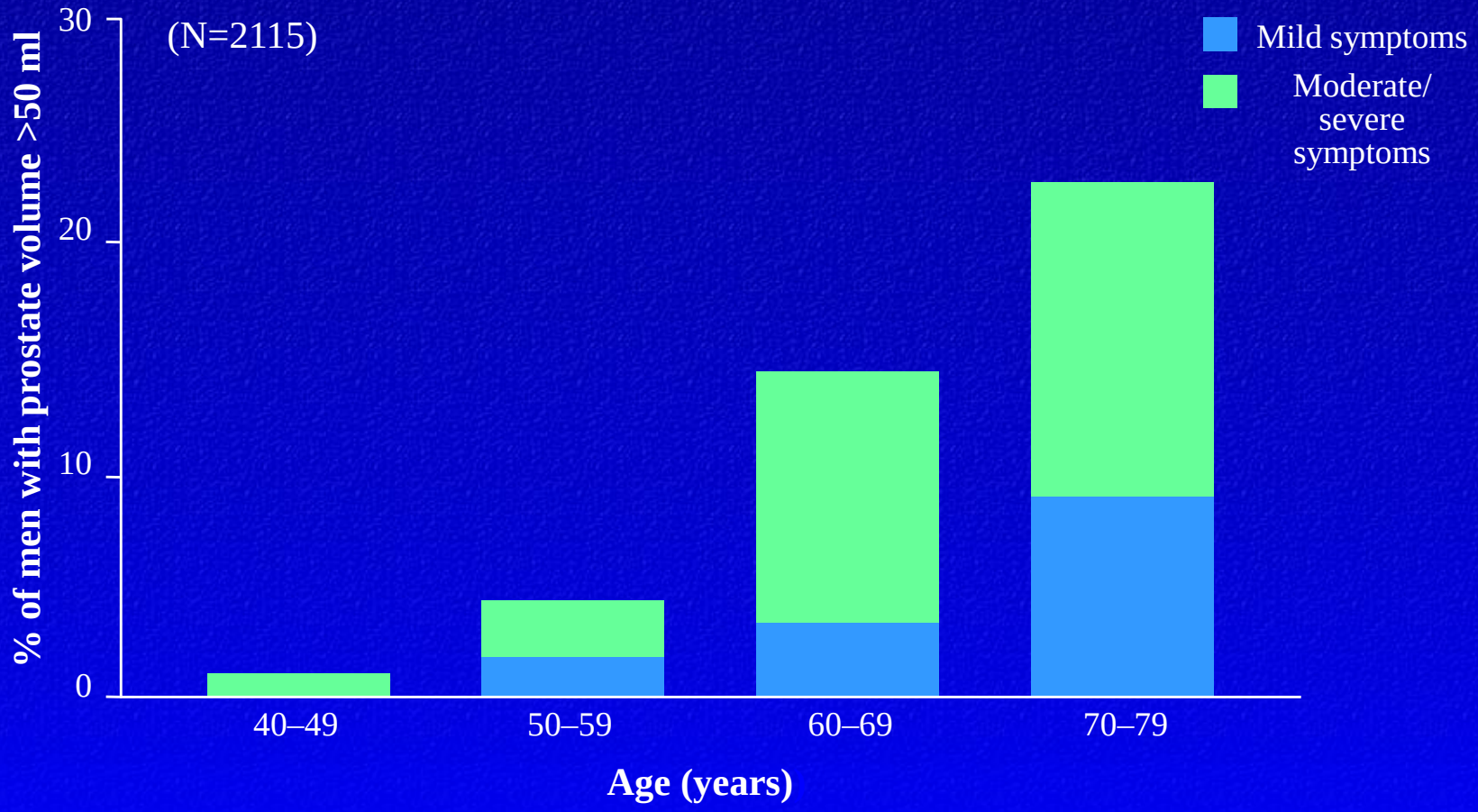
Hong SJ et al. *BJU Int.* 2005;95:15–19.

Prevalence of BPH

Age (years)	Prevalence
31-40	8%
51-60	40-50%
80+	80%

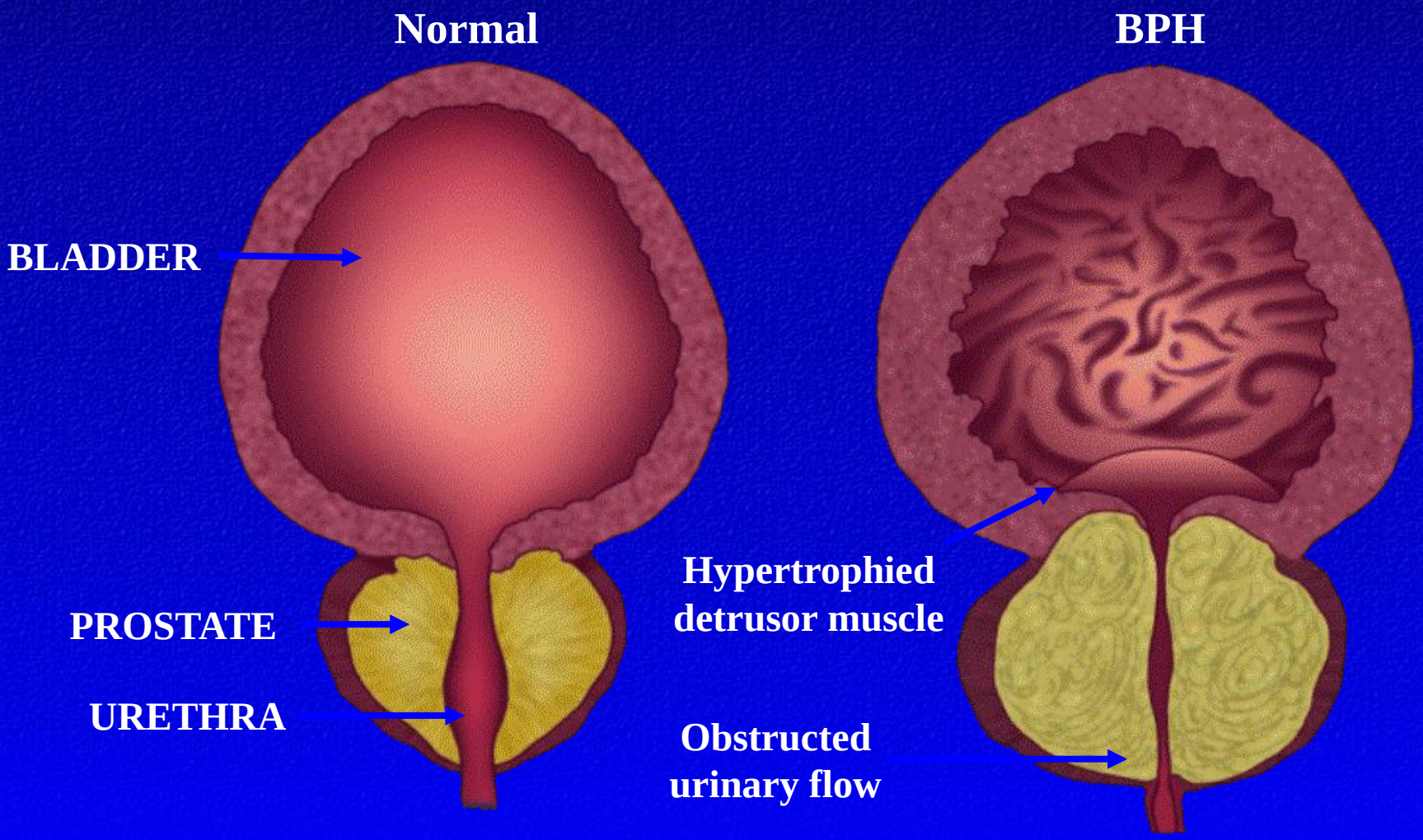
Guess HA et al. Prostate 1990; 17:241.

Natural History of BPH: Relationship Between Symptoms and Prostate Volume



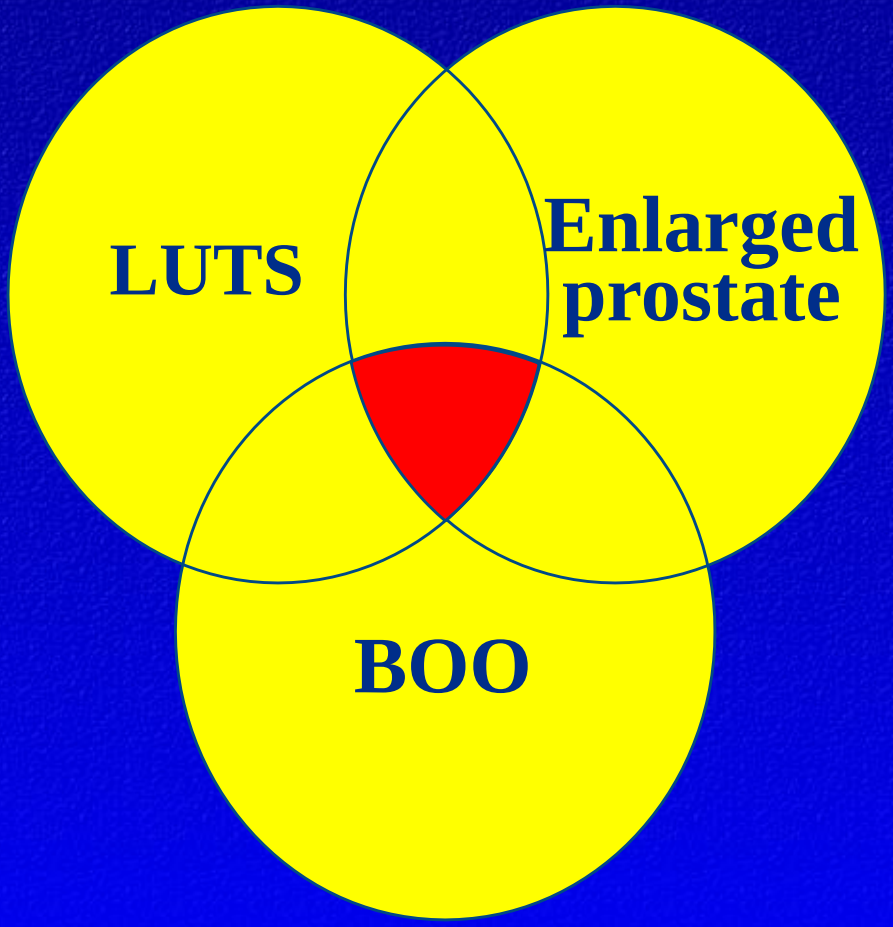
Adapted from Girman CJ et al *J Urol* 1995;153:1510-1515.

Anatomy of Benign Prostatic Hyperplasia



Kirby RS et al. *Benign prostatic hyperplasia*. Health Press, 1995.

Pathophysiology of Clinical BPH: Overlapping but Independent Features



LUTS= lower urinary tract symptoms
BOO= bladder outlet obstruction

LUTS – Bladder or Prostate?

LUTS = Lower Urinary Tract Symptoms

- Voiding (Obstructive)
  - Incomplete urination
  - Stopping / starting
  - Weak stream
  - Pushing / straining
- Irritative (Storage)
  - Frequency
  - Urgency
  - Nocturia

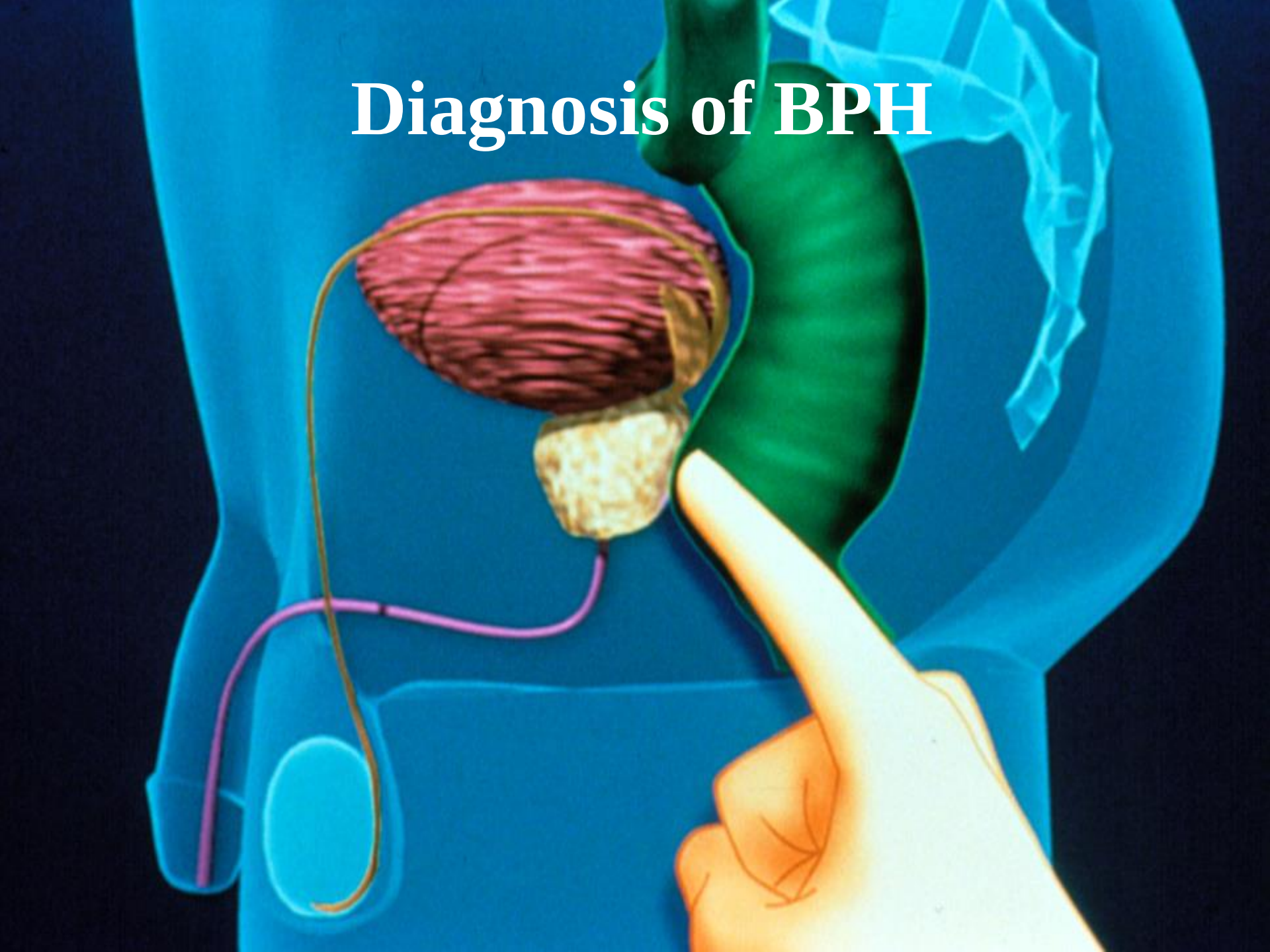
AUA Symptom Score

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time time	Almost always
1. Over the past month, how often have you had the sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. 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. Over the past month, 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 month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, 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 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 Symptom Score						

AUA Symptom Index Scoring

SCORE	INTERPRETATION
0-7	Mild
8-19	Moderate
20-35	Severe

Diagnosis of BPH



LUTS: History

- How long?
- Most bothersome symptom? **Degree of bother?**
- Voiding (Obstructive)
  - Incomplete urination
  - Stopping/starting
  - Weak stream
  - Pushing/straining
- Irritative (Storage - OAB)
  - Frequency
  - Urgency
  - Nocturia
- Other: fluid intake, UTI, pain, hematuria, LE swelling
- IPSS/AUA Symptom Score

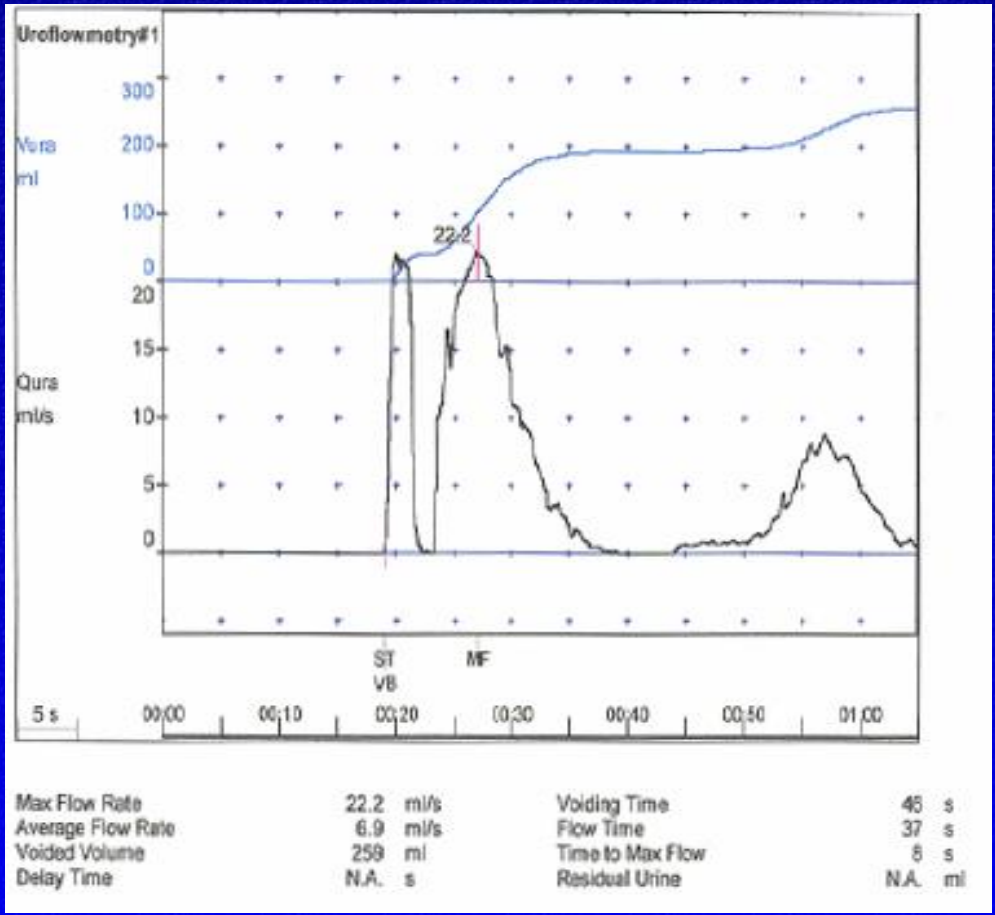
LUTS: Exam

- Digital rectal exam
  - Estimate prostate size, asymmetry, induration, nodule or bogginess (exclude carcinoma or chronic prostatitis)
  - Check for rectal sphincter tone
- Bladder percussion/palpation for distention
- Focused neurologic examination
  - Rule out neurologic conditions that might contribute to voiding dysfunction

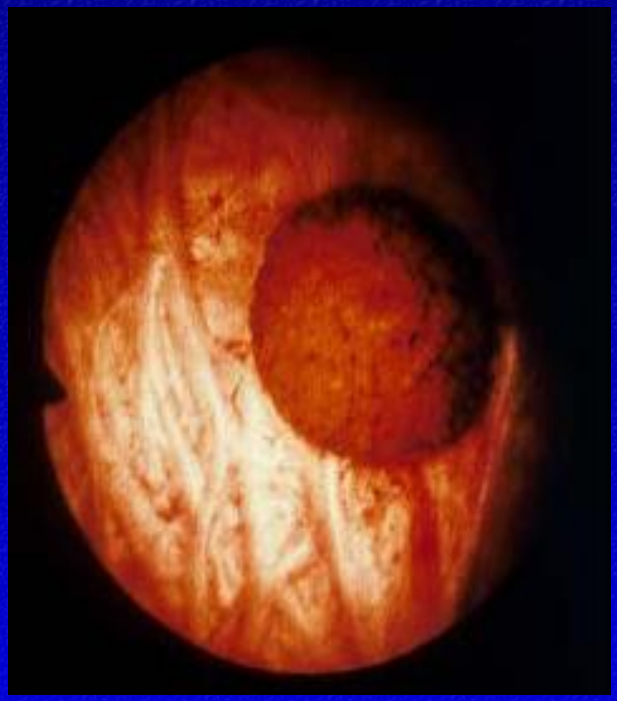
LUTS: Labs/Studies

- Urinalysis – rule out other urinary tract pathology
- PSA – appropriately aged male to screen for prostate cancer
- Upper tract imaging – only if recurrent UTI, hematuria, renal insufficiency, urolithiasis or prior urinary tract surgery
- Urodynamics/cystoscopy NOT required for initial evaluation or prior to starting therapy in standard patient
- Urolflow

Uroflow

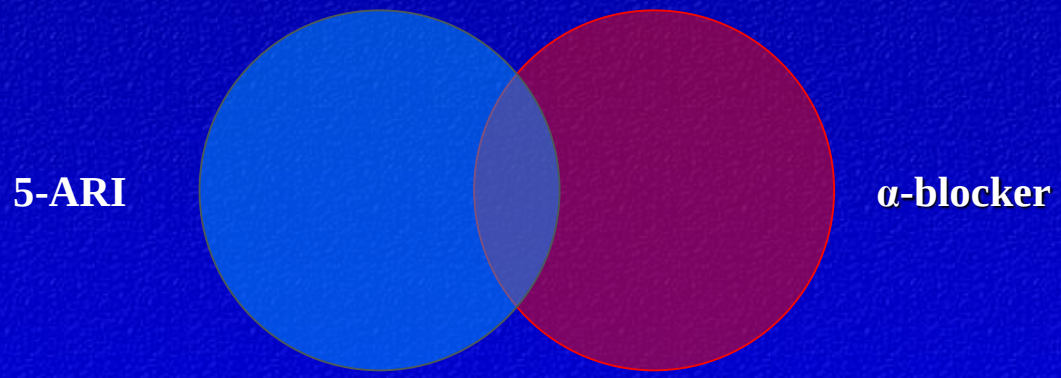

Uroflowmetry#1
300
200
100
0
Vura
ml
22.2
20
15
Qura
ml/s
10
5
0
ST
VB
MF
5 s
00:00
00:10
00:20
00:30
00:40
00:50
01:00
Max Flow Rate 22.2 ml/s
Average Flow Rate 6.9 ml/s
Voided Volume 259 ml
Delay Time N.A. s
Voiding Time 45 s
Flow Time 37 s
Time to Max Flow 5 s
Residual Urine N.A. ml

Male LUTS
When Should Therapy Be Started?



- Absolute indications
  - Urinary retention
  - Renal insufficiency
  - Recurrent UTI
  - Recurrent hematuria
  - Bladder stones
- Otherwise…are you bothered?
  - Poor flow
  - Nocturia
  - Frequency

Evolution of Medical Therapy for LUTS/BPH/BOO/BPE



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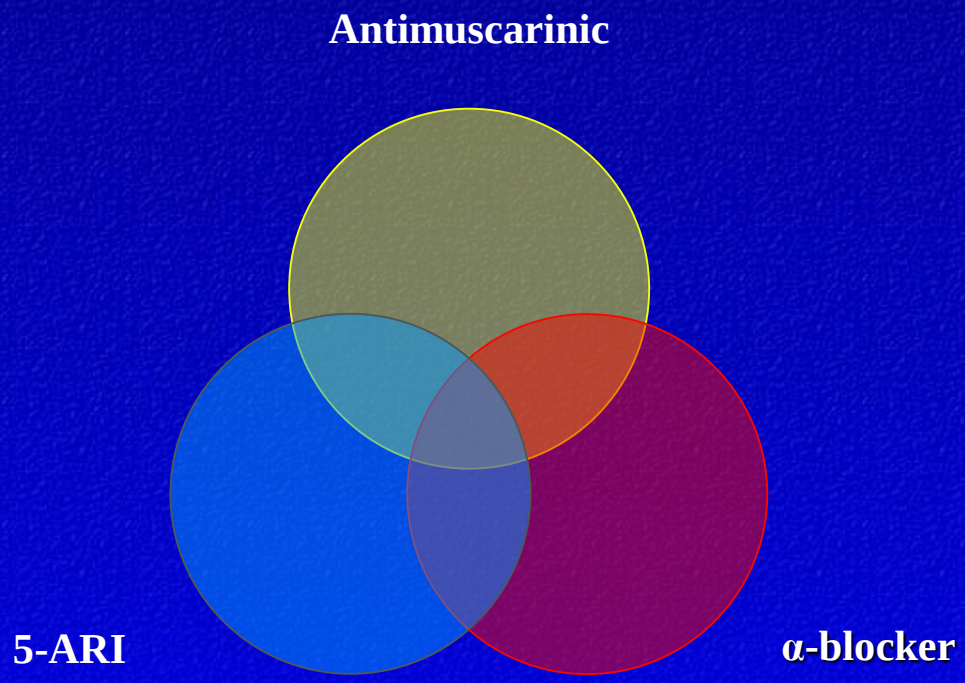

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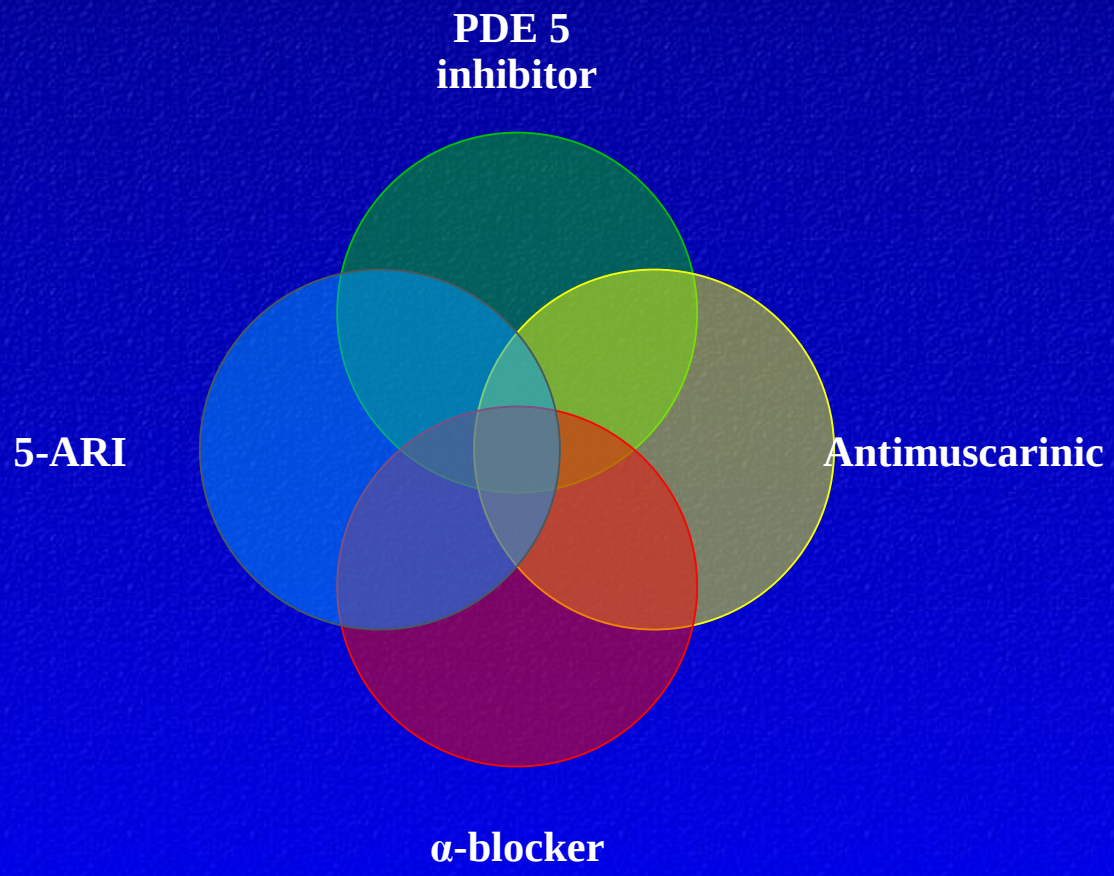
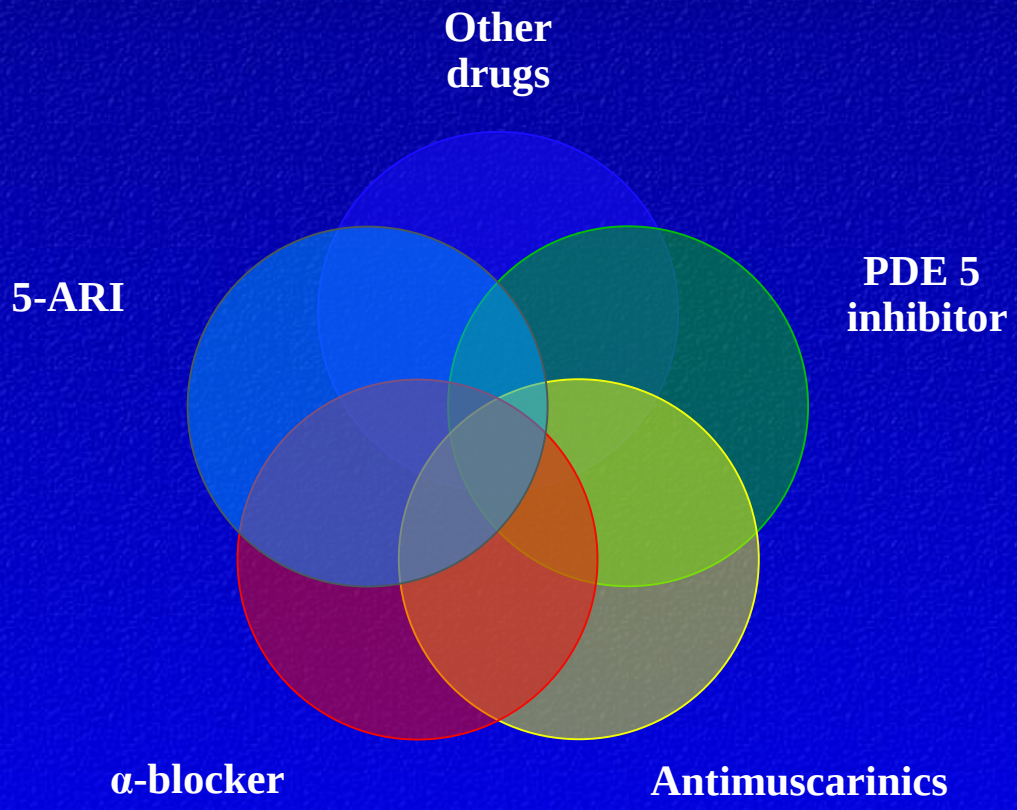
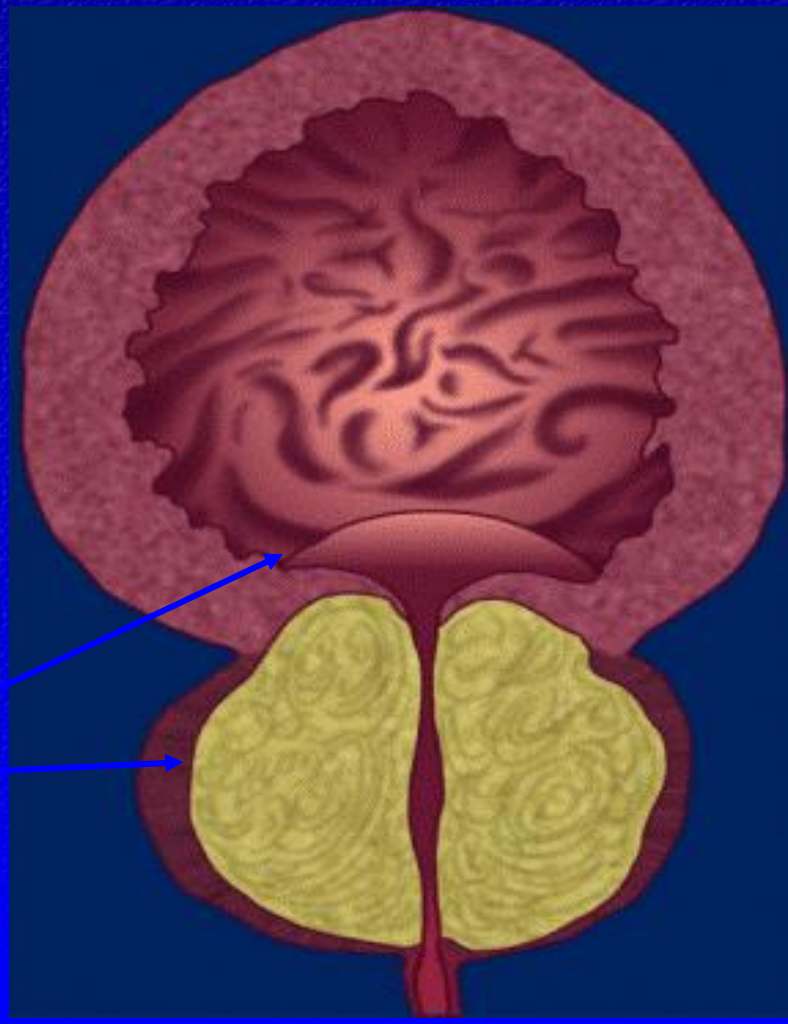


Evolution of Medical Therapy for LUTS/BPH/BOO/BPE



α-Blocker Therapy

- α -adrenergic receptors found at bladder neck and smooth muscle capsule of prostate
- α-1 receptors have many subtypes: A1a,A1b,A1d, A1L
- A1a found in prostate gland and bladder neck



Alpha blockers: how to choose?

Agent	Trade name	Typical titration schedule	Available dosing	Advantages	Disadvantages
Prazosin	Minipress	1 mg QD x1wk 1 mg BID x 1wk then 2 mg BID	1, 2 mg	-Low cost	-BID dosing -↑↑ Side effects
Terazosin	Hytrin	2 mg qhs x 1wk 5 mg qhs x 1wk then 10 mg qhs	2, 5 and 10 mg	-QD dosing	-Need to titrate -↑ side effects
Doxazosin	Cardura	2 mg qhs x 1wk 4 mg qhs x 1wk then 8 mg qhs	2, 4 and 8 mg	-QD dosing	-Need to titrate -↑ side effects
Alfusozin (long acting)	Uroxatral	No titration needed	10 mg	-QD dosing -No titration -↓ retrograde ejaculation	
Tamsulosin	Flomax	No titration needed	0.4 and 0.8 mg	-QD dosing -No titration -Low side effects	- May need to titrate
Silodosin	Rapaflo	No titration needed	8 mg	-QD dosing -No titration -No impact on BP or HR	-Higher RE and cost

Alpha-blockers
Adverse Events

- Postural hypotension
- Dizziness
- Somnolence
- Nasal congestion
- Retrograde ejaculation

Intraop Floppy Iris Syndrome (IRIS)

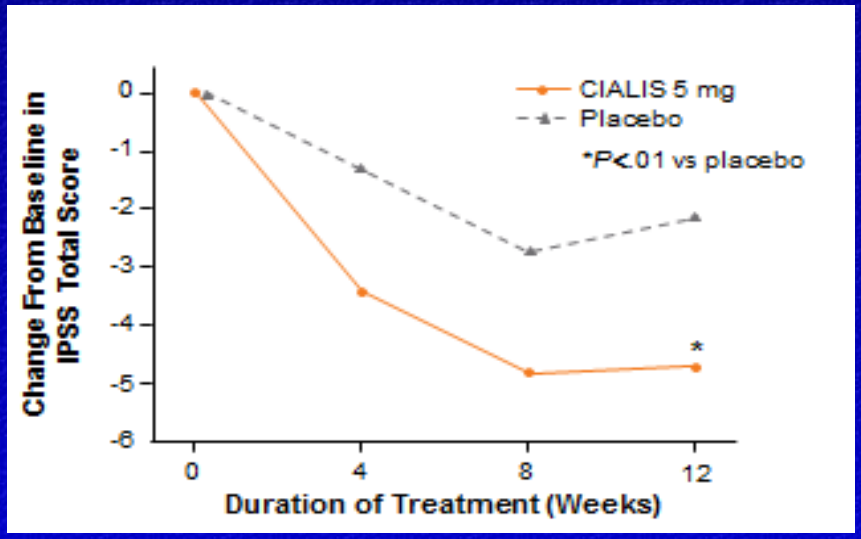
- Risk with tamsulosin or other alpha-blockers
- Flaccid iris during cataract surgery
- Impacts surgical technique – well known in ophthalmologic community
- Benefit of stopping alpha-blocker pre-op is questionable

5-alpha Reductase Inhibitors Finasteride/Dutasteride

- Blocks conversion of testosterone to DHT
- Reduces volume of enlarged prostate as DHT primary androgen responsible for prostate growth
- Reduces risk of AUR/surgery by 50% (prostates $\geq$ 40 gm)
- Reduces PSA by 50%
- Takes 3-6 months to show maximal effects
- Common side effects: erectile dysfunction, decreased libido, decreased ejaculate volume

Cialis for Once Daily Dose

- FDA Indications
  - ED
  - BPH
  - ED + BPH
- Side effects
  - Headache (4.1%)
  - Dyspepsia (2.4%)
  - Back pain (2.4%)
  - Nasopharyngitis (2.1%)

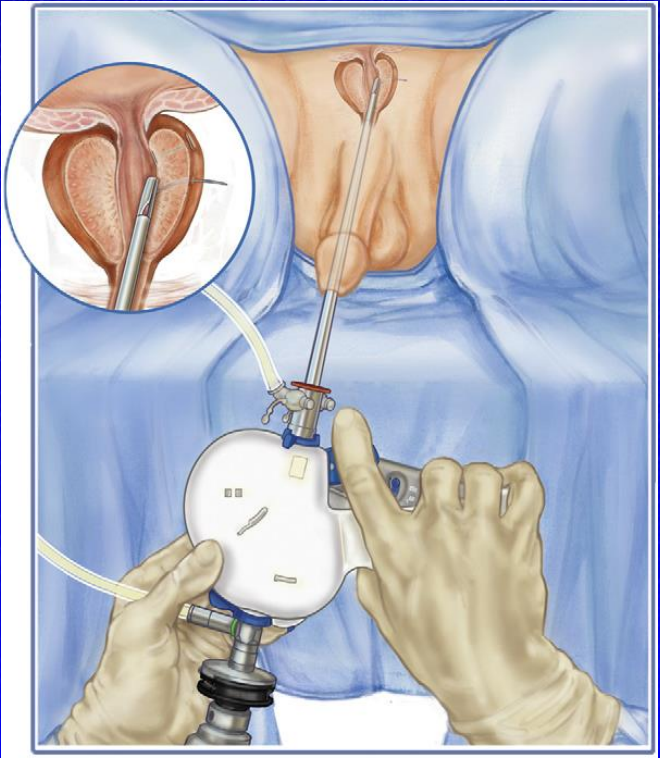


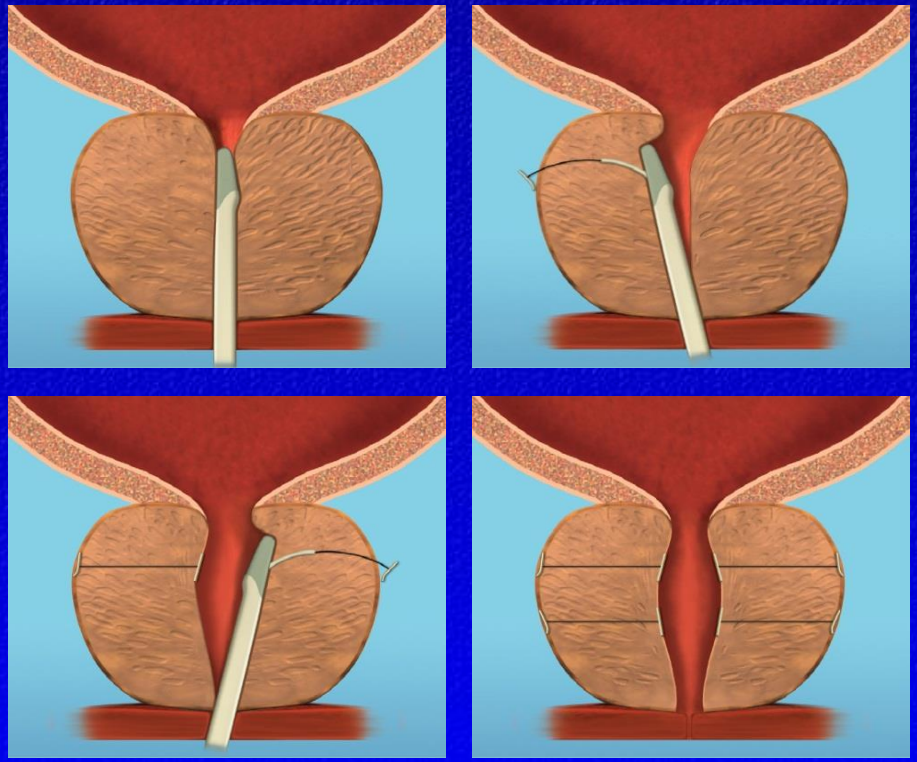
Tadalafil full prescribing information 2011

Surgical Options

- Transurethral resection of the prostate (TURP)
- Open prostatectomy
- Minimally invasive options
  - Aqua ablation
  - Prostate arterial embolization (PAE)
  - Rezume™
  - Urolift™

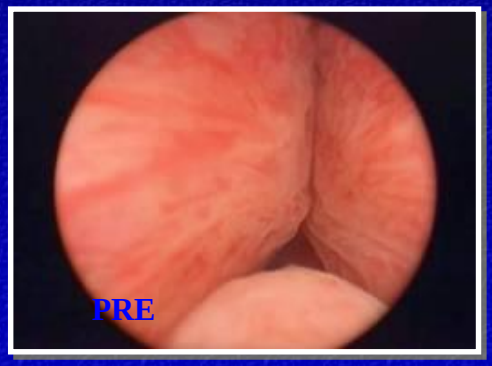
UroLift® Prostatic Urethral Lift

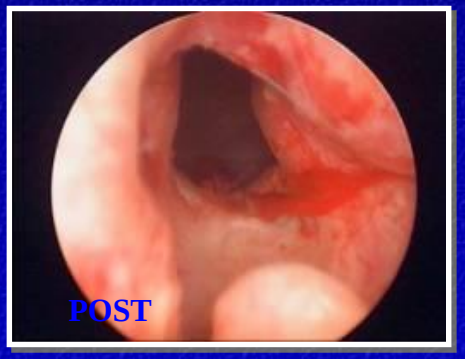


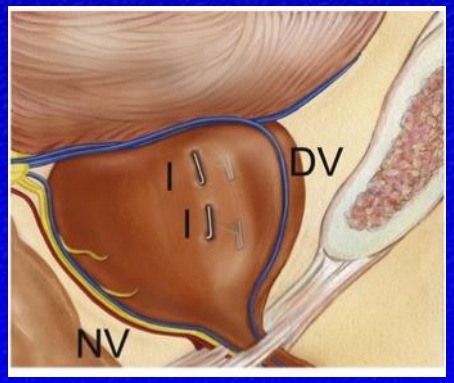


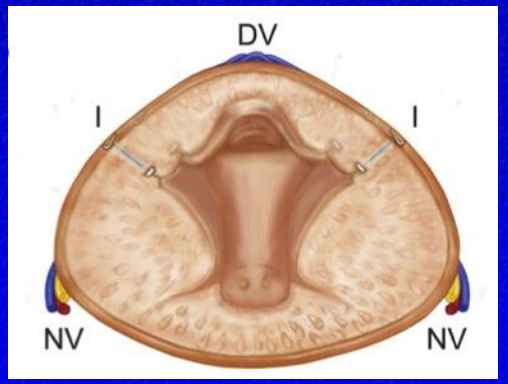
UroLift® Effect

- Mechanically opens prostatic urethra
- Result is visible under cystoscopy
- Implants are anterolateral, away from NV bundles or dorsal venous complex









Complementary Medicines

- Serenoa repens (saw palmetto)
- Cernilton (Rye Grass Pollen)
- Permixon
- Pygeum africanum (african plum)
- Stinging nettle (urtica dioica)
- African star grass (hypoxis rooperi)
- Pumpkin seeds (cucurbita peopo)
- Pruce (picea)
- Pine (pineas)
- Zinc

Saw Palmetto

- Lack of evidence
  - Few trials
  - Study limitations: poor design, small numbers, variable drug preparation
- 2006 NEJM RCT*
  - 225 men, moderate-severe BPH, saw palmetto vs. placebo
  - No advantage with saw palmetto at one year
    - AUA score
    - Peak flow
    - Prostate size
    - Bother score/QOL
- Multiple formulations problematic without FDA regulation

Prostate Cancer

Estimated New Cases of Cancers in Men

Estimated New Cases

Males

Prostate	164,690	19%
Lung & bronchus	121,680	14%
Colon & rectum	75,610	9%
Urinary bladder	62,380	7%
Melanoma of the skin	55,150	6%
Kidney & renal pelvis	42,680	5%
Non-Hodgkin lymphoma	41,730	5%
Oral cavity & pharynx	37,160	4%
Leukemia	35,030	4%
Liver & intrahepatic bile duct	30,610	4%
All Sites	**856,370**	**100%**

Siegel R et al, CA Cancer J Clin 2018

Probability of Prostate Cancer Increases with Age

		BIRTH TO 49	50 TO 59	60 TO 69	≥70	BIRTH TO DEATH
All sites†	Male	3.4 (1 in 30)	6.1 (1 in 16)	13.4 (1 in 7)	32.2 (1 in 3)	39.7 (1 in 3)
	Female	5.5 (1 in 18)	6.1 (1 in 16)	9.9 (1 in 10)	26.0 (1 in 4)	37.6 (1 in 3)
Breast	Female	1.9 (1 in 52)	2.3 (1 in 43)	3.4 (1 in 29)	6.8 (1 in 15)	12.4 (1 in 8)
Colorectum	Male	0.3 (1 in 287)	0.7 (1 in 145)	1.2 (1 in 85)	3.4 (1 in 29)	4.5 (1 in 22)
	Female	0.3 (1 in 306)	0.5 (1 in 194)	0.8 (1 in 122)	3.1 (1 in 32)	4.2 (1 in 24)
Kidney & renal pelvis	Male	0.2 (1 in 456)	0.4 (1 in 284)	0.6 (1 in 155)	1.3 (1 in 74)	2.1 (1 in 48)
	Female	0.1 (1 in 706)	0.2 (1 in 579)	0.3 (1 in 320)	0.7 (1 in 136)	1.2 (1 in 83)
Leukemia	Male	0.2 (1 in 400)	0.2 (1 in 573)	0.4 (1 in 260)	1.4 (1 in 71)	1.8 (1 in 56)
	Female	0.2 (1 in 515)	0.1 (1 in 887)	0.2 (1 in 446)	0.9 (1 in 111)	1.3 (1 in 80)
Lung & bronchus	Male	0.1 (1 in 682)	0.7 (1 in 154)	1.9 (1 in 54)	6.1 (1 in 16)	6.9 (1 in 15)
	Female	0.2 (1 in 635)	0.6 (1 in 178)	1.4 (1 in 70)	4.8 (1 in 21)	5.9 (1 in 17)
Melanoma of the skin‡	Male	0.5 (1 in 218)	0.5 (1 in 191)	0.9 (1 in 106)	2.6 (1 in 38)	3.6 (1 in 27)
	Female	0.7 (1 in 152)	0.4 (1 in 254)	0.5 (1 in 202)	1.1 (1 in 91)	2.4 (1 in 42)
Non-Hodgkin lymphoma	Male	0.3 (1 in 382)	0.3 (1 in 349)	0.6 (1 in 174)	1.8 (1 in 54)	2.4 (1 in 42)
	Female	0.2 (1 in 545)	0.2 (1 in 480)	0.4 (1 in 248)	1.3 (1 in 74)	1.9 (1 in 54)
Prostate	Male	0.2 (1 in 403)	1.7 (1 in 58)	4.8 (1 in 21)	8.2 (1 in 12)	11.6 (1 in 9)
Thyroid	Male	0.2 (1 in 517)	0.1 (1 in 791)	0.2 (1 in 606)	0.2 (1 in 425)	0.6 (1 in 160)
	Female	0.8 (1 in 124)	0.4 (1 in 271)	0.3 (1 in 289)	0.4 (1 in 256)	1.8 (1 in 56)
Uterine cervix	Female	0.3 (1 in 368)	0.1 (1 in 845)	0.1 (1 in 942)	0.2 (1 in 605)	0.6 (1 in 162)
Uterine corpus	Female	0.3 (1 in 342)	0.6 (1 in 166)	1.0 (1 in 103)	1.3 (1 in 75)	2.8 (1 in 35)

Siegel R et al, CA Cancer J Clin 2018

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Siegel R et al, CA Cancer J Clin 2018

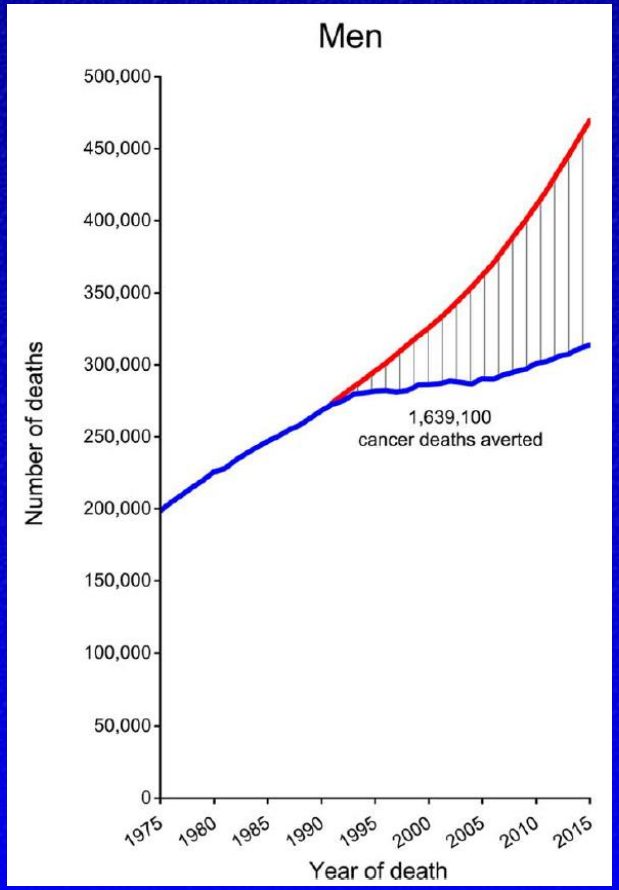
Prostate Cancer Screening

- H&P → Rectal exam
- Assess comorbid conditions → life expectancy estimation
- Discuss individual risks + define personal goals of care
- PSA (prostate specific antigen)

Prostate Cancer Screening

- Abnormal PSA → > 4ng/mL or > 2.5ng/mL
- Prostate biopsy
- Surgery or radiation therapy

Effects of PSA Screening



U.S. Preventive Services Task Force - USPSTF

Table 1. What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	*Note: The following statement is undergoing revision.* Clinicians may provide this service to selected patients depending on individual circumstances. However, for most persons without signs or symptoms there is likely to be only a small benefit from this service.	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

U.S. Preventive Services Task Force - USPSTF

Annals of Internal Medicine | CLINICAL GUIDELINES

Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

U.S. Preventive Services Task Force*

Description: Update of the 2002 U.S. Preventive Services Task Force (USPSTF) recommendation statement about screening for prostate cancer.

Methods: The USPSTF evaluated randomized, controlled trials of the benefits of prostate cancer screening; cohort and cross-sectional studies of the psychological harms of false-positive prostate-specific antigen test results; and evidence on the natural history of prostate-specific antigen–detected prostate cancer to address previously identified gaps in the evidence from the 2002 USPSTF recommendation.

Recommendations: Current evidence is insufficient to assess the balance of benefits and harms of screening for prostate cancer in men younger than age 75 years (I statement).

Do not screen for prostate cancer in men age 75 years or older (Grade D recommendation).

Ann Intern Med. 2008;149:185-191. www.annals.org

For author affiliation, see end of text.

*For a list of Task Force members, see the **Appendix** (available at www.annals.org).

U.S. Preventive Services Task Force - USPSTF

CLINICAL GUIDELINE | Annals of Internal Medicine

Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, PhD, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2008 U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for prostate cancer.

Methods: The USPSTF reviewed new evidence on the benefits and harms of prostate-specific antigen (PSA)–based screening for prostate cancer, as well as the benefits and harms of treatment of localized prostate cancer.

Recommendation: The USPSTF recommends against PSA-based screening for prostate cancer (grade D recommendation).

This recommendation applies to men in the general U.S. population, regardless of age. This recommendation does not include the use of the PSA test for surveillance after diagnosis or treatment of prostate cancer; the use of the PSA test for this indication is outside the scope of the USPSTF.

Ann Intern Med. 2012;157:120-134. www.annals.org

For author affiliation, see end of text.

* For a list of the members of the USPSTF, see **Appendix 1** (available at www.annals.org).

This article was published at www.annals.org on 22 May 2012.

USPSTF Critiques

- Preliminary conclusions based on incomplete data (both trials had longer follow-up + Swedish trial)
- Pooling data with other poor quality trials and MA
- Statistical issues with CI comparisons (CI of difference vs. CI of each value separately
- Overestimation of risk of radical prostatectomy
- Overall mortality issue
- No detrimental effect on men's anxiety

Updated USPSTF recommendations

Figure 2. Clinical Summary: Screening for Prostate Cancer

Population	Men aged 55 to 69 y	Men 70 y and older
Recommendation	The decision to be screened for prostate cancer should be an individual one. Grade: C	Do not screen for prostate cancer. Grade: D

Informed Decision Making	Before deciding whether to be screened, men aged 55 to 69 years should have an opportunity to discuss the potential benefits and harms of screening with their 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, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and erectile dysfunction. Harms are greater for men 70 years and older. 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 benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening and should not routinely screen men 70 years and older.
Risk Assessment	Older age, African American race, and family history of prostate cancer are the most important risk factors for prostate cancer.
Screening Tests	Screening for prostate cancer begins with a test that measures the amount of prostate-specific antigen (PSA) protein in the blood. An elevated PSA level may be caused by prostate cancer but can also be caused by other conditions, including an enlarged prostate (benign prostatic hyperplasia) and inflammation of the prostate (prostatitis). Some men without prostate cancer may therefore have false-positive results. Men with a positive PSA test result may undergo a transrectal ultrasound-guided core-needle biopsy of the prostate to diagnose prostate cancer.
Treatments	The 3 most common treatment options for men with screen-detected, localized prostate cancer are surgical removal of the prostate gland (radical prostatectomy), radiation therapy (external-beam radiation therapy, proton beam therapy, or brachytherapy), and active surveillance.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to https://www.uspreventiveservicestaskforce.org.

U.S. Preventive Services TASK FORCE

JAMA

Individualizing risks and personalizing assessment PSA Derivatives

- PSA density → 0.15ng/mL/cc
- PSA velocity
  - Calculated with minimum of 3 readings
  - Suggested ideal interval of 18 months
  - PSA < 4ng/mL → PSAv cutoff of 0.35ng/mL/year
  - PSA 4-10ng/mL → PSAv cutoff of 0.75ng/mL/year

NCCN guidelines; AUA – PSA Best Practice Guidelines

New Emerging Prostate Cancer Markers

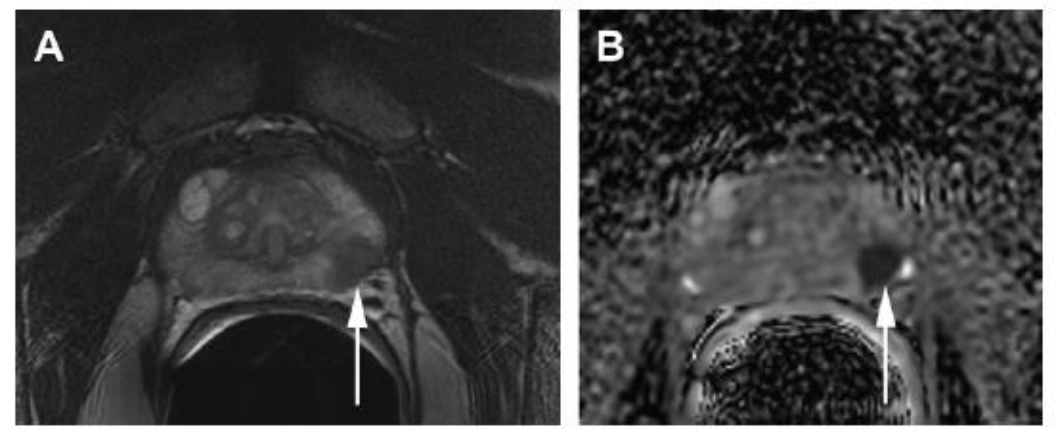
- **Blood:**
- PHI (Prostate Health Index)
- 4K

- **Urine:**
- PCA-3 (post DRE)
- Select MDx (post DRE)
- ExoDx Prostate IntelliScore – EPI (no DRE)

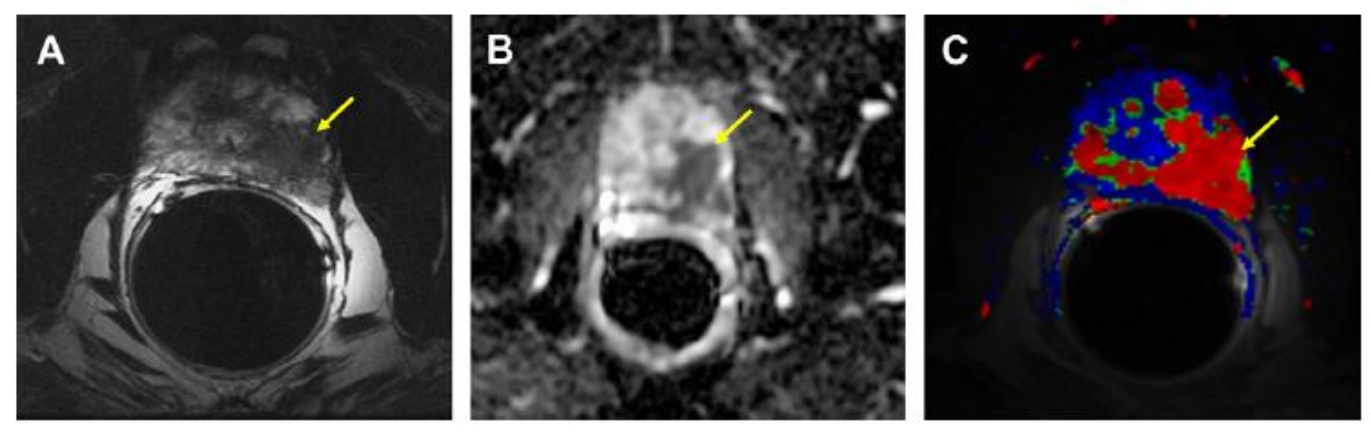
- **Tissue:**
- Confirm MDx (previous bx sample)

- **Imaging based:**
- mpMRI → also benefit for MRI/US Fusion bx

Multiparametric MRI of the Prostate



Multiparametric MRI of the Prostate



Review AUA Guidelines: Disorders of Ejaculation

Premature Ejaculation Definitions:

- **ISSM: "Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE) or a clinically significant and bothersome reduction in latency time, to about 3 minutes or less (acquired PE) associated with lack of control and negative interpersonal consequences."**
- **DSM-V: "A persistent or recurrent pattern of ejaculation occurring during partnered sexual activity within approximately 1 minute following vaginal penetration and before the individual wishes it…associated with distress."**
- **ICD-11: "Ejaculation that occurs prior to or within a very short duration of the initiation of vaginal penetration or other relevant sexual stimulation, with no or little perceived control over ejaculation…and is associated with distress."**

PE Definitions

Lifelong premature ejaculation is defined as consistently poor ejaculatory control, associated bother, and ejaculation within about 2 minutes of initiation of penetrative sex that has been present since sexual debut. (Data-driven/ expert opinion)

LPE Criteria #1: Latency

Evidence favoring a longer ELT includes:

- **Studies using PE self-identification or Ejaculatory Control as validating covariates show *median* ELTs of 1-2 min**
- **Men who report ELTs between 1-2 min are more similar to men reporting ELTs of < 1 min on ejaculatory control and bother/distress than those with ELTs between 2-5 min**
- **Even lifelong PE men (untreated) show variation above 1 min when re-examined 6 years later (Jern group)**

LPE Criteria #2: Ejaculatory Control

AUA definition requires poor ejaculatory control (sine qua non)

What is ejaculatory control?

- **Measure of self-efficacy by which the man feels he can effect a particular outcome, assessed by such language as:**
  - **Not being able to "control ejaculation"**
  - **Not being able to "delay or postpone ejaculation"**
  - **Ejaculating "before wanting/wishes to"**
- **>70% of men with PE report poor/very poor ejaculatory control**

LPE Criteria #3: Associated Bother/Distress

The AUA definition includes associated bother/distress

What is meant by bother/distress?

- **Negative psycho-behavioral effects on man, partner, or relationship**
- **Bother stands as a proxy for terms as: dissatisfied", "anxious," "concerned" "depressed," "frustrated,"etc.**
- **Behaviors may include (but not limited to) catastrophizing about the effect of PE, avoidance of intimacy, post-coital apologizing, etc.**

PE Definitions

Acquired **premature ejaculation is defined as consistently poor ejaculatory control, associated bother, and ejaculation latency that is *markedly reduced from prior sexual experience* during penetrative sex. (Expert Opinion)**

APE Criteria: ELT

Clinical experience suggests that men with APE:

- **Have an ELT under about 2-3 minutes, or**
- **ELT is reduced by about 50% or more from prior (e.g., 8 min to about 4 min, etc.)**

This flexibility allows clinical judgment, and reflects the thinking that the consequence for false positives in terms of treatment strategies is relatively low

Psychological/Behavioral Interventions

- **May be useful alone or combined with medical/pharma therapy**
  - **Typically require half a dozen to 10 sessions**
  - **May include relationship therapy**
  - **Can be integrated with pharmacotherapy (combination therapy seems more effective than either by itself)**

First Line Pharmacotherapy

Clinicians should recommend daily SSRIs; on demand clomipramine or dapoxetine (where available); and topical penile anaesthetics (ie Promescent) as first-line pharmacotherapies in the treatment of premature ejaculation. (Strong Recommendation; Evidence Level: Grade B)

NB: All pharmacotherapies for PE are off-label use in the US

SSRI

- SSRI have been used off-label in management of PE for years
  - Daily Dosing with paroxetine (10-40 mg), sertraline (50-200 mg), citalopram (20-40 mg), & fluoxetine (20-40 mg)
  - On Demand Dosing with paroxetine, sertraline, and fluoxetine

Althof 2014

Second Line Pharmacotherapy

Clinicians may consider treating men with premature ejaculation who have failed first-line therapy with on-demand dosing of tramadol* (Conditional Recommendation; Evidence Level: Grade C)

Clinicians may consider treating men with premature ejaculation who have failed first-line therapy with a1-adrenoreceptor antagonists* (Expert Opinion)

PE and comorbid ED

Clinicians should treat comorbid erectile dysfunction in patients with premature ejaculation according to the AUA Guidelines on Erectile Dysfunction. (Expert Opinion)

DE Definitions

Lifelong delayed ejaculation is defined as lifelong, consistent, bothersome inability to achieve ejaculation, or as an excessive latency to ejaculation, despite adequate sexual stimulation and the desire to ejaculate. (Expert Opinion)

Acquired delayed ejaculation is defined as an acquired, consistent, bothersome inability to achieve ejaculation, or an increased latency of ejaculation, despite adequate sexual stimulation and the desire to ejaculate. (Expert Opinion)

Some preliminaries

- Most men ejaculate between about 5-10 min following penetration
  - Ejaculation within this timeframe is typical
  - Ejaculation requiring 15-20 min or more after penetration may be delayed, depending on individual circumstances (e.g., age, physical condition)
- Many men with DE are able to masturbate to orgasm

Mental Health Evaluation

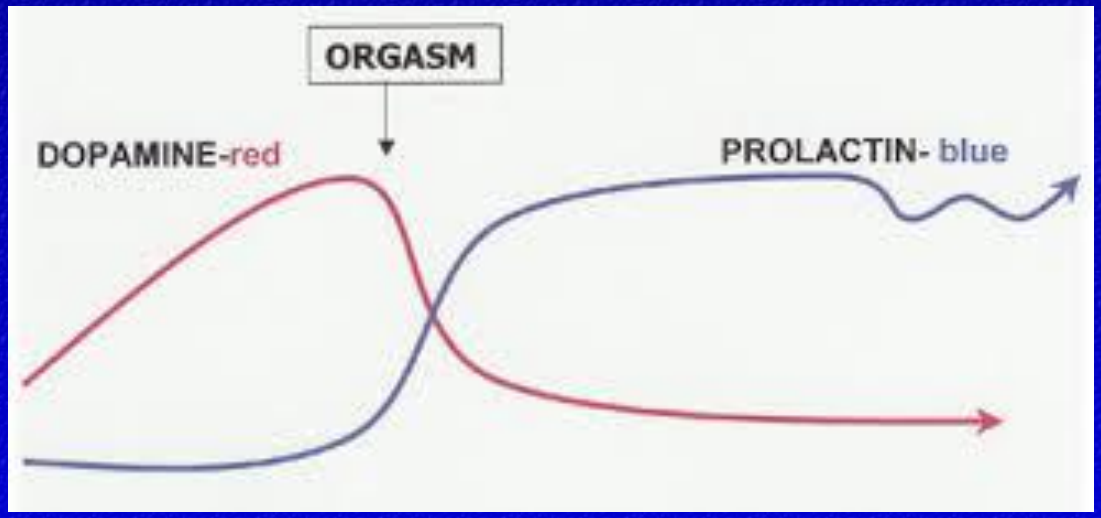
Clinicians should consider referring men diagnosed with lifelong or acquired delayed ejaculation to a mental health professional with expertise in sexual health. (Expert Opinion)

Penile Vibratory Stimulation (PVS)

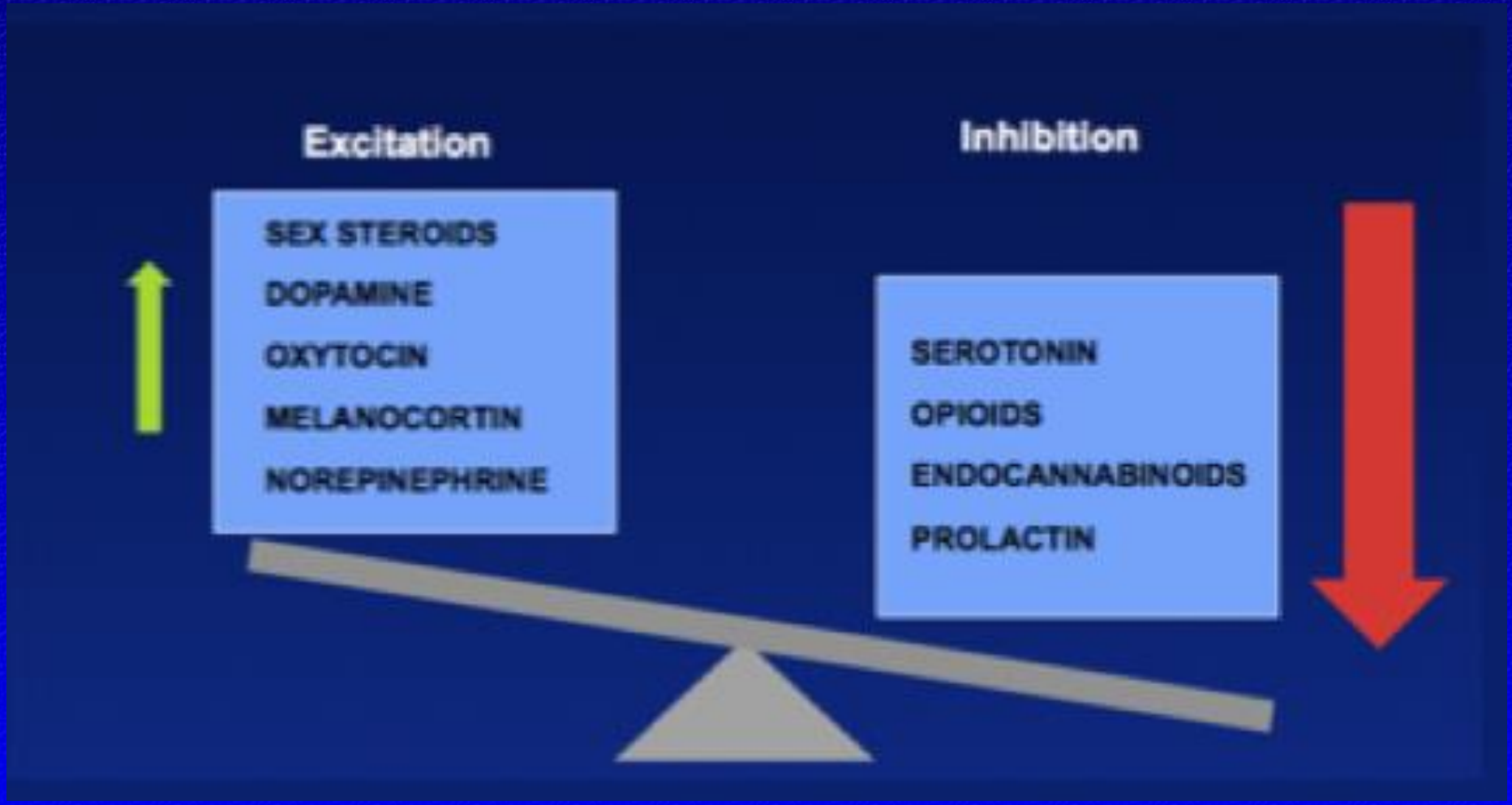
- **Intensified sensation/arousal**
  - **Nelson 2007: 36 patients with secondary anorgasmia for ≥3 months treated with intermittent PVS to frenulum**
    - **72% had at least "some" restoration of orgasm**
      - **62% of sexual encounters resulted in orgasm**
    - **Improvements in Orgasm and Satisfaction sustained to 6 months post-treatment**

Sadowski 2016

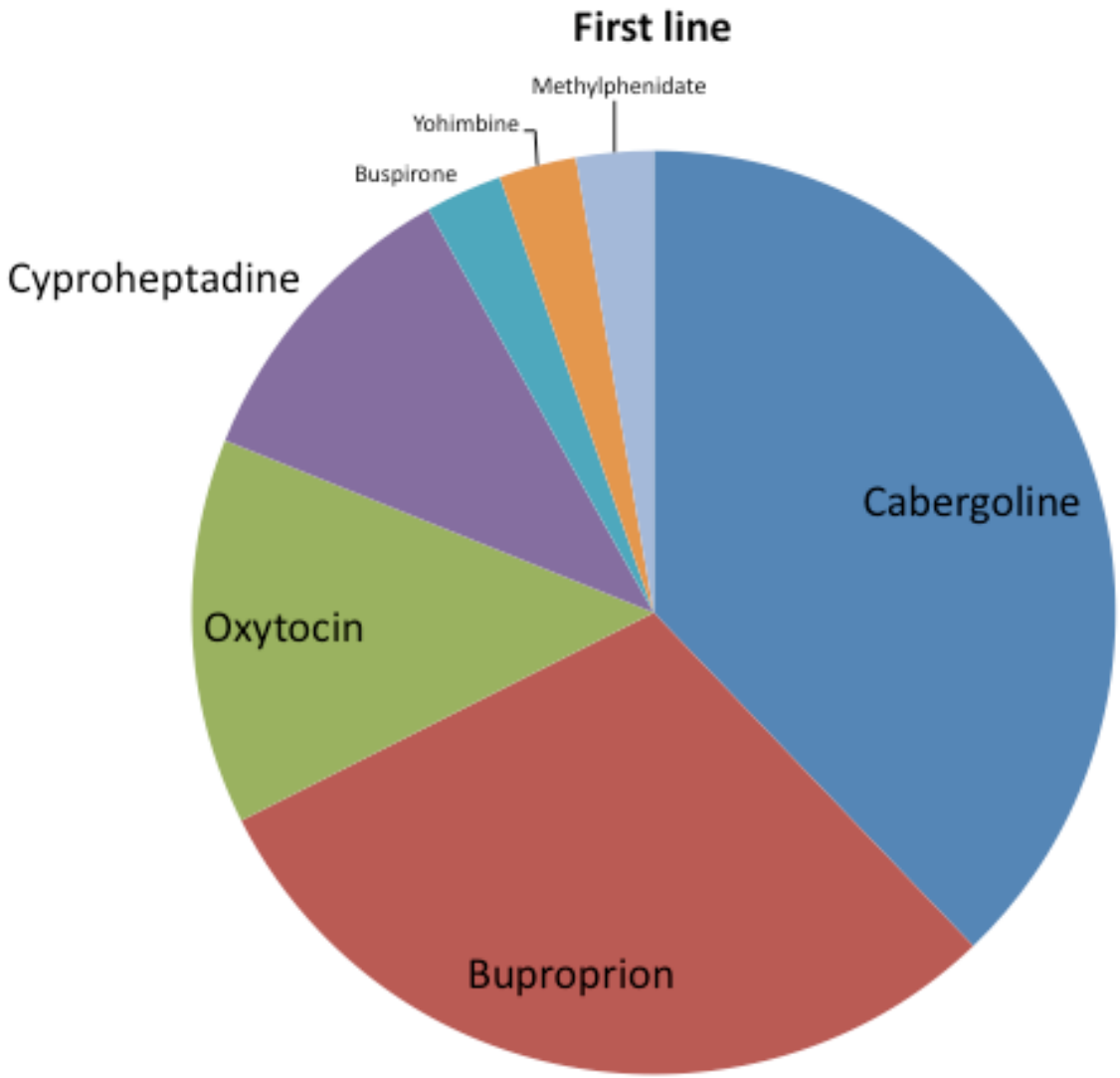
Dopamine and Prolactin and Orgasm



Delayed Ejaculation:
High Inhibition, Low Excitation



First Line Medications



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Thank You