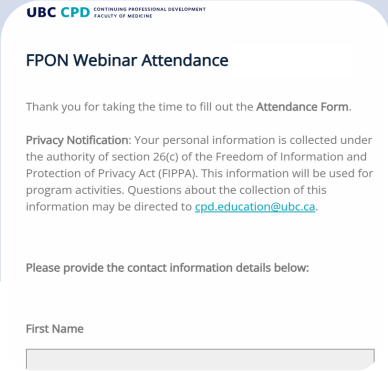


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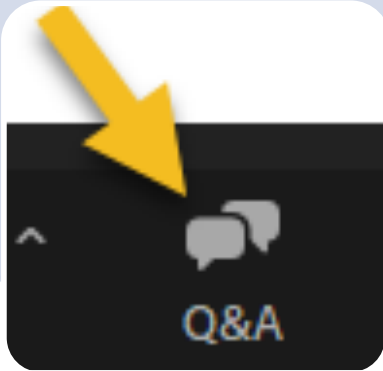
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Androgen Deprivation Therapy: Endocrine Toxicities

Justin (Jasmeet) S. Bhullar MD FRCPC
Clinical Assistant Professor
UBC Division of Endocrinology
Endocrinologist at St. Paul's Hospital, Vancouver BC
Sept 17th, 2026

Presenter Disclosures

Financial Disclosure: Consultation honorarium from Tolmar Pharmaceuticals

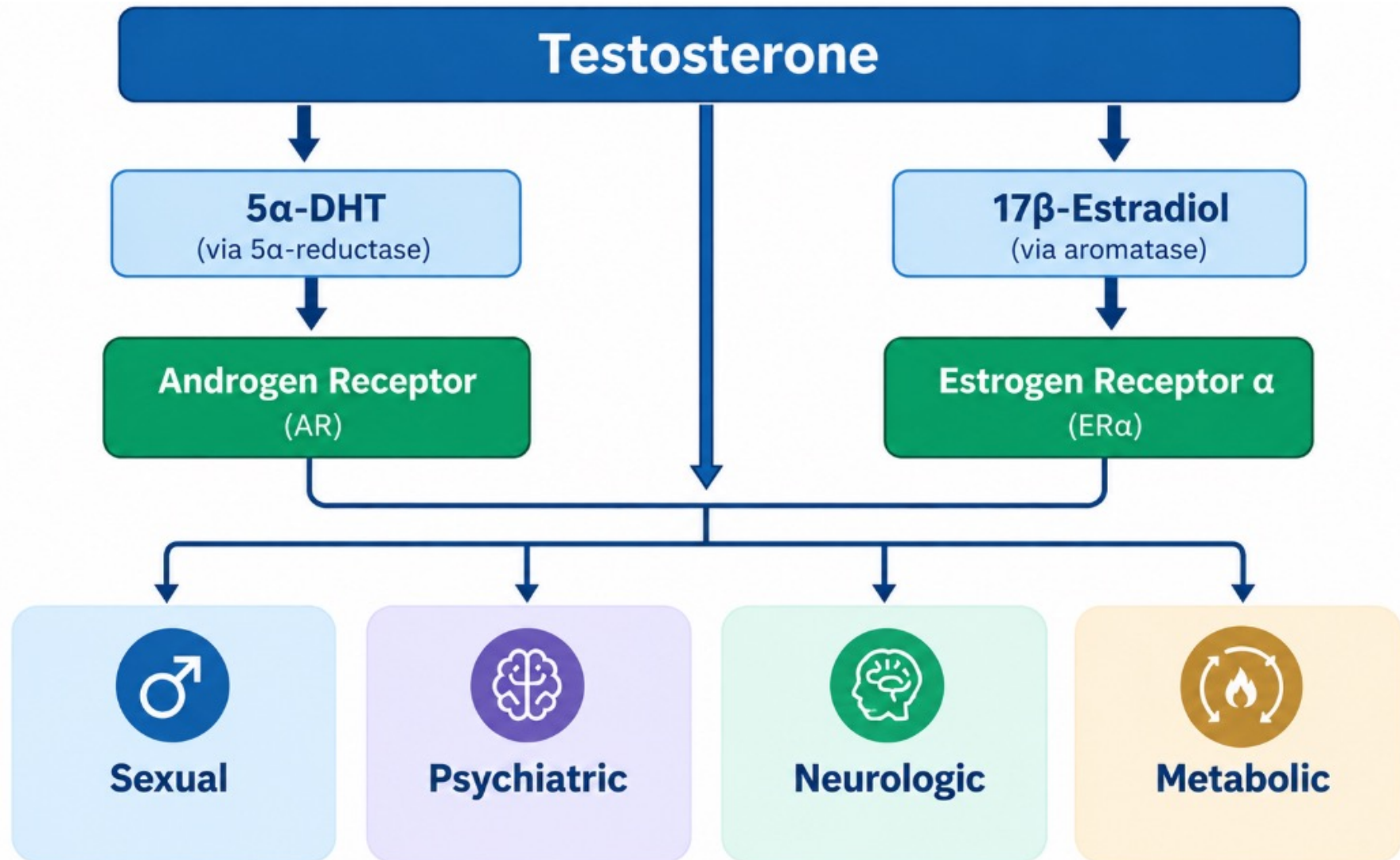
AI Disclosure: *OpenAI ChatGPT (GPT-5.6 Sol)* was used for visual design and formatting of figures. All scientific content and references were independently researched and verified by the presenter.



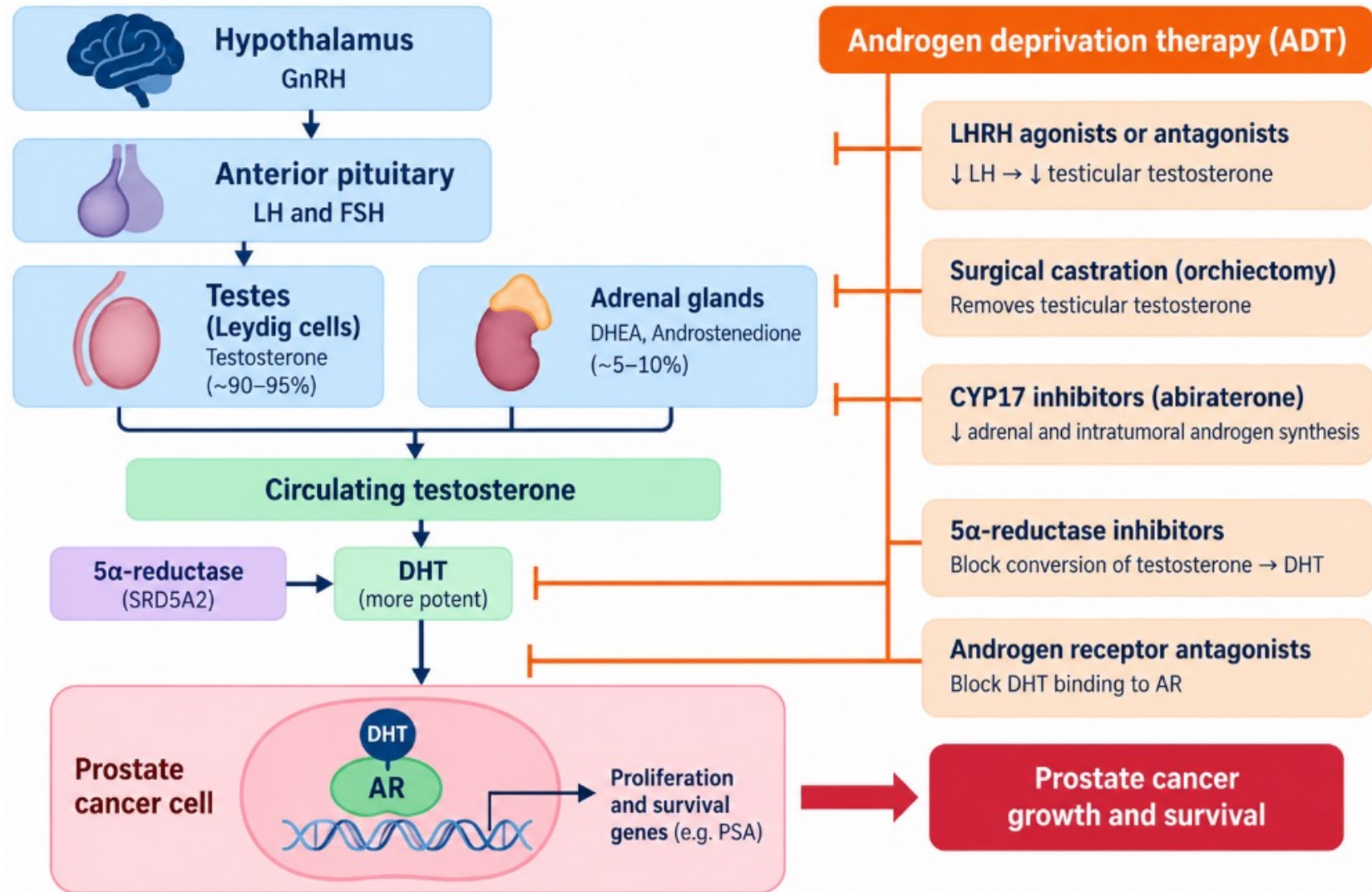
Learning Objectives

1. Physiologic effects of Testosterone
2. Signs and symptoms of ADT
3. Review of ADT-related complications
 1. Sexual Dysfunction
 2. Bone Health
 3. Cardiometabolic Risk
 4. Vasomotor Symptoms & Gynecomastia (Quality of Life)
4. Testosterone Therapy in treated low risk Prostate Cancer
5. Future Direction

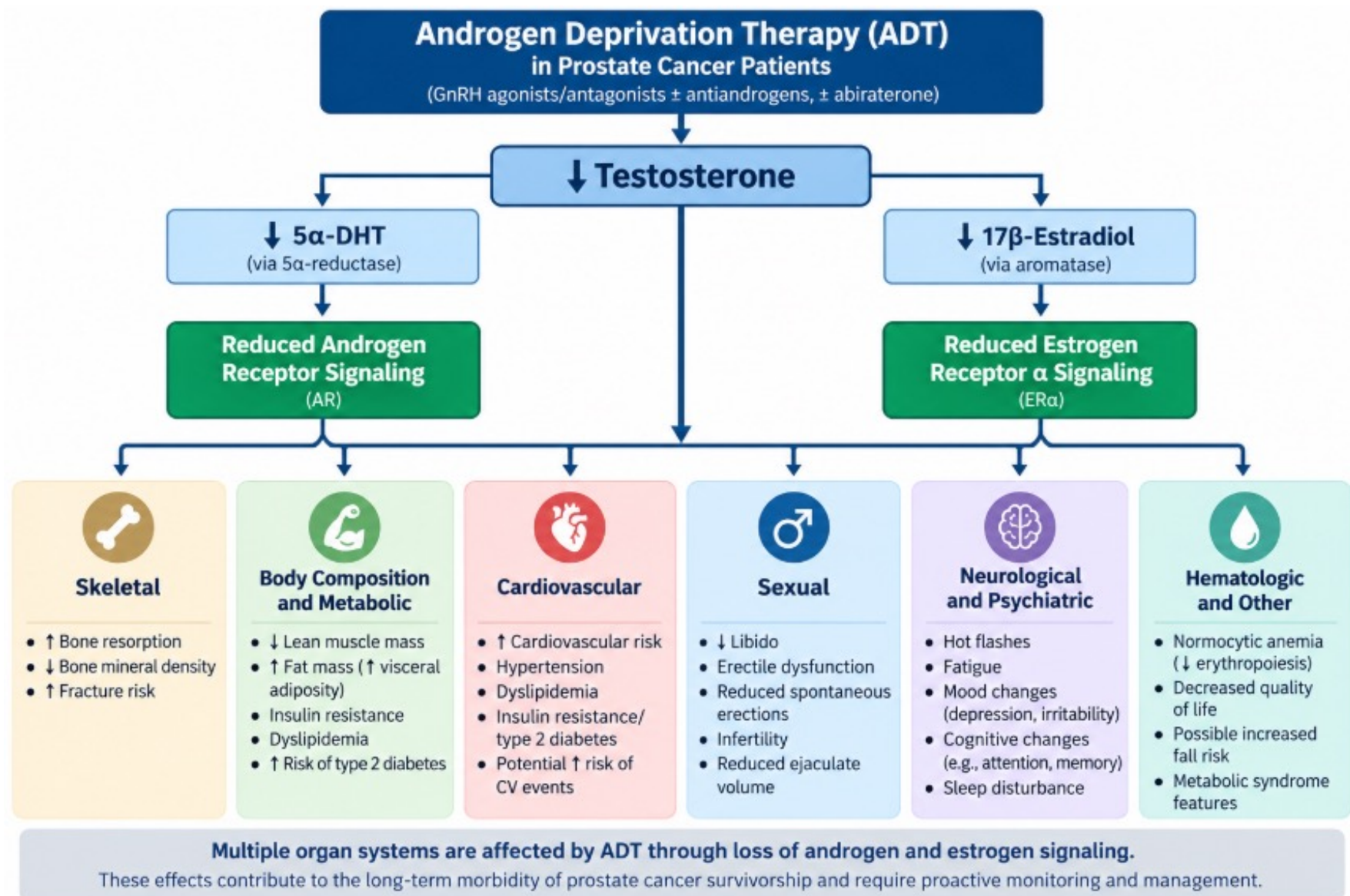
Physiological effects of Testosterone in Men



Androgens effects on the Prostate



Physiological effects of ADT in PrCa





Spectrum of Signs & Symptoms

Weight gain
Gynecomastia
Sarcopenia
Testicular atrophy
Hypertension

Bone loss
Metabolic syndrome
Anemia
CV risk
Hypogonadism

Fatigue
Mood lability
Hot flashes
Memory changes
Libido loss and ED

CLINICALLY APPARENT

PHYSIOLOGIC EFFECTS

PATIENT REPORTED EFFECTS



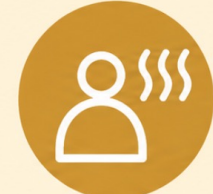
Sexual Health



Bone Health



**Cardiometabolic
Risk**



**QoL: VMS and
Gynecomastia**



Sexual Health: Assessment

Assessing Sexual Function in Patients on ADT

A practical checklist for primary care

Patient starting or currently on ADT

Assess and monitor sexual function using a biopsychosocial approach

**Clinical**
Medical and treatment factors

- ☐ **Baseline sexual/erectile function**
(ask before ADT if possible)
- ☐ **Prior prostate cancer treatments**
(prostatectomy, radiotherapy)
- ☐ **Comorbidities**
(vascular disease, diabetes, obesity)
- ☐ **Medications**
(e.g., antihypertensives, antidepressants)
- ☐ **ADT regimen and planned duration**

 Use a **validated tool**
(e.g., SHIM/IIEF-5)
and re-assess over time

**Psychological**
Emotional and mental health

- ☐ **Depression** (screen with brief tool
if indicated, e.g., PHQ-9)
- ☐ **Anxiety**
- ☐ **Emotional lability**
- ☐ **Grief over loss of sexual function**
- ☐ **Body image concerns**
(gynecomastia, genital shrinkage,
muscle loss)
- ☐ **Loss of sexual confidence or
self-esteem**
- ☐ **Altered sense of masculinity**

**Social / Relational**
Partner and relationship factors

- ☐ **Partnership status**
(partnered or single)
- ☐ **Partner's concerns and sexual health**
- ☐ **Impact on intimacy and
relationship satisfaction**
- ☐ **Communication patterns**
- ☐ **Each patient's priorities**
(e.g., survival vs. maintaining intimacy)
- ☐ **Consider partner inclusion
in discussions**



Integrate findings
Use a biopsychosocial assessment to guide individualized counselling and management.
Reassess periodically, as needs and priorities may change over time.

Proactive discussion helps normalize these issues and supports patients and their partners.



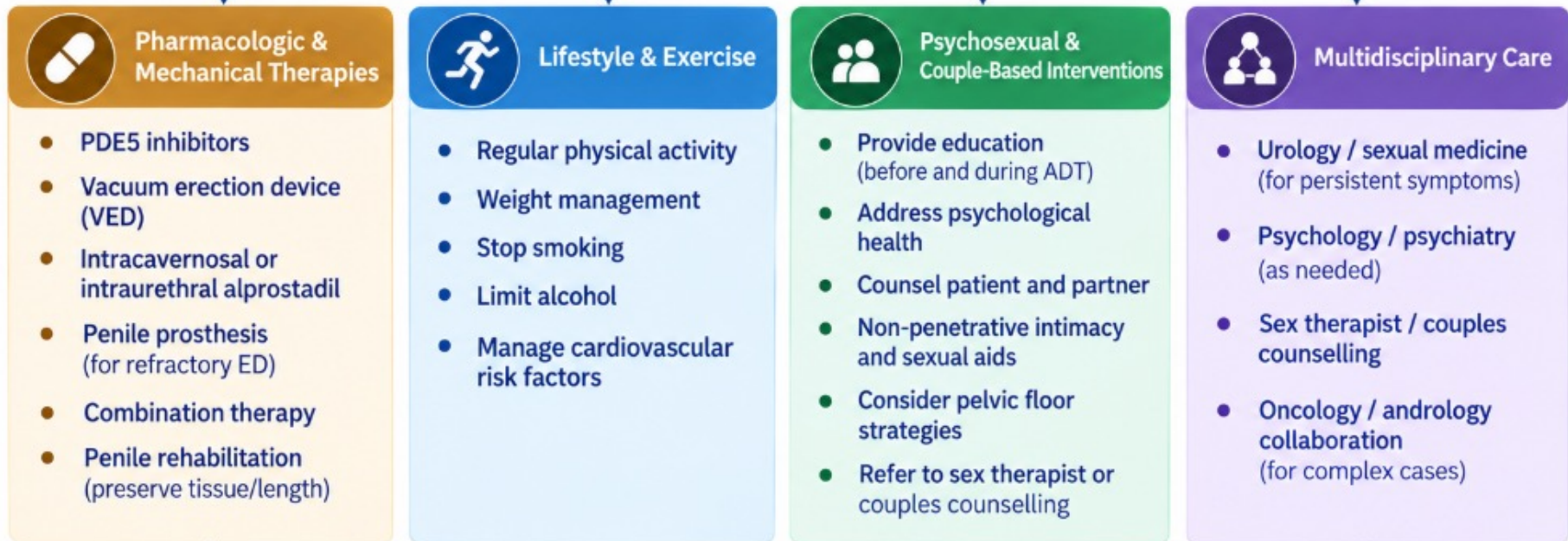
Sexual Health: Treatment

Multimodal Approach to Sexual Dysfunction in Patients on ADT

Integrate medical, lifestyle, psychosocial and specialist care

Patient with sexual dysfunction on ADT

Individualize management based on goals and preferences



Goals of treatment

Maintain sexual function and intimacy, preserve quality of life, and support the patient and their partner.

Reassess regularly and adjust the plan over time.



Sexual Health: Treatment

PDE5 Inhibitors for Erectile Dysfunction Key prescribing information for primary care

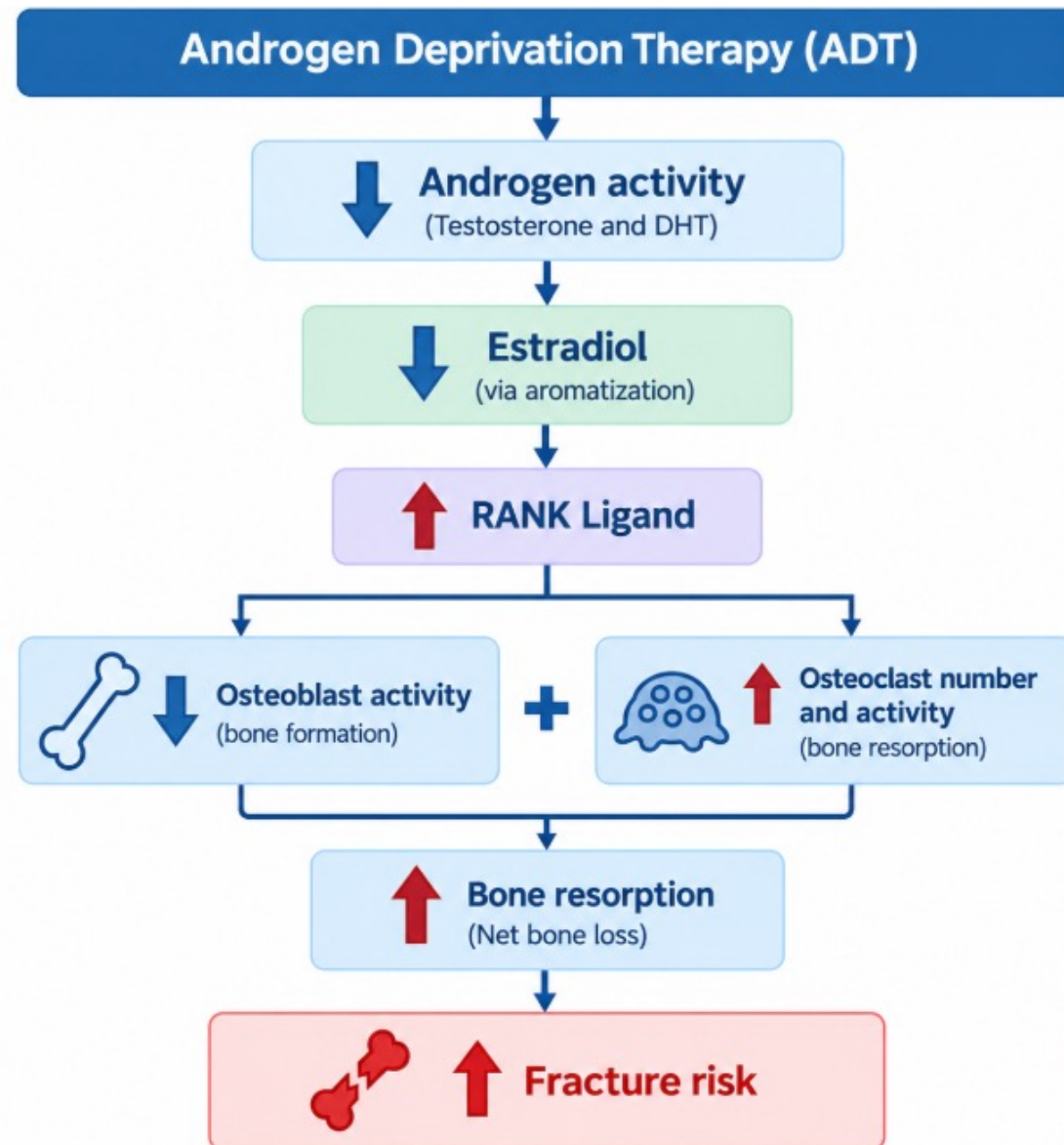
Agent	Usual starting dose (on-demand)	Maximum dose	Timing (before sexual activity)	Duration of effect	Dose adjustments	Key points
Sildenafil (Viagra)	50 mg (can start 25 mg if older or frail)	100 mg once daily	~1 hour (range 30–60 min)	4–6 hours	Renal: start 25 mg if CrCl <30 mL/min Hepatic: start 25 mg in severe impairment	- Take on empty stomach (best absorption) - Can titrate 25–100 mg - Common side effects: headache, flushing, dyspepsia, nasal congestion, visual changes
Tadalafil (Cialis)	10 mg (can start 5 mg if older or frail)	20 mg once daily (on-demand) or 5 mg once daily (daily use)	≥30 minutes	Up to 36 hours	Renal: reduce dose if CrCl <30 mL/min Hepatic: max 10 mg daily in moderate–severe impairment	- Longest duration of action - Can be taken with or without food - Daily low-dose option (2.5–5 mg) for spontaneous activity - Similar side effects to other PDE5i
Vardenafil (Levitra, Staxyn)	10 mg (can start 5 mg if older or frail)	20 mg once daily	~60 minutes (range 30–60 min)	4–6 hours	Renal: no adjustment usually needed Hepatic: start 5 mg, max 10 mg in moderate impairment; avoid in severe impairment	- Can be taken with or without food - Avoid with strong CYP3A4 inhibitors (e.g., some antifungals, macrolide antibiotics) - Similar side effects to other PDE5i

General considerations

- Contraindicated with nitrates or riociguat (risk of severe hypotension).
- Use with caution in unstable cardiovascular disease.
- Efficacy may be reduced in men on ADT due to low testosterone and changes in erectile tissue.
- Assess response and tolerability; if inadequate, consider dose optimization, alternate PDE5i, or referral for other therapies (e.g., VED, injections).



Bone Health: ADT effects on bone





Bone Health: Osteoporosis Risk

Key Facts: ADT and Bone Health



BMD loss of ~3–5% per year on ADT
(vs. 0.5–1% in normal aging)



Bone loss most pronounced in first year
of treatment



Fracture incidence 19.4% and 12.6%
(in ADT vs no ADT)



Risk amplified
with duration, concurrent glucocorticoids, and ARPIs



Bone Health: Assessment

Assessment of Fracture Risk in Patients on ADT



Risk stratify with FRAX

- 10-year probability of hip fracture or major osteoporotic fracture
- Select “YES” for secondary osteoporosis



Obtain DXA

- In most patients before initiating ADT



Monitor

- Annual reassessment
- Consideration for DXA every 1–2 years for those on ADT
- Check Ca, eGFR, 25OHD



Bone Health: Management

Management of Bone Health in Patients on ADT



Non-pharmacotherapy (all ADT patients)

- Ca 1000–1200 mg daily
- Vitamin D₃ supplementation (target 25OHD 75–125 nmol/L)
- Lifestyle: Weight-bearing exercise (30 min/day), balance training, limiting alcohol, smoking cessation



Pharmacotherapy considered

- Patients ≥ 50 with osteopenia (T-score -1.0 to -2.5) at Femoral Neck or Total Hip with hip fracture risk $>3\%$ or major osteoporotic fracture risk $>20\%$



Pharmacotherapy options

- Denosumab 60 mg SC q6months
- Zoledronic Acid 5 mg IV q12months
- Alendronate 70 mg PO q7days



Cardiometabolic Health: ADT effect on Metabolism

Metabolic Complications in Patients on ADT



Castration levels of Testosterone

lead to sequelae of metabolic disturbances



Body composition

~9% increase in body fat with concurrent reduction in muscle mass



Insulin resistance and Diabetes Mellitus

GnRH-agonist users had higher diabetes incidence (29.0 vs 20.9 per 1000 person-years) than non-ADT patients



Metabolic syndrome

Prevalence exceeding 50% on long-term ADT.



Cardiometabolic Health: ADT and CV Risk



Cardiovascular risk and ADT



Cardiovascular disease is the leading non-cancer cause of death in prostate cancer.



ADT raises major cardiovascular events (MI, stroke, CV death) by ~20–30% with long-term use.



Androgen Receptor Pathway Inhibitor add-on to ADT ~2x cardiovascular events.



Cardiovascular risk is front-loaded in the first ~6 months.



Cardiometabolic Health: Assessment and Risk Stratification



Baseline stratification: Estimate risk with ASCVD Risk Estimator



High risk

Established CVD: prior MI, stroke/TIA, CAD requiring intervention, peripheral artery disease, AAA, or VTE



Intermediate risk

No prior event but ≥ 1 risk factor (smoking, diabetes mellitus, HTN, DLD, obesity)



Low risk

No event history or risk factors



Cardiometabolic Health: Management



ABCDE Framework (NCCN Prostate Cancer, 2026)



A

Awareness/Assessment

Review CV symptoms; periodically re-estimate risk; address aspirin for secondary prevention.



B

Blood pressure

Check and treat every visit (hypertension is the most common ADT-related CV effect).



C

Cholesterol & Cigarettes

At least annual lipid panel with statin discussion; support tobacco cessation.



D

Diet, weight & Diabetes

Track BMI/weight; screen for metabolic syndrome; monitor glucose/HbA1c (ADT raises new-onset diabetes risk).



E

Exercise & ECG

Counsel aerobic + resistance exercise; obtain baseline/follow-up ECG when QTc is prolonged or with concomitant QT-prolonging drugs.



Quality of Life: Vasomotor Symptoms

Hot Flashes in Men on ADT



Prevalence

Hot flashes most common ADT related complaint (~60-80% of men).



Clinical impact

Driver of sleep disturbance, fatigue, impaired QoL, and reduced ADT adherence.



Mechanism

Driven by E2 deficiency and altered sex-steroid feedback, leading to dysregulation in thermoregulatory circuits.



Quality of Life: Vasomotor Symptoms

Assessment of Hot Flashes in Men on ADT



Clinical assessment

Confirm frequency, severity, nocturnal component, QoL and functional impact.

- Utilize validated clinical tools (HFRDIS).



Rule out other etiologies

Thyroid disease, diabetes mellitus, review medications and identify triggers (e.g. alcohol).



Investigations as indicated

- Total T, E2, FSH, LH, PRL, TSH.
- Confirm adequate castration levels.



Use results to guide management

Tailor treatment based on severity, impact and underlying contributors.



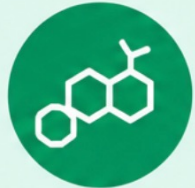
Quality of Life: Vasomotor Symptoms

Management of Hot Flashes in Men on ADT



Non-hormonal Pharmacotherapy (First-line)

- Venlafaxine: target 75 mg PO daily
- Gabapentin: ~900 mg/day (qHS dosing for sedation/night sweats)
- Oxybutynin: 2.5–5 mg BID



Hormonal Pharmacotherapy (cautious use)

- Medroxyprogesterone
- Estrogen



Non-pharmacological

- Acupuncture
- Exercise
- Cognitive behavioural therapy (CBT)
- Evidence for superiority over placebo lacking.



Emerging therapies

- NK3-pathway antagonists (Fezolinetant, elinzanetant) are under active study in ADT population but not validated in men.



Quality of Life: Gynecomastia

Gynecomastia Associated with ADT



Nonsteroidal antiandrogens (highest risk)

- Bicalutamide and flutamide are associated with the highest rates of gynecomastia.
- Enzalutamide is also associated with a high rate (~49% gynecomastia).



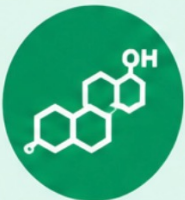
GnRH agonists/antagonists (lower risk)

- Associated with a lower risk of gynecomastia (~13–25%).



Bilateral orchiectomy (lowest risk)

- Associated with the lowest incidence of gynecomastia.



Estrogen therapy (highest risk)

- Directly stimulates breast tissue and is associated with the highest rate of gynecomastia.



Quality of Life: Gynecomastia

Assessment of Gynecomastia



History and Physical Exam

- Medication history (e.g., current and prior androgen deprivation therapies and other drugs)
- Confirm glandular gynecomastia versus pseudogynecomastia (adiposity)
- Assess duration, symptoms (pain/tenderness), and impact on QoL



Red Flags

- Unilateral, hard, fixed, or rapidly enlarging breast tissue
- Nipple discharge (especially if bloody)



Consider imaging or biopsy (if indicated)

- Breast ultrasound and/or referral for biopsy in the presence of concerning features (e.g., unilateral, hard/fixed mass, nipple discharge, or suspicion for malignancy).



Rule out other etiologies

- Thyroid disease (TSH)
- Hepatic/renal dysfunction (LFTs, renal function)
- Assess sex hormones as clinically indicated: estradiol, total/free testosterone, LH, FSH, and prolactin



Quality of Life: Gynecomastia

Management of Gynecomastia



Tamoxifen

- 10–20 mg daily.
- Most effective when initiated early (e.g., within 6–12 months of onset).



Prophylactic radiotherapy

- Consider in men at high risk or with anticipated long-term antiandrogen therapy.
- Preferred in men with thrombotic risk or contraindications to tamoxifen.



Reduction mammoplasty / surgery

- Reserved for severe or refractory cases.



Anastrozole (aromatase inhibitors)

- No significant benefit for gynecomastia in men on ADT.

TRT in PrCa: T and the Prostate

Rationale for Caution with Exogenous Testosterone and Prostate Cancer Risk



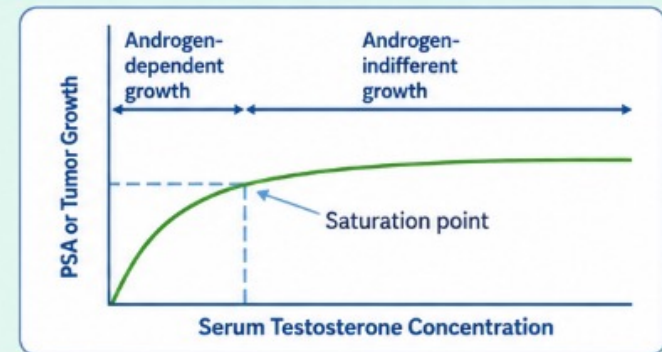
Huggins-Hodges Hypothesis

- Prostate cancer is androgen-dependent and regresses with testosterone withdrawal.



Saturation Model

- Androgen receptors are finite and saturated at low testosterone levels.



Clinical Implication

- Major societies remain cautious on exogenous testosterone after prostate cancer due to limited long-term safety data.



TRT in PrCa: TRT in patients with Hx of Treated PrCa

Testosterone replacement therapy following definitive treatment for prostate cancer: a scoping review of safety and efficacy

John Gibson ^{1,2}, Michael George ^{1,2}, Peter Grice ^{1,2}, Amar Mohee¹, Theodora Stasinou^{1,2}, Ian Pearce ^{1,2} and Vaibhav Modgil ^{1,2,3} on Behalf of Manchester Andrology Research Collaborative (MARC)



Objective

Evaluate the safety and efficacy of testosterone replacement therapy (TRT) following definitive treatment for prostate cancer.



Studies included

12 studies performed between 2005 and 2025

6

Included patients treated with radical prostatectomy

6

Included patients treated with radiation therapy



Key findings

TRT was not associated with increased biochemical recurrence after definitive treatment for prostate cancer.



Conclusion

Current evidence suggests that TRT was not associated with increased biochemical recurrence.



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Take home point: TRT may be cautiously considered in hypogonadal men with stable post-cancer treatment course with regular monitoring.



TRT in PrCa: TRT in patients with Hx of Treated PrCa

JAMA Internal Medicine | [Original Investigation](#)

Testosterone Treatment in Prostate Cancer Survivors With Hypogonadism A Randomized Clinical Trial



Objective

Determine effects of TRT on prostatic tissue of aging men with low testosterone levels.



Participants

136

men, >40 years
(mean age 68.6)



Localized low-grade
(Gleason 6 or 3+4=7)



Undetectable PSA
for ≥ 2 years post
radical prostatectomy



Serum T level
<9.54 nmol/L
and hypogonadal
symptoms

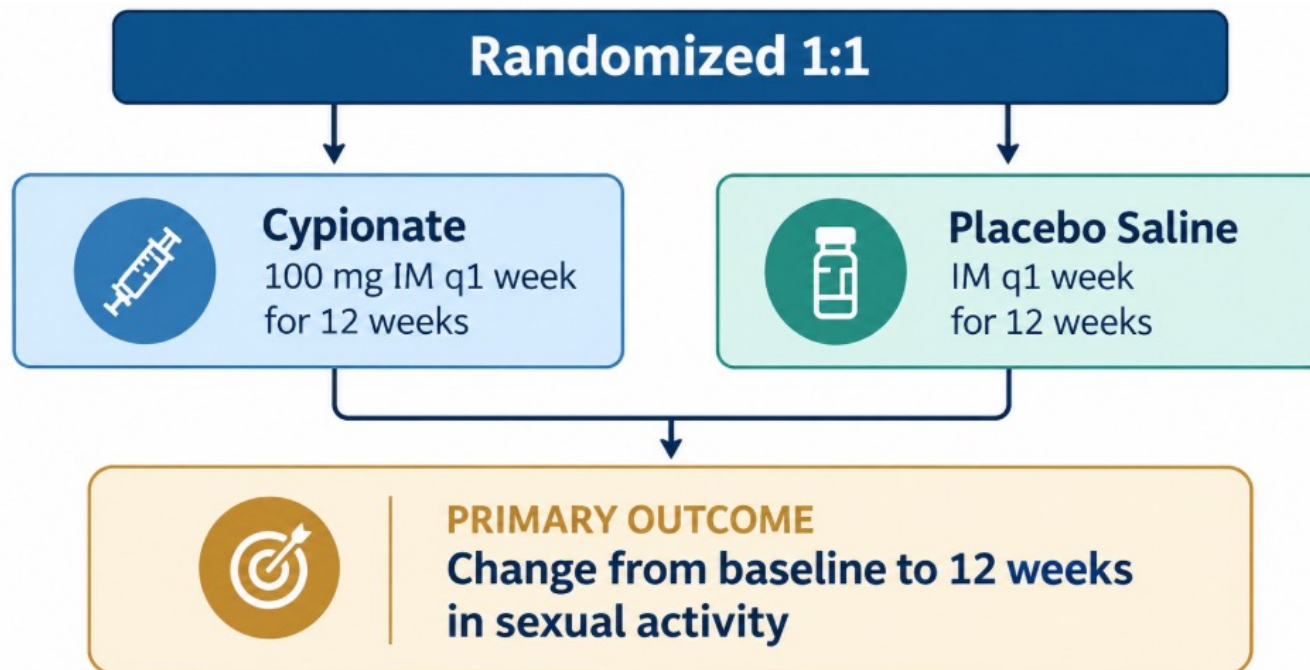


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Yusnie Memish-Beleva, BS; Helen Lam, MPH; Adam S. Kibel, MD; Karol M. Pencina, PhD





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Summary



TRT was associated with improvements in:

- Sexual activity
- Sexual desire
- Well-being
- Lean-body mass
- Peak VO₂
- Loaded stair-climbing power



Erectile dysfunction

No significant change



Safety

No evidence of biochemical recurrence



TRT in PrCa: TRT in patients with Hx of Treated PrCa



What do the current guidelines recommend?

AUA

American
Urological
Association

AUA (2018/2024)

"...inadequate evidence to quantify the risk benefit ratio of testosterone therapy."



ENDOCRINE
SOCIETY

Endocrine Society (2018, Predating SPIRIT Trial)

"Recommend against initiation of testosterone therapy in men with prostate cancer."



NCCN
National
Comprehensive
Cancer Network®

NCCN Survivorship (2025)

"...timing of initiating or resuming testosterone is "controversial" and requires coordination with oncologic team. Testosterone is contraindicated in metastatic or active prostate cancer and must not be given to men currently on ADT."



TRT in PrCa: TRT in patients with Hx of Treated PrCa

European Association of Urology

Criteria for offering testosterone replacement therapy after prostate cancer treatment



Treatment may be offered in the meeting the following criteria:



Low-risk and localized prostate cancer



T1-T2a staging



Disease-free after treatment



Maximal pre-treatment PSA <10 ng/mL



Gleason Score <7



Undetectable PSA for at least 1 year after surgery



Clinical approach

Individualized, shared decision-making process between the patient and provider.



TRT in PrCa: TRT in patients with Hx of Treated PrCa



What can I do for my patient in my office today?



Informed discussion

Review the available evidence, discuss potential benefits and risks
for a shared-decision-making process.



TRT in PrCa: TRT in patients with Hx of Treated PrCa



Practical framework for patient selection and monitoring



1 Confirm diagnosis of hypogonadism

- ≥ 2 AM and fasting total T levels < 9 nmol/L with free T, cBAT, SHBG, LH, PRL
- Assessment for cardinal symptoms of hypogonadism



2 Stratify by risk

- Meet EAU criteria
- Avoid in high-grade, active, or metastatic disease
- ≥ 1 year post-prostatectomy



3 Shared decision making

- Coordinate with UROLOGY, ONCOLOGY, and ENDOCRINOLOGY
- Discuss potential benefits and risks
- Incorporate patient values and preferences



4 Monitor on therapy

- PSA and hematocrit ~ 3 –12 months
- Monitor for clinical response and adverse effects
- Evaluate for concerning rise in PSA (> 0.2 ng/dL)



TAKE HOME POINTS

Sexual function requires multimodal approach with benefits seen in proactive and early intervention

ADT accelerates bone loss

Cardiometabolic health encompasses a multitude of complications necessitating early assessment and regular follow-up



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