Canadian Urological Association
The Voice of Urology in Canada

Association des Urologues du Canada
La voix de l'urologie au Canada

Erectile Dysfunction

Speaker

Trustin Domes MD, MEd, FRCSC
Urologist

Disclosures | Trustin Domes

- No relationships with financial sponsors to disclose.

Disclosure of Financial Support

Potential for conflict(s) of interest:

- Members of the SPC committee (Alan Bell, Peter Lin, and Arthur Kushner) received honorarium from the Canadian Urological Association.
- Trustin Domes received honorarium from the Canadian Urological Association at the start of this program.

Mitigating Potential Bias

The scientific planning committee of this program have complete control over the content of this program.

There has been no influence from the sponsors on the content.

Disclosures

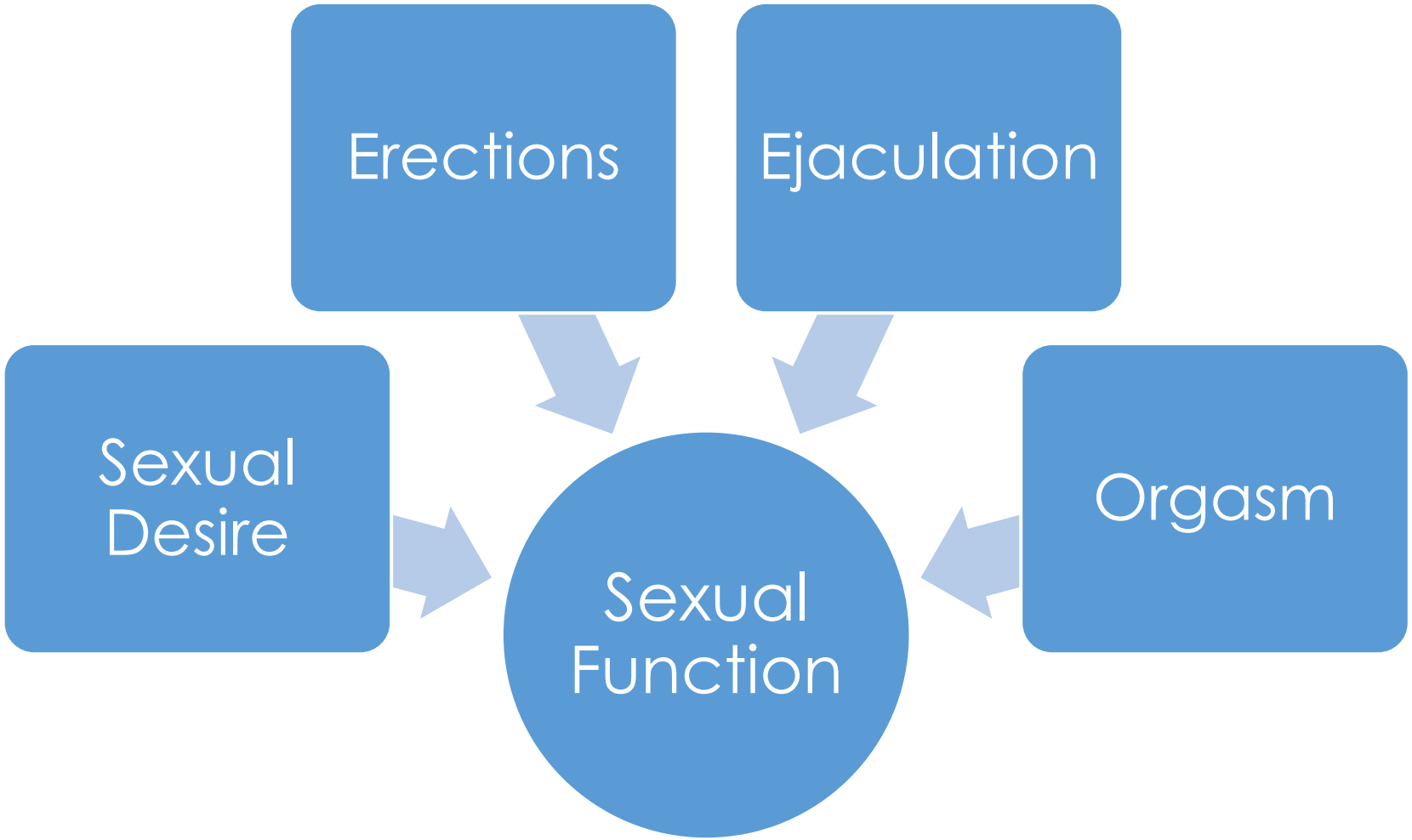
- No relationships to disclose.

Learning Objectives

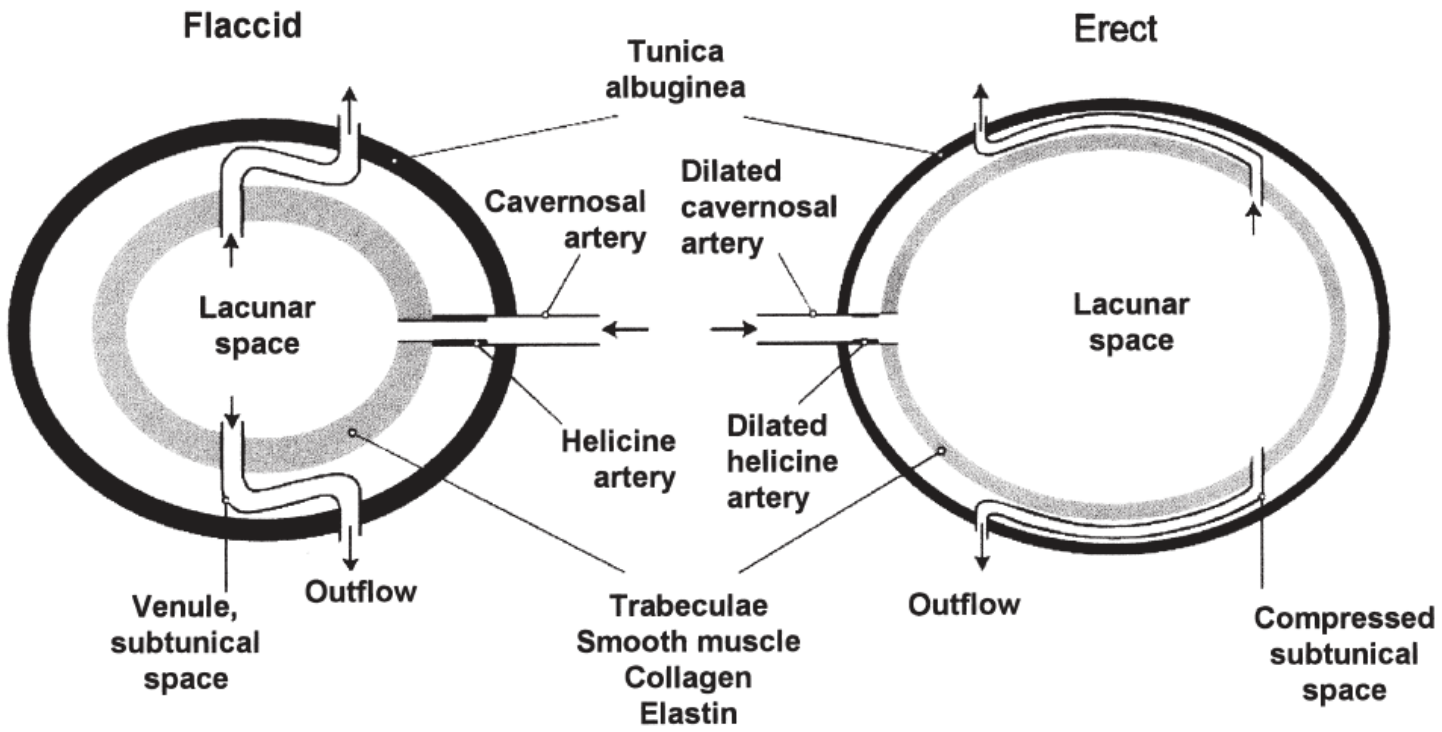
Upon completion of this program, participants will be able to:

- Describe the physiology of erection
- Classify erectile dysfunction (ED)
- Discuss the assessment of a patient presenting with ED
- Outline the key features of management for a patient presenting with ED

Four Domains of Male Sexual Function



Physiology of Erection: Cavernosal Level

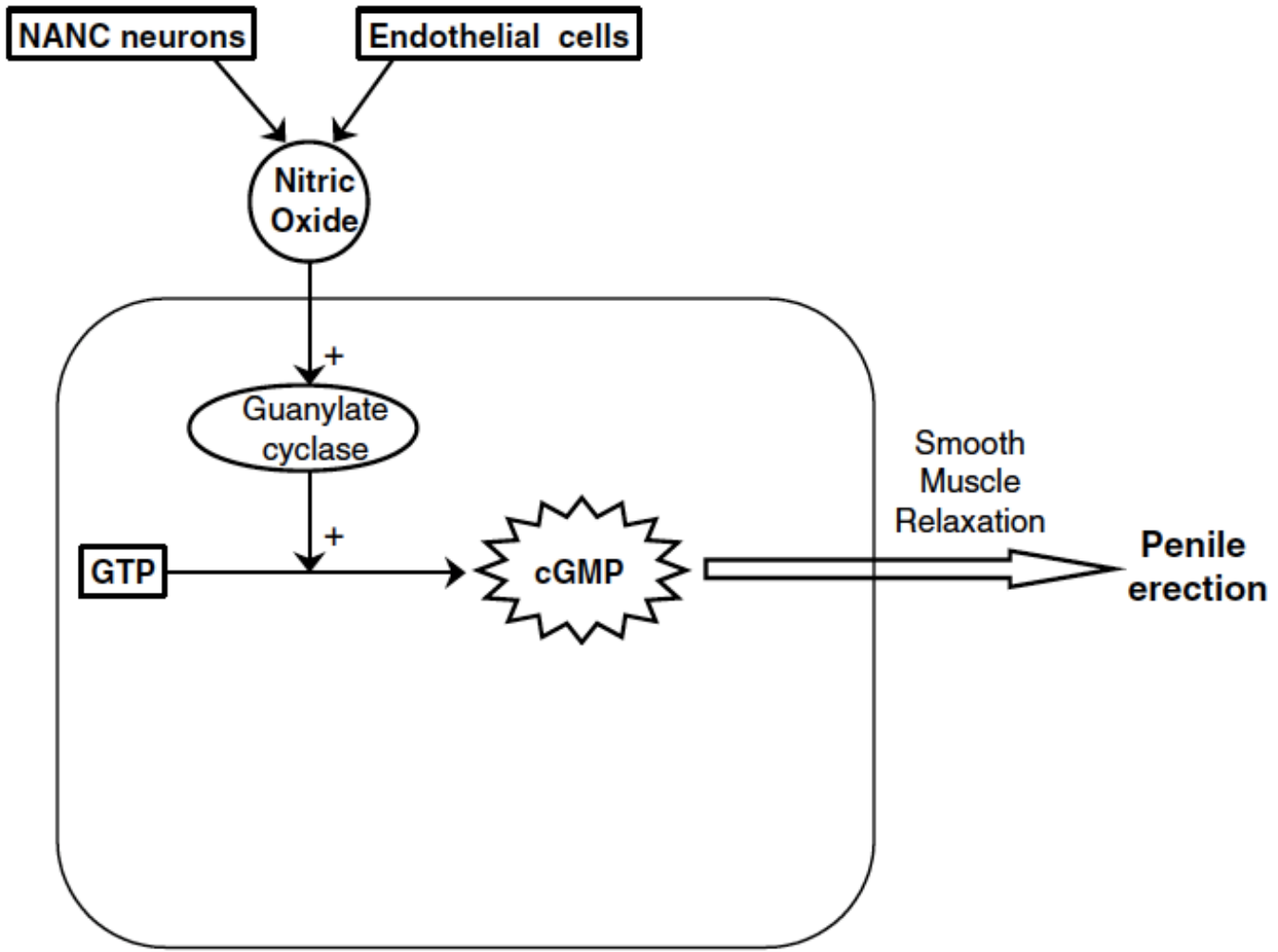


4 processes:

1) Dilation of arteries
2) Enlargement of sinusoidal spaces
3) Compression of subtunical veins
4) Increase in cavernosal pressure

Adapted from *BMJ* 1998;316:678–82

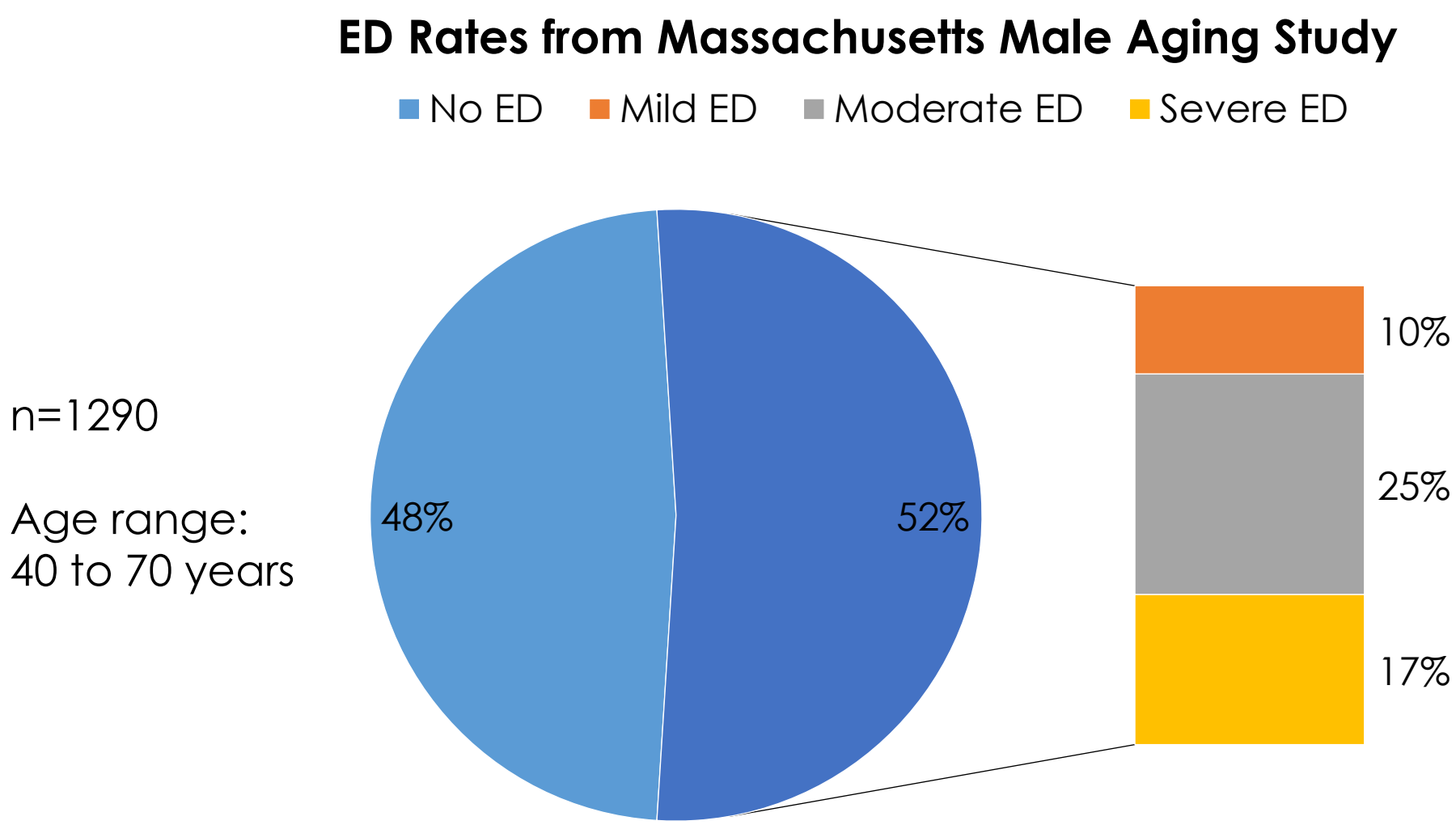
Physiology of Erection: Cellular Level



Cavernosal Smooth Muscle Cell

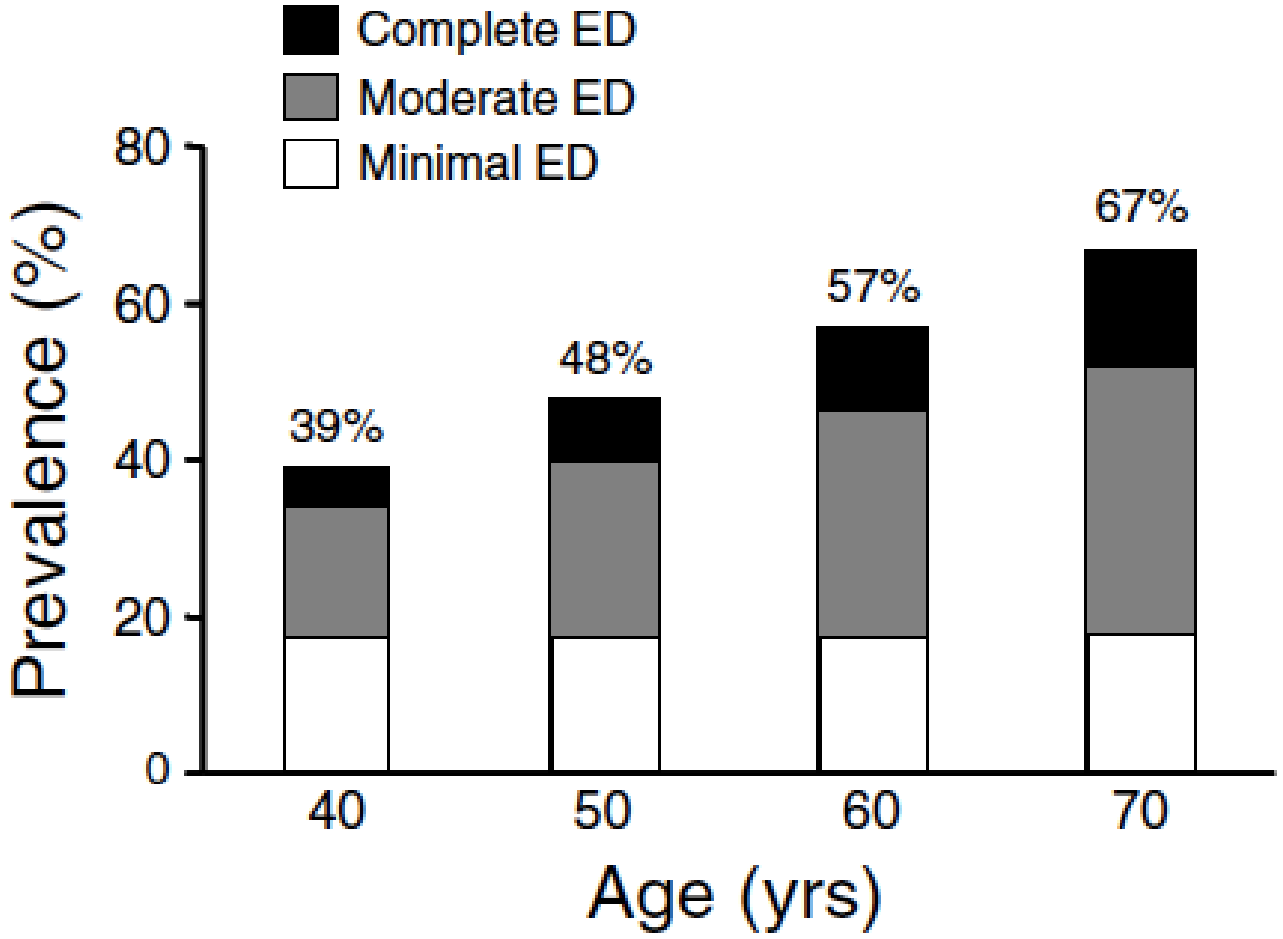
Adapted from *J Sex Med* 2004;1(3):254-65

Prevalence of ED



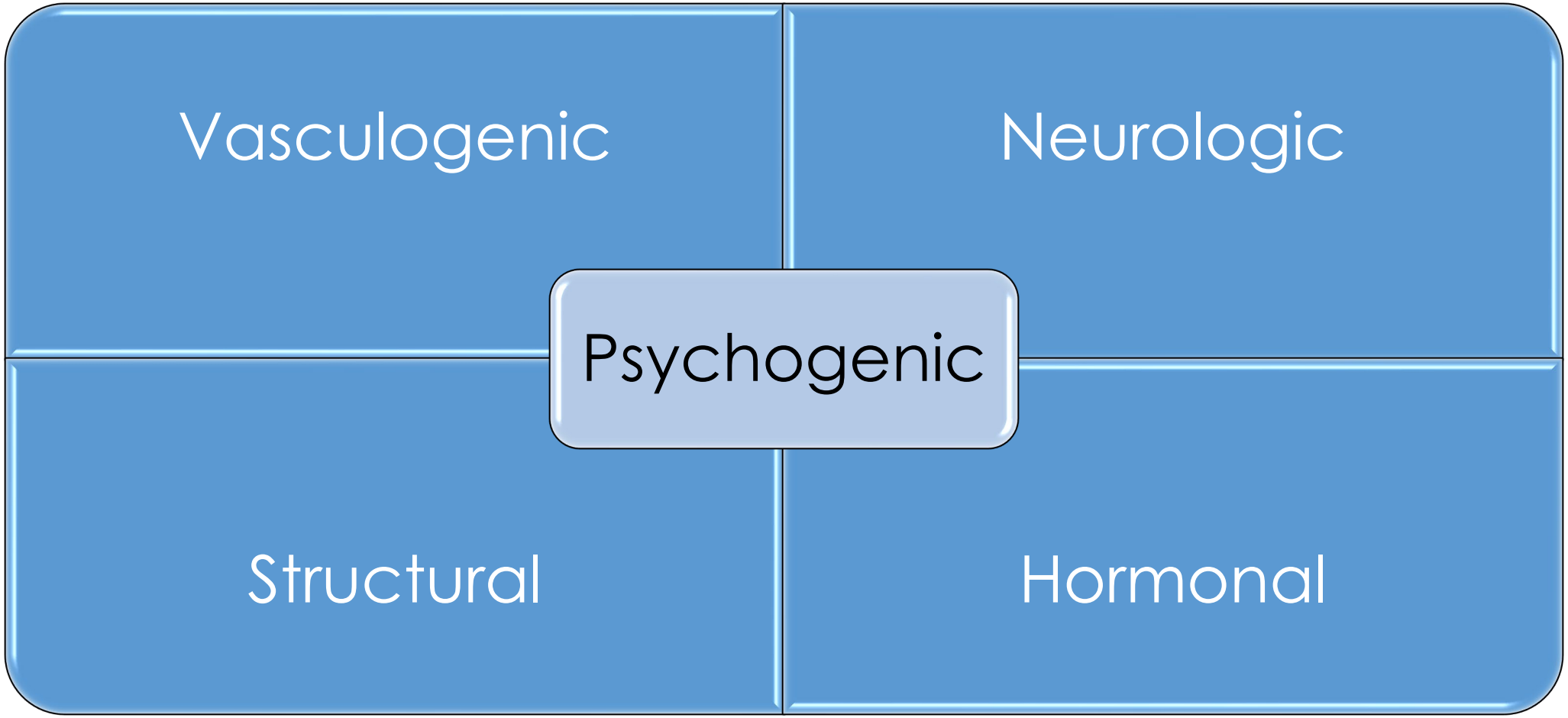
J Urol 1994;151:54-61

Severity of ED Increases with Age



Adapted from *J Urol* 1994;151:54-61

Classification of ED



Adapted from *Urology* 1993;42:468-81

Vasculogenic

- Microvascular disease and resulting endothelial dysfunction is a significant underlying cause of ED

- Risk factors for vasculogenic ED:
  - Hypertension
  - Dyslipidemia
  - Diabetes
  - Smoking
  - Pelvic Radiation
  - Vessel injury from trauma/surgery

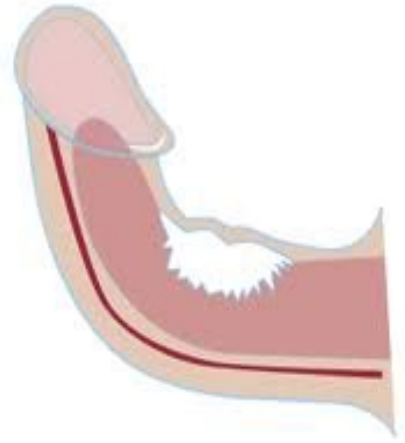
Some patients may present with ED as their only clinical sign otherwise subclinical vascular disease

ED may be an early marker of cardiovascular disease and may predict future cardiac events, especially in younger men

Am J Med 2014;127:174-82
Am Heart J. 2012;164(1):21-8

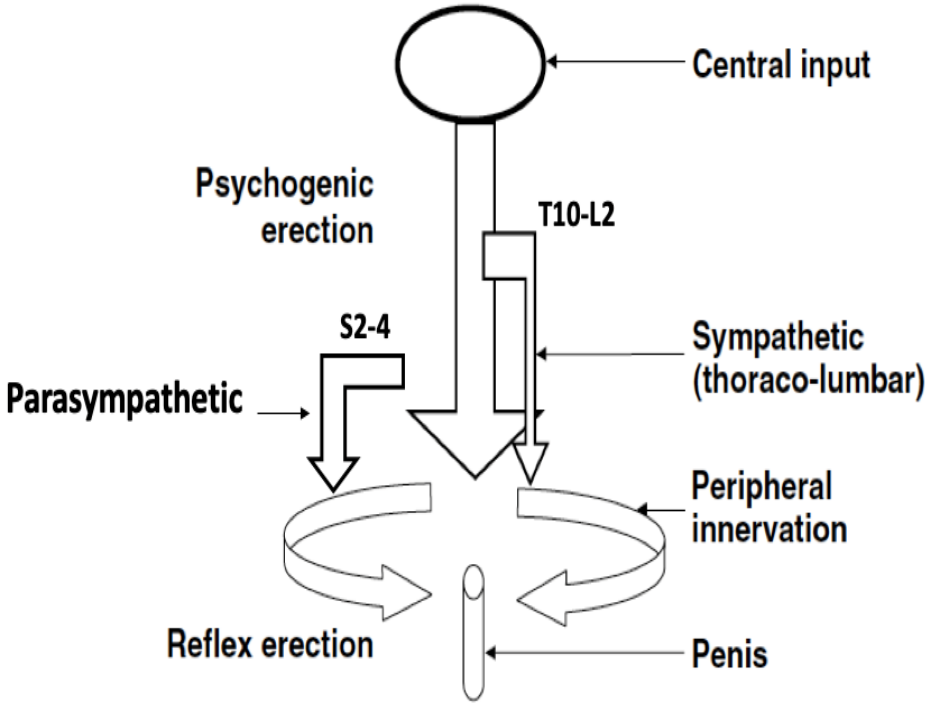
Structural

- Conditions that affect the structure and function of the cavernosal bodies
  - Peyronie's Disease is the most common
    - Benign scarring condition of the tunica albuginea of the penis affecting up to 9% of the male population
    - Affects the elastic tissues and expansion capabilities of the corpora cavernosa



Neurogenic

- Numerous neurological conditions can affect erectile function
- CNS:
  - Stroke, Parkinson's Disease, MS, Spinal Cord Inju Trauma
- PNS:
  - Neuropathies (Diabetes, Alcoholism, Vitamin Deficiencies), Trauma
- Demyelinating diseases:
  - Multiple System Atrophy, MS
- Surgery:
  - Pelvic/Retroperitoneal
  - Most common: Radical Prostatectomy and Proctectomy



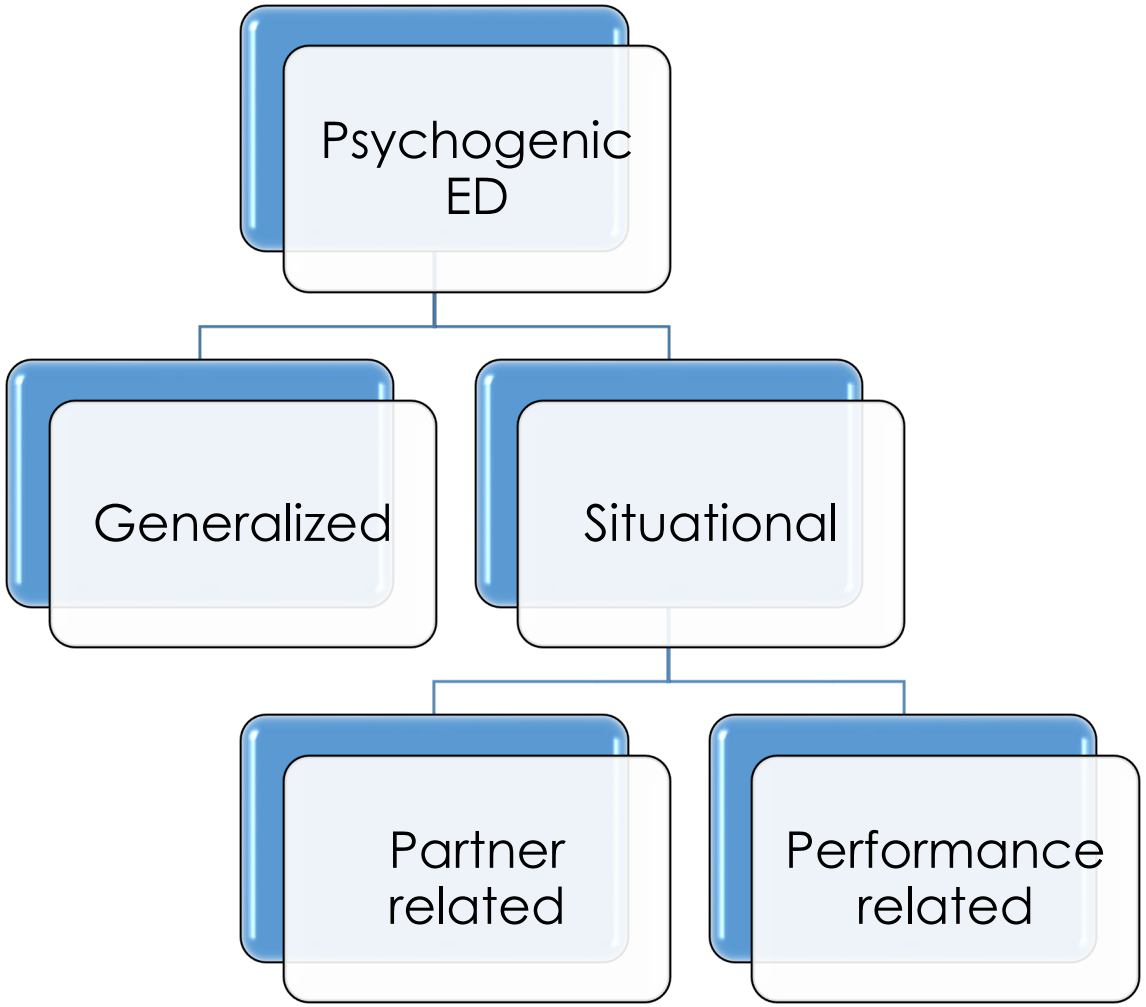
Hormonal

- All domains of male sexual function require testosterone

  Libido > Mood > Erections > Body Composition Changes

- Causes of Hypogonadism:
  - Idiopathic, often associated with aging (most common)
  - Primary testicular failure: genetic and non-genetic
  - Associated with other medical conditions
    - Liver disease, hemochromatosis, HIV/AIDS, obesity
  - Surgical, traumatic and infectious
    - Hypothalamus/Pituitary
    - Testicle(s)
  - Medications: LHRH agonists and antagonists, opioids, corticosteroids

Pyschogenic



ED History

- ED significantly impacts both the patient and their partner
  - Encourage partner involvement in patient assessment
- Onset, duration, consistency and severity of ED
  - Situational versus generalized
  - Response to prior treatments
- Issues with other domains of male sexual function
  - Desire, orgasm, ejaculation, any penile deformity/curvature
- Co-morbid risk factors
  - Medical, surgical, psychological and social factors
- Medication review
  - Antipsychotics (Risperidone and classical), antidepressants (SSRI, SNRI, TCAs) antihypertensives (thiazides, beta-blockers) and anti-androgens

Psychogenic versus Organic ED

Question	Psychogenic ED	Organic ED
Presence of nocturnal erections?	Often present	Reduced
Presence of erection during masturbation or with alternate partners?	Often present	Reduced
Significant recent psychosocial stress?	Strong impact	Minimal impact
Feelings of performance anxiety around sexual activity?	Strong impact	Minimal impact
Situational variability of erectile dysfunction (improved while on vacation)?	Potential for wide variability	Minimal variability

CUA ED Guideline, 2021

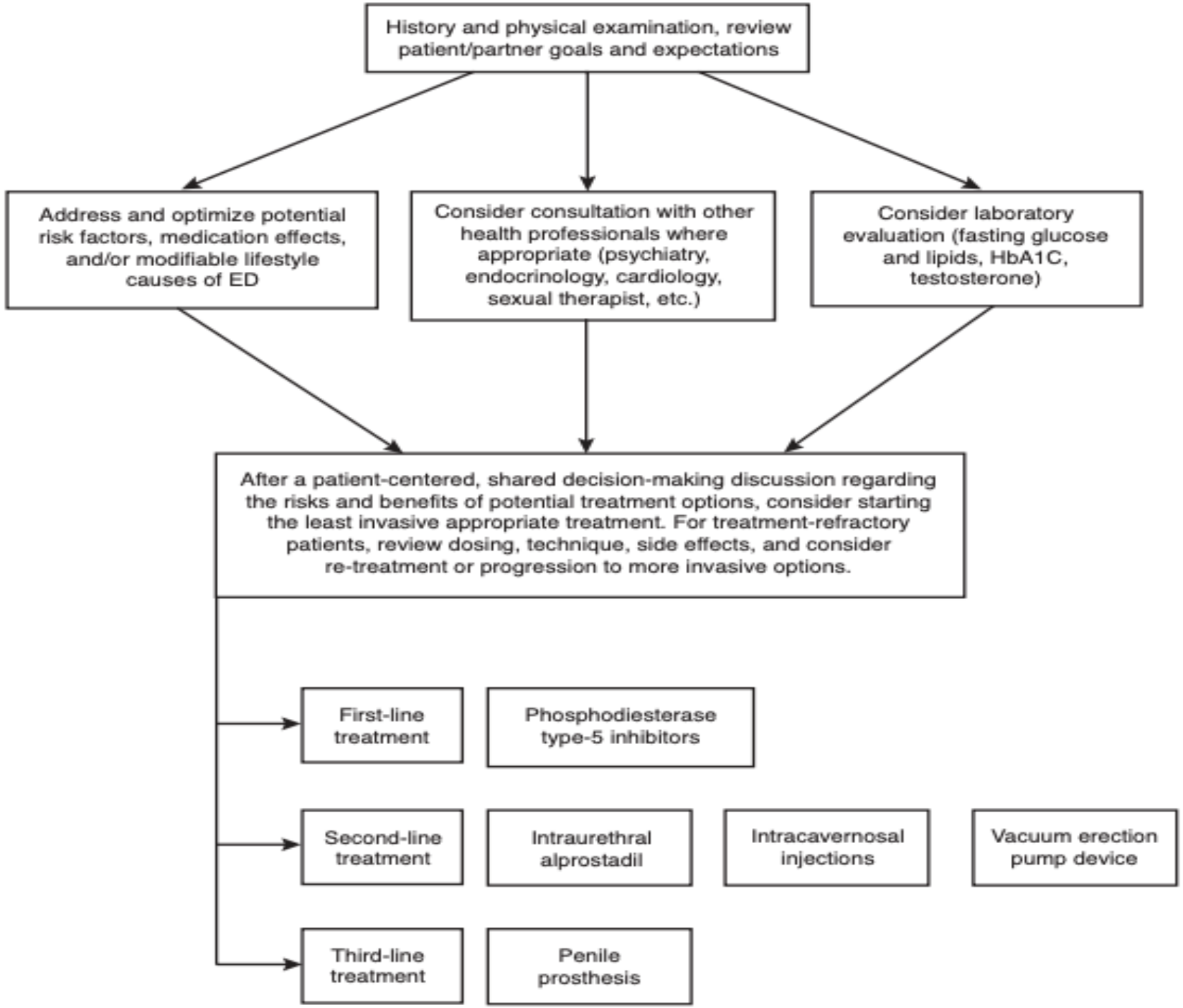
Physical Examination

Area	Factors to be assessed
Overall	Blood pressure, body habitus, virilization, mood, gynecomastia
Penis and groins	Penile length and girth, presence of penile plaques, phimosis, frenular tether, meatal stenosis, quality of femoral pulses
Testicles	Volume and consistency

CUA ED Guideline, 2021

Investigations

- Morning serum testosterone
  - Hypogonadal symptoms (low sexual desire)
  - Failure to respond to PDE5-inhibitors
- Fasting glucose, lipids, hemoglobin A1C
  - Idiopathic or suspected vasculogenic ED cases where occult diabetes and dyslipidemia should be ruled out
- More advanced vascular and neurological testing rarely indicated



CUA ED Guideline, 2021

Conservative treatment

- Should be discussed with all patients with ED
- Medication review and potential medication change
  - ACE inhibitor/ARB, calcium channel blocker less impact on erections
  - Bupropion, mirtazapine less impact on erections
- Focus on optimizing vascular risk factors and impacts on overall health
- Smoking, alcohol and cannabis negatively impact erectile function
- Increasing physical activity improves erectile function (conditional recommendation, low certainty of evidence)

CUA ED Guideline, 2021

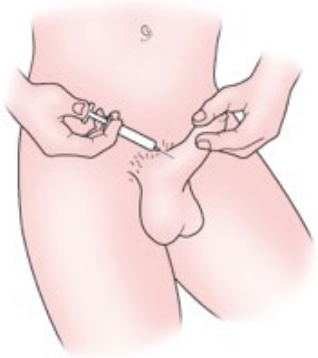
Management of Psychogenic ED

- Psychological counseling is typically used in combination with medical management
- Individual and couple counseling sessions are encouraged
- Psychological counseling techniques used by therapists:
  - Anxiety reduction
  - Cognitive-behavioral interventions
  - Discussions regarding adequate sexual stimulation/non-intercourse forms of stimulation
  - Interpersonal assertiveness and couple communication training

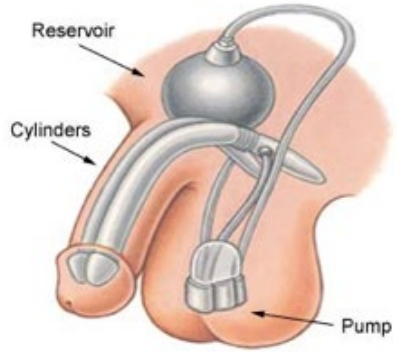
Urology Clinics NA 2001;28(2):269-78

Management of ED

Intraurethral alprostadil



Intracavernosal injection



Penile prosthesis

PDE5 inhibitors

Vacuum erection pump device

Most Invasive

Therapeutic Ladder

Least Invasive

Phosphodiesterase Type 5 inhibitors (PDE5-inhibitors)

- Facilitate erection by promoting vascular and cavernosal smooth muscle relaxation in response to sexual stimulation
- Highly effective first-line therapy
  - All three agents in Canada (Sildenafil, Tadalafil, Vardenafil) have similar efficacy with improvement in IIEF-EF score of around 7 in RCTs
- Absolute contraindications: organic nitrate use and allergy
- Side effects:
  - Headache
  - Flushing
  - Dyspepsia
  - Rhinitis
  - Back pain (Tadalafil specific)
  - Alteration in color vision (Sildenafil specific)

Pharmacology of PDE5-inhibitors

Characteristic	Sildenafil	Tadalafil	Vardenafil
Tmax	1.0 h	2.0 h	0.7 h – 0.9 h
Half-life	4 h	17.5 h	4 h – 5 h
Absorption affected by food	Yes	No	Yes
Interaction with alcohol	Yes	Yes	Yes

P. T. 2013; 31:31-5

Daily versus On-demand Tadalafil

- Given the pharmacokinetics of Tadalafil, daily dosing is possible
- Clinical efficacy and side effect profiles are very similar between daily and on-demand regimens
- Decision to prescribe daily versus on-demand PDE5-inhibitor is based on patient preference
- Patient-centered factors influencing daily dosing preference:
  - Increases sexual spontaneity (less concerns regarding timing)
  - Less anticipatory anxiety
  - Treatment of comorbid lower urinary tract symptoms
  - May be more cost-effective depending on frequency of use and whether a low (2.5 mg) or high (5 mg) daily dose is used

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Low-intensity shockwave therapy (Li-SWT) [experimental]

- Painless shockwaves delivered to different areas of the penis in multiple sessions using a wand-like device
- Hypothesized to improve erectile function through regeneration
  - Induces angiogenesis and nerve regeneration
- Limited research demonstrating clinical efficacy
  - 7 RCTs, varied treatment protocols, 3 trials have high risk of bias
  - IIEF-EF score improvement of 2.07 (95% CL 0.19, 3.96) with moderate certainty of evidence
- NOT Health Canada approved for treatment of ED
- Recommend against Li-SWT as a treatment for patients with ED at this time (conditional, low certainty of evidence)

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SEXUAL MEDICINE

SOCIETY REPORT

Restorative Therapies for Erectile Dysfunction: Position Statement From the Sexual Medicine Society of North America (SMSNA)

James L. Liu, MD,[1,*] Kevin Y. Chu, MD,[2,*] Andrew T. Gabrielson, MD,[1] Run Wang, MD,[3] Landon Trost, MD,[4] Gregory Broderick, MD,[5] Kelvin Davies, PhD,[6] Gerald Brock, MD,[7] John Mulhall, MD,[8] Ranjith Ramasamy, MD,[2] and Trinity J. Bivalacqua, MD, PhD[1]

ABSTRACT

Introduction: Current non-invasive treatments for erectile dysfunction (ED) include oral medications, intracavernosal injections, and vacuum-assisted devices. Though these therapies work well for many, a subset of patients have contraindications or are unsatisfied with these options. Restorative therapies for ED are a new frontier of treatments focused on regenerating diseased tissue and providing a potential "cure" for ED.

Aim: The aim of this position statement is to examine existing clinical trial data for restorative therapies and identify elements that require further research before widespread adoption.

Methods: A literature review was performed to identify all clinical trials performed with regenerative therapy for ED. This includes treatments such as stem cell therapy (SCT), platelet rich plasma (PRP), and restorative related technologies like low-intensity shockwave therapy (LiSWT).

Main Outcome Measures: Most clinical trials in restorative therapies were assessed for safety, feasibility, or efficacy. This included recording adverse events, changes in sexual function and erectile function questionnaires, and

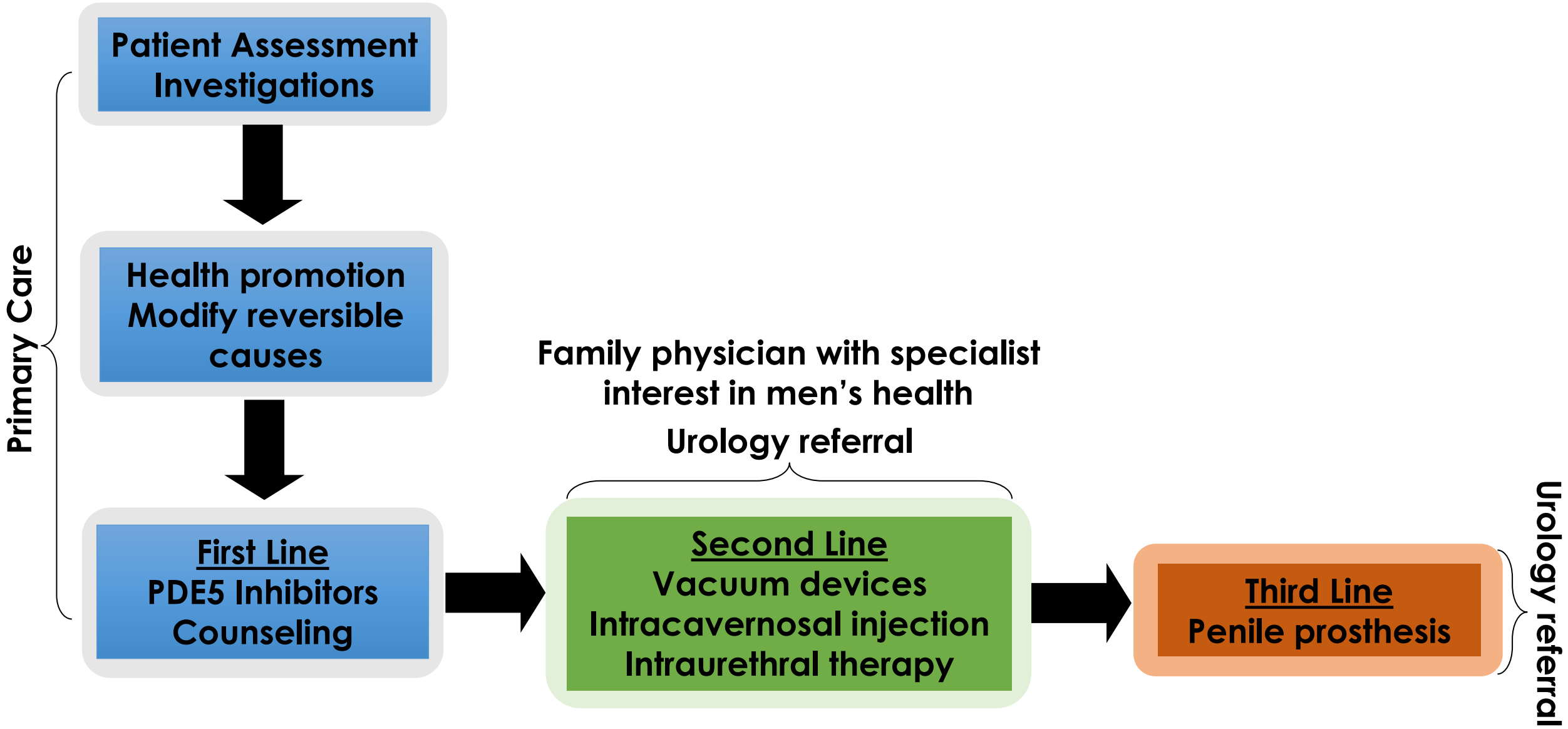
Conclusions: Restorative therapies are a promising technology that represents a new frontier of treatment geared towards reversing disease pathology rather than just treating symptoms. However, current published clinical studies are limited. Future work needs to be adequately powered, multi-center, randomized, sham/placebo-controlled trials in well-characterized patient populations to ensure safety and demonstrate efficacy. Until these studies are done, restorative therapies should be reserved for clinical trials and not offered in routine clinical practice. **Liu JL, Chu KY, Gabrielson AT, et al. Restorative Therapies for Erectile Dysfunction: Position Statement From the Sexual Medicine Society of North America (SMSNA). J Sex Med 2021;9:100343**

Second-line therapies

- Vacuum erection pump device
  - Negative pressure promotes blood flow which is trapped by a constriction ring placed at base of penis
  - Good option for patients who cannot tolerate or have contraindications to other medical or surgical options
- Intracavernosal injections (ICI)
  - Injection of vasoactive agent into corpus cavernosum prior to intercourse
  - Highly effective, but risk of pain, bruising, scarring and priapism
- Intraurethral alprostadil (MUSE™)
  - Preferred for patients with needle phobia
  - Risk of urethral/penile pain, very low risk of priapism

Penile prosthesis

- All non-surgical options should at least be discussed with the patient prior to considering surgical intervention
- 2 types of implants
  - Malleable and inflatable
- Very high patient and partner satisfaction rates
- Complications:
  - Infection
  - Device erosion
  - Device mechanical failure



J Sex Reprod Med 2002; 2: 61-65

Take home points

- ED is common and may be associated with reversible factors or undiagnosed conditions that need to be optimized
- History, physical examination and laboratory investigations (when applicable) narrow down the primary cause of ED in the vast majority of cases
- There are numerous treatment options for ED, typically starting with the least invasive to most invasive using a therapeutic ladder approach
- Family physicians and other primary care providers are the initial point of contact and play a huge role in the diagnosis and treatment of ED
  - Urology referral required only for treatment refractory cases

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Chair, 2021 CUA ED Guideline Committee