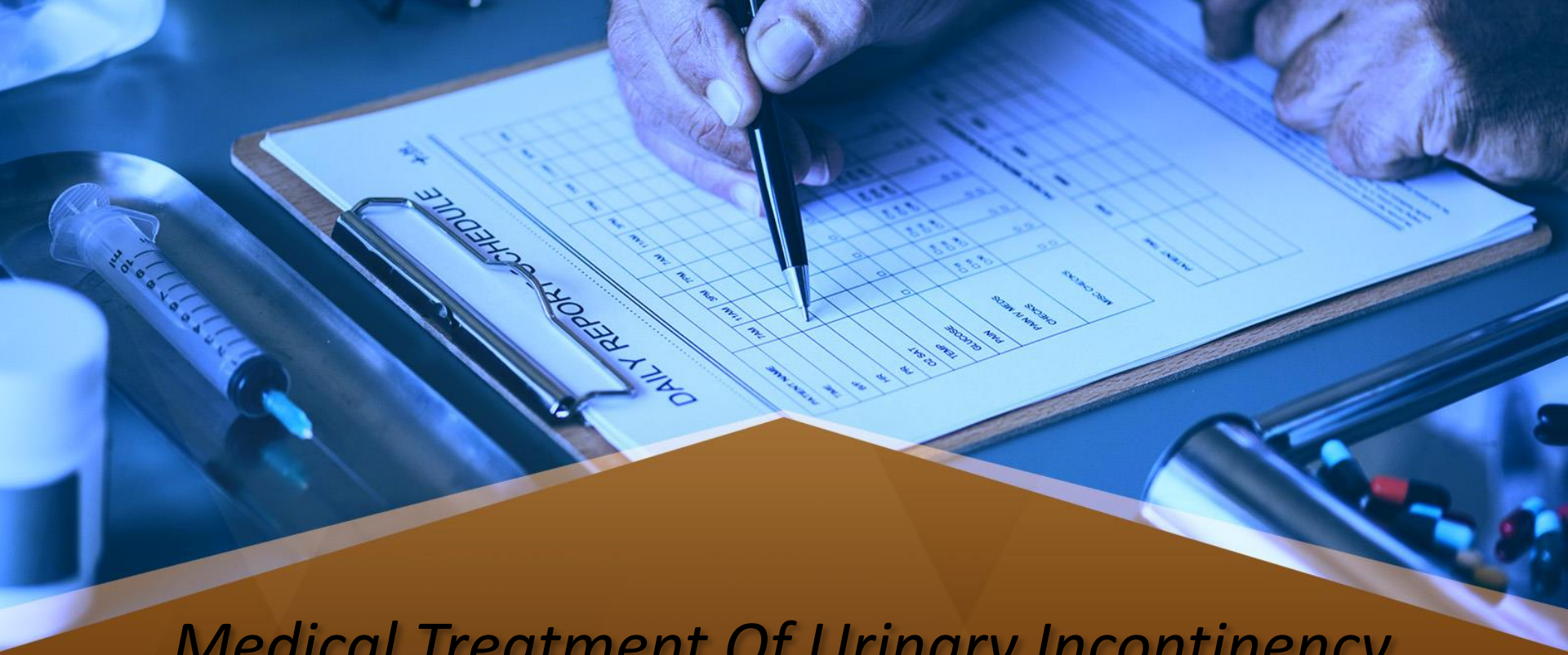
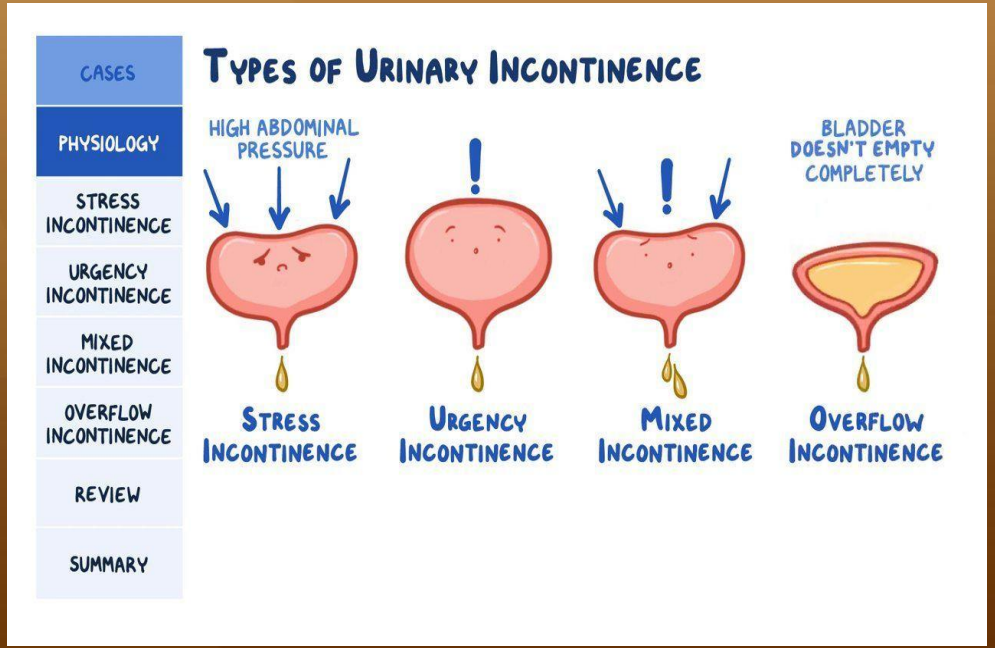


Medical Treatment Of Urinary Incontinency

Ardalan Akhavan MD

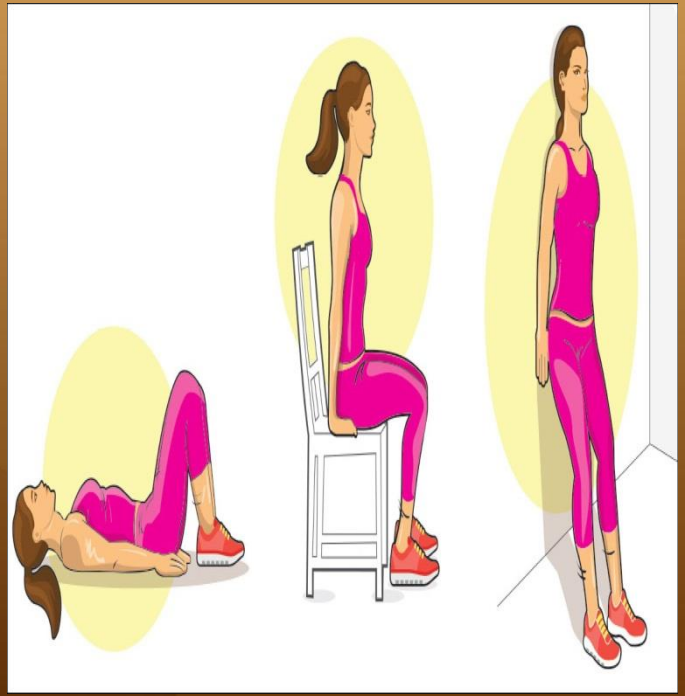
Approach to Treatment

- Etiology
- Pathophysiology
- Patient goals and expectations
- Risk-benefit
- Cost-benefit



Urge Urinary Incontinence (UUI)

- Lifestyle interventions :
  - Caffeine intake
  - Fluid intake
  - Obesity and weight loss
  - Smoking
- Behavioral and physical therapies:
  - Prompted voiding and timed voiding
  - Bladder Training
  - Pelvic floor muscle training
  - Electrical stimulation
  - Acupuncture



UUI *Pharmacological management*

- Anticholinergic
- Beta-3 agonists
- Estrogen

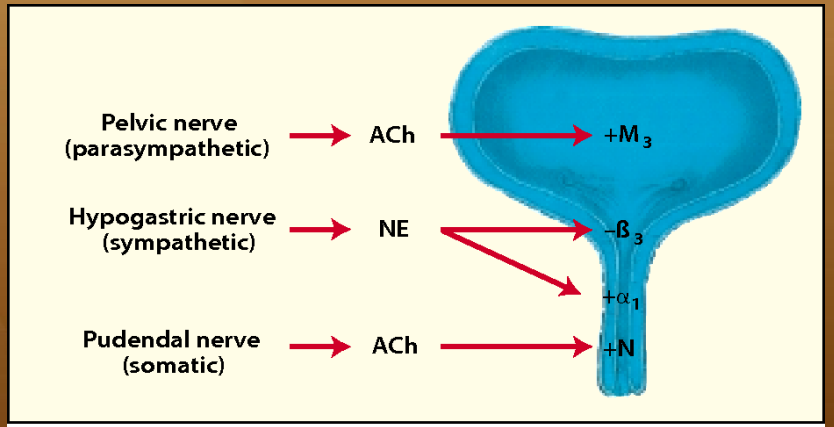


Figure 1. *Innervation of the lower urinary tract: The parasympathetic pelvic nerve stimulates the bladder detrusor muscle, mediated by muscarinic receptors (M_3) being activated by acetylcholine (ACh). The sympathetic hypogastric nerve stimulates urethral smooth muscle and inhibits bladder detrusor, mediated by α_1-adrenergic and β_3-adrenergic receptors, respectively. The somatic pudendal nerve stimulates striated muscle of the external urethral sphincter, mediated by ACh activating nicotinic (N) receptors. NE, norepinephrine. Plus and minus signs indicate neural stimulation and inhibition, respectively.*

Anticholinergic

Quaternary

Propantheline

Tropium

Tertiary

Darifenacin

Solifenacin

Fesoterodine

Tolterodine

Oxybutynin

Propiverine

	LEVEL OF EVIDENCE	GRADE OF RECOMMENDATION
ANTIMUSCARINIC DRUGS		
Atropine, hyoscyamine	3	C
Darifenacin	1	A
Fesoterodine	1	A
Imidafenacin	1	A
Propantheline	2	B
Solifenacin	1	A
Tolterodine	1	A
Trospium	1	A
DRUGS WITH MIXED ACTIONS		
Oxybutynin	1	A
Propiverine	1	A
Flavoxate	2	D

Anticholinergic

Medication/formulation	Uroselective	Usual dosage	Comments
Oxybutynin (Ditropan)	No	2.5–5 mg orally 2–4 times per day (geriatric dose 2.5 mg)	• Effective and inexpensive • Side effects include constipation, dry mouth, blurred vision • May precipitate acute urinary retention • In the elderly may cause confusion and sedation • Available on the PBS
Oxybutynin transdermal patch (Oxytrol)	No	39 cm^2 patch 2 times/week (3.9 mg/day	• Side effects of oxybutynin are due to metabolites which may be reduced by newer transdermal delivery system • Not available on the PBS
Tolterodine (Detrol)	Yes	2–4 mg orally per day	• Comparable efficacy to oxybutynin • Improved side effect profile • No PBS listing as yet
Darifenacin hydrobromide (Enablex)	Yes	7.5–15 mg orally once per day	• Comparable efficacy to oxybutynin • Improved side effect profile • No PBS listing as yet
Solifenacin (Vesicare)	Yes	5 mg/day orally	• Comparable efficacy to oxybutynin • Improved side effect profile • No PBS listing as yet

Anticholinergic

Summary of evidence	LE
No anticholinergic drug is clearly superior to another for cure or improvement of OAB/UUI.	1a
Higher doses of anticholinergic drugs are more effective to improve OAB symptoms, but exhibit a higher risk of side effects.	1a
Once daily (extended release) formulations are associated with lower rates of adverse events compared to immediate release preparations, although similar discontinuation rates are reported in clinical trials.	1b
Dose escalation of anticholinergic drugs may be appropriate in selected patients to improve treatment effect although higher rates of adverse events can be expected.	1b
Transdermal oxybutynin (patch) is associated with lower rates of dry mouth than oral anticholinergic drugs, but has a high rate of withdrawal due to skin reaction.	1b
There is no consistent evidence to show superiority of drug therapy over conservative therapy for treatment of OAB.	1b
Behavioural treatment may have higher patient satisfaction rates than drug treatment.	1b
There is insufficient evidence as to the benefit of adding PFMT to drug treatment for OAB.	1b
Adherence to anticholinergic treatment is low and decreases over time because of lack of efficacy, adverse events and/or cost.	2a
Most patients will stop anticholinergic agents within the first three months.	2a

Anticholinergic

Recommendations	Strength rating
Offer anticholineric drugs to adults with overactive bladder (OAB) who fail conservative treatment.	Strong
Consider extended release formulations of anticholinergic drugs, whenever possible.	Strong
If an anticholinergic treatment proves ineffective, consider dose escalation or offering an alternative anticholinergic formulation, or mirabegron, or a combination.	Strong
Encourage early review (of efficacy and side effects) of patients on anticholinergic medication for OAB.	Strong

Discontinuing anticholinergics

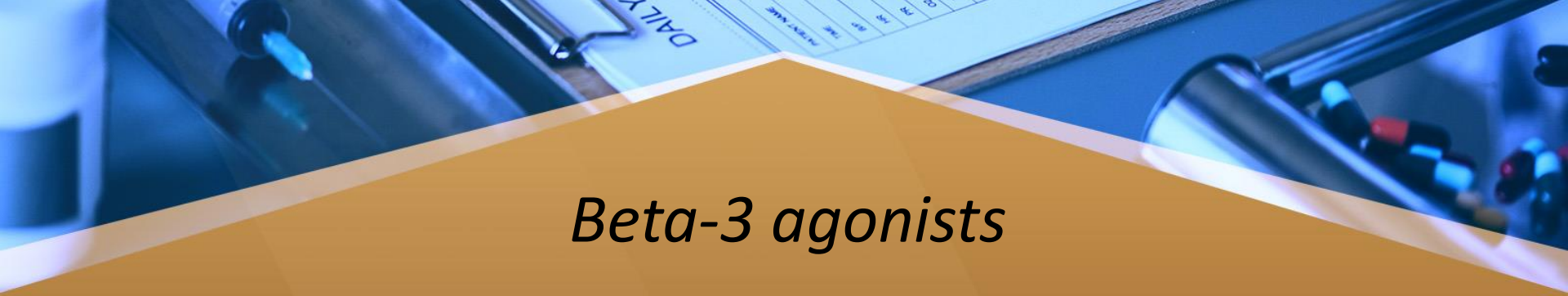
- *low level of efficacy (41.3%)*
- *adverse events (22.4%)*
- *cost (18.7%)*
- *age (lower persistence among younger adults)*
- *unrealistic expectations of treatment*
- *gender distribution(better adherence/persistence in female patients)*

Beta-3 agonists

4.1.4.2.2.1. Summary of evidence and recommendation for mirabegron

Summary of evidence	LE
Mirabegron is better than placebo and as efficacious as anticholinergics for improvement of OAB/UUI symptoms.	1a
Adverse event rates with mirabegron are similar to placebo.	1a
Patients inadequately treated with solifenacin 5 mg may benefit more from the addition of mirabegron than dose escalation of solifenacin.	1b

Recommendation	Strength rating
Offer mirabegron as an alternative to anticholinergics to women with overactive bladder who fail conservative treatment.	Strong



Beta-3 agonists

- *QT Prolongation On Electrocardiogram*
- *Intraocular Pressure*
- *Uncontrolled Hypertension*
- *Cardiac Arrhythmia*

Oestrogens

- *Oestrogens treatment : oral, transdermal and vaginal routes of administration*
- *Vaginal (local) treatment : symptoms of vaginal atrophy in post-menopausal women*

LUTS and Genitourinary Syndrome of Menopause (GSM)

- mucosal pallor/erythema
- loss of vaginal reggae
- tissue fragility/fissures
- vaginal petechia
- urethral mucosal prolapse
- introital retraction
- vaginal dryness

Oestrogens

- Vaginal oestrogen therapy may improve symptoms associated with GSM, of which OAB may be a component

- Offer vaginal oestrogen therapy to women with lower urinary tract symptoms and associated symptoms of genito-urinary syndrome of menopause (Weak)

Stress Urinary Incontinence(SUI)

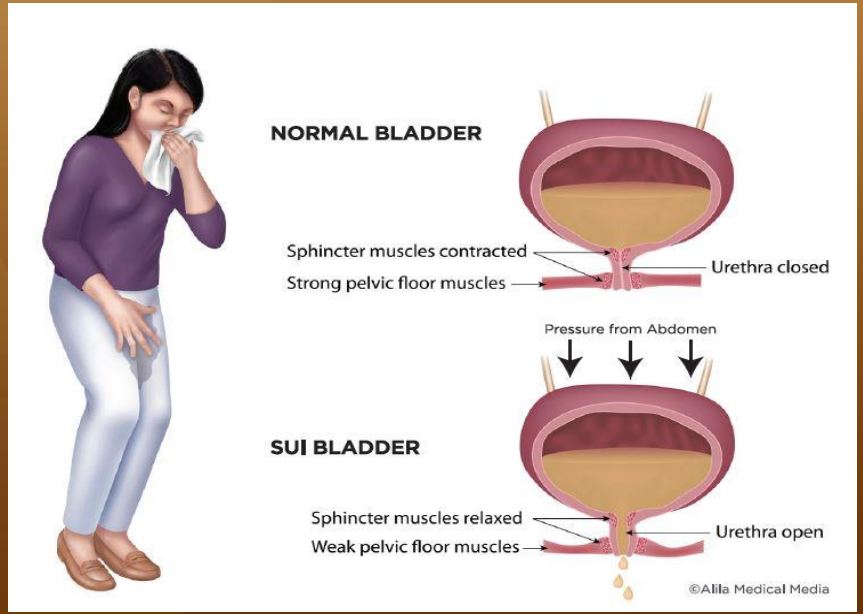
Conservative management

Obesity and weight loss

Urinary containment

Pelvic floor muscle training

Electromagnetic stimulation



SUI Pharmacological management

- Oestrogen
- Duloxetine

TABLE 120.4 Drugs Used in the Treatment of Stress Urinary Incontinence: Assessments According to the Oxford System (Modified)

DRUG	LEVEL OF EVIDENCE	GRADE OF RECOMMENDATION
Clenbuterol	3	C
Duloxetine	1	B
Ephedrine	3	D
Estrogen	2	D
Imipramine	3	D
Methoxamine	2	D
Midodrine	2	C
Norephedrine (phenylpropanolamine)	3	D

From Andersson K-E, Cardozo L, Cruz F, et al. Pharmacological treatment of urinary incontinence. In: Abrams P, Cardozo L, Wagg A, Wein AJ, eds. Incontinence. 6th International Consultation on Incontinence. Paris: ICUD-EAU; 2017:805–957.

Oestrogen

4.2.4.2.1.1. Summary of evidence and recommendations for oestrogens

Summary of evidence	LE
Vaginal oestrogen therapy improves SUI for post-menopausal women in the short term.	1a
Neoadjuvant or adjuvant use of local oestrogens are ineffective as an adjunct to surgery for SUI.	2b
Systemic hormone replacement therapy using conjugated equine oestrogens does not improve SUI and may worsen pre-existing UI.	1a

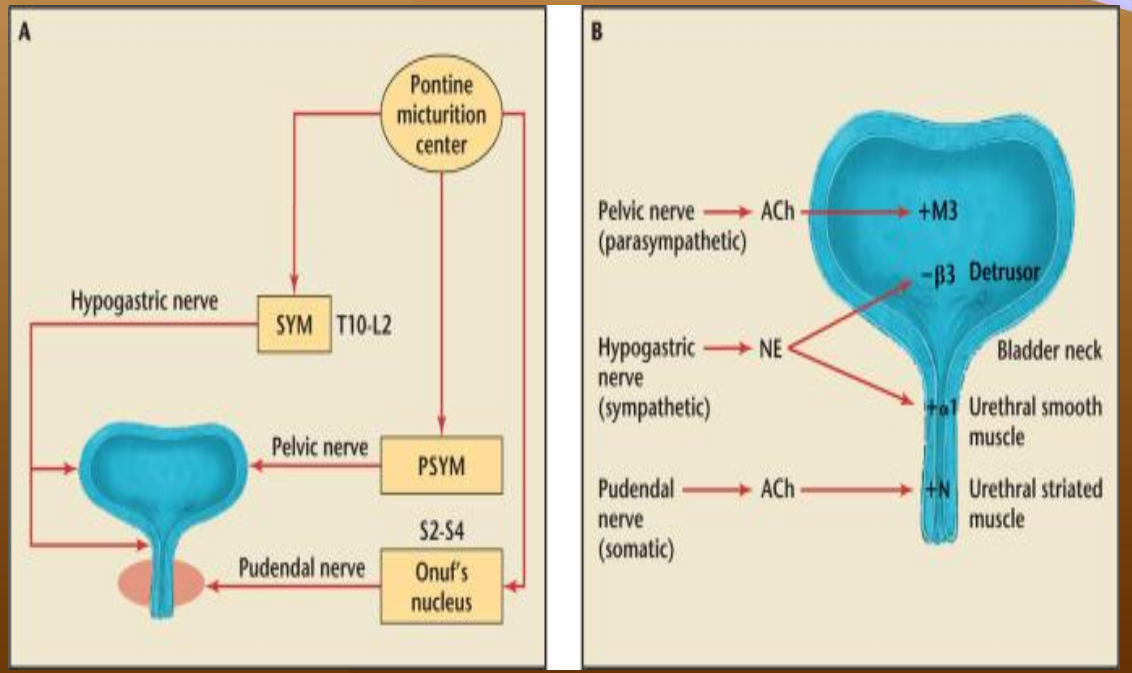
Recommendations	Strength rating
Offer vaginal oestrogen therapy to post-menopausal women with stress urinary incontinence (SUI) and symptoms of vulvo-vaginal atrophy.	Strong
In women taking oral conjugated equine oestrogen as hormone replacement therapy who develop or experience worsening SUI discuss alternative hormone replacement therapies.	Strong

Oestrogen

- *Raloxifene was not associated with development or worsening of UI*
- *oral oestriol or oestradiol as HRT may improve UI symptoms although the evidence was unclear*

Duloxetine

- Increasing concentration of 5-HT and NE in the synaptic cleft by inhibiting the presynaptic re-uptake
- Increases stimulation of 5-HT and NE receptors on the pudendal motor neurons
- Increases the resting tone and contraction strength of the urethral striated sphincter.



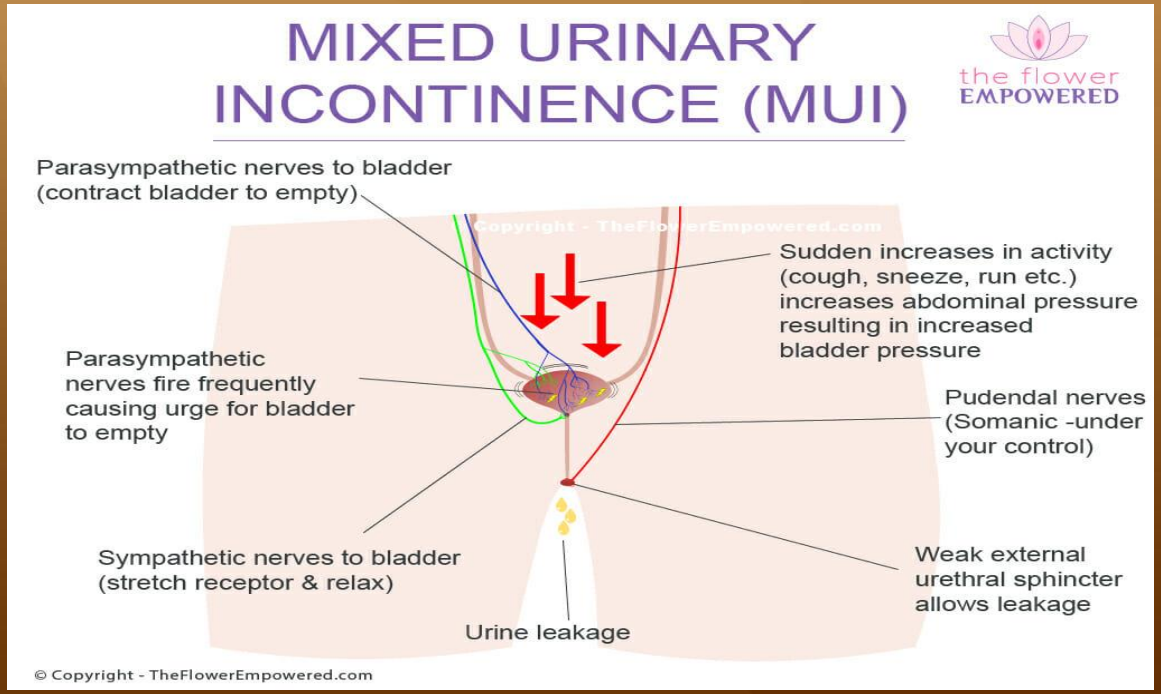
Duloxetine

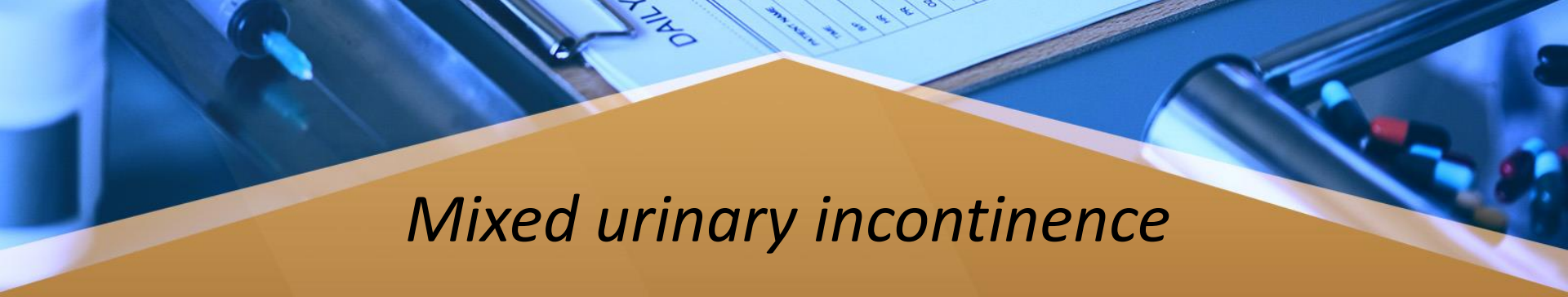
4.2.4.2.2.1. Summary of evidence and recommendations for duloxetine

Summary of evidence	LE
Duloxetine improves SUI in women, but the chances of cure are low.	1a
Duloxetine may cause significant gastrointestinal and central nervous system side effects leading to a high rate of treatment discontinuation, although these symptoms may be limited to the first weeks of treatment.	1a

Recommendations	Strength rating
Offer duloxetine (where licensed) to selected patients with SUI unresponsive to other conservative treatments and who want to avoid invasive treatment, counselling carefully about the risk of adverse events.	Strong
Duloxetine should be initiated and withdrawn using dose titration because of the high risk of adverse events.	Strong

Mixed urinary incontinence





Mixed urinary incontinence

- *Conservative management*
  - Pelvic floor muscle training in mixed urinary incontinence
  - Bladder training
  - Electrical stimulation
- *Pharmacological management*
  - Tolterodine
  - Duloxetine

Mixed urinary incontinence

4.3.3.3.3. Summary of evidence and recommendations for pharmacological management of MUI

Summary of evidence	LE
Limited evidence suggests that anticholinergic drugs are effective for improvement of the UUI component in patients with MUI.	2
Duloxetine is effective for improvement of both SUI and MUI symptoms, but adverse event rates are high.	1b

Recommendations	Strength rating
Treat the most bothersome symptom first in patients with mixed urinary incontinence (MUI).	Weak
Offer anticholinergic drugs or beta-3 agonists to patients with urgency-predominant MUI.	Strong
Offer duloxetine (where licensed) to selected patients with stress-predominant MUI unresponsive to other conservative treatments and who want to avoid invasive treatment, counselling carefully about the risk of adverse events.	Weak

با تشکر از توجه شما