Overactive Bladder and Urge Urinary incontinence (OAB & UUI)

泌尿科 吳書雨醫師

Outline

- Definition and terminology
- Prevalence
- Pathophysiology
- Diagnosis
- Treatments

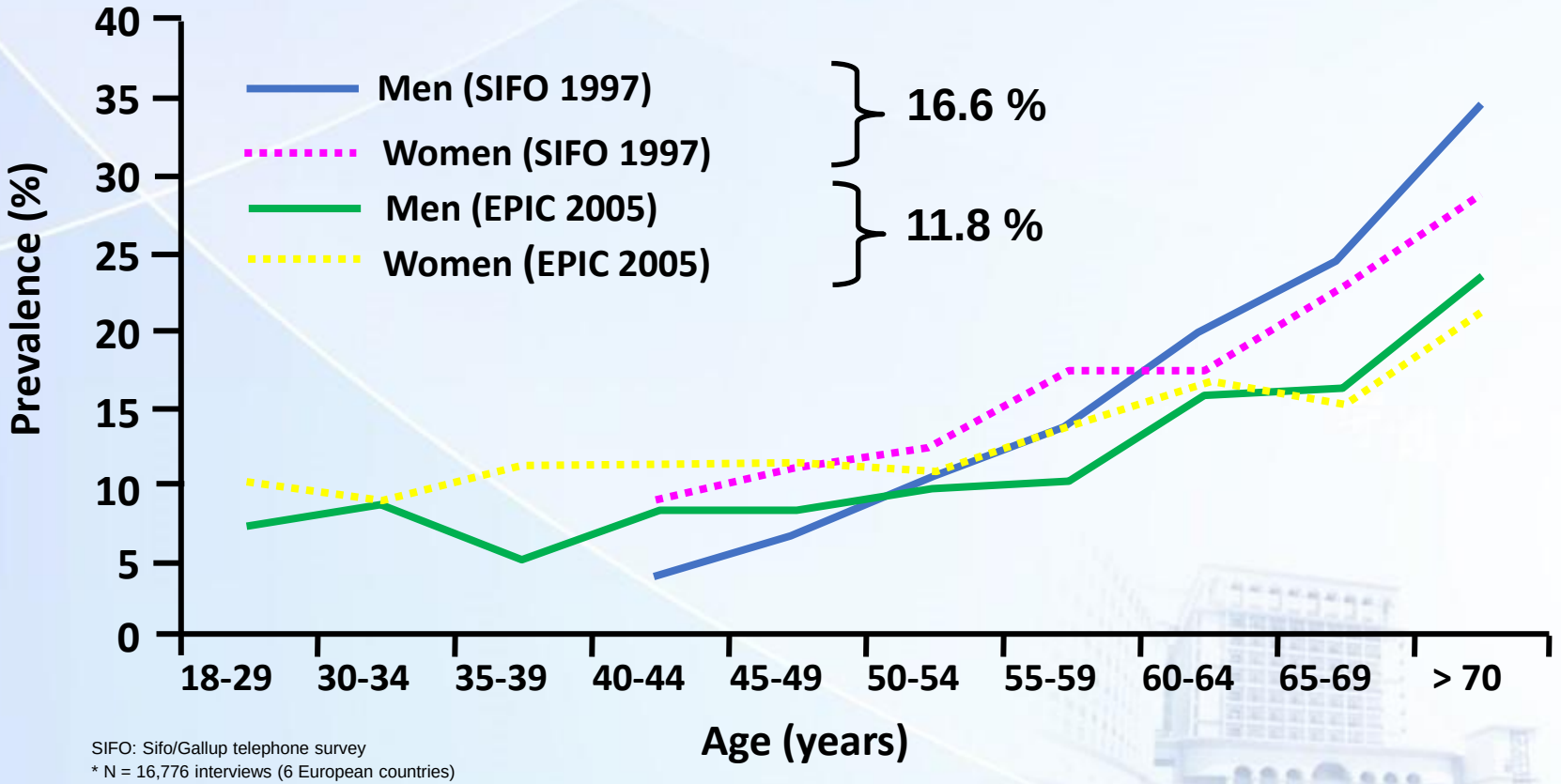
Definition & Terminology

- Overactive bladder
  - A symptom syndrome
  - Urinary urgency, with or without urge incontinence, usually accompanied by frequency and nocturia
  - No signs of other pathology or infection
- Urgency
  - The complaint of a sudden compelling desire to pass urine, which is difficult to defer
- Urge urinary incontinence
  - The complaint of involuntary loss of urine accompanied by or immediately preceding by urgency

Definition & Terminology

- Nocturia
  - Walking to pass urine during the main sleep period
  - The first nocturia episode must be preceded by sleep
  - Nocturia once was thought to be normal
- Nocturnal polyuria
  - More than 33% of the total daily urine output occurs at night (or sleep)
- Frequency
  - Average voiding times: 8/day
  - Many times in a short time

Prevalence



SIFO: Sifo/Gallup telephone survey
* N = 16,776 interviews (6 European countries)
† N = 19,165 interviews (4 European countries and Canada)

Prevalence

- Up to 100 million worldwide
  - 16.6% of adult population in US
  - OAB dry: 13.6% men, 7.6% women
  - OAB wet: 2.4% men, 9.3% women
  - <40% seek treatment
- In Taiwan
  - 16.9% of adult population
  - 30~79 y/o: 18.2%
  - OAB dry: 13.7%
  - OAB wet: 4.5%

Impact of incontinence

- Quality of life
  - Associated with depression and anxiety, work impairment, and social isolation
- Sexual dysfunction
  - 30% (fear of) coital incontinence
- Morbidity
  - Perineal infections
  - Falls and fractures
- Caregiver burden
  - 6-10% of nursing home admissions

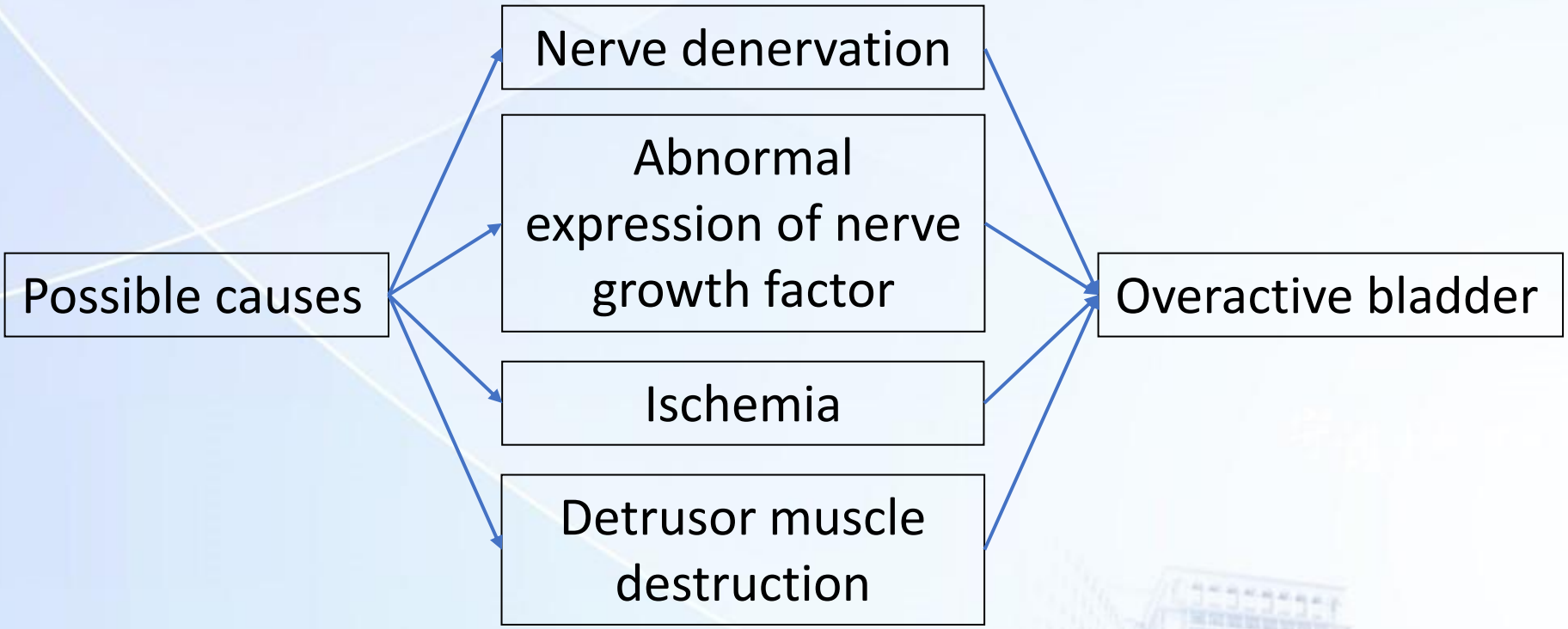
Pathophysiology

- Myogenic
  - Alterations in structural and functional properties of the detrusor muscle
  - Partial denervation of the detrusor muscle
  - Supersensitivity to acetylcholine (ACh)
  - Abnormal spontaneous mechanical activity
- Neurogenic
  - Increased afferent activity
  - Decreased central inhibitory control
  - Increased detrusor sensitivity to motor input

Pathophysiology

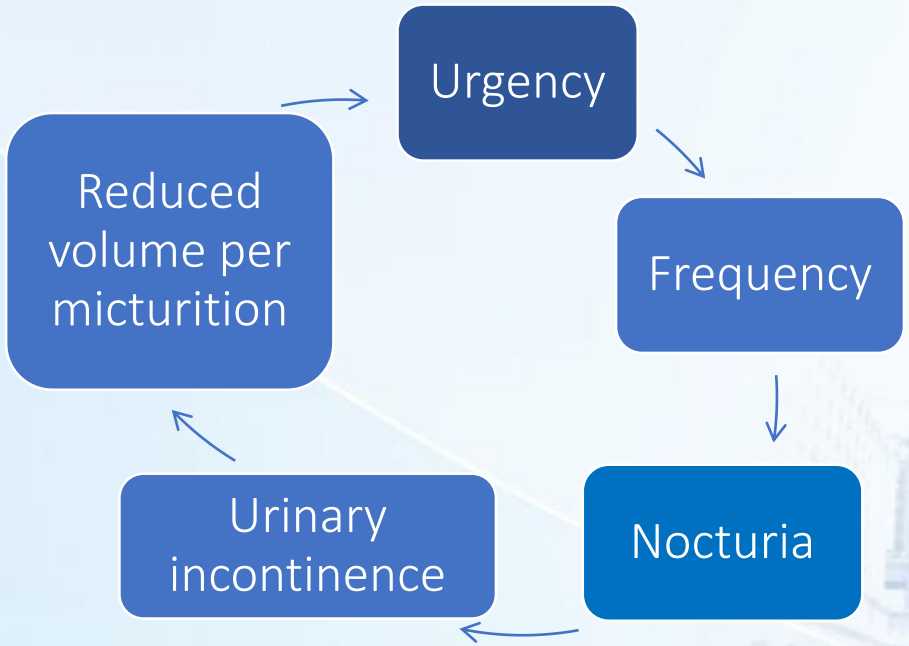
- Possible causes
  - Aging
  - Idiopathic
  - Cerebrovascular disease
    - Stroke, Alzheimer disease, multi-infarct or other dementias, Parkinson disease, or multiple sclerosis
  - Spinal cord injury or spine surgery
  - Metabolic, degenerative, or neurogenic diseases
  - Disorders of the PFM(POP, fecal incontinence)
  - Abdominal or pelvic operation
  - Bladder outlet obstruction
  - Depression or anxiety

Pathophysiology



Diagnosis

- Symptoms
  - Urinary urgency, with or without urge incontinence, usually accompanied by frequency and nocturia



Diagnosis

- Urinalysis to exclude urinary tract infection
- Bladder sonography to exclude urine retention

OABSS

以下症狀大約出現的頻率為何? 請選出一個與最近幾周內您的狀態最接近的選項

您早上起床到睡前為止大約要小便幾次?		您晚上就寢到早上起床為止大約要醒來小便幾次?		您多長有突然想小便且感覺難以延後(感覺憋不住)		您多常有因尿急難以延後(憋不住)而漏尿	
	分數		分數		分數		分數
7次以下	0	無	0	無	0	無	0
8-14次	1	1次	1	每週少於1次	1	每週少於1次	1
15次以上	2	2次	2	每週1次以上	2	每週1次以上	2
		3次以上	3	每天1次左右	3	每天1次左右	3
				每天2-4次	4	每天2-4次	4
				每天5次以上	5	每天5次以上	5

分數 5 分或 5 分以下	輕度膀胱過動
分數 6-11 分	中度膀胱過動
分數 12 或 12 分以上	較嚴重膀胱過動

總分 _____

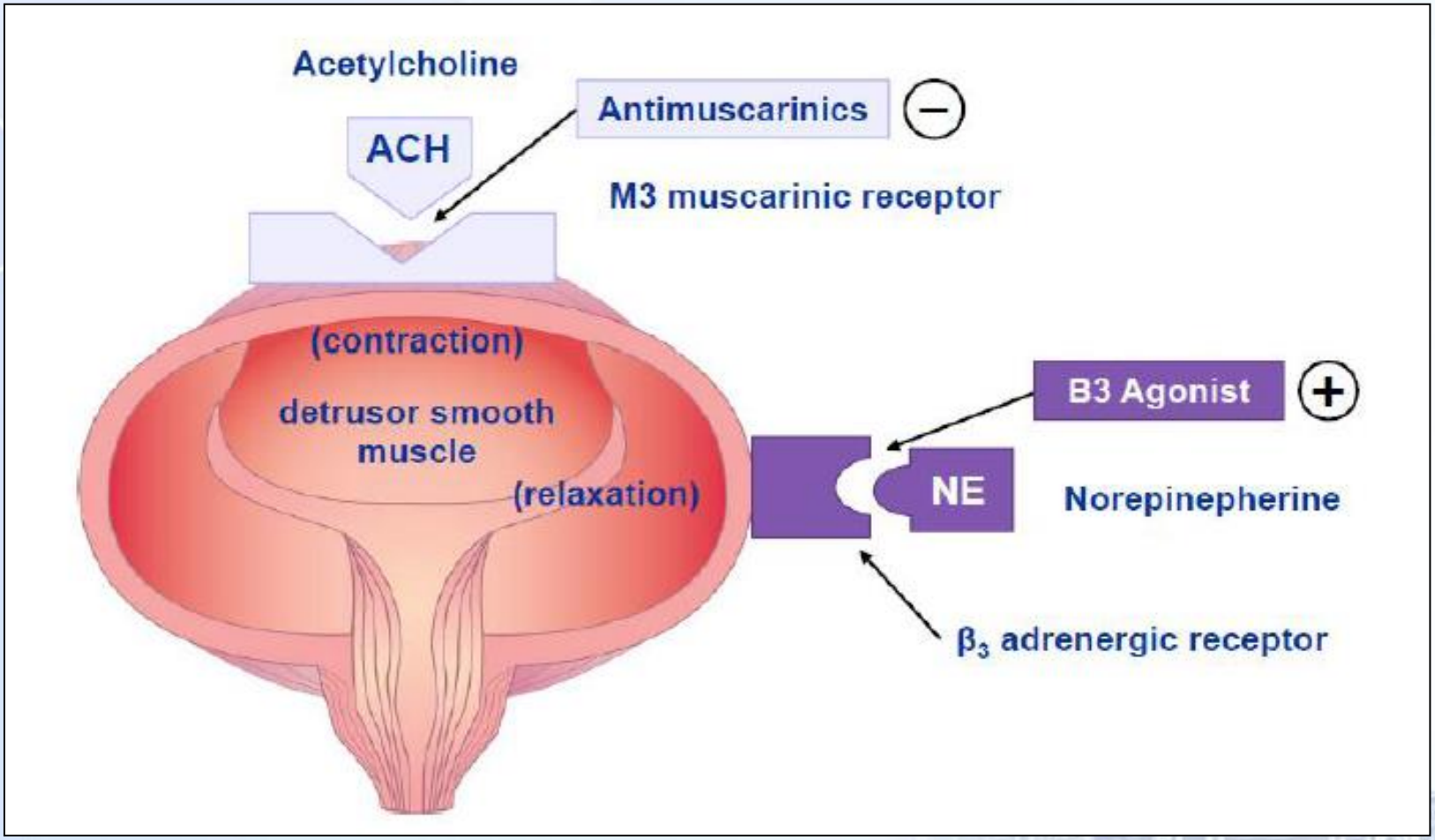
Treatments

- First line
  - Behavioral therapies (Standard)
  - Above may be combined with pharmacotherapy (Recommendation)
- Second line
  - Oral antimuscarinics (Standard)
  - ß-3 agonist (Standard)
  - Extended release should be preferentially offered (Recommendation)
  - Transdermal oxybutynin

Treatments

- Third line
  - OnabotulinumtoxinA (Standard)
  - Sacral neuromodulation (Recommendation)
  - Percutaneous Tibial Nerve Stimulation (PTNS) (Recommendation)
- Additional treatments
  - Indwelling catheters as last resort (Expert opinion)
  - Augmentation cystoplasty/diversion (Expert opinion)
  - Severe, refractory complicated cases only

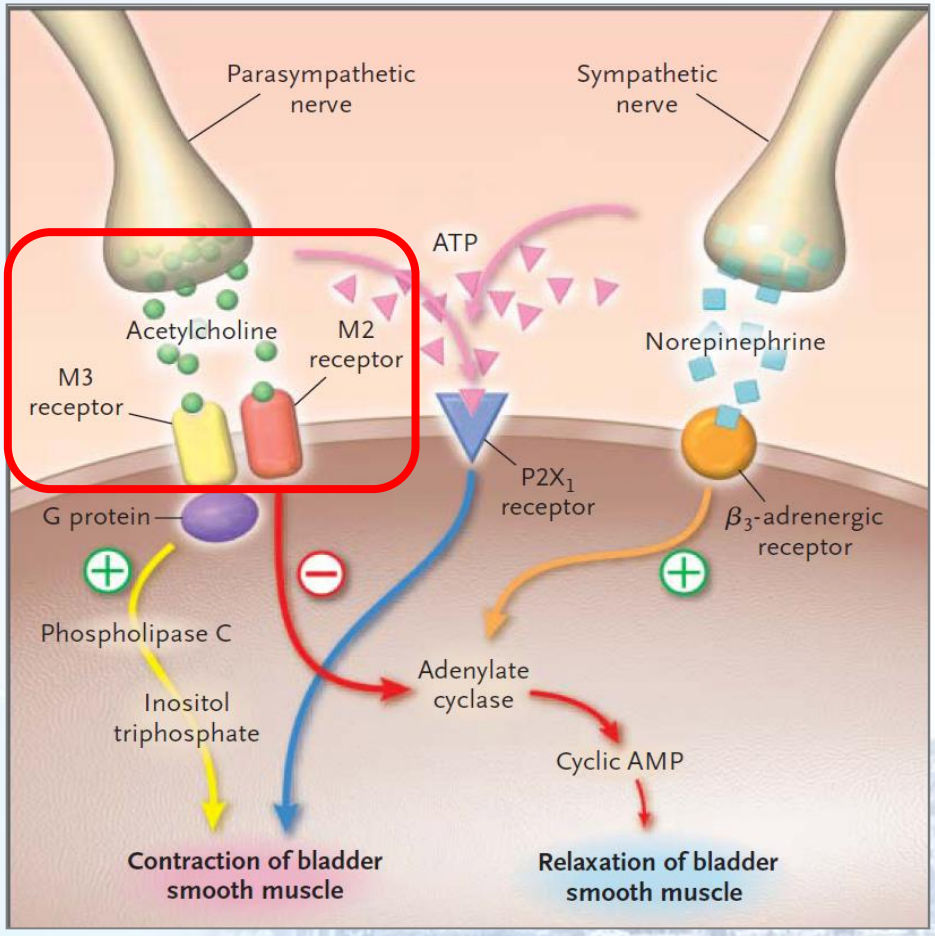
Neurogenic Innervation and Control of Bladder Musculature



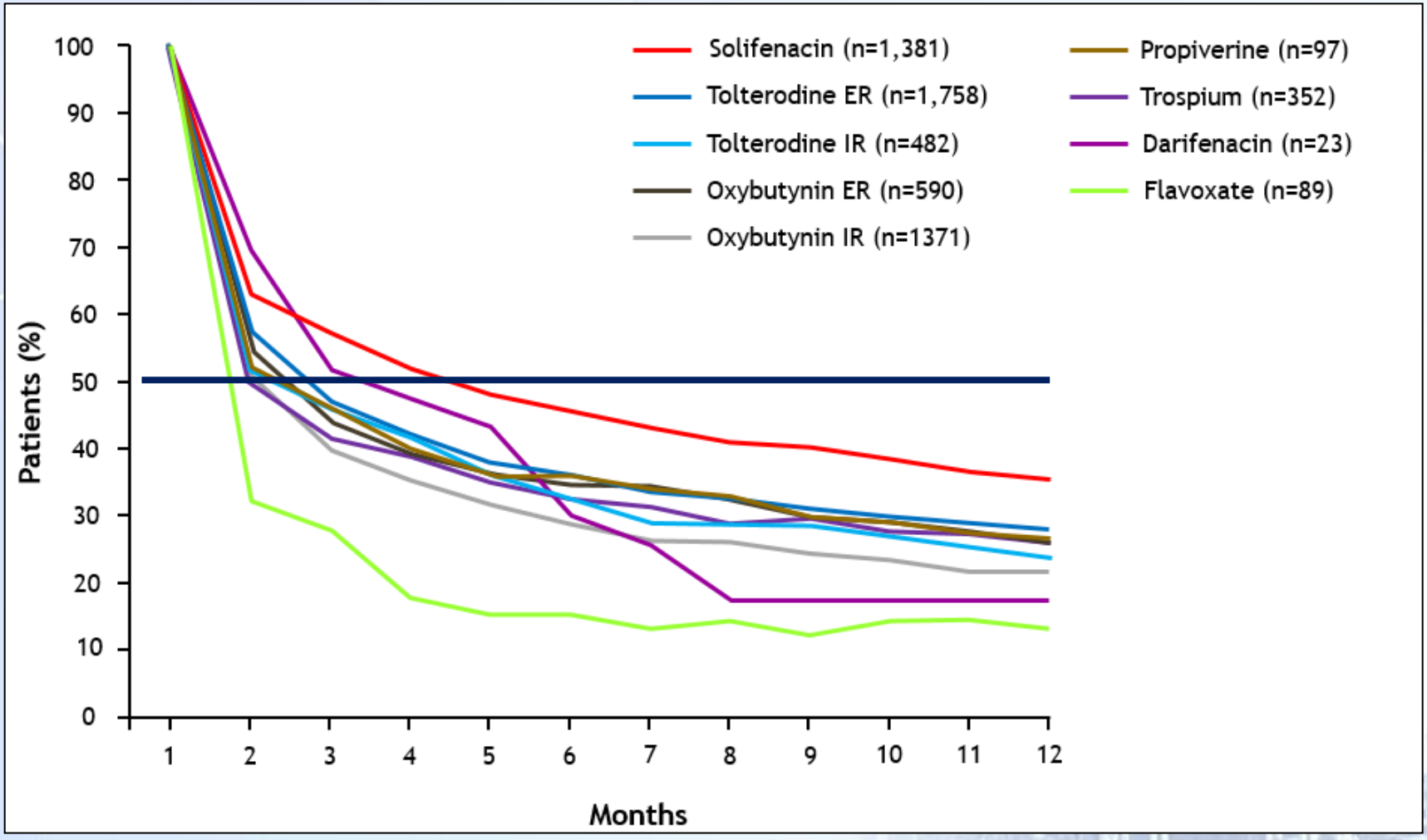
OAB Medications in Taiwan

- Anticholinergic agents
  - 1974- Trospium
  - 1975- Oxybutynin IR (Ditropan)
  - 1983- Atropine sulfate, Propantheline (Grade B)
  - 1983- Propiverine
  - 1996- Tolterodine (Detrusitol)
  - 2006- Solifenacin (Vesicare)
  - 2011- Oxybutynin ER (Oxbu)
- β-3 adrenergic agonist
  - 2015- Mirabegron (Betmiga)
- Flavoxate (平滑肌鬆弛劑) (Grade D)
- Imipramine (三環抗憂鬱劑) (Grade C)

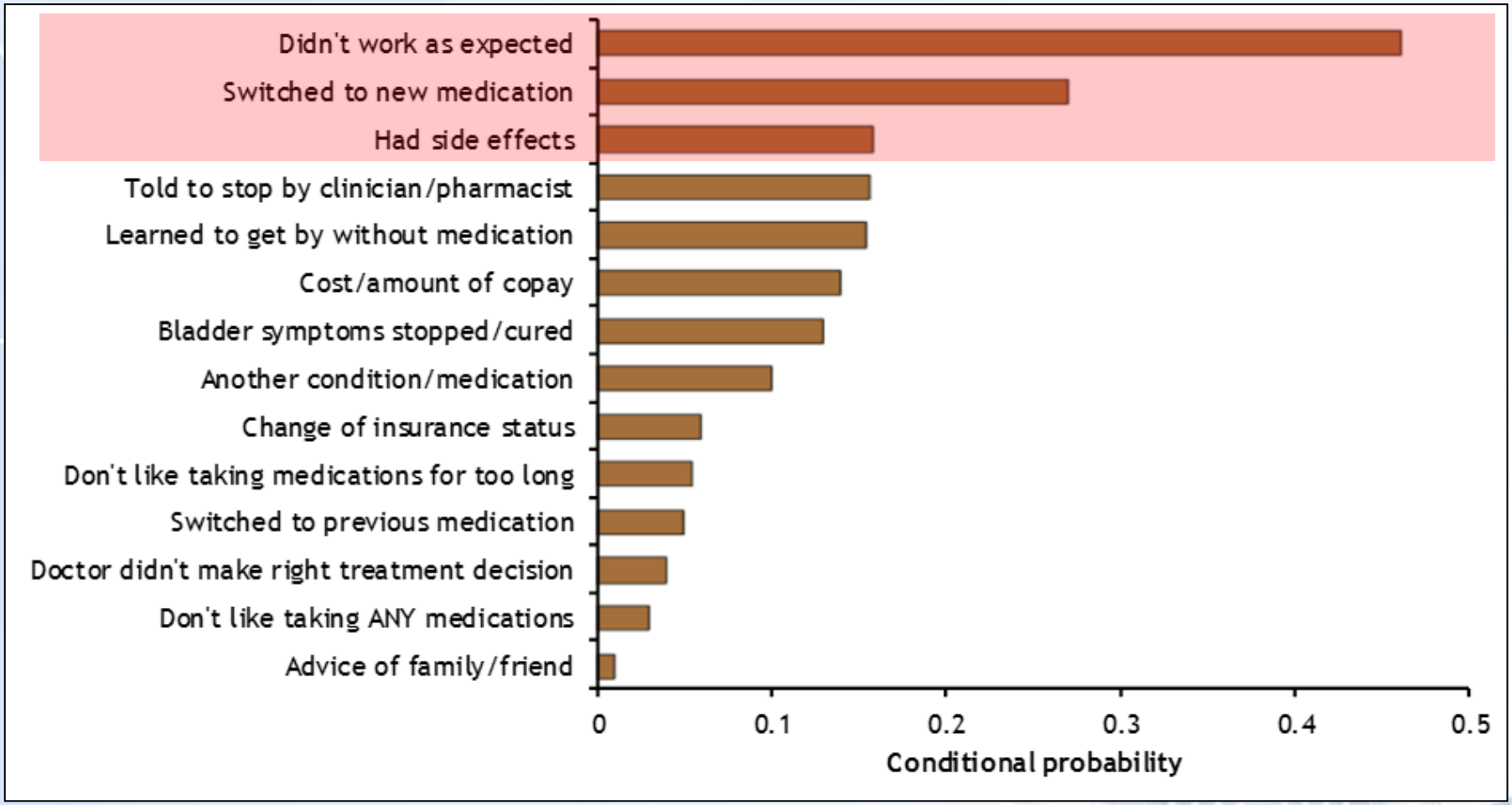
- Parasympathetic pathway
  - Muscarinic receptor M2 and M3 → Bladder contraction
  - Antimuscarinics
    - Solifenacin (Vesicare)
    - Tolterodine (Detrusitol)
    - Trospium (Uracare)
    - Oxybutynin (Diropan)
    - Propiverine (Urotrol)
    - Flavoxate



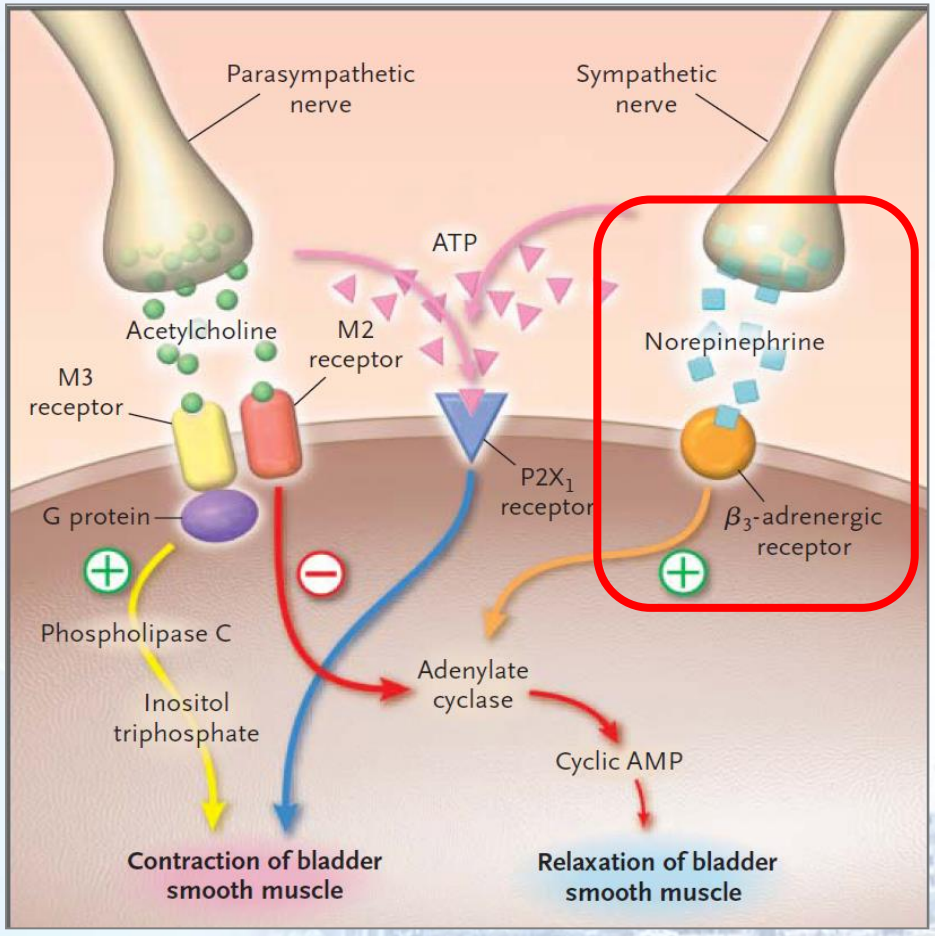
Adherence to Antimuscarinics



Why Discontinue?



- Sympathetic pathway
  - β_3-adrenergic receptor → Bladder relaxation
  - β_3-agonist
    - Mirabegron (Betmiga)



禁忌症

- Anti-muscarinic medications
  - 尿液滯留
  - 腸道阻塞
  - 未控制的狹角性青光眼
  - 心律不整引起之心博過速
  - 重度腎功能障礙或中度肝功能障礙患者
- ß3-agonist
  - 嚴重未控制的高血壓
  - 收縮壓>180mmHg或舒張壓>110mmHg

Treatment in OAB

- EAU guidelines:
  - Non-neurogenic Female LUTS
  - Management of Non-neurogenic Male LUTS

Non-neurogenic Female LUTS

- Lifestyle interventions

Recommendations	Strength rating
Encourage overweight and obese adults with overactive bladder (OAB)/urinary incontinence to lose weight and maintain weight loss.	Strong
Advise adults with OAB that reducing caffeine intake may improve symptoms of urgency and frequency, but not incontinence.	Strong
Review type and amount of fluid intake in patients with OAB.	Weak
Provide smoking cessation strategies to patients with OAB who smoke.	Strong

Non-neurogenic Female LUTS

- Behavioral and physical therapies
  - Bladder training, pelvic floor muscle training, electrical stimulation, acupuncture, posterior tibial nerve stimulation (PTNS)

Electrical stimulation may improve symptoms of OAB in some women, but the type and mode of delivery of ES remains variable and poorly standardised.	1a
Percutaneous-posterior tibial nerve stimulation appears effective in the short-term for improving UUI in women who have had no benefit from anticholinergic medication but in general is not curative.	2b
A maintenance programme of P-PTNS has been shown to be effective for up to 3 years.	1b
Percutaneous-PTNS has comparable effectiveness to tolterodine for improvement of UUI in women.	1b
No serious adverse events have been reported for P-PTNS in UUI.	3
Transcutaneous-PTNS appears to be effective in reducing OAB symptoms compared to sham treatment.	1a

Non-neurogenic Female LUTS

- Behavioral and physical therapies

Recommendations	Strength rating
Offer prompted voiding for adults with overactive bladder (OAB) who are cognitively impaired.	Strong
Offer bladder training as first-line therapy to adults with OAB/UUI.	Strong
Ensure that pelvic floor muscle training programmes are as intensive as possible.	Strong
Consider posterior tibial nerve stimulation as an option for improvement of OAB/UUI in women who have not benefitted from anticholinergic medication.	Strong

Non-neurogenic Female LUTS

- Anticholinergic drugs and beta-3 agonist

Recommendations	Strength rating
Offer anticholineric drugs to woman 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, offering an alternative anticholinergic formulation, or the use of mirabegron (alone or in combination with an anticholinergic).	Strong
Encourage early review (of efficacy and adverse effects) of patients on anticholinergic medication for OAB.	Strong
Offer beta-3 agonists as an alternative to anticholinergics to women with OAB who fail conservative treatment.	Strong

Non-neurogenic Female LUTS

- Bladder wall injection of botulinum toxin A

Recommendations	Strength rating
Offer bladder wall injections of onabotulinum toxin A (100 U) to patients with OAB/UUI refractory to conservative therapy or drug treatment.	Strong
Warn patients of the limited duration of response, risk of UTI and possible prolonged need for clean intermittent self catheterisation prior to treatment with onabotulinum toxin A.	Strong

Non-neurogenic Female LUTS

- Sacral nerve stimulation

Recommendation	Strength rating
Offer sacral nerve stimulation to patients who have overactive bladder/urge urinary incontinence refractory to anticholinergic therapy.	Strong

- Laser treatment

Recommendation	Strength rating
Do not offer vaginal laser therapy to treat overactive bladder symptoms outside of a well regulated clinical research trial.	Strong

Non-neurogenic Female LUTS

- Cystoplasty/urinary diversion

Recommendations	Strength rating
Ensure patient counselling and lifelong support both prior to and after major surgery as a treatment for overactive bladder (OAB).	Strong
Offer augmentation cystoplasty to patients with OAB/UUI who have failed all other treatment options and have been warned about the possible small risk of malignancy.	Weak
Inform patients undergoing augmentation cystoplasty of the high risk of clean intermittent self-catheterisation (ensure they are willing and able to do so) and that they need life-long surveillance.	Strong
Do not offer detrusor myectomy as a treatment for UUI.	Weak
Only offer urinary diversion to patients who have failed less-invasive therapies for the treatment of OAB/UUI, who will accept a stoma and have been warned about the possible small risk of malignancy.	Weak

Management of Non-neurogenic Male LUTS

- Behavioral and Physical therapies
  - Bladder training, pelvic floor muscle training, electrical stimulation, posterior tibial nerve stimulation (PTNS)

Electrical stimulation may add benefit to PFMT up to six months.	2
Electrical stimulation may improve UI compared to sham up to six months.	2
There is limited evidence for the effectiveness of PTNS in male population.	2
There is no evidence that PTNS cures UUI in male population.	2

Management of Non-neurogenic Male LUTS

- Muscarinic receptor antagonists and Beta-3 agonist

Recommendations	Strength rating
Use muscarinic receptor antagonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Strong
Do not use antimuscarinic overactive bladder medications in men with a post-void residual volume > 150 mL.	Weak

Recommendation	Strength rating
Use beta-3 agonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Weak

Management of Non-neurogenic Male LUTS

- Combination therapies

Recommendations	Strength rating
Use combination treatment of a α1-blocker with a muscarinic receptor antagonist in patients with moderate-to-severe LUTS if relief of storage symptoms has been insufficient with monotherapy with either drug.	Strong
Do not prescribe combination treatment in men with a post-void residual volume > 150 mL.	Weak

Recommendations	Strength rating
Use combination treatment of a α1-blocker with mirabegron in patients with persistent storage LUTS after treatment with α1-blocker monotherapy.	Weak

Management of Non-neurogenic Male LUTS

- Bladder wall injection of botulinum Toxin A

Recommendations	Strength rating
Offer bladder wall injections of onabotulinum toxin A (100 U) to patients with overactive bladder/urgency urinary incontinence refractory to medical therapy.	Weak
Warn patients of the limited duration of response, risk of urinary tract infection and the possible prolonged need for clean intermittent self-catheterisation (ensure that they are willing and able to do so).	Strong

- Sacral nerve stimulation (neuromodulation)

Recommendation	Strength rating
Offer sacral nerve stimulation to patients who have urgency urinary incontinence refractory to medical therapy and are willing to undergo surgical treatment.	Weak

Management of Non-neurogenic Male LUTS

- Cystoplasty/urinary diversion

Recommendations	Strength rating
Offer augmentation cystoplasty to patients with overactive bladder (OAB)/urgency urinary incontinence (UUI) who have failed all other treatment options and are able and willing to perform self-catheterisation.	Weak
Inform patients undergoing augmentation cystoplasty of the high risk of complications; the risk of having to perform clean intermittent self-catheterisation and the need for life-long surveillance.	Strong
Only offer urinary diversion to patients who have failed less invasive therapies for the treatment of OAB/UUI, who will accept a stoma.	Weak

Summary in current OAB treatment

- Lifestyle interventions
- Behavioral and physical therapies
  - Bladder training, pelvic floor muscle training, electrical stimulation, acupuncture, posterior tibial nerve stimulation (PTNS)
- Drug treatments
  - Anticholinergic drugs and beta-3 agonist
  - Intravesical drug treatment
- Botulinum toxin injections in the bladder
- Sacral nerve stimulation
- Cystoplasty/urinary diversion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