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BUDDHIST TZU CHI GENERAL HOSPITAL, TAIPEI BRANCH

# 膀胱過動症 (Overactive bladder)

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# Outline

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





# 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



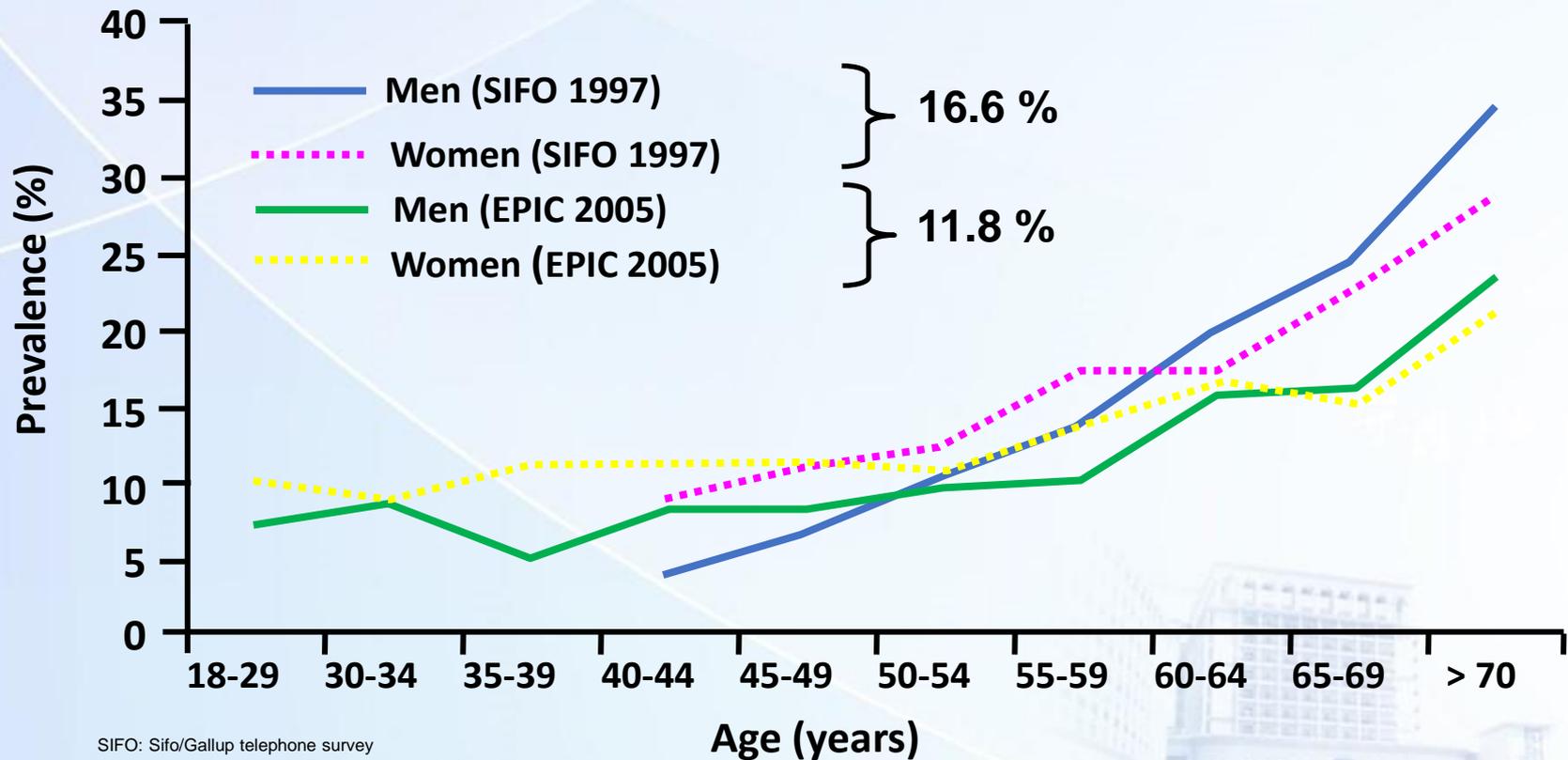


# Definition & Terminology

- 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



# 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

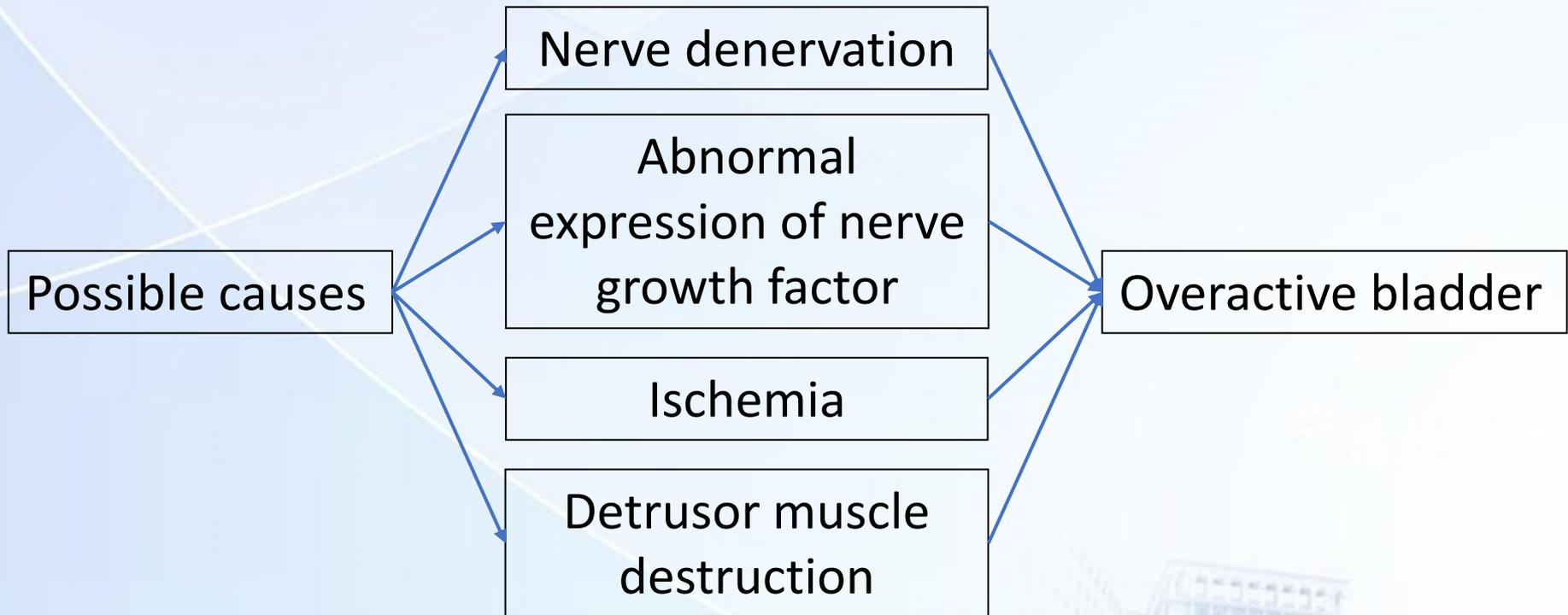


# Pathophysiology

- 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

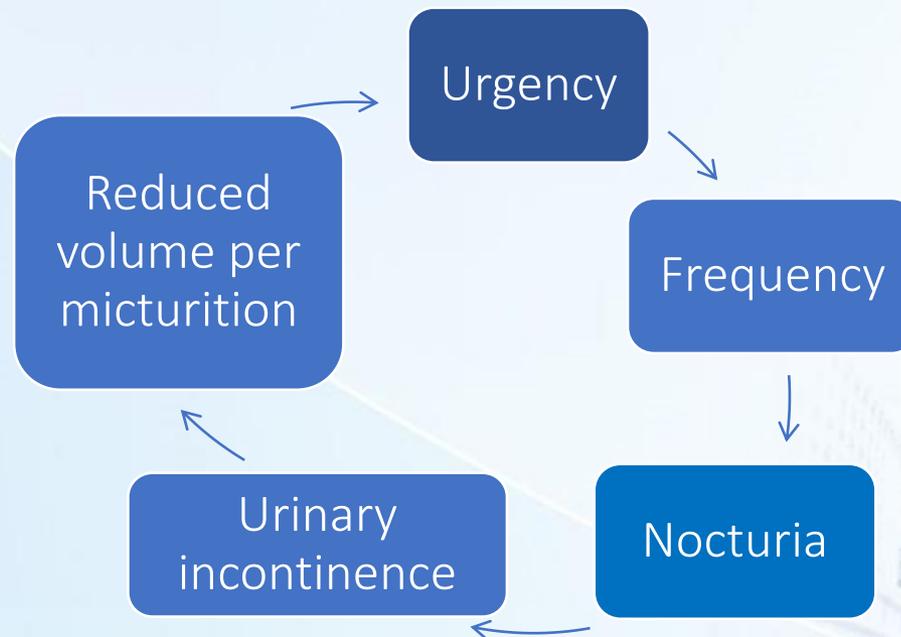




# Diagnosis

- Symptoms

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







# 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)
  - $\beta$ -3 agonist (Standard)
  - Extended release should be preferentially offered (Recommendation)
  - Transdermal oxybutynin



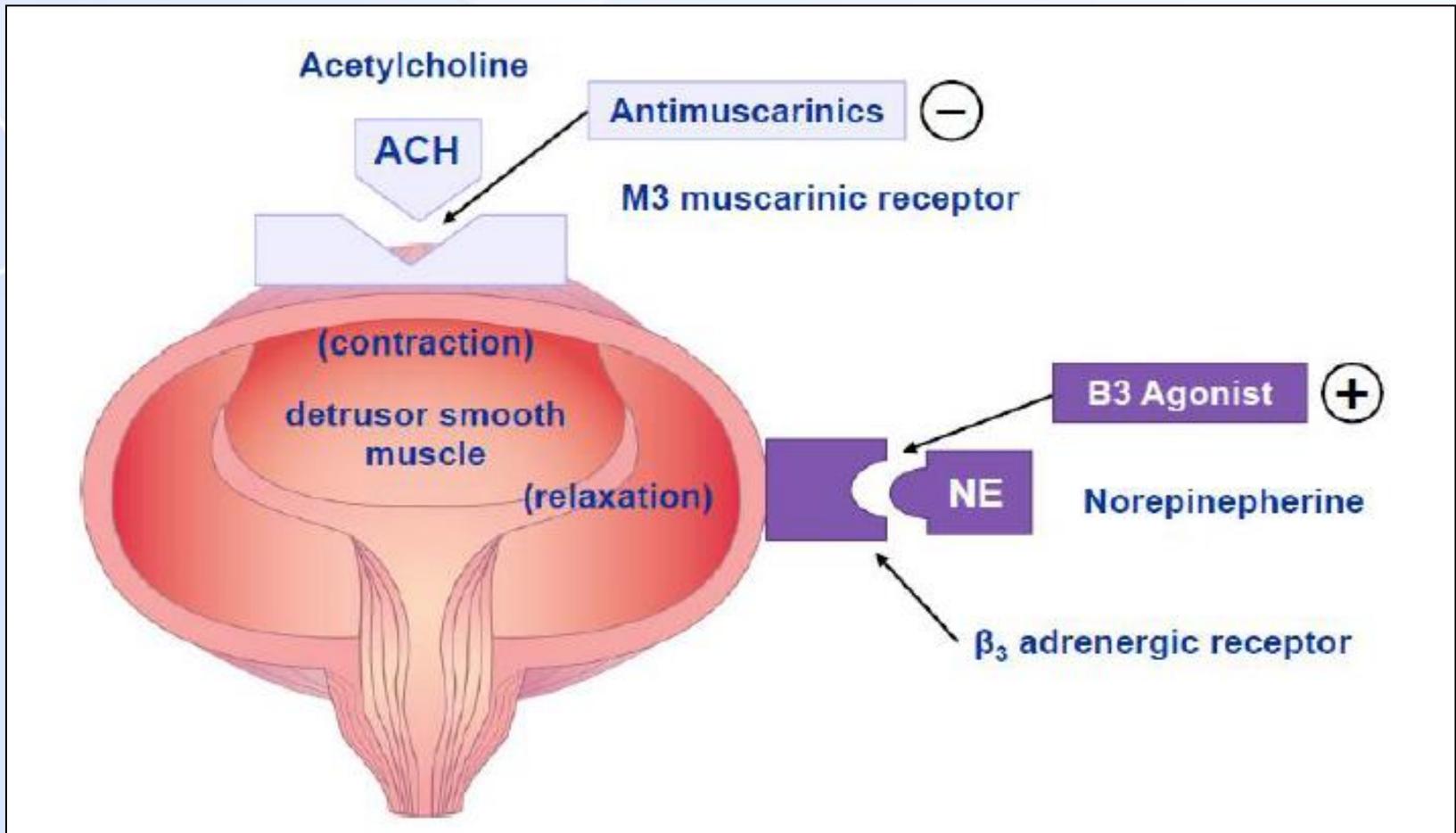


# Treatments

- 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)**
- $\beta$ -3 adrenergic agonist
  - 2015- **Mirabegron (Betmiga)**
- Flavoxate (平滑肌鬆弛劑) (Grade D)
- Imipramine (三環抗憂鬱劑) (Grade C)

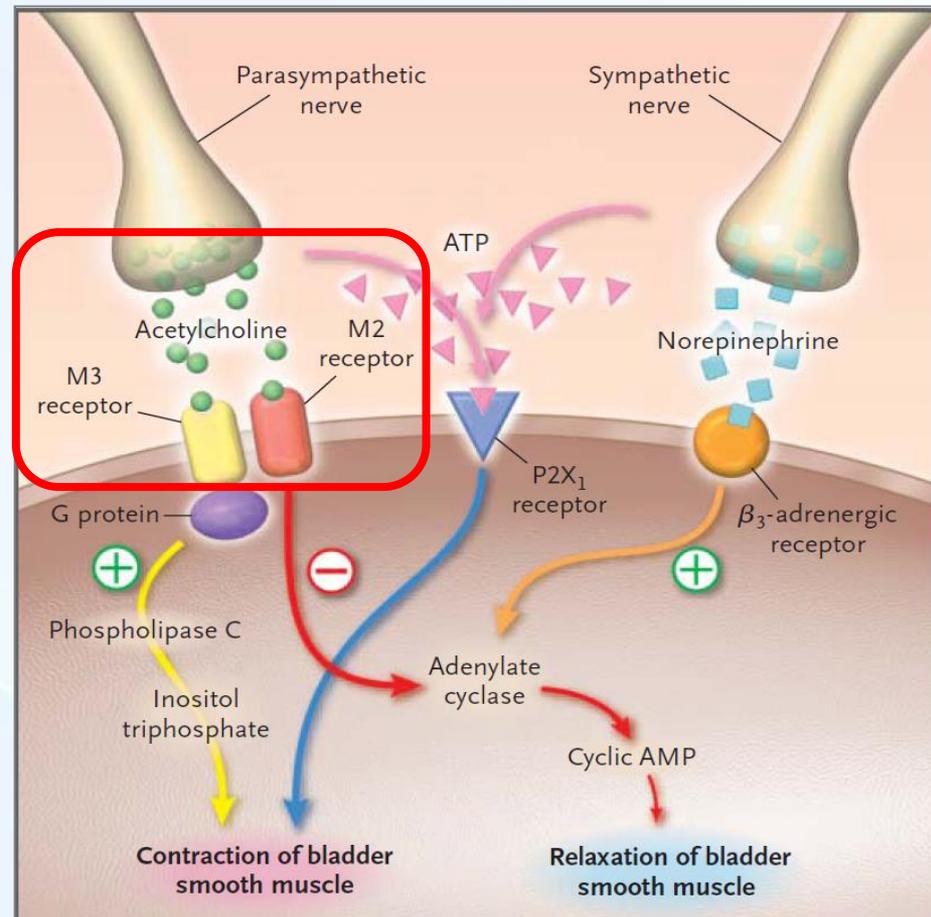


- Parasympathetic pathway

- Muscarinic receptor M2 and M3 → Bladder contraction

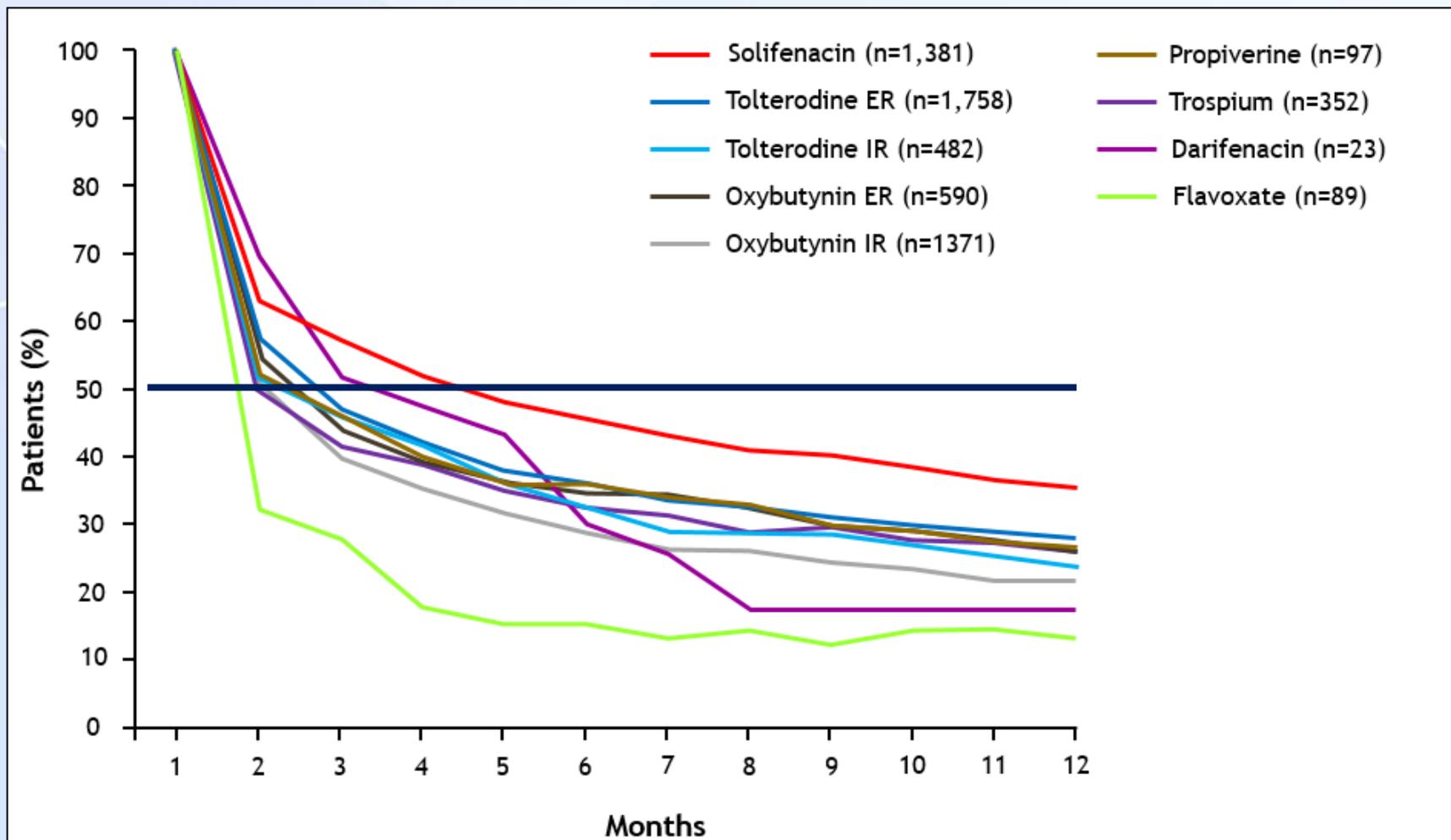
- Antimuscarinics

- Solifenacin (Vesicare)
- Tolterodine (Detrusitol)
- Trospium (Uracare)
- Oxybutynin (Dipropan)
- Propiverine (Urotrol)
- Flavoxate



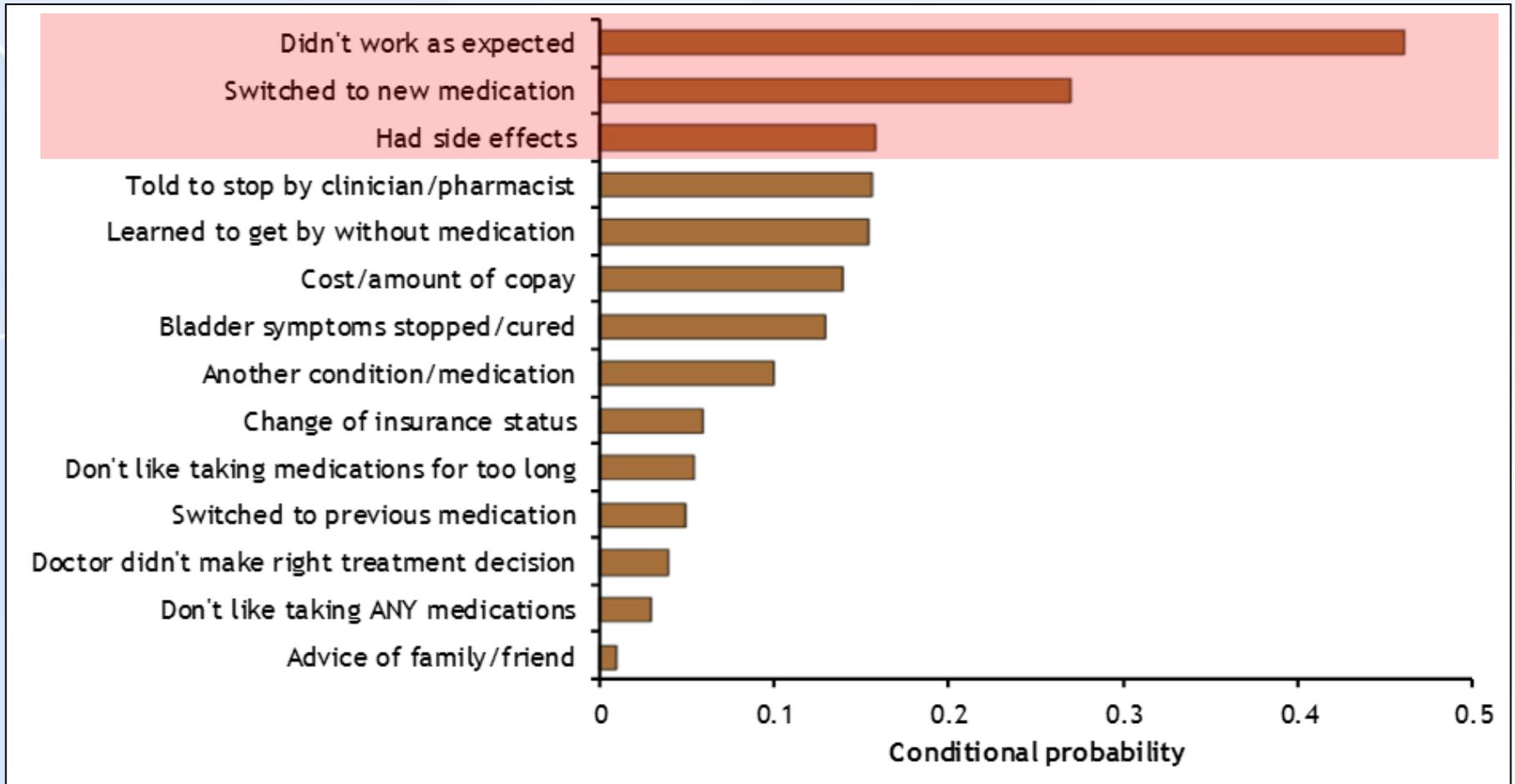


# Adherence to Antimuscarinics





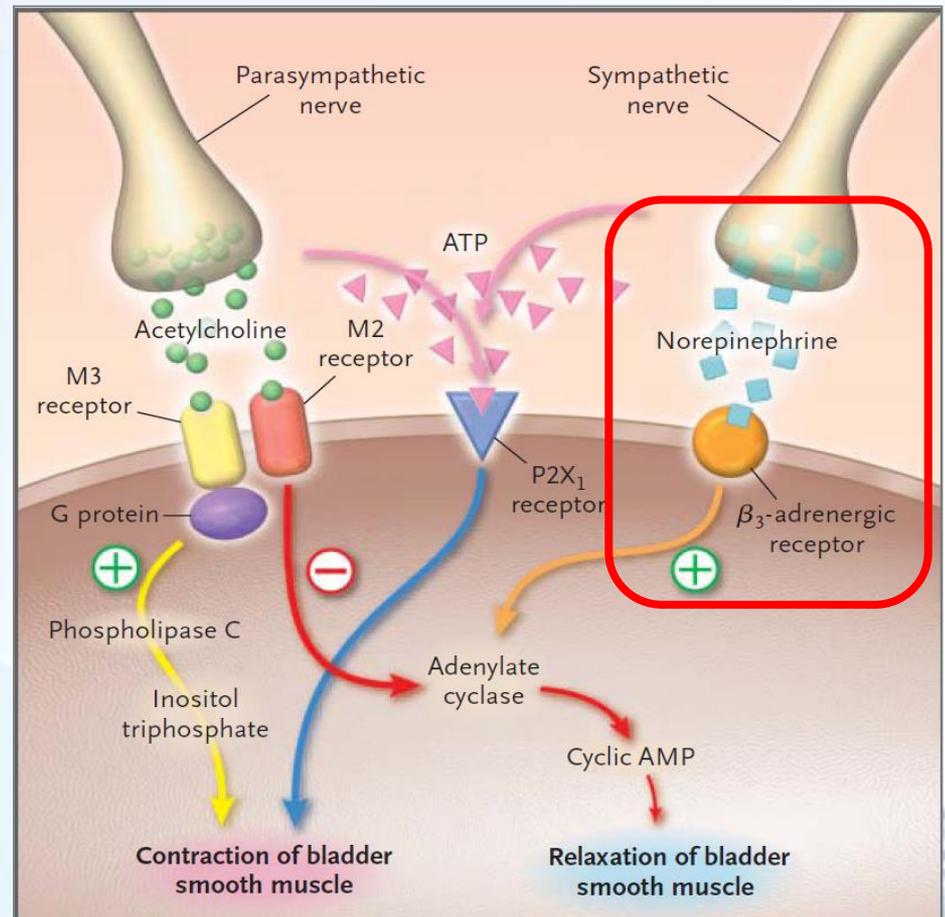
# Why Discontinue?





- Sympathetic pathway

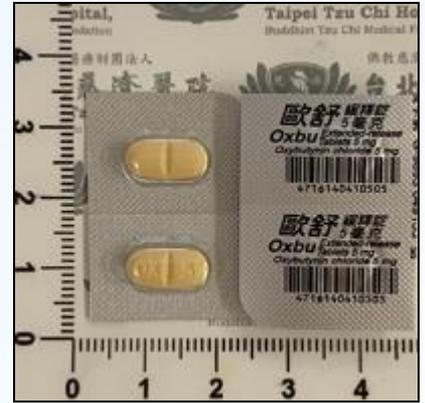
- $\beta_3$ -adrenergic receptor → Bladder relaxation
- $\beta_3$ -agonist
  - Mirabegron (Betmiga)





# Oxibu ER 5mg/tab (Oxybutynin)

- 中文：歐舒緩釋錠
- 廠商：健喬信元醫藥生技股份有限公司
- 適應症：治療伴有急尿、頻尿或急迫性尿失禁症狀的膀胱過動症
- 劑量：起始5~10mg，最高30mg/每天一次
- 副作用：
  - 胃腸道：口腔乾燥症(35~72%)、便秘(9~15%)、噁心(5~12%)
  - 中樞神經(10%)：頭暈、嗜睡、頭痛、失眠
  - 心血管(1~5%)：血壓降低、水腫、血壓升高、心悸、心律不整
  - 泌尿生殖道(1~5%)：解尿困難、尿滯留、尿路感染、殘尿增加





# Detrusitol 2mg/tab (Tolterodine)

- 中文：得舒妥
- 廠商：輝瑞大藥廠股份有限公司
- 適應症：治療伴有急尿、頻尿或急迫性尿失禁症狀的膀胱過動症
- 劑量：2mg/每天兩次
- 副作用：
  - 胃腸道：口腔乾燥症(35%)、便秘(7%)、腹痛/腹瀉/消化不良(4%)
  - 中樞神經(1~5%)：頭痛、頭暈、疲勞、嗜睡、焦慮症
  - 泌尿生殖道(1~2%)：解尿困難





# Propiverine (Urotrol) 15mg/FC tab

- 中文：優合膜衣錠
- 廠商：健亞生物科技股份有限公司
- 適應症：
  - 尿失禁
  - 不穩定性膀胱狀態之尿急及頻尿
- 劑量：15mg/每天2~3次
- 副作用：
  - 口乾、視覺模糊、胃腸不適、疲倦、低血壓





# Solifenacin (Vesicare) 5mg/tab

- 中文：衛喜康膜衣錠
- 廠商：台灣安斯泰來製藥股份有限公司
- 適應症：對於膀胱過動症病人所伴隨之急迫性尿失禁、頻尿、尿急等之症狀性治療
- 劑量：5mg/每天一次
- 副作用：
  - 胃腸道：口腔乾燥症(11~28%)、便秘(5~13%)、腹痛/噁心/消化不良(3%)
  - 視力模糊(4~5%)、乾眼症(2%)
  - 尿路感染(3~5%)、尿滯留(1%)





# Mirabegron 50 mg/tab (Betmiga)

- 中文：貝坦利持續性藥效錠
- 廠商：台灣安斯泰來製藥股份有限公司
- 適應症：治療伴有急尿、頻尿和/或急迫性尿失禁症狀的膀胱過動症
- 劑量：50mg/每天一次
- 副作用：
  - 心血管：高血壓(10%)、心搏過速(2%)
  - 中樞神經系統(1~4%)：頭痛、頭暈
  - 泌尿系統感染(3~6%)
  - 胃腸道(1~4%)：便秘、口乾、腹瀉、腹痛
  - 呼吸道(3~4%)：鼻咽炎、鼻竇炎





# 禁忌症

- 抗毒蕈鹼藥物
  - 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
- $\beta_3$ -腎上腺素受體活化劑
  - 嚴重未控制的高血壓
  - 收縮壓 $>180\text{mmHg}$ 或舒張壓 $>110\text{mmHg}$



# Botulinum toxin type A (BOTOX) 100U/vial

- 中文：保妥適乾粉注射劑
- 廠商：台灣愛力根藥品股份有限公司
- 適應症：
  - 因脊髓病變所引起的逼尿肌過動而導致尿失禁之成人病患，且經抗膽鹼類藥物治療無效或無法耐受者。治療有尿失禁、尿急與頻尿等膀胱過動症的成人病患，經抗膽鹼類藥物治療反應不佳或無法耐受必須停藥，且如有需要時，願意及能夠於治療後進行乾淨間歇性導尿者。
- 劑量：200~300U/次



## Botulinum toxin type A (BOTOX) 100U/vial

- 禁忌症：對於罹患尿道感染的病患，以及未定期進行乾淨間歇性導尿(CIC)的急性尿滯留及排尿後餘尿量超過200mL的病患而言，不應投與
- 副作用：膀胱功能障礙
  - 尿路感染(18~49%)、血尿(4%)
  - 排尿困難(4~9%)、殘餘尿量增加(3%，不需導尿)、尿滯留(6~17%)
- 70% improvement, need repeat injection

感謝聆聽

