# PHARMACAL TREATMENT FOR OAB

DATE: 111.2.23
SPEAKER: Dr. 張嘉珮

# DEFINITION OF OAB

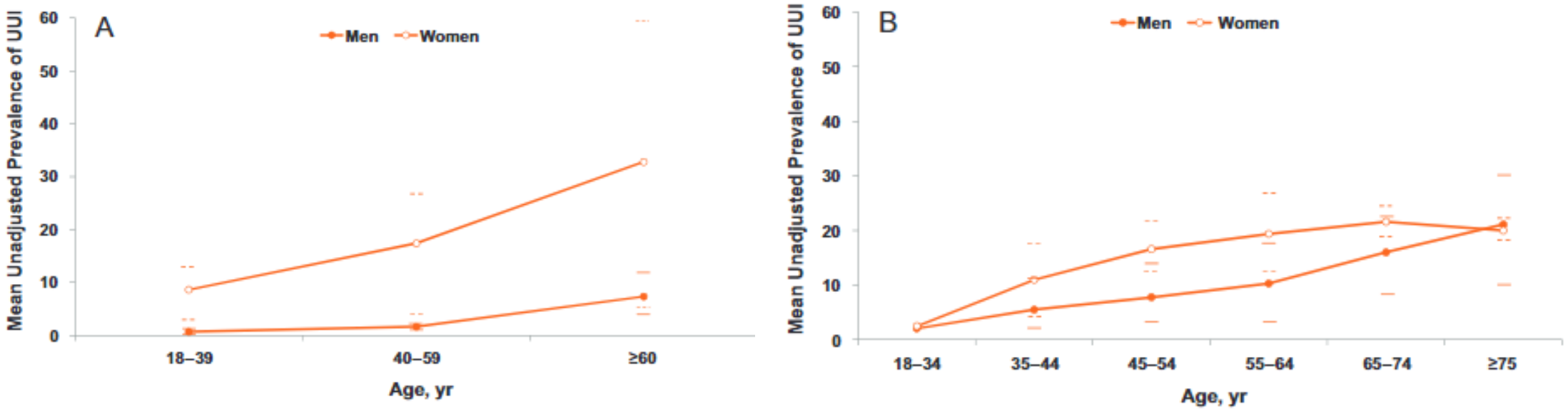
**OAB is syndrome or symptom complex defined as:**
"**Urgency,** with or without **urgency incontinence**, usually with **frequency and nocturia.**"

Urgency is the key symptom of OAB

Urgency is defined as "a sudden compelling desire to void, which is difficult to defer"

AbramsP, et al. *Urology.*2003;61:37-49. Rosenberg MT, et al*. Int J Clin Pract.* 2007;61:1535-1546.

# PREVALENCE




The individual study data and the unadjusted mean prevalence estimates across studies demonstrate that the prevalence of UUI increases with age.

I. Milsom, K.S. Coyne, S. Nicholson, M. Kvasz, C.-I. Chen, A.J. Wein**Global prevalence and economic burden of urgency urinary incontinence: a systematic review** Eur Urol, 65 (2014), pp. 79-95

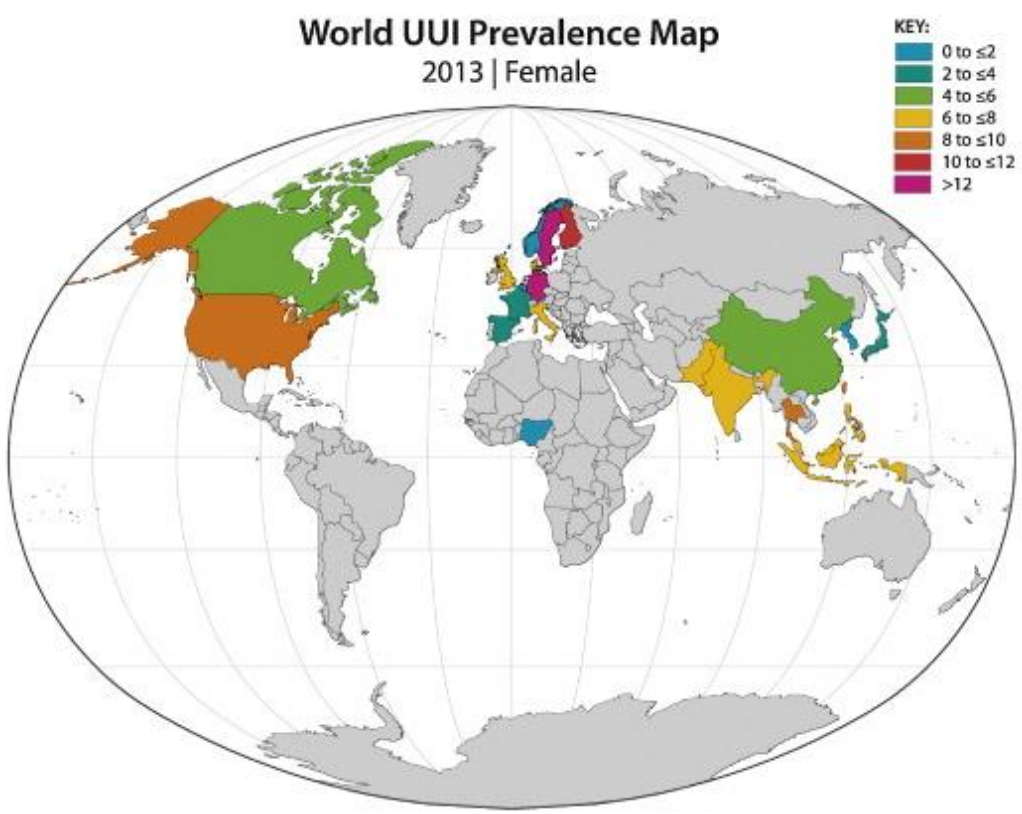
# PREVALENCE

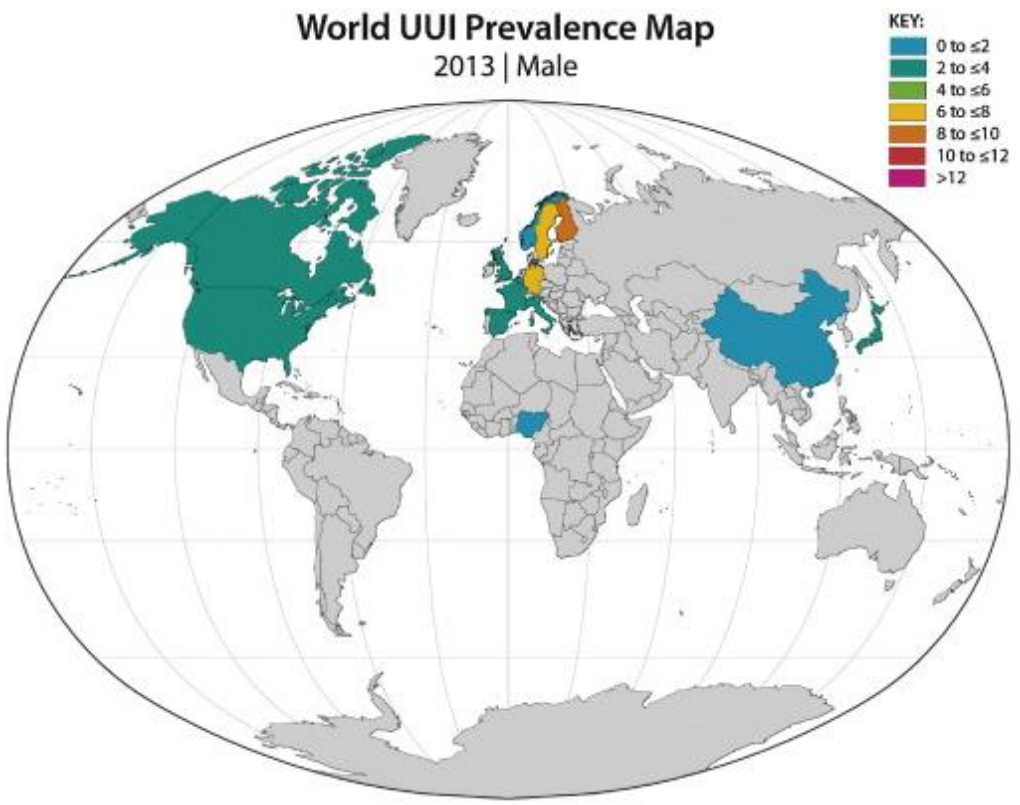
In 54 articles (50 studies); 22 large-scale

population-based surveys indicated varying UUI prevalence estimates with ranges of

- 1.8 ~30.5% in European populations
- 1.7 ~36.4% in US populations
- 1.5 ~15.2% in Asian population

I. Milsom, K.S. Coyne, S. Nicholson, M. Kvasz, C.-I. Chen, A.J. Wein**Global prevalence and economic burden of urgency urinary incontinence: a systematic review** Eur Urol, 65 (2014), pp. 79-95




Rates of UUI were **relatively high** for both men and women in **Germany, Sweden, and Finland**

UUI prevalence was **higher in women** than in men in all countries(Japan (men: 4.0%; women: 3.6%))

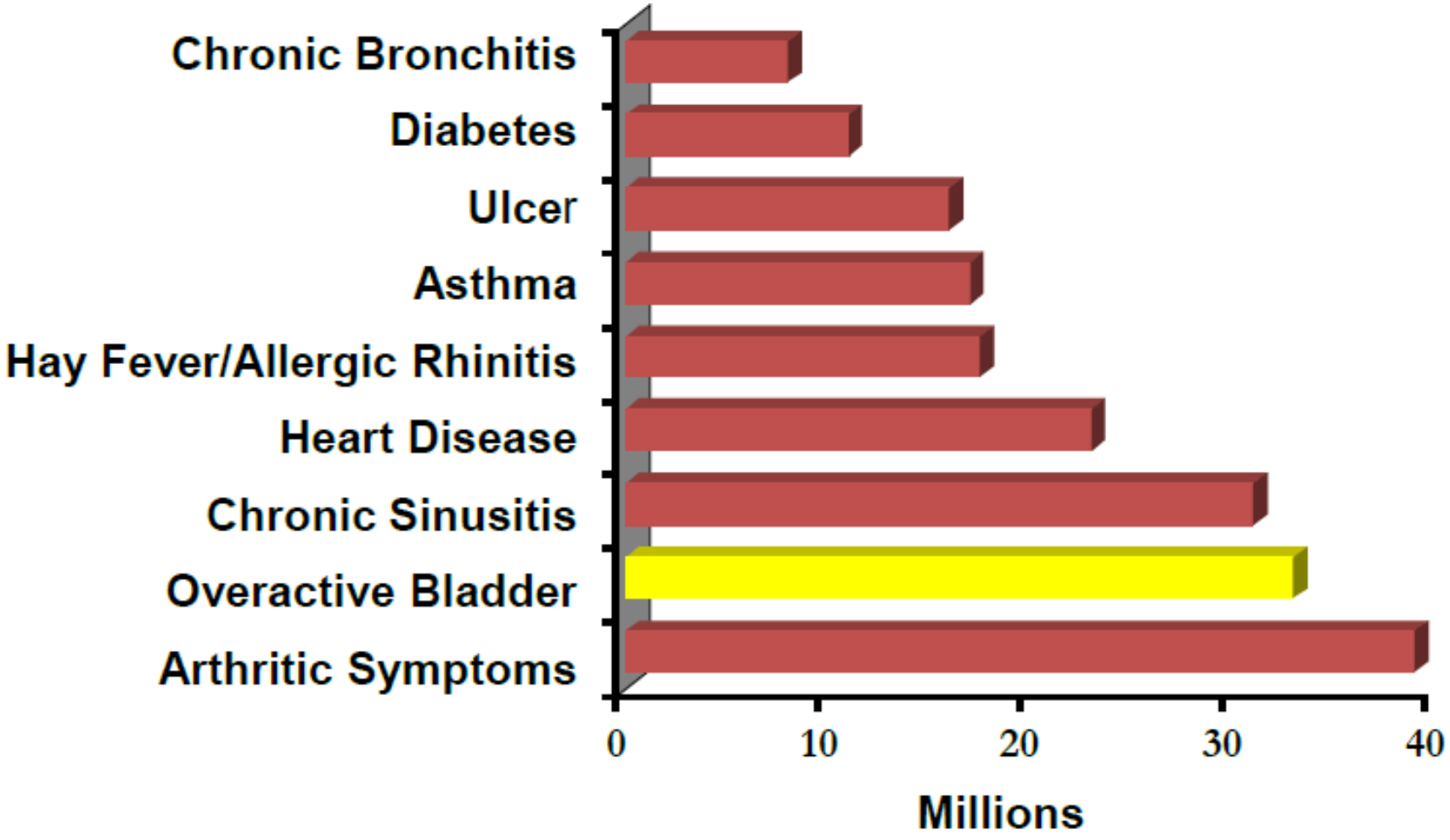
Data from Asian countries: M < F

Few or no data from large-scale studies on UUI prevalence in men and women from **Africa, Australia, western Asia, Central America, eastern Europe, and South America.**



I. Milsom, K.S. Coyne, S. Nicholson, M. Kvasz, C.-I. Chen, A.J. Wein**Global prevalence and economic burden of urgency urinary incontinence: a systematic review** Eur Urol, 65 (2014), pp. 79-95

# OAB & OTHER DISORDERS




Stewart WF, et al. *World J Urol*. 2003;20(6):327-336. PleisJR, Coles R. Summary health statistics for U.S. adults: National Health Interview Survey, 1998. V*ital Health Stat 10*. 2002;209:1-113. Centers for Disease Control and Prevention/National Center for Health Statistics. Vital and Health Statistics. Hyattsville, MD: U.S. Department of Health and Human Services; 1997. DHHS Publication No. (PHS) 97-1522. «http://www.cdc.gov/nchs/data/series/sr_10/sr10_194.pdf».

# MANAGEMENT AND TREATMENT

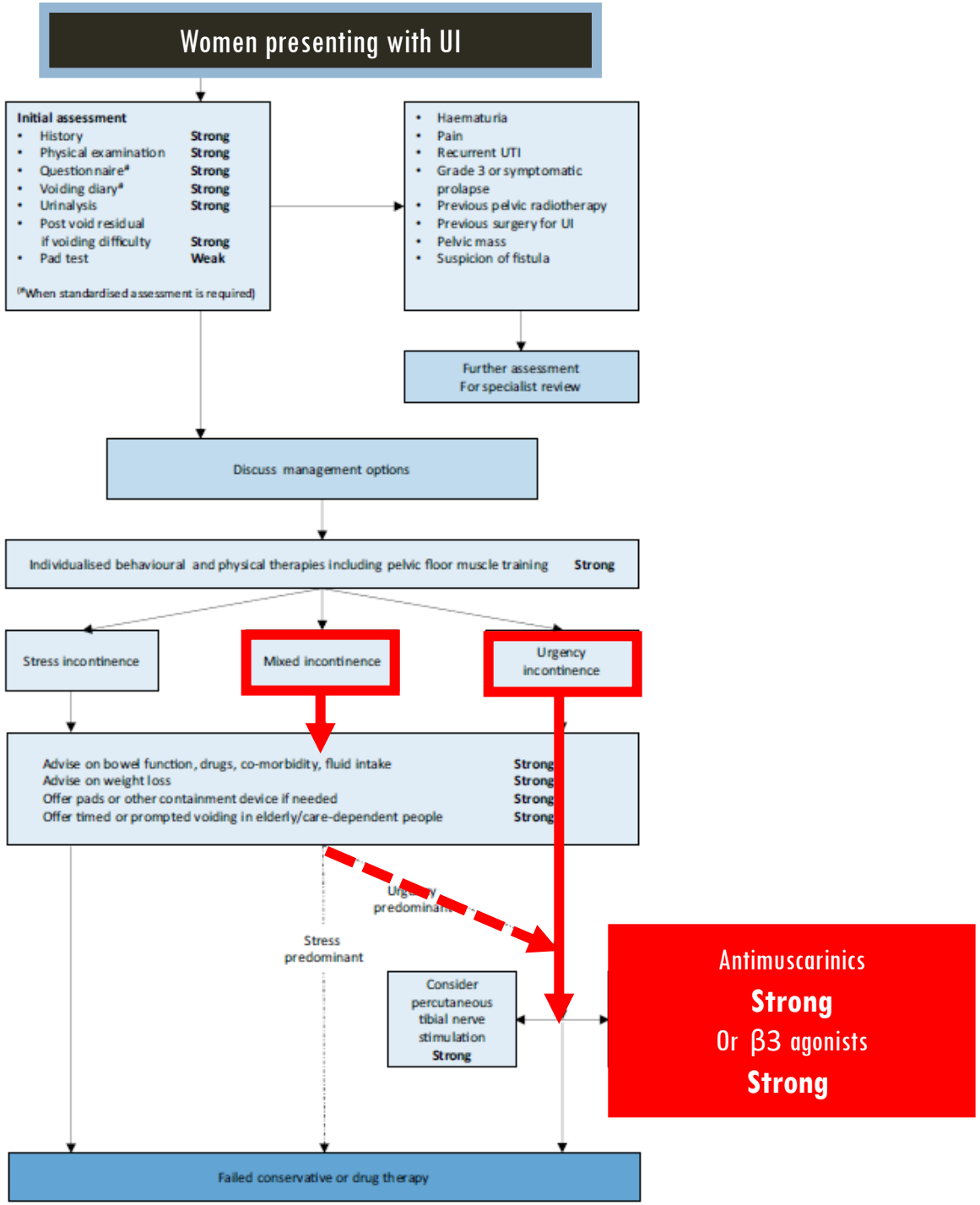
The AUA and FUSA guidelines from 2019 categorize the management of OAB into four steps :

- 1st line treatments – Conservative management;
- 2nd line treatments- pharmacologic therapy;
- 3rd line treatments- Intradetrusor onabotulinumtoxin A injections, sacral neuromodulation and peripherical tibial nerve stimulation;
- 4th line treatments: Augmentation Cystoplasty and Urinary Diversion .

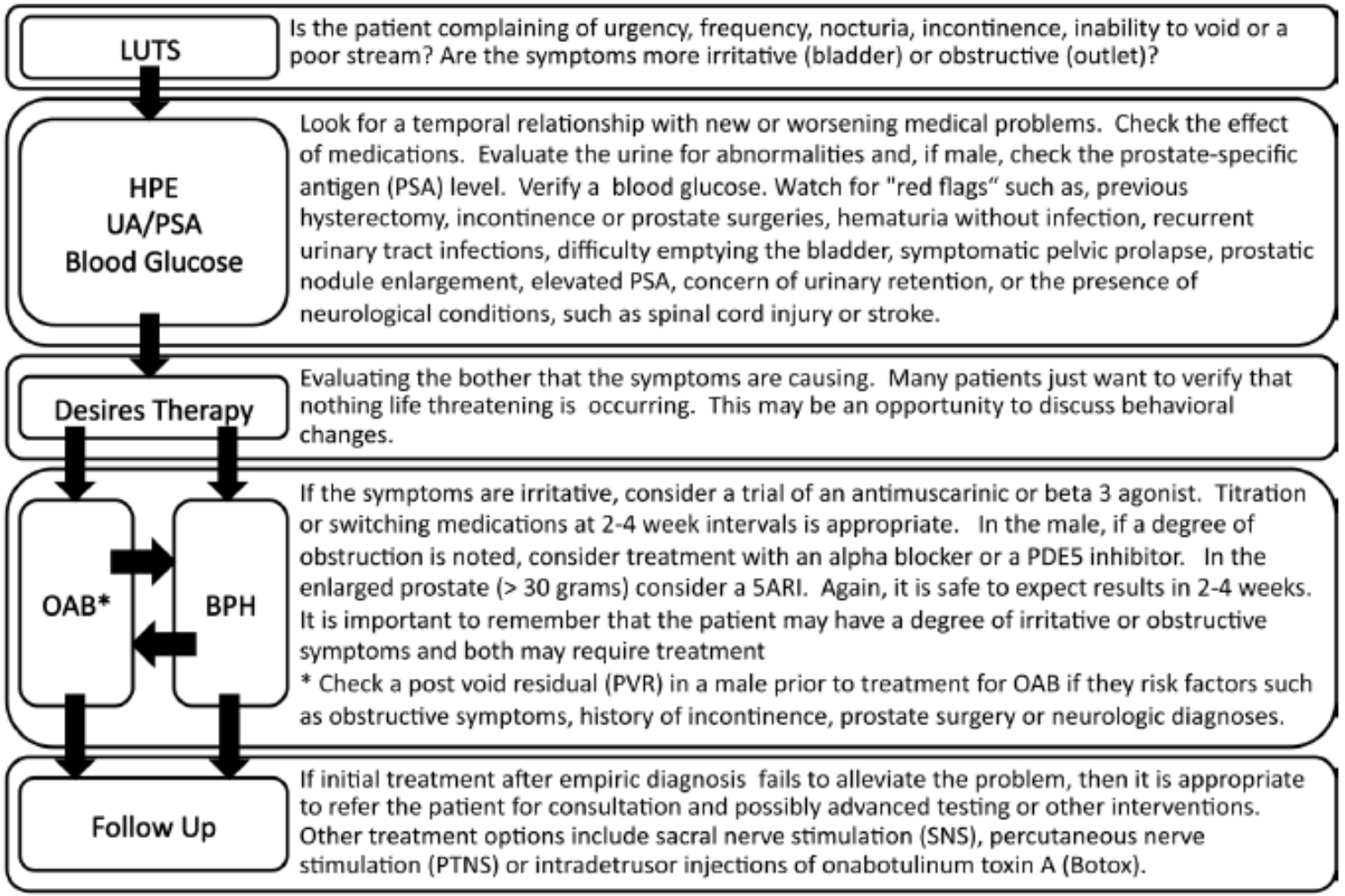
D.J. Lightner, A. Gomelsky, L. Souter, S.P. Vasavada**Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment 2019** J Urol, 202 (2019), pp. 558-563

European Association of Urology

# 2021 EAU GUIDELINES ON URINARY INCONTINENCE IN ADULTS



# PRACTICAL APPROACH IN EVALUATING THE PTS WITH OAB






*The Canadian Journal of Urology™; 21(Supplement 2); June 2014*

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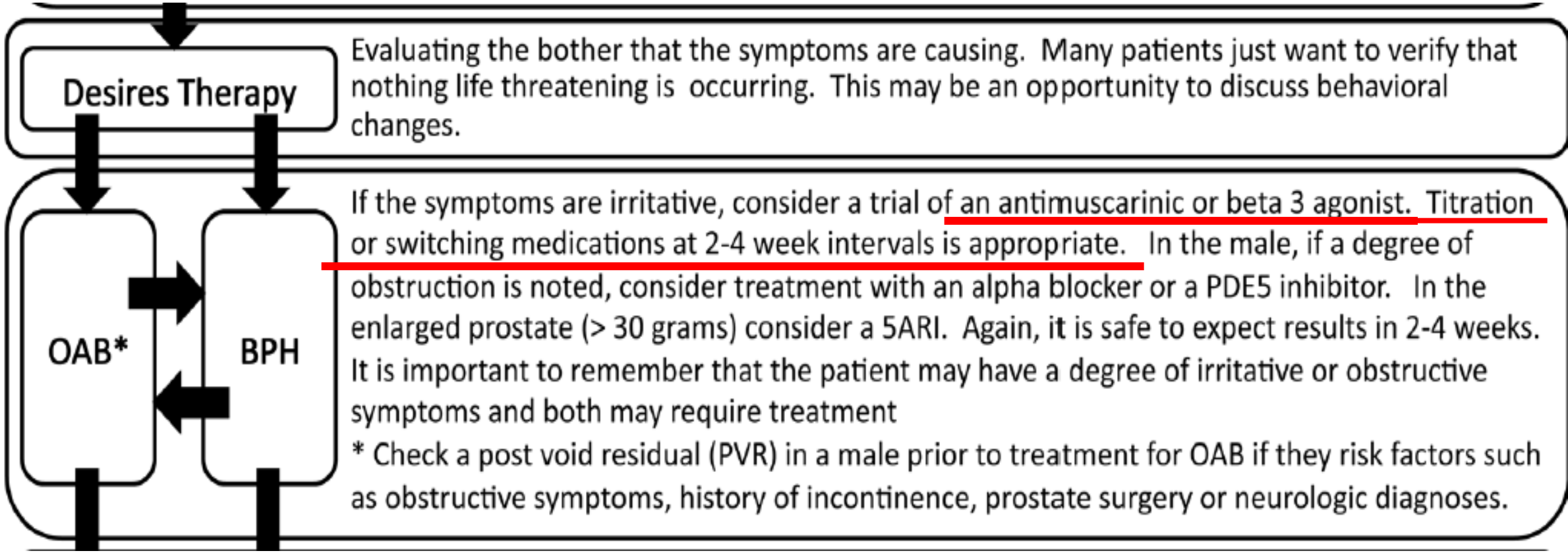





*The Canadian Journal of Urology™; 21(Supplement 2); June 2014*

# GUIDELINES

**2020 EAU** Guidelines on urinary incontinence:

**Consider** **extended release formulations** of antimuscarinic drugs whenever possible (Strength Rating: Strong)

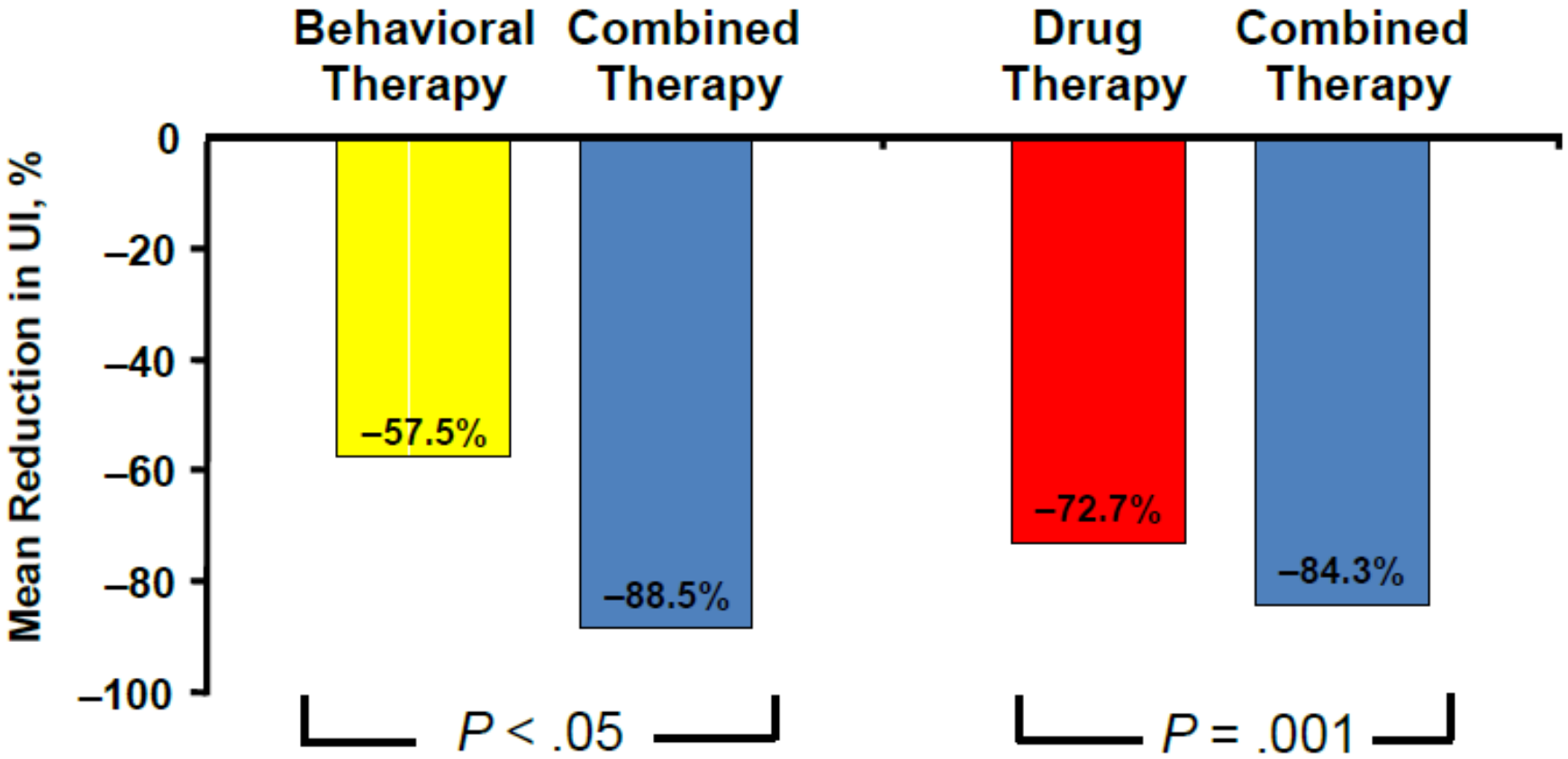
**2019 AUA/SUFU** Guidelines on OAB:

**ER formulations** should **preferentially** be prescribed over IR formulations because of lower rates of dry mouth(Grade B)

**2019 NICE** Guidelines on urinary incontinence:

Do not offer **oxybutynin (immediate release)** to **the elderly** who may be at higher risk of a sudden deterioration in their physical or mental health (強調是針對IR劑型!!)

# ADDITIVE EFFECT OF COMBINING BEHAVIORAL AND DRUG THERAPY




BurgioKL, et al. *J Am GeriatrSoc.*2000;48:370-374.

# PHARMACOLOGIC MANAGEMENT

6 antimuscarinics

1 beta-3 adrenergic agonist

All medications have been proven effective for OAB treatment

Choice is based of efficacy, dose flexibility, adverse event profiles and drug interactions.

Finney SM, et al. *BJU Int.*2006;98:503-507. Chapple C, et al. *EurUrol*. 2005;48:5-26. Myrbetriq™ (mirabegron) prescribing information, AstellasPharma US, Inc. June 2012. Rosenberg M, Newman DK, Tallman CT, et al. *Cleve ClinJ Med.*2007;74(suppl3):S21-S29. *Physcians' Desk Reference*. 64st ed. Montvale, NJ: Thomson PDR; 2010.

# ANTIMUSCARINICS—EXTENDED RELEASE

TABLE 3. **Medications for overactive bladder**[20]

| Drug | Brand name | Dose | Dosing | Indications |
|---|---|---|---|---|
| **Antimuscarinics - immediate release (IR)** | | | | |
| Oxybutynin IR | Ditropan | 5 mg | 2-4 x/day | OAB |
| Tolterodine IR | Detrol | 1 mg-2 mg | Twice daily | OAB |
| Trospium chloride | Sanctura (US)<br>Trosec (Canada) | 20 mg | Twice daily | OAB |
| **Antimuscarinics - extended release (ER)** | | | | |
| Darifenacin ER | Enablex | 7.5 mg, 15 mg | Daily | OAB |
| Fesoterodine ER | Toviaz | 4 mg, 8 mg | Daily | OAB |
| Oxybutynin ER | Ditropan XL | 5 mg-30 mg | Daily | OAB |
| Oxybutynin TDS | Oxytrol | 3.9 mg = 1 patch | Twice weekly | OAB |
| Oxybutynin 10% gel | Gelnique | 100 mg = 1 g of gel | Daily | OAB |
| Solifenacin | Vesicare | 5 mg, 10 mg | Daily | OAB |
| Tolterodine ER | Detrol LA | 2 mg-4mg | Daily | OAB |
| Trospium chloride | Sanctura XR (US) | 60 mg | Daily | OAB |
| **Beta 3 agonists** | | | | |
| Mirabegron | Myrbetriq | 25 mg, 50 mg | Daily | OAB |

# FOLLOW UP ON THE PATIENT TREATED FOR OAB

Review the patient after 2 –4 weeks

--Be prepared to titrate as studies show > 50 % will increase dose if given the option

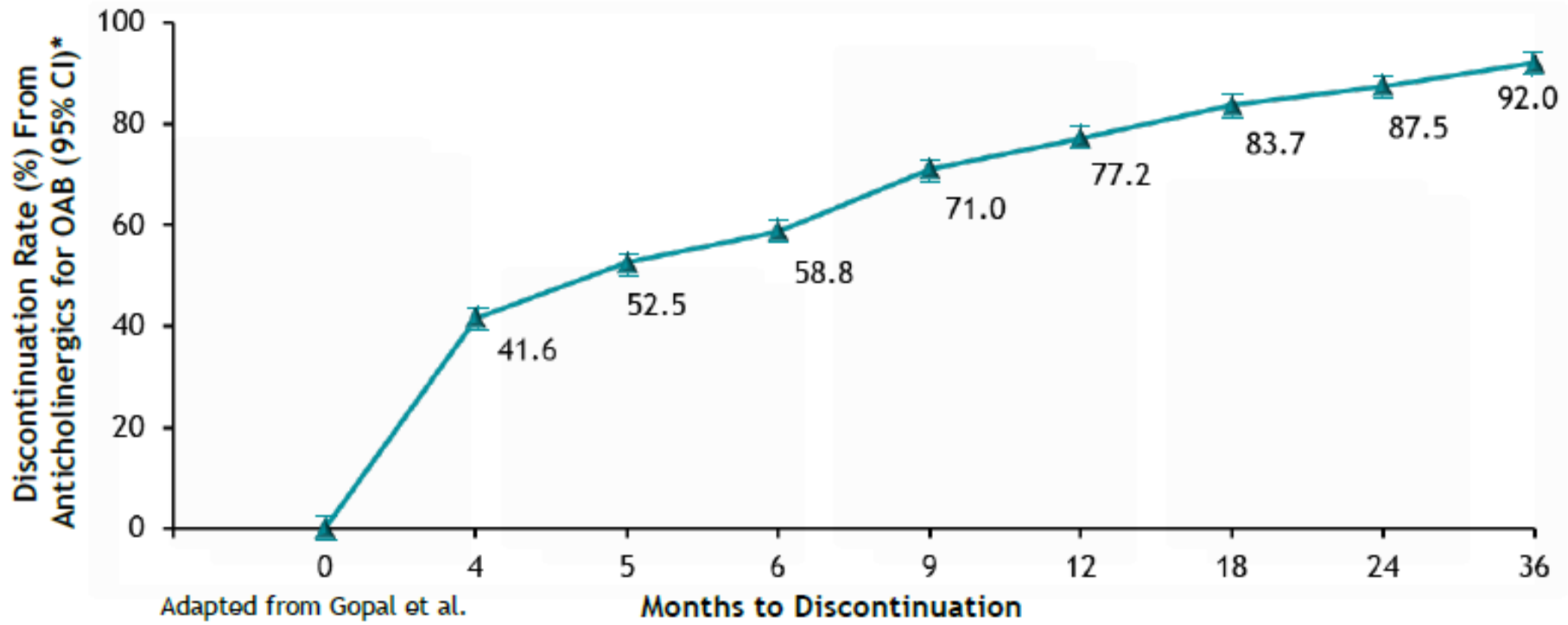
--Be prepared to try different agent or class

Consider checking PVR to ensure volume not increasing significantly in the complex patient

--Studies on medication usage in males show safety and minimal increase in post void residual over time of follow up

--The risk of urinary retention (although low) is highest during the first 30 days of treatment

# HIGH DISCONTINUATION RATE FOR PATIENTS ON OAB THERAPY




**Study Design:**UK study. Overall drug discontinuation for all women prescribed anticholinergic medications (N=29,369). Unadjusted cumulative incidence of discontinuation (95% CI).

*Cumulative incidence of discontinuation was determined using the Kaplan-Meier method.GopalM, et al. *ObstetGynecol.* 2008;112:1311-1318.

# IMPROVING PATIENT ADHERENCE BY ADDRESSING EXPECTATIONS

Effects on urgency

Limiting incontinence

Decreasing nocturia

Improved quality of life

Tolerability of medication

Rosenberg MT. *Cur Uro*2008, 9:428–432.DeCastroJ, et al. *Am J Med*.2008;121:S27-S33.

ORIGINAL PAPER

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

# Prescription pattern of oxybutynin ER in patients with overactive bladder in real life practice: a multicentre, open-label, prospective observational study

D.-S. Yoo,[1] J.-Y. Han,[1] K.-S. Lee,[2] M.-S. Choo[1]

Aims of study:

To investigate the prescription pattern and dose distribution of the antimuscarinic agent oxybutynin extended release (ER) in patients with overactive bladder (OAB) in actual clinical practice.

ORIGINAL PAPER

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Materials and methods:

- In this multicentre, prospective, observational, flexible-dosing study, the dosage of oxybutynin ER for each patient was **adjusted after discussions of efficacy and tolerability between doctor and patient**, over a 12 week treatment period.
- Efficacy was measured by administering the **Primary OAB Symptom Questionnaire (POSQ)** before and after treatment. Patients were also administered, the **patient perception of treatment benefit (PPTB)** questionnaire at the end of the study. Adverse events (AE) were documented at each study visit.

# RESULTS:

- Of the 809 patients enrolled, 590 (73.2%) continued to take study medication for 12 weeks. Most patients were prescribed 5 (24.2%) or 10 (68.8%) mg/day oxybutynin ER at the start of treatment.
- Most were also prescribed 5 (19.1%) or 10 (67.4%) mg/day at the end of treatment, with a dose escalation rate of 14.9%.

**Table 3** Distribution and changes in prescribed oxybutynin doses

| Starting dose | Final dose | | | | | | Starting dose |
|---|---|---|---|---|---|---|---|
| | 5 mg/day | 10 mg/day | 15 mg/day | 20 mg/day | 25 mg/day | 30 mg/day | |
| 5 | 118 | 49 | 4 | 1 | | | 172 (24.2) |
| 10 | 17 | 424 | 22 | 24 | | 3 | 490 (68.8) |
| 15 | 1 | | 11 | 1 | | 2 | 15 (2.1) |
| 20 | | 7 | | 26 | | | 33 (4.6) |
| 25 | | | | | | | |
| 30 | | | | | | 2 | 2 (0.3) |
| Final dose | 136 (19.1) | 480 (67.4) | 37 (5.2) | 52 (7.3) | | 7 (1.0) | 712 (100) |

Dose escalation 14.9% (106/712), Dose maintenance 81.6% (581/712), Dose reduction 3.5% (25/712).

2011 Int J Clin Pract

# RESULTS:

All OAB symptoms evaluated by the POSQ were improved;
94.1% of patients reported benefits from treatment and
89.3% were satisfied.

**Table 4** Symptom scores evaluated by primary overactive bladder questionnaire at baseline and end-point

| | Mean symptom score | | | | |
|---|---|---|---|---|---|
| Symptoms | Baseline | End-point | Change from baseline to end-point | 95% CI | p-value |
| Urgency | 3.83 | 2.29 | −1.54 | −1.44, −1.65 | < 0.001 |
| Frequency | 3.36 | 2.16 | −1.21 | −1.10, −1.32 | < 0.001 |
| Nocturia | 3.25 | 2.14 | −1.12 | −1.00, −1.23 | < 0.001 |
| Urge incontinence | 2.99 | 1.87 | −1.12 | −0.98, −1.26 | < 0.001 |

2011 Int J Clin Pract

**Table 5** Adverse events of oxybutynin ER

| Adverse events | *n* | % |
|---|---|---|
| Dry mouth | 97 | 60.2 |
| Urinary disorder | 25 | 15.5 |
| urinary hesitation | 14 | 8.5 |
| dysuria | 9 | 5.6 |
| urinary retention | 2 | 1.2 |
| Constipation | 15 | 9.3 |
| Dyspepsia | 4 | 2.5 |
| Abdominal pain upper | 3 | 1.9 |
| Headache | 3 | 1.9 |
| Keratoconjunctivitis sicca | 3 | 1.9 |
| Blurred vision | 1 | 0.6 |
| Insomnia | 1 | 0.6 |
| Oedema | 1 | 0.6 |
| Others | 8 | 5.0 |
| Total | 161 | 100 |

ER, extended release.

在所有809 位患者中，

有161 位 **(19.9%)** 有副作用,其中最常見的是口乾(60.2%):

✓ 大部分的副作用程度**輕微 (76.5%)** 或中等 (20.8%)，

✓ 僅32 位(4 %)患者因副作用而中斷療程。

我們同時發現:

比過去Oxybutynin ER 試驗的 7.6 % 和6.7% **中斷率低!**

2011 Int J Clin Pract

# CONCLUSIONS:

Most patients were prescribed 5–10 mg/day oxybutynin ER as both starting and maintenance doses, with a dose escalation rate of only 14.9%.
Prescription of > 10 mg/day oxybutynin ER was not frequent in real life practice.

Individualised dosing with oxybutynin ER was associated with highly effective and well tolerated control of urinary incontinence in clinical trials.

Oxybutynin 彈性劑量(5~30mg)的方式，能為OAB 患者提供更為有效、安全和良好耐受性的治療!

Received: 22 May 2017 | Accepted: 21 August 2017
DOI: 10.1002/nau.23413

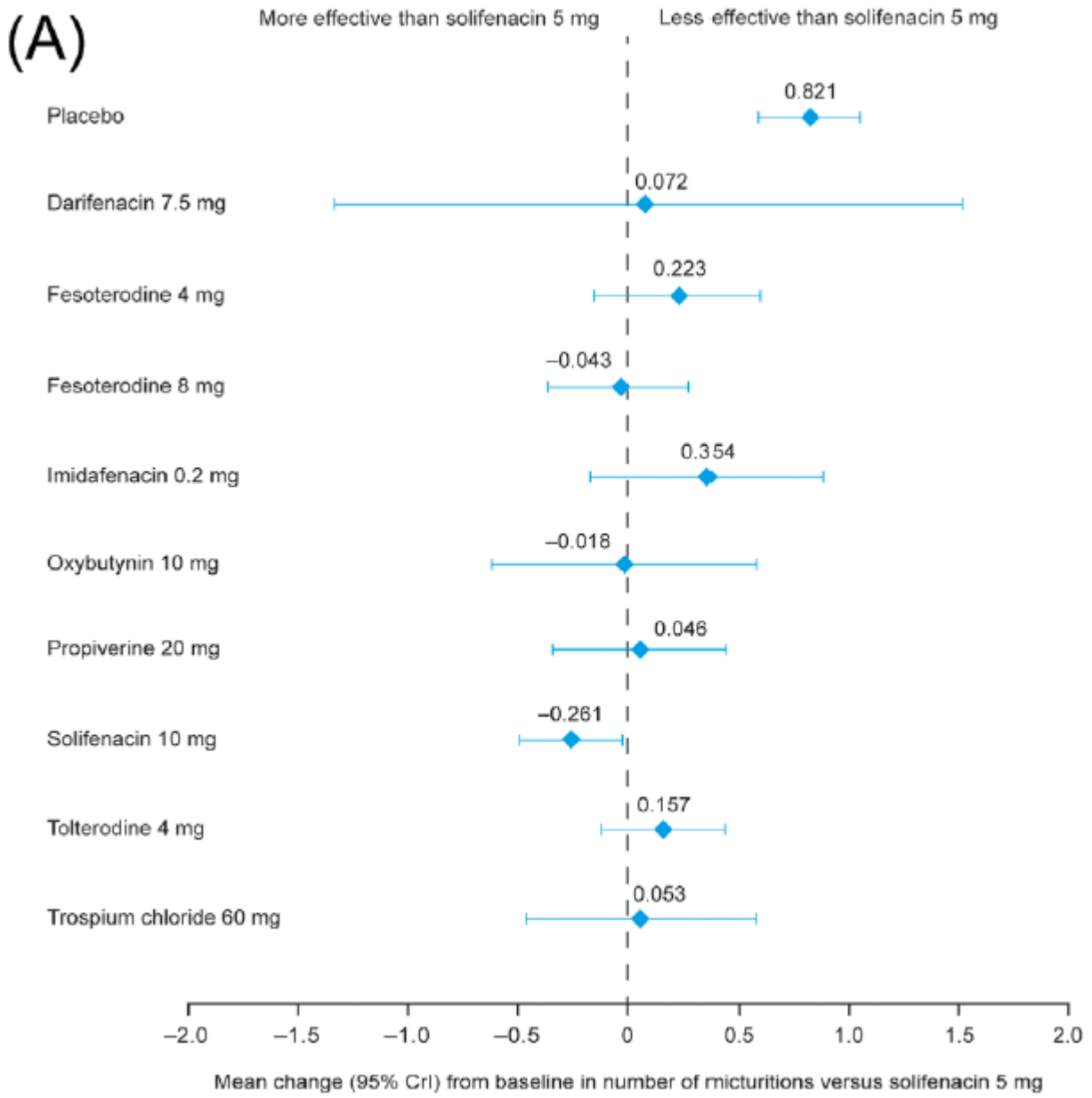
ORIGINAL BASIC SCIENCE ARTICLE

WILEY Neurourology Urodynamics ICS SUFU

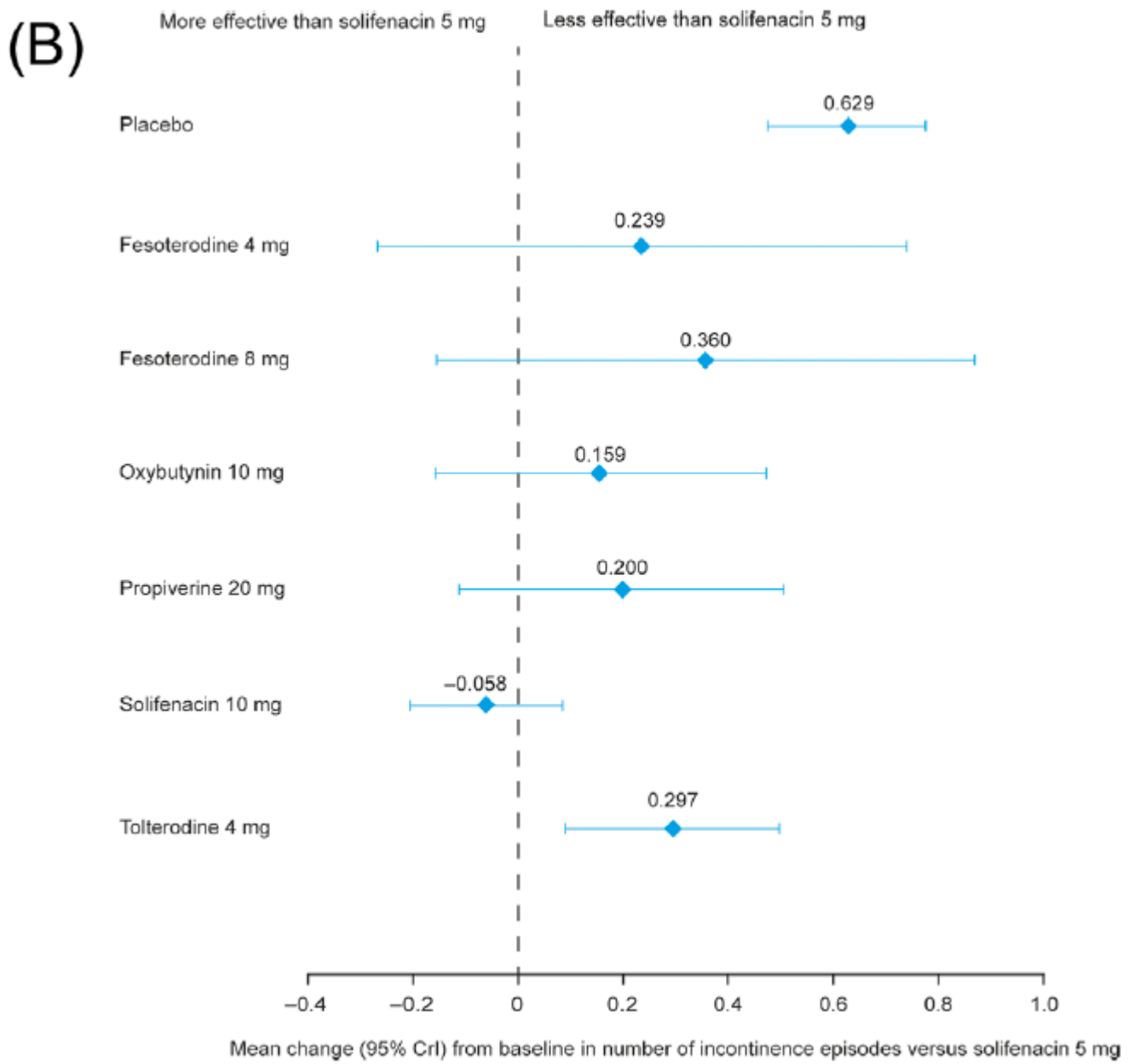
# Comparative efficacy and tolerability of solifenacin 5 mg/day versus other oral antimuscarinic agents in overactive bladder: A systematic literature review and network meta-analysis

Jameel Nazir PhD[1] | Con Kelleher MD, FRCOG[2] | Samuel Aballéa PhD[3] | Khaled Maman MSc[4] | Zalmai Hakimi PharmD[5] | Colette Mankowski PhD[1] | Isaac Odeyemi PhD[1]

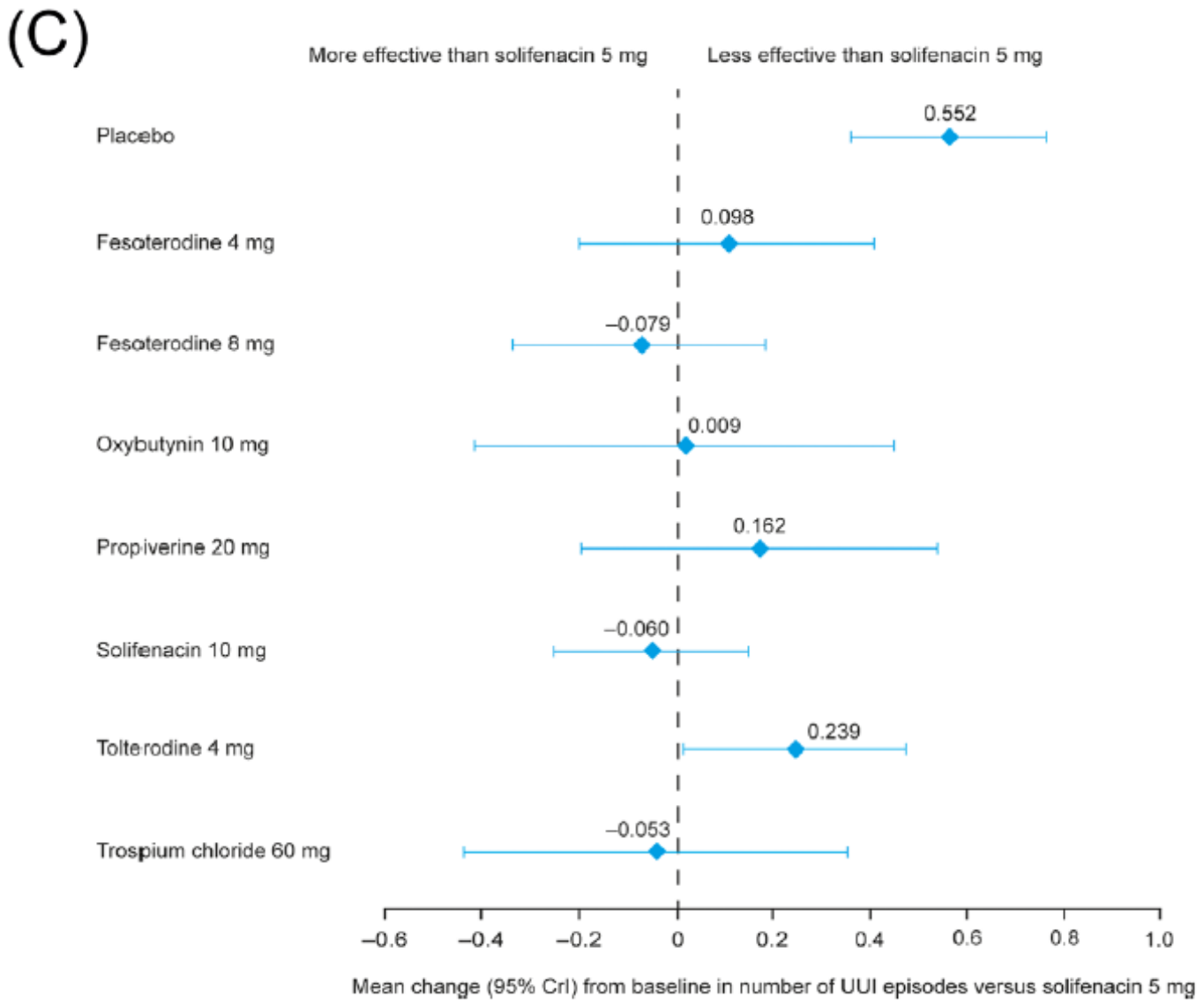
# IN THE NUMBER OF MICTURITIONS (VS SOLIFENACIN)



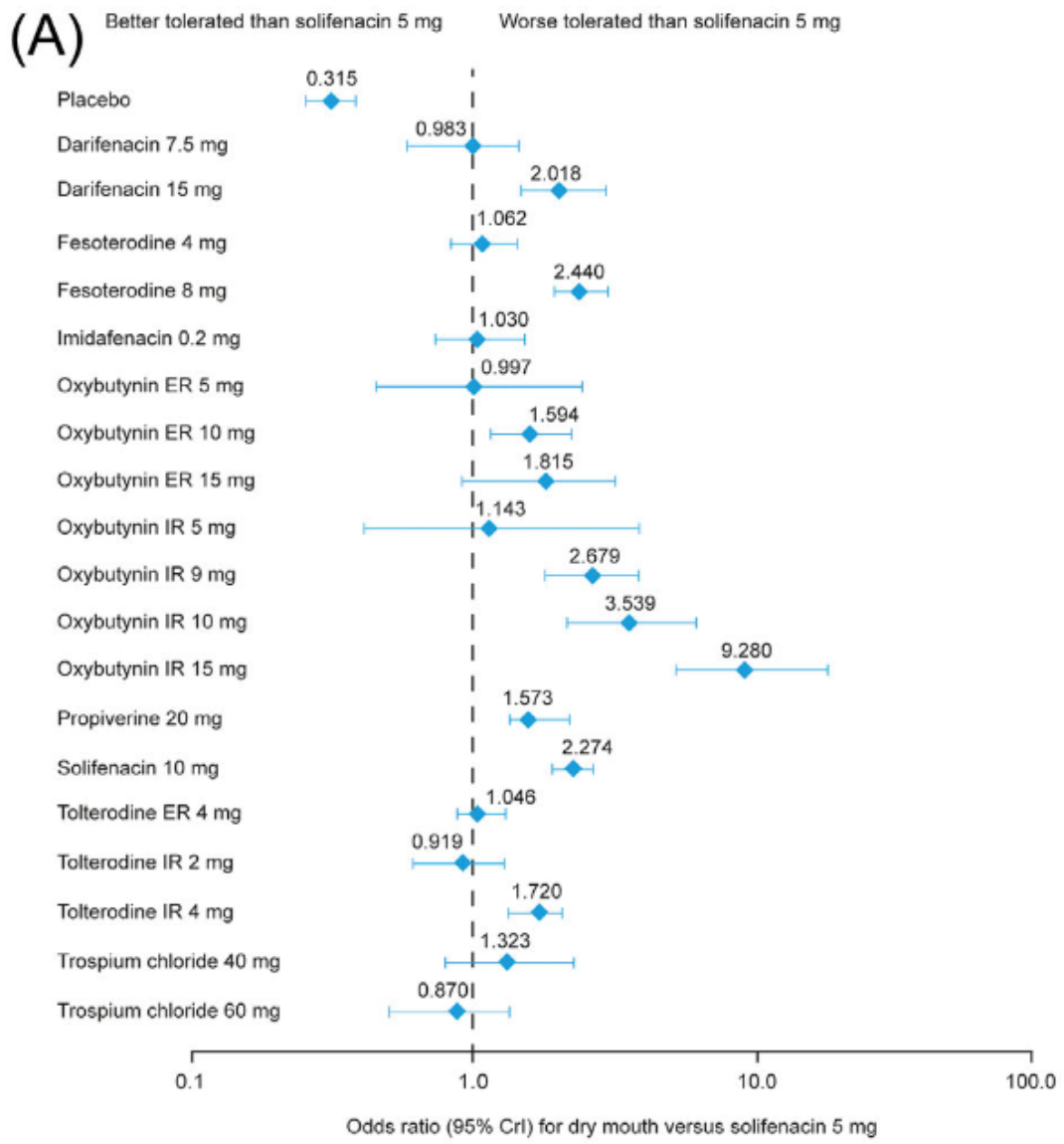
# In the number of incontinence episodes (vs Solifenacin)



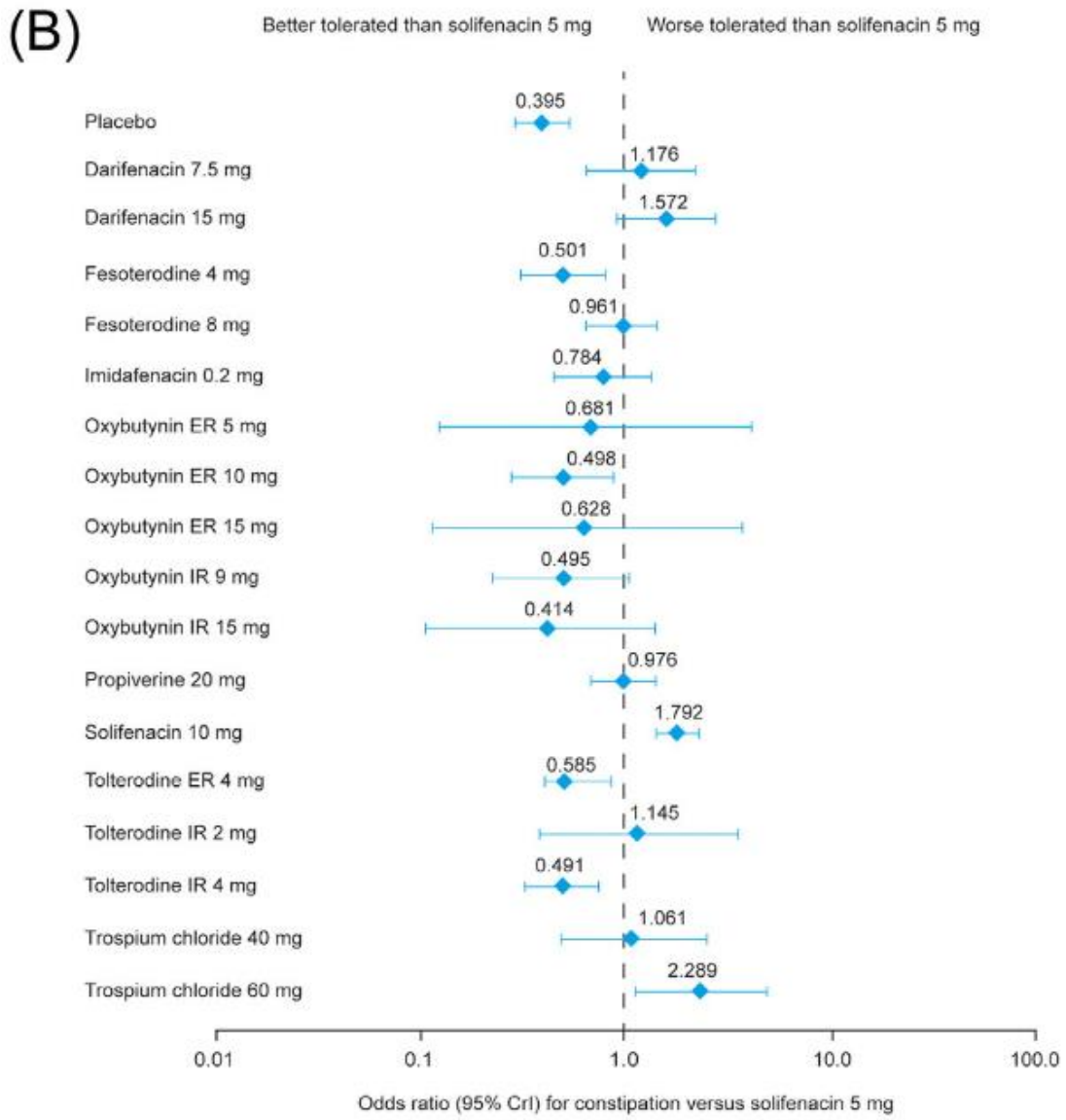
# In the number of UUI episodes (vs Solifenacin)



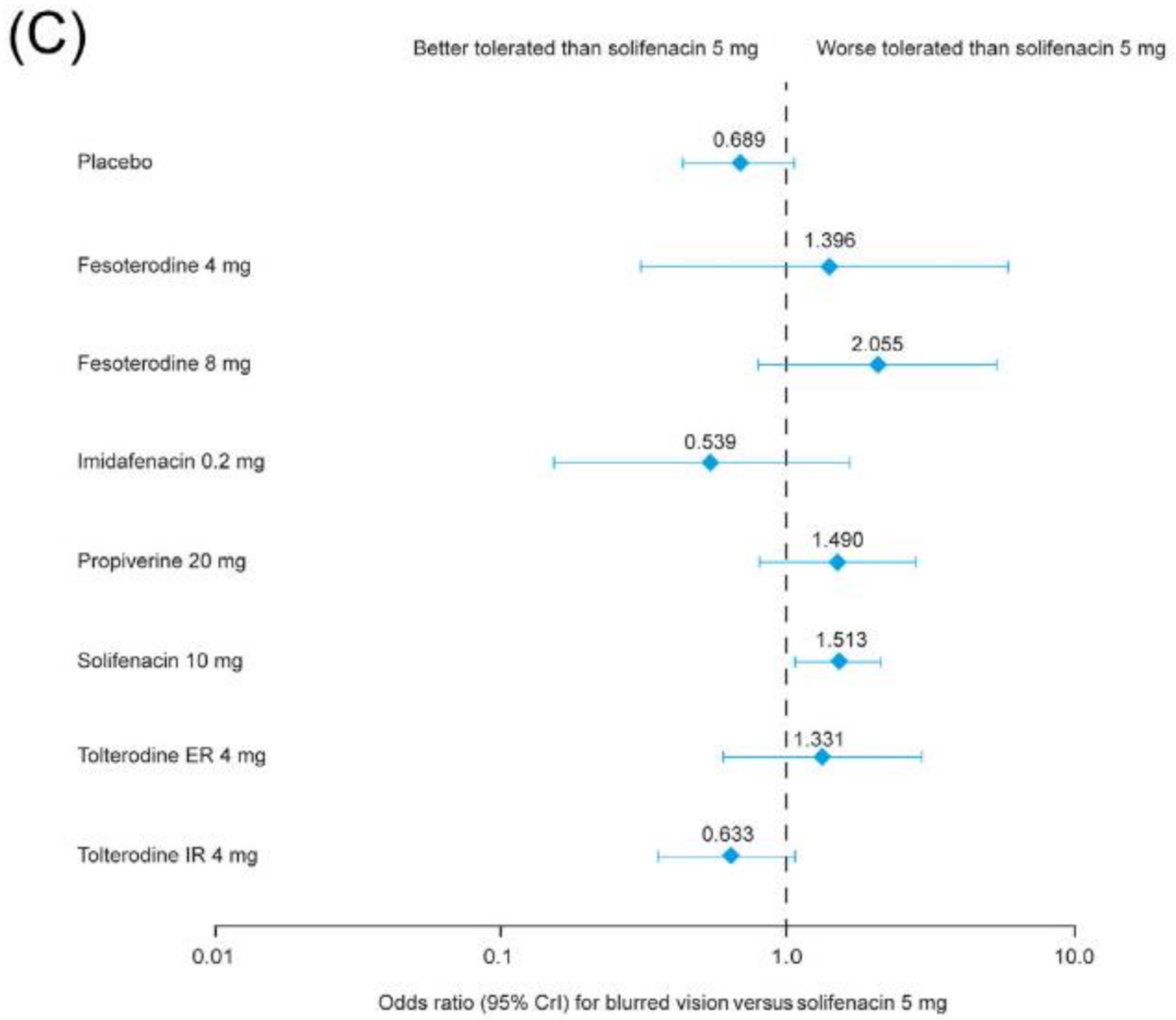
# In the number of dry mouth (vs Solifenacin)



# In the number of constipatient (vs Solifenacin)



# In the number of blurred vision (vs Solifenacin)



*Neurourology and Urodynamics*. 2018;**37**:986–996.

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**CONCLUSIONS:** This NMA suggests that solifenacin 5 mg/day is more effective than tolterodine 4 mg/day in reducing OAB incontinence and UUI episodes, but does not differ significantly in terms of efficacy compared with other oral antimuscarinics.

# THE EFFECT AND SIDE EFFECT OF AM

- Antimuscarinic agents (AM) differ in molecular size, charge and lipophilicity.
- They are categorized as tertiary or quaternary amines.
  - Tertiary agents have higher lipophilicity and less molecular charge, both of which along with small molecular size increase the passage through the blood-brain barrier . They include atropine, darifenacin, fesoterodine, oxybutynin, propiverine, solifenacin, and tolterodine.

Chancellor MB, Staskin DR, Kay GG, Sandage BW, Oefelein MG, Tsao JW. Blood-brain barrier permeation and efflux exclusion of anticholinergics used in the treatment of overactive bladder. Drugs Aging. 2012; 29:259-73

  - Quaternary agents such as propantheline and trospium have greater molecular charge and less lipophilicity with limited passage into the central nervous system (CNS) and lower risk of CNS side effects .

Todorova A, Vonderheid-Guth B, Dimpfel W. Effects of tolterodine, trospium chloride, and oxybutynin on the central nervous system. J Clin Pharmacol. 2001; 41:636-44.

# CNS RELATED AE

**Table III** Distribution of Central Nervous System (CNS)-Related Adverse Events

| Adverse Event | Placebo (*n*) | Tolterodine (*n*) | Trospium Chloride (*n*) | Oxybutynin (*n*) |
|---|---|---|---|---|
| Headache | 3 | 2 | 5 | 5 |
| Tiredness | — | 1 | 2 | 6 |
| Impaired concentration | — | 1 | 1 | 3 |
| Restless sleep | — | — | 1 | — |
| Listlessness | — | — | — | 1 |
| Single myoclonia | — | — | 1 | — |
| Motor restlessness | — | — | — | 1 |
| Sensation of cold | — | 1 | 1 | 1 |
| Total number of events | 3 | 5 | 11 | 17 |
| Total number of subjects | 3 | 4 | 8 | 8 |

Todorova A, Vonderheid-Guth B, Dimpfel W. Effects of tolterodine, trospium chloride, and oxybutynin on the central nervous system. J Clin Pharmacol. 2001; 41:636-44.

AJOG American Journal of Obstetrics & Gynecology

# Extended-release formulations of oxybutynin and tolterodine exhibit similar central nervous system tolerability profiles: A subanalysis of data from the OPERA trial

Franklin M. Chu, MD,[a,*] Roger R. Dmochowski, MD,[b] Daniel J. Lama, MD,[a] Rodney U. Anderson, MD,[c] Peter K. Sand, MD[d]

treatment 12 wks

**Table I** Incidence of selected CNS adverse events* (≥1%) by treatment

| | Treatment | | | | |
|---|---|---|---|---|---|
| | Oxybutynin ER 10mg(n=391) | | Tolterodine 4mg (n=399) | | |
| AE | n | % | N | % | *P* value† |
| Any CNS AE | 35 | 9.0 | 33 | 8.3 | .8001 |
| Dizziness | 15 | 3.8 | 10 | 2.5 | .3150 |
| Somnolence | 4 | 1.0 | 9 | 2.3 | .2632 |
| Insomnia | 7 | 1.8 | 3 | 0.8 | .2193 |
| Depression | 5 | 1.3 | 3 | 0.8 | .5015 |
| Hypertonia | 2 | 0.5 | 4 | 1.0 | .6864 |

*AE*, Adverse event.
Other CNS AEs were reported in <1% of each treatment group (0.6% and 0.9% for extended-release oxybutynin and extended-release tolterodine, respectively).
* Based on FDA classification.[18]
† *P* values were computed using the Fisher exact test.

**Conclusion:**

The extended-release formulations of **oxybutynin (10mg) and tolterodine (4mg)** given to 790 women with OAB for **12 weeks** were observed to be associated with **a similar low incidence of CNS** adverse events, which were mostly **mild or moderate** in severity.



American Journal of Obstetrics and Gynecology (2005) 192, 1849–55

AJOG American Journal of Obstetrics & Gynecology

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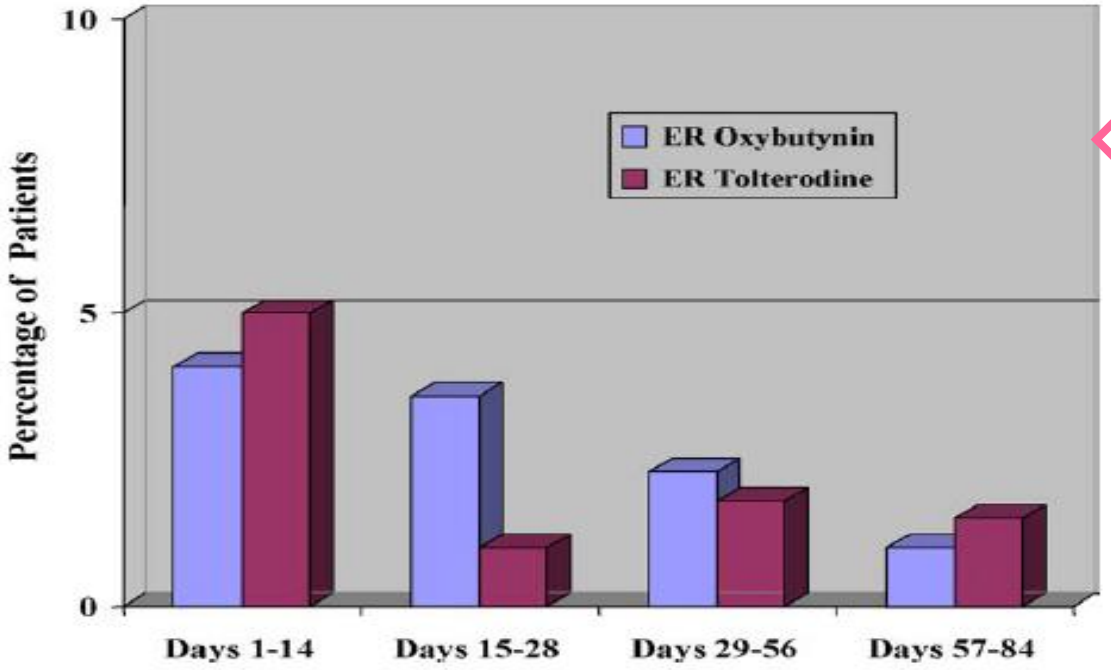



**Onset of CNS adverse events** over the course of the trial.

- These figures indicate a trend toward **increased tolerance** in both treatment groups.
- The differences between the 2 groups are small and do not indicate a clear distinction between treatments.



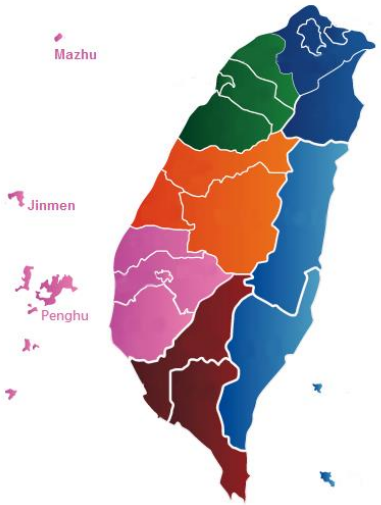
American Journal of Obstetrics and Gynecology (2005) 192, 1849–55

LUTS LOWER URINARY TRACT SYMPTOMS

*LUTS* (2018) 10, 21–26

ORIGINAL ARTICLE

# Treatment Outcome of Overactive Bladder Patients Receiving Antimuscarinic Therapy for More than One Year




Sheng-Mou HSIAO,[1] Ho-Hsiung LIN,[2] and Hann-Chorng KUO[3,*]

[1]Department of Obstetrics and Gynecology, Far Eastern Memorial Hospital, Banqiao, Taiwan, [2]Department of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan, and [3]Department of Urology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

# BASELINE CHARACTERISTICS OF PATIENTS

| Variables | All patients ($n = 140$) | ≥75 years ($n = 94$) | *P*-values† |
|---|---|---|---|
| Age (years) | 76.4 ± 10.5 | 82.0 ± 4.6 | <0.001 |
| Sex | | | |
| Male | 106 (76) | 71 (76) | 0.94 |
| Female | 34 (24) | 23 (24) | — |
| Subgroups | | | |
| OAB wet | 87 (62) | 65 (69) | 0.02 |
| OAB dry | 53 (38) | 29 (31) | — |
| Treatment | | | |
| Solifenacin | 105 (75) | 73 (78) | 0.30 |
| Tolterodine | 27 (19) | 15 (16) | 0.15 |
| Oxybutynin | 20 (14) | 14 (15) | 0.77 |
| Concomitant therapy | | | |
| Alpha-blocker | 38 (27) | 28 (30) | 0.32 |
| Dutasteride | 13 (9) | 9 (10) | 1.00 |
| Benign prostate hyperplasia | 62 (44) | 41 (44) | 0.86 |
| Diabetes mellitus | 43 (31) | 36 (38) | 0.005 |
| Coronary artery disease | 14 (10) | 13 (14) | 0.04 |
| Cerebral vascular accident | 11 (8) | 8 (9) | 1.00 |
| Parkinsonism | 3 (2) | 2 (2) | 1.00 |
| Chronic obstructive pulmonary disease | 1(1) | 0(0) | 0.33 |
| Chronic renal disease | 1 (1) | 1 (1) | 1.00 |
| Medical comorbidity‡ | 59 (42) | 55 (59) | 0.02 |

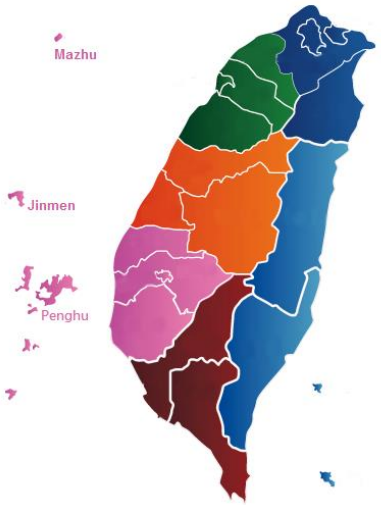
| Variables | All patients ($n = 140$) | ≥75 years ($n = 94$) | $P$-values† |
|---|---|---|---|
| Treatment | | | |
| Solifenacin | 105 (75) | 73 (78) | 0.30 |
| Tolterodine | 27 (19) | 15 (16) | 0.15 |
| Oxybutynin | 20 (14) | 14 (15) | 0.77 |

Side-effects were observed in 81patients (57.9%)

- ✓ dry mouth (n=58, 41.4%),
- ✓ constipation (n=48, 34.3%)
- ✓ and blurred vision (n=4,2.9%);
- ✓ **all side-effects were tolerable.**

**Conclusion:** Sustained therapeutic effects were observed in patients who received 12 months or more of antimuscarinic therapy, even in elderly patients. In addition, side-effects in patients receiving long-term therapy were also common but tolerable.

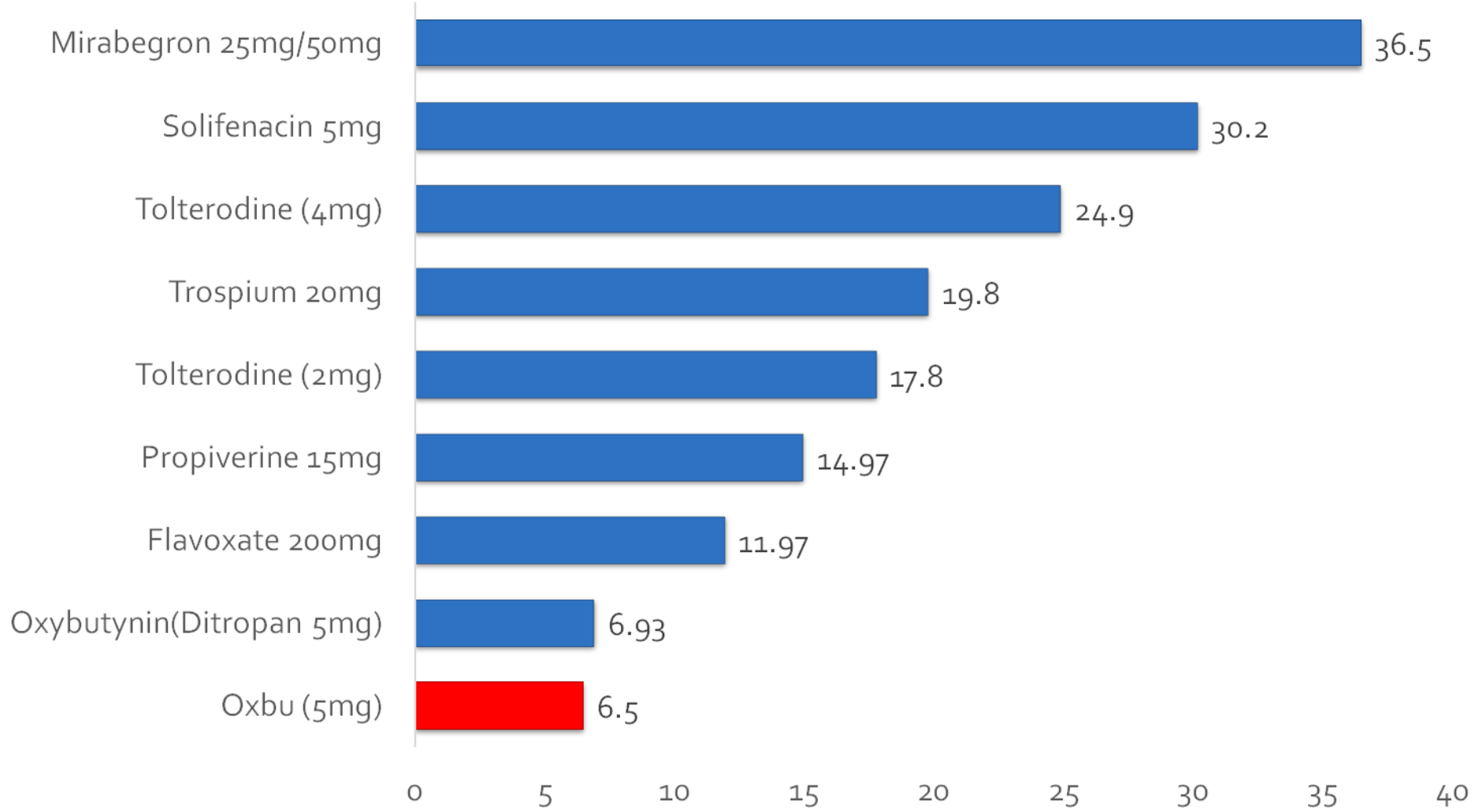
# Treatment for more than 1 year!!!




No significant between-group differences in side-effects were observed between different antimuscarinic (Solifenacin 5mg /Tolterodine 4mg /Oxybutynin ER ) medications.

# 每日最低藥價

108.05.01最新健保價生效



# Oxybutynin 已上市47年, 但仍有新用途:

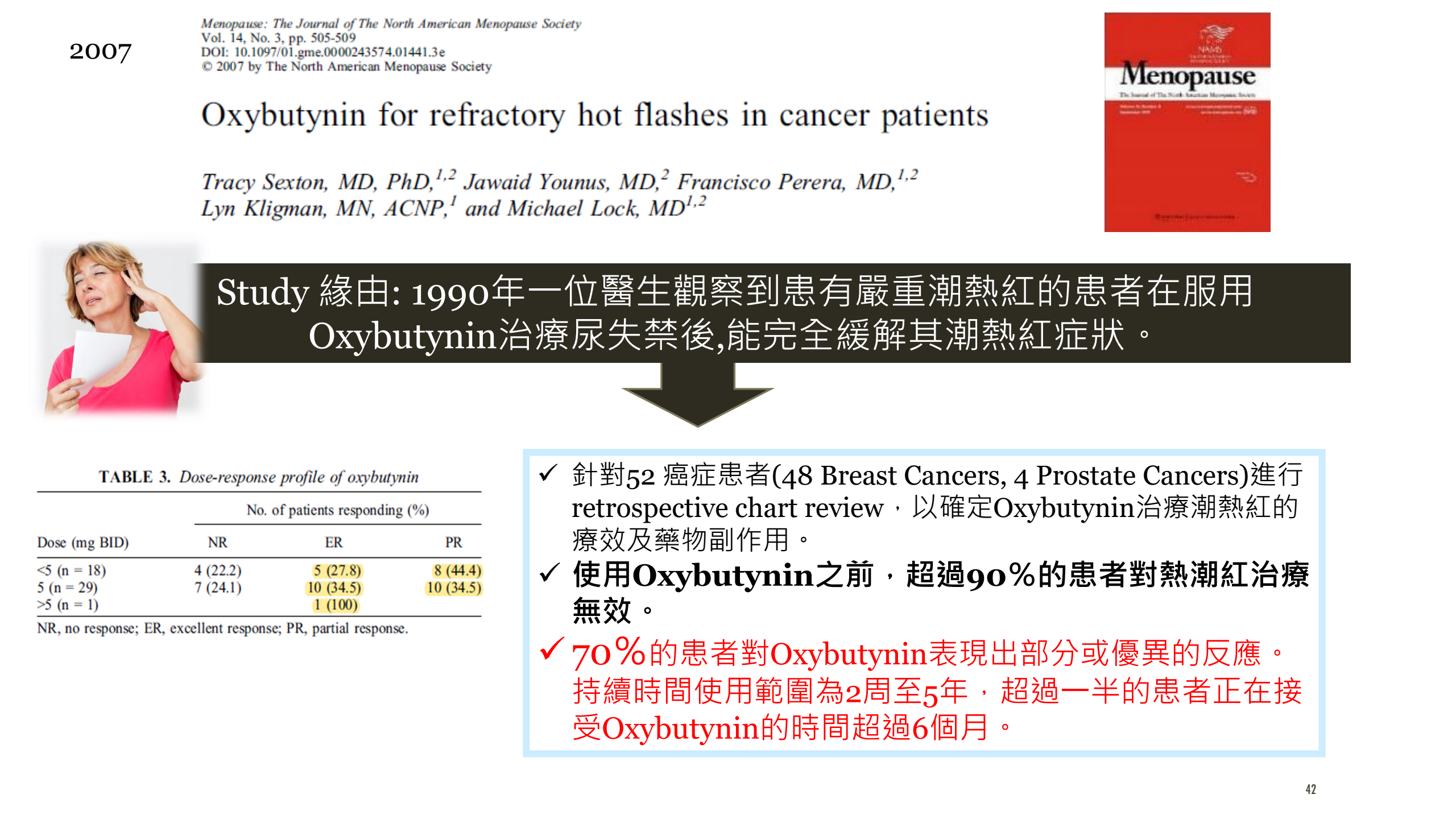
**Few interesting studies about "Oxybutynin"**

2007

*Menopause: The Journal of The North American Menopause Society*
Vol. 14, No. 3, pp. 505-509
DOI: 10.1097/01.gme.0000243574.01441.3e


# Oxybutynin for refractory hot flashes in cancer patients

*Tracy Sexton, MD, PhD,[1,2] Jawaid Younus, MD,[2] Francisco Perera, MD,[1,2] Lyn Kligman, MN, ACNP,[1] and Michael Lock, MD[1,2]*






## Study 緣由: 1990年一位醫生觀察到患有嚴重潮熱紅的患者在服用Oxybutynin治療尿失禁後,能完全緩解其潮熱紅症狀。

**TABLE 3.** *Dose-response profile of oxybutynin*

| | No. of patients responding (%) | | |
|---|---|---|---|
| Dose (mg BID) | NR | ER | PR |
| <5 (n = 18) | 4 (22.2) | 5 (27.8) | 8 (44.4) |
| 5 (n = 29) | 7 (24.1) | 10 (34.5) | 10 (34.5) |
| >5 (n = 1) | | 1 (100) | |

NR, no response; ER, excellent response; PR, partial response.

- ✓ 針對52 癌症患者(48 Breast Cancers, 4 Prostate Cancers)進行retrospective chart review，以確定Oxybutynin治療潮熱紅的療效及藥物副作用。
- ✓ **使用Oxybutynin之前，超過90%的患者對熱潮紅治療無效。**
- ✓ 70%的患者對Oxybutynin表現出部分或優異的反應。持續時間使用範圍為2周至5年，超過一半的患者正在接受Oxybutynin的時間超過6個月。

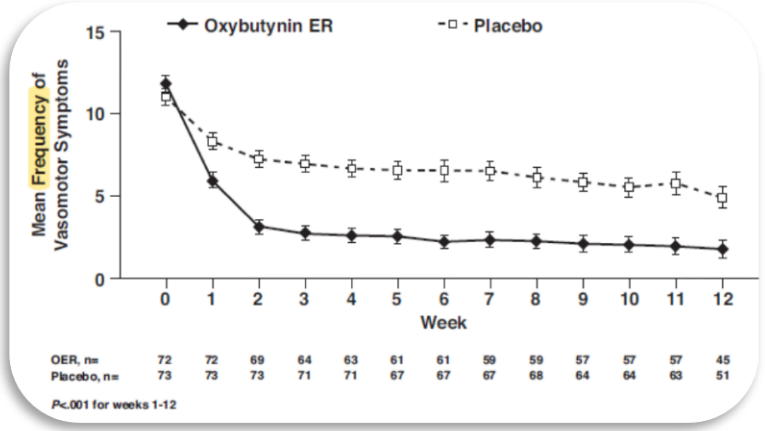
2016

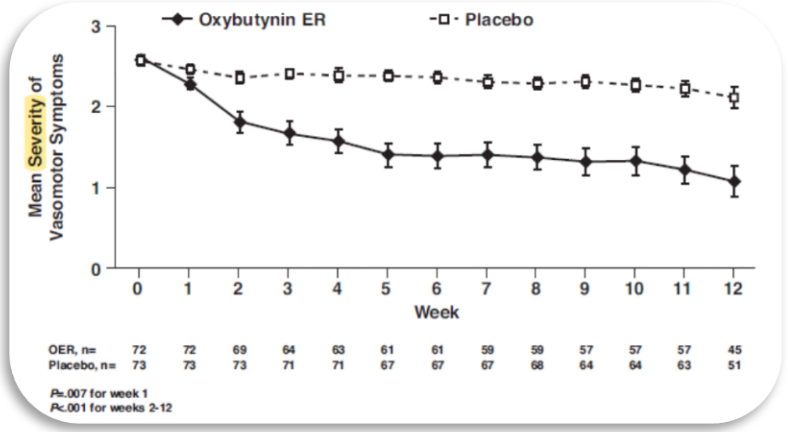

*Menopause: The Journal of The North American Menopause Society*
Vol. 23, No. 11, pp. 1214-1221
DOI: 10.1097/GME.0000000000000773


# Extended-release oxybutynin therapy for vasomotor symptoms in women: a randomized clinical trial

*James A. Simon, MD, CCD, NCMP, IF, FACOG,[1] Tatiana Gaines, MD, MPH,[2] Katherine D. LaGuardia, MD, MPH,[3] for the Extended-Release Oxybutynin Therapy for VMS Study Group*

為期12週隨機多中心雙盲安慰劑對照的Phase II 臨床試驗: 針對每天至少有**7次中~重度血管舒縮症狀VMS**的更年期婦女(mean age: 54 y/o), 每天一次 15 mg Oxybutynin ER（n=73）或安慰劑（n=75).



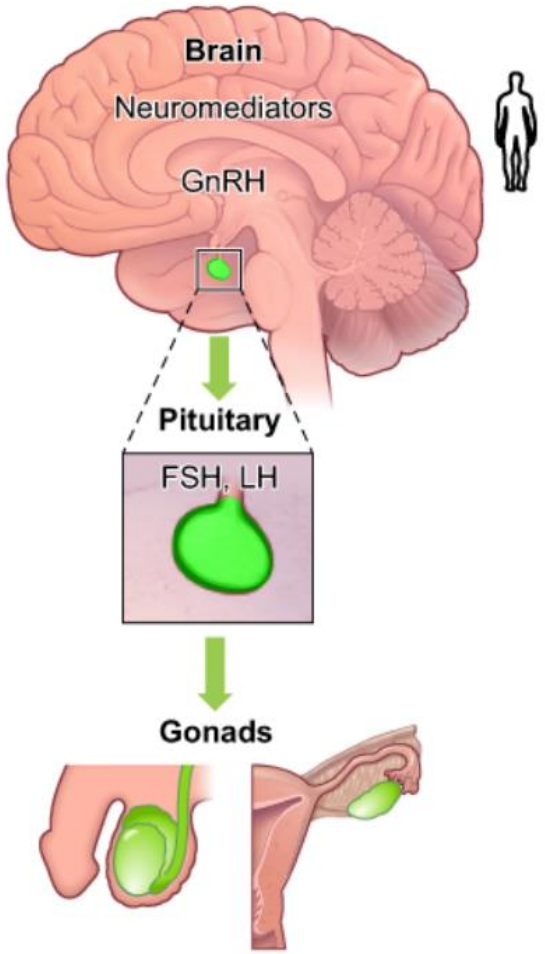




服用Oxybutynin 組口乾 比例 52.1% vs Placebo 5.3%，有6.8%的參與者停用

**結論：Oxybutynin ER (15mg/qd)是一種有效的non-hormonal therapy ， 可治療有中度至重度血管舒縮症狀的更年期婦女。**

# THE MECHANISM OF ACTION OF OXYBUTYNIN

- ✓ The mechanism of action of oxybutynin in reducing vasomotor symptoms is also not well-understood.
- ✓ As an antimuscarinic agent, oxybutynin causes **relaxation of smooth muscle** and has specificity for both M1 and M3 receptors, which are found in the brain, bladder, and small vessels.
- ✓ Additional reported properties of anticholinergics in **suppression of luteinizing hormone (LH) release** and **inhibition of small artery vasodilation** may explain some of the effect seen.




- ✓ Chiodera et al demonstrated that LH and FSH secretion are mediated in part by a muscarinic pathway and **that antimuscarinic agents can inhibit gonadotropic secretion. If gonadotropins play a role in temperature regulation, it is possible that oxybutynin exerts its effect through this pathway.** A peripheral effect is also possible through small-vessel constriction.

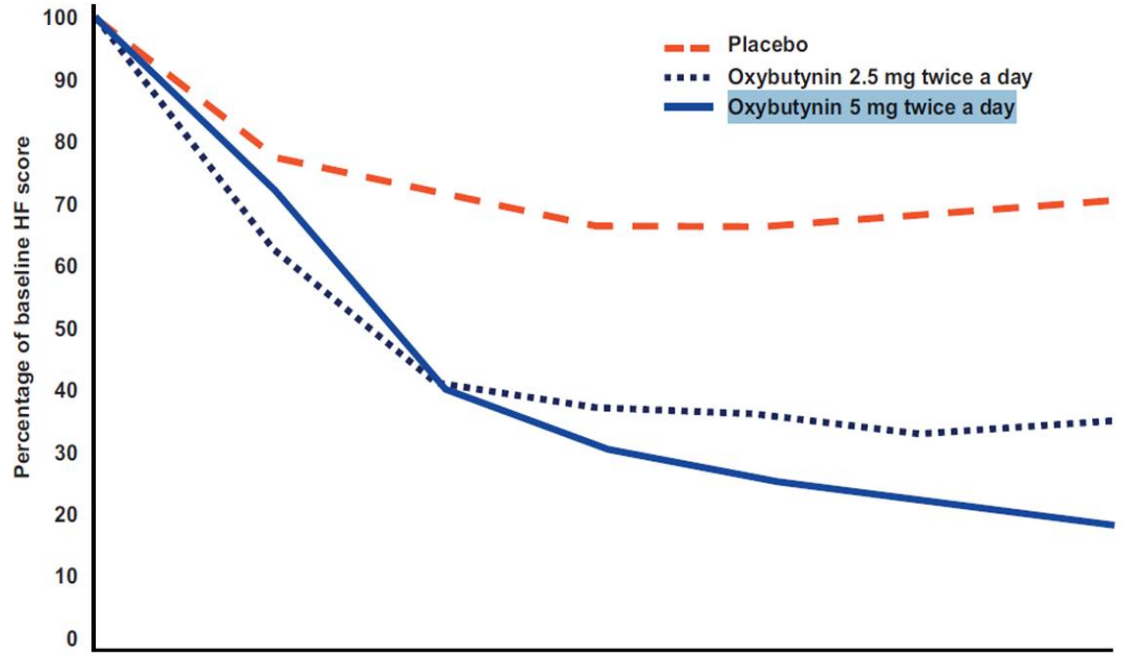

Menopause, Vol. 23, No. 11, 2016

ARTICLE

# Oxybutynin vs Placebo for Hot Flashes in Women With or Without Breast Cancer: A Randomized, Double-Blind Clinical Trial (ACCRU SC-1603)

Roberto A. Leon-Ferre *, Paul J. Novotny, Eric G. Wolfe, Stephanie S. Faubion, Kathryn J. Ruddy , Daniel Flora, Christopher S. R. Dakhil, Kendrith M. Rowland, Mark L. Graham, Nguyet Le-Lindqwister, Thomas J. Smith , Charles L. Loprinzi

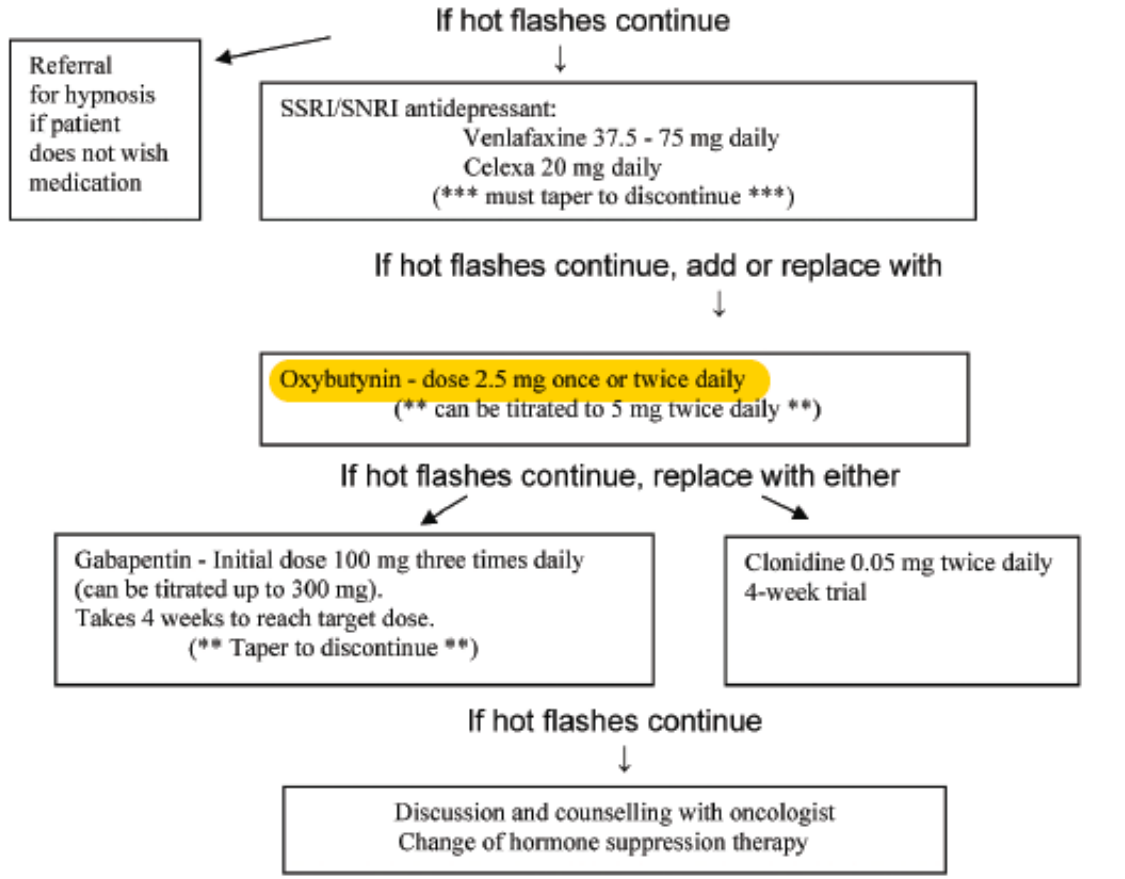
**Oxybutynin is an effective and relatively well-tolerated treatment option for women with HFs.**




| Weeks | Baseline | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| Placebo | 38 | 38 | 38 | 37 | 35 | 35 | 35 |
| Oxybutynin 2.5 mg twice a day | 40 | 40 | 38 | 36 | 35 | 35 | 34 |
| Oxybutynin 5 mg twice a day | 35 | 35 | 34 | 32 | 32 | 31 | 31 |

# Management of hot flashes in women with breast cancer

*L. Kligman RNEC and J. Younus MD*




[** For male patients with hot flashes, consider megestrol 20 mg twice daily **]

Journal of the Formosan Medical Association (2018) xx, 1–8

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfma-online.com


Review Article

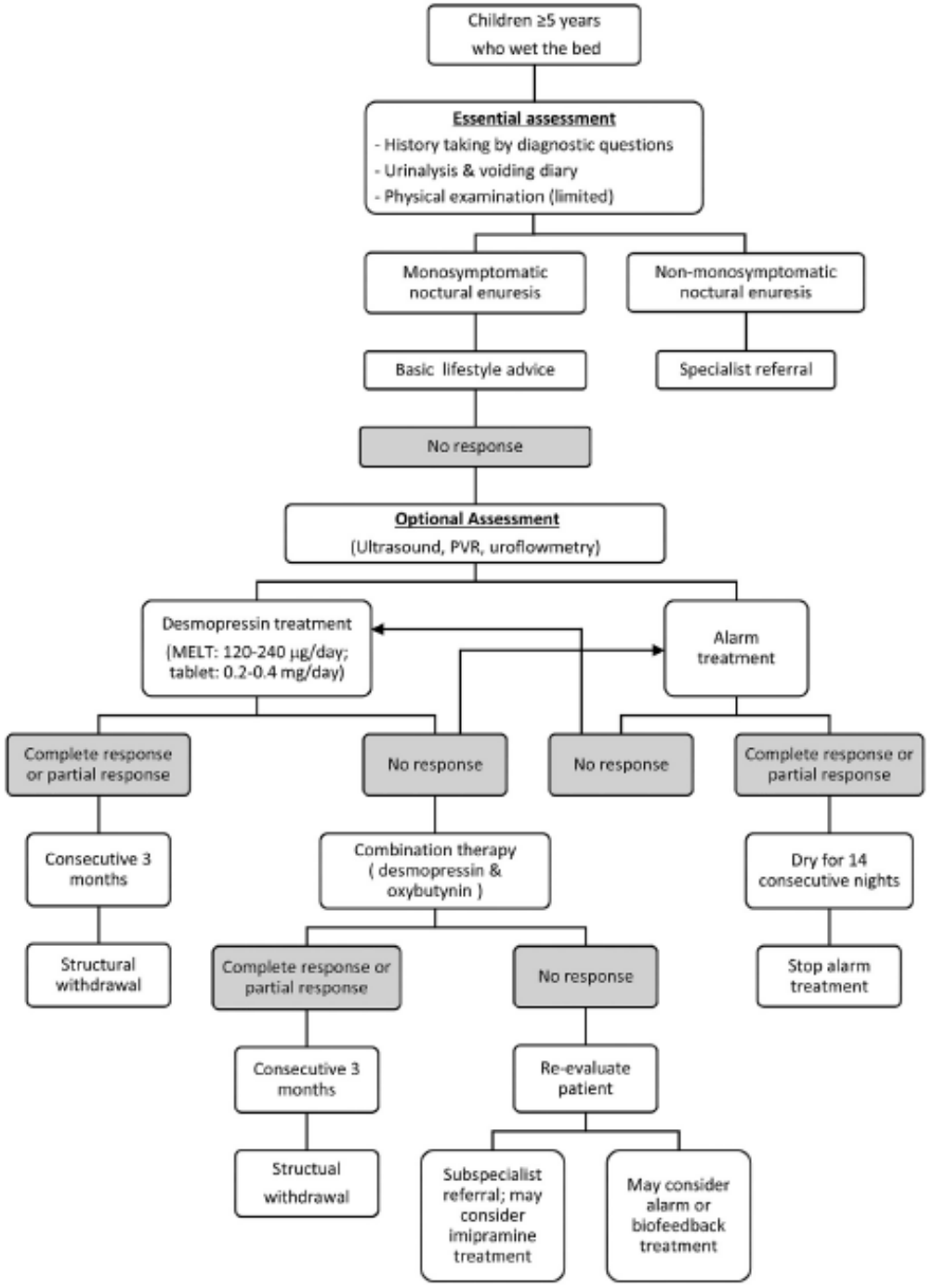
2018

# Management of nocturnal enuresis in Taiwan: Consensus statements of the Taiwan enuresis expert committee

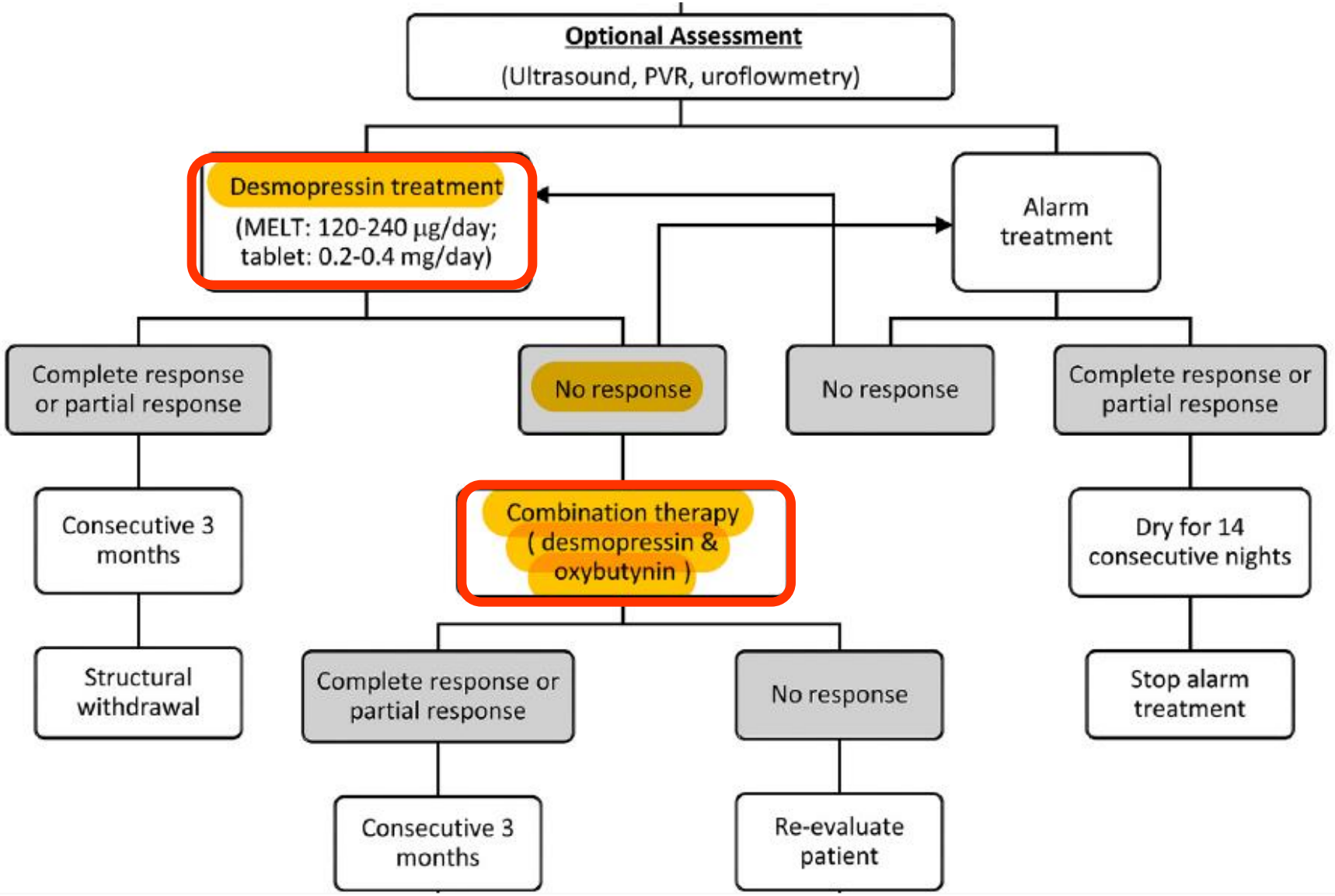
Ta-Min Wang [a], Stephen Shei-Dei Yang [b,*], Jeng-Daw Tsai [c], Mei-Ching Yu [d], Yee-Hsuan Chiou [e], Kuo-Liang Chen [f], Hong-Lin Cheng [g], Jesun Lin [h], Hsiao-Wen Chen [i], Hann-Chorng Kuo [j], Shyh-Chyan Chen [k]

2018.03

# 台灣小兒夜間遺尿症專家共識聲明及推薦強度



# 夜間遺尿 (尿床) nocturnal enuresis (NE) 治療指引



UROLOGY

# PRELIMINARY STUDY OF THE SAFETY AND EFFICACY OF EXTENDED-RELEASE OXYBUTYNIN IN CHILDREN

KATRIN YOUDIM AND BARRY A. KOGAN

***Objectives.***

A new extended-release formulation of oxybutynin has some benefits versus traditional oxybutynin but has never been evaluated in children.

***Methods.***

A retrospective study was performed on 25 children [ age from 5 to 18 years (mean 9.5) ]who had been treated with ER oxybutynin. 14 had neurogenic bladder dysfunction and 11 had urinary frequency and urgency and urge incontinence but no neurologic abnormalities.

- The dosage prescribed was as close as possible to 0.3 mg/kg daily using the 5, 10, and 15-mg tablets.

Katrin Yet al. Urology. **2002;59:428-432**

UROLOGY

# PRELIMINARY STUDY OF THE SAFETY AND EFFICACY OF EXTENDED-RELEASE OXYBUTYNIN IN CHILDREN

KATRIN YOUDIM AND BARRY A. KOGAN

***Results.***

- All 25 patients had improvement in incontinence and/or voiding dysfunction on extended-release oxybutynin. Twelve (48%) experienced no side effects. Of the 13 who did, 10 complained of dry mouth (grade 4.6 ± 0.5), 4 had constipation (grade 5.8 ± 1.8), 4 had heat intolerance (grade 5.1 ± 0.9), and 3 had drowsiness (grade 5.3 ± 2.4).

- Of patients previously treated with oxybutynin, the extended-release oxybutynin was equally or more efficacious and had the same or fewer side effects, especially less dry mouth.

UROLOGY

# PRELIMINARY STUDY OF THE SAFETY AND EFFICACY OF EXTENDED-RELEASE OXYBUTYNIN IN CHILDREN

KATRIN YOUDIM AND BARRY A. KOGAN

**Conclusions.** **ER oxybutynin is safe and efficacious in children**. In this preliminary evaluation, it had benefits over traditional, immediate-release oxybutynin.

Patient and family satisfaction was very high, **84 %** have **continued** using the medication.

Iran Red Crescent Med J. 2015 July; 17(7): e16174. DOI: 10.5812/ircmj.16174v2
Published online 2015 July 01. Research Article

# Desmopressin, Imipramine, and Oxybutynin in the Treatment of Primary Nocturnal Enuresis: A Randomized Clinical Trial

Maryam Seyfhashemi [1,*]; Raheb Ghorbani [2]; Abbas Zolfaghari [1]

**Background:** Nocturnal enuresis is the most common pediatric urologic problem in outpatient clinics.
**Objectives:** To assess the effect of various monotherapies, and comparing the effects of desmopressin, imipramine, and oxybutynin in children with enuresis, as well as the influence of socioeconomic and cultural factors of their families on the response and relapse rates.
**Patients and Methods:** The study was a randomized clinical trial conducted on 92 children aged 5 - 14 years, referred to the pediatric clinic of Semnan University Hospital in Semnan, Iran. Children with primary nocturnal enuresis were randomly allocated to three different treatment groups: desmopressin (n = 30), imipramine (n = 31), and oxybutynin (n = 31) all for 6 weeks. The socioeconomic and demographic characteristics of all participants were recorded. The number of wet nights per week was noted at the end of the 6-week-trial, and children were followed up to three months for relapse.
**Results:** Children in the oxybutynin group showed a slightly higher response rate (71.0% success) and a lower relapse rate (31.8%), while in the desmopressin group the response and relapse rates were 63.3% and 57.9%, respectively, and in the imipramine group 61.3% and 63.2%, respectively. However, the difference between the 3 groups in terms of response (P = 0.701) and relapse rates (P = 0.095) was not statistically significant.
**Conclusions:** There is no significant difference between monotherapy with desmopressin, imipramine or oxybutynin in children with enuresis. However, oxybutynin showed a higher response rate and a lower relapse rate compared to other medications. More clinical trials with a larger sample size are needed to clarify these uncertainties.

**Table 2.** Treatment Outcomes (Response and Relapse Rates) in Groups [a]

10-20 ug of nasal DDAVP 25 - 75 mg 5-15mg

| Variables | Whole sample (n = 92) | Desmopressin (n = 30) | Imipramine (n = 31) | Oxybutynin (n = 31) | P Value |
|---|---|---|---|---|---|
| **Response** | 60 (65.2) | 19 (63.3) | 19 (61.3) | 22 (71.0) | 0.701 |
| **Relapse** | 30 (50.0) | 11 (57.9) | 12 (63.2) | 7 (31.8) | 0.095 |

[a] Data are presented as No. (%).

# TREATMENT PRINCIPLES WITH AM

- AM act mainly by blocking M3 receptors; Because there are no AM with significant selectivity for the bladder, adverse effects (AEs) of treatment are common;
- All commercially available AM improve OAB symptoms and quality of life with comparable efficacy, but different tolerability profiles;
- The most frequent AEs are gastrointestinal, with dry mouth as the most common;
- Immediate-release AM have a greater risk of side effects than extended-release formulations;
- AM should be avoided in the elderly population(> 75 Y/O) since the cumulative use of medications with anticholinergic activity may be associated with the risk of dementia;
- Persistence in treatment with AM is low, with only 20% persisting after 1 year;
- Due to specific pharmacologic properties and dosing schedule, AM treatment must be individualized;

Evgenyi I. Kreydin, Cristiano M. Gomes, and Francisco Cruz
Current pharmacotherapy of overactive bladder
Int Braz J Urol. 2021 Nov-Dec; 47(6): 1091–1107

# 1.6.3. .TOLTERODINE L-TARTRATE（如DETRUSITOL）; SOLIFENACIN SUCCINATE（如VESICARE）; MIRABEGRON (如BETMIGA):(90/7/1、93/10/1、96/4/1、104/2/1、106/6/1)

1. 限符合下列診斷標準條件之一者：
   (1) 頻尿：每天（24小時）排尿次數超過八次，並有詳實病歷紀錄。
   (2) 急尿：病患自述經常有一種很突然、很強烈想解尿的感覺。
   (3) 急迫性尿失禁：對於尿急的感覺無法控制，並於24小時內至少也有一次漏尿之情形。
2. 不宜使用本類藥品者：
   (1) **小兒夜尿**。
   (2) 單純性應力性尿失禁。
   (3) 膀胱逼尿肌無反射（detrusor areflexia）或膀胱不收縮所引起之排尿困難或尿失禁之症狀。
3. Solifenacin succinate（如Vesicare）及Mirabegron (如Betmiga) 藥品每天限使用1錠。 (104/2/1)
4. 每一種antimuscarinics 或Beta-3 agonist都可當作膀胱過動症之第一線治療藥物。(106/6/1)
5. 當使用一段時間(如3個月)病人治療效果仍不佳時，在侵入性治療前，可以考慮增加劑量或增加第二種antimuscarinics或合併Mirabegron使用。(106/6/1)

# OAB藥品評估表(ANTIMUXCARINICS)

| 商品名 | Oxbu ER | Detrusitol SR | Vesicare |
|---|---|---|---|
| 學名 | Oxybutynin | Tolterodine L-Tartrate | Solifenacin Succinate |
| 劑量劑型 | 5 mg | 4 mg | 5 mg,10 mg / Tab |
| 腎功能不全之劑量 | NA | 腎功能嚴重受損患者(CCr: 10 ~ 30 ml/mi)降低劑量 | 重度腎功能障礙 (CCr< 30 ml/min)每天不得多於 5 mg |
| 肝功能不全之劑量 | NA | 肝硬化病患降低劑量使用 | ■ 中度肝功能障礙 (Child-Pugh B) 每天不得多於5 mg ;<br>■ 重度肝功能障礙 (Child-Pugh C)不建議使用 |
| 兒童使用劑量 | 6歲以上兒童；一天5~20mg | 兒童不可使用 | 兒童不可使用 |
| FDA懷孕分級 | B | C | C |
| 特殊注意事項 | 可剝半使用、不可磨粉 | 不可剝半使用、不可磨粉 | NA |
| 健保給付規範 | 無 | 有 | 有 |

# Thank You !