

Urgency Urinary Incontinence

Definition – Epidemiology – Diagnosis - Therapy

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Definitions and Epidemiology

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TYPES OF UI^{1,2}

- **UUI:** Urgency Urinary Incontinence
- **SUI:** Stress Urinary Incontinence
- **MUI:** Mixed urinary Incontinence
- **OAB:** Overactive Bladder
- **Mixed Symptoms:** SUI accompanied by urgency but not UUI

1. Abrams et al., Urology 2003;61:37-49; 2. Wein AJ et al., J Urol 2006;175:55-610

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URGENCY URINARY INCONTINENCE (UUI)^{1,2}

- Sometimes the trigger can be:
 - Warm/cold
 - Noise or streaming water
 - Coming home, key on the door

1. Abrams et al., Urology 2003;61:37-49; 2. Wein AJ et al., J Urol 2006;175:55-610

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STRESS URINARY INCONTINENCE (SUI)^{1,2}

- **Mild:** when sneezing, coughing, laughing, coitus
- **Moderate:** when walking or walking up stairs
- **Severe:** when standing up from a chair

1. Abrams et al., Urology 2003;61:37-49; 2. Wein AJ et al., J Urol 2006;175:55-610

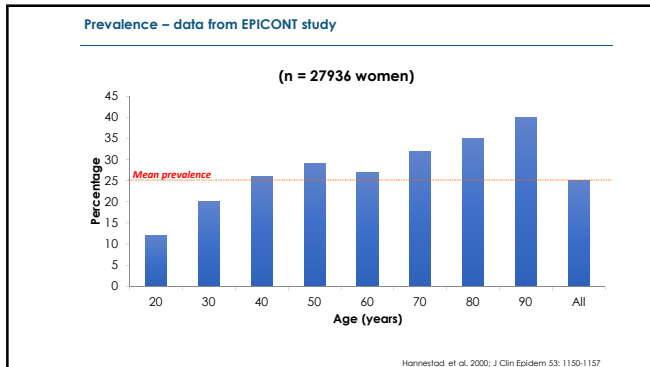
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MIXED URINARY INCONTINENCE(MUI)^{1,2}

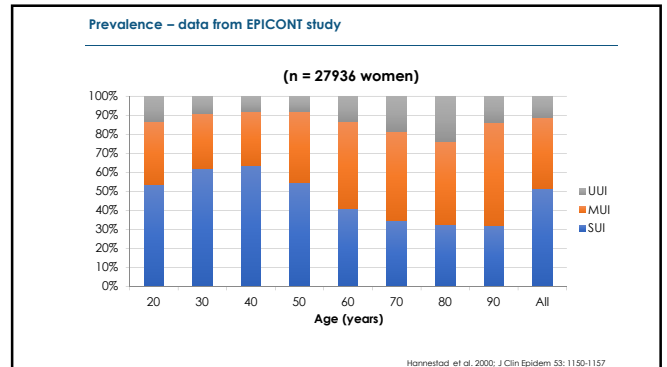
UUI: Urgency Urinary Incontinence
SUI: Stress Urinary Incontinence
MUI: Mixed Urinary Incontinence
OAB: Overactive Bladder

1. Abrams et al., Urology 2003;61:37-49; 2. Wein AJ et al., J Urol 2006;175:55-610

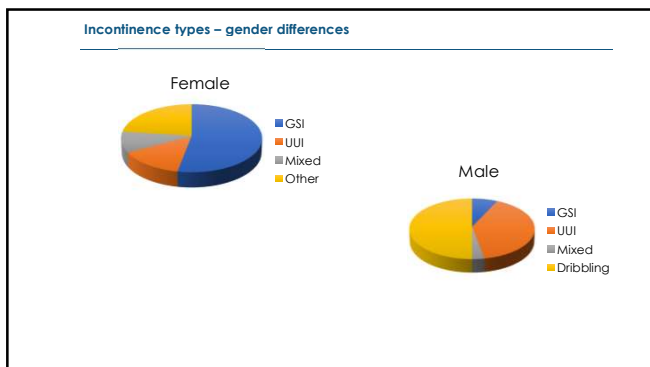
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Overactive bladder – WET or DRY SYMPTOM COMPLEX

- ICS definition¹⁸ (2002) **Overactive Bladder (OAB)**

Storage **syndrome** defined as urgency with or without urgency incontinence, usually with frequency and nocturia (no signs of infection or other pathology)

Sudden, irresistible urge to urinate with or without urgency urinary incontinence. This is often associated with increased frequency of micturition during the day and night (nocturia) (no signs of an infection or other pathology)

18. Abrams P et al. Neurourol Urolyn. 2002;21:167-78

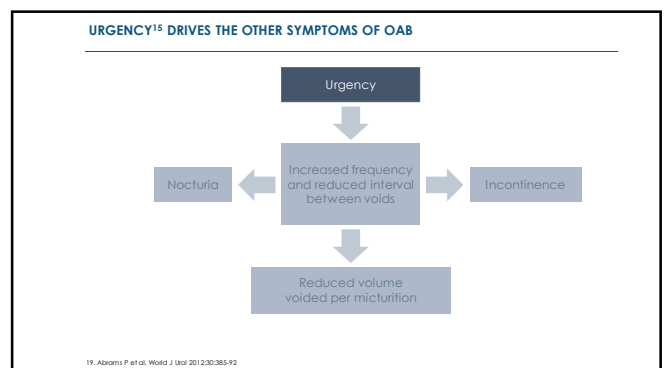
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URGENCY – Key symptom

- “Complaint of sudden, compelling desire to pass urine which is difficult to defer”^{20,18,12}
- Increased bladder sensation: “complaint that the desire to void occurs earlier”
- Micturition can be postponed despite desire to void**

20. Abrams et al. Sand J Urol Nephrol Suppl. 1998; 18. Abrams et al. Neurourol.2002; 12. Haylen et al. Int Urogynecol. 2010

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PATHOPHYSIOLOGY OF OAB

- Can be the result from an overactive bladder muscle
- The bladder muscle contracts involuntarily and excessively during the filling of the bladder

Normale blaas
Blaaspier trekt samen als blaas vol is

Overactieve blaas
Blaaspier trekt samen tijdens vullen blaas

1. Abrams P et al. Urology 2003;61:37-49; 24. Chapple CR. Eur Urol 2006;49:651-9

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PREVALENCE OF OAB SYMPTOMS ²¹

21. Stewart WF, et al. World J Urol 2003;20:327-33

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Causes – Risk factors

- Neurogenic disorders
 - Multiple Sclerosis – Parkinson's disease – Cerebrovascular accident
- Non neurogenic disorders
 - Bladder stone, UTI, PVR, urethral instabiliteit, decreased compliance (post RT), pelvic floor hypertonicity
- Idiopathic
- Psychogenic
- Age – postmenopausal state
- Obesity – Smoking
- Pregnancy
- Faecal incontinence (OR 5.8); Constipation (OR 1,6-3.9)

Abrams. Urology 2003;62 (Suppl 5B):28; 37; 4th International Consultation on Incontinence (ICI) 2009

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URGENCY... BOTHERSOME SYMPTOM ²²

22. Coyne et al. BJU Int 2009

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Diagnosis

It's a symptom complex

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Initial assessment

- "presumed diagnosis is sufficient to start conservative treatment"

BUT
RULE OUT COMPLICATED FORMS OF INCONTINENCE

Recurrent Incontinence
Pain
Hematuria
Recurrent UTI
Voiding symptoms
Pelvic Irradiation
Radical pelvic surgery
Suspected fistula

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Diagnostic tools

- History
- Bladder diaries
- Urinalysis
- Postvoid residual
- More specialized diagnostics
 - Urodynamics
 - Electrophysiological evaluation
 - Cystoscopy
 - ...

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DIFFERENTIAL DIAGNOSIS UUI-SUI^{1,4}

Symptoms	Urge Incontinence	Stress Incontinence
Urgency (strong, sudden desire to void)	Yes	No
Frequency with urgency (>8 times/24 h)	Yes	No
Leaking during physical activity; eg, coughing, sneezing, lifting	No	Yes
Amount of urinary leakage with each episode of incontinence	Large (if present)	Small
Ability to reach the toilet in time following an urge to void	Often no	Yes
Waking to pass urine at night	Usually	Seldom

UUI: urgency urinary incontinence
SUI: stress urinary incontinence

1. Abrams et al., Urology 2003;61:37-49; 4. Wein, AJ et al., Int J Feil 1999;44(2):54-66

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Bladder diaries

date: _____

surname - name _____

wake up time: _____

sleep time: _____

Time	Drink	Fluid intake (ml)	Void	Voided volume (ml)	Grade of bladder sensation (1-4)	Urinary leakage	Grade of urine loss (1-3)	Wake up to void (no / yes)

Desire to void was graded according to the following definitions:
 grade 1 – no desire to void (convenience void);
 grade 2 – desire to void but voiding can be delayed for at least 30 min;
 grade 3 – desire to void but voiding can not be delayed for more than 15 min;
 grade 4 – desire to void but voiding can not be delayed for more than 5 min.

Severity of leakage:
 grade 1 – some drops;
 grade 2 – moderate loss (wet undergarments);
 grade 3 – extensive loss (wet upper clothes).

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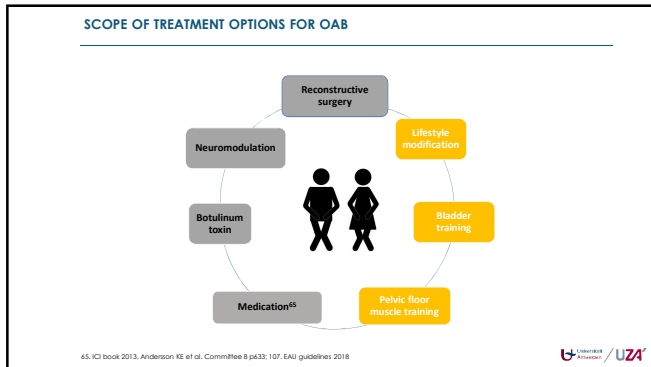
SPECIALISED MANAGEMENT OF URINARY INCONTINENCE IN WOMEN

HISTORY/ SYMPTOM ASSESSMENT	Incontinence on physical activity	Incontinence with mixed symptoms	Incontinence with urgency / frequency	"Complicated" Incontinence:
CLINICAL ASSESSMENT	<ul style="list-style-type: none"> • Assess for pelvic organ mobility / prolapse • Consider imaging of the UT/pelvic floor • Urodynamics (see notes) 			<ul style="list-style-type: none"> • Recurrent incontinence • Incontinence associated with: <ul style="list-style-type: none"> ◦ Pain ◦ Hematuria ◦ Recurrent infection ◦ voiding symptoms ◦ Pelvic irradiation ◦ Radical pelvic surgery ◦ Suspected fistula
				Consider: <ul style="list-style-type: none"> • Urothycystoscopy • further imaging • Urodynamics

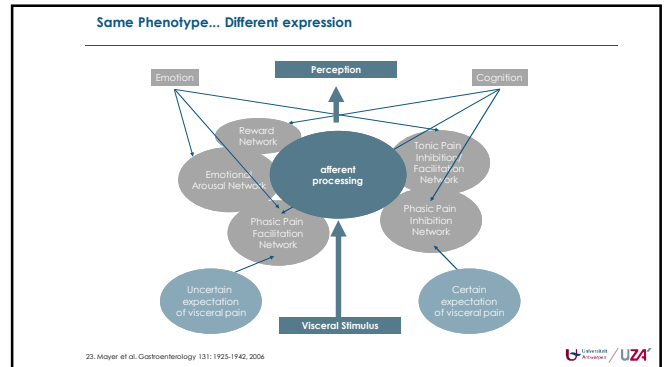
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Treatments

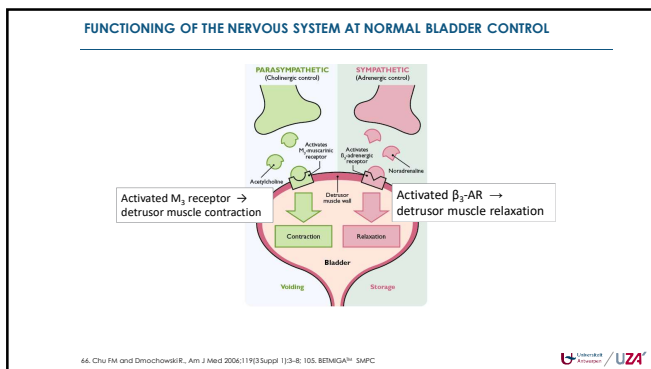
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TYPES OF ANTICHOLINERGICS

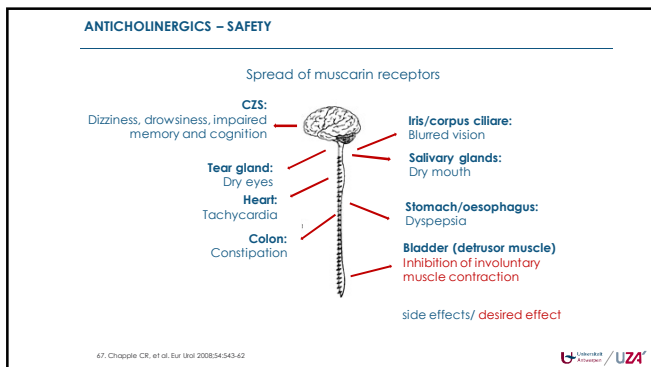
Dose/day	Darifenacin	Fesoterodine	Oxybutynin ER	Propiverin ER	Solifenacin	Tolterodine ER
Dose/day	7.5-15 mg	4-8 mg	5-30 mg	30 mg	5-10 mg	4 mg

- The efficacy of various anticholinergics is similar³⁵(and limited)
- Important placebo effect: decrease of ~30% in incontinence episodes³⁶
- Compliance varies greatly between formulations
- Start with a low dose, evaluate after 4-6 weeks

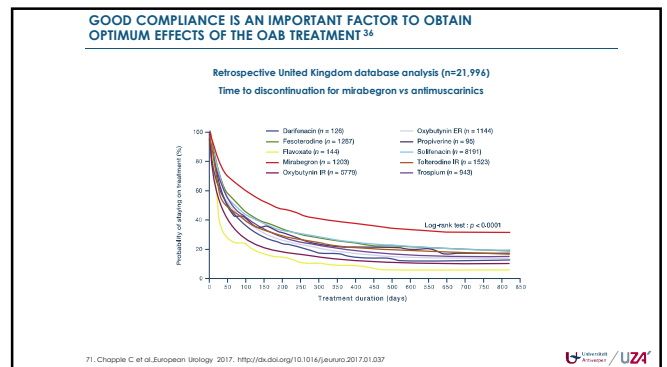
* There are differences between agents, both in terms of effectiveness and side effects

68. Lee S. et al. BMC Med Res methodol 2009;9:55-93. Busir H, et al. Eur Urol 2012;62:1040-40

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BETA-3 AR AGONIST – MODE OF ACTION

- β_3 AR agonists relax the detrusor muscle:
 - Increased bladder capacity without changing the micturition pressure
 - Increased interval between micturitions
- Developed for the treatment of OAB

66. Chu FM and Dmochowski R. Am J Med 2006;119(3 Suppl 1):3-B; 105. BETMIGA™ 5MPC

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BETA-3 AR AGONIST – EFFICACY AND SAFETY

- Superior efficacy in comparison with placebo with regard to:
 - Number of incontinence episodes: decreased
 - Number of micturitions per day: decreased
- Effective for both patients never before treated with anticholinergics as well as patients ending an anticholinergics treatment
- Number of patients with a dry mouth was similar for mirabegron and placebo, and considerably lower than for tolterodine ER 4 mg
- Contraindicated for use with serious uncontrolled hypertension (systolic blood pressure (BP) \geq 180 mm Hg and/or diastolic BP \geq 110 mm Hg)
- Use with caution in patients with a history of QT interval prolongation or patients who use medicines that are known to prolong QT interval

105. BETMIGA™ 5MPC; 76. Khullar 2013; 89. Chapple 2013

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TREATMENT STRATEGIES FOR REFRACTORY OAB

- Botulinum toxin injection
- Sacral neuromodulation
- Tibial nerve stimulation
- Pudendal nerve stimulation

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BOTULINETOXINE A-INJECTIONS : NOT ONLY FOR WRINKLES

- Injection of botulinum toxin type A-protein in bladder wall
- Results:
 - Significant improvement of the OAB symptoms, positive effect on their quality of life
 - Patients with an average of 5.5 UI-episodes/day, improved to an average of 2.5 UI-episodes per day after 2 weeks (compared with 4.5 with placebo)
- Duration of the effect: ~ 24 weeks
- Most important adverse events (AEs):
 - UTI, postvoid residual urine volume (PVR) elevation
 - and initiation of clean intermittent catheterisation

76. Chapple C et al. Eur Urol 2013;64(4):56-62. 5PC Botox

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BOTULINUM TOXIN INJECTION - CLINICAL RESULTS

- Pooled data 2 phase III trials
- 1105 patients: 557 onabot 100U – 548 placebo
- 12 week results

81. Sievert et al. Int J Clin Pract 2014

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SACRAL NEUROMODULATION

- Sacral nerves control the functioning of the bladder (and intestines)
- Neurostimulator normalises the functioning of the bladder through a change in nerve activity → nerve stimulation
 - Neurostimulator is implanted under the skin
 - Connection between neurostimulator and sacral nerves
 - Patient programming unit
- Results
 - Urgency urinary incontinence: improved in 68% of patients 5 years after implantation
 - New intervention is required for 25-30%
 - long-term effect (years)

88. Van Kerrebroeck PEV et al. J Urol 2007;178:2229-34.

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1982 2002 2006 2013 2014 2019

+ / 300 000 patients

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Sacral Neuromodulation – Conventional indications

- Overactive bladder
- Urgency Urinary Incontinence
- Non Obstructive Urinary Retention / Hypocontractile or Acontractile bladder
- Faecal Incontinence
- Only treatment that may alleviate symptoms of bladder and bowel dysfunction

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PHASE I – 6 MONTHS RESULTS

Efficacy

PP: Only patients with baseline and end data ITT: Failed to follow up were failures

Device	ITT	Continence
SNM	76*	61*
SMT	49**	42*

Improvement in QoL

QoL Domain	SNM	SMT
Continence	47	16
Coping	45	14
Sleep	37	11
Social	27	9
HRQL total	40	13

Device-related AE occurred in 31% of SNM patients
Medication – related AE occurred in 27% of SMT patients

*p<0.05; **p<0.01.

90. Siegel et al. Neurourol Urodyn. 34:224-230, 2015

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ROSETTA TRIAL 24 MONTHS FU

- In botox group – 2 additional injections were allowed after 6 months

44. Amundsen et al. Eur Urol 2018

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POSTERIOR TIBIAL NERVE STIMULATION

- PTNS* sends indirect electrical impulses to the sacral micturition centres
- Stimulation is percutaneous with a fine needle with an adhesive electrode inserted just above the ankle (posterior tibial nerve)
- Treatment cycles usually consist of 12 weekly treatments of 30 minutes each (to be long-term when effective)

*PTNS: posterior tibial nerve stimulation

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SUMIT TRIAL – SHAM CONTROLLED TRIAL

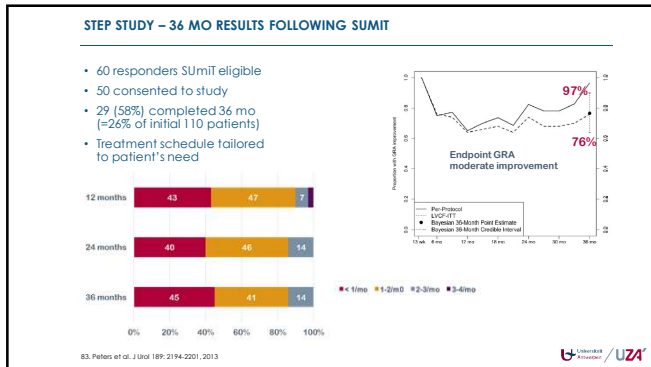
Endpoint GRA: Moderate improvement

	Baseline	13 Wks	Change From Baseline	p Value	Difference (PTNS – sham)	p Value
Mean ± SD PTNS:						
Frequency*	123 ± 32	98 ± 28	-24 ± 25	<0.001	-0.8 ± 2.5	0.01
Nighttime voids†	2.9 ± 1.6	2.1 ± 1.4	-0.7 ± 1.2	<0.001	-0.4 ± 1.3	0.04
Voided vol	1695 ± 789	1930 ± 756	114 ± 450	0.01	5.5 ± 42.1	0.35
Mean ± SD sham:						
Frequency	124 ± 30	110 ± 31	-15 ± 24	<0.001		
Nighttime voids	2.9 ± 1.7	2.9 ± 1.6	-0.2 ± 1.4	0.02		
Voided vol	1987 ± 840	1726 ± 906	-5.9 ± 390	0.13		
Median PTNS:						
Moderate to severe urgency*	63	37	-37	<0.0001		<0.001
Urge incontinence†	30	63	-1.3	<0.0001		0.002
Median sham:						
Moderate to severe urgency	80	50	-2.0	<0.0001		
Urge incontinence	1.8	1.0	-0.3	<0.0001		

82. Peters et al. J Urol 183:1438, 2010

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Summary Urgency Urinary Incontinence

- Prevalent condition - often associated with other disorder
 - Other urological disorders like stress incontinence
 - Other gynecological disorders like prolapse
 - Other gastrointestinal disorders like faecal incontinence / constipation
- Symptom complex
 - Diagnosis often made on history alone – certainly for conservative treatment
- More advanced diagnosis necessary when considering invasive treatments
- Some treatment have dual effect, on bladder and bowel

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Thank you for listening...

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