Female Urinary Incontinence

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Objectives

- Differentiate the types of female urinary incontinence
- Evaluate, diagnose and treat female urinary incontinence
Female Urinary Incontinence (UI)

- Any involuntary leakage of urine
- Stress urinary incontinence (SUI)
  - Involuntary loss of urine associated with provocative maneuvers-coughing, laughing, sneezing, listing, exercise
- Urinary urgency incontinence (UUI)
  - Involuntary loss of urine associated with urgency
- Mixed urinary incontinence (MUI)
  - Both SUI & UUI

- Female UI is a highly prevalent condition affecting 50% of women
- Only 25% seek care and <50% of those that do receive treatment
• Population-based studies have reported that UI is more common in women than men
• Prevalence increases with increasing age
• Older women with UI are 1.5-2.3 times more likely to experience falls leading to increased mortality, morbidity and health care dollars

Cumulative Incidence of Incontinence in Women According to Age and Definition of UI

*Per International Continence Society; requires objective demonstrability and presence of hygienic or social problem for uncontrolled loss of urine to be acknowledged as UI.

• According the U.S. National Health and Nutrition Examination Survey (NHANES) 49.6% of women reported any UI with:
  – 49.8% reporting pure SUI
  – 34.4% reporting mixed UI (MUI)
  – 15.9% reporting pure urgency UI (UUI)
Stress Urinary Incontinence Is the Most Common Type in Women

- Stress: 49%
- Urge: 22%
- Mixed: 29%

Prevalence of UI in Women

### Differential Diagnosis: Overactive Bladder, Stress Incontinence, and Mixed Symptoms

**Medical History and Physical Examination**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Overactive Bladder</th>
<th>Stress Incontinence</th>
<th>Mixed Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgency (strong, sudden desire to void)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Frequency with urgency (&gt;8 times/24 h)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Leaking during physical activity, eg, coughing, sneezing, lifting, etc.</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Amount of urinary leakage with each episode of incontinence</td>
<td>Large (if present)</td>
<td>Small</td>
<td>Variable</td>
</tr>
<tr>
<td>Ability to reach the toilet in time following an urge to void</td>
<td>Often no</td>
<td>Yes</td>
<td>Variable</td>
</tr>
<tr>
<td>Waking to pass urine at night</td>
<td>Usually</td>
<td>Seldom</td>
<td>Maybe</td>
</tr>
</tbody>
</table>


### Risk Factors for SUI

**Predispose**
- Gender
- Race
- Neurologic
- Muscular
- Anatomic
- Collagen
- Family

**Incite**
- Childbirth
- Hysterectomy
- Vaginal surgery
- Radical pelvic surgery
- Radiation
- Injury

**Promote**
- Obesity
- Lung disease
- Smoking
- Menopause
- Constipation
- Recreational activity
- Occupation
- Medications
- Infection

**Intervene**
- Behavioral
- Pharmacological
- Devices
- Surgical

**Decompensate**
- Aging
- Dementia
- Debility
- Disease
- Environment
- Medications

SUI

• Peak incidence 45-49 years

• Risk Factors
  – White race
  – Obesity
    • BMI >30 have twice the risk, independent of age and parity
  – Pregnancy
  – Childbirth
  – Parity

Evaluation

• History
  – Focused History
    • Elicit symptoms
    • Duration of symptoms
    • Severity- does it require pads, diapers
    • Associated factors- hematuria, dysuria, pain, straining, post void dribbling, UTIs
  • Past Medical History
    – Neurological conditions- MS, DM, CVA, Parkinson’s, SCI
    – GU trauma
    – Previous or current XRT
  • Past OBGYN history
    – Gravity, parity
    – Estrogen status- pre, peri, post-menopausal
  • Past Surgical History
    – Previous anti-incontinence or POP surgery
    – Previous GU surgeries
    – APR, radical hysterectomy
  • Medications
PE

—Focused PE

• GU examination
  » Estrogen status
  » Pelvic Organ Prolapse
    • Pelvic Organ Quantification System

—Urethra
  » Supine cough stress test- involuntary leakage from the urethra with valsalva or cough

Testing

• UA
• PVR

Per AUA guidelines a PVR is not indicated in uncomplicated patients. It is recommended in patients with obstructive symptoms, history of previous incontinence or prostatic surgery, neurological diagnoses and in patients with SUI that may are considering invasive therapy
Testing

• UDS
  – VALUE Trial
    • For women with uncomplicated, demonstrable stress urinary incontinence, preoperative office evaluation alone was not inferior to evaluation with urodynamic testing for outcomes at 1 year.

SUI Care Pathway

[Diagram of SUI Care Pathway]
Treatment of Stress Incontinence

- Observation
- Pelvic Floor Exercises
- Incontinence devices
- Injectable Therapy – Bulking Agents
- Retropubic procedures
- Slings

Pelvic Floor Muscle Training

- Perception of cure is more common in women who perform pelvic floor exercises than in those who do not

- Efficacy has been shown with 30-50 daily contractions

- Not all women can perform Kegels correctly with oral instruction alone
Surgery versus Physiotherapy for Stress Urinary Incontinence

• 460 women randomized to PT or MUS
• 49.0% PT and 11.2% of women in the surgery group crossed over
• Subjective cure rates 85.2% in MUS & and 53.4% PT
• Objective cure were 76.5% in MUS and 58.8%, PT


Conclusion

• For women with stress urinary incontinence, initial midurethral-sling surgery, as compared with initial physiotherapy, results in higher rates of subjective improvement and subjective and objective cure at 1 year.
Medications

• No FDA approved medications

Devices-Pessary

See Figure 2. Pessaries for Treating Stress Incontinence.
Devices

• Approximately ½ of women successfully fitted with a pessary use it for the next 1-2 years

• A randomized controlled trial comparing use of super tampon and pessary to no device in women with incontinence only with exercise found that the tampon and pessary were equally effective

History of Surgery for Female Stress Urinary Incontinence


Kelly Plication
MMK
Burch
Pereya
Stamey
Needle suspension
PVS
Raz
Gitte
Lap
Burch
TVT
TOT
TVT Secur
Surgical Treatment of SUI

- Bulking Agents
- Retropubic Suspensions
  - Burch
- Slings
  - Autologous fascia
  - Mid-urethral
    - Retropubic
    - Transobturator
    - Mini-sling

Urethral Bulking Agents

[Images: Bladder neck incompetence, Bladder neck after Macroplastique injection]
Bulking Agents—Results

• In office under local or in the OR under MAC
• 12 month cure rates 24- 36%

• Bulkamid (polyacrylamide hydrogel)
  – 70% cure rate at 60 months

Burch Long Term Results

De Novo Detrusor Instability = 14.7%
Long Term Complaints of Voiding Difficulty = 22%
Recurrent UTI = 4.6%
After 12 years, long term cure rate plateaus at 69%

Autologous Fascial Sling/ Pubovaginal Sling

See Figure 3 - Surgical Procedures for Treating Stress Incontinence.


Autologous Fascia—Long Term Results

• 15 x 2 cm autologous rectus fascia
• N = 251
• Minimum of 1 year follow up
• Median follow up 3 years
• 92% cure of SUI
• 95% cure of SUI in 20 patients with 10 yr fu

Chaikin & Blaivas, J Urol, 1998
Autologous Fascia – Long Term Results

• Multiple authors report 75-85% cure with > 5 year f/u
• No dyspareunia (without bone anchors)
• 5-15% voiding dysfunction
• Gold standard sling

Midurethral Sling

• TVT
  – Introduced in 1995
  – Rapidly became the most widely-performed procedure for SUI
• TOT
  – Introduced in 2001
  – Created to avoid common complications associated with TVT
Retropubic Midurethral Sling Outcomes

<table>
<thead>
<tr>
<th>Author</th>
<th>Success Rate</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulmsten et al</td>
<td>86%</td>
<td>36 months</td>
</tr>
<tr>
<td>Olsson et al</td>
<td>90%</td>
<td>36 months</td>
</tr>
<tr>
<td>Wang et al</td>
<td>83-87%</td>
<td>24 months</td>
</tr>
<tr>
<td>Moran</td>
<td>80%</td>
<td>24 months</td>
</tr>
</tbody>
</table>

TVT Complications

- Multicenter retrospective review of 241 patients who underwent TVT (22 patients had a secondary procedure)
- Mean Follow-up 6 months
  - Sling Lysis for BOO 4.1%
  - De Novo Urgency 15%
  - Intravaginal Tape Erosion 0.4%

Current Surgical Treatments

• Bulking agents
  – Pros: Minimally invasive, can do in the office or under MAC, no post-operative restrictions
  – Cons: 50% efficacy

• Midurethral slings:
  – Pros: High success rate 85%
  – Cons: 4 week recovery, mesh complications, urinary retention

• Fascial slings
  – Pros: High success rate 87%
  – Cons: Voiding dysfunction 10%, SSI 5%, 6 week recovery, foley X 1 week post-op

• 188,454 sling performed
UUI Epidemiology

- Affects 33 million Americans — 500 million worldwide
- Prevalence — 11-19% men and women
- OAB sx prevalence and severity increase with age

Impact on Psychosocial Functioning and Quality of Life

- Negatively affects sleep, mental health, work productivity, overall QOL
- UUI independently associated with increased risk of falls and non-spine non-traumatic fractures in older woman

References:
- Irwin D et al. BJU Int 2011;108:1132
- Haab F et al. Neuro Urol 2014;33:S2
- Coyne et al. BJU 2008; 101:1388
Concerning Statistics

- Nearly 2/3 of patients are symptomatic for 2 years before seeking treatment
- 76% of diagnosed pts remain untreated
- 50% pts on current treatment regimens say treatment is not helping their symptoms
- 73.5% stop medications within 1 yr due to SE or lack of efficacy

D’Souza et al. J Manag Care Care Pharm 2008;14:291
Guideline Statement 1

• The clinician should engage in a diagnostic process to document symptoms and signs that characterize OAB and exclude other disorders that could be the cause of the patient’s symptoms
  – UTI, IC/PBS, Diabetes insipidous, Polydipsia

• The minimum requirements for this process are a careful history, physical exam and urinalysis.

History

• Duration of symptoms
• Severity of incontinence
• Inciting events (post-op, neurological symptoms)
• Obstructive voiding symptoms
• Fluid intake habits
  – Caffeine and alcohol intake
• Medications
• Surgeries/radiation/chemo
• Does it BOTHER the pt enough to warrant treatment?
Co-Morbid Conditions: DIAPPERS

- Diabetes Mellitus
- Infection
- Atrophy
- Psychological
- Pharmacologic
- Excessive urine production
- Restricted mobility
- Stool impactions

Physical Exam

- Vital signs: BP
- Cognitive function- dementia?
- Mobility/gait/ dexterity
- Abdominal exam
  - Scars
  - Suprapubic distention
- Pelvic exam
  - Atrophic vaginitis
  - Pelvic organ prolapse
  - Levator spasm
  - Perineal skin – rash/breakdown
  - Lower extremities – edema
**Urinalysis**

- **UA**
  - Rule out UTI
  - Rule out hematuria
  - Microscopic hematuria ≥ 3 or more RBC on 1 properly collected specimen in absence of obvious benign cause*

- Urine Culture – **NOT** indicated unless there are signs of infection on UA

- **PVR:** Is it indicated?

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**Post-Void Residual**

“Measurement of the post-void residual (PVR) is not necessary for patients who are receiving first-line behavioral interventions or for uncomplicated patients (i.e., patients without a history of or risk factors for urinary retention) receiving anti-muscarinic medications”

PVR should be assessed in patients with:
- obstructive symptoms
- history of incontinence surgery
- neurologic diagnoses
- when PVR deemed necessary to optimize care and minimize potential risks
• Useful in pts who cannot describe or are not familiar with intake and voiding patterns
• Useful to document baseline symptoms & treatment assessment
• Components – # voids – Voided volume – Fluid intake – # of incontinence episodes
• Helpful in determining if nocturia is secondary to nocturnal polyuria – >20

Guideline Statement 3

• Urodynamics, cystoscopy and diagnostic renal and bladder ultrasound should not be used in the initial workup of the uncomplicated patient
Treatment

• First-line treatment with behavioral therapy presents essentially no risks and should be offered to all

Behavioral Treatment

• Education
  – Normal and abnormal bladder function
  – “Normal” fluid intake

• Modifying voiding habits
  – Bladder training
  – Delayed voiding

• Pelvic floor muscle training
  – Biofeedback
  – Vaginal weights
  – Manual training

• Weight loss
Fluid Management

• 25% reduction in fluid intake reduced urinary frequency and urgency
  – daytime frequency ↓ 23%
  – urgency ↓ 34%
  – nocturia ↓ 7%
• Reducing caffeine decreases urgency & frequency by 37%

Pelvic Floor Muscle Training

• PFMT via biofeedback, verbal feedback or self-administered via pamphlet
  – Similar outcomes for incontinence reduction (60%) and increased bladder capacity (40-60cc)
  – Pts in both feedback groups reported higher patient satisfaction
Weight Loss

• 6 mo weight loss program vs education program
• 8% weight loss in obese women
• Reduced urgency incontinence episodes:
  – 47% in weight loss group
  – 28% in control group

Subak L et al. NEJM 2009; 360:481.

2nd Line: Pharmacologic Treatment

• Choice of oral anti-muscarinics as second-line therapy reflects the fact that these medications reduce symptoms but also can commonly have non-life-threatening side effects
  – Antimuscarinics
  – Tricyclic antidepressants
  – Beta-3 agonists
Anti-muscarinics

- Oxybutynin IR
- Oxybutynin ER
- Tolterodine ER
- Trospium
- Solifenacin (vesicare)
- Darifenacin (enablex)
- Fesoterodine (toviaz)

Available as generics

- Oxytrol
- Gelnique

Over the counter

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**Table 1** Characteristics of pharmacologic agents for treatment of overactive bladder

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose range</th>
<th>Dosage form</th>
<th>Metabolism</th>
<th>Receptor affinity</th>
<th>Other notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darifenacin (Enablex)</td>
<td>7.5-15 mg once daily</td>
<td>Tablet, ER</td>
<td>Hepatic by CYP450 isoforms</td>
<td>M3</td>
<td>Low rate of CNS side effects; high rate of constipation (14.6% to 21.3%)</td>
</tr>
<tr>
<td>Fesoterodine (Toviaz)</td>
<td>4-8 mg once daily</td>
<td>Tablet, ER</td>
<td>Hepatic by CYP450 isoforms</td>
<td>M1, M2, M3, M5</td>
<td>Low CNS penetration; possibly fewer CNS side effects</td>
</tr>
<tr>
<td>Oxybutynin IR (Ditropan)</td>
<td>5 mg 2-3 times/day, max 4 times/day (IR)</td>
<td>Tablet</td>
<td>Hepatic by CYP450 isoforms</td>
<td>M1, M2, M3, M4</td>
<td>IR is limited by high rates of dry mouth; ER associated with cognitive impairment</td>
</tr>
<tr>
<td>Oxybutynin ER (Ditropan XL)</td>
<td>5-30 mg once daily (ER)</td>
<td>Tablet, ER</td>
<td>Hepatic by CYP450 isoforms</td>
<td>M1, M2, M3, M4</td>
<td>Low rate of dry mouth; ER associated with cognitive impairment</td>
</tr>
<tr>
<td>Oxybutynin transdermal patch (Oxytrol)</td>
<td>1 patch applied twice weekly</td>
<td>Transdermal patch</td>
<td>Hepatic by CYP450 isoforms; second pass</td>
<td>M1, M2, M3, M4</td>
<td>Transdermal patch and gel associated with lower rates of dry mouth; transdermal patch associated with significant rate of skin reaction (lower with gel)</td>
</tr>
<tr>
<td>Oxybutynin transdermal gel (Gelnique) 3% and 10%</td>
<td>Applied once daily</td>
<td>Transdermal gel</td>
<td>Hepatic by CYP450 isoforms</td>
<td>M1, M2, M3, M4</td>
<td>Transdermal patch and gel associated with lower rates of dry mouth; transdermal patch associated with significant rate of skin reaction (lower with gel)</td>
</tr>
<tr>
<td>Solifenacin (VESicare)</td>
<td>5-10 mg once daily</td>
<td>Tablet</td>
<td>Hepatic by CYP450 isoforms</td>
<td>M3</td>
<td>High rate of dry mouth at 10 mg dose (27.8% vs 13.9% at 5 mg)</td>
</tr>
<tr>
<td>Tolterodine LA (Detro LA)</td>
<td>2-4 mg once daily</td>
<td>Capsule, ER</td>
<td>Hepatic by CYP450 isoforms</td>
<td>M1, M2, M3, M5</td>
<td>Constipation</td>
</tr>
<tr>
<td>Trospium (Sanctura, Sanctura XR)</td>
<td>20 mg twice daily (non-XR) 60 mg in the morning (XR)</td>
<td>Tablet</td>
<td>Active renal tubular secretion; no CYP450 involvement</td>
<td>M1, M2, M3, M4, M5</td>
<td>Low penetration across blood-brain barrier (quaternary amine); XR formulation should be taken in the morning</td>
</tr>
</tbody>
</table>

Anti-muscarinic activity

Anti-muscarinics

- Class side effects
  - Dry mouth
  - Constipation
  - Dry/itchy eyes
  - Blurred vision
  - Dyspepsia
  - Impaired cognitive function
Choice of Anti-muscarinic

• An extensive review of the randomized trials that evaluated pharmacologic therapies for OAB revealed no compelling evidence for differential efficacy across medications

• Choice of medication should be based on:
  – Prior history of anti-muscarinic use
  – Side effect profiles
  – Delivery system
  – Comorbidities
  – Cost/Coverage

Guideline 9

• If an immediate release (IR) and an extended release (ER) formulation are available, ER formulations should preferentially be prescribed over IR formulations because of lower rates of dry mouth
Guideline Statement 11

• If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with 1 anti-muscarinic medication, then a dose modification or a different anti-muscarinic medication or a β3-adrenoceptor agonist may be tried.

Guideline Statement 12

• Clinicians should not use anti-muscarinics in patients with narrow angle glaucoma and should used with extreme caution in patients with impaired gastric emptying or a history of urinary retention.
  – Do not use in patients taking solid oral formulations of potassium chloride.
Guideline Statement 14

• Clinicians must use caution in prescribing anti-muscarinics in patients who are using other medications with anti-cholinergic properties
  – Tricyclic antidepressants
  – Parkinsons drugs
  – Alzheimer's meds
  – Anti-nausea drugs with atropine like effects
  – Anti-cholinesterase inhibitors

Guideline Statement 15

• Clinicians should use caution in prescribing anti-muscarinics or β3-adrenoceptor agonists in the frail OAB patient
  – Start with the lowest possible dose and increase slowly
  – Watch out for poly-pharmacy & cognitive changes
Mirabegron

- Beta-3 adrenergic agonist
- FDA approved in 2012
- β3 receptors in detrusor smooth muscle & urothelium
- Promotes storage by activating sympathetic nervous system (hypogastric nerve) via norepinephrine

Ellsworth et al. J Fam Prac 2014;S63:38

Takeda et al. J Pharm Sci 2010;2110:121
**Mirabegron**

- Pooled efficacy date 3 randomized, double blind, placebo controlled multi-center study- 151 sites
- N=3452
- Placebo, tolterodine 4mg, mirabegron 25, 50, 100 mg
- Significantly greater decreases in UI and freq than placebo
- “Efficacy” similar to anti-muscarinics
- AE- NO difference in dry mouth or HTN vs placebo

**Medical Therapy Follow-up**

- Telehealth visit 4-6 weeks after prescribe a medication
  - Assess SEs
  - Dose Escalation
  - If have tried & failed medications discuss 3rd line therapies
    - Botox after 1 med
    - PTNS & SNS most insurances make pts fail 2 meds
3rd Line Therapies:
OnabotulinumtoxinA

Guideline Statement 17
• Clinicians may offer intradetrusor onabotulinumtoxinA (100U) as third-line treatment in the carefully-selected and thoroughly-counseled patient who has been refractory to first- and second-line OAB treatments. The patient must be able and willing to return for frequent post-void residual evaluation and able and willing to perform self-catheterization if necessary

Botulinum Toxin
• Most potent neurotoxin known to man
• Seven immunologically distinct serotypes: A, B, C1, D, E, F, G
• Only A & B are available for use clinically
• Works by inhibiting acetylcholine release from presynaptic cholinergic junction leading to chemodenervation, reduced muscle contractility and likely reduce afferent input
• Reversible in 5-12 months
• FDA approved for NDO in 2011 & OAB 2013
Botulinum Toxin Injection

See Figure 1. Injection-site pattern for the administration of onabotulinumtoxinA in the detrusor.

Onabotulinum Toxin A injection

• 100 units (200 units for neurogenic bladder)
  – 20 injection sites 0.5cc/site
• In office or OR
• Flexible or rigid scope
• Negative UA
• 1% lidocaine instilled in bladder
• Discontinue antiplatelet therapy ≥3 days

Botulinum Toxin

• Decreases OAB symptoms
• Increases bladder capacity
• Needs to be repeated roughly every 8-10 months
• Costly
• Up to 6% risk of need for temporary CIC w 100u
• Risk of UTI

• There are other types of botulinum toxin
  – Dosages/strengths differ
Onabotulinum Toxin A Outcomes

UII episodes decreased by 2.65 vs 0.87 for placebo (p<0.001)

Onabotulinum Toxin A Outcomes

| Table 3. Key safety parameters in first 12 weeks after treatment 1 and at any time during treatment cycle 1 in safety population |
|---|---|---|---|
| No. First 12 Wks (%) | No. Any Time (%)* |
| Placebo | OnabotulinumtoxinA 100 U | Placebo | OnabotulinumtoxinA 100 U |
| No. pts | 272 | 278 | 272 | 278 |
| AE with 5% or greater incidence: | | | | |
| UIIE | 16 (5.9) | 43 (15.5) | 59 (21.7) | 86 (34.5) |
| Dysuria | 26 (9.6) | 34 (12.2) | 27 (9.9) | 40 (14.4) |
| Bacteriuria | 5 (1.8) | 14 (5.0) | 10 (3.7) | 23 (8.3) |
| Urinary retention | 1 (0.4) | 15 (5.4) | 1 (0.4) | 16 (5.8) |
| Serious AE | 8 (2.9) | 9 (3.2) | 16 (5.9) | 19 (7.0) |
| Death | 0 | 0 | 1 (0.4) | 0 |
| PNE AE | 0 | 0 | 0 | 0 |
| 1.00 or Greater change from baseline | | | | |
| Placebo | 19 (6.9) | | 24 (8.7) |
| OnabotulinumtoxinA 100 U | 19 (6.9) | | 19 (6.9) |

6.1% pts initiated CIC
PTNS: Percutaneous Tibial Nerve Stimulation

• Needle electrode inserted medial/above medial malleolus
• Impulses travel from the ankle along the tibial nerve to the sacral nerves
  – Tibial nerve has input from S 2, 3 and 4 roots
• Weekly x 12 weeks
• Maintenance Therapy – varies
  – 1/month

Interstim

• Must fail or be intolerant to 2 meds
• Now MRI compatible
• Two approaches:
  – PNE followed by combined
  – Stage 1 & 2
So which 3rd line therapy

• Botox
  – Contraindicated in pregnancy
  – Can’t be used in Jehovah's’ witnesses
  – Increases risk of UTIs
  – Should not be used in pts with incomplete emptying or elevated PVRS
  – Must be willing to cath
  – Must hold anti-coagulation 5-7 days before procedure

PTNS

• Time commitment – 12 weeks then maintenance therapy
• Cannot have lower extremity edema- will not stimulate PTN
Interstim

- Good for pts with dual incontinence - UI & FI
- Now MRI compatible
- Does require reprogramming

Mixed Urinary Incontinence

- Treat the most bothersome symptom
- Caveat- if the pt has significant SUI surgical correction of SUI can improve OAB symptoms in 50-70% of patients
Conclusion

• Female urinary incontinence is a common, life altering condition affecting 50% of women
• It is important to differentiate the type of incontinence as the treatment algorithms are different