

Committee 11

Incontinence in the Frail Elderly

Chair-person

C.E. DUBEAU (USA)

Members

G.A. KUCHEL (USA),

T. JOHNSON (USA),

M.H. PALMER (USA),

A. WAGG (U.K)

CONTENTS

I. INTRODUCTION	VIII. URINARY RETENTION IN THE FRAIL ELDERLY
II. SEARCH STRATEGY	IX. NOCTURIA
III. DEFINING THE FRAIL ELDER POPULATION	X. MODELS OF CARE FOR THE FRAIL ELDERLY WITH UI
IV. AETIOLOGY	XI. RECOMMENDATIONS FOR MANAGEMENT
V. ASSESSMENT OF THE FRAIL ELDERLY WITH UI	XII. RECOMMENDATIONS FOR RESEARCH
VI. FACTORS IN MANAGEMENT	XIII. ALGORITHM
VII. TREATMENT	REFERENCES

ABBREVIATIONS USED

ADE =	adverse drug effect	ICS =	International Continence Society
ADL =	activities of daily living	IR =	immediate release
ANP =	atrial natriuretic peptide	ISC =	intermittent straight catheterization
AVP =	arginine vasopressin	LTC =	long term care
BOO =	bladder outlet obstruction	LUT =	lower urinary tract
BPH =	benign prostate hyperplasia	LUTS =	lower urinary tract symptoms
CEI =	cholinesterase inhibitor	NH =	nursing home
CI =	confidence interval	OAB =	overactive bladder
CNS =	central nervous system	OR =	odds ratio
DHIC =	detrusor hyperactivity with impaired contractility	PVR =	postvoid residual volume
DO =	detrusor overactivity	RCT =	randomized controlled trial
ER =	extended release	SUI =	stress urinary incontinence
FI =	faecal incontinence	UI =	urinary incontinence
IADL =	instrumental activities of daily living	UK =	United Kingdom
ICI =	International Consultation on Incontinence	US =	United States
		UTI =	urinary tract infection

Incontinence in the Frail Elderly

C.E. DUBEAU

G.A. KUCHEL, T. JOHNSON, M.H. PALMER, A. WAGG

I. INTRODUCTION

Older persons have the highest known prevalence of urinary incontinence (UI) of any group, other than persons with specific neurological disorders (e.g., spinal cord injury). The absolute numbers of older persons with UI is increasing exponentially worldwide with the global phenomenon of population aging [1].

In developed countries, the population of centenarians has doubled every decade since 1960, mostly as a result of increases in survival after age 80 [1]. As the baby boomers age, the number of persons aged 85 or older will rise steadily from just under 2 percent of the population now to nearly 5 percent by 2050. Thus, the absolute numbers of older persons will increase dramatically [2]. Even if the observed improvements in physical functioning among older persons continue, and research is able to demonstrate improved health and lower costs, the impact on future health care and long-term care costs will be profound [1].

Throughout the world, no matter how one defines “older” or “elderly,” this population is characterized by its variety, ranging from active, community-dwelling, working, healthy nonagenarians to bed-bound, chronically ill, functionally- and cognitively-impaired persons in their late 60’s. The former healthier group is closer in phenotype and physiology to middle aged persons than to frailer older persons. For these reasons, beginning with the Third Consultation, information about persons older than 65 years of age is organized by health status. Data regarding healthier older persons is integrated in the chapters covering anatomy, physiology, evaluation, and treatment, and this chapter focuses on frailer older persons, emphasizing not only the different aetiologies and treatment of UI, but the additional issues of disease burden, disability, altered responses to drug therapy, the role of caregivers, and goals and organization of care. This chapter is aimed at all types of providers who work with populations of frail elderly, and is also intended to be relevant to specialists who find standard approaches ineffective in this population. Faecal incontinence in frail elderly is now covered in the report of Committee ?.

UI in the frail elderly is uniquely different from UI in healthy older persons. The pathophysiology of UI in the frail requires a broader conception of “disease,” which centers on patient-level factors rather than just the lower urinary tract (LUT) and its neurological control. UI in the frail elderly constitutes a syndromic model of multiple interacting risk factors, including age-related physiologic changes, comorbidity, and potentially common pathways between them. Unlike UI in healthy older persons, the impact of UI in the frail elderly includes functional impairment, and extends beyond affected individuals to their caregivers, leading to outcomes of caregiver stress and institutionalization.

Therefore, the assessment of UI in frail persons requires a much broader medical and functional scope. Failure to address the multifactorial nature of UI limits not only clinical care and research regarding aetiology and treatment, but also important opportunities to improve function and quality of life [3]. Treatment must always be multicomponent, and must address the multiple associated factors and shared underlying impairments with other geriatric syndromes (for example, by combining lower extremity exercise with prompted voiding) [4]. Drug therapy must be placed in context of altered pharmacology, polypharmacy, and susceptibility to adverse effects. Effective management requires system-level approaches, with different models of care (e.g., for institutionalized persons).

A final challenge in providing a review of UI and FI in frail older people is the relative dearth of Level 1 evidence for interventions. This is not to say that existing studies are not robust, as the frail present multiple challenges for research (not the least of which is substantial trial drop-out due to intervening illness and death). What it does indicate is the **continuing paucity of new clinical trials**, despite the clear epidemiological imperative that the oldest-old are the fastest growing group of affected individuals. Reasons for this are myriad, including a lack of funding for multi-component interventions and “riskier” trials involving drug therapy. At the same time, one cannot assume that treatment outcomes from conventional therapy will be worse in the frail elderly than the healthy elderly without special data to so prove.

Intervention studies and outcomes need to be more broadly based, incorporating caregivers, a range of care settings, alternative models of care, and goals of care unique to this population [5].

II. SEARCH STRATEGY

Given the broad range of this report, we used multiple searches using the following MESH terms (in caps) and phrases, alone and in combination, using the PubMed and Ovid search engines: AGED, AGED OVER 80, ACTIVITIES OF DAILY LIVING, DEPRESSION, elderly, FALLS, frail, FRAIL ELDERLY, FRAILITY, function, geriatrics, LONG TERM CARE, MEDICATIONS, NURSING HOME, older, QUALITY OF LIFE, RANDOMIZED CONTROLLED TRIAL; and BLADDER, GYNAECOLOGICAL SURGICAL PROCEDURES, PELVIC FLOOR, PROSTATE, STRESS INCONTINENCE, SURGERY, URETHRA, URINARY INCONTINENCE, URINATION DISORDERS, UROGYNECOLOGY, UROLOGY, VAGINA, VOIDING DYSFUNCTION; Ovid Expert Search Filter; Publication years 2004-08. We included, where possible, information from non-English language articles where an English language abstract with sufficient information was available. References in retrieved articles were reviewed for additional relevant articles. We also searched the Cochrane Database and National Guideline Clearinghouse for relevant systematic reviews, meta-analyses, and evidence-based recommendations.

III. DEFINING THE FRAIL ELDER POPULATION

1. FRAILITY

Who, then, are the frail elderly? Consistent with increasing consensus in the geriatric literature, we define “frail older persons” as those over the age of 65 with a clinical presentation or phenotype combining impaired physical activity, mobility, balance, muscle strength, motor processing, cognition, nutrition, and endurance (including feelings of fatigue and exhaustion) [6-8]. Frailty is not, however, identical to disability and comorbidity. Among persons meeting strict phenotypic criteria for frailty, only 22% also had both comorbidity and disability, 46% had comorbidity without disability, 6% disability without comorbidity, and 27% had neither comorbidity nor disability [7]. Frail persons usually have multiple chronic medical conditions, take multiple medications, require care by other persons and assistance to perform some or all of the activities of daily living (ADLs) (e.g., bathing, dressing, toileting, and ambulation), are often homebound or in care institutions, and have a high risk of intercurrent disease, increased disability, hospitalisation, and death [1-6]. For example, in Japan,

10% of all persons over 65 require help or supervision with at least one ADL, [9] and the total prevalence of frail elders has been estimated at 6.1% [10].

Several studies suggest that the relationship between UI and frailty is not unidirectional. Incident UI in persons over age 65 has been associated with a two-fold increased risk of impairment in ADLs, instrumental activities of daily living (IADLs – e.g., transportation, finances, shopping, laundry, housekeeping), and poor performance on three physical measures, suggesting that incident UI may be an early marker of the onset of frailty [10]. In a population-based study of older Mexican Americans, incident but not prevalent UI was independently associated with functional decline in ADLs, IADLs, and physical performance [11]. Another population-based study found an association between UI and IADL decline, but not ADL decline, nursing home admission, or death, after adjustment for age and comorbidity [10A]. The authors suggest that the relationship between UI and adverse outcomes may be mediated by baseline illness severity and functional impairment [10A].

2. IMPACT OF UI ON MORBIDITY AND INSTITUTIONALIZATION

UI in frail persons can have much more severe consequences than in healthy older persons. Although one early study suggested that older persons with UI had a higher mortality risk, [12] subsequent studies that more fully adjusted for comorbidity and functional status have not found any association [10A, 10, 13, 14]. Several multivariate studies suggest that patients with new onset UI at the time of stroke have higher rates of death or disability at 2 years (OR 4.43; 95% CI 1.76 to 11.2) [15] and 6 months (OR 3.21 [95% CI 1.04-9.91]), [16] especially if UI persists (OR 7.47 [95% CI 2.29-24.42]) [16].

Given its association with frailty, it is not surprising that UI remains a risk factor for nursing home admission, despite global variation in services and temporal changes in elder care. Studies showing a significant association between UI and institutionalization have been done in: Finland (men [not women] with urgency UI); [17] Germany; [18] New Zealand (persons \geq age 65); [19] US (men more than women), [20] after hip fracture, [21] among Hispanic elderly, [11] and patients attending a dementia clinic [22]; and Japan (men only) [23]. Two studies failed to find a significant association after controlling for comorbidity, using US [10A] and Canadian databases [24]. It is estimated that the fraction of US NH admissions attributable to UI in men is 0.10 (95% CI 0.08–0.13) and in women 0.06 (95% CI 0.05–0.09) [25]. The prevalence of UI at NH admission in the U.S. shows small area variation of almost 50% and differs by race, [26] suggesting that patient and caregiver factors and local resources affect the role UI plays in institutionalization. An important methodological issue for such studies is

the erroneously low prevalence of UI in administrative long-term care databases when UI is defined by physician diagnosis in the medical record [27,28]. Another issue, particularly in studies of institutionalization in persons with dementia, is the failure to include UI as a risk factor [29] or defining it only by a composite function score [30].

IV. AETIOLOGY

1. BACKGROUND

As noted above, the aetiology of UI in frail older adults is grounded in the concept of a classic geriatric syndrome, involving multiple interacting risk factors, including age-related changes, comorbidity, and potentially common pathways between them. This section addresses all of these components.

2. QUALITY OF THE DATA

The data on the aetiology of UI in the frail elderly population is limited, and the Consultation does not grade the level of observational studies, which constitute much of this literature. Moreover, longitudinal studies of large numbers of frail individuals are difficult to carry out. Despite the lack of such studies, many relatively large, careful descriptive studies and case series, as well as expert consensus processes, have made important contributions to our understanding of the aetiology of UI in this population.

3. UI AS A GERIATRIC SYNDROME

In older adults, especially those who are frail, UI is considered to be a *geriatric syndrome*, because many of its risk factors are not directly related to the genitourinary tract [31, 32]. Geriatric syndromes have been defined as “multifactorial health conditions that occur when the accumulated effects of impairments in multiple systems render an older person vulnerable to situational challenges [31]. Thus, large numbers of different baseline as well as precipitating risk factors may interact with each other in influencing the ability of an older individual to remain continent in the face of common daily challenges (**Figure 1**). This multifactorial complexity, combined with the fact that most individual risk factors typically account for only a small proportion of the overall risk, have greatly complicated the development of a pathophysiological framework for the study of common geriatric syndromes [31].

Nevertheless, because common risk factors (e.g. lower and upper extremity weakness, sensory and affective impairment) may be shared by different geriatric syndromes (such as UI, falls, and functional dependence), [33] they may represent particularly attractive sites for intervention development [31]. For example, as proposed by Kuo and Lipsitz, [34] the presence of brain white matter hyperdensities within

critical periventricular and subcortical regions could represent key risk factors for the development of different geriatric syndromes such as falls, impairment in executive cognitive function, depressive symptoms, and UI. In fact, recent functional magnetic resonance imaging (fMRI) studies have begun to identify central nervous system areas that are particularly relevant to an individual’s ability to suppress urgency [35-37]. Therefore, failure of activation within orbitofrontal regions may contribute to individuals’ decreased ability to suppress urgency [37]. Connectivity pathways within the right insula and anterior cingulate gyrus may also play a role maintaining continence, [36, 37] supporting the concept that declines in connectivity [38] and coordination [39] between different brain regions represent early critical events in aging. These findings suggest the possibility that interventions to prevent the develop of white matter hyperdensities, such as control of vascular risk factors, could also prevent UI.

4. AGE-RELATED CHANGES RELEVANT TO UI IN THE FRAIL ELDERLY

Age-related changes in the LUT can function as risk factors for the development, continuation, and worsening of UI in frail elderly persons (**Table 1**). At the same time, they rarely are alone sufficient to cause UI, and in some persons have no effect on lower urinary tract symptoms (LUTS) or UI. Furthermore, the literature on “normal” LUT ageing has many potentially confounding methodological limitations. Normal ageing changes are difficult to study, because longitudinal data including large numbers of individuals spanning many years are necessary to definitively separate “normal LUT ageing” from confounding factors and comorbidity. Cross sectional studies are subject to confounding by comorbidity and time-dependent cohort effects, such as change in labour and delivery practices. Thus, to date many studies actually describe “age-related” associations, as opposed to normal ageing. Other limitations include: derivation of much of the cellular and neurochemical data from animal studies; morphologic studies based on cadavers with unknown parity, comorbidity, and LUT symptoms; “age-effects” derived from studies of symptomatic persons; and use of surgical patients at tertiary centres as “normal” controls. Even the definition of “normal” can be difficult: is it continence, absence of LUTS, lack of comorbid disease, or normal physiologic testing? [40] The following sections focus on findings from more robust and, where possible, confirmatory studies.

a) Bladder

Understanding age-related changes in the bladder is complicated by a paucity of longitudinal data, variable definitions of “normal,” and use of potentially biased (and symptomatic) referral populations. It is difficult to isolate such factors as the role of decreased blood flow, poor voiding habits, comorbidity, central and peripheral

Table 1. Age-related changes that could potentially contribute to UI in frail elderly persons

Age-Related Change	Potential Effects on Continence
Bladder ultrastructure on electron microscopy - Dysjunction pattern - Muscle and axon degeneration	Bladder overactivity and urgency UI Impaired bladder contractility, increased residual urine, and decreased functional bladder capacity
Bladder function - Decreased capacity - Increased detrusor overactivity - Decreased detrusor contractility - Increased residual urine	Increased likelihood of urinary symptoms and UI
Urethra - Decreased closure pressure in women	Increased likelihood of stress and urgency UI
Prostate - Increased incidence of benign prostatic obstruction - Increased incidence of prostate cancer	- Increased likelihood of urinary symptoms and UI
Decreased oestrogen (women)	- Increased incidence of atrophic vaginitis and related symptoms - Increased incidence of recurrent urinary tract infections
Increased night-time urine production	Increased likelihood of nocturia and night-time UI
Altered central and peripheral neurotransmitter concentrations and actions	Increased likelihood of lower urinary tract dysfunction
Altered immune function	Increased likelihood of recurrent urinary tract infections

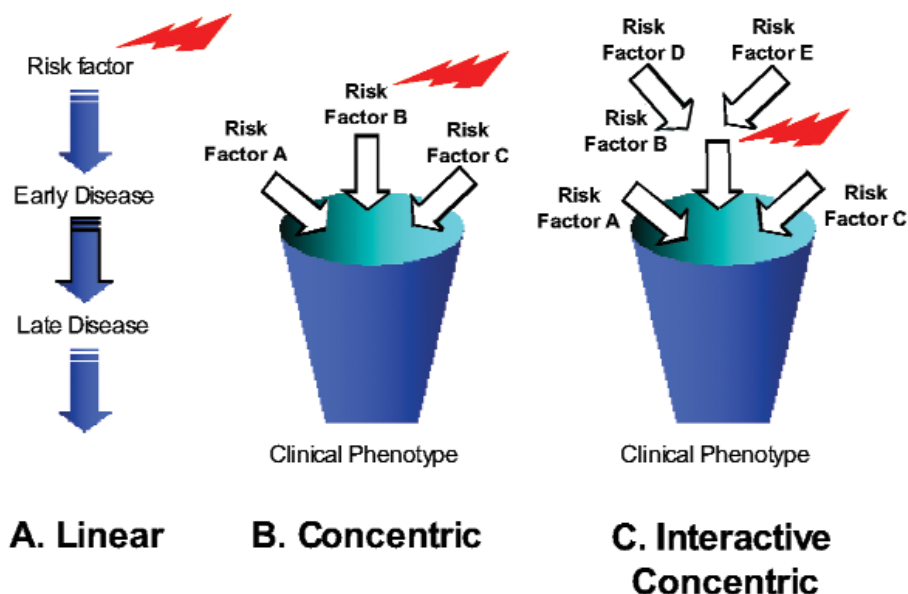


Figure 1 : Mechanistic Model of Geriatric Syndromes. Traditional pathophysiological models are based on a linear relationship proceeding from risk factors to early disease and then advanced disease (A), with prevention and treatment (red) directed at the causative risk factor. These models, while effective for many conditions, do not address the multifactorial nature of geriatric syndromes. Cancer researchers have used an alternative “concentric” model (B), in which a set number of risk factors (e.g., oncogenic pathways) lead to the clinical phenotype, and can become targets for therapy. This model also is insufficient for geriatric syndromes. Targeting individual RFs is unlikely to be effective because each RF accounts for only a small portion of the overall risk of disease. Geriatric syndromes are best described by an interactive concentric model (C), in which multiple risk factors likely interact with one another and (either common or separate) modulating factors. Interventions may be best targeted at those points that alter “downstream” risk factors [adapted from reference 31].

nervous system innervation, and reflex patterns as determinants of bladder function in older persons [41]. The research focus has been urodynamic function, neurohumoral responsiveness of detrusor smooth muscle, and ultrastructure. While the key role of the urothelium and afferent systems on micturition are increasingly appreciated (See Committee 2, Cell Biology; Committee 3, Neural Control; and Committee 4, Pathophysiology), there are only limited human data on urothelial changes with age.

Urodynamic changes associated with age typically include smaller voided volume, increased residual volume, smaller bladder capacity, and increased involuntary detrusor contractions (detrusor overactivity [DO]). Correlations with age are often small, suggesting that other factors are at least as important [42]. Urodynamic findings may not relate to symptoms: in a urodynamic study of community-based healthy persons over age 55, [40] DO was found in 42% of continent women, one-third of whom were totally free of LUTS. Within this older healthy cohort the prevalence of DO did not increase with age. Notably, completely normal urodynamic studies were found in only 18%. Nevertheless, in a cross-sectional study involving ambulatory, cognitively intact, community-dwelling older female volunteers, maximum urethral closure pressure, detrusor contraction strength, and urine flow rate all declined significantly with age, regardless of whether DO was present or not [43].

Detrusor contractility also declines in healthy older men who have no evidence of bladder outlet obstruction (BOO) or significant confounding disease [40]. A variety of different risk factors associated both with ageing and common comorbid conditions may contribute to age-related declines in detrusor contractility, which may ultimately lead to detrusor underactivity [44]. Decreased contractility during voiding in older persons is associated with lower urine flow rates and a small increase in postvoiding residual volume (PVR) (generally to ≤ 50 ml) [45]. Even in men with BOO, an elevated PVR may reflect decreased bladder contractility rather than obstructed voiding [46]. While some studies suggest a myogenic origin of impaired contractility, others suggest that impaired blood supply, with concomitant ischemic-reperfusion injury causing patchy denervation, leads to decreased contractility (see Committee 3, Neural Control). Incomplete bladder emptying from all causes can reduce functional bladder capacity, and thereby contribute to the urinary frequency and nocturia common in frail older persons [44].

The observation that bladder volume at the initial desire to void declines with age [48] may have been confounded by comorbid conditions and concurrent medications. Furthermore, unlike the positive association between detrusor contraction strength and DO found in younger subjects, older adults fail to

demonstrate this DO-associated increase in detrusor contractility [49]. Moreover, many frail older persons with UI present with a combination of DO on filling and poor contractility during voiding, a condition termed detrusor hyperactivity with impaired contractility (DHIC) [44, 50]. In such cases, the bladder contraction does not empty the bladder fully, leaving a large PVR otherwise not explained by BOO. Because DHIC symptoms can include urgency UI, stress and mixed UI, dribbling, frequency, and nocturia, they may be mistaken for other conditions. At the same time, DHIC may be mistaken for DO with normal contractility because significant detrusor underactivity may be present in the absence of any relevant symptoms.

Ultrastructural studies demonstrate cellular changes associated with age-related changes in detrusor function. One series of such studies involved symptomatic and asymptomatic persons aged 65 to 96, using urodynamic testing and electron microscopy of bladder biopsy specimens, which were read in a blinded fashion using explicit protocols [45, 51-57]. A consistent, one-to-one correlation between specific urodynamic findings and bladder ultrastructure was observed. Patients with urodynamic DO had a "dysjunction pattern" with "protrusion junctions" and "ultra-close abutments." The latter were postulated to be the anatomic explanation for the propagation of involuntary detrusor contractions in older patients. Patients with impaired bladder contractility had fibrosis with widespread degeneration of detrusor muscle and axons. A subgroup of patients had both types of pathology and urodynamic DHIC [50]. In the small number of asymptomatic patients with no DO, normal contractility, and no obstruction, detrusor muscle fascicles were largely intact, with two distinctive ultrastructural findings that may be related to ageing alone: muscle cell membranes characterized by numerous "dense bands" and markedly depleted caveolae, and slightly widened spaces between muscle cells with limited content of collagen and elastin. Depletion of caveolae may be related to de-differentiation of muscle cells, which could eventually result in the reversion of actively contractile cells to inactive, synthetically immature cells. A similar phenomenon has been reported in atherosclerotic blood vessels and postmenopausal myometrium, and may be related to reports of increased collagen in bladders from older women [45, 58]. Moreover, lack of oestrogen contributes to, and oestrogen replacement reverses, both caveolar depletion [59] and detrusor fibrosis [60] Thus, both ageing and postmenopausal decline in oestrogen levels may contribute to bladder muscle cell differentiation and contractility [44].

The natural history of these ultrastructural changes remains largely unknown. From the ultrastructural studies described above, a subset of 23 patients was followed longitudinally [54]. The previously observed

one-to-one correlation between ultrastructure and function was maintained, but it was unclear whether urodynamic or ultrastructural changes occurred first in subjects who developed or had a change in LUTS. The pattern of dense-bands and nondisruptive muscle cell degeneration varied over time: the DO with dysjunction pattern developed in some subjects, and impaired detrusor contractility and the corresponding degeneration pattern was observed to progress in severity or develop. Other investigators have found similar results but without the one-to-one correlation (e.g., see Brierly et al [61]).

b) Urethra

Due to their common embryological origin, the urethra undergoes age-related mucosal and stromal changes similar to the vagina, and urethral changes in older women can be partially inferred from examination of vaginal tissue. Because of the difficulty of obtaining non-cadaveric urethral tissue, data on urethral smooth and striated muscle changes with age are complicated by confounding factors and definitions of controls.

Urethral closure pressure decreases with age [62, 63]. Based on a sample of 82 women aged 20-70, urethral closure pressure was found to decrease by 15 cmH₂O per decade [64]. A number of anatomical and physiologic changes may account for this decline. Mucosal thinning and lack of proteoglycans reduce urethral wall apposition; this also may contribute to retrograde movement of perineal bacteria into the bladder causing urinary tract infections [65]. These mucosal changes may extend up to the bladder trigone, causing irritation of sensory afferent nerves, and possibly triggering DO [66]. The submucosal venous plexus in the proximal urethra loses its corkscrew shape, the number and volume of arterial vessels decrease, and vascular pulsations lessen [67]. Several studies, using different measurement techniques, have shown that urethral vascular density and blood flow decrease with age, but not vascular flow velocity [68-70]. However, age explained only 9% of the variability in vascular density in one study, [68] and none of the studies controlled for vascular risk factors such as hypertension and diabetes. The relative importance of decreased vascular volume versus hypoxia on urethral functional integrity is unclear. Other alterations in the urethral stroma are increased volume of connective tissue, decreased ratio of proteoglycans to collagen, and decrease in nerve density [71, 72].

Cadaver studies suggest that the number and density of urethral striated muscle fibres decrease with age, especially in the ventral wall of the proximal urethra [73, 74]. These authors estimated that striated fibers decrease by 1% per year. Large inter-individual variations were observed, with age and parity accounting for only a small part of the variability, suggesting that other yet to be defined factors are

important. These studies also found that cross-sectional striated muscle fibre area decreased while fibre diameter was preserved. Another cadaver study by the same group found that circular smooth muscle width was 25%-50% higher in younger women (aged 20-39 years) than older (aged 70-89), and that younger women had higher fibre counts [75]. Smooth muscle loss in the older women correlated with loss of striated muscle in the anterior urethra.

Urethral sensation, measured as current perception thresholds, was significantly impaired in older women in two studies (by the same authors), one comparing 48 asymptomatic women and 13 with urgency UI, [66] and another in asymptomatic women [76]. The authors concluded that age-related LUT sensory neuropathy could contribute to the higher prevalence of overactive bladder (OAB) symptoms with age; however, urethral sensation thresholds were higher in women with urgency UI when controlled for age and parity, [66] and the "asymptomatic" older women may have had urodynamic DO [76].

With age, the urethral meatus generally moves toward the vaginal introitus, and may be difficult to see if there is considerable introital stenosis. Caruncles—benign violaceous soft swellings—often appear at the meatus, and are not problematic unless they cause discomfort or obstruction. Urethral diverticula can be a diagnostic challenge, especially in older women, because the symptoms (dysuria, pain, UI, frequency, urgency, dyspareunia) may be attributed to postmenopausal changes, age, OAB, or urgency UI [77]. Diverticula should be considered in women who have repeatedly failed "conventional" UI treatment. Diagnosis requires imaging by either voiding cystourethrography, ultrasound, or magnetic resonance scans.

Urethral obstruction is relatively uncommon in older women, and is nearly always secondary to other LUT dysfunction (e.g., pelvic organ prolapse) or is iatrogenic (from LUT/pelvic surgery or radiation).

In men, age-related decrease in striated sphincter muscle cell density occurs as well, [78, 79] and has been associated with increased muscle cell apoptosis [78]. While some investigations describe an increase in resting prostatic urethral pressure with age, [80] others note the increase occurs only to the sixth decade then subsequently decreases, along with a shortening of sphincteric urethral length [81]. These discrepancies may reflect differences in prostate volume and morphology.

c) Pelvic floor

Pelvic floor changes in normal older men have not been well studied. In women, the effect of age on pelvic floor structure and function is difficult to differentiate from the effects of hormonal status and parity. A number of studies are cross sectional rather

than longitudinal, and focus on symptomatic women. For example, a questionnaire study of over 4,000 community women aged 25-84 found no association between age and stress UI (SUI), OAB, or anal UI, after adjustment for obesity, birth history, menopause, and hormone use [82]. Similarly, in a random sample of 343 Austrian women aged 18-79 years, impaired pelvic muscle contraction (graded by the Modified Oxford Scale) was weakly associated with parity and body mass index but not age [83]. Evidence of denervation and changes in pelvic striated muscle fibre number, type, and diameter have been found in asymptomatic and nulliparous women (see Committee 2, Cell Biology). For example, in a sample of 82 nulliparous women, neither levator function (measured by resting vaginal closure force and augmentation of vaginal closure force) nor pelvic organ support (on pelvic exam) showed an association with age [64]. A histomorphometric study, using levator ani muscle from 94 female cadavers (aged 15-58), 10 male cadavers (aged 23-35), and 24 women undergoing pelvic surgery, found that myogenic cell damage was associated with both parity and age (</> age 35), but there was no difference between nulliparous women, men, and women with pelvic organ prolapse and/or UI [84]. Total collagen content in pelvic muscle and fascia declines with age, with increased cross-linking and decreased elasticity, [85] but this association does not imply a direct causative effect of "ageing." Constipation may independently contribute to pelvic floor dysfunction in older women [86, 87].

d) Vagina

The prevalence of age-related changes in the vagina varies with hormonal status, coexistent vascular disease, and the continuation or lack of sexual activity [88]. The postmenopausal decrease in oestrogen plays a part in many age-associated vaginal changes. Oestrogen is trophic for much of the LUT track in women, with oestrogen receptors found in the vagina, vestibule, distal urethra, bladder trigone, pelvic muscles, and ligamentum rotundum [89]. Yet, as the Women's Health Initiative trial has shown, [90 91] one cannot assume that the association between low oestrogen levels and physiological changes implies that hormone replacement will reverse these changes, restore function, or reduce symptoms. Moreover, the data are equivocal whether and how LUT oestrogen receptors change in number, density, or function with age [67].

Following menopause, the vaginal epithelium loses the majority of its superficial and intermediate layers. Mucosal thinning may be associated with inflammation, evident as erythema, telangiectasia, petechiae, friability, and erosions. This may be responsible for urgency and frequency in some frail elderly women. In addition, there is loss of epithelial glycogen and lubrication, and mucosal pH increases from 4.5-5.5 to 7.0-7.4 [67]. These changes can lead to loss of

normal adherent flora (lactobacillus), colonization with pathogenic organisms such as *E. coli* and enterococci, and the observed increase in bacteriuria and recurrent symptomatic urinary tract infections (UTIs) in older women [92].

Vaginal blood flow, which is important for mucosal integrity and submucosal fullness, decreases with age [67]. Whether this is oestrogen-related, and/or due to concomitant vascular disease is not known. Collagen and lipofuscin deposition in the stroma increases, and may be accompanied by invasion by lymphocytes and plasma cells [67]. The combined epithelial and stromal changes are associated with vaginal wall thinning and flattening of rugae [89]. The vaginal vault may shorten and narrow, and the introital opening decrease (and in severe cases become stenotic), which may make vaginal examination, intercourse, and use of pessaries difficult. However, it is not clear that vaginal shortening is clinically relevant: in one case series of over 3,000 women attending a general clinic, total vaginal length decreased by only 0.08 cm every 10 years [93]. Vaginal shape also may be altered by POP.

Because of the multiple potential confounding factors discussed above, a causal relationship between urogenital atrophy and urogenital symptoms/LUTS should not be automatically assumed. Very few randomized trials of oestrogen (oral or topical) for urogenital symptoms include women over age 75, use patient-defined outcomes in addition to physiological measures, or evaluate quality of life outcomes [94]. There are insufficient data to provide an evidence-based approach to symptomatic urogenital atrophy in older women. Oral oestrogen should not be used, but expert opinion supports topical oestrogen treatment (cream, intravaginal tablets, or oestrogen-impregnated pessary-like ring).

e) Prostate

Histological benign prostate hyperplasia (BPH) is strongly age-related, [95] and may lead to prostate enlargement (BPE) and outlet obstruction (BOO). While many LUT changes in women are associated with lower oestrogen levels, BPH results from the development of an oestrogen-predominant hormonal milieu in the prostate. The trophic prostatic androgen, dihydrotestosterone, is formed by the 5- α reduction of testosterone. Dihydrotestosterone levels decrease with age, while estradiol concentrations increase in the prostate stroma and remain constant in epithelial tissues, leading to an increase in the estradiol/dihydrotestosterone ratio [96, 97] and promoting stromal proliferation. Epithelial hyperplasia in turn is mediated by an array of stromal factors [98].

Histological BPH occurs in nearly 80% of men by age eighty [95]. Mean prostate volume increases with age but is very variable; its strongest predictor is prostate

specific antigen level of >1.4-2 ng/mL [99]. LUTS in men increase linearly over time, with the fastest increase during the seventh decade, such that by age 80 approximately one-third of men have received treatment for moderate to severe LUTS [100]. Natural history studies and randomized intervention trials, however, consistently demonstrate that symptomatic progression of benign prostate disease is not inevitable. LUTS remits in about one-third of symptomatic men without treatment [101]. Approximately one-third to one-half of affected men develop DO [102]. Thus, even in the presence of demonstrable BPE and/or BOO, the aetiology of LUTS is multifactorial, making prostate-related LUTS in older men a diagnosis of exclusion.

Although most patients are asymptomatic at the time of prostate cancer diagnosis, this is another possible cause of LUTS, including urgency UI, in older men. However, evaluation for prostate cancer in frail elderly men is rarely if ever indicated, given the high likelihood of limited remaining life expectancy.

The evidence is contradictory as to whether prostatic inflammation, either acute or chronic, contributes to urinary retention and LUTS in frail older men. In a single institution case series of 374 men undergoing TURP for acute urinary retention (AUR) or LUTS, pathological evidence of acute inflammation was significantly more common men presenting with AUR than LUTS (70% vs. 45%) [103]. However, in a much smaller case series of 70 men presenting with AUR, there was no association between inflammation from prostate infarction and AUR [104].

f) Other changes

The role of various neurotransmitters in the central and peripheral nervous system in UI is under active investigation (see Committee 2, Cell Biology). Nevertheless, age-related changes in the actions of these neurotransmitters, their receptors, or the cellular events they stimulate may contribute to the development of UI in frail older persons.

The prevalence of both asymptomatic bacteriuria and UTIs increase with age, [92] and the two are often found together in the frail elderly. Age-related changes in immune function, vaginal epithelium, faecal incontinence, and insufficient hygiene related to disability, cognitive impairment, and/or lack of caretakers may predispose the frail elderly to bacteriuria and recurrent UTIs. However, the role of otherwise asymptomatic bacteriuria (often found in association with pyuria), [105] in the aetiology of UI in frail elderly people remains unclear [106]. Treating otherwise asymptomatic bacteriuria in frail elderly patients with chronic, stable UI does not, in general, reduce UI severity [107]. UTI symptoms may be subtle and non-specific in this population, and include worsening of UI, altered mental status in patients with

dementia, decreased oral intake, or a minor but important decline in functional ability [106]. At the same time, current consensus criteria for UTI are poorly sensitive and only fairly specific for UTI in frail elderly. In a prospective cohort of 340 nursing home residents, in which UTI was defined as pyuria (>10 white cells) with >100,000 colony forming units on culture, the McGeer, Loeb, and revised Loeb UTI criteria had sensitivities of only 19-30% and specificities of 79-89% [92].

5. FACTORS OUTSIDE THE LOWER URINARY TRACT CAUSING OR CONTRIBUTING TO UI

A hallmark of UI in the frail elderly population is the wide variety of factors and conditions outside the lower urinary tract that can cause or contribute to leakage (**Table 2**).

a) Comorbid medical illness

Numerous comorbid conditions are common in frail elderly with UI, and many patients have multiple such conditions. For example, in a large population-based observation study, [108] UI (defined as use of pads) was independently associated with one or more other geriatric conditions (cognitive impairment, injurious falls, dizziness, vision impairment, hearing impairment) in 60%, two or more conditions in 29%, and three or more in 13%. Comorbid conditions can affect continence through multiple mechanisms: e.g., diabetes mellitus, present in approximately 15-20% of frail elderly, may cause UI by diabetes-associated LUT dysfunction (DO, cystopathy), poor diabetic control (causing osmotic diuresis and polyuria), medications (see below), and/or diabetes-associated comorbidity (e.g., constipation) and impairment (amputation, vascular dementia).

b) Neurological and psychiatric disorders

Neurological and psychiatric disorders are highly prevalent in the frail elderly population. Stroke, dementia syndromes (most commonly Alzheimer's disease, multi-infarct dementia, or a combination of the two [109]), and Parkinson's disease can each contribute to UI through multiple mechanisms. First, these disorders may affect the brain's pontine micturition centre and frontal lobes, and interfere with the normal ability to inhibit voiding. Second, each of these disorders can impair cognition. And third, each can impair mobility, and interfere with the ability to toilet independently. Frail older persons with these neurological conditions usually have multiple impairments and are at high risk for worsening disability. For example, in a UK cross-sectional survey of over 15,051 subjects, persons with cognitive impairment (MiniMental State Exam score \leq 23, prevalence 18%), were significantly more likely to have UI (odd ratio [OR] 1.3), impaired hearing (OR 1.7), poor vision (OR 1.7), have had at least two falls in the previous six months (OR 1.4), and report poorer

Table 2. Comorbid conditions that can cause or contribute to UI in frail elderly persons

Conditions	Comments	Implications for Management
Comorbid medical illnesses		
Diabetes mellitus	Poor control can cause polyuria and precipitate or exacerbate incontinence; also associated with diabetic neuropathic bladder	Better control of diabetes can reduce osmotic diuresis and associated polyuria, and improve incontinence
Degenerative joint disease	Can impair mobility and precipitate urgency UI	Optimal pharmacologic and non-pharmacologic pain management can improve mobility and toileting ability
Chronic pulmonary disease	Associated cough can worsen stress UI	Cough suppression can reduce stress incontinence and cough-induced urgency UI
Congestive heart failure Lower extremity venous insufficiency	Increased urine production at night can contribute to nocturia and UI	Optimizing pharmacologic management of congestive heart failure, sodium restriction, support stockings, leg elevation, and a late afternoon dose of a rapid acting diuretic may reduce nocturnal polyuria and associated nocturia and night-time UI
Sleep apnoea	May increase night-time urine production by increasing production of atrial natriuretic peptide	Diagnosis and treatment of sleep apnoea, usually with continuous positive airway pressure devices, may improve the condition and reduce nocturnal polyuria and associated nocturia and UI
Severe constipation and faecal impaction	Associated with “double” incontinence (urine and faecal)	Appropriate use of stool softeners Adequate fluid intake and exercise Disimpaction if necessary
Neurological and psychiatric conditions		
Stroke	Can precipitate urgency UI and less often urinary retention ; also impairs mobility	UI after an acute stroke often resolves with rehabilitation; persistent UI should be further evaluated Regular toileting assistance essential for those with persistent mobility impairment
Parkinson’s disease	Associated with urgency UI and less often urinary retention; also causes impaired mobility and cognition in late stages	Optimizing management may improve mobility and improve UI
Normal pressure hydrocephalus	Presents with UI, along with gait and cognitive impairments	Regular toileting assistance essential for those with mobility and cognitive impairment in late stages Patients presenting with all three symptoms should be considered for brain imaging to rule out this rare condition, as it may improve following a ventricular-peritoneal shunt
Dementia (Alzheimer’s, multi-infarct, others)	Associated with urgency UI; impaired cognition and apraxia interferes with toileting and hygiene	Regular toileting assistance essential for those with mobility and cognitive impairment in late stages
Depression	May impair motivation to be continent; may also be a consequence of incontinence	Optimizing pharmacologic and non-pharmacologic management of depression may improve UI
Medications	See Table 3	Discontinuation or modification of drug regimen

Table 2. Comorbid conditions that can cause or contribute to UI in frail elderly persons (To be Continued)

Conditions	Comments	Implications for Management
Functional impairments		
Impaired mobility	Impaired cognition and/or mobility due to a variety of conditions listed above and others can interfere with the ability to toilet independently and precipitate UI	Regular toileting assistance essential for those with severe mobility and/or cognitive impairment
Impaired cognition		
Environmental factors		
Inaccessible toilets	Frail, functionally impaired persons require accessible, safe toilet facilities, and in many cases human assistance in order to be continent	Environmental alterations may be helpful; supportive measures such as pads may be necessary if caregiver assistance is not regularly available
Unsafe toilet facilities		
Unavailable caregivers for toileting assistance		

UI = urinary incontinence

health (OR 1.9) [110]. Older persons with cognitive impairment have a nearly 6-fold increased risk of developing UI when they are hospitalized [111]. However, not all patients with neurological conditions causing cognitive impairment develop UI: in a six year longitudinal study, cognitive decline had only borderline association with UI, and only with UI that interfered with activities [112].

With the introduction of magnetic resonance brain imaging into routine clinical practice, radiology reports in older patients have increasingly emphasized the presence of structural abnormalities involving the white matter [113]. Terminology has also undergone a great change, moving away from subcortical atherosclerotic encephalopathy (a specific and relatively rare form of dementia), towards leukoaraiosis and, most recently, to the concept of white matter signal abnormalities (WMSA) [113, 114]. As noted above in Aetiology, recent fMRI studies [35, 37 36] demonstrate failure of activation within orbitofrontal regions in older persons with urgency UI, possibly contributing to a decreased ability to suppress urgency [37]. To date, there are no published studies of quantitative regional assessments of WMSA within these critical regions. Although a dichotomous diagnosis of “cerebral white matter lesions” provided by a radiologist demonstrated no relationship to the presence or absence of UI, [115] a semi-quantitative measure of global WMSA appears to be associated with increased urgency UI and nocturnal frequency [116].

Normal pressure hydrocephalus should be a diagnostic consideration in any frail elderly patient who presents with new onset of UI in association with gait disturbance and cognitive impairment. A subset of

these patients benefits from surgical implantation of a cerebrospinal fluid shunt [117].

LUTS, UI, and urodynamic DO are common in older persons with Parkinson’s disease, yet they may be related more to age and comorbidity than Parkinson’s-specific CNS pathophysiology [118-120]. The presence of UI in persons with Parkinson’s may in turn increase their risk for disability: in one series of patients with Parkinson’s, UI increased the risk of falling by nearly six-fold [121].

c) Depression

As in younger persons, frail elderly with UI have a higher risk of depression, a finding that has been replicated across cultures. Depression in older persons with UI may be under-diagnosed and under-treated: in one study of homebound adults with UI and severe depression, only 35% carried a previous diagnosis of depression and only 34% had been prescribed an antidepressant [122]. UI may add to the burden of depression by decreasing life satisfaction [123, 124] and self-rated health, [125] and by its association in frail elders with comorbidity [126].

Studies of the association of depression and UI in older persons are consistent across several depression measures. The validated Center for Epidemiologic Studies-Depression was used in two U.S. studies: a cross-sectional analysis of nearly 10,000 community-based persons (adjusted risk ratio for depression with UI 1.39 [95% CI 1.24, 1.55]), [127] and a large community-based study of older Mexican Americans (adjusted OR for depression 1.94 [95% CI 1.46-2.59]) [128]. Other multivariate studies finding significant associations between depression and UI in older patients used the Beck Depression index, [129] the

emotional disturbances and social isolation subscales of the Nottingham Health Profile Questionnaire, [130] and have included studies in Asia [131]. Although no association between UI and depression was found in a Korean study, it used a higher cut-off on the Geriatric Depression Scale and, unlike many other studies, found no association between UI and mobility [132]. Self-report of sadness has [133] and has not been associated with UI [134]. Psychological distress, assessed by the General Health Questionnaire, was associated with UI in African Americans (adjusted OR 5.60 [95% CI 1.88–16.67]), but not in whites, in a cross-sectional study of community based older persons with mean age 67 [135]. However, a longitudinal analysis of the same population over 13 years found that persons with UI and psychological distress were more likely to report UI-specific functional impairment (e.g., avoidance of social activities, shopping, and physical activities) (adjusted OR 6.55 [95% CI 1.94–22.12]). Additionally, persons with UI and condition-specific functional loss were more likely to develop psychological distress (OR 3.66 [95% CI 1.61–8.33]).

The direction of the causal relationship between UI and depression in frail persons is unclear, as nearly all of these studies were cross-sectional. The results of the one longitudinal study suggested that it is not UI itself but UI-specific functional loss (e.g., avoidance of social activities, attending church, etc.) that is most closely associated with psychological distress, even after controlling for important covariates [122].

d) Medications

Older persons consume the majority of prescription medications and are therefore at greater risk of experiencing adverse events associated with their use. The risk of difficulty in controlling urination in community dwelling older women taking medications with LUT effects was about 30% higher compared to those who did not take such medications (OR 1.31 [95% CI 1.05–1.21]) [136]. UI was independently associated with antianxiety/hypnotic medications in one large sample of US nursing home residents [109]. Many classes of medications commonly prescribed for the frail elderly can cause or contribute to the development of UI (**Table 3**). The possibility that UI could be caused by a medication should be taken into account before prescribing drug treatment for UI in older persons.

e) Functional impairment

Impaired functional ability is a common pathway by which several medical and neuropsychiatric disorders cause or contribute to UI in frail elderly (see above). Impaired mobility can preclude a frail older person with urinary urgency from reaching the toilet in adequate time to prevent UI. The apraxia associated with moderate to severe dementia can interfere with

independence in toileting and hygiene. Visual impairment is common in frail elderly, and may affect the ability to toilet independently.

Numerous studies support a close association between functional impairment and UI in frail elderly [33, 109, 137–141]. For example, UI was significantly associated with perceived limitations in usual role activities among community-based older persons [142]. In a longitudinal population-based study of older Mexican-Americans, prevalent UI was associated with an almost 60% increased risk of difficulty walking 8 feet (nearly 3 metres), and incident UI was associated with a two-fold increased risk for difficulty with ADLs and IADLs, as well as poor performance on three physical performance tasks [11]. Older women who experience a significant decline in physical performance over six years were more likely to report weekly UI (OR 1.31–1.40, depending on the physical measure) [112]. In the Health and Retirement Study, a population-based observational study of Americans aged ≥ 65 living in the community and nursing homes ($n = 11,093$), UI sufficient to require pads was independently associated with multiple impairments, including toileting (OR 2.9 [95% CI 2.3–3.4]), transferring (OR 2.8 [2.4–3.2]), dressing (OR 2.3 [2.0–2.6]), eating (OR 2.1 [1.8–2.4]), bathing (OR 2.0 [1.8–2.2]), and dependency in one or more ADLs (OR 1.9 [1.7–2.0]) [108]. Among NH residents in one US state, both baseline UI and FI were associated with ADL loss over one year (for UI, adjusted OR 3.1; for FI, adjusted OR 2.9; combined UI-FI (adjusted OR 3.4) [143].

UI may have particular prognostic implications after stroke. Among Italian stroke patients admitted to home care program after post-acute rehabilitation, those with UI were more likely have a significant decline in physical function at one year (OR 1.64 [95% CI, 1.01–3.29]) [144]. Similarly, stroke patients admitted to a Spanish multidisciplinary geriatric rehabilitation unit who had UI on admission made less functional gains in mobility and self-care [16].

International studies demonstrate a bi-directional association between UI and falls, including those resulting in fractures. In a study of elderly women using day-care services in Japan, mixed UI (but not urgency or stress alone) was associated with falls over one year (RR 3.05 [95% CI 1.01–10.2]) [145]. Baseline UI was an independent risk for falls in longitudinal studies of frail elders in residential care in Australia, [146] long-term care in Germany, [147] and in the community in the Netherlands [148]. There is a significant association between UI and fractures as well. Supporting studies include: a secondary analysis of an observational study of community-dwelling women in the US (adjusted relative hazard ratio for non-spine nontraumatic fracture 1.34 [95% CI, 1.06–1.69]); [149] a cross-sectional analysis of the Canadian National Population Health Survey; [150] a cross-sectional analysis of older women attending a

Table 3. Medications that can cause or contribute to UI in frail elderly persons

Medications	Effects on Continence
Alpha adrenergic agonists	Increase smooth muscle tone in urethra and prostatic capsule and may precipitate obstruction, urinary retention, and related symptoms
Alpha adrenergic antagonists	Decrease smooth muscle tone in the urethra and may precipitate stress urinary incontinence in women
Angiotensin converting enzyme inhibitors	Cause cough that can exacerbate UI
Anticholinergics	May cause impaired emptying, urinary retention, and constipation that can contribute to UI. May cause cognitive impairment and reduce effective toileting ability.
Calcium channel blockers	May cause impaired emptying, urinary retention, and constipation that can contribute to UI. May cause dependent oedema which can contribute to nocturnal polyuria
Cholinesterase inhibitors	Increase bladder contractility and may precipitate urgency UI
Diuretics	Cause diuresis and precipitate UI
Lithium	Polyuria due to diabetes insipidus
Opioid analgesics	May cause urinary retention, constipation, confusion, and immobility, all of which can contribute to UI
Psychotropic drugs	
Sedatives	May cause confusion and impaired mobility and precipitate UI
Hypnotics	
Antipsychotics	Anticholinergic effects
Histamine1 receptor antagonists	Confusion
Selective serotonin re-uptake inhibitors	Increase cholinergic transmission and may lead to urinary UI
Others	
Gabapentin	Can cause oedema, which can lead to nocturnal polyuria and cause nocturia and night-time UI
Glitazones	
Non-steroidal anti-inflammatory agents	

UI = urinary incontinence

university hospital geriatric outpatient department in Sweden; [151] and in a population based postal questionnaire study of 10,000 Swedish women born between 1900 and 1940 [152].

f) Environmental factors

Inaccessible toilets can be a major factor in the aetiology of UI in frail elderly persons, especially those with functional impairments. A study of 5,418 older persons receiving home care found that physical restraints and environmental barriers, along with UTIs, were the most common reversible risk factors for UI [153]. Among nursing home residents, UI has been independently associated with use of restraints [109]. Falls among frail elderly persons in long-term care institutions commonly occur while attempting to reach a bathroom [154]. Thus, the appropriate use of toilet substitutes (e.g., urinals, bedside commodes, bedpans for immobile women) and attention to potential environmental hazards (e.g. obstacles on the path to the bathroom, inadequate lighting, lack of handrails, low toilets) may be helpful in preventing UI as well as injuries. The availability of capable and motivated caregivers is often essential for effective toileting and prevention of UI. Clothing also may be altered to make toileting easier (e.g., Velcro fasteners and pants with elastic waist bands rather than buttons and zippers).

V. ASSESSMENT OF THE FRAIL ELDERLY WITH UI

Recommendations for the basic assessment of the frail elderly persons with UI are summarized in the Algorithm (see Summary Document). Because UI in the frail elderly is multifactorial, it is essential to conduct a comprehensive assessment with the goal of identifying all potential contributing factors. Collaboration among primary care physicians, geriatricians, surgical specialists, nurses, other health professionals, and caretakers is usually necessary for optimal assessment and management.

We could find no evidence-based guidelines for the assessment of UI in frail elderly. The United Kingdom (UK) NICE guidelines for UI in women do not address the assessment of frailer elderly women [155]. The US Agency for Health Care Policy and Research Clinical Practice Guideline on UI is significantly out of date (last revision 1996). The US government sets minimum quality standards for UI assessment and management in long term care, but these standards, along with basic fundamental principles of UI, are poorly understood by long term staff [156]. Two groups, the US Assessing Care of Vulnerable Elders (ACOVE) project and the UK Clinical Effectiveness and Evaluation Unit, have developed quality performance measures for UI care in frailer older persons, using structured literature review and expert panel review

[157-160]. These measures are not guidelines *per se*, and in some instances lack sufficient detail. Unfortunately, both groups have demonstrated using their measures the poor quality of UI assessment and care by community practitioners in the US and the UK, including inadequate integration of continence services. Thus, there is an urgent need to re-establish the fundamentals of UI assessment and management for all personnel who care for frail older persons with UI.

1. COMPONENTS

a) Identification of frail older persons

Health care providers can screen older patients with UI for frailty using the Vulnerable Elders Survey, which can be administered in person or by phone (**Table 4**) [161]. Persons with a score of 3 or greater have four-fold increase in the risk of death and functional decline compared with persons with lower scores.

b) Primary care assessment

Geriatricians' and primary care physicians' (PCPs) UI assessments were compared in a randomized multicentre study involving 364 subjects, 42% of whom self-reported UI to the investigators. Geriatricians were significantly more likely to detect UI (59% of cases vs. 16%), regardless of the severity of UI, and were more likely to refer to Continence Programs (25%); all referrals by PCPs were to urologists [162]. An assessment strategy based on clinical evaluation, simple cystometry, and several criteria for referral was compared with urodynamic diagnosis. Approximately 25% of patients met criteria for referral, half of patients accepted urodynamic evaluation, yet urodynamics changed the treatment plan in only 12% of the patients who did not meet the *a priori* criteria for referral [163].

Practice patterns and adherence to US UI guidelines were evaluated by retrospective chart review of 300 consecutive patients aged ≥ 65 , seen by either an internist or geriatrician for UI at a tertiary care centre. Geriatricians ordered more testing, such as urodynamics, before referring patients to a surgical specialist [164]. Overall, primary care practitioners rarely follow the US Agency for Healthcare Research and Quality UI guidelines, [165] and nursing home practitioners rarely follow the Federal guidance for UI care regarding recommended physical examination, PVR testing, urinalysis, and identification of potentially reversible causes [166].

Systematic review of articles identified only 5 studies meeting eligibility criteria, and all were in women. None of studies found sufficient diagnostic evidence (defined as positive > 5 and negative likelihood ratios < 0.02) for different types of UI. The best was a general population study reporting the utility of history and exam for the diagnosis of SUI (positive and negative likelihood ratios 3.23 and 0.40, respectively) [167].

Table 4. Vulnerable Elders Survey (VES-13)161: see text for scoring

1. Age_____ (1 point for age 75-84, 3 points for age 85 or greater)
2. In general, compared to other persons your age, would you say that your health is:
 - A. Poor (1 Point)
 - B. Fair (1 Point)
 - C. Good
 - D. Very Good, or
 - E. Excellent
3. How much difficulty, on average, do you have with the following physical activities: (SCORE 1 POINT FOR EACH BOLD RESPONSE, MAXIMUM OF 2 POINTS)

	No difficulty	A little difficulty	Some difficulty	A lot of difficulty	Unable to do
Stooping, crouching or kneeling					
Lifting, or carrying objects as heavy as 10 pounds					
Reaching or extending arms above shoulder level					
Writing, or handling and grasping small objects					
Walking a quarter of a mile					
Heavy housework such as scrubbing floors or washing windows					

4. Because of your health or a physical condition, do you have any difficulty: (SCORE 4 POINTS FOR ONE OR MORE YES RESPONSES IN THIS SECTION)
 - A. Shopping for personal items (like toilet items or medicine)?

<input type="radio"/> YES>> Do you get help with shopping?	YES	NO
<input type="radio"/> NO		
<input type="radio"/> DON'T DO: Is that because of your health?	YES	NO
 - B. Managing money (like keeping track of expenses or paying bills)?

<input type="radio"/> YES>> Do you get help with managing money?	YES	NO
<input type="radio"/> NO		
<input type="radio"/> DON'T DO: Is it because of your health?	YES	NO
 - C. Walking across the room? (USE OF CANE OR WALKER ALLOWED)

<input type="radio"/> YES>> Do you get help with walking	YES	NO
<input type="radio"/> NO		
<input type="radio"/> DON'T DO: Is that because of your health?	YES	NO
 - D. Doing light housework (like washing dishes, straightening up, or light cleaning)?

<input type="radio"/> YES>> Do you get help with light housework?	YES	NO
<input type="radio"/> NO		
<input type="radio"/> DON'T DO>> Is that because of your health?	YES	NO
 - E. Bathing or showering?

<input type="radio"/> YES>> Do you get help with bathing or showering?	YES	NO
<input type="radio"/> NO		
<input type="radio"/> DON'T DO>> Is that because of your health?	YES	NO

c) Cough stress test

Utility of the cough stress test was studied in 97 incontinent female long-term care residents using blinded comparison with single channel cystometry. Of the 77% in whom single channel cystometry diagnosis was congruent with the stress test (i.e., urodynamic DO with negative cough test, no DO and positive cough test), all were correctly classified; no woman with SUI was missed nor were any with DO misclassified [168]. An analysis 200 older women with UI found that provocative full-bladder cough test was as effective as radiographic or urodynamic pressure measurement in detecting SUI. Clinical diagnosis incorporating the cough test with leakage symptoms was 78% accurate, with only 6% false negatives for SUI, but was only 44% accurate with 45% false negatives for urgency UI [169].

d) Postvoiding residual measurement

We identified no studies evaluating the impact of PVR measurement on clinical diagnosis and treatment outcomes. Frail elderly may have a higher prevalence of elevated PVR, especially in association with DHIC. One study of 100 patients consecutively admitted to a geriatric ward found that 34% had PVR > 50 mL; these patients tended to have more UI (57% vs. 38%, $p > .05$), greater functional dependency, and a higher mortality rate (36% vs. 9%) [170].

However, the prevalence of elevated PVR in community dwelling frail elderly, especially those without associated disability or comorbidity, is not known.

e) Urodynamic testing

Urodynamic testing is feasible and safe, even in frail nursing home residents [171]. There is no evidence, however, that urodynamic diagnosis changes the outcome of treatment. Expert guidelines have recommended urodynamic testing before surgical or minimally invasive UI treatment in frail elders [172].

2. SUMMARY OF EVIDENCE

1. Active case finding and screening for UI should be done in all frail older persons because many do not spontaneously report their symptoms. (Level 1)
2. Screening for frailty is possible with short screening instruments (Level 1)
3. Current quality of primary care assessment of UI in frail elders is poor (Level 2)
4. Cough stress test has moderate accuracy in frail institutionalized women (Level 2)
5. No recommendation is possible on the utility of PVR testing in the assessment of UI in frail elderly (Level 4)

6. Urodynamic testing is feasible in frail elderly (Level 1) but it is unlikely change management or outcomes except in frail persons considered for surgical treatment of UI (Level 4)

3. RECOMMENDATIONS FOR EVALUATION (SEE ALGORITHM)

The essential first step is to screen all frail elders for UI, as the condition may be underreported across settings. The second is to identify treatable, potentially reversible conditions and other factors (medications, environment) that can cause or contribute to UI. Although UI associated with such factors has been commonly called “transient UI,” most frail elderly with UI have it as a chronic and often progressive condition. It is important to evaluate for such contributing factors because their amelioration may improve UI directly, make UI more amenable to other interventions, and overall improve the patient’s (and carer’s) quality of life [173].

Tables 2 and 3 list the common, treatable, potentially reversible conditions that can contribute to UI in frail older people. A mnemonic, “DIAPPERS” (delirium, infection [urinary tract], atrophic vaginitis, pharmaceuticals, psychological, excess fluid (in/out), restricted mobility, and stool impaction [and constipation]), has been commonly used to teach and remember these conditions [174]. However, treatment of two of these elements, atrophic vaginitis and UTI, may not improve UI (see Treatment section) and over-treatment of what is actually asymptomatic bacteriuria as UTI can lead to serious adverse outcomes (resistant organisms, secondary infections such as *Clostridium difficile*).

VI. FACTORS IN MANAGEMENT

1. BACKGROUND

This section, introduced in the 3rd ICI, highlights the issues that distinguish management of UI in frail elderly persons from that of healthier older adults. These include preferences for care, goals of care, determination of costs and benefits, special issues in drug treatment and issues unique to frail elderly men. They incorporate knowledge of physiological, psychological, sociological, and economic changes associated with frailty and advanced age, and reflect the importance of patient-centred goals and the role of caregivers in this population. These factors provide the context of continence care and should be incorporated into the management of all incontinent frail persons, *regardless* of the choice of specific treatment.

2. ROLE OF COMORBIDITY IN MANAGEMENT DECISIONS

Many frail elderly have concomitant disability and comorbidity, both of which can influence the clinical presentation and assessment of UI, as well as responsiveness to interventions. Frail older persons are not only at higher risk for unintended adverse effects from treatment (e.g., fulminate *Clostridium difficile* colitis from antibiotics used to treat otherwise asymptomatic bacteriuria in the setting of UI), but also may realize **additional benefits in domains other than UI** [173] from UI treatment that is aimed at underlying comorbidity and impairment (e.g., topical oestrogen for irritating atrophic vaginitis reduces recurrent UTIs; a nursing home exercise programme done in the course of toileting improves both physical function and UI [4]).

3. DEFINING OUTCOMES FOR TREATMENT

Outcome measures for frail older persons with UI must be fundamentally different from those used in healthy older persons, because of the heterogeneity of this frail population regarding comorbidity, remaining life expectancy (RLE), patient perceptions, personal values, and the involvement of caretakers and proxy decision makers. Unfortunately, intervention studies in the frail elderly remain focused on UI frequency and not these factors, and comorbidity is frequently used as an exclusion criteria in therapeutic trials. Also, there are no data on patients' or carers' expectations for the outcome of UI therapy.

Although quality of life (QoL) is a key concern for UI in all persons (see Committee 5, Initial Assessment Including Quality of Life), and has special relevance in the frail elderly with limited RLE, there are few validated QoL outcome measures applicable to this population. Only one validated UI-related QoL measure is derived specifically from patient-based data among persons older than 65, and these subjects were community-dwelling and relatively healthy [175]. None of the ICI-endorsed UI-related QoL measures have been validated in oldest-old or cognitively and/or functionally impaired persons. Traditional UI QoL domains—e.g., impact on IADLs, travel, sexual relations—are often not relevant to frail elderly, and there could be significant “floor effects” for social and role function domains. One alternative QoL domain for frail elderly is social interaction, especially for nursing home residents; [176] an analysis of cross sectional and longitudinal data from over 100,000 US nursing home residents found that prevalent and especially incident UI had negative impact on social interactions, particularly among persons with moderate ADL impairment [176].

The profound question when considering UI outcomes in frail older persons is, Is cure possible? The short answer is: it depends on patient factors, specific

treatment(s), and the target outcome. While no geriatrician endorses “ageism” and therapeutic nihilism, research evidence suggests that complete dryness is unlikely for certain frail patients, particularly frail institutionalized persons with severe cognitive and functional impairment. Even “intractable” UI is amenable to interventions that may improve the patient’s urinary and bowel function and quality of life [3]. The Frail Elderly Committee of the Third ICI introduced an alternative continence paradigm for frail elderly (**Figure 2**), which subsequently was generalized for all persons with UI [177]. In this paradigm, persons with “dependent continence” are dry as a result of ongoing assistance, behavioural treatment, and/or medications. UI would return if the interventions ceased, a situation analogous to chronic disease models [178] such as “controlled hypertension” or “controlled diabetes.” Persons with “independent continence” are cured without need for ongoing treatment (e.g., dry after successful anti-incontinence surgery). For patients who are unable to achieve independent or dependent continence, “contained incontinence” should be possible by use of appropriate products such pads, catheters, and appliances (See Committee 20, Management Using Continence Products), thus providing “social continence” or “accepted incontinence” [179, 180]. The balance between the types of continence achieved may vary as UI severity changes, and in conjunction with patient and caregiver preferences. All of the continence outcomes encompass a common need: to be both realistic and hopeful about UI in frail elders while avoiding nihilism and neglect, and maintaining comfort and dignity, and preventing avoidable complications of UI.

Although the ICS standardization document on outcomes in older patients is now 10 years old, little progress has been made and many of the identified needs still pertain (see Recommendations for Research) [5].

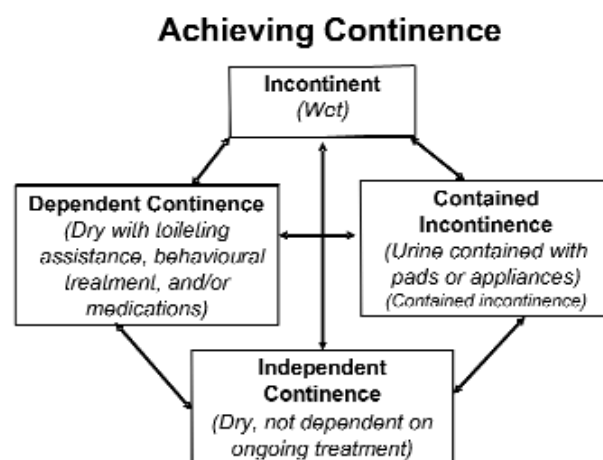


Figure 2 : A Paradigm for Continence

4. ROLE OF REMAINING LIFE EXPECTANCY IN TREATMENT DECISIONS

Remaining life expectancy (RLE) is a key yet often misunderstood concept in treatment decisions for frail older persons. RLE is *not* uniformly short in this population; moreover, there is a demographic trend of increasing RLE, with a smaller proportion of persons spending their remaining years living with disability [181]. Incorporation of RLE into treatment decisions in urology and gynaecology has been studied only in relation to cancer treatment. Only two studies, both in prostate cancer, examined specialists' ability to estimate RLE. Canadian urologists were more accurate in estimating longer RLE: using scenarios based on actual patient data, 31% were accurate within 1 year, 67% within 3 years, and 82% in estimating greater than or less than 10 years in 82% of responses [182].

Walter and Covinsky [183] developed a graphical tool for estimating quintiles of RLE by age (**Figure 3**). Medical conditions most closely associated with shorter RLE are class III/IV congestive heart failure, end-stage renal disease, and oxygen-dependent chronic obstructive pulmonary disease. Estimates of RLE are significantly affected by frailty and cognitive and

functional impairment [184]. Alzheimer's dementia decreases RLE profoundly (by nearly 75%) among older persons who otherwise would be in the top quintile of RLE [185]. Compared to older persons with at most one IADL deficit, persons with more deficits have significantly higher 5-year mortality (with two deficit, adjusted RR 1.46 [95% CI 1.20 – 1.78] ; with three or more deficits, adjusted RR 1.64 [1.26 – 2.14]) [184].

5. PREFERENCES FOR CARE

Because there are multiple treatment options available for frail older adults with UI, and individualised care is emphasised, obtaining patients' and carers' opinions regarding preference is essential for quality care planning. It should not be assumed that persons with cognitive impairment are unable to make their care preferences known or participate in treatment decisions.

Three studies have directly addressed patient and caregiver preferences for UI care. Preferences for toileting and changing were studied in 111 nursing home residents with UI; residents preferred an average of 2 pad changes, 1.5 toilet assists, and 2 walking assists more than they actually received, yet even these levels were lower than guidelines recommend, suggesting that residents may have reduced expectations based on their experience [186]. In the second, residents of board-and-care facilities and two nursing homes, their family members, and facility nursing staff were given definitions of and information about five UI treatment options (indwelling catheter, prompted voiding, adult diapers [sic], electrical stimulation, and medications) [187].

Respondents were asked their preferences between pairs of treatment options (e.g., "diapers" versus prompted voiding). Most of the board-and-care respondents were continent, although some were undergoing UI treatment at an outpatient clinic. Patients and family members were evenly divided between "definitely" and "probably" preferring prompted voiding versus diapers. Almost 80% of nursing staff, however, preferred prompted voiding to diapers. Families perceived staff members as unwilling to perform prompted voiding, and some thought prompted voiding was degrading to the resident and that it was bothersome to be asked to go to the toilet frequently. Using a similar method, a German study with 117 geriatric hospital patients (mean age 85; 43% with UI), 72 staff members, and 71 family members, found that most patients preferred diapers (79%), medications (78%) and scheduled toileting (79%) over urinary catheters and 64% preferred scheduled toileting [188].

When choosing between diapers and medication, equal proportions preferred each option. Patients with greater functional dependence were more likely to

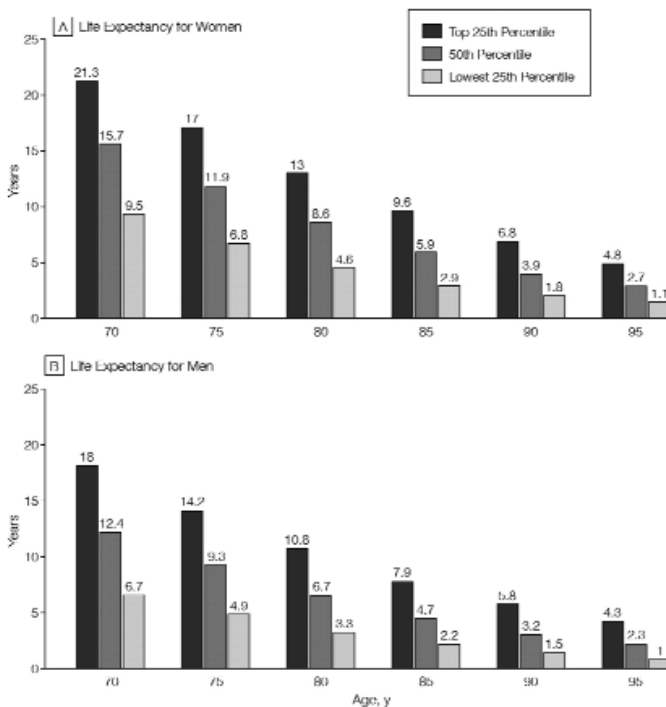


Figure 3 : Estimating Remaining Life Expectancy (reproduced from [183]). The graphs represent the quartiles of remaining life expectancy by age for women (A) and men (B). The lower quintile (25%) can be thought to represent persons with extensive comorbidity and dependence, the middle two quintiles (50%) represent persons with moderate comorbidity, and the top quintile (75%) represents the healthiest group.

prefer catheters, and those with experience with diapers were more likely to prefer medications and toileting. Notably, spouses showed moderate to almost perfect agreement with patient preferences, but those of other family proxies had only slight to fair agreement.

6. COSTS AND BENEFITS OF UI TREATMENT IN FRAIL ELDERLY

An overall discussion regarding UI-related costs is covered by Committee 22, Economics of Incontinence. The following discusses UI cost issues specific to the frail elderly.

a) *Estimating Costs*

Successful ageing is a hallmark of modern society. For many populations, the greatest increase in population is occurring in the oldest old, those \geq age 85. This group has the highest prevalence of UI, and accordingly their increased prevalence number will result in higher UI care costs. Such an increase has already been observed between 1992 and 1998 amongst US women aged \geq 65 [189]. The costs of care for older persons has been estimated at double that for people under 65, but care for those older persons living in institutions was less than for community dwelling individuals [190]. Likewise, the cost of OAB in five European countries is estimated to rise by one billion Euros between 2000 and 2020, [191] and in the US it has been estimated that by 2030 the greatest increase in demand for UI care (81%) will be in older women aged 60-89 with OAB symptoms [192]. In one US study using of a community managed care population, the presence of OAB and comorbidity doubled the associated costs of UI care [193].

Costs can be expressed as direct costs, indirect costs, and intangible costs [194]. Previous estimates have focused on diagnostic costs, treatment (including routine care and pads), and consequence costs (skin irritation, urinary tract infection, falls, fractures, additional nursing home and hospital admissions, longer hospital length of stay). Direct healthcare costs are most often estimated but there is a lack of meaningful research into indirect costs and those related to comorbidity often present in the frail elderly. Intangible costs have not been considered in these estimates because of their subjective nature and the methodological difficulty of collection and estimation. Much of the evidence for the cost of UI in older persons has been gathered from either epidemiological surveys or analyses of claims from insurance databases, and have often involved many assumptions or complicated formulae to calculate final costs. There is a consistent theme that the cost of caring for older adults with UI will increase, but the estimated magnitude of this increase is variable.

For the frail elderly, especially those in long term care, cost calculation is especially complex. The greatest costs for UI care in nursing homes are by far nursing

labour costs [195]. Extrapolated costs for nursing home admission due to UI was \$6 billion (2000 US dollars), [25] with institutional costs of UI management and consequences of \$5 billion (2000 U.S. dollars) [196]. In one small 6-month study, the mean daily cost of UI care, including direct nursing care, indirect nursing overhead, and supplies, was \$9.09 (\pm \$ 10.52) per resident (2003 U.S. dollars) [197]. The costs for UI pads alone in Dutch long-term care has been estimated at 160 million Euros [198]. In an Australian sub-acute care setting, the costs of daily UI care was \$49 AU, with most spent on staff wages [199]. In Canada, researchers found that 1% increase in UI prevalence was associated with an 11-12% increase in costs [200]. The extra nursing time needed to maintain toileting programmes contributes to high costs [201]. Routine garment and laundry costs may be lower than estimated because in practice residents are not changed as often as needed. In addition, for prompted voiding to remain effective, such things as regular refresher education programmes for staff or wet sensors may be necessary, and thus are rarely considered in cost estimates.

Moreover, the time period over which the costs and benefit are calculated needs to be explicit because both benefit and costs will change, and patient morbidity and mortality need to be considered. The costs of correcting functional and medical causes of UI are rarely considered. Also, the potential differential in costs across the span of cognitive and functional impairment has seldom been assessed, [202] despite evidence that UI care costs are closely related to the degree of functional impairment [203]. Costs related to caregivers of frail persons with UI living in the community include lost wages, decreased productivity (both within and outside of the home), the additional number of caretaking hours when a frail person develops UI, [204] and the cumulative effect of increased strain and burden, along with any resulting illness. Overall, there are still limited data on costs of UI treatment in other residential (such as assisted living or rest homes) and acute care settings [205 2004]. Costs may vary by access to care; because so many frail elderly are homebound or live in institutions, they often do not have the same access to the UI therapies as other populations. Their health care providers may be limited to primary care physicians, community nurses, and care assistants or aides with little to no expertise in UI management. Specialist consultation may be minimally available in home or long term care settings, leading to a focus solely on behavioural management and/or containment products.

Cost relates strongly to reimbursement, which varies considerably from country to country, depending not only on structure of the health system but special programmes for the aged and persons with UI (see Models of Care below). Within particular countries, there may be further variation based on insurance, co-

insurance, drug versus procedure coverage and incentives, access to care, programmes for vulnerable populations and urban/rural differences.

b) Benefit and effectiveness of treatment

The ability to define the benefit of UI treatment in frail older people is highly dependent on the individual, their caregivers, and the health care system. Outcomes research indicates that patients value quality of life, which encompasses many domains besides reduction in UI (See Committee 6, Symptom and Quality of Life Assessment). Even in cognitively impaired persons, one can still elicit treatment preferences, [188, 206] evaluate domains of quality of life (e.g., social interaction), [176] and assess treatment satisfaction directly or behaviourally. At the same time, we found no data on the value or utilities the frail elderly or their caregivers assign to varying degrees of UI (with or without treatment intervention) versus “dryness.” Standard outcomes such as quality adjusted life years (QALYs) may overestimate effectiveness in older people, [207] not just because of potentially different utilities but the altered importance of “years of life saved” in a population with variable and sometimes limited remaining life expectancy.

The above issues underline the need for novel and specific outcomes for use in both trials of UI

interventions and clinical care of the incontinent frail elderly. Outcomes measured by single item tools of perceived benefit or satisfaction with treatment are unlikely to be generalizable across the heterogeneous frail elderly population. It should not be assumed that perceived benefit of treatment can be measured with the same tools across cultures and health systems, unless such tools are sensitive to differences in such things as reimbursement for continence services and supplies. Associations between expectations, preferences, and outcomes need to be prospectively studied. New approaches and tools to assess UI-specific quality of life in the cognitively-impaired frail elderly are needed, as well as better understanding of the interaction between functional impairment and the impact of UI [176]. When QALYs are included as an outcome in UI treatment trials in older persons, they should be specifically analyzed by age and also possibly health status.

7. ISSUES IN DRUG TREATMENT

a) Age-related changes in pharmacology

Specific age-related changes in pharmacokinetics, alteration in drug absorption, distribution, metabolism and clearance, and their potential effect on UI drugs, are shown in **Table 5**. Age-related pharmacokinetic changes are rarely if ever considered in planning the

Table 5. Pharmacokinetic changes in older persons

Parameter	Age-associated Changes	UI Drugs Potentially affected
Absorption	Minimal quantitative change despite ↓ gastric motility, yet little known regarding effect on slow-release agents	Extended release preparations
	∅ Skin thickness	Transdermal preparations
Distribution	Decrease in lean body mass leads to ↓ Vd / ↓ T 1/2 for hydrophilic drugs and ↑ Vd / ↑ T 1/2 for lipophilic agents	Lipophilic agents, tricyclic antidepressants
	Decreased protein binding in frail patients with low albumin, leading to higher concentration of free drug	Tolterodine
Hepatic metabolism	↓ Phase I reactions (oxidation/ reduction)	Tricyclic antidepressants
	No change in Phase II reactions (glycosylation)	
	↓ Hepatic blood flow and ↓ hepatic mass, leading to reduced clearance for agents with first-pass metabolism	Oxybutynin Tolterodine Solifenacin Darifenacin
	Stereoselective selectivity in metabolism (hypothetical)	Enantiomers
	Cytochrome P450	Oxybutynin Tolterodine Solifenacin Fesoterodine Darifenacin
Clearance	Decrease in renal clearance	Tolterodine

Vd = volume of distribution, T 1/2 = half life

duration of time off previous UI medications, placebo-run in periods, and wash-out periods in UI drug trials in older persons. The numerous factors potentially affecting drug clearance in such patients, as well as previous and/or cross-over compounds, may confound observed drug effects. Age-related changes in pharmacodynamics have been described for benzodiazepines, beta-adrenergic agents, and opiates [208, 209] but there are little available data concerning changes in the frail elderly.

b) Availability of low dose agents

One effect of the under-representation (if not exclusion) of frail older persons in UI drug studies is a lack of knowledge regarding minimal effective drug doses for this population. The age-related changes in pharmacology noted above suggest that some UI drugs may be effective at lower than standard doses in frail elderly with concomitant decreased adverse effects [210]. This issue is especially relevant for extended-release preparations, which cannot be divided into smaller doses. There are some data supporting the effective use of low dose oxybutynin in older persons, but such studies are exceptional [211, 212].

c) Inappropriate polypharmacy

Approximately 60% of persons over age 65 take at least one prescribed medication, and about one-third take more than five prescribed drugs. In addition, many take over-the-counter and naturopathic or herbal agents, with the rate of use varying across countries and cultures. The likelihood of adverse drug reactions (ADEs) and drug interactions rises exponentially as the number of medications increases. This has led to the recommendation in geriatric prescribing to “subtract before adding,” to consider whether target symptoms might be due to medications before adding another drug targeting those symptoms. This approach is relevant in geriatric UI, as UI may have been precipitated and/or worsened by medications (see Table 3). Changes to existing drug regimens should be considered in the management of UI in all frail older people.

d) Adverse drug effects

ADEs are extremely common in older persons, [213] with rates up to 35% among community-dwelling persons aged ≥ 65 in the US, [214] to two-thirds of long term care residents. [215]. In a recent UK study, 59% of ADEs requiring hospital admission involved patients aged ≥ 60 [216]. Factors associated with higher ADEs in the elderly are higher drug doses, age-related pharmacological changes, polypharmacy, comorbid conditions, and the interactions between them. Older people are at higher risk of ADEs from antimuscarinics because of age- and comorbidity-related changes in muscarinic receptor number and distribution, blood-brain barrier transport, and drug

metabolism [217]. Whereas antimuscarinic ADEs in younger persons are bothersome, in the frail elderly they can result in serious morbidity such as increased heart rate, sedation, heat intolerance, delirium, and falls with fractures [3].

A major antimuscarinic ADE of concern in frail adults is cognitive decline, yet there are little data about its actual incidence or prevalence. Cognitive effects may be under-detected because they are clinically subtle, neither asked about nor reported by the patient, or mistaken for age-related diseases and ageing [218]. Persons with pre-existing cognitive impairment (especially from conditions known to affect central cholinergic pathways) may be at greater risk for this ADE. Actual incidence rates of cognitive impairment with antimuscarinic agents for UI are difficult to estimate because of probable under-reporting, the different measures used across studies, failure to specify the measure in published trials, the use of proxy measures (such as quantitative EEG), and differences in psychometrics and clinical relevance of self-report, physiologic and performance measures of cognition.

Antimuscarinic agents for UI also cause dry mouth (xerostomia), which is already present in approximately 30% of persons over age 65. Most older persons take at least one drug that causes xerostomia [219]. The morbidity from xerostomia-dental caries, problems chewing, poorly fitting dentures, dysphagia, and sleeping difficulty should be included when assessing the risks and benefit of antimuscarinics in frail older persons. Another antimuscarinic ADE to which the frail elderly may be predisposed is decreased visual accommodation, yet this has been specifically evaluated only in young healthy volunteers, [220] and drug trials typically report only “blurred vision,” without further characterization.

The incidence of a increased PVR as an ADE is seldom reported in clinical trials of antimuscarinics for UI or OAB. When it has been reported, the magnitude of increase is seldom of clinical significance. The incidence of acute urinary retention with antimuscarinics in general is low, but it has not been systematically evaluated in frail elderly. There is no consensus as to what constitutes a sufficiently high PVR to preclude antimuscarinic treatment or to require dose adjustment of an already prescribed agent. If urinary frequency or UI worsens after an antimuscarinic is started or increased, then PVR should be checked because an increased PVR will lower functional bladder capacity and worsen UI. PVR should be monitored in frail older men treated with antimuscarinics who may not reliably report change in LUTS or voiding difficulty.

e) Drug interactions

Because frail older persons take higher numbers of drugs and usually have several comorbid conditions,

drug interactions are more common [221]. All antimuscarinic agents for UI will have additive side effects when combined with other anticholinergic agents. Antimuscarinics could potentially alter absorption of other drugs by slowing gastrointestinal motility.

Drug-drug interactions for oxybutynin, solifenacin, darifenacin, and tolterodine include potent CYP3A4 inhibitors (azole antifungals, macrolide antibiotics, cyclosporin, vinblastine). Fesoterodine, a prodrug that is converted to tolterodine by non specific esterases, is also dependent upon CYP3A4 for its excretion. There is one case report of interaction between tolterodine and warfarin in 2 older patients, [222] which has not been seen in healthy volunteers. Naturopathic/ herbal preparations should also be considered for potential interactions, especially in areas where these agents are used frequently.

There is still uncertainty regarding interactions between antimuscarinic agents for UI and cholinesterase inhibitors (CEIs) used for dementia. There is evidence CEIs can cause or worsen UI from a case report [223] and also a case series of 216 consecutive patients with probable Alzheimer's disease attending a memory treatment center [224]. In the latter, CEI treatment was overall associated with 7% risk of new UI: the highest risk was observed in patients with more behaviour problems, and lower risk in patients who demonstrated positive cognitive and/or behavioural response to CEI. Evidence for an interaction between antimuscarinics and CEIs comes from a database study of nursing home residents in one US state [225]. Residents with dementia newly treated with cholinesterase inhibitors were subsequently more likely to be prescribed a bladder antimuscarinic than dementia patients not given CEIs, suggesting a classic geriatric "prescribing cascade" [226]. Concomitant use of antimuscarinic and CEIs in nursing home residents was associated with a decline in ADL function but not worsening cognition, possibly because the cognitive measure (MDS-COG) was inadequately sensitive [227].

Drugs also may interact with comorbid conditions (*drug-disease interactions*), such as diseases that affect hepatic or renal metabolism and clearance, slow gastric motility (e.g., advanced diabetes), predispose to delirium, or are associated with impaired central cholinergic transmission (Alzheimer's and Parkinson's diseases).

f) Potentially inappropriate drugs for older persons

Efforts at quality improvement for older populations have led to the development in several countries of expert consensus guidelines regarding inappropriate drugs for older persons, [228, 229] although the continuing relevance of these guidelines has been questioned and alternative systems suggested [230, 231]. These guidelines focus on drugs with lower risk-

benefit ratios and higher potential for drug-drug and drug-disease interactions, and are used for nursing home regulation and quality performance measurement. Several UI drugs are included in the US guidelines (the "Beers criteria"): immediate-release oxybutynin (because of "high risk of anticholinergic adverse effects, sedation, and weakness"); oxybutynin (immediate- and extended-release), tolterodine, and flavoxate in the patients with BOO (because of "high risk of decrease[d] urinary flow, leading to urinary retention"); all anticholinergic drugs in patients with cognitive impairment (because of "high risk of CNS-altering effects") or constipation (because of "risk of exacerbat[ing] constipation"); and tricyclic antidepressants in patients with stress UI (because of "high risk of produc[ing] polyuria and worsening of incontinence"). Whether or not one agrees with these recommendations, there is value in the concerns they raise, especially their emphasis on the level of thought needed for "best practice" prescribing for frail older persons.

8. SPECIAL ISSUES UNIQUE TO FRAIL OLDER MEN

Although their ranks thin into the ninth decade, men still comprise a significant portion of frail older persons. The prevalence of UI increases in men after age 80, going from about one-third of the rate in women to the same. Over the past ten years, the prevalence of UI in US male nursing home residents aged 65-74 has increased to a greater extent than in female residents (from 39% to 60%, compared with 45% to 59%) [232]. At the same time, frail men are under-represented in UI treatment trials, whether behavioural, pharmacological, or surgical (see also Committee 15: Surgery for Urinary Incontinence in Men).

This under representation is unfortunate, because results from treatment trials in frail women cannot be directly extrapolated to men for several reasons:

- Differences in comorbidity: frail older women have higher rates of functional impairment, [233] which may mean that frail men may be more likely to respond to behavioural interventions.
- Differences in caregivers: more older men have living spouses who can provide care, with a potential impact on the risk and type of caregiver burden associated with UI management.
- Differences in the relationship between UI and cognition: one systematic urodynamic study of nursing home residents with UI found a significant association between DO and more severe cognitive impairment in women, but not in men (although power was likely low, as the number of men was only 17) [171].
- Benign prostate disease: the prevalence of histological BPH, BPE, and BOO increase with age, and is associated with LUTS, UI, and DO. In the urodynamic study cited above, 29% of men had

BOO and 59% had DO as the predominant cause of UI, [171] *versus* 4% BOO and 61% DO in women.

- Prostate cancer: nearly all men in their ninth decade have histological evidence of prostate cancer. However, it is not clear that frail elderly men have an increased risk of prostate cancer-specific mortality, especially given that their RLE is primarily affected by comorbid conditions. The need to screen for and treat prostate cancer diminishes with functional status, comorbidity, and RLE [234]. At the same time, more men are living with the sequelae of prostate cancer treatment, particularly stress UI after radical surgery.
- Risk of urinary retention: because of age-related decrease in detrusor contractility and increased likelihood of BPE and BOO, it is often assumed that frail elderly men have a higher prevalence and risk of urinary retention. However, this has never been demonstrated. Among NH residents with UI, the prevalence of underactive detrusor was similar in women and men (38% and 41%, respectively), despite the higher prevalence of BOO in men [171].

Despite the issues noted above, evaluation and management of UI in most frail older men follows the same roadmap as for frail women (see Algorithm).

9. SUMMARY OF THE EVIDENCE

1. Patients and caregivers have clear preferences for the type of UI management, and they are often discordant between the two groups (Level 2)
2. Age-related changes in pharmacokinetics affect antimuscarinic drugs for UI and should be incorporated into treatment planning. (Levels 1-2)
3. Drugs may be effective at lower doses in frailer compared with healthier older persons (Level 3)
4. Polypharmacy increases the chance of adverse reactions to drug therapy. (Level 1)
5. Adverse drug events are more common in the frail elderly. (Level 2)
6. Drug-drug and drug-disease interactions are common in frail older persons (Level 1-3).
7. The economic burden of UI in frail elderly, as well as the cost-benefit, cost-effectiveness, and cost-utility of its treatment, has been incompletely characterized (Level 4)

VII. TREATMENT

1. LIFESTYLE INTERVENTIONS

As potentially treatable correlates of and risk factors for UI are determined, interventions that ameliorate their effects have been devised. Several lifestyle interventions have been evaluated in healthier older and younger women, including weight loss regimens, diet, fluid selection and management, smoking cessation, and constipation management (See Committee 12, Adult Conservative Management). Although many health care professionals advocate lifestyle interventions to treat UI, [196, 235, 236] we did not locate any studies of these interventions for the frail elderly. Several of these interventions may be inappropriate in frail elders (e.g., weight loss), yet advanced age alone should not preclude their use if assessment warrants. Inadequate fluid intake and dehydration are common in incontinent frail elderly in long-term care, in part because nursing assistants offer them less fluids in the belief that this will reduce UI [237]. Dehydration may actually increase the risk of UI in frail elders, because of the former's significant association with constipation [238] and impaired cognition, [239] both known risk factors for UI.

a) Quality of data and results

We located articles addressing lifestyle interventions for UI in older women, but the number of oldest-old subjects was very small, few to none appeared to be frail, and no studies stratified results by age. Two very small older trials point to the possibility that increased hydration for incontinent frail elderly may actually decrease UI [240, 241].

b) Summary of the evidence (see Table 6)

No recommendations are possible regarding lifestyle interventions for UI in the frail elderly (Level 4)

2. BEHAVIOURAL INTERVENTIONS

Behavioural interventions have been especially designed for frail older people with cognitive and physical impairments that may affect their ability to learn new behaviours or to actively participate in self-care activities. These interventions evolved from classical behavioural change theory, using antecedent and/or consequent conditioning to shape the desired behaviour. Because behavioural interventions have no side effects, they have been the mainstay of UI treatment in the frail elderly [242]. Behavioural therapies used predominantly in frail adults, ***all of which require active caregiver participation***, include:

Table 6. Lifestyle Interventions

Intervention	Authors	Study Design	Sample	Methods	Results
Fluid management	Kincade et al, 2007 [236]	Two arm, randomized trial	224 community-dwelling women aged 18 years and older with UI	Self monitoring was individualized and women were counselled on fluid consumption, quick pelvic floor muscle contraction, management of constipation and voiding frequency.	After adjusting for age, hormone status, and race women in the self-monitoring group had statistically significant less urine loss (average 13.3 g less urine loss) than women in the wait list group.
Caffeine reduction	Bryant et al, 2002 [466]	Prospective randomized controlled trial	95 consecutive adults with UI coming to two continence nurse advisors	Treatment group received education regarding caffeine reduction; control received no information.	Caffeine intake was significantly reduced in treatment group and frequency and urgency was significantly improved compared to control group one month post intervention.

Prompted voiding, involving prompts to toilet with contingent social approval, is designed to increase patient requests for toileting and self-initiated toileting, and decrease the number of UI episodes. It was first used in the 1980s for incontinent nursing home residents [243].

- **Habit training**, which requires the identification of the incontinent person’s individual toileting pattern, including UI episodes, usually by means of a bladder diary. A toileting schedule is then devised to pre-empt UI episodes [244, 245]. There is no attempt in habit retraining to alter an individual’s voiding pattern.
- **Timed voiding** involves toileting an individual at fixed intervals, such as every 3 hours. This is considered a passive toileting programme; no attempts are made at patient education or reinforcement of behaviours, or to re-establish voiding patterns [246]. Other terms used to describe timed voiding are scheduled toileting, routine toileting, and fixed toileting [247].
- **Combined toileting and exercise therapy.** Functional Intervention Training incorporates strengthening exercises into toileting routines by nursing home aides [248]. Another combination intervention, administered by occupational or physical therapist, involves toileting and mobility skills [249].

Cognitive and functional impairments common in frail elderly and/or lack of caregivers may preclude the use of some of these interventions.

Although pelvic floor muscle rehabilitation has not been studied extensively in frail elderly, age and frailty alone should not preclude their use in appropriate patients with sufficient cognition to participate [250]. Similarly, a combined behavioural modification programme involving pelvic muscle exercises, bladder training, and information about lifestyle modifications prevented UI in community-dwelling older women (aged 55 to 80 years) [251]. could be effective in some frailer older women.

a) Quality of data

We identified a systematic review of prompted voiding (9 trials, 674 patients) [252] and a Cochrane review of habit training in nursing home and home care patients updated since the last ICI (4 trials, 378 patients) [253]. The majority of trials did not determine the type of UI, or sufficiently describe whether comorbidity possibly contributing to UI was evaluated or treated. Randomized trials in long term care have overwhelmingly depended on research personnel to supervise or even conduct the interventions. Studies repeatedly show that, once a trial ends, indigenous long-term care staff rarely maintain the intervention at the same level, if at all (see, e.g. [4]) Outcome eva-

uation is usually limited to “wet checks” (percentage of times the patient is found to be wet on a set schedule of checks) and not UI, and no studies report cure or patient-based outcomes such as satisfaction with treatment and quality of life. Little intervention research has been conducted with incontinent hospitalised and homebound frail elders.

Limitations in many studies include: small samples with low power to detect significant differences; variable terminology and operational definitions, making comparisons across studies difficult; little ethnic or cultural diversity; data limited to women, especially in nursing home trials; little focus on night-time UI; little consideration to the psychological impact of toileting programmes on patients and caregivers; [254] and no long-term follow up. Many studies excluded frail older adults with terminal illness, [255] inability to respond to an one-step command, [255, 256] or poor language ability [256-258]. Ethical concerns for human subjects prohibits withholding treatment, thus true “control” groups were nearly impossible to create. Two studies used delayed treatment as controls [257, 258]. The frequency of the intervention varied across studies as well, with toileting conducted every two hours over 12-hour, 14-hour, and 24-hour schedules [243].

b) Efficacy (Table 7).

Prompted voiding is more effective than no intervention for improving daytime dryness in nursing home residents and some home care clients (Level 1) [252]. Prompted voiding is not effective and should not be used for persons with end-stage dementia (unable to state name or point to one of two named objects), who are bedbound or require 2-person assist to transfers, or who have more than four UI episodes during a 12 hr daytime period; such persons should be managed by “check and change,” with the goal of dependent continence. Eligible persons should have a three-day trial of prompted voiding, and the intervention should be continued after only in those that achieve appropriate toileting rates (the number of times the resident voided into the toilet divided by the total number of voids) of $\geq 66\%$ or a wet check rate (number of times the resident was wet when physically checked) of $\leq 20\%$ [259]. All others should be managed by check and change. This approach allows prompted voiding to be targeted to only the approximately one-third of residents who are eligible for and respond to prompted voiding, and could help decrease the considerable time and labour costs now used for inappropriate, unsuccessful toileting [195]. The 2005 revised US guidelines for continence care in nursing homes approved this approach as quality care [260].

No data are available about the long-term effects of prompted voiding. Self-initiated toileting increased, as anticipated, in some trials but concern was raised about increased dependence on the caregiver for toileting assistance.

There is insufficient evidence to determine if **timed voiding** improves continence (Level 4) [246]. No additional intervention studies on timed voiding since the previous Consultation were located. Several of the studies included in a systematic review had only female subjects with cognitive impairment, and included use of additional interventions such as antimuscarinic drugs (propantheline or flavoxate), staff education, bedside commodes, and absorbent products.

There is insufficient evidence to determine if **habit training** improves continence (Level 4) [253, 254].

Functional Incidental Training (FIT) incorporates endurance and strengthening exercises (e.g., sit-to-stand, bicep curls) while an aide conducts prompted voiding with a resident [248]. FIT significantly improves physical endurance and UI (measured by wet check). Across several different long-term populations, FIT led to a 38% reduction in daily urine loss [4, 249] However, all FIT efficacy trials relied on trained research nursing staff, FIT costs more than usual care, [4] and it may be difficult to implement in nursing homes without changes in existing staffing levels, [261] limiting its generalizability [262].

Operant behavioural strategies have shown some effectiveness in improving UI in long-term care residents (Level B) [243, 263]. The underlying principle is that behaviour is modified by its consequences, [264] even in frail adults. A balance must be struck, however, between encouraging self-care activities and patient functional status.

c) Summary of evidence

1. Prompted voiding is effective in the short-term treatment of daytime UI in nursing home residents and home-care clients, if caregivers comply with the protocol (Level 1).
2. Prompted voiding is ineffective and should not be used in persons who are unable to state their name or need the assistance of more than one person to transfer, and these persons should be managed with “check and change.” (Level 1).
3. Prompted voiding should not be continued in eligible persons who after a three day trial have less than a 20% reduction in wet checks (Level 1) or toilet successfully less than two-thirds of the time; these persons should be managed with “check and change.” (Level 1).
4. Interventions combining toileting and exercise decrease wet checks and improve endurance in nursing home residents, including those with psychiatric disease (Level 1).
5. Efficacy of behavioural interventions decrease when implemented by indigenous nursing home staff (Level 1) and the associated labour costs may be difficult to offset (Level 2).

Table 7. Behavioural interventions

Intervention	Authors	Study Design	Sample	Methods	Results
Prompted Voiding	Palmer, 2005 [243]	Systematic literature review	1 quasi-experimental, 1 repeated measures, 1 prospective case series, and 1 systematic (Cochrane) review	Sample, methods, and results were examined to address: is prompted voiding effective in reducing wetness episodes and increasing requests for toileting?	Different prompted voiding protocols were used limiting comparison across studies. Sample sizes were small and mainly white elderly female long-term care residents participated. Staff adherence to the protocol was important to its success. Little evidence exists that self-initiated requests for toileting is increased. Wetness episodes decreased in the short-term.
	Eustice, Roe, & Paterson, 2008 [252]	Cochrane Review update	Nine trials included, N = 674 older adults.	Literature searched according to protocol (all randomized or quasi-experimental studies). Two reviewers evaluated studies for methodological quality; third reviewer proof-read the review.	Insufficient evidence to reach firm conclusions for practice. Suggestive evidence exists for short-term benefit from prompted voiding, longer effects are not known.
Habit Retraining	Ostaszkiwicz, Chestney & Roe, 2004 [253]	Cochrane Review	Four trials included, N = 378.	Literature searched and evaluated per protocol. Trials too heterogeneous to for meta-analysis.	Adherence to habit retraining protocols is difficult for staff. Evidence is too limited to judge if improvements in continence make habit re-training protocols worth investment.
	Nikolleti, Young & King, 2004 [467]	Randomized controlled trial	41 elderly incontinent patients on acute care rehabilitation units in Australian hospitals	Patients in the treatment group were monitored for 72-hours with an electronic device. Patients in the control group received standard habit training. Prescribed voiding times for both groups (control and monitoring group) were developed and continence outcomes were measured.	No statistically significant improvements in self-reported or carer reported UI frequency. Significant reduction in self-reported and carer reported severity of UI in one-month follow up of treatment group. Missing data and problems with using the electronic monitoring device were noted.
Timed Voiding	Ostaszkiwicz, Johnston & Roe, 2008 [246]	Cochrane Review	Two trials met inclusion criteria, N= 298 female subjects with reduced mobility and cognitive impairments.	Literature searched and evaluated per protocol.	Nighttime incontinence was significantly lower in intervention group. Data were considered too few to make a recommendation for or against timed voiding.
Mobility and Toileting Interventions	Ouslander, Griffiths, McConnell, Riolo, Kulner & Schnelle, 2005 [4]	Randomized controlled trial cross-over design.	102 residents in four Veterans Affairs nursing home	Research staff implemented the Functional Incidental Training (FIT) intervention four times daily, five days a week for eight weeks.	FIT improved endurance, strength and UI; 64 residents completed the intervention.
	Van Houten, Achterberg & Ribbe, 2007 [249]	Randomized single blinded trial.	57 dependent women with no cognitive impairment with longstanding UI living in 24 long-term care institutions.	Physiotherapists or occupational therapist administered the intervention to the treatment group for an individualized eight-week long programme of mobility and toileting skills.	Intervention group experienced 37.7% reduction in the daily amount of urine loss, but results were not statistically significant.
Prevention Interventions	Diokno et al, 2004 [251]	Randomized controlled trial comparing behavioural modification programme (BMP) to no treatment group.	Ambulatory postmenopausal continent volunteer women, N = 359.	Women in behavioural intervention group received educational sessions and individualized evaluations of knowledge, adherence and skills.	At 12 months follow up, women in behavioural group had significantly better continence status, pelvic muscle strength and displacement score.

6. It is uncertain whether habit retraining reduces UI in frail older persons (Level 4).
7. It is uncertain whether timed voiding reduces UI in frail older persons (Level 4).
8. There are no proven interventions to reduce night-time UI in frail elders (Level 4)

3. INTERVENTIONS WITH LONG TERM CARE STAFF AND CAREGIVERS

Many frail elderly persons must rely on family, caregivers, or residential and/or nursing staff for toileting assistance and personal care. These carers may not be available as frequently as necessary for the frail elder to maintain continence, and even if available they may not be able or willing to provide the needed assistance. Research has shown that the frequency of toileting assistance actually provided in US nursing homes is too low to maintain continence [265].

There is dissonance between nursing home surveyors, nursing staff, and nursing home administrators' knowledge and beliefs about UI and its management, which may be an important barrier to effective UI care [156]. One study suggests that nurses in the acute and long-term care settings continue to provide urine containment interventions rather than promoting continence [266 267]. Nursing staff preferences for UI management (toileting) are in conflict with those of residents and their families patient treatment preferences (medications and garments) [187, 188].

In long term care, a two-prong behavioural intervention to UI care, one geared towards the resident and the other geared towards staff members, appears necessary [268, 270]. Nursing assistants play a key role in the success of behavioural programmes, and organisational schemes need to be devised to create incentives for them to keep residents continent [271]. Direct care providers will be unlikely to implement programmes unless residents and their families advocate for them [272].

This advocacy, however, appears unlikely if, based on their experiences, nursing home residents have reduced expectations and do not anticipate receiving sufficiently frequent and prompt toileting, and therefore express no desire for more frequent toileting [265]. One documented barrier to toileting programmes in long term care is their labour intensity. Bladder training programmes are considered one of the three most time consuming activities for long-term care staff [197].

A specialty practice exemplar model has been proposed to improve continence care in long-term care, with a nursing faculty member with expertise in the assessment and treatment of UI having a clinical practice in a facility. Graduate nursing students, working with this individual, focus on the Minimum Data Set Resident Assessment Protocol for UI.

Assessment and treatment skills ultimately are transferred to the facility nursing staff members through several mechanisms, including staff education and improved continence care systems [273]. Quality assurance programmes using incontinence quality indicators have also been proposed [157]. A clinical leadership model in the sub-acute setting in Australia used a staff empowerment and mentorship model to make evidence based changes related to continence care during patient's stay and on discharge [244].

a) Quality of data

Several authors point to the difficulty of conducting research in long-term care settings [268, 269, 274]. Factors such as staffing ratios, changes in administrative and regulatory policies, and fiscal issues are beyond researchers' control. Several investigators report that staff compliance was less than total, and some experienced problems with staff training. For instance, in one study several staff members did not attend group-training sessions and needed one-on-one training, and other staff members did not perform the protocol or document its use, especially when staffing levels were low [269]. Little staff intervention research to improve continence in older persons has been conducted in the acute-care setting.

b) Results

One group of researchers investigated the effect of a scheduled toileting programme on nursing home staff injury using a quasi-experimental design using a 75 bed unit and a similar comparison unit [275]. Fifty residents in the intervention unit were selected to participate based on an assessment indicating their eligibility for a toileting programme. Mechanical lifts were purchased for the intervention unit in anticipation of an increase in toilet transfers. Regular toileting increased from 12% pre-intervention to 67% in the intervention and 26% in the comparison unit. Staff injuries related to toileting did not increase in the intervention group, and the staff also noted less resident agitation. In-service classes on UI did not change staff knowledge and attitudes about UI, or improve resident toileting (only 70% of toileting assists were completed) [268]. The authors noted that staff members believed that toileting was "not worthwhile" for some residents. In a randomized study using advanced practice nurses (with post-graduate training) to work with staff to implement evidence-based protocols, residents in the intervention arm experienced significantly greater improvement in UI compared with those receiving usual care [276].

Several studies detail extensive barriers to UI care [166, 277, 278]. A staff survey revealed that nursing assistants believed prompted voiding was very helpful to residents in reducing the frequency and volume of incontinent voids, but that inadequate staffing, staff work load, turnover, and absenteeism were significant

barriers to prompted voiding. They believed that increased numbers of staff, improved communication, ongoing education, and alternative modes of care delivery were necessary to facilitate prompted voiding. Overall, staff believed toileting programmes improved resident quality of life but the realities of long-term care made them difficult to implement [279]. Nursing assistants believed that UI was a normal part of ageing and that nothing could be done for it, 99% of residents with UI in the study facility wore absorbent products and only 3% had received UI treatment [166].

When staff perceptions regarding completed toileting assistance were compared to research staff observations, staff over-inflated the percent of toilet assists they completed (stating 80-90% when the observed was 70%) [280]. Staff members also believed that residents were happier with a prompted voiding programme, yet only 52% thought the programme improved residents' continence. In another study, long-term care facility residents reported a mean of 1.8 daily assists to the toilet, regardless of whether they were on a toileting programme or not [272].

Continence care creates additional needs for family caregivers. In a small pilot study, caregivers at home felt that the requirements of a behavioural protocol were more than they could manage [281]. Other family caregivers report embarrassment and social isolation as their most frequent emotional responses to UI, and a need for information about resources [282]. In contrast to long term care staff, family caregivers were adherent with prompted voiding 89% of the time, and 93% were somewhat or completely satisfied with the decrease in UI [257]. A descriptive study found that caregivers of frail elders with UI report a high level of physical fatigue (70%) [282]. Caregivers dealing with different levels of UI (mild, moderate, catheter managed) have different educational needs and require different levels of support from healthcare professionals. For example, carers of frail persons with mild UI expressed the greatest need for professional care, but those of persons with moderate UI or catheters spent the highest number of daily hours providing care [283].

A computerised quality management programme for prompted voiding was tested in a convenience sample of 85 residents in eight US nursing homes [273]. Each facility was asked to identify staff members for the following roles: main contact person; quality control specialist; two licensed personnel who would conduct UI assessments; and two nursing/health care assistants who would implement the prompted voiding intervention. Information on the computer system included UI assessment and residents wetness rates. Research staff monitored the database and provided the nursing staff feedback by telephone consultation. The programme was effective in improving dryness for six months while research staff monitored the database, but only one facility continued the

programme after the research ended [278]. The researchers noted that current incentives for nursing homes to maintain UI management systems are insufficient.

A scheduled toileting programme, designed to explore risk of injury to staff members and resident agitation and aggressive behaviour, required statistically significantly more staff time than "check and change," with cleaning soiled patients while they were in their bed (slightly longer than 6 minutes to toilet versus slightly longer than 4 minutes to clean) [275].

Acute care patients have preferences for urinary incontinence treatment that is significantly discordant to hospital staff. For example, nurses and physicians preferred scheduled toileting over diapers more than did the patients [188]. The authors suggested that communication about treatment preferences should occur.

c) Summary of evidence

1. Although long term care nursing staff generally believe prompted voiding to be helpful, they fail to implement such programmes. (Level 2)
2. Interventions designed to maintain implementation of patient-focused behavioural interventions by long-term care staff are helpful in promoting continence care. (Level 2)
3. Family caregivers in the community setting can be adherent to behavioural interventions but experience fatigue and social isolation. (Level 2)
4. The use of computerised programmes to manage quality control for UI management does not persist after research studies have ended. (Level 2)
5. Toileting programmes including mechanical lifts may reduce staff injury and decrease resident agitation associated with toileting. (Level 2)
6. There is insufficient data to determine whether long-term care UI quality improvement efforts have an impact on costs related to UI (Level 4)

4. PHARMACOLOGICAL TREATMENT OF UI IN FRAIL ELDERLY PERSONS

a) Background

The pharmacological management of UI in healthy older persons is discussed in Chapter 10, Drug Treatment. This section deals with the management of frail elderly, using the definition at the beginning of the chapter. Specific treatments for bladder outlet obstruction and associated LUTS in frail elderly men are outside the scope of this chapter; special issues in the care of frail older men with UI are discussed above.

Frail persons with UI should be considered for drug treatment only following a comprehensive evaluation

of remediable causative factors, and if they are appropriate for and have had a trial of behavioural and lifestyle interventions. Drug treatment should not generally be used for persons who make no attempt to toilet when aided, become agitated with toileting, or are so functionally and cognitively impaired that there is no prospect of meaningful benefit. Even so, a recent study of US nursing home residents suggested that only a small proportion of incontinent residents potentially suitable for drug therapy ever received it [284]. There is still much to do, with potential benefit for many.

b) Quality of data

We located 17 randomised placebo controlled trials (RCTs) of antimuscarinic medication, predominantly involving subjects over the age of 80. The majority were of modest quality often reflecting their publication date (up to 40 years ago). The available RCTs were predominantly done in the US, with a small number in the UK, Germany, Taiwan and Japan. Approximately half of identified studies were conducted in long-term care facilities, whose residents are overwhelmingly female. All focus on antimuscarinic treatment of presumed urgency UI. UI diagnosis was overwhelmingly symptom-based; only three studies included urodynamic evaluation. The majority of newer studies including older persons but whom overwhelmingly appear to be “fit.” For most studies it was impossible to identify whether subjects were indeed frail, except where the study was performed in an institutional environment, in which it is reasonable to assume a high prevalence of functional and cognitive dependence.

Many older trials used a randomised cross-over design, which lessens power and increases the non-drug effect. The methods of blinding and randomisation in RCTs was seldom specified.

Other than those conducted by the pharmaceutical industry, most studies were generally small and under-powered, and others lost power because of high drop out rates due to illness and death (inevitable in trials with frail elderly persons). Because of these issues, many RCTs provide only Level 2 evidence. Some larger studies in older persons without clear frailty are included here, to recognise that, since the last consultation, there has been an increasing emphasis on including older persons in drug trials.

Precise descriptions of the target population—including the definition of “frail persons” and a comprehensive description of the degree of cognitive and functional impairment—were usually absent. Although some investigators included information on patients’ functional and cognitive status, as well as comorbid conditions, the descriptions were often only qualitative, and none addressed these issues adequately in the analyses. Explicit, concurrent behavioural therapy

was used in most nursing home studies, yet may have occurred in many others. Combination therapy and high comorbidity could have attenuated differences between drug and placebo, and make it difficult to compare results directly with studies in healthy older and younger persons. Outcomes were universally assessed by UI frequency (pad-weighing, bladder diaries, and wet-checks), and none reported quality of life outcomes.

Treatment of some reversible causes of UI also may have affected the ability to detect drug effects. In at least six studies, investigators treated subjects with “urinary tract infection” (usually defined as pyuria and bacteriuria in the presence of UI) before initiating antimuscarinic therapy, and one study excluded such subjects. In another, investigators treated urogenital atrophy with oestrogen prior to antimuscarinic therapy, possibly leading to an additional amelioration of symptoms. However, no other reversible causes were addressed prior to entry or randomisation in most studies.

The generally low quality of these trials reflects not just study design, but the larger issue of the difficulty of doing large, prospective intervention trials in frail populations. Moreover, UI in frail elderly is universally a multifactoral problem involving a large number of factors beyond the bladder. Thus, the expectation that drug therapy targeted solely at urodynamic DO or SUI would markedly improve/cure UI in this population is unlikely to be realised.

c) Results

Results from randomised trials are summarised in **Table 8**; the following sections discuss specific drugs in detail, and include randomised trials as well as non-randomised trials in older persons.

1. OXYBUTYNIN

The majority of studies in frail older persons used immediate-release oxybutynin (oxybutynin-IR). There are two studies of extended release oxybutynin (oxybutynin-ER), one examining cognitive effects in nursing home residents with dementia and urgency UI, [285] and the other involving community-dwelling women over age 65 [286]. Published trials of the efficacy of transdermal oxybutynin included subjects up to age 100 and in institutional care settings, but did not stratify results by age or comorbidity [287].

The pharmacokinetics of oxybutynin-IR and its active metabolite, N-desethyloxybutynin, in one study tended to show greater plasma levels and bioavailability with increasing frailty and age [288]. Another found peak levels in 21 octogenarians similar to those reported in young normal males (12.5 ng/mL vs. 8.9 ng/mL) [289]. A study of the pharmacokinetics of transdermal oxybutynin showed no significant difference in plasma levels between young and old (up to 77 years) subjects [290].

Table 8. Evaluable drug trials in frail elderly persons (see text for explanation)

Drug	Study	Design	Setting and pts	Results	Comments
Oxybutynin	Zorzitto 1989 [293]	8 day RCT; Oxy-IR 5 mg twice daily	Long term care residents (n=24)	No difference from PLC	
	Ouslander 1988 [291]	RCT Oxy-IR vs. PLC vs. habit training	15 long term care patients who failed prompted voiding	No difference in % of checks wet, but 40% Oxy pts had \leq 1 daytime UI episodes vs. 18% PLC (p <0.05)	
	Szonyi 1995 [294]	2 mos RCT; titrated Oxy IR with bladder retraining vs. bladder retraining alone	Frail, community-dwelling	Significant drug effect on frequency (95% CI 6-27 fewer voids/2 wk) but not on UI	
	Zorzitto 1989 [293]	8 day cross over RCT; Oxy IR 5 mg twice daily	Long term care residents (n=24)	No difference from PLC	Subjects toileted 10 times daily, trial short
Propiverine	Dorschner 2003 [327]	4 weeks RCT propiverine 15 mg three times daily	"Elderly" (mean age 68) with urgency or mixed UI (n=98)	54% decrease in UI episodes (p<0.05 vs. baseline; PLC response not described)	Low AE (2% drug mouth on drug), no QTc prolongation. Efficacy reportedly better for urgency than mixed UI
Imipramine	Castleden 1986 [343]	RCT titrated imipramine 25 mg/day, increased monthly by 25 mg	Older women referred to continence clinic (n=34) with urodynamic involuntary detrusor contraction	No statistical difference in continence rate (78% drug, 43% plc) at trial end (36 months); concluded no benefit over the habit training that all subjects received	Subjects "clinically well" and "could understand nature of the study". Type II error possible. AE "frequent": dry mouth, constipation, one episode of confusion
Emepronium	Williams 1981 [335]	Cross over	"Organic brain syndrome" and psychiatric pts	No significant effect on daytime or night-time UI	
	Walter 1982 [336]	Cross over	"Elderly" patients with urgency UI and urodynamic involuntary detrusor contractions	Subjective cure/improvement rate 79% for drug and PLC; no change in cystometric parameters	
Emepronium and Flavoxate	Robinson 1983 [337]	RCT 14-20 days Emepronium 200 mg 4x/day plus Flavoxate 100 mg 4x/day vs. PLC with cross over	22 frail women seen in a Geriatric continence clinic with urodynamic involuntary detrusor contractions	No significant change in UI episodes or cystometric detrusor overactivity, but all subjectively felt better on drug	Data presented only on 14 pts who completed trial; underpowered
Propantheline	Zorzitto 1986 [338]	4 day cross over RCT Prop 15 mg 4x/day vs. PLC; non responders repeated cross over with doubled doses	43 long term car patients (42% female) with urodynamic involuntary detrusor contractions	Only 30 mg 4x/day dose statistically better than PLC	50% experienced ADEs (dry mouth, constipation); 1 pt at 30 mg dose developed retention and another bowel obstruction)
	Dequeker 1965 [341]	Cross over RCT, each period 10 day treatment with Propantheline 15 mg 4x/day, or Vasopressin 5 units 2x/day or PLC	27 women in long term care	No differences in wet checks between the drugs and PLC. Patients who could use a bed pan had better response to vasopressin	No ADEs reported
	Whitehead 1967 [340]	2 week RCT Propantheline 75 mg at bedtime vs. PLC, cross over at 1 week without washout, all received habit training	40 long term care residents with severe dementia (50% female)	Propantheline moderately yet significantly better than PLC, especially in women	Urinary retention in one man found in a related case series
	Doig 1956 [339]	9 week RCT Propantheline 15 mg 4x/day vs. PLC	31 "senile" long term care residents (71% female)	No difference between drug and PLC	AE: dry mouth (2 persons), hesitancy (1), transient blurred vision (1)

Table 8. Evaluable drug trials in frail elderly persons (see text for explanation) (Continued)

Drug	Study	Design	Setting and pts	Results	Comments
Propantheline and Flavoxate	Tobin 1986 [468]	RCT Flavoxate 4x/day with Propantheline 3x/day	Long term care residents, all also toileted every 2 hours	Significant improvement in nocturia but not daytime UI with drugs	
Procaine haematoporphyrin	Hall 1987 [346]	26 week RCT 200 mg/day vs. PLC	65 long term care residents (85% women) with "urge UI from neurogenic bladder"	Intention to treat analysis: significantly better with drug only for pls with UI > 2x/week	Subjects recruited in 2 tiers after 9 pts dropped out at 12 weeks. No AE reported
Flurbiprofen	Palmer 1983 [345]	RCT Flurbiprofen 50 mg 4x/day vs. PLC with 2 week cross over periods	37 community dwelling subjects attending hospital (65% women, 25% with dementia) with urodynamic involuntary detrusor contractions	Drug significantly increased in total bladder capacity, decreased UI episodes, and increased maximum contractile pressure; no difference for volume at first sensation, volume at first contraction, or number of voids/day	Only 27 with complete data; bladder diary data available only in 12 patients. Three patients on drug withdrawn for leukopenia, hematemesis, pneumonia
Oestrogens	Judge 1969 [323]	RCT quinestradiol 0.25 mg 4x/day with cross over after 4 weeks + 4 week washout	20 long term care residents (50% "mentally confused," only 3 ambulatory)	12% decrease in UI with drug compared with 22% increase with Plc, p<0.01; equivalent to 4 fewer changes/week	Vaginal bleeding in one pt treated after the trial; optimum effect may not have been reached; no pt became dry;
	Ouslander 2001 [333]	RCT oral oestrogen (0.625 mg) combined with progesterone (2.5 mg) daily vs. placebo for 6 months	32 female long term care residents with incontinence	No difference in UI at 3 or 6 months, despite clinical changes and vaginal pH and cytology evidence of a partial oestrogenic effect	

• **Efficacy**

An early, small (n=15) trial of **oxybutynin-IR** and habit training in long-term care residents showed no effect on UI episodes [291]. However, in a subsequent and larger study in long-term care residents who had failed prompted voiding alone, the addition of titrated oxybutynin-IR resulted in a significant but modest reduction versus placebo [292]. Wet-checks decreased from 27% at baseline to 20% on drug and 24% on placebo, leading the authors to conclude that the improvement was not clinically significant, especially given the continuing requirement for nursing intervention. However, their *a priori* definition of "clinically significant improvement" (one or fewer episodes of daytime UI) was achieved by 40% on drug but only 18% on placebo (p<0.05). The dose generally associated with improvement was 2.5 mg three times daily. In another controlled study of UI in long-term care residents (n=24), there was little effect of oxybutynin-IR 5 mg twice daily given for 8 days, but all residents were toileted 10 times daily, and the dose may have been too high and given too infrequently [293]. In a randomised two month trial in frail community-dwelling elderly, oxybutynin-IR plus bladder training was subjectively and objectively superior to bladder training alone in improving urinary frequency (95% CI 6-27 fewer voids per 2 weeks) but not UI

[294]. Insufficient information was available regarding a Japanese study in 75 "elderly" patients to assess the population and outcomes [295]. A study in 416 community dwelling older persons, including the fitter elderly, found 68% reported a partial or complete symptomatic cure with 2.5 mg three times daily; 30% of subjects experienced ADEs, but only 10% withdrew because of them [211].

Only one of the two identified RCTs examined efficacy of **oxybutynin-ER** [286]. The other examined the effect on cognition [285] and is discussed below. No published RCTs of **transdermal oxybutynin** in the frail elderly were found, and post hoc sub-analyses of efficacy in subjects over the age of 65 has been published only in abstract form. In a small Japanese case series (n=13, mean age 75) in persons with urgency UI and cystometric DO, **intravesical oxybutynin** caused no significant increase in mean bladder capacity one hour after installation of 5 mg oxybutynin at pH 5.85 [296]. In four patients who continued twice daily installation, two had UI "disappear" and one "markedly decrease" (duration until effect not noted). No patient developed an "increased PVR" (not defined).

• **Predictors of efficacy**

Predictors of efficacy were studied in one study in

persons with urgency UI and urodynamic DO (n=41, mean age 79) treated with 2-4 weeks of oxybutynin-IR (5-15 mg/day) [297]. Factors associated with baseline urine loss (by pad weighing) were impaired cognitive orientation (on the Cambridge Mental Disorders of the Elderly Examination), number of daily voids, and fluid intake. Persistent urine loss after treatment was associated with impaired orientation, reduced sensation of bladder filling during cystometry, and most significantly global cortical under-perfusion on single photon emission computed tomography scan, suggesting that cortical factors are the main determinant of the severity of urgency UI before and after oxybutynin. In a study of 80 older patients (mean age 74), patients with dementia (by Hasegawa dementia scale) were less likely than cognitively intact patients to report subjective improvement in UI with antimuscarinic agents, despite similar objective outcomes [298]. However, these results could reflect treatment-associated cognitive effects.

• **Adverse reactions**

Cognitive side effects from oxybutynin have been reported in older persons. In one case series, four older men with Parkinson's disease and mild-severe cognitive impairment developed confusion, psychosis, hallucinations, behavioural disturbance, and/or paranoia after receiving oxybutynin-IR (5-15mg/day), which resolved when oxybutynin was stopped [299]. Of note, each patient was also on L-dopa (co-beneldopa) and selegiline, and the observed effects could reflect drug-drug interactions. However, these results are belied by a large RCT in which oxybutynin-ER 5 mg daily did not cause more delirium than placebo in NH residents with UI and dementia [285].

There are case reports of reversible peripheral neuropathy confirmed by re-exposure in a 70 year old woman taking oxybutynin-IR 5-7.5 mg/day [300] and recurrent heat stroke associated with oxybutynin in one elderly patient [301]. Few studies have addressed cardiac effects. A small study of older persons in the community with UI (n=20, mean age 75) found no change in resting heart rate or electrocardiograph evidence of either prolonged PR interval or QTc, or QTc dispersion after 4 weeks of oxybutynin-IR (mean daily dose 7.6 mg [range 2.5-10 mg]) [302]. Using a large administrative utilisation database, no association was found between antimuscarinics (oxybutynin, flavoxate, hyoscyamine) and ventricular arrhythmia and sudden death [303]. Post-marketing adverse events with extended release oxybutynin include tachycardia and hallucinations [304].

2. TOLTERODINE

Studies of tolterodine in "older patients" do not include frail persons. For example, "older" patients in one RCT of **tolterodine-ER** were all community-dwelling,

able to complete a 7-day bladder diary, had a high prevalence of previous antimuscarinic treatment (53-57%), and a low prevalence of arthritis (15-18%), unlike most frail older persons [305]. Although several trials include elderly persons in their ninth and tenth decades, [305-307] mean age (~64 years) was much lower, persons with "[unspecified] disease which the investigator thought made the patient unsuitable" and/or "renal disease" were excluded, and results were not stratified by age. In a secondary analysis of a large, open label German trial of **tolterodine-IR** 2 mg twice daily, higher age was significantly associated with "less favourable efficacy"[308]. However, the absolute difference in odds was only 0.019, there was no association of tolerability with age, only mean age is described, and UI frequency was based on patient report, not bladder diaries, all of which fail to add up to a clinically meaningful difference. In a non-randomised study, tolterodine was given to 48 nursing home residents who did not respond to toileting alone; 31 of these patients had a 29% increase in dryness (versus 16% in residents on toileting alone) [309].

• **Adverse reactions**

There are no prospective systematic data on tolerability in frail patients. There have been case reports of hallucinations (73 year old woman with dementia [310]) and worsening memory, [311] including a 65 year old cognitively intact woman [312]. There is a case reports of delirium when tolterodine was given with a cholinesterase inhibitor [313]. Analysis of prescription-event monitoring in the UK (mean patient age 63) found a significant association between age (>74 years) and psychiatric events and tachycardia (odds ratios not given) [314]. In a similar database study, the age- and sex-adjusted risk of hallucinations with tolterodine was 4.85 (95% CI 2.72-8.66) compared with 10 other drugs (acarbose, alendronate, famotidine, 3 proton pump inhibitors, finasteride, meloxicam, misoprostol, and nizatidine) chosen for presumed lack of antimuscarinic, cardiovascular, and CNS activity, and available in the database. Important confounders such as other drugs and comorbidity were not evaluated. Similar to oxybutynin-ER, post-marketing information on tachycardia and hallucinations was added to the tolterodine-ER package insert in 2003 [315].

3. FESOTERODINE

There are no published data in the frail elderly. Older, fitter subjects have been included in clinical trials, with persons over age 65 comprising approximately one-third of the total number of subjects studied, [316] yet no published results stratify by age.

4. SOLIFENACIN

Pharmacokinetics of solifenacin were evaluated in 23 older subjects (mean age 68); t_{max} was longer and there was a higher maximum plasma concentration,

but the differences from results in younger patients were small and deemed by the authors to be clinically irrelevant [317]. There are no randomized controlled trials specifically examining its efficacy in frail elderly. A secondary analysis of pooled Phase III data in patients aged 65 and older (all community dwelling and fit, mean age 72) found similar efficacy to that reported for younger and middle aged persons [318]. However, direct comparison with subjects < 65 yrs from the same pooled trials was not done. Adverse effects in older frailer patients have not been specifically reported. However, data from an open-label, 12-week trial in patients treated by community urologists found that overall treatment-emergent adverse events were more likely in patients aged >80 years (OR 3.9 [95% CI 1.3-11.5]) and taking concomitant medications (OR 1.8 [95% CI 1.2-2.6]) [319]. Patients with concurrent medications were more likely to be male and on average about 12-14 years older, have comorbid disease, and be administered higher doses of solifenacin, yet had no observed increase in heart rate or blood pressure with solifenacin.

5. DARIFENACIN

We located one RCT of darifenacin for OAB in persons aged ≥ 65 (mean 72), in which there was no statistically significant difference between drug and placebo for the primary end point, UI frequency [320]. There were statistically significant improvements with drug for urinary frequency (-25.3% vs. -18.5% with placebo; $p < 0.01$) and quality of life, as measured by OAB-q and patient perception of bladder condition. Although subjects were not frail, this is the only prospective study of a more modern antimuscarinic in older persons.

• Adverse effects

Cognitive adverse effects of darifenacin have been prospectively studied in a series of trials. The first was a 3-period crossover RCT in 129 older subjects (mean age 71, 54% of those screened), 88% of whom had comorbid medical conditions and 93% were on other medications [321]. Cognition was assessed using a standardized computerized battery. Darifenacin at variable doses did not adversely affect cognition compared to placebo, but results were aggregated so that patients did not serve as their own controls. A subsequent study in cognitively intact older persons ($n = 49$, mean age 66) using a similar computer cognitive battery compared titrated darifenacin and oxybutynin-ER with placebo over 3 weeks [322]. Oxybutynin-ER but darifenacin or placebo adversely affected the primary endpoint, delayed recall on the Name-Face Association test. However, oxybutynin was titrated one week earlier than darifenacin, and to a final dose (20 mg daily) much higher than is commonly used in clinical practice. Also, there were no differences between the two drugs and placebo for many other domains of the cognitive battery.

6. TROSPIMUM CHLORIDE

Although often promoted for use in the elderly because of the reduced likelihood that the drug crosses the blood-brain barrier, we found no studies that evaluated the agent specifically in frail older persons. All studies have included “younger elderly,” but even the most recent have not stratified results by age [323].

7. PROPIVERINE

In 46 patients with dementia (mean age 81), there was a 40% decrease in urgency UI with propiverine 20 mg/day for 2 weeks, [324] similar to two small Japanese trials [325, 326] and a German trial in 98 patients [327]. The agent’s high protein binding, extensive first pass metabolism, 15-hour half life (in normal younger persons), and renal clearance [324] need to be considered if used in frail older persons.

8. DULOXETINE

There was a statistically significantly reduced rate of clearance of duloxetine in patients over age 65, based on a study in 12 fit women aged 65-77 [328]. The authors felt the differences were not clinically significant given the “similar safety profile” of the drug in older and younger women. In three large RCTs in women (with SUI, aged 24-83 years, $n = 494$ [none frail]; [329] with OAB, aged 21-84 years [none frail], $n = 306$; [330] and with mixed UI, up to age 85 [331]), duloxetine decreased UI and urinary frequency, but none stratified outcomes or adverse effects by age. Duloxetine is not approved by the US FDA and is not recommended by the UK National Institute of Healthcare and Clinical Excellence.

9. OESTROGEN

Oral oestrinol 3 mg/day was compared to placebo for 12 weeks in 34 women aged 75 [65]. The group was highly self-selected; complete results were available for 11 with SUI, 12 with urgency UI, and 8 with mixed. Two-thirds of urgency UI and 75% of mixed UI patients reported improvement; there was no effect on SUI. Four patients reported metrorrhagia and mastodynia. A 10 week crossover trial comparing quinestradol 0.25 mg four times a day with placebo in 18 women in long-term care (type of UI not reported) found a mean 12% decrease in UI episodes vs. 22% increase with placebo [332]. The combination of conjugated oestrogen 0.625 mg/day and progesterone 2.5 mg/day was evaluated in a 6 month, placebo-controlled trial in 32 female NH residents with predominantly urgency UI, who also received prompted voiding [333]. In the 21 women who finished the trial, there was no difference in wet checks between drug and placebo despite increased serum oestrogen levels and partial oestrogen effect on vaginal cytology and pH in the women on drug. Two women on the drug developed vaginal spotting, and 10% developed breast tenderness. Similar lack of efficacy despite vaginal

changes were found in a case series of 9 frail women (mean age 83) with urgency or mixed UI using an oestrogen-implanted vaginal ring (Estring®) [334].

10. MISCELLANEOUS MEDICATIONS

Most of these agents are not widely used in clinical practice, and are included here for primarily historical purposes. **Emepronium bromide** had no significant effect on daytime or nocturnal UI among patients with chronic “organic brain syndrome” or chronic “functional psychiatric illness,” [335] similar to another RCT [336]. In 20 frail patients seen in a continence clinic (only 14 completed the trial), treatment with **both emepronium and flavoxate** for two weeks had no effect on UI or cystometric DO, but did increase in PVR [337]. **Propantheline** (15 mg three to four times daily) had no effect on daytime UI [338] or nocturia [339-341]. When the dose was increased to 30 mg four times daily, useful clinical effects were overwhelmed by antimuscarinic side effects [338]. In a similar small NH study, nocturia but not daytime UI improved with **concomitant propantheline and flavoxate** [342]. Titrated **imipramine** was no different than placebo in a small trial in ambulatory older persons also treated with habit training [343]. **Flavoxate** 200 mg at bedtime reduced nocturia in a small uncontrolled trial (n=40, age 51-79) [344]. An even smaller trial (6 “elderly” patients with urgency UI and cystometric DO) found no cystometric or clinical effect of a loading dose of 100 mg intravenous followed by 200 mg orally four times daily for 7 days [344].

Flurbiprofen 50 mg 4 times daily for four weeks decreased UI by nearly 50% (vs. no change with placebo) in 37 older persons (median age 78) with “idiopathic detrusor instability,” yet complete data were available for only 11 subjects [345]. **Procaine haematoporphyrin** 200 mg/day had only borderline effect in an 26 week RCT among 65 residents (mean age 85) of UK care homes with clinical “urge UI due to neurogenic bladder.” [346]. No studies were identified that evaluated **bethanechol chloride** specifically for frail elderly with UI and impaired detrusor emptying.

11. COMPARATIVE TRIALS

We found no studies that compared antimuscarinic agents in frail older persons.

5. SUMMARY OF THE EVIDENCE

1. Short-term treatment with oxybutynin-IR has small to moderate efficacy in reducing urinary frequency and urgency UI when added to behavioural therapy in long term care residents. (Level 2)
2. Low dose oxybutynin-ER does not cause delirium in cognitively impaired nursing home residents (Level 1)
3. Oxybutynin-IR has been associated with cognitive

adverse effects in persons with dementia and/or Parkinson’s disease (Level 3), although the incidence and prevalence are unknown (Level 4)

4. Oxybutynin has been associated with tachycardia (Level 3), but not associated with QTc prolongation (Level 3) or ventricular arrhythmia (Level 2).
5. Oxybutynin is less effective in persons with impaired orientation, cerebral cortical under-perfusion, and reduced bladder sensation (Level 2).
6. There is insufficient evidence to determine the efficacy, tolerability, and safety of the following agents in frail elderly (Level 4):
 - a. Intravesical oxybutynin
 - b. Trospium
 - c. Tolterodine
 - d. Fesoterodine
 - e. Darifenacin
 - f. Solifenacin
 - g. Duloxetine
 - h. Oral and topical oestrogen
 - i. Bethanechol
7. Tolterodine is associated with cognitive impairment and tachycardia (Level 3), although the incidence and prevalence are unknown. (Level 4)
8. There is evidence for lack of efficacy in the frail elderly for:
 - a. Emepronium bromide (Level 2-3)
 - b. Propantheline (Level 2)
 - c. Imipramine (Level 2)
 - d. Flavoxate (Level 3)
9. Combination of propantheline and flavoxate reduces nocturia but cannot be recommended because of unknown tolerability and safety (Level 4)
10. Flurbiprofen, propiverine, and procaine haematoporphyrin cause a small reduction in UI (Level 3) but tolerability and safety are uncertain (Level 4).

6. SURGICAL TREATMENT

a) Background

Very little is known about surgical treatment of UI in the frail elderly, likely reflecting a bias toward conservative therapy in a group with high prevalence of comorbidity and functional impairment. There are still very few studies of gynaecological surgery in women, surgical treatment for post-prostatectomy UI in frail men, minimally invasive procedures, or peri-operative care (including prevention of common post-operative complications) in urological and gynaeco-

logical patients. We reviewed the available data and general issues regarding peri-operative care which could improve surgical outcomes in this group. Surgical treatment of UI in healthy older persons is covered in Chapter 15: Surgery for Urinary Incontinence in Men, Chapter 16: Surgery for Urinary Incontinence in Women, and Chapter 17: Surgery for Pelvic Organ Prolapse.

An exhaustive review of surgical management of UI in the frail elderly is beyond the scope of this chapter. Therefore, in providing an evidence-based summary on this topic, we have taken advantage of the recent literature review and research recommendations from the American Geriatric Society, *New Frontiers in Geriatrics Research: An Agenda for Surgical and Related Medical Specialities* [347]. This project involved systematic literature reviews that were used to generate summary statements and recommendations for research. Their findings and recommendations pertinent to the frail elderly regarding surgical treatment of geriatric UI, [348] geriatric gynaecological surgery, [349] and general care of the geriatric surgical patient [350] are included in the summary statements below. Data supporting these conclusions are available in the monograph [351].

b) Incontinence surgery in frail elderly women

Data on surgery rates in older frail women are difficult to find and overall appear very low. Several studies have used U.S. national hospital discharge databases to examine surgery rates, but unfortunately they either age-adjusted results [352] or used relatively younger cut-points (e.g., $</> 50$ years) [353]. Even in series that specifically looked at elderly women (mean age 78, range 68-90), most patients were cognitively intact (95%) [354]. Cognitive impairment appears to bias against having surgery: in one study, only 0.11% of operations for UI were done in women with dementia, cerebrovascular disease, or hemiplegia combined [353]. While absolute numbers of ambulatory UI surgery cases in women increased from 1994-1996, the percent done in those aged ≥ 80 years remained the same (4-5%), [355] and the results were similar for pelvic organ prolapse surgery (5%) [356]. In the US, surgery rates in elderly women vary by region of the country and race [355, 356].

One single-centre, community-based series of 54 patients aged 70 years and above provides a picture of this surgical population [357]. Twenty-eight percent of patients were aged ≥ 80 , four resided in a nursing home or assisted living facility, 82% had significant comorbidity, and 32% were classified as American Society of Anaesthesiology class III risk. Intra-operative complications occurred in 11% of patients; post-operatively, 11% required intensive care monitoring, 6% had serious complications, 7% became delirious, and 9% had slow return of bowel function [357]. The

authors concluded that discharge planning is especially important for these patients, and recommend pre-surgery planning of place of discharge and likely care assistance needs [357].

Although higher complication rates generally reflect the comorbidity common in frail elders (10.4% complication rate with comorbidity vs. 5.8% without it, $p < .001$), [353] some studies have found age protective (in one, age ≥ 73 years was associated with lower risk of vaginal cuff infection and recurrent prolapse following vaginal sacrospinous fixation [358]). Overall, the morbidity and mortality for geriatric patients undergoing anti-UI procedures are similar to those of other major non-cardiac surgical procedures [348]. Mortality is inconsistently associated with increased age, and most strongly related to cardiac or cancer complications [349]. Many studies do not uniformly control for the impact of comorbidity on mortality [348, 349]. Pre-operative administration of oestrogen appears ineffective in promoting wound healing [350]. Patient-controlled analgesia provides adequate pain control and sedation and increased patient satisfaction compared with standard fixed-dose and time-administered medications in cognitively intact geriatric patients [350]. Choice of anaesthetic agent may affect postoperative cognition [350] and urinary retention. The use of methylalantrexone to treat opioid-related urinary retention may become an important adjunct to surgical care in frailer patients [359]. Very few age-specific data on outcomes are available, and no studies systematically examine quality of life, functional outcome, and discharge site.

With the advent of newer "minimally invasive" procedures, there has come some modicum of testing in older, albeit, not frail, patients. Injection of bulking agents in women appears to be effective in older women, and age does not appear to correlate with outcomes [348]. In a randomized controlled trial of tension-free vaginal tape (TVT) versus 6-month wait-list control, [360] at 6 months the intervention group had a statistically significantly greater improvement in mean I-QOL score, patient satisfaction score, and urinary problem score. There was no objective measure of cure. Peri-operative complications were not insignificant, with bladder perforation by needle in one-in-five (22.6%) which required 24 hours of indwelling catheterization, urinary retention (12.9%), and less than 5% with either a urinary tract infection or new urinary urgency (3.2%). In an uncontrolled case series examining the use of the suprapubic arch (SPARC) sling procedure, the outcomes in 43 older women (ages 65-91) were separately examined. Objective cure rate was evaluated by clinical and urodynamic examination and subjective cure rate was assessed using a visual analogue score and a global patient impression questionnaire, all at 3, 6, and 12 months. At a mean follow-up of 36 months (range, 12-54 months), objective and subjective cure rates with

surgery were 91% and 95%, respectively [361]. There were statistically significant improvement in pad weight and pad numbers (from a mean of 5 to 0) and the visual analogue score. No severe intra- or post-operative complications were observed, and no patient developed *de novo* urgency UI.

c) Incontinence surgery in frail elderly men

No specific conclusions can be drawn regarding surgical treatment of UI in frail men. Typical studies of anti-UI surgery in elderly men are very small or fail to stratify results by age and/or comorbidity (e.g., see references [362, 363]). One small study (n=46) found that advanced age was not a risk factor for poor outcome after collagen injection for post-prostatectomy UI, [364] while another (n=12, mean age 80 years) of trans-urethral resection prostatectomy (TURP) for obstruction-associated urgency UI found that cognitively impaired men had the greatest UI improvement [365]. In a single-institution case series of men aged > 80 years old undergoing TURP (68% of whom had urinary retention), 80% were satisfied with their outcome. Of the men with retention, 80% were able to void with a small PVR by six weeks. Complication rates were 41% (early) and 22% (late) [366]. Urodynamic evaluation of post-prostatectomy UI is recommended prior to surgical treatment (see, for example, reference [363]).

d) General issues in surgical care of the frail elderly

Important factors in the surgical care of frail patients include: pre-operative risk stratification (e.g., American Society of Anaesthesiology class, Charlson index, Modified Cardiac Risk Index, [367] Burden of Illness Score [368]); ensuring adequate nutrition, especially when patients cannot take oral feeding or become delirious; proactive management of comorbid heart disease, diabetes, and pulmonary disease; prevention, [369, 370] recognition, [371] and treatment of post-operative delirium; [370, 372] adequate pain assessment and treatment, especially in cognitively impaired persons; [373] recognition of the hazards of prolonged bed rest [374] and the prevention [375] and treatment of functional impairment; use of specialised care units for the elderly; [376] and discharge planning regarding rehabilitation, need for assistance, and site of discharge. These issues should be factored into any plan of surgical care of frail elderly persons.

e) Summary of evidence

1. No studies were identified regarding gynaecological surgery in institutionalized elderly women. (Level 4)
2. Exogenous administration of oestrogen is ineffective in promoting wound healing after gynaecological surgery in older women. (Level 3)

3. Injection of bulking agents appears to be effective in older women, and age does not appear to correlate with outcomes. (Level 3)
4. No studies were identified that evaluated functional or quality of life outcomes after UI surgery in frail older persons (Level 4)
5. Risks of morbidity and mortality for frail patients undergoing anti-UI procedures are similar to those of other major non-cardiac surgical procedures. (Level 2)
6. Surgical mortality risks are still low in elderly persons, and often due to cardiac or cancer complications. (Level 2-3)
7. Operative mortality is inconsistently associated with increased age, and many studies did not uniformly control for comorbid conditions. (Level 2-3)
8. Patient-controlled analgesia provides adequate pain control and sedation and increased patient satisfaction compared with standard fixed-dose and time-administered medications in cognitively intact geriatric patients. (Level 2)
9. Choice of agent for patient-controlled analgesia may affect postoperative cognition. (Level 3)
10. Some case series and waitlist-controlled trials suggest that minimally invasive surgical approaches may be useful in older adults, yet these trials may have little to do with whether surgical treatments are appropriate in the frail elderly (Level 3)

VIII. URINARY RETENTION IN THE FRAIL ELDERLY

The association of both detrusor underactivity and bladder outlet obstruction with age, comorbidity, and medications makes urinary retention (UR), either acute or chronic, a potential problem in frail older adults. Although bothersome in younger and middle-aged persons, in older frail persons UR and acute UR (AUR) carry significant morbidity, including delirium, [377] bradycardia (possibly related to alteration in the reflex loop involving the vagal and the sympathetic nerves), [378] higher mortality in the year following hip fracture, [379] and persistent UI.[380]. UR and elevated PVR have [380] and have not been [381] associated with an increased risk of UTI in this population. Data from the UK NHS data base found that the 1-year mortality in older men without significant comorbidity presenting with AUR was 12% (age 75-84) and 29% (age > 85); in men with comorbidity, the respective mortality rates were 27% and 43%, and rates were even higher in men with "precipitated" retention (not associated with BPO) [382]. Of concern is the fact that UR may be asymptomatic in frail elders, particularly women.[383].

1. QUALITY OF THE DATA

Studies of the prevalence of UR among frail elders suffer from lack of standardization of the definition of UR, which ranges from inability to void to PVR cut-offs as low as 50 mL. PVR is usually reported as a volume and not percent of bladder emptying; results often are based on a single measurement; and whether or not the patient strained is rarely reported. Many studies do not exclude patients with medical reasons for impaired emptying, such as advanced diabetes mellitus and anticholinergic medications. There is also extensive heterogeneity in the populations studied, and there is a relative paucity of data on UR in women. The 1996 US Agency for Health Care Policy Research consensus guidelines on UI in adults suggested that PVR > 200mL is abnormal, <50 mL normal, and 50-200 mL intermediate [172]. Using data from symptomatic patients referred for urodynamics, Madersbacher et al estimated that, starting at age 40, PVR increased by 13 mL per decade in men and 4 mL per decade in women [42]. In two studies of postmenopausal women without DO, both with and without LUTS, Pfisterer et al found median PVR to be < 20 mL [43, 49]. Efforts to establish normative means for PVR in women only compared those less than age 65 versus those older; only 25 were aged \geq 65, and their mean PVR was 34 ± 31 mL [384].

2. RESULTS

Frail elders in hospital and rehabilitations units may be at special risk for UR and impaired bladder emptying. Amongst 100 consecutive patients admitted to a geriatric hospital ward (mean age 81), 34% had PVR >50 mL, and they had greater functional impairment and subsequent mortality than those with smaller PVR [170]. UR (defined as PVR \geq 150 mL) was present in 22% of older patients on admission to a subacute, predominantly geriatric, rehabilitation unit; [380] patients with UR were more likely to be male and have poor mobility, neurologic disorders (e.g., stroke or multiple sclerosis), cognitive impairment, UI, previous prostate problems, previous LUTS, take anticholinergic medications, or have a UTI diagnosed on admission. Other risk factors for UR in this population include previous history of UR, [385] faecal impaction, [386] and several classes of medications. [44] UR is common after hip fracture: in consecutive series of patients admitted to hospital with hip fracture, a PVR >300 was present in 79-97% on admission, [379,387] 36% immediately pre-operatively, 56% post-operatively, and 22% during the recovery phase [379]. Randomized trials have shown both short-term indwelling and intermittent catheterization to be effective in restoring normal voiding in frail elderly [44, 388].

Impaired emptying is common among nursing home residents. In separate case series, 35% of residents had a PVR \geq 100 mL (n=150), [381] 11% had PVR

\geq 150 mL, [386] and 59% had urodynamic evidence of detrusor underactivity [171].

Less is known about the prevalence of UR in frail elders in the community. In a case series of 167 frail elderly outpatients, 11% had UR (two consecutive ultrasound PVR measurements \geq 150 mL), which was independently associated with advanced age, use of anticholinergic medication, diabetes, and faecal impaction [386]. Women attending a Female Pelvic Medicine Clinic who were found to have a high PVR (\geq 100 mL) were significantly older than women with normal emptying (62 ± 14 vs. 59 ± 13 years, $p=0.005$) [389]. Studies involving older men focus on AUR. Cathcart et al evaluated AUR among men in the UK NHS data base, defining AUR by ICD-10 coding; men with TURP, prostatic cancer, multiple sclerosis, or Parkinson's disease were excluded. AUR incidence rose sharply with age, even amongst the oldest old, from 9.13/1000 person-years among men aged 75-84, to 16.8/1000 person-years among men aged 85-100 [390]. AUR incidence in older men (aged 70-83) was also evaluated in a prospective observational study of over 6,000 American male health professionals without baseline history of TURP, prostate cancer, or AUR. The estimated AUR incidence over 3 years was 7.9/1000 person-years among men with no or only mild LUTS at baseline, and 11.3/1000 person-years among men with moderate to severe LUTS [391].

Intermittent catheterisation (ISC) can be helpful in the management of patients with UR with or without UI. ISC can be carried out by either the patient or a caregiver, with the frequency based on PVR. The assumption that older patients are unwilling or unable to manage UR with ISC has not been borne out [392]. The ability to reliably and safely use ISC to manage UR in hospital and long term care settings is highly dependent on staff availability and training. In addition, using ISC in institutional settings (where multi-resistant organisms are common) may yield an unacceptable risk of nosocomial infections, and use of sterile catheter trays are very expensive. Thus, it may be extremely difficult to implement such a programme in a typical nursing home setting.

3. SUMMARY OF EVIDENCE

1. There is no consensus regarding a standardized definition of UR in frail older persons (Level 4)
2. UR is common in hospitalized frail elders and long term care residents (Level 2), but not in healthy, asymptomatic older persons (Level 2)
3. Hip fracture and orthopaedic surgery are associated with very high rates of UR in older persons (Level 2)
4. Risk factors for UR in frail elders include male sex, impaired mobility, cognitive impairment,

neurologic disorders, prior UI and LUTS, history of prostate disease, prior UR or AUR, faecal impaction, anticholinergic medications, and orthopaedic surgery (Level 2)

5. UR is associated with increased morbidity in frail elders, including delirium and increased mortality (Level 2)
6. There is no consistent data on the risk of UTI in frail elders with UR (Level 4)
7. UR in frail elders can be effectively treated with either indwelling or intermittent catheterization (Level 2)

IX. NOCTURIA

1. BACKGROUND

Nocturia is defined as waking at night from sleep one or more times to void, with each void being preceded and followed by sleep [393]. While a single episode of awakening to urinate would be considered nocturia, patients are more likely to consult a provider about nocturia if they have three or more episodes [394]. Several reviews [395, 396] and an entire journal supplement [397] have discussed various aspects of nocturia in detail. This section specifically focuses on what is known about the prevalence, impact, pathophysiology, diagnostic assessment, and treatment of nocturia in the frail elderly. Similar to UI, nocturia is usually multifactorial in frail elderly persons. Thus, diagnostic assessment must be comprehensive, and multi-component interventions may be necessary for successful treatment.

2. QUALITY OF THE DATA

There are good epidemiological data from multiple cultures and countries on the prevalence of nocturia, but limited data on associated factors and impact. Studies of the pathophysiology of nocturia in the elderly have generally been small and highly focused on one aspect of potential underlying causes. As with UI, there are limited data on optimal diagnostic assessment, and therefore recommendations are generally based on expert opinion [19, 393]. Data on treatment in elderly patients are very limited. Although there are some treatment RCTs, they are small, include few very elderly subjects, and have focused primarily on vasopressin. We located no data on the effectiveness of multi-component interventions for nocturia in the elderly.

3. PREVALENCE AND IMPACT

The prevalence of nocturia increases with age, and has been reported to be as high as 90% for one episode per night in persons over age 80 [398-402]. The prevalence of two or more episodes among men

between 70 and 79 is nearly 50 percent [403]. This increasing prevalence is largely due to age-related conditions that underlie the pathophysiology of nocturia (see below). Nocturia is more common in young adult women than in men, but the gender ratio reverses after age 60 [403]. Nocturia has been variably associated with chronic medical conditions such as hypertension and diabetes, [404, 405] advancing renal failure, [406] and cardiovascular disease [407, 408]. Nocturia in the frail elderly can cause accidental falls [409]. Frail elderly persons with nocturia, who also have gait and balance disorders and other risk factors for falls, are clearly at increased risk for injury and consequent morbidity, yet no nocturia treatment trials have evaluated any impact on fall reduction. Nocturia also has adverse effects on quality of life, including an increased risk of depression and poor self-rated health, probably as the result of the impact on sleep [410, 411]. Adults with nocturia also complain that nocturia “makes them feel old” and they worry about falling at night [412].

4. PATHOPHYSIOLOGY

In elderly persons, the pathophysiology of nocturia is usually multifactorial and can be related to one or a combination of three primary underlying causes, all of which increase with age: low bladder capacity usually as a component of OAB, DO, urgency UI, or BOO in men; nocturnal polyuria; and primary sleep disorders [395-397].

The proportion of 24-hour urine volume produced at night increases with age, even among healthy older adults free of overt comorbid conditions [413, 414]. Studies of frail elderly have shown that the proportion of urine produced at night is close to 50%, rather than less than 30% as in young healthy adults [415-417]. Nocturnal polyuria is more common in older compared to younger nocturics [418]. In some elderly persons, this is due to mobilisation of excess volume caused by peripheral oedema, which may be due to venous insufficiency, medications, and/or heart failure. Some studies have suggested that there is an abnormality in the secretion and/or action of arginine vasopressin (AVP) or a loss of its normal diurnal rhythm (with inappropriately low values at night) in many elderly patients with nocturia [419, 420]. Another, however, failed to find an association between AVP deficiency (detected by water deprivation testing) and nocturnal polyuria in a series of elderly persons with nocturia [421]. Other research suggests that some frail elderly persons with nocturia have high atrial natriuretic peptide (ANP) levels at night; [422, 423] however, these investigators did not use echocardiography or brain natriuretic peptide levels to detect occult heart failure. Sleep disordered breathing and sleep apnoea also have been associated with nocturia and nocturnal UI in the elderly [422, 424-426]. Whether this relates to increased ANP production, [422] mechanical forces on the bladder generated during apnoea events, [424] or other mechanism(s) is unknown.

5. DIAGNOSTIC ASSESSMENT

The approach to the assessment of nocturia should be similar to that for UI described above. Special considerations include:

- A frequency-volume chart of at least 24 hours duration that includes timing and volume of each void at night as well as during the day, as well as a specific indication of when the individual went to bed with the intention of going to sleep at night and awoke in the morning. Some patients may find this difficult to perform, [427] but face-to-face explanation of the procedure, a receptacle to place in the toilet to measure volumes, and involvement of carers may improve compliance and accuracy.
- Additional questions in the history that focus on the possibility of a primary sleep disorder, such as asking about sleep quality, daytime sleepiness, snoring, and leg movements at night (this history is enhanced by questioning the bed partner).
- Additional history and focused physical examination related to volume overload (e.g., lower extremity venous insufficiency, heart failure); in some cases additional testing such as an echocardiogram or a brain natriuretic peptide level may be helpful in ruling out the latter diagnosis.

6. TREATMENT

Treatment of nocturia in elderly patients should be based on individualized identification of all potential underlying causes. The most commonly used measure of nocturia treatment efficacy is a reduction in nocturia episodes. However, studies have not related the number of nocturia episodes to the hours spent in bed, which may vary considerably in older persons. The impact of three episodes of nocturia is considerably different in someone in bed for seven compared with twelve or more hours. Cure, or the complete resolution of nocturia, is infrequently achieved in either clinical practice or in research. Some trials have reported percent of trial participants achieving a 50% reduction in nocturia or the percent of individuals reporting one fewer nightly episodes of nocturia. It is important to recognize that most reports of treatment have shown only a small reduction in episodes of nocturia, ranging from 0 to 0.8 fewer episodes of nocturia versus placebo. Patient-based outcomes are important and may include general satisfaction questions, nocturia-related bother, and nocturia-specific quality of life. Most trials examining nocturia as an outcome were performed prior to the validation testing of the ICIQ-NQOL instrument [428]. An additional important target for therapy is reduction in bother due to nocturia.

Although no specific data are available on multi-component interventions, elderly patients with nocturia may benefit from an approach to treatment that combines behavioural strategies, therapy for medical and sleep disorders, and nocturia-specific drug therapy.

a) Behavioural approaches and treatment of comorbidity

There are no specific data on the impact of behavioural strategies (e.g. altering fluid or sodium intake, leg elevation for oedema) on nocturia in older patients. Using bedside commodes or urinals, and minimising the distance necessary to reach a toilet and providing a safe, adequately lit path may be helpful in reducing the risk of night-time falls related to nocturia, especially in those with underlying gait instability and other risk factors for falls. Reducing volume overload associated with lower extremity venous insufficiency or congestive heart failure with a late afternoon dose of a rapid acting diuretic may be helpful in reducing nocturnal polyuria and nocturia in selected patients [429, 430]. Treating sleep apnoea with continuous positive airway pressure can reduce nocturia severity, but these trials have not usually included the frail elderly [431]. Treatment with very short-acting benzodiazepines for patients with primary insomnia, and with dopaminergic agonists for patients with restless leg syndrome, may improve sleep quality, but there are no data to support these approaches. There is one secondary data analysis of a RCT which demonstrated that behavioural therapy, with an emphasis on pelvic floor muscle exercises and urgency suppression strategies, reduced nocturia in women with urgency-predominant UI [432]. The median reduction of 0.5 episodes per night was significantly more effective than antimuscarinic (0.3 episodes) or placebo (no reduction). There are no trials of pelvic floor muscle exercises or urgency suppression strategies with nocturia as the primary outcome.

There are several approaches to drug therapy for elderly patients with nocturia. Most of the published guidelines suggest targeting a “primary” or “principal” causes of nocturia (e.g., nocturnal polyuria). Because most older adults with nocturia have multiple potential causes, treatment often will require combination treatment.

b) Antimuscarinic therapy

In general, if the history, bladder diary, and physical examination suggest that nocturia is related primarily or in part to OAB/DO/urgency UI, then treatment with an antimuscarinic agent should be considered (see Pharmacological Treatment above). There are several trials examining the effect of antimuscarinics for nocturia reduction, including trials of oxybutynin-IR, [432] solifenacin, [318] and tolterodine [433, 434]. Even when these agents have shown statistically significant reductions in nocturia, the net benefit of reduction in nocturia (above that effect shown with placebo) is only 0.0 to 0.3 episodes. There is evidence to suggest that these agents may be best used in combination with other therapies [433] rather than as single modality therapy.

c) Agents for benign prostatic obstruction

Alpha-adrenergic blockers used in patients with symptoms suggestive of BPO have a modest impact on nocturia, with a mean reduction of slightly less than one episode per night [421]. 5-alpha reductase inhibitors have mostly shown no statistical benefit for nocturia [421] except in one study among a subset of participants age ≥ 70 [435]. This statistical advantage did not persist beyond one year, and the net benefit compared to placebo was a difference of < 0.2 fewer nocturia episodes. Among postmenopausal women, one uncontrolled trial of estradiol in combination with a progestational agent showed a dramatic reduction in nocturia over 6 months, [436] but this was not replicated in another RCT [437]. There are few studies that have focused on treatment of nocturia with the use of medications for sleep. One RCT evaluated melatonin for treatment of nocturia associated with BOO in older men [438]. Melatonin showed only a trend towards reduction in nocturia compared to placebo (-.03 and -0.05 episodes from baseline 3.1 episodes, respectively) but did significantly reduce reported bother from nocturia.

d) Anti-diuresis treatment: Desmopressin

A large number of studies over the last 20 years have examined the potential role of exogenous AVP (desmopressin or DDAVP) for the treatment of nocturia in older patients [439-451] (Table 9). The majority have been uncontrolled case series involving relatively small numbers of subjects, and the inclusion criteria, outcome measures, and route, dosing, and duration of DDAVP treatment varied considerably. The two largest studies were RCTs of oral DDAVP using essentially identical designs, one conducted in men [449] and the other in women [450]. Although they included some patients older than 75, the mean age of the participants was closer to "middle" rather than "old" age (65 and 57, respectively). Both found significant reductions in nocturia and nocturnal urine volume, and increases in mean duration of self-reported first night-time sleep episode. However, the trials' designs were unusual: the randomised controlled portion was preceded by a dose-titration run-in, with the subsequent exclusion of subjects who did not experience $>20\%$ reduction in nocturnal urine volume or who were intolerant to the medication. Although this approach may be useful for targeting therapy in clinical practice, it raises questions about selection bias and the generalizability of the results.

Most individuals in DDAVP trials were titrated up to an oral dosage of 0.4 mg, [449, 450] yet older patients can have a significant reduction in night-time urine with much lower doses of 0.1 or 0.2 mg orally [452]. A major concern related to DDAVP treatment in elderly patients is fluid retention (which can exacerbate underlying cardiovascular disease) and hyponatremia. Many older persons may have pre-existent hypo-

natremia due to a variety of medical conditions and drugs. A recent review [453] found the incidence of hyponatremia with DDAVP in older persons to be 0-9% (depending on definition), with the exception of the RCT in men discussed above, in which the incidence of any hyponatremia was 22% (4% with sodium < 130 mmol/L). Because so few frail elderly were included in these trials, the actual incidence of clinically significant hyponatremia from DDAVP is unknown. A further review of pooled trial results found that the incidence of hyponatremia in subjects with normal baseline sodium was $<1\%$ (3/336 subjects) in persons < 65 and 8% (22/260) in those ≥ 65 , and 75% (6/8) in older patients with a low baseline serum sodium [454]. Pharmacodynamic studies in younger older men (aged 55-70) found that DDAVP had a prolonged half-life which was in part responsible for hyponatremia [455]. DDAVP is not useful in frail older persons in nursing homes with nocturia and/or night-time UI because of the lack of efficacy for reducing night-time voids and the very high rate of hyponatremia [452].

7. SUMMARY OF EVIDENCE

- Late afternoon administration of a diuretic may reduce nocturia in persons with lower extremity venous insufficiency or congestive heart failure unresponsive to other interventions. (Level 2)
- If OAB, DO, and/or urgency UI is felt to be a major contributor to nocturia, antimuscarinic agents should be considered. (Level 3)
- If nocturia is due to insomnia alone, then a very-short acting sedative hypnotic may be considered. (Level 3)
- DDAVP should not be used in frail elderly because of the risk of hyponatremia. (Level 1)

X. MODELS OF CARE FOR THE FRAIL ELDERLY WITH UI

1. BACKGROUND

Throughout the world, frail elderly persons are cared for in a variety of settings using many different models of care. While there continues to be very few studies that examine these models in relation to UI management, a discussion of selected models is useful in identifying the challenges and opportunities to improve continence care in this population. This descriptive section briefly outlines four models of UI care particularly relevant to the frail elderly: home care, continence nurse advisors, collaborative practices between advance practice nurses and physicians, and long term institutional care. A

Table 9. Selected studies of desmopressin (DDAVP) for nocturia involving older patients

Reference [No.]	Study Design	N	Sex	Age (Mean)	Nocturia Definition	DDAVP Dose ¹	Outcomes		Level of Evidence
							Nocturnal Urine Volume	Nocturnal Frequency Pre/Post	
Seiler et al, 1992 [439]	Open label	9	M/F	73-90	_ nocturnal volume	10 µg 20 µg 40 µg	_33% _10% _50%		4
Asplund et al, 1993 [440]	Open label	21	M/F	(73)	_ nocturnal volume	40 µg	20-34%		4
Asplund et al, 1993 [441]	Open label	20	F	(71)	_ nocturnal volume	20 µg (2 nights)	_355 ± 205 mL		4
Obara et al, 1993 [442]	Open label	8	M/F	(64)	_ nocturnal volume	5-10 mg		4.6 / 2.5	4
Asplund et al, 1993 [443]	Open label	19	M/F	(73)	_ nocturnal volume	40 µg 2 months	_38%		4
Asplund et al, 1998 [444]	Dose titration	23	M/F	60-74 (68)	nocturia ≥ 2, nocturnal volume ≥ 0.9 mL/min	0.1 mg 0.2 mg 0.4 mg (oral)	_31% _44% no further _		3
Asplund et al, 1999 [445]	RCT	17	M/F	60-74 (68)	nocturnal volume ≥ 0.9 mL/min	10-40 mg (oral)	_38%	1.7 / 1.1	2
Cannon et al, 1999 [446]	Double blind controlled trial	20	M	52-80	Nocturnal volume > 33% of 24 hr volume	20 ng 40 ng	_15% _26%	3.0 / 2.3	2
Chancellor et al, 1999 [447]	Open label	12	M	"Elderly"				3.6 / 1.8	4
Kuo, 2002 [448]	Open label	30	M/F	(75)	Nocturia ≥ 3, nocturnal polyuria	0.1 mg (oral)	20 patients responded _956 mL to 523 mL	5.2 / 2.2	4

Table 9. Selected studies of desmopressin (DDAVP) for nocturia involving older patients (Continued).

Reference [No.]	Study Design	N	Sex	Age (Mean)	Nocturia Definition	DDAVP Dose ^a	Outcomes		Level of Evidence
							Nocturnal Urine Volume	Nocturnal Frequency Pre/Post	
Mattiason et al, 2002 [449]	Initial dose titration then responders randomized to optimal dose vs. placebo for 3 weeks	115 randomized	M	18 – 88 (65)	Nocturia ≥ 2 , nocturnal urine production greater than functional bladder capacity	0.1 – 0.4 mg (oral)	-36% vs. 6% in placebo	3.0 / 1.7 vs. 3.2 / 2.7 placebo	2
Lose et al, 2003 [450]	Initial dose titration then responders randomized to optimal dose vs. placebo for 3 weeks	144 randomized	F	21-89 (55)	Nocturia ≥ 2 and nocturnal urine production greater than functional bladder capacity	0.1 – 0.4 mg (oral)	-44% vs. 6% in placebo	2.9 / 1.6 vs. 2.9 / 2.4 placebo	2
Rembratt et al, 2003 [451]	Open label	72	M/F	66-90 (76)	Nocturia ≥ 2	0.2 mg oral (3 nights)	-306 mL mean reduction	-1 episode mean reduction	4
Lose et al, 2004 [469]	One year extension of Lose [451] and Mattiason [449] studies above	249 continued treatment	M/F	21 – 88 (65 men, 56 women)	Nocturia ≥ 2 and nocturnal urine production greater than functional bladder capacity			Men 3.1 baseline, 1.6 end Women 2.9 baseline 1.3 end	4 (as above)
Ho et al, 2005 [470]	Open label trial of men with bladder outlet obstruction on alpha blockers who failed antimuscarinics and had no nocturnal polyuria	28	M	43 – 91 (70.8)	Not defined	0.1 – 0.4 mg (oral) average dosage 0.104			
van Kerrebroeck et al, 2007 [471]	Initial dose titration then responders randomized to optimal dose vs. placebo for 3 wks	127 randomized	M/F	19-94 (62)	Nocturia ≥ 2	0.1 – 0.4 mg (oral)			
Johnson et al, 2007 [472]	Double-blinded, RCT with titration	14 randomized	M	67 – 80 (74)	Nocturia ≥ 2 without evidence of bladder outlet obstruction	0.1 – 0.4 mg (oral), average dosage 0.31	-197 mL reduction from baseline vs. -126 mL reduction with placebo		

comprehensive review of worldwide care models is outside the purview of this section. Of note, we located little new information since the 3rd ICI.

2. HOME CARE

Most care for the frail elderly who live at home is provided by spouses, children, other relatives, and in some cases neighbours or friends. Overall, there has been little research on UI interventions for this population. One trial found that behavioural interventions can be effective in selected frail homebound persons with UI and motivated caregivers [456]. Overall, however, the informal nature of care at home may lead to important barriers to effective continence care. First, caregivers may not be available 24 hours per day, and thus regular toileting assistance may only be intermittently available. Toileting programmes (e.g., prompted voiding) and intermittent catheterisation therefore may be impossible to implement consistently. Second, many caregivers for frail persons are in fact frail themselves. Spouses and even adult children may have medical illnesses and/or functional problems that make it physically difficult and stressful for them to provide continence care. Third, even among caregivers who are physically capable and available to assist with continence care, negative attitudes and lack of education may pose substantial barriers to providing the required care.

Trained, paid caregivers for frail elderly living at home are variably available throughout the world. Such services may include nurses to teach patients and caregivers UI care and management of intermittent or indwelling catheterisation; health aides who can assist with continence care; and provision of continence care supplies (e.g., pads and catheter supplies). In the US, for example, Medicare (health insurance for persons aged ≥ 65) does not pay for ongoing UI care, only some catheter care and supplies period and need-based, home skilled nursing and physical therapy, and usually only on a limited basis and following hospitalisation. For patients who do not have access to continence home care and/or do not have an available and motivated caregiver, UI management remains pads and other protective products, which can be expensive if not provided or reimbursed through available health insurance. In these cases, some frail elders will devise homemade alternatives to pads, which are neither effective, comfortable, nor safe (especially for skin protection).

3. CONTINENCE NURSE ADVISORS

In many countries (e.g., UK, Australia, and Canada, among others), continence nurse advisors are available who can provide extremely valuable services for frail elderly with UI. Continence nurse advisors are highly trained in UI assessment and management. They are generally funded by the government and function as public health nurses for a region associated

with one or more hospitals. They serve as advisors and provide education to physicians, nurses, and other health care professionals, as well as patients and their caregivers. They may also assist hospital staff in the assessment and management of UI in hospitalised frail elderly, and coordinate follow up care in the home or in an outpatient clinic. One Canadian study found that continence nurse advisors had a positive impact in improving management of UI in older persons [457].

4. COLLABORATIVE PRACTICES BETWEEN ADVANCE PRACTICE NURSES AND PHYSICIANS

In many countries, publicly supported continence nurse advisors are not available. However, other models have developed that generally involve collaborative practices between nurses with special interest, advanced training, and expertise in continence care and physicians (usually an urologist, gynaecologist, or geriatrician). These collaborations can be vital for providing optimal continence care for the frail elderly because of the multicomponent therapy required. Such nurses may provide reimbursable services in private offices and clinics; provide education, consultation, and/or direct services to nursing homes, other long term care facilities, and assisted living facilities; and assist with the assessment and management of UI for frail elders in their homes. Reimbursement for advance practice nurses and their ability to provide direct care independently of a physician varies across countries, and in some case within countries (e.g., in the US their scope of practice can vary by state). In some countries there are specialty organisations for this type of continence nurse (e.g., the US, Wound Ostomy Continence Nurses Society and Society of Urological Nurses and Associates). Although little data on the effectiveness of this model exist, it is becoming more widespread (e.g., Israel and Italy).

5. INSTITUTIONAL LONG TERM CARE

Long term care for the frail elderly is provided in a variety of types of institutional settings throughout the world. Continence care in these settings is dependent upon many factors, including: type of resident (only long-term care or also short-term rehabilitation post-hospitalization patients as well); physical environment; the organisational culture and leadership commitment to providing high quality care; the number, education, and motivation of direct care staff; access to physicians with interest and understanding of continence care; and financial and regulatory incentives to provide appropriate continence care. Nursing home staffing is a major barrier to translating research on prompted voiding and other interventions into practice (see Behavioural interventions above), and because resource constraints are stringent and will become more challenging with the rapid growth in the frail elderly population [267, 458].

The section on Interventions with Long-term Care Staff above reviews studies of interventions with nursing home staff to improve continence care. These interventions have generally met with limited success because they have not addressed the culture, staffing, and overall system of care in these facilities.

Three broad strategies have been employed to improve the quality of continence care for frail elderly nursing home residents. The first are standardised approaches to identification, assessment, and management of UI. One is the Resident Assessment Instrument for nursing facilities, whose use is mandated in the US and other countries [460]. The Resident Assessment Instrument combines information from the Minimum Data Set (including data on individual resident demographics, medical conditions, function, cognition, and care needs) with Resident Assessment Protocols for specific conditions and impairments. The continence section of the Minimum Data Set is generally accurate in identifying incontinent patients, but not for determining the type or severity of UI or determining especially smaller changes in continence over time [459]. The original version of the Resident Assessment Protocol for UI was partially validated in a sample of approximately 100 frail, incontinent patients in one large academically-affiliated US nursing home [460]. Another approach is national guidance directives, such as that for surveyors who conduct yearly quality evaluations of all US nursing homes. A recent revision of the US guideline for UI attempted to replace the existing emphasis on nursing documentation of continence care plans with an emphasis on UI assessment and provision of patient-focused care [461]. However, a subsequent study found that both surveyors and nursing home staff did not understand this shift in emphasis, and that dissonance between these two groups in basic UI knowledge and elements of the guidance is a likely barrier to any change in quality of UI care [156]. The American Medical Directors Association (for nursing home physicians) publishes a clinical practice guideline for continence care, based on the US Agency for Healthcare Policy and Research guideline and the federal guidance mentioned above, [462] yet its implementation and effectiveness has not been studied. However, despite the existence and dissemination of these approaches, several studies document an ongoing discrepancy between their recommendations and regulations and the continence care actually delivered in the US [166, 272, 463, 464] and UK [160]. The second strategy has been the use of principles of continuous quality improvement and total quality management developed for business management [465]. The key elements of these approaches are education and involvement of direct care staff, identification of a "continence champion" and team to implement the programme, and the continuous collection and analysis of quantitative outcome data using principles of statistical quality control. Quality

assurance programmes using UI quality indicators have also been proposed [157]. One study successfully used a computerised assessment and quality improvement software programme and external oversight to maintain a 50% reduction in UI in eight diverse, geographically dispersed US nursing homes [273]. A second implemented a quality improvement programme in five diverse US nursing homes, but UI reduction was more modest (20-30%) in this effort to translate research into practice [309].

The third approach is a specialty practice exemplar model for continence care, with an academic nursing faculty member with expertise in the assessment and treatment of UI conducting a clinical UI practice in a long-term care facility (see Interventions with Long-term Care Staff, above). Graduate nursing students working with this individual focus on the Resident Assessment Protocol for UI. UI assessment and management skills are transferred to the facility nursing staff members through several mechanisms, including staff education and improved continence care systems [273].

Assisted living communities are social care residential models, in which older persons are provided primarily IADL assistance (meals, laundry, cleaning), are becoming more common (primarily in the developed world). There is substantial variation in the functional status and medical care needs of their residents, availability of nursing and physician care, reimbursement, regulation, and whether and how residents are allowed to age "in place" versus transferred to nursing facilities. In some countries and localities, assisted living residents may substantially resemble the nursing home population. There are no data on the quality of management of UI for frail elderly residing in assisted living facilities, or intervention trials specifically in this population. The US National Association for Continence (www.nafc.org) has published a "blueprint" for continence care in assisting living facilities, based primarily on expert opinion.

XI. RECOMMENDATIONS FOR MANAGEMENT

1. BASIC ASSESSMENT (SEE ALGORITHM FOR SPECIFICS)

- a. Active case finding for UI should be done in all older persons (Grade A).
- b. Screening for frailty is possible (Grade A) and encouraged (Grade C).
- c. The basic assessment of UI should focus on identification of potentially treatable conditions and factors that may cause or worsen UI, contribute to its burden, and impact management decisions (Grades A-C).

Table 10. Challenges of and recommendations for research studies on UI in frail older persons

Challenges	Recommendations
Incomplete standard criteria of “frailty” for research	Provide specific definition of frailty. Explicitly define variables in the domains of mobility, cognition, and nutrition.
Incomplete understanding of natural history of UI	Include control/placebo arms that consider time effects and measurement of primary and secondary outcomes of interest
Multifactorial nature of incontinence	Collect and describe measures to assess and address relevant comorbidity, e.g.: <ul style="list-style-type: none"> • Medication changes • Interval illnesses • Interval bacteriuria <ul style="list-style-type: none"> - Care setting - Interventions affecting domains of continence (e.g., exercise programmes)
Complexity and expense of enrollment	Multistage selection process: <ul style="list-style-type: none"> • Exclude robust/healthy • Identify the frail • Identify subset according to specific domain of frailty (e.g., need for toileting assistance). • Prepare to contact family members or other proxy decision makers for consent [41]
High trial attrition rates	Plan for intention to treat analysis with explicit plans for dealing with drop-outs/deaths in the analysis. Improve intervention adherence by: <ul style="list-style-type: none"> • Designing interventions feasible for most, and incorporating caregivers/care setting in that consideration • Allowing flexible time frame for follow-up assessments • Prioritising safety • Providing transportation • Preplanning alternatives to clinic-based follow-up (e.g., home visit, telephone) • Establishing good relationship and incentives to participate for family, caregivers, and/or care setting • Understanding priority rank and definition of important potential outcomes to patients, caregivers, and care settings <p>Anticipated attrition rates should not preclude attempts at long-term follow-up.</p>
Exclusions that decrease generalizability	Principle exclusion should be factors that prevent participation. Avoid exclusions for comorbidity. Exclude only those persons whose cognition is not compatible with the specific intervention. Use explicit procedures for consenting participants; involve a surrogate/proxy when needed. Include discussion of ethical concerns and how they were addressed in the report.
Problems using self-report to assess outcomes	Supplement self-report of primary outcomes with “hard” measures, e.g. assist with toileting. Collect “objective” measures of function and proxy information in parallel, e.g. percent of wet checks, hours of caregiver time. Set outcomes to be less sensitive to random fluctuations (e.g., end point of “50% decrease in UI”). Use outcome measures specific to the target population: e.g., for quality of life, use established measures of social interaction [42] rather than existing UI-specific scales; re-validate existing UI-specific scales; for community-dwelling persons, transfer to setting with higher level of care (e.g., from home to residential/institutional care) Include measures related to caregiver time commitment, burden, costs, morbidity, quality of life, and satisfaction with intervention (regarding the patient and themselves). Assess possible caregiver(s) preference(s) for care.

Table 10. Challenges of and recommendations for research studies on UI in frail older persons (Continued)

Challenges	Recommendations
Mechanism by which intervention changes continence status is unclear	<p>Use as secondary outcomes or covariates any physiological, functional, and care measures that are in the theoretical pathway between the intervention target and need for continence care: e.g., improvement in mobility; changes in functional MRI or SPECT; change in nursing home staffing.</p> <p>Evaluate multi-component interventions</p>
Improvements in continence status may not translate into well-being or better quality of life	<p>Develop and use standardised measures of adverse effects particular to/of special importance for frail persons: e.g., assessment of cognitive and behavioural effects of drug therapy in persons with cognitive impairment (ranging from mild to end-stage dementia); visual changes; bowel frequency; falls.</p> <p>Use secondary outcome measures that assess perceived well-being and factors (such as somatic symptoms, social interaction, activities of daily living) that are important for frail older persons and their caretakers.</p> <p>Include assessment not just of intervention efficacy but also its effectiveness, durability, and applicability.</p> <p>Emphasise patient- and caregiver-centred outcome measures; minimize use of/dependence on researcher-based outcomes assessment.</p> <p>Consider development of clinical global impression scales (i.e., as used in dementia and depression studies)</p>
Translating research into clinical practice	<p>Imbed qualitative research into quantitative trials in order to determine potential barriers to implementation</p> <p>Conduct feasibility studies of evidence-based interventions within non-research settings, preferably using pre-existing services (e.g. care home staff, primary care providers) rather than research staff</p>

2. PRINCIPLES OF MANAGEMENT

- a. Initial management should be individualized (Grade B).
- b. Decisions on specific management of frail older persons with UI should incorporate:
 - i. Most likely type of UI (Grade C)
 - ii. Patient and caregiver preferences for care (Grade B)
 - iii. Patient-centred care goals of care (Grade C)
 - iv. The chance that a specific treatment will achieve the patient's/carer's goals within the patient's expected remaining life expectancy (Grade C)
 - v. Understanding of the potential direct and indirect costs and benefits of treatment for the individual, their caregiver(s), and health systems (Grade C)
- c. Decisions to use drug therapy and choice of specific agent should incorporate:
 - i. Age-related changes in pharmacology (Grade B)
 - ii. Adding to pre-existent polypharmacy (Grade B)
 - iii. Drug-drug interactions (Grade A)

- iv. Drug-disease interactions (Grade B)
- d. Management of UI in frail older men should incorporate consideration of gender differences in:
 - i. Comorbidity and functional impairment (less in men) (Grade C)
 - ii. Caregivers (men more likely to have living spouses) (Grade C)
 - iii. The relationship between UI and cognition (less strong in men) (Grade C)
 - iv. Benign prostate disease (Grade C)
 - v. Prostate cancer (Grade C)
- e. No recommendation is possible regarding gender differences in the risk of urinary retention from antimuscarinic therapy (Grade D).
- f. No recommendation is possible regarding the cost-benefit, cost-effectiveness, or cost-utility of specific interventions (Grade D).

3. LIFESTYLE INTERVENTIONS

- a. Fluid restriction should be avoided in long-term care residents and other frail elders who may not have ready access to fluids or accurately sense thirst (e.g., persons with dementia) (Grade C).
- b. No recommendation can be made regarding other lifestyle interventions (Grade D).

4. BEHAVIOURAL THERAPY

- a. Prompted voiding should be offered to nursing home residents and homebound older adults with UI who: are able to state their name or point to one of two named objects; transfer with a maximum assist of one person; and have less than four UI episodes during the day (Grade A).
- b. Prompted voiding should be continued only in those frail elders who, after a three-day trial, demonstrate at least a 20% reduction in leakage or toilet appropriately at least two-thirds of the time (Grade A).
- c. Efforts must be made to increase and maintain caregiver compliance with prompted voiding (Grade B).
- d. Combined toileting and exercise programs should be considered for frail elderly with UI who are physically inactive, when there are resources to conduct and continue the intervention (Grade A).
- e. No recommendation can be made for behavioural treatment of night-time UI (Grade D).
- f. No recommendation can be made for habit retraining in frail elderly (Grade D).
- g. No recommendation can be made for timed voiding with in frail elderly (Grade D).

5. PHARMACOLOGICAL THERAPY

- a. Antimuscarinic treatment should be considered for those frail persons with UI who have symptoms of OAB, urgency UI, or mixed UI, and who have been assessed for contributing comorbid factors (including existing medications), and who are appropriate for and have had a trial of behavioural treatment (Grade C).
- b. Choice of specific antimuscarinic should be based on:
 - i. Age-related changes in pharmacokinetics that could affect the metabolism and clearance of a specific agent
 - ii. Likelihood of the agent causing any adverse effects the patient already experiences, such as pre-existing constipation, dry mouth, and visual impairment (Grade C)
 - iii. Potential drug-drug and drug-disease interactions (Grade C)
- c. Drugs should be started at the lowest possible dosage (Grade C).
- d. There should be proactive monitoring and re-evaluation of drug therapy for achievement of explicit efficacy goals, any adverse drug effects, and appropriateness of continued drug therapy (Grade C).
- e. Oxybutynin-IR can be considered for additional

benefit for frail elders with OAB, urgency UI, or mixed UI in whom behavioural therapy is feasible, with careful monitoring for adverse effects (Grade C).

- f. Topical oestrogens (cream, tablet, ring) may be considered for adjunctive treatment of urogenital atrophy in women (Grade B).
- g. No recommendation can be made for the use of oral or topical oestrogen for the treatment of UI in frail elderly women (Grade D).
- h. No specific recommendation can be made for use of the following agents for the treatment of UI in frail elderly (Grade D):
 - i. Tolterodine
 - ii. Topical or extended-release oxybutynin
 - iii. Darifenacin
 - iv. Solifenacin
 - v. Trospium
 - vi. Fesoterodine
 - vii. Bethanacol
 - viii. Duloxetine
 - ix. Propiverine
 - x. Flurbiprofen
- i. The following agents should not be used in the frail elderly:
 - i. Emepronium bromide (Grade B)
 - ii. Propantheline (Grade B)
 - iii. Imipramine (Grade B)
 - iv. Flavoxate (Grade B)
 - v. Procaine haemtoporphyrin (Grade C)
- J. Combinations of bladder antimuscarinics should not be used (Grade C).

6. SURGICAL THERAPY

- a. Age alone is not a contraindication to surgical treatment of UI (Grade C).
- b. Urodynamic evaluation should be done before considering surgical treatment of UI in frail older persons (Grade B).
- c. Pre-operative risk should be stratified using established indexes (Grade A).
- d. Insure adequate post-operative nutrition especially in patients who cannot take oral feeding or who become delirious (Grade C).
- e. Programmes to prevent post-operative delirium should be used (Grade A) along with proactive use of established measures to diagnose delirium (Grade A).
- f. Pain assessment in cognitively impaired persons

should use measures specially-designed for this population and not general pain scoring tools (Grade B).

- g. Proactive preventative approaches to hospitalisation-related functional impairment should be used (Grade A).
- h. Specialised care units may improve selective outcomes for frail older patients (Grade A).
- i. Discharge planning should begin before surgery takes place (Grade C).
- j. Patient controlled analgesia can be used in cognitively-intact frail older persons (Grade B).
- k. Analgesic agents associated with delirium (e.g., meperidine) should be avoided (Grade B).

7. NOCTURIA

- a. Older patients with bothersome nocturia should undergo a diagnostic assessment that focuses on identifying the potential underlying cause(s), including nocturnal polyuria, a primary sleep disorder, OAB/DO/urgency UI, or a combination of these conditions (Grade C).
- b. Treatment of elderly patients with nocturia should focus on the underlying causes:
 - i. For patients with OAB/DO/urgency UI, consider an antimuscarinic agent. (Grade B)
 - ii. Patients with nocturnal polyuria must be evaluated and treated for contributing factors (peripheral oedema [and its potential medical and drug aetiologies], congestive heart failure, and type and timing of fluids [all Grade C], and sleep apnoea [Grade B]).
 - iii. In patients with nocturnal polyuria unresponsive to treatment of contributing factors or of uncertain cause, afternoon dose of a rapid-acting diuretic can be considered with careful monitoring of efficacy, volume status, and electrolytes and renal function. (Grade C)
 - iv. Patients with a primary sleep disorder should be treated for the underlying cause(s), and the impact of treatment on nocturia monitored. (Grade C)
 - v. For patients without cognitive impairment and nocturia inadequately responsive to the above approaches who remain most bothered by inability to achieve sleep after an episode of nocturia, a low dose of short-acting hypnotic may be considered, (Grade C)
- c. DDAVP should not be used in frail elderly with nocturia because of the risk of hyponatremia (Grade B).

8. INTERVENTIONS WITH LONG-TERM CARE STAFF

- a. Long-term care institutions should implement staff development programmes to increase knowledge and skills about continence care and the efficacy of behavioural methods (Grade C).
- b. Computerised databases may help caregivers determine the effectiveness of UI programmes (Grade C).
- c. Family caregivers need monitoring for and resources to counteract fatigue, social isolation, and other burdens related to continence care. (Grade C)
- d. Use of mechanical lifts may help to reduce staff injury and increase adherence to toileting programmes (Grade C).

XII. RECOMMENDATIONS FOR RESEARCH

1. AETIOLOGY

- a. Racial and ethnic differences in LUT- and comorbidity-related causes of UI
- b. Aetiological models and translational research in the causes of UI in frailer older persons, incorporating principles of concentric, interacting, multiple risk factors models of geriatric syndromes
- c. Relationship between emerging models of frailty and vulnerability and development of UI
- d. Relative roles of lower urinary tract disorders, medical conditions, hormonal factors, sleep disorders, and other conditions in the pathophysiology of nocturia in frail older persons
- e. Longitudinal studies incorporating basic science as well as clinical measures

2. EVALUATION

- a. Efficacy and effectiveness of current evaluation guidelines and recommendations across settings (home, clinic, assisted living, long-term care)
- b. Development and validation of consensus standards for the definition of elevated PVR and UR for both frail elderly men and women, in both clinical and research settings
- c. Development and validation of consensus standards for evaluation of nocturia in frail older persons

3. TREATMENT

- a. Proactive incorporation of frailer, older-old persons in all UI intervention trials
- b. New outcome measures relevant to geriatric care, including quality of life, socialisation, need for institutionalisation, impact on comorbidity, caregiver burden, and alternatives to wet-checks for long-term care residents
- c. Outcome measures that are sensitive to differences across cultures and health care systems, e.g., reimbursement for continence services and supplies
- d. Association between expectations, preferences, and outcomes
- e. New approaches and tools to assess UI-specific quality of life in cognitively-impaired frail elderly
- f. Increased understanding of the interaction between functional impairment and the impact of UI
- g. Investigation of the utilities frail elderly and their caregivers assign to varying degrees of UI (with or without treatment intervention) versus “dryness”
- h. Multicomponent interventions
- i. Development and validation of predictive models for guiding treatment decisions
- j. Family caregiver characteristics associated with and optimum interventions to improve their effective use of behavioural interventions for UI in the home
- k. Racial-ethnic differences in UI treatment efficacy, tolerability, and safety in frail older persons across care settings (home, assisted living, long-term care, hospital)
- l. Racial-ethnic disparities in UI treatment in frail older persons across care settings
- m. Efficacy and effectiveness of policy and regulatory approaches to improve UI care quality in long-term care
- n. Efficacy and tolerability of antimuscarinics in older-old and frail persons across care settings
 - i. Include adequate numbers of patients (including those with cognitive and/or functional impairment, and comorbid conditions common in this population); use outcome measures specific for this population and include impact on caregivers; stratify outcomes by age, comorbidity, function, and frailty; specify diagnostic methods; and continue interventions for clinically-relevant periods
 - ii. Determine the characteristics of frail older persons who respond to drug therapy
 - iii. Incidence, prevalence, and risk factors for adverse cognitive and functional effects, and optimum research and clinical measures to detect them
 - iv. Cost-benefit, cost-effectiveness, and cost-utility studies of UI treatments, using models incorporating the special issues of patient and caregiver preferences, definitions of “benefit” in this population, and a comprehensive approach to costs across a range of care settings
- o. Inclusion of older-old and frailer patients in surgical studies, with stratification of outcomes by age, comorbidity, oestrogen status (women), and urodynamic findings
- p. Prospective studies to determine the magnitude and severity of common geriatric complications following anti-incontinence surgery
- q. Develop and validate guidelines for identifying frail elders who would benefit from gynaecological/urological anti-incontinence surgery
- r. Efficacy and effectiveness of specific devices and procedures to prevent complications from long term indwelling catheters in frail elderly
- s. Efficacy and effectiveness of multicomponent treatment for nocturia, including interventions targeted at comorbidity and drug therapy
- t. Compare the efficacy of specific models of UI care for frail elderly around the world.
- u. Determine the factors associated with the effectiveness of care models in countries with different health care systems

XIII. ALGORITHM

1. URINARY INCONTINENCE IN FRAIL OLDER MEN AND WOMEN

Healthy older persons should receive the **similar range of treatment options** as younger persons, but **frail older persons** require a **different approach** addressing the **potential role of comorbid disease, current medications (prescribed, over-the-counter, and/or naturopathic), and functional and/or cognitive impairment in UI**. The **extent of investigation and management** should take into account the **degree of bother** to the patient and/or carer, **goals for care**, cooperation, and **overall prognosis and life expectancy**. Effective management to meet the goals of care should be possible for most frail elderly.

2. HISTORY AND SYMPTOM ASSESSMENT

Active case finding and screening for UI should be done in all frail older persons (Grade A). **History**

should include **comorbid conditions and medications** that could cause or worsen UI. The physical should include **rectal exam for faecal loading or impaction** (Grade C), **functional assessment (mobility, transfers, manual dexterity, ability to toilet)** (Grade A), **screening test for depression** (Grade B), and **cognitive assessment** (to assist in planning management, Grade C). The mnemonic DIAPPERS (see algorithm) covers some of these comorbid factors, with two alterations: 1) **atrophic vaginitis** does not itself cause UI and **should not be treated for this purpose** (Grade B); and 2) current consensus diagnostic criteria for urinary tract infection (UTI) are poorly sensitive and specific in nursing home residents. The patient and/or carer should be asked about the **degree of bother** of UI (Grade B), **goals for UI care** (dryness, decrease in specific symptom[s], quality of life, reduction of comorbidity, lesser care burden) (Grade B), likely cooperation with management (Grade C), and the patient's **overall prognosis and remaining life expectancy** (Grade C). **Urinalysis** is recommended for all patients, primarily to screen for hematuria (Grade C); **treatment of otherwise asymptomatic bacteriuria/pyuria is not beneficial** (Grade D), and it may cause harm by increasing the risk of antibiotic resistance and severe adverse effects, e.g., *Clostridium difficile* colitis (Grade C). Utility of clinical stress test in this population is uncertain (Grade D). **Wet checks** can assess UI frequency in **long-term care residents** (Grade C).

Postvoiding residual volume (PVR) testing is impractical in many care settings, and there is no consensus for the definition of "high" PVR in any population. Yet, there is compelling clinical experience for PVR testing **in selected frail older persons** with: diabetes mellitus (especially longstanding), prior urinary retention or high PVR; recurrent UTIs; medications that impair bladder emptying (e.g., opiates); severe constipation; persistent or worsening urgency UI despite antimuscarinic treatment; or prior urodynamics showing detrusor underactivity and/or bladder outlet obstruction (Grade C). Treatment of contributing comorbidity may reduce PVR. Trial with catheter may be considered for PVR > 200–500 ml if the PVR is felt to contribute to UI or frequency (Grade C).

Assessment of frail elders with bothersome nocturia should identify potential underlying cause(s) including nocturnal polyuria (by **bladder diary [frequency-volume chart] or wet checks** or oedema on exam) (Grade C); primary sleep problem (e.g., sleep apnoea); and low voided volumes (e.g., from high PVR).

3. CLINICAL DIAGNOSIS

The most common types of UI in frail older persons are urgency, stress, and mixed UI. Frail elderly with urgency UI also may have detrusor underactivity and high PVR (without outlet obstruction), called detrusor

hyperactivity with impaired contractility (DHIC). There is no evidence that antimuscarinics are less effective or cause retention in DHIC (Grade D).

4. INITIAL MANAGEMENT

Initial treatment should be individualized and influenced by **goals of care, treatment preferences,** and **estimated remaining life expectancy**, as well as the most likely clinical diagnosis (Grade C). In some frail elders the only possible outcome may be contained UI (managed with pads), especially for persons with minimal mobility (require assistance of ≥ 2 persons to transfer), advanced dementia (unable to state their name), and/or nocturnal UI.

Conservative and behavioural therapy for UI include lifestyle changes (Grade C), bladder training for more fit alert patients (Grade B), and prompted voiding for frailer, more impaired patients (Grade A). For select cognitively intact patients, pelvic muscle exercises may be considered, but there are few studies (Grade C). Antimuscarinics may be added to conservative therapy of urgency UI (Grade A-C, depending on agent). Alpha-blockers may be cautiously considered in frail men with suspected prostatic outlet obstruction (Grade C). All drugs should be started at the lowest dose and titrated with regular review until either care goals are met or adverse effects are intolerable. DDAVP (vasopressin) has a high risk of severe hyponatremia in frail persons and should not be used (Grade B).

5. ONGOING MANAGEMENT AND REASSESSMENT

Optimal UI management is usually possible with the above approaches. If initial management fails to achieve desired goals, next steps are reassessment and treatment of contributing comorbidity and/or functional impairment.

6. SPECIALIZED MANAGEMENT

If frail elderly have either **other significant factors** (e.g., pain, haematuria), **UI symptoms that cannot be classified** as urgency, stress, or mixed, or **other complicated comorbidity** which the primary clinician cannot address (e.g., dementia, functional impairment), then **specialist referral** should be considered. Referral also may be appropriate for **insufficient response to initial management**. Type of specialist will depend on local resources and the reason for referral: surgical specialists (urologists, gynaecologists); geriatrician or physical therapist (functional and cognitive impairment); continence nurse specialists (homebound patients). **Referral decisions** should consider **goals of care, patient/carer desire for invasive therapy,** and **estimated remaining life expectancy**.

Age per se is not a contraindication to UI surgery (Grade C), but before surgery is considered, all patients should have:

- Evaluation and treatment for any comorbidity, medications, and cognitive and/or functional impairments contributing to UI and/or which could compromise surgical outcome (e.g., dementia that precludes patient ability to use artificial sphincter) (Grade C)
- Adequate trial of conservative therapy (Grade C)
- Discussion (including the carer) to insure that the anticipated surgical outcome is consistent with goals of care in the context of the patient's remaining life expectancy (Grade C)
- Urodynamic testing, because clinical diagnosis may be inaccurate (Grade B)
- Preoperative assessment and perioperative care to establish risk for and minimise common geriatric post-operative complications such as delirium and infection (Grade A) and dehydration and falls (Grade C).

REFERENCES

- Baltes, P.B. & Smith, J. New frontiers in the future of aging: from successful aging of the young old to the dilemmas of the fourth age. *Gerontology* 49, 123-135 (2003).
- Lutz W., Sanderson W., Scherbow S. The coming acceleration of global population aging. *Nature* 451, 716-9 (2008).
- Fonda, D. Improving management of urinary incontinence in geriatric centres and nursing homes. Victorian Geriatricians Peer Review Group. *Australian Clinical Review* 10, 66-71 (1990).
- Ouslander, J.G. et al. Functional incidental training: a randomized, controlled, crossover trial in Veterans Affairs nursing homes. *J Am Geriatr Soc* 53, 1091-1100 (2005).
- Fonda, D. et al. Outcome measures for research of lower urinary tract dysfunction in frail older people. *Neurourology & Urodynamics* 17, 273-281 (1998).
- Ferrucci, L. et al. Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons: a consensus report. *Journal of the American Geriatrics Society* 52, 625-634 (2004).
- Fried, L. et al. Frailty in older adults: evidence for a phenotype. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 56, M146-156 (2001).
- Centers for Disease Control National Center for Health Statistics.
- Imuta, H., Yasumura, S., Abe, H. & Fukao, A. The prevalence and psychosocial characteristics of the frail elderly in Japan: a community-based study. *Aging-Clinical & Experimental Research* 13, 443-453 (2001).
- Thom, D.H., Haan, M.N. & Van Den Eeden, S.K. Medically recognized urinary incontinence and risks of hospitalization, nursing home admission and mortality. *Age & Ageing* 26, 367-374 (1997).
- Holroyd-Leduc, J.M., Mehta, K.M. & Covinsky, K.E. Urinary incontinence and its association with death, nursing home admission, and functional decline. *Journal of the American Geriatrics Society* 52, 712-718 (2004).
- Miles, T.P. et al. New-onset incontinence and markers of frailty: data from the Hispanic Established Populations for Epidemiologic Studies of the Elderly. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 56, M19-24 (2001).
- Donaldson, L. & Jagger, C. Survival and functional capacity: three year follow up of an elderly population in hospitals and homes. *Journal of Epidemiology & Community Health* 37, 176-179 (1983).
- Herzog, A., Diokno, A., Brown, M., Fultz, N. & Goldstein, N. Urinary incontinence as a risk factor for mortality. *J Am Geriatr Soc* 42, 264-268 (1994).
- Johnson, T.M. 2nd, Bernard, S., Kincade, J. & Defriese, G. Urinary incontinence and risk of death among community-living elderly people: results from the National Survey on Self-Care and Aging. *Journal of Aging & Health* 12, 25-46 (2000).
- Patel, M., Coshall, C., Rudd, A. & Wolfe, C. Natural history and effects on 2-year outcomes of urinary incontinence after stroke. *Stroke* 32, 122-127 (2001).
- Baztan, J.J., Arias, E., Gonzalez, N. & de Prada, M.I.R. New-onset urinary incontinence and rehabilitation outcomes in frail older patients. *Age Ageing* 34, 172-175 (2005).
- Nuotio, M., Tammela, T.L.J., Luukkaala, T. & Jylha, M. Predictors of institutionalization in an older population during a 13-year period: The effect of urge incontinence. *J Gerontol A Biol Sci Med Sci* 58, M756-762 (2003).
- Welz-Barth, A., Garcia-Schurman, C. & Fusgen, I. [Incontinence, dementia and multiple morbidity—predictive factors for nursing care requirement and nursing home admission] [German]. *Wiener Medizinische Wochenschrift* 148, 305-308 (1998).
- Weatherall, M., Slow, T. & Wiltshire, K. Risk factors for entry into residential care after a support-needs assessment. *New Zealand Medical Journal* 117, U1075 (2004).
- Coward, R.T., Horne, C. & Peek, C.W. Predicting nursing home admissions among incontinent older adults: a comparison of residential differences across six years. *Gerontologist* 35, 732-743 (1995).
- Steiner, J., Kramer, A., Eilertsen, T. & Kowalsky, J. Development and validation of a clinical prediction rule for prolonged nursing home residence after hip fracture. *J Am Geriatr Soc* 45, 1510-1514 (1997).
- O'Donnell, B. et al. ncontinence and troublesome behaviors predict institutionalization in dementia. *Journal of Geriatric Psychiatry & Neurology* 5, 45-52 (1992).
- Matsumoto, M. & Inoue, K. Predictors of institutionalization in elderly people living at home: the impact of incontinence and commode use in rural Japan. *Journal of Cross-Cultural Gerontology* 22, 421-432 (2007).
- Hebert, R., Dubois, M.-F., Wolfson, C., Chambers, L. & Cohen, C. Factors associated with long-term institutionalization of older people with dementia: data from the Canadian Study of Health and Aging. *J Gerontol A Biol Sci Med Sci* 56, M693-699 (2001).
- Morrison, A. & Levy, R. Fraction of nursing home admissions attributable to urinary incontinence. *Value Health* 9, 272-274 (2006).
- Boyington, J. et al. Differences in resident characteristics and prevalence of urinary incontinence in nursing homes in the southeastern United States. *Nursing Research*. 56, 97-107 (2007).
- Anger, J.T., Saigal, C.S., Pace, J., Rodríguez, L.V. & Litwin, M.S. True prevalence of urinary incontinence among female nursing home residents. *Urology* 67, 281-287 (2006).
- Berlowitz, D., Brand, H. & Perkins, C. Geriatric syndromes as outcome measures of hospital care: can administrative data be used? *J Am Geriatr Soc* 47, 692-696 (1999).
- Tomiak, M., Berthelot, J.-M., Guimond, E. & Mustard, C.

- Factors associated with nursing-home entry for elders in Manitoba, Canada. *J Gerontol A Biol Sci Med Sci* 55, M279-287 (2000).
30. Yaffe, K. et al. Patient and caregiver characteristics and nursing home placement in patients with dementia. *JAMA* 287, 2090-2097 (2002).
 31. Inouye, S.K., Studenski, S., Tinetti, M.E. & Kuchel, G.A. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. *J.Am.Geriatr.Soc.* 55, 780-791 (2007).
 32. DuBeau, C.E. Beyond the bladder: management of urinary incontinence in older women. *Clin.Obstet.Gynecol.* 50, 720-734 (2007).
 33. Tinetti, M., Inouye, S., Gill, T. & Doucette, J. Shared risk factors for falls, incontinence, and functional dependence. Unifying the approach to geriatric syndromes. *JAMA* 273, 1348-1353 (1995).
 34. Kuo, H.K. & Lipsitz, L.A. Cerebral white matter changes and geriatric syndromes: is there a link? *J.Gerontol.A Biol.Sci.Med.Sci.* 59, 818-826 (2004).
 35. Griffiths, D., Derbyshire, S., Stenger, A. & Resnick, N. Brain control of normal and overactive bladder. *J.Urol.* 174, 1862-1867 (2005).
 36. Tadic, S.D., Griffiths, D., Schaefer, W. & Resnick, N.M. Abnormal connections in the supraspinal bladder control network in women with urge urinary incontinence. *Neuroimage.* 39, 1647-1653 (2008).
 37. Griffiths, D. & Tadic, S.D. Bladder control, urgency, and urge incontinence: Evidence from functional brain imaging. *Neurourol.Urodyn.* (2007).
 38. Hof, P.R. & Morrison, J.H. The aging brain: morphomolecular senescence of cortical circuits. *Trends Neurosci.* 27, 607-613 (2004).
 39. Andrews-Hanna, J.R. et al. Disruption of large-scale brain systems in advanced aging. *Neuron* 56, 924-935 (2007).
 40. Resnick, N.M. & Yalla, S.V. Age and the lower urinary tract: what is normal? *Neurourology & Urodynamics* 14, 577-579 (1995).
 41. Nordling, J. The aging bladder—a significant but underestimated role in the development of lower urinary tract symptoms. *Experimental Gerontology* 37, 991-999 (2002).
 42. Madersbacher, S. et al. The aging lower urinary tract: a comparative urodynamic study of men and women. *Urology.* 51, 206-212 (1998).
 43. Pfisterer, M.H., Griffiths, D.J., Schaefer, W. & Resnick, N.M. The effect of age on lower urinary tract function: a study in women. *J.Am.Geriatr.Soc.* 54, 405-412 (2006).
 44. Taylor, J.A., III & Kuchel, G.A. Detrusor underactivity: Clinical features and pathogenesis of an underdiagnosed geriatric condition. *J.Am.Geriatr.Soc.* 54, 1920-1932 (2006).
 45. Elbadawi, A., Yalla, S.V. & Resnick, N.M. Structural basis of geriatric voiding dysfunction. II. Aging detrusor: normal versus impaired contractility. *Journal of Urology.* 150, 1657-1667 (1993).
 46. Abrams, P.H. & Griffiths, D.J. The assessment of prostatic obstruction from urodynamic measurements and from residual urine. *British Journal of Urology* 51, 129-134 (1979).
 47. Taylor, J., III. Null mutation for macrophage migration inhibitory factor (MIF) is associated with less aggressive bladder cancer in mice. *BMC Cancer* 7, 135 (2007).
 48. Collas, D.M. & Malone-Lee, J.G. Age-associated changes in detrusor sensory function in women with lower urinary tract symptoms. *International Urogynecology Journal* 7, 24-29 (1996).
 49. Pfisterer, M.H., Griffiths, D.J., Rosenberg, L., Schaefer, W. & Resnick, N.M. The impact of detrusor overactivity on bladder function in younger and older women. *J.Urol.* 175, 1777-1783 (2006).
 50. Resnick, N.M. & Yalla, S.V. Detrusor hyperactivity with impaired contractile function. An unrecognized but common cause of incontinence in elderly patients. *Jama.* 257, 3076-3081 (1987).
 51. Elbadawi, A., Yalla, S.V. & Resnick, N.M. Structural basis of geriatric voiding dysfunction. I. Methods of a prospective ultrastructural/urodynamic study and an overview of the findings. *Journal of Urology.* 150, 1650-1656 (1993).
 52. Elbadawi, A., Yalla, S.V. & Resnick, N.M. Structural basis of geriatric voiding dysfunction. IV. Bladder outlet obstruction. *Journal of Urology.* 150, 1681-1695 (1993).
 53. Elbadawi, A., Yalla, S.V. & Resnick, N.M. Structural basis of geriatric voiding dysfunction. III. Detrusor overactivity. *Journal of Urology.* 150, 1668-1680 (1993).
 54. Elbadawi, A., Hailemariam, S., Yalla, S.V. & Resnick, N.M. Structural basis of geriatric voiding dysfunction. VII. Prospective ultrastructural/urodynamic evaluation of its natural evolution. *Journal of Urology.* 157, 1814-1822 (1997).
 55. Elbadawi, A., Hailemariam, S., Yalla, S.V. & Resnick, N.M. Structural basis of geriatric voiding dysfunction. VI. Validation and update of diagnostic criteria in 71 detrusor biopsies. *Journal of Urology.* 157, 1802-1813 (1997).
 56. Hailemariam, S., Elbadawi, A., Yalla, S.V. & Resnick, N.M. Structural basis of geriatric voiding dysfunction. V. Standardized protocols for routine ultrastructural study and diagnosis of endoscopic detrusor biopsies. *Journal of Urology.* 157, 1783-1801 (1997).
 57. Elbadawi, A., Diokno, A.C. & Millard, R.J. The aging bladder: morphology and urodynamics. *World Journal of Urology.* 16, S10-34 (1998).
 58. Levy, B. & Wight, T. Structural changes in the aging submucosa: New morphologic criteria for the evaluation of the unstable human bladder. *J Urol* 144, 1044-1055 (1990).
 59. Zhu, Q., Resnick, N.M., Elbadawi, A. & Kuchel, G.A. Estrogen and postnatal maturation increase caveolar number and caveolin-1 protein in bladder smooth muscle cells. *J.Urol.* 171, 467-471 (2004).
 60. Zhu, Q. et al. Role of ovarian hormones in the pathogenesis of impaired detrusor contractility: evidence in ovariectomized rodents. *J.Urol.* 166, 1136-1141 (2001).
 61. Brierly, R.D., Hindley, R.G., McLarty, E., Harding, D.M., Thomas, P.J. A prospective evaluation of detrusor ultrastructural changes in bladder outlet obstruction. *BJU International* 91, 360-364 (2003).
 62. Rud, T. Urethral pressure profile in continent women from childhood to old age. *Acta Obstet Gynecol Scand* 59, 331-335 (1980).
 63. Hilton, P. & Stanton, S. Urethral pressure measurement by microtransducer: the results in symptom-free women and in those with genuine stress incontinence. *BJOG* 90, 919-933 (1983).
 64. Trowbridge, E., Wei, J., Fenner, D., Ashton-Miller, J. & Delancey, J. Effects of aging on lower urinary tract and pelvic floor function in nulliparous women. *Obstet Gynecol* 109, 715-720 (2007).
 65. Samsioe, G., Jansson, I., Mellstrom, D. & Svanborg, A. Occurrence, nature and treatment of urinary incontinence in a 70-year-old female population. *Maturitas* 7, 335-342 (1985).
 66. Kenton, K., Lowenstein, L., Simmons, J. & Brubaker, L. Aging and overactive bladder may be associated with loss of urethral sensation in women. *Neurourol Urodyn* 26, 981-984 (2007).

67. Forsberg, J.G. A morphologist's approach to the vagina—age-related changes and estrogen sensitivity. *Maturitas* 22, S7-S15 (1995).
68. Yang, J., Yang, S. & Huang, W. Functional correlates of Doppler flow study of the female urethral vasculature. *Ultrasound Obstet Gynecol* 28, 96-102 (2006).
69. Siracusano, S. et al. Application of ultrasound contrast agents for the characterization of female urethral vascularization in healthy pre- and postmenopausal volunteers. *Eur Urol* 50, 1316-1322 (2006).
70. Liang, C. et al. Three-dimensional power Doppler measurement of perfusion of the periurethral tissue in incontinent women: a preliminary report. *Acta Obstetrica et Gynecologica Scandinavica* 85, 608-613 (2006).
71. Carlile, A., Davies, I., Rigby, A. & Brocklehurst, J.C. Age changes in the human female urethra: a morphometric study. *Journal of Urology* 139, 532-535 (1988).
72. Verelst, M., Maltau, J.M. & Orbo, A. Computerised morphometric study of the paraurethral tissue in young and elderly women. *Neurourology & Urodynamics* 21, 529-533 (2002).
73. Perucchini, D., DeLancey, J.O., Ashton-Miller, J.A., Peschers, U. & Kataria, T. Age effects on urethral striated muscle. I. Changes in number and diameter of striated muscle fibers in the ventral urethra. *American Journal of Obstetrics & Gynecology* 186, 351-355 (2002).
74. Perucchini, D., DeLancey, J.O., Ashton-Miller, J.A., Galecki, A. & Schaer, G.N. Age effects on urethral striated muscle. II. Anatomic location of muscle loss. *American Journal of Obstetrics & Gynecology* 186, 356-360 (2002).
75. Clobes, A., DeLancey, J. & Morgan, D. Urethral circular smooth muscle in young and old women. *J Obstet Gynecol* 198, 587e581-585 (2008).
76. Kenton, K., Simmons, J., FitzGerald, M., Lowenstein, L. & Brubaker, L. Urethral and bladder current perception thresholds: normative data in women. *J Urol* 178, 189-192 (2007).
77. Romanzi, L.J., Groutz, A. & Blaivas, J.G. Urethral diverticulum in women: diverse presentations resulting in diagnostic delay and mismanagement. *Journal of Urology* 164, 428-433 (2000).
78. Strasser, H., Tiefenthaler, M., Steinlechner, M., Bartsch, G. & Konwalinka, G. Urinary incontinence in the elderly and age-dependent apoptosis of rhabdosphincter cells. *Lancet* 354, 918-919 (1999).
79. Rother, P., Loffler, S., Dorschner, W., Reibiger, I. & Bengs, T. Anatomic basis of micturition and urinary continence. Muscle systems in urinary bladder neck during ageing. *Surgical & Radiologic Anatomy* 18, 173-177 (1996).
80. Bagi, P., Vejborg, I., Colstrup, H. & Kristensen, J.K. Pressure/cross-sectional area relations in the proximal urethra of healthy males. Part 1: Elastance and estimated pressure in the uninstrumented urethra. *European Urology* 28, 51-57 (1995).
81. Hammerer, P., Michl, U., Meyer-Moldenhauer, W.H. & Huland, H. Urethral closure pressure changes with age in men. *Journal of Urology* 156, 1741-1743 (1996).
82. Lawrence, J., Lukacz, E., Nager, C., Hsu, J. & Luber, K. Prevalence and co-occurrence of pelvic floor disorders in community-dwelling women. *Obstet Gynecol* 111, 678-685 (2008).
83. Talasz, H. et al. Evaluation of pelvic floor muscle function in a random group of adult women in Austria. *Int Urogynecol J* 19, 131-135 (2008).
84. Jundt, K. et al. Is the histomorphological concept of female pelvic floor and its changes due to age and vaginal delivery correct? *Neurourol Urodyn* 24, 44-50 (2005).
85. Norton, P.A. Pelvic floor disorders: the role of fascia and ligaments. *Clinical Obstetrics & Gynecology* 36, 926-938 (1993).
86. Spence-Jones, C., Kamm, M.A., Henry, M.M. & Hudson, C.N. Bowel dysfunction: a pathogenic factor in uterovaginal prolapse and urinary stress incontinence. *British Journal of Obstetrics & Gynaecology* 101, 147-152 (1994).
87. Buntzen, S., Nordgren, S., Delbro, D. & Hulten, L. Anal and rectal motility responses to distension of the urinary bladder in man. *Int J Colorectal Dis* 10, 148-151 (1995).
88. Bachmann, G. Urogenital ageing: an old problem newly recognized. *Maturitas*. 22 Suppl, 51-55 (1995).
89. Stenberg, A., Heimer, G. & Ulmsten, U. The prevalence of urogenital symptoms in postmenopausal women. *Maturitas* 22, S17-S20 (1995).
90. Rossouw, J.E. et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 288, 321-333 (2002).
91. Grady, D. et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II). *JAMA* 288, 49-57 (2002).
92. Juthani-Mehta, M. et al. Diagnostic accuracy of criteria for urinary tract infection in a cohort of nursing home residents. *J Am Geriatr Soc* 55, 1072-1077 (2007).
93. Tan, J. et al. Determinants of vaginal length. *Am J Obstet Gynecol* 195, 1846-1850 (2006).
94. Cardozo, L., Lose, G., McClish, D., Versi, E. & de Koning Gans, H. A systematic review of estrogens for recurrent urinary tract infections: third report of the hormones and urogenital therapy (HUT) committee. *International Urogynecology Journal* 12, 15-20 (2001).
95. Berry, S., Coffey, D., Walsh, P. & Ewing, L. The development of human benign prostatic hyperplasia with age. *J Urol* 132, 474-479 (1984).
96. Shibata, Y. et al. Changes in the endocrine environment of the human prostate transition zone with aging: simultaneous quantitative analysis of prostatic sex steroids and comparison with human prostatic histological composition. *Prostate* 42, 45-55 (2000).
97. Griffiths, K. Estrogens and prostatic disease. *International Prostate Health Council Study Group. Prostate* 45, 87-100 (2000).
98. Kramer, G., Mitteregger, D. & Marberger, M. Is benign prostatic hyperplasia (BPH) an immune inflammatory disease? *Eur Urol* 51, 1202-1216 (2007).
99. Roehrborn, C.G. et al. Serum prostate-specific antigen and prostate volume predict long-term changes in symptoms and flow rate: results of a four-year, randomized trial comparing finasteride versus placebo. *PLESS Study Group. Urology* 54, 662-669 (1999).
100. Jacobsen, S.J. et al. Treatment for benign prostatic hyperplasia among community dwelling men: the Olmsted County study of urinary symptoms and health status. *Journal of Urology* 162, 1301-1306 (1999).
101. McConnell, J.D., Barry, M.J. & Bruskewitz, R.C. Benign prostatic hyperplasia: diagnosis and treatment. Agency for Health Care Policy and Research. *Clinical Practice Guideline - Quick Reference Guide for Clinicians*, 1-17 (1994).
102. Coolsaet, B., van Venrooij, G. & Block, C. Prostatism: rationalization of urodynamic testing. *World Journal of Urology* 2, 216-221 (1984).
103. Mishra, V. et al. Does intraprostatic inflammation have a role in the pathogenesis and progression of benign prostatic hyperplasia? *BJU International* 100, 327-331 (2007).

104. Anjum, I., Ahmed, M., Azzopardi, A. & Mufti, G. Prostatic infarction/infection in acute urinary retention secondary to benign prostatic hyperplasia. *J Urol* 160, 792-793 (1998).
105. Ouslander, J.G., Schapira, M., Schnelle, J.F. & Fingold, S. Pyuria among chronically incontinent but otherwise asymptomatic nursing home residents. *Journal of the American Geriatrics Society* 44, 420-423 (1996).
106. Nicolle, L.E. Urinary tract infection in geriatric and institutionalized patients. *Current Opinion in Urology* 12, 51-55 (2002).
107. Ouslander, J.G. et al. Does eradicating bacteriuria affect the severity of chronic urinary incontinence in nursing home residents? *Annals of Internal Medicine* 122, 749-754 (1995).
108. Cigolle, C.T., Langa, K.M., Kabeto, M.U., Zhiyi, T. & Blaum, C.S. Geriatric conditions and disability: The Health and Retirement Study. *Annals of Internal Medicine* 147, 156-W126 (2007).
109. Brandeis, G., Baumann, M., Hossain, M., Morris, J. & Resnick, N. The prevalence of potentially remediable urinary incontinence in frail older people: a study using the Minimum Data Set. *J Am Geriatr Soc* 45, 179-184 (1997).
110. Rait, G. et al. Prevalence of cognitive impairment: results from the MRC trial of assessment and management of older people in the community. *Age Ageing* 34, 242-248 (2005).
111. Mecocci, P. et al. Cognitive impairment is the major risk factor for development of geriatric syndromes during hospitalization: results from the GIFA study. *Dementia & Geriatric Cognitive Disorders* 20, 262-269 (2005).
112. Huang, A., Brown, J., Thom, D., Fink, H. & Yaffe, K. Study of Osteoporotic Fractures Research Group. Urinary incontinence in older community-dwelling women: the role of cognitive and physical function decline. *Obstetrics & Gynecology* 109, 909-916 (2007).
113. Pantoni, L. Leukoaraiosis: from an ancient term to an actual marker of poor prognosis. *Stroke* 39, 1401-1403 (2008).
114. Pantoni, L. & Garcia, J.H. The significance of cerebral white matter abnormalities 100 years after Binswanger's report. A review. *Stroke* 26, 1293-1301 (1995).
115. Sitoh, Y.Y. & Sahadevan, S. Clinical significance of cerebral white matter lesions in older Asians with suspected dementia. *Age Ageing* 33, 67-71 (2004).
116. Sakakibara, R., Hattori, T., Uchiyama, T. & Yamanishi, T. Urinary function in elderly people with and without leukoaraiosis: relation to cognitive and gait function. *J.Neurol.Neurosurg.Psychiatry* 67, 658-660 (1999).
117. Meier, U., Konig, A. & Miethke, C. Predictors of outcome in patients with normal-pressure hydrocephalus. *European Neurology* 51, 59-67 (2004).
118. Gray, R., Stern, G. & Malone-Lee, J. Lower urinary tract dysfunction in Parkinson's Disease: changes relate to age and not disease. *Age & Ageing* 24, 499-504 (1995).
119. Wullner, U. et al. Autonomic dysfunction in 3414 Parkinson's disease patients enrolled in the German Network on Parkinson's disease (KNP e.V.): the effect of ageing. *Eur J Neurol* 14, 1405-1408 (2007).
120. Chaudhuri, K. Nocturnal symptom complex in Parkinsons disease and its management. *Neurology* 61(Suppl 3), S17-S23 (2003).
121. Balash, Y. et al. Falls in outpatients with Parkinson's disease. *Journal of Neurology* 252, 1310-1315 (2005).
122. Engberg, S. et al. Prevalence and recognition of depressive symptoms among homebound older adults with urinary incontinence. *Journal of Geriatric Psychiatry & Neurology* 14, 130-139 (2001).
123. Dugan, E. et al. The association of depressive symptoms and urinary incontinence among older adults. *J Am Geriatr Soc* 48, 413-416 (2000).
124. Chesterman, J., Bauld, L. & Judge, K. Satisfaction with the care-managed support of older people: an empirical analysis. *Health & Social Care in the Community* 9, 31 (2001).
125. Johnson, T.M. 2nd, et al. The association of urinary incontinence with poor self-rated health. *J Am Geriatr Soc* 46, 693-699 (1998).
126. Herzog, A., Fultz, N., Brock, B., Brown, M. & Diokno, A. Urinary incontinence and psychological distress among older adults. *Psychology & Aging* 3, 115-121 (1988).
127. Fultz, N.H. et al. The impact of own and spouse's urinary incontinence on depressive symptoms. *Social Science & Medicine* 60, 2537-2548 (2005).
128. Black, S., Goodwin, J. & Markides, K. The association between chronic diseases and depressive symptomatology in older Mexican Americans. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 53, M188-194 (1998).
129. Chiverton, P., Wells, T., Brink, C. & Mayer, R. Psychological factors associated with urinary incontinence. *Clinical Nurse Specialist* 10, 229-233 (1996).
130. Grimby, A., Milsom, I., Molander, U., Wiklund, I. & Ekelund, P. The influence of urinary incontinence on the quality of life of elderly women. *Age & Ageing* 22, 82-89 (1993).
131. Yoshida, Y. et al. Prevalence and characteristics of urinary incontinence in community-dwelling-elderly as determined by comprehensive health examination and interview for the prevention of geriatric syndrome and bed-ridden state. *Nippon Ronen Igakkai Zasshi - Japanese Journal of Geriatrics* 44, 83-89 (2007).
132. Song, H. & Bae, J. Prevalence of urinary incontinence and lower urinary tract symptoms for community-dwelling elderly 85 years of age and older. *Journal of Wound, Ostomy, & Continence Nursing* 34, 535-541 (2007).
133. Ko, Y., Lin, S., Salmon, J. & Bron, M. The impact of urinary incontinence on quality of life of the elderly. *Am J Managed Care* 11(4 Suppl), S103-111 (2005).
134. Fultz, N.H. & Herzog, A.R. Self-Reported Social and Emotional impact of urinary incontinence. *Journal of the American Geriatrics Society* 49, 892-899 (2001).
135. Bogner, H.R. et al. Urinary incontinence and psychological distress in community-fwelling older adults. *Journal of the American Geriatrics Society* 50, 489-495 (2002).
136. Ruby, C. & et al. Medication use and control of urination among community-dwelling older adults. *J Aging & Health* 17, 661-674 (2005).
137. Ouslander, J.G. et al. Clinical, functional, and psychosocial characteristics of an incontinent nursing home population. *Journal of Gerontology* 42, 631-637 (1987).
138. Ouslander, J.G., Uman, G.C., Urman, H.N. & Rubenstein, L.Z. Incontinence among nursing home patients: clinical and functional correlates. *Journal of the American Geriatrics Society* 35, 324-330 (1987).
139. Wyman, J.F., Elswick, R.K., Jr., Ory, M.G., Wilson, M.S. & Fantl, J.A. Influence of functional, urological, and environmental characteristics on urinary incontinence in community-dwelling older women. *Nursing Research* 42, 270-275 (1993).
140. Chiang, L., Ouslander, J., Schnelle, J. & Reuben, D.B. Dually incontinent nursing home residents: clinical characteristics and treatment differences. *Journal of the American Geriatrics Society* 48, 673-676 (2000).
141. Ouslander, J.G., Palmer, M.H., Rovner, B.W. & German, P.S. Urinary incontinence in nursing homes: incidence, remission and associated factors. *Journal of the American Geriatrics Society* 41, 1083-1089 (1993).

142. Kutner, N., Schechtman, K., Ory, M., Baker, D. Older adults' perceptions of their health and functioning in relation to sleep disturbance, falling, and urinary incontinence. *J Am Geriatr Soc* 42, 757-762 (1994).
143. Nelson, R.L. & Furner, S.E. Risk factors for the development of fecal and urinary incontinence in Wisconsin nursing home residents. *Maturitas* 52, 26-31 (2005).
144. Landi, F. et al. The Silvernet-HC study group. Functional decline in frail community-dwelling stroke patients. *Journal of Neurology* 13, 17-23 (2006).
145. Takazawa, K. & Arisawa, K. Relationship between the type of urinary incontinence and falls among frail elderly women in Japan. *Journal of Medical Investigation* 52, 165-171 (2005).
146. Chen, J.S. et al. A multivariate regression model predicted falls in residents living in intermediate hostel care. *Journal of Clinical Epidemiology* 58, 503-508 (2005).
147. Becker, C. et al. An algorithm to screen long-term care residents at risk for accidental falls. *Aging-Clinical & Experimental Research* 17, 186-192 (2005).
148. Tromp, E. Risk profiles and preventive measures of falls in elderly persons [Risicoprofielen en preventie van vallen bij ouderen]. *Tijdschrift voor Gerontologie en Geriatrie* 33, 21-25, (2002).
149. Brown, J.S. et al. Urinary incontinence: does it increase risk for falls and fractures? Study of Osteoporotic Fractures Research Group. *Journal of the American Geriatrics Society*. 48, 721-725 (2000).
150. Wilkins, K. Medications and fall-related fractures in the elderly. *Health Reports* 11, 45-53 (1999).
151. Johansson, C., Hellstrom, L., Ekelund, P. & Milsom, I. Urinary incontinence: a minor risk factor for hip fractures in elderly women. *Maturitas* 25, 21-28 (1996).
152. Johansson, C., Molander, U., Milsom, I. & Ekelund, P. Association between urinary incontinence and urinary tract infections, and fractures in postmenopausal women. *Maturitas* 23, 265-271 (1996).
153. Landi, F. et al. Potentially reversible risk factors and urinary incontinence in frail older people living in community. *Age Ageing* 32, 194-199 (2003).
154. Robbins, A.S. et al. Predictors of falls among elderly people. Results of two population-based studies. *Archives of Internal Medicine* 149, 1628-1633 (1989).
155. Woodford, H. & George, J. NICE guidelines on urinary incontinence in women. *Age Ageing* 36, 349-350 (2007).
156. DuBeau, C.E., Ouslander, J.G. & Palmer, M.H. Knowledge and attitudes of nursing home staff and surveyors about the revised federal guidance for incontinence care. *Gerontologist* 47, 468-479 (2007).
157. Fung, C., Spencer, B., Eslami, M. & Crandall, C. Quality indicators for the screening and care of urinary incontinence in vulnerable elders. *J Am Geriatr Soc* 55 Suppl 2, S443-449 (2007).
158. Schnelle, J.F. & Smith, R.L. Quality indicators for the management of urinary incontinence in vulnerable community-dwelling. *Annals of Internal Medicine* 135, 752 (2001).
159. Wagg, A. et al. National audit of continence care for older people: management of urinary incontinence. *Age & Ageing* 37, 39-44 (2008).
160. Wagg, A., Mian, S., Lowe, D., Potter, J. & Pearson, M. National audit of continence care for older people: results of a pilot study. *J Eval Clin Pract* 11, 525-532 (2005).
161. Saliba, S., Elliott, M., Rubenstein, L., Solomon, D. & et al. The Vulnerable Elders Survey (VES-13): a tool for identifying vulnerable elders in the community. *J Am Geriatr Soc* 49, 1691-1699 (2001).
162. McDowell, B., Silverman, M., Martin, D., Musa, D. & Keane, C. Identification and intervention for urinary incontinence by community physicians and geriatric assessment teams. *J Am Geriatr Soc* 42, 501-505 (1994).
163. Ouslander, J. et al. Prospective evaluation of an assessment strategy for geriatric urinary incontinence. *J Am Geriatr Soc* 37, 715-724 (1989).
164. Torres, C., Ciocon, J., Galindo, D. & Ciocon, D. Clinical approach to urinary incontinence: a comparison between internists and geriatricians. *International Urology & Nephrology* 33, 549-552 (2001).
165. Bland, D.R. et al. The effects of implementation of the Agency for Health Care Policy and Research Urinary Incontinence Guidelines in primary care practices. *Journal of the American Geriatrics Society* 51, 979 (2003).
166. Watson, N., Brink, C., Zimmer, J. & Mayer, R. Use of the Agency for Health Care Policy and Research Urinary Incontinence Guideline in nursing homes. *J Am Geriatr Soc* 51, 1779-1786 (2003).
167. van Gerwen, M. & Lagro-Janssen, A. Diagnostic value of patient history and physical examination in elderly patients with urinary incontinence; a literature review [De diagnostische waarde van anamnese en lichamelijk onderzoek bij ouderen met urine-incontinentie; een overzicht van de literatuur]. *Nederlands Tijdschrift voor Geneeskunde* 150, 1771-1775, (2006).
168. Resnick, N., Brandeis, G., Baumann, M., DuBeau, C. & Yalla, S. Misdiagnosis of urinary incontinence in nursing home women: prevalence and a proposed solution. *Neurourology & Urodynamics* 15, 599-613 (1996).
169. Diokno, A., Wells, T. & Brink, C. Urinary incontinence in elderly women: urodynamic evaluation. *J Am Geriatr Soc* 35, 940-946 (1987).
170. Grosshans, C., Passadori, Y. & Peter, B. Urinary retention in the elderly: a study of 100 hospitalized patients. *J Am Geriatr Soc* 41, 633-638 (1993).
171. Resnick, N.M., Yalla, S.V. & Laurino, E. The pathophysiology of urinary incontinence among institutionalized elderly persons. *New England Journal of Medicine* 320, 1-7 (1989).
172. Urinary Incontinence Guideline Panel. (Agency for Healthcare Quality and Research) (US Department of Health and Human Services, Rockville, MD; 1992).
173. Ouslander, J.G. Intractable incontinence in the elderly. *BJU International* 85, 72-78; (2000).
174. Resnick, N. An 89-year-old woman with urinary incontinence. *JAMA* 276, 1832-1840 (1996).
175. DuBeau, C., Kiely, D. & Resnick, N. Quality of life impact of urge incontinence in older persons: a new measure and conceptual structure. *J Am Geriatr Soc* 47, 989-994 (1999).
176. DuBeau, C., Simon, S. & Morris, J. Impact of urinary incontinence on quality of life in nursing home residents. *J Am Geriatr Soc*, 1325-1333 (2006).
177. Fonda, D. & Abrams, P. Cure sometimes, help always—a "continence paradigm" for all ages and conditions. *Neurourology & Urodynamics* 25, 290-292 (2006).
178. Mitteness, L.S. & Barker, J.C. Stigmatizing a "normal" condition: urinary incontinence in late life. *Medical Anthropology Quarterly* 9, 188-210 (1995).
179. DuBeau, C.E. Urinary incontinence management: new questions from old assumptions. *Journal of the American Geriatrics Society* 49, 829-830 (2001).
180. Houghman, G.W. et al. Empirical research on informed consent with the cognitively impaired. *IRB: a Review of Human Subjects Research* Suppl 25, S26-S32 (2003).
181. Cai, L. & Lubitz, J. Was there compression of disability for older Americans from 1992 to 2003? *Demography* 44, 479-495 (2007).

182. Murray, D., Krahn, K., Bremner, J. & et al The ten-year rule revisited: accuracy of clinicians' estimates of life expectancy in patients with localized prostate cancer. *Urology* 60, 258–263 (2002).
183. Walter, L. & Covinsky, K. Cancer screening in elderly patients: a framework for individualized decision making. *JAMA* 285, 2750-2756 (2001).
184. Fried, L. et al. Risk factors for 5-year mortality in older adults: the Cardiovascular Health Study. *JAMA* 279, 585-592 (1998).
185. Larson, E. et al. Survival after initial diagnosis of alzheimer disease. *Ann Intern Med* 140, 501-509 (2004).
186. Simmons, S.F. & Schnelle, J.F. Strategies to measure nursing home residents' satisfaction and preferences related to incontinence and mobility care: implications for evaluating intervention effects. *Gerontologist* 39, 345-355 (1999).
187. Johnson, T.M., Ouslander, J.G., Uman, G.C. & Schnelle, J.F. Urinary incontinence treatment preferences in long-term care. *Journal of the American Geriatrics Society* 49, 710-718 (2001).
188. Pfisterer, M.H., Johnson, T.M., 2nd, Jenetzky, E., Hauer, K. & Oster, P. Geriatric patients' preferences for treatment of urinary incontinence: a study of hospitalized, cognitively competent adults aged 80 and older. *J Am Geriatr Soc* 55, 2016-2022 (2007).
189. Anger, J. et al. Increasing costs of urinary incontinence among female Medicare beneficiaries. *J Urol* 176, 247–251 (2006).
190. Wilson, L., Brown, J., Shin, G., Luc, K. & Subak, L. Annual direct cost of urinary incontinence. *Obstet Gynecol* 98, 398-406 (2001).
191. Reeves, P. et al. The current and future burden and cost of overactive bladder in five European countries. *Eur Urol* 50, 1050-1057 (2006).
192. Ouslander, J.G., Shih, Y.T., Malone-Lee, J. & Luber, K. Overactive bladder: special considerations in the geriatric population. *American Journal of Managed Care* 6, S599-606 (2000).
193. Darkow, T., Fontes, C. & Williamson, T. Costs associated with the management of overactive bladder and related comorbidities. *Pharmacotherapy* 25, 511–519 (2005).
194. Hu, T.W. et al. Estimated economic costs of overactive bladder in the United States. *Urology* 61, 1123-1128 (2003).
195. Schnelle, J.F., Sowell, V.A., Hu, T.W. & Traughber, B. Reduction of urinary incontinence in nursing homes: does it reduce or increase costs? *Journal of the American Geriatrics Society* 36, 34-39 (1988).
196. Landefeld, C.S. et al. National Institutes of Health State-of-the-Science Conference statement: Prevention of fecal and urinary incontinence in adults. *Ann Intern Med* 148, 449-458 (2008).
197. Frantz, R.A., Xakellis, G.C., Jr., Harvey, P.C. & Lewis, A.R. Implementing an incontinence management protocol in long-term care. *Clinical outcomes and costs. Journal of Gerontological Nursing* 29, 46-53 (2003).
198. Albers-Heitner, P. et al. The effects of involving a nurse practitioner in primary care for adult patients with urinary incontinence: the PromoCon study (Promoting Continence). *BMC Health Serv Res* 8, 84 (2008).
199. Morris, A.R. et al. Costs of managing urinary and faecal incontinence in a sub-acute care facility: a "bottom-up" approach. *Neurourological Urodyn* 24, 56-62 (2005).
200. Wodchis, W.P., Teare, G.F. & Anderson, G.M. Cost and quality: evidence from Ontario long term care hospitals. *Med Care* 45, 981-988 (2007).
201. Shih, Y.C., Hartzema, A.G. & Tolleson-Rinehart, S. Labor costs associated with incontinence in long-term care facilities. *Urology* 62, 442-446 (2003).
202. Borrie, M.J. & Davidson, H.A. Incontinence in institutions: costs and contributing factors. *CMAJ Canadian Medical Association Journal* 147, 322-328 (1992).
203. Green, J., Smoker, I., Ho, M. & Moore, K. Urinary incontinence in subacute care—a retrospective analysis of clinical outcomes and costs. *Medical Journal of Australia* 178, 550-553 (2003).
204. Langa, K.M., Fultz, N.H., Saint, S., Kabeto, M.U. & Herzog, A.R. Informal caregiving time and costs for urinary incontinence in older individuals in the United States. *Journal of the American Geriatrics Society* 50, 733-737 (2002).
205. Engberg, S., Kincade, J. & Thompson, D. Future directions for incontinence research with frail elders. *Nurs Res* 53, S22-29 (2004).
206. Mezey, M., Teresi, J., Ramsey, G., Mitty, E. & Bobrowitz, T. Decision-making capacity to execute a health care proxy: development and testing of guidelines. *Journal of the American Geriatrics Society* 48, 179-187 (2000).
207. Baltussen, R., Leidl, R. & Ament, A. The impact of age on cost-effectiveness ratios and its control in decision making. *Health Economics* 5, 227-239 (1996).
208. Bressler, R. & Bahl, J.J. Principles of drug therapy for the elderly patient. *Mayo Clinic Proceedings* 78, 1564-1577 (2003).
209. Avorn, J. & Rochon, P.A. in *Geriatric Medicine: An Evidenced Based Approach*. (eds. C. Cassel, R.M. Leipzig, H.J. Cohen, E.B. Larson & D.E. Meier) 65-81 (Springer, New York; 2003).
210. Rochon, P.A. et al. Age- and gender-related use of low-dose drug therapy: the need to manufacture low-dose therapy and evaluate the minimum effective dose. *Journal of the American Geriatrics Society* 47, 954-959 (1999).
211. Bemelmans, B., Kiemeney, L. & Debruyne, F. Low-dose oxybutynin for the treatment of urge incontinence: good efficacy and few side effects. *Eur Urol* 37, 709-713 (2000).
212. Malone-Lee, J., Lubel, D. & Szonyi, G. Low dose oxybutynin for the unstable bladder. *Br Med J* 304 (1992).
213. Cresswell, K., Fernando, B., McKinstry, B. & et al. Adverse drug events in the elderly. *Br Med Bull* 83, 259-274 (2007).
214. Hanlon, J.T. et al. Adverse drug events in high risk older outpatients. *Journal of the American Geriatrics Society* 45, 945-948 (1997).
215. Bootman, J.L., Harrison, D.L. & Cox, E. The health care cost of drug-related morbidity and mortality in nursing facilities. *Archives of Internal Medicine* 157, 2089-2096 (1997).
216. Patel, H. & et al. Trends in hospital admissions for adverse drug reactions in England: analysis of national hospital episode statistics 1998-2005. *Clin Pharmacol* 7, 9 (2007).
217. Feinberg, M. The problems of anticholinergic adverse effects in older patients. *Drugs & Aging* 3, 335-348 (1993).
218. Kay, G. & et al. Antimuscarinic drugs for overactive bladder and their potential effects on cognitive function in older patients. *J Am Geriatr Soc* 53, 2195-2201 (2005).
219. Ship, J.A., Pillemer, S.R. & Baum, B.J. Xerostomia and the geriatric patient. *Journal of the American Geriatrics Society* 50 (2002).
220. Chapple, C.R. & Nilvebrant, L. Tolterodine: selectivity for the urinary bladder over the eye (as measured by visual accommodation) in healthy volunteers. *Drugs in R & D* 3, 75-81 (2002).
221. Laroche, M.-L., Charnes, J.-P., Nouaille, Y., Picard, N. & Merle, L. Is inappropriate medication use a major cause of adverse drug reactions in the elderly? *Br J Clin Pharmacol* 63, 177-186 (2007).
222. Colucci, V.J. & Rivey, M.P. Tolterodine-warfarin drug interaction. *Annals of Pharmacotherapy* 33, 1173-1176 (1999).

223. Hashimoto, M., Imamura, T., Tanimukai, S., Kazui, H. & Mori, E. Urinary incontinence: an unrecognised adverse effect with donepezil. *Lancet* 356, 568 (2000).
224. Starr, J. Cholinesterase inhibitor treatment and urinary incontinence in Alzheimer's disease. *J Am Geriatr Soc* 55, 800-801 (2007).
225. Siegler, E.L. & Reidenberg, M. Treatment of urinary incontinence with anticholinergics in patients taking cholinesterase inhibitors for dementia. *Clinical Pharmacology & Therapeutics* 75, 484-488 (2004).
226. Gill, S.S. et al. A prescribing cascade involving cholinesterase Inhibitors and anticholinergic drugs. *Arch Intern Med* 165, 808-813 (2005).
227. Sink, K. et al. Dual use of bladder anticholinergics and cholinesterase inhibitors: long-term functional and cognitive outcomes. *J Am Geriatr Soc* 56, 847-853 (2008).
228. Fick, D.M. et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Archives of Internal Medicine* 163, 2716-2724 (2003).
229. McLeod, P.J., Huang, A.R., Tamblyn, R.M. & Gayton, D.C. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. *CMAJ Canadian Medical Association Journal* 156, 385-391 (1997).
230. Barry, P., O'Keefe, N., O'Connor, K. & O'Mahony, D. Inappropriate prescribing in the elderly: a comparison of the Beers criteria and the Improved Prescribing in the Elderly tool (IPET). *J Clin Pharm Ther* 31, 617-626 (2006).
231. O'Mahony, D. & Gallagher, P. Inappropriate prescribing in the older population: need for new criteria. *Age & Ageing* 37, 138-141 (2008).
232. Sahyoun, N.R., Pratt, L.A., Lentzner, H., Dey, A. & Robinson, K.N. The changing profile of nursing home residents: 1985-1997. *Aging Trends*, 1-8 (2001).
233. Health United States 2003 Special excerpt trend tables on 65 and older population, National Center for Health Statistics Centers for Disease Control and Prevention, 2004.
234. Scherr, D., Swindle, P.W., Scardino, P.T. National Comprehensive Cancer Network Guidelines for the management of prostate cancer. *Urology* 61(suppl2A), 14-24 (2003).
235. Brown, C.T., Van Der Meulen, J., Mundy, A.R. & Emberton, M. Lifestyle and behavioural interventions for men on watchful waiting with uncomplicated lower urinary tract symptoms: a national multidisciplinary survey. *BJU International* 92, 53-57 (2003).
236. Kincade, J.E., Dougherty, M.C., Carlson, J.R., Hunter, G.S. & Busby-Whitehead, J. Randomized clinical trial of efficacy of self-monitoring techniques to treat urinary incontinence in women. *Neurourol Urodyn* 26, 507-511 (2007).
237. Kayser-Jones, J., Schell, E., Porter, C., Barbaccia, J. & Shaw, H. Factors contributing to dehydration in nursing homes: inadequate staffing and lack of professional supervision. *J Am Geriatr Soc* 47, 1187-1194 (1999).
238. Arnaud, M. Mild dehydration: a risk factor of constipation? *Eur J Clin Nutrition* 57 (Suppl 2), S88-S95 (2003).
239. Wilson, M.-M. & Morley, J. Impaired cognitive function and mental performance in mild dehydration. *Eur J Clin Nutrition* 57 (Suppl 2), S24-S29 (2003).
240. Dowd, T., Campbell, J. & Jones, J. Fluid intake and urinary incontinence in older community-dwelling women. *J Comm Health Nurs* 13, 179-186 (1996).
241. Spangler, P., Risley, T. & Bilyew, D. The management of dehydration and incontinence in nonambulatory geriatric patients. *J Appl Behavior Anal* 17, 397-401 (1984).
242. Teunissen, T.A., de Jonge, A., van Weel, C. & Lagro-Janssen, A.L. Treating urinary incontinence in the elderly—conservative therapies that work: a systematic review. *Journal of Family Practice* 53, 25-30, 32 (2004).
243. Palmer M.H: Effectiveness of prompted voiding for incontinent nursing home residents, in Melnyk BM and Fineout-Overholt E: *Evidence-Based Practice in Nursing & Healthcare: A Guide to the Best Practice*. Philadelphia, Lippincott Williams & Williams, 2005, pp 20-30.
244. Ostaszkiwicz, J. A clinical nursing leadership model for enhancing continence care for older adults in a subacute inpatient care setting. *J Wound Ostomy Continence Nurs* 33, 624-629 (2006).
245. Loening-Baucke, V. & Anuras, S. Effects of age and sex on anorectal manometry. *American Journal of Gastroenterology* 80, 50-53 (1985).
246. Ostaszkiwicz, J., Johnston, L. & Roe, B. Timed voiding for the management of urinary incontinence in adults. *Cochrane Database of Systematic Reviews*, CD002802 (2004).
247. Ostaszkiwicz, J., Roe, B. & Johnston, L. Effects of timed voiding for the management of urinary incontinence in adults: systematic review. *J Adv Nurs* 52, 420-431 (2005).
248. Schnelle, J.F., MacRae, P.G., Ouslander, J.G., Simmons, S.F. & Nitta, M. Functional Incidental Training, mobility performance, and incontinence care with nursing home residents. *Journal of the American Geriatrics Society* 43, 1356-1362 (1995).
249. van Houten, P., Achterberg, W. & Ribbe, M. Urinary incontinence in disabled elderly women: a randomized clinical trial on the effect of training mobility and toileting skills to achieve independent toileting. *Gerontology* 53, 205-210 (2007).
250. Perrin, L., Dauphinee, S.W., Corcos, J., Hanley, J.A. & Kuchel, G.A. Pelvic floor muscle training with biofeedback and bladder training in elderly women: a feasibility study. *J Wound Ostomy Continence Nurs* 32, 186-199 (2005).
251. Diokno, A.C. et al. Prevention of urinary incontinence by behavioral modification program: a randomized, controlled trial among older women in the community. *J Urol* 171, 1165-1171 (2004).
252. Eustice, S., Roe, B. & Paterson, J. Prompted voiding for the management of urinary incontinence in adults. *Cochrane Database Syst Rev*, CD002113 (2000).
253. Ostaszkiwicz, J., Chestney, T. & Roe, B. Habit retraining for the management of urinary incontinence in adults. *Cochrane Database Syst Rev*, CD002801 (2004).
254. Roe, B. et al. Translating research on incontinence into practice. *Nursing Research*. 53(6 Suppl), S56-60 (2004).
255. Bates-Jensen, B.M., Alessi, C.A., Al-Samarrai, N.R. & Schnelle, J.F. The effects of an exercise and incontinence intervention on skin health outcomes in nursing home residents. *Journal of the American Geriatrics Society* 51, 348-355 (2003).
256. Simmons, S.F. & Schnelle, J. Effects of an exercise and scheduled-toileting intervention on appetite and constipation in nursing home residents. *J Nutr Health Aging* 8, 116-121 (2004).
257. Engberg, S., Sereika, S.M., McDowell, B.J., Weber, E. & Brodak, I. Effectiveness of prompted voiding in treating urinary incontinence in cognitively impaired homebound older adults. *Journal of Wound, Ostomy, & Continence Nursing* 29, 252-265 (2002).
258. Colling, J., Owen, T.R., McCreedy, M. & Newman, D. The effects of a continence program on frail community-dwelling elderly persons. *Urologic Nursing* 23, 117-122, 127-131 (2003).
259. Ouslander, J.G. et al. Predictors of successful prompted

- voiding among incontinent nursing home residents. *Jama*. 273, 1366-1370 (1995).
260. Tag F315, in State Operations CMS Manual System, US Department of Health & Human Services Centers for Medicare & Medicaid Services, 2005.
 261. Schnelle, J.F. et al. Does an exercise and incontinence intervention save healthcare costs in a nursing home population? *Journal of the American Geriatrics Society* 51, 161-168 (2003).
 262. DuBeau, C. Urinary incontinence in nursing home patients: Are we FIT to be tied? *J Am Geriatr Soc* 55, 1254-1256 (2005).
 263. Palmer, M.H. Use of health behavior change theories to guide urinary incontinence research. *Nurs Res* 53, S49-55 (2004).
 264. Baldwin, J. & Baldwin, J. Behavioral principles in everyday life, Edn. 2nd. (Prentice-Hill Co., Englewood, NJ; 1986).
 265. Schnelle, J.F. et al. The minimum data set urinary incontinence quality indicators: do they reflect differences in care processes related to incontinence? *Medical Care* 41, 909-922 (2003).
 266. Dingwall, L. & McLafferty, E. Do nurses promote urinary continence in hospitalized older people?: An exploratory study. *J Clin Nurs* 15, 1276-1286 (2006).
 267. Schnelle, J.F., Ouslander, J.G. & Cruise, P.A. Policy without technology: a barrier to improving nursing home care. *Gerontologist* 37, 527-532 (1997).
 268. Colling, J., Ouslander, J., Hadley, B.J., Eisch, J. & Campbell, E. The effects of patterned urge-response toileting (PURT) on urinary incontinence among nursing home residents. *Journal of the American Geriatrics Society*. 40, 135-141 (1992).
 269. Creason, N.S. et al. Prompted voiding therapy for urinary incontinence in aged female nursing home residents. *Journal of Advanced Nursing* 14, 120-126 (1989).
 270. Schnelle, J.F., Cruise, P.A., Rahman, A. & Ouslander, J.G. Developing rehabilitative behavioral interventions for long-term care: technology transfer, acceptance, and maintenance issues. *Journal of the American Geriatrics Society* 46, 771-777 (1998).
 271. Hu, T.W. et al. A clinical trial of a behavioral therapy to reduce urinary incontinence in nursing homes. Outcome and implications. *JAMA* 261, 2656-2662 (1989).
 272. Schnelle, J.F. et al. A standardized quality assessment system to evaluate incontinence care in the nursing home. *Journal of the American Geriatrics Society* 51, 1754-1761 (2003).
 273. Schnelle, J.F., McNees, P., Crooks, V. & Ouslander, J.G. The use of a computer-based model to implement an incontinence management program. *Gerontologist* 35, 656-665 (1995).
 274. Palmer, M.H., German, P.S. & Ouslander, J.G. Risk factors for urinary incontinence one year after nursing home admission. *Research in Nursing & Health* 14, 405-412 (1991).
 275. Engst, C. et al. Implementation of a scheduled toileting program in a long term care facility: evaluating the impact on injury risk to caregiving staff. *AAOHN J* 52, 427-435 (2004).
 276. Ryden, M. et al. Value-added outcomes: the use of advanced practice nurses in long-term care facilities. *Gerontologist* 40, 654-662 (2000).
 277. Schnelle, J.F. et al. Translating clinical research into practice: a randomized controlled trial of exercise and incontinence care with nursing home residents. *Journal of the American Geriatrics Society* 50, 1476-1483 (2002).
 278. Remsburg, R.E., Palmer, M.H., Langford, A.M. & Mendelson, G.F. Staff compliance with and ratings of effectiveness of a prompted voiding program in a long-term care facility. *Journal of Wound, Ostomy, & Continence Nursing* 26, 261-269 (1999).
 279. Lekan-Rutledge, D., Palmer, M. & Belyea, M. In their own words: Nursing assistants' preceptions of barriers to implementation of prompted voiding in long-term care. *Gerontologist* 38, 370-378 (1998).
 280. Bear, M., Dwyer, J.W., Benveneste, D., Jett, K. & Dougherty, M. Home-based management of urinary incontinence: a pilot study with both frail and independent elders.[see comment]. *Journal of Wound, Ostomy, & Continence Nursing* 24, 163-171 (1997).
 281. Cassells, C. & Watt, E. The impact of incontinence on older spousal caregivers. *Journal of Advanced Nursing* 42, 607-616 (2003).
 282. Shimanouchi, S., Kamei, T. & Hayashi, M. Home care for the frail elderly based on urinary incontinence level. *Public Health Nursing* 17, 468-473 (2000).
 283. Lekan-Rutledge, D. Diffusion of innovation. A model for implementation of prompted voiding in long-term care settings. *Journal of Gerontological Nursing* 26, 25-33 (2000).
 284. Narayanan, S., Cerulli, A., Kahler, K. & Ouslander, J. Is drug therapy for urinary incontinence used optimally in long-term care facilities? *J Am Med Dir Assoc*, 98-104 (2007).
 285. Lackner, T., Wyman, J., McCarthy, T., Monigold, M. & Davey, C. Randomized, placebo-controlled trial of the cognitive effect, safety, and tolerability of oral extended-release oxybutynin in cognitively impaired nursing home residents with urge urinary incontinence. *J Am Geriatr Soc* 56, 862-870 (2008).
 286. Minassian, V. & et al Randomized trial of oxybutynin extended versus immediate release for women aged 65 and older with overactive bladder; lessons learned from conducting a trial. *J Obstet Gynaecol Can* 29, 726-732 (2007).
 287. Sand, P. & et al Oxybutynin transdermal system improves the quality of life in adults with overactive bladder: a multi-centre community based, randomized study. *BJU International* 99, 836-844 (2007).
 288. Hughes, K.M. et al. Measurement of oxybutynin and its N-desethyl metabolite in plasma, and its application to pharmacokinetic studies in young, elderly and frail elderly volunteers. *Xenobiotica* 22, 859-869 (1992).
 289. Ouslander, J.G., Blaustein, J., Connor, A., Orzeck, S. & Yong, C.L. Pharmacokinetics and clinical effects of oxybutynin in geriatric patients. *Journal of Urology* 140, 47-50 (1988).
 290. Zobrist, R., Quan, D., Thomas, H., Stanworth, S. & Sanders, S. Pharmacokinetics and metabolism of transdermal oxybutynin: in vitro and in vivo performance of a novel delivery system. *Pharmaceut Res* 20, 103-109 (2003).
 291. Ouslander, J.G., Blaustein, J., Connor, A. & Pitt, A. Habit training and oxybutynin for incontinence in nursing home patients: a placebo-controlled trial. *Journal of the American Geriatrics Society*. 36, 40-46 (1988).
 292. Ouslander, J.G. et al. Does oxybutynin add to the effectiveness of prompted voiding for urinary incontinence among nursing home residents? A placebo-controlled trial. *Journal of the American Geriatrics Society*. 43, 610-617 (1995).
 293. Zorziito, M.L., Holliday, P.J., Jewett, M.A., Herschorn, S. & Fernie, G.R. Oxybutynin chloride for geriatric urinary dysfunction: a double-blind placebo-controlled study. *Age & Ageing*. 18, 195-200 (1989).
 294. Szonyi, G., Collas, D.M., Ding, Y.Y. & Malone-Lee, J.G.

- Oxybutynin with bladder retraining for detrusor instability in elderly people: a randomized controlled trial. *Age & Ageing* 24, 287-291 (1995).
295. Uchibayashi, T., Nakajima, K., Nihino, A. & Hisazumi, H. [Assessment of the use of oxybutynin hydrochloride (Pollakis tablets) in the elderly]. *Hinyokika Kyo - Acta Urologica Japonica* 37, 1077-1085 (1991).
 296. Mizunaga, M. et al. [Intravesical oxybutynin hydrochloride in the treatment of urge incontinence in the elderly]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology* 87, 923-927 (1996).
 297. Griffiths, D.J., McCracken, P.N., Harrison, G.M. & Moore, K.N. Urge incontinence in elderly people: factors predicting the severity of urine loss before and after pharmacological treatment. *Neurourology & Urodynamics* 15, 53-57 (1996).
 298. Sugiyama, T. et al. [Anticholinergic therapy of urinary incontinence and urinary frequency associated with the elderly—with special reference to dementia]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology* 84, 1068-1073 (1993).
 299. Donnellan, C., Fook, L., McDonald, P. & Playfer, J. Oxybutynin and cognitive dysfunction. *BMJ* 315, 1363-1364 (1997).
 300. Patel, H.R., Albehussi, S., Arya, M. & Miller, R.A. Can oxybutynin cause peripheral neuropathy? *Journal of Urology* 168, 646 (2002).
 301. Adubofour, K.O., Kajiwaru, G.T., Goldberg, C.M. & King-Angell, J.L. Oxybutynin-induced heatstroke in an elderly patient. *Annals of Pharmacotherapy* 30, 144-147 (1996).
 302. Hussain, R.M., Hartigan-Go, K., Thomas, S.H. & Ford, G.A. Effect of oxybutynin on the QTc interval in elderly patients with urinary incontinence. *British Journal of Clinical Pharmacology* 41, 73-75 (1996).
 303. Wang, P.S., Levin, R., Zhao, S.Z. & Avorn, J. Urinary antispasmodic use and the risks of ventricular arrhythmia and sudden death in older patients. *Journal of the American Geriatrics Society* 50, 117-124 (2002).
 304. Detrol LA package insert, Pfizer Inc, 2008.
 305. Zinner, N.R., Mattiasson, A. & Stanton, S.L. Efficacy, safety, and tolerability of extended-release once-daily tolterodine treatment for overactive bladder in older versus younger patients. *Journal of the American Geriatrics Society* 50, 799-807 (2002).
 306. Millard, R. et al. Clinical efficacy and safety of tolterodine compared to placebo in detrusor overactivity. *Journal of Urology* 161, 1551-1555 (1999).
 307. Drutz, H.P., Appell, R.A., Gleason, D., Klimberg, I. & Radomski, S. Clinical efficacy and safety of tolterodine compared to oxybutynin and placebo in patients with overactive bladder. *International Urogynecology Journal* 10, 283-289 (1999).
 308. Michel, M.C., Schneider, T., Kregge, S. & Goepel, M. Does gender or age affect the efficacy and safety of tolterodine? *Journal of Urology* 168, 1027-1031 (2002).
 309. Ouslander, J.G., Maloney, C., Grasela, T.H., Rogers, L. & Walawander, C.A. Implementation of a nursing home urinary incontinence management program with and without tolterodine. *J Am Med Dir Assoc* 2, 207-214 (2001).
 310. Tsao, J.W. & Heilman, K.M. Transient memory impairment and hallucinations associated with tolterodine use. *New England Journal of Medicine* 349, 2274-2275 (2003).
 311. Womack, K.B. & Heilman, K.M. Tolterodine and memory: dry but forgetful. *Archives of Neurology* 60, 771-773 (2003).
 312. Salvatore, S., Serati, M., Cardozo, L., Uccella, S. & Bolis, P. Cognitive dysfunction with tolterodine use. *Am J Obstet Gynecol* 197 (2007).
 313. Edwards, K.R. & O'Connor, J.T. Risk of delirium with concomitant use of tolterodine and acetylcholinesterase inhibitors. *Journal of the American Geriatrics Society* 50, 1165-1166 (2002).
 314. Layton, D., Pearce, G.L. & Shakir, S.A. Safety profile of tolterodine as used in general practice in England: results of prescription-event monitoring. *Drug Safety* 24, 703-713 (2001).
 315. Ditropan X.L prescribing information, Ortho-McNeil Pharmaceutical, Inc, 2008.
 316. Nitti, V. & et al. Efficacy, safety and tolerability of fesoterodine for overactive bladder syndrome. *J Urol* 178, 2488-2494 (2007).
 317. Krauwinkel, W., Smulders, R., Mulder, H., Swart, P. & Taekema-Roelvink, M. Effect of age on the pharmacokinetics of solifenacin in men and women. *Int J Clin Pharmacol Ther* 43, 227-238 (2005).
 318. Wagg, A., Wyndaele, J. & Sieber, P. Efficacy and tolerability of solifenacin in elderly subjects with overactive bladder syndrome: a pooled analysis. *Am J Geriatr Pharmacother* 4, 14-24 (2006).
 319. Michel, M., Wetterauer, U., Vogel, M. & De la Rosette, J. Cardiovascular safety and overall tolerability of solifenacin in routine clinical use: A 12-week, open-label, post-marketing surveillance study. *Drug Safety* 31, 505-514 (2008).
 320. Chapple, C., DuBeau, C., Ebinger, U., Reked, L. & Viegas, A. Darifenacin treatment of patients > or = 65 years with overactive bladder: results of a randomized, controlled, 12-week trial. *Curr Med Res Opin* 23, 2347-2358 (2007).
 321. Lipton, R., Kolodner, K. & Wesnes, K. Assessment of cognitive function of the elderly population: effects of darifenacin. *J Urol* 173, 493-498 (2005).
 322. Kay, G. & et al. Differential effects of the antimuscarinic agents darifenacin and oxybutynin ER on memory in older subjects. *Eur Urol* 50, 317-326 (2006).
 323. Dmochowski, R., Sand, P., Zinner, N. & Staskin, D. Trospium 60 mg once daily (QD) for overactive bladder syndrome: results from a placebo-controlled interventional study. *Urology* 71, 449-454 (2008).
 324. Madersbacher, H. & Murtz, G. Efficacy, tolerability and safety profile of propiverine in the treatment of the overactive bladder (non-neurogenic and neurogenic). *World Journal of Urology* 19, 324-335 (2001).
 325. Mori, S., Kojima, M., Sakai, Y. & Nakajima, K. [Bladder dysfunction in dementia patients showing urinary incontinence: evaluation with cystometry and treatment with propiverine hydrochloride]. *Nippon Ronen Igakkai Zasshi - Japanese Journal of Geriatrics* 36, 489-494 (1999).
 326. Otomo, E., Maruyama, S., Kobayashi, I. & al, e. Clinical evaluation of propiverine hydrochloride (P-4) on urinary disturbances due to neurological diseases. *Japan J Pharmacol* 18, 1731-1740 (1990).
 327. Dorschner, W. et al. [The elderly patient with urge incontinence or urge-stress incontinence - efficacy and cardiac safety of propiverine]. *Aktuelle Urologie* 34, 102-108 (2003).
 328. Skinner, M. & et al. Effect of age on the pharmacokinetics of duloxetine in women. *Br J Clin Pharmacol* 57, 54-61 (2004).
 329. van Kerrebroeck, P. & et al. Duloxetine versus placebo in the treatment of European and Canadian women with stress urinary incontinence. *Br J Obstet Gynaecol* 111, 249-257 (2004).
 330. Steers, W. & et al. Duloxetine compared with placebo for treating women with symptoms of overactive bladder. *BJU International* 100, 337-345 (2007).

331. Bent, A. & et al. Duloxetine compared with placebo for the treatment of women with mixed urinary incontinence. *Neurourol Urodyn* 27, 212-221 (2008).
332. Judge, T. The use of quinestrol in elderly incontinent women, a preliminary report. *Gerontol Clin* 11, 159-164 (1969).
333. Ouslander, J.G. et al. Effects of oral estrogen and progestin on the lower urinary tract among female nursing home residents. *Journal of the American Geriatrics Society* 49, 803-807 (2001).
334. Ouslander, J.G., Cooper, E. & Godley, D. Estrogen treatment for incontinence in frail older women. *Journal of the American Geriatrics Society* 47, 1383-1384 (1999).
335. Williams, A.J., Prematalake, J.K. & Palmer, R.L. A trial of emepronium bromide for the treatment of urinary incontinence in the elderly mentally ill. *Pharmatherapeutica* 2, 539-542 (1981).
336. Walter, S. et al. Urinary incontinence in old age. A controlled clinical trial of emepronium bromide. *British Journal of Urology* 54, 249-251 (1982).
337. Robinson, J.M. & Brocklehurst, J.C. Emepronium bromide and flavoxate hydrochloride in the treatment of urinary incontinence associated with detrusor instability in elderly women. *British Journal of Urology* 55, 371-376 (1983).
338. Zorzitto, M.L., Fernie, G.R., Holliday, P.J. & Bartlett, S. Effectiveness of propantheline bromide in the treatment of geriatric patients with detrusor instability. *Neurourology & Urodynamics* 5, 133-140 (1986).
339. Doig, A. Enuresis. *British Medical Journal*. 1, 1045-1046 (1956).
340. Whitehead, J.A. Urinary incontinence in the aged. Propantheline bromide as an adjunct to treatment. *Geriatrics* 22, 154-158 (1967).
341. Dequeker, J. Drug treatment of urinary incontinence in the elderly. Controlled trial with vasopressin and propantheline bromide. *Gerontol Clin* 7, 311-317 (1965).
342. Tobin, G.W. & Brocklehurst, J.C. The management of urinary incontinence in local authority residential homes for the elderly. *Age & Ageing* 15, 292-298 (1986).
343. Castleden, C.M., Duffin, H.M. & Gulati, R.S. Double-blind study of imipramine and placebo for incontinence due to bladder instability. *Age & Ageing*. 15, 299-303 (1986).
344. Briggs, R.S., Castleden, C.M. & Asher, M.J. The effect of flavoxate on uninhibited detrusor contractions and urinary incontinence in the elderly. *Journal of Urology* 123, 665-666 (1980).
345. Palmer, J. Report of a double-blind crossover study of flurbiprofen and placebo in detrusor instability. *Journal of International Medical Research* 11, 11-17 (1983).
346. Hall, M., Lee, P. & Dewar, S. Procaine haematoporphyrin and its effect on urinary incontinence in the institutionalized elderly. *J Clin Exper Gerontol* 9, 43-55 (1987).
347. Solomon, M.J., Pager, C.K., Rex, J., Roberts, R. & Manning, J. Randomized, controlled trial of biofeedback with anal manometry, transanal ultrasound, or pelvic floor retraining with digital guidance alone in the treatment of mild to moderate fecal incontinence. *Diseases of the Colon & Rectum* 46, 703-710 (2003).
348. Griebling T.: Geriatric Urology, in Solomon D.H, LoCicero L. and Rosenthal R: *New Frontiers in Geriatric Research*. New York, American Geriatrics Society, 2004, pp 269-302.
349. Miller K., Stenchever M., Richter H., Granieri E. and Andrews W. : Geriatric Gynecology, in Solomon D., LoCicero L. and Rosenthal R: *New Frontiers in Geriatrics Research: An Agenda for Surgical and Related Medical Specialities*. New York, American Geriatrics. Society, 2004, pp 225-267.
350. LoCicero J., Bierman A., Coleman A. and et al. Cross-cutting issues, in Solomon D, LoCicero L and Rosenthal R: *New Frontiers in Geriatrics Research. An Agenda for Surgical and Related Medical Specialities*. New York, American Geriatric Society, 2004, pp 369-419.
351. LoCicero J., Bierman A.S, Coleman A.L and et al. *New Frontiers in Geriatrics Research. An agenda for surgical and related medical specialties*. New York, 2004, pp 369-419.
352. Olsen, A.L., Smith, V.J., Bergstrom, J.O., Colling, J.C. & Clark, A.L. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. *Obstetrics & Gynecology* 89, 501-506 (1997).
353. Boyles, S.H., Weber, A.M. & Meyn, L. Procedures for urinary incontinence in the United States, 1979-1997. *American Journal of Obstetrics & Gynecology* 189, 70-75 (2003).
354. FitzGerald, M.P. & Brubaker, L. Colpocele and urinary incontinence. *American Journal of Obstetrics & Gynecology* 189, 1241-1244 (2003).
355. Boyles, S.H., Weber, A.M. & Meyn, L. Ambulatory procedures for urinary incontinence in the United States, 1994-1996. *American Journal of Obstetrics & Gynecology* 190, 33-36 (2004).
356. Brown, J.S. et al. Pelvic organ prolapse surgery in the United States, 1997. *American Journal of Obstetrics & Gynecology* 186, 712-716 (2002).
357. Toglia, M.R. & Nolan, T.E. Morbidity and mortality rates of elective gynecologic surgery in the elderly woman. *American Journal of Obstetrics & Gynecology* 189, 1584-1587; discussion 1587-1589 (2003).
358. Nieminen, K., Huhtala, H. & Heinonen, P.K. Anatomic and functional assessment and risk factors of recurrent prolapse after vaginal sacrospinous fixation. *Acta Obstetrica et Gynecologica Scandinavica* 82, 471-478 (2003).
359. Rosow, C. et al. Reversal of opioid-induced bladder dysfunction by intravenous naloxone and methylnaltrexone. *Clin Pharm Ther* 82, 48-53 (2007).
360. Campeau, L. et al. A multicenter, prospective, randomized clinical trial comparing tension-free vaginal tape surgery and no treatment for the management of stress urinary incontinence in elderly women. *Neurourol Urodyn* 26, 990-994 (2007).
361. Dalpiaz, O., Primus, G. & Schips, L. SPARC sling system for treatment of female stress urinary incontinence in the elderly. *Eur Urol* 50, 826-831 (2006).
362. Gousse, A.E., Madjar, S., Lambert, M.M. & Fishman, I.J. Artificial urinary sphincter for post-radical prostatectomy urinary incontinence: long-term subjective results. *Journal of Urology* 166, 1755-1758 (2001).
363. Groutz, A., Blaivas, J.G., Chaikin, D.C., Weiss, J.P. & Verhaaren, M. The pathophysiology of post-radical prostatectomy incontinence: a clinical and video urodynamic study. *Journal of Urology* 163, 1767-1770 (2000).
364. Martins, F.E. et al. Adverse prognostic features of collagen injection therapy for urinary incontinence following radical retropubic prostatectomy. *Journal of Urology* 158, 1745-1749 (1997).
365. Gormley, E.A., Griffiths, D.J., McCracken, P.N., Harrison, G.M. & McPhee, M.S. Effect of transurethral resection of the prostate on detrusor instability and urge incontinence in elderly males. *Neurourology & Urodynamics* 12, 445-453 (1993).
366. Briery, R. et al. Is transurethral resection of the prostate safe and effective in the over 80-year-old? *Ann Roy Coll Surg Egn* 83, 50-53 (2001).
367. Detsky, A.S. et al. Predicting cardiac complications in patients undergoing non-cardiac surgery. *Journal of General Internal Medicine* 1, 211-219 (1986).

368. Inouye, S.K. et al. Burden of illness score for elderly persons: risk adjustment incorporating the cumulative impact of diseases, physiologic abnormalities, and functional impairments. *Medical Care* 41, 70-83 (2003).
369. Inouye, S.K., Bogardus, S.T., Jr., Baker, D.I., Leo-Summers, L. & Cooney, L.M., Jr. The Hospital Elder Life Program: a model of care to prevent cognitive and functional decline in older hospitalized patients. *Journal of the American Geriatrics Society* 48, 1697-1706 (2000).
370. Bogardus, S.T., Jr. et al. The effects of a targeted multicomponent delirium intervention on postdischarge outcomes for hospitalized older adults. *American Journal of Medicine* 114, 383-390 (2003).
371. Inouye, S.K. et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Annals of Internal Medicine* 113, 941-948 (1990).
372. Britton, A. & Russell, R. Multidisciplinary team interventions for delirium in patients with chronic cognitive impairment. *Cochrane Database of Systematic Reviews*, CD000395 (2001).
373. Herr, K.A. & Garand, L. Assessment and measurement of pain in older adults. *Clinics in Geriatric Medicine* 17, 457-478, (2001).
374. Allen, C., Glasziou, P. & Del Mar, C. Bed rest: a potentially harmful treatment needing more careful evaluation. *Lancet* 354, 1229-1233 (1999).
375. Sager, M.A. et al. Hospital admission risk profile (HARP): identifying older patients at risk for functional decline following acute medical illness and hospitalization. *Journal of the American Geriatrics Society* 44, 251-257 (1996).
376. Counsell, S., Holder, C.M. & Laebenauer, L.L. Effects of a multicomponent intervention on functional outcomes and process of care in hospitalized older patients: a randomized controlled trial of Acute Care for Elders (ACE) in a community hospital. *JAGS* 48, 1572-1581 (2000).
377. Waale, W., Buijns, E. & Dautzenberg, P. [Delirium due to urinary retention: confusing for both the patient and the doctor] [Dutch] *Tijdschrift voor Gerontologie en Geriatrie* 32, 100-103 (2001).
378. Koch, H., Szecsey, A. & Raschka, C. Severe bradyarrhythmia in a patient with Alzheimer's disease and a patient with cerebral ischaemia, both induced by acute distension of the bladder. *Int J Clin Pract* 55, 323-325 (2001).
379. Smith, N. & Albazzaz, M. A prospective study of urinary retention and risk of death after proximal femoral fracture. *Age & Ageing* 25, 150-154 (1996).
380. Wu, J. & Baguley, I. Urinary retention in a general rehabilitation unit: prevalence, clinical outcome, and the role of screening. *Arch Phys Med Rehab* 86, 1772-1777 (2005).
381. Omli, R., Skotnes, L., Mykletun, A., Bakke, A. & Kuhry, E. Residual urine as a risk factor for lower urinary tract infection: a 1-year follow-up study in nursing homes. *J Am Geriatr Soc* 56, 871-874 (2008).
382. Armitage, J., Sibanda, N., Cathcart, P., Emberton, M. & van der Meulen, J. Mortality in men admitted to hospital with acute urinary retention: database analysis. *BMJ* 335, 1199-1202 (2007).
383. Williams, M., Wallhagen, M. & Dowling, G. Urinary retention in hospitalized elderly women. *J Gerontol Nurs* 19, 7-14 (1993).
384. Gehrich, A., Stany, M., Fischer, J., Buller, J. & Zahn, C. Establishing a mean postvoid residual volume in asymptomatic perimenopausal and postmenopausal women. *Obstetrics & Gynecology* 110, 827-832 (2007).
385. Tan, T., Lieu, P. & Ding, Y. Urinary retention in hospitalised older women. *Ann Acad Med Singapore* 30, 588-592 (2001).
386. Borrie, M. et al. Urinary retention in patients in a geriatric rehabilitation unit: prevalence, risk factors, and validity of bladder scan evaluation. *Rehabilitation Nursing* 26, 187-191 (2001).
387. Skelly, J., Guyatt, G., Kalbfleisch, R. & et al Management of urinary retention after surgical repair of hip fracture. *Can Med Assoc J* 146, 185-1189 (1992).
388. Tang, M.W.S., Kwok, T.C.Y., Hui, E. & Woo, J. Intermittent versus indwelling urinary catheterization in older female patients. *Maturitas* 53, 274-281 (2006).
389. Lukacz, E., DuHamel, E., Menefee, S. & Luber, K. Elevated postvoid residual in women with pelvic floor disorders: prevalence and associated risk factors. *Int Urogynecol J* 18, 397-400 (2007).
390. Cathcart, P., van der Meulen, J., Armitage, J. & Emberton, M. Incidence of primary and recurrent acute urinary retention between 1998 and 2003 in England. *J Urol* 176, 00-04 (2006).
391. Meigs, J. et al. Incidence rates and risk factors for acute urinary retention: the health professionals followup study. *J Urol*, 376-382 (1999).
392. Bennett, C. & Diokno, A. Clean intermittent self-catheterization in the elderly. *Urology* 24, 43-45 (1984).
393. van Kerrebroeck, P. et al. The standardisation of terminology in nocturia: report from the Standardisation Sub-committee of the International Continence Society. *Neurourology & Urodynamics* 21, 179-183 (2002).
394. Chen, F. et al. Perception of nocturia and medical consulting behavior among community-dwelling women. *Int Urogynecol J* 18, 431-436 (2007).
395. Ouslander, J. & Johnson, T. Nocturia in the elderly. *J Geront* 65, 375-379 (1998).
396. Weiss, J.P. & Blaivas, J.G. Nocturia. *Journal of Urology* 163, 5-12 (2000).
397. Abrams, P. & Wein, A. Nocturia. *BJU International Supplement* 3, 1-37 (2002).
398. Hale, W.E., Perkins, L.L., May, F.E., Marks, R.G. & Stewart, R.B. Symptom prevalence in the elderly. An evaluation of age, sex, disease, and medication use. *Journal of the American Geriatrics Society* 34, 333-340 (1986).
399. Malmsten, U.G., Milsom, I., Molander, U. & Norlen, L.J. Urinary incontinence and lower urinary tract symptoms: an epidemiological study of men aged 45 to 99 years. *Journal of Urology* 158, 1733-1737 (1997).
400. Pinnock, C. & Marshall, V.R. Troublesome lower urinary tract symptoms in the community: a prevalence study.[see comment]. *Medical Journal of Australia* 167, 72-75 (1997).
401. Perry, S. et al. An epidemiological study to establish the prevalence of urinary symptoms and felt need in the community: the Leicestershire MRC Incontinence Study. *Journal of Public Health Medicine* 22, 427-434 (2000).
402. Schatzl, G. et al. Cross-sectional study of nocturia in both sexes: analysis of a voluntary health screening project. *Urology* 56, 71-75 (2000).
403. Tikkinen, K., Tammela, T., Huhtala, H. & Auvinen, A. Is nocturia equally common among men and women? A population based study in Finland. *J Urol* 175, 2006 (2006).
404. Fitzgerald, M., Litman, H., Link, C. & McKinlay, J. The association of nocturia with cardiac disease, diabetes, body mass index, age and diuretic use: results from the BACH survey. *J Urol* 177, 1385 (2007).
405. Johnson TM 2nd, Sattin, R., Parmelee, P., Fultz, N. & Ouslander, J. Evaluating potentially modifiable risk factors for prevalent and incident nocturia in older adults. *J Am Geriatr Soc* 53, 1011-1016 (2005).

406. Hillier, P., Knapp, M. & Cove-Smith, R. Circadian variations in urine excretion in chronic renal failure. *Q J Med* 49, 461 (1980).
407. Rembratt, A., Norgaard, J.P. & Andersson, K.E. Nocturia and associated morbidity in a community-dwelling elderly population. *BJU International* 92, 726-730 (2003).
408. Asplund, R. Nocturia in relation to sleep, somatic diseases and medical treatment in the elderly. *BJU International* 90, 533-536 (2002).
409. Stewart, R.B., Moore, M.T., May, F.E., Marks, R.G. & Hale, W.E. Nocturia: a risk factor for falls in the elderly. *Journal of the American Geriatrics Society* 40, 1217-1220 (1992).
410. Coyne, K.S. et al. The prevalence of nocturia and its effect on health-related quality of life and sleep in a community sample in the USA. *BJU International* 92, 948-954 (2003).
411. Newman, A.B. et al. Daytime sleepiness predicts mortality and cardiovascular disease in older adults. The Cardiovascular Health Study Research Group. *Journal of the American Geriatrics Society* 48, 115-123 (2000).
412. Mock, L., Parmelee, P., Kutner, N., Scott, J. & Johnson TM 2nd. Content validation of a symptom-specific Nocturia Quality of Life instrument developed in men: Issues expressed by women as well as men. *Urology in press* (2009).
413. Kirkland, J.L., Lye, M., Levy, D.W. & Banerjee, A.K. Patterns of urine flow and electrolyte excretion in healthy elderly people. *British Medical Journal Clinical Research Ed* 287, 1665-1667 (1983).
414. Blanker, M.H. et al. Normal values and determinants of circadian urine production in older men: a population based study. *Journal of Urology* 168, 1453-1457 (2002).
415. Miller, M. Nocturnal polyuria in older people: pathophysiology and clinical implications. *Journal of the American Geriatrics Society*. 48, 1321-1329 (2000).
416. Rembratt, A., Norgaard, J.P. & Andersson, K.E. Differences between nocturics and non-nocturics in voiding patterns: an analysis of frequency-volume charts from community-dwelling elderly. *BJU International* 91, 45-50 (2003).
417. Ouslander, J., Schnelle, J., Simmons, S., Bates-Jensen, B. & Zeitlin, M. The dark side of incontinence in nursing home residents. *JAGS* 41, 1083-1089 (1993).
418. Weiss, J., Blaivas, J., Jones, M. & et al Age related pathogenesis of nocturia in patients with overactive bladder. *J Urol* 178, 548 (2007).
419. Asplund, R. & Aberg, H. Diurnal rhythm of antidiuretic hormone in elderly subjects with nocturia. *Med Sci Res* 19, 765-766 (1991).
420. Ouslander, J.G. et al. Arginine vasopressin levels in nursing home residents with nighttime urinary incontinence. *Journal of the American Geriatrics Society* 46, 1274-1279 (1998).
421. Johnson, T.M., 2nd et al. Changes in nocturia from medical treatment of benign prostatic hyperplasia: secondary analysis of the Department of Veterans Affairs Cooperative Study Trial. *Journal of Urology* 170, 145-148 (2003).
422. Umlauf, M.G. et al. Obstructive sleep apnea, nocturia and polyuria in older adults. *Sleep* 27, 139-144 (2004).
423. Ouslander, J., Johnson, T., Nasr, S., Schnelle, J. & Miller, M. Atrial natriuretic peptide levels in geriatric patients with nocturia and nursing home residents with nighttime incontinence. *Journal of the American Geriatrics Society* 47, 1439-1444 (1999).
424. Bliwise, D.L., Adelman, C.L. & Ouslander, J.G. Polysomnographic correlates of spontaneous nocturnal wetness episodes in incontinent geriatric patients. *Sleep* 27, 153-157 (2004).
425. Pressman, M.R., Figueroa, W.G., Kendrick-Mohamed, J., Greenspon, L.W. & Peterson, D.D. Nocturia. A rarely recognized symptom of sleep apnea and other occult sleep disorders. *Archives of Internal Medicine* 156, 545-550 (1996).
426. Dahlstrand, C., Hedner, J., Wang, Y.H. & Pettersson, S. Snoring—a common cause of voiding disturbance in elderly men. *Lancet* 347, 270-271 (1996).
427. Abrams, P. & Klevmark, B. Frequency volume charts: an indispensable part of lower urinary tract assessment. *Scand J Urol Nephrol Suppl* 179, 47 (1996).
428. Abraham L., Hareendran A., Mills I. and et al.: Development and validation of a quality-of-life measure for men with nocturia. *Urology*. 63: 481-486, 2004.
429. Pedersen, P.A. & Johansen, P.B. Prophylactic treatment of adult nocturia with bumetanide. *British Journal of Urology* 62, 145-147 (1988).
430. Reynard, J.M., Cannon, A., Yang, Q. & Abrams, P. A novel therapy for nocturnal polyuria: a double-blind randomized trial of frusemide against placebo. *British Journal of Urology* 81, 215-218 (1998).
431. Fitzgerald, M., Mulligan, M. & Parthasarathy, S. Nocturic frequency is related to severity of obstructive sleep apnea, improves with continuous positive airways treatment. *Am J Obstet Gynecol* 194, 1399-1403 (2006).
432. Johnson TM 2nd, Burgio, K., Redden, D., Wright, K. & Goode, P. Effects of behavioral and drug therapy on nocturia in older incontinent women. *J Am Geriatr Soc* 53, 846-850 (2005).
433. Kaplan, S.A. & D'Alisera, P.M. Tolerability of alpha-blockade with doxazosin as a therapeutic option for symptomatic benign prostatic hyperplasia in the elderly patient: a pooled analysis of seven double-blind, placebo-controlled studies. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences*. 53, M201-206 (1998).
434. Rackley, R., Weiss, J., Rovner, E., Wang, J. & Guan, Z. Nighttime dosing with tolterodine reduces overactive bladder-related nocturnal micturitions in patients with overactive bladder and nocturia. *Urology* 67, 731-736 (2006).
435. Johnson TM 2nd, Burrows, P., Kusek, J. & et al Medical Therapy of Prostatic Symptoms Research Group. The effect of doxazosin, finasteride and combination therapy on nocturia in men with benign prostatic hyperplasia. *J Urol* 178, 2045-2050 (2007).
436. Kok, A.L. et al. Micturition complaints in postmenopausal women treated with continuously combined hormone replacement therapy: a prospective study. *Maturitas* 31, 143-149 (1999).
437. Fantl, J.A., Bump, R.C., Robinson, D., McClish, D.K. & Wyman, J.F. Efficacy of estrogen supplementation in the treatment of urinary incontinence. The Continence Program for Women Research Group. *Obstetrics & Gynecology*. 88, 745-749 (1996).
438. Drake, M., Mills, I. & Noble, J. Melatonin pharmacotherapy for nocturia in men with benign prostatic enlargement. *Urology* 171, 1199-1202 (2004).
439. Seiler, W.O., Stahelin, H.B. & Hefti, U. Desmopressin reduces night urine volume in geriatric patients: implication for treatment of the nocturnal incontinence. *Clinical Investigator* 70, 619 (1992).
440. Asplund, R. & Aberg, H. Desmopressin in elderly subjects with increased nocturnal diuresis. A two-month treatment study. *Scandinavian Journal of Urology & Nephrology* 27, 77-82 (1993).
441. Asplund, R. & Aberg, H. Desmopressin in elderly women with increased nocturnal diuresis. A short-term study. *British Journal of Urology* 72, 42-45 (1993).
442. Obara, K., Takahashi, H., Takeda, M. & Sato, S. [The effect of desmopressin (DDAVP) in patients complaining of nocturia]. *Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology* 84, 2131-2136 (1993).

443. Asplund, R., Sunberg, B. & Bengtsson, P. Desmopressin for the treatment of nocturnal polyuria in the elderly: a dose titration study. *British Journal of Urology* 72, 38-41 (1993).
444. Asplund, R., Sundberg, B. & Bengtsson, P. Desmopressin for the treatment of nocturnal polyuria in the elderly: a dose titration study. *British Journal of Urology* 82, 642-646 (1998).
445. Asplund, R., Sundberg, B. & Bengtsson, P. Oral desmopressin for nocturnal polyuria in elderly subjects: a double-blind, placebo-controlled randomized exploratory study. *BJU International* 83, 591-595 (1999).
446. Cannon, A., Carter, P.G., McConnell, A.A. & Abrams, P. Desmopressin in the treatment of nocturnal polyuria in the male. *BJU International* 84, 20-24 (1999).
447. Chancellor, M.B. et al. Beneficial effect of intranasal desmopressin for men with benign prostatic hyperplasia and nocturia: preliminary results. *Techniques in Urology* 5, 191-194 (1999).
448. Kuo, H.C. Efficacy of desmopressin in treatment of refractory nocturia in patients older than 65 years. *Urology* 59, 485-489 (2002).
449. Mattiasson, A., Abrams, P., Van Kerrebroeck, P., Walter, S. & Weiss, J. Efficacy of desmopressin in the treatment of nocturia: a double-blind placebo-controlled study in men. *BJU International* 89, 855-862 (2002).
450. Lose, G., Lalos, O., Freeman, R.M., van Kerrebroeck, P. & Nocturia Study, G. Efficacy of desmopressin (Minirin) in the treatment of nocturia: a double-blind placebo-controlled study in women. *American Journal of Obstetrics & Gynecology* 189, 1106-1113 (2003).
451. Rembratt, A., Norgaard, J.P. & Andersson, K.E. Desmopressin in elderly patients with nocturia: short-term safety and effects on urine output, sleep and voiding patterns. *BJU International* 91, 642-646 (2003).
452. Johnson TM 2nd, Miller, M., Tang, T., Pillion, D. & Ouslander, J. Oral ddAVP for nighttime urinary incontinence in characterized nursing home residents: a pilot study. *J Am Med Dir Assoc* 7, 6-11 (2006).
453. Wetherall, M. & Arnold, T. Nocturia in adults: draft New Zealand guidelines for its assessment and management in primary care. *NZ Med J* 119 (2006).
454. Rembratt, A., Riis, A. & Norgaard, J. Desmopressin treatment in nocturia; an analysis of risk factors for hyponatremia. *Neurourol Urodyn* 25, 105-109 (2006).
455. Rembratt, A., Graugaard-Jensen, C., Senderovitz, T. & et al. Pharmacokinetics and pharmacodynamics of desmopressin administered orally versus intravenously at daytime versus night-time in healthy men aged 55-70 years. *Eur J Clin Pharmacol*, 397 (2004).
456. McDowell, B.J. et al. Effectiveness of behavioral therapy to treat incontinence in homebound older adults. *Journal of the American Geriatrics Society* 47, 309-318 (1999).
457. Borrie, M.J., Bawden, M., Speechley, M. & Kloseck, M. Interventions led by nurse continence advisers in the management of urinary incontinence: a randomized controlled trial. *CMAJ Canadian Medical Association Journal* 166, 1267-1273 (2002).
458. Fonda, D., Ouslander, J.G. & Norton, C. Continence across the continents. *Journal of the American Geriatrics Society* 42, 109-112 (1994).
459. Crooks, V.C., Schnelle, J.F., Ouslander, J.P. & McNees, M.P. Use of the Minimum Data Set to rate incontinence severity. *Journal of the American Geriatrics Society* 43, 1363-1369 (1995).
460. Resnick, N., Brandeis, G., Baumann, M. & Morris, J. Evaluating a national assessment strategy for urinary incontinence in nursing home residents: reliability of the minimum data set and validity of the resident assessment protocol. *Neurourology & Urodynamics* 15, 583-598 (1996).
461. Vaizey, C.J., Carapeti, E., Cahill, J.A. & Kamm, M.A. Prospective comparison of faecal incontinence grading systems. *Gut* 44, 77-80 (1999).
462. American Medical Directors Association: Urinary Incontinence Clinical Practice Guidelines. Columbia, Maryland, 1996.
463. Palmer, M.H., Umphlet, H.W., Umphlet, T.L. & Johnson, T.M., 2nd. Quality of incontinence management in U.S. nursing homes: a failing grade. *Journal of the American Geriatrics Society* 51, 1810-1812 (2003).
464. Ouslander, J.G. & Johnson, T.M., 2nd. Continence care for frail older adults: it is time to go beyond assessing quality. *Journal of the American Medical Directors Association* 5, 213-216 (2004).
465. Schnelle, J.F., Ouslander, J.G., Osterweil, D. & Blumenthal, S. Total quality management: administrative and clinical applications in nursing homes. *Journal of the American Geriatrics Society* 41, 1259-1266 (1993).
466. Bryant, C.M., Dowell, C.J. & Fairbrother, G. Caffeine reduction education to improve urinary symptoms. *British Journal of Nursing* 11, 560-565 (2002).
467. Nikolett, S., Young, J. & King, M. Evaluation of an electronic monitoring device for urinary incontinence in elderly patients in an acute care setting. *J Wound Ostomy Continence Nurs* 31, 138-149 (2004).
468. Tobin, G.W. & Brocklehurst, J.C. Faecal incontinence in residential homes for the elderly: prevalence, aetiology and management. *Age & Ageing* 15, 41-46 (1986).
469. Lose, G. et al. Clinical experiences with desmopressin for long-term treatment of nocturia. *J Urol* 172, 1021-1025 (2004).
470. Ho, D. et al. Clinical observations of the effect of antidiuretic hormone on nocturia in elderly men. *BJU International* 96, 1310-1313 (2005).
471. van Kerrebroeck, P. et al. Desmopressin in the treatment of nocturia: a double-blind, placebo-controlled study. *Eur Urol* 52, 221-229 (2007).
472. Johnson, T. et al. The relationship between the action of arginine vasopressin and responsiveness to oral desmopressin in older men: a pilot study. *J Am Geriatr Soc* 55, 562-569 (2007).