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Urinary Incontinence: Economic Burden and New Choices in Pharmaceutical Treatment

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ABSTRACT

In the year 2000, an estimated 17 million community-dwelling adults in the United States had daily urinary incontinence (UI), and an additional 33 million suffered from the overlapping condition, overactive bladder. Estimates of the total annual cost of these conditions range up to $32 billion; the largest components are management costs and the expenses associated with nursing home admissions attributable to UI. In most cases, patients with UI can be treated with pharmaceutical agents, in addition to behavioral therapy. Until recently, pharmaceutical therapy for UI has been limited, especially because the adverse effects of available agents resulted in poor adherence to treatment regimens. Recent innovations in molecular design and new dosage forms of UI medications offer the promise of fewer and less severe adverse effects and, thus, better treatment outcomes for patients. Additionally, the availability of multiple agents within a therapeutic class offers health care providers a spectrum of choices with which to personalize treatment for each individual patient. New pharmacologic treatment options for UI have the potential to allow greater independence for older persons who reside at home and to delay or avoid the costs of admission to long-term care facilities. Alternate dosage forms, which include patches and sustained-release formulations, may benefit patients who have difficulty chewing, swallowing, or remembering to take medications. Although these newer products are generally more expensive than older forms of therapy, they typically have more favorable cost-effectiveness ratios. Access to these new medications for patients enrolled in public and private health care plans may help to reduce the economic and social burden of UI care.

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INTRODUCTION

Urinary incontinence (UI), which is defined as the involuntary leakage of urine,[1] is a stigmatized, underreported, underdiagnosed, and undertreated condition that is often erroneously believed to be a normal part of aging. It is a significant cause of decline in overall health status among older persons and a primary cause of institutionalization because of the burden placed on caregivers.[2]

Several different types of UI have been described—the most common classifications are urge, stress, and mixed incontinence (see Table 1 for definitions). Symptoms of urge incontinence may overlap with those of overactive bladder (OAB), and these 2 conditions lie on a continuum, so that about one third of those with OAB also have urge incontinence.[3,4] OAB affected 33 million community-dwelling adults in the United States in the year 2000, and an estimated 17 million had daily UI.[5] OAB and UI occur about twice as frequently in women as in men and become more prevalent in both sexes with advancing age (Fig 1).[6] Prevalence rates of the various types of UI vary with age, with stress incontinence predominating in younger women and mixed incontinence in older women (Fig 2).[7] Prevalence rates of OAB and UI are comparable with those of other major chronic illnesses in US women (Fig 3).[8]

As men age, they become increasingly vulnerable to OAB and benign prostatic hyperplasia (BPH), or enlarged prostate. The irritative symptoms of BPH—frequency, urgency, and nocturia—are the same as those reported by individuals with OAB. Starting at age 60, men who report these symptoms begin to outnumber women who do so, with about 42% of men over the age of 74 reporting symptoms of OAB compared with only about 32% of women in the same age group.[9] In addition to these symptoms of OAB, men with BPH typically report obstructive symptoms, including slow stream of urination, the sensation of incomplete emptying, and dribbling. Both irritative and obstructive symptoms are more likely to be experienced by men who have been given a clinical diagnosis of BPH than by those in whom BPH has not been diagnosed.[10] Although severe BPH causes urine retention and strain on the bladder, more serious problems may develop over time, such as urinary tract infections, bladder or kidney damage, bladder stones, and overflow incontinence. Overflow incontinence is relatively rare in the general population, but it adds to the complications of medication management in this population because the symptoms of OAB and BPH may overlap.

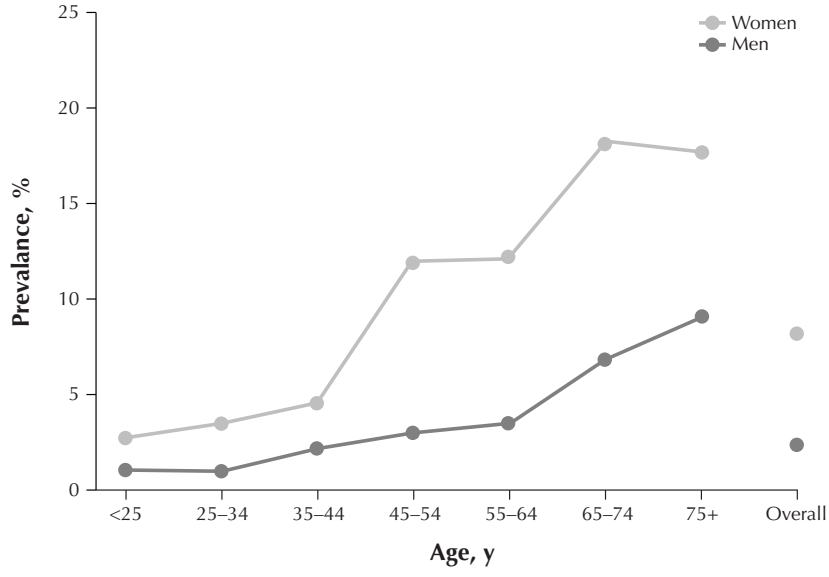
The total number of people with UI may be far greater than current estimates because fewer than half of individuals with UI who are living in the community consult health care providers about their problem.[11] This may be due to embarrassment, low expectations of benefit, a lack of understanding of UI, an assumption that leakage is normal with age, or a lack of information regarding management options.[12]

In addition, when help is sought, many clinicians are not familiar with the latest information on appropriate evaluation and treatment of patients with UI. Substantial variations in the adequacy of examination, assessment, and management of UI have been reported. In one study, less than one third of women with newly identified UI were actively treated by general practitioners.[13] UI is often undetected and underreported by hospital and nursing home personnel.[14]

Table 1. Classification of Types of Urinary Incontinence

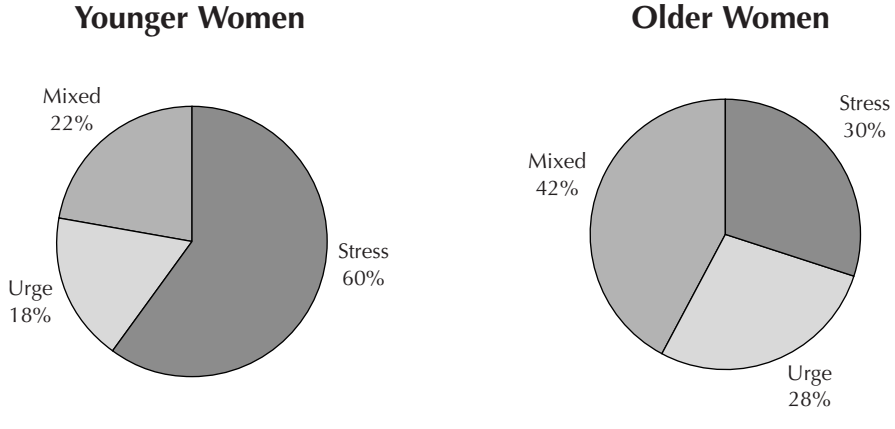
Type of UI	Symptoms	Causes
Overactive bladder syndrome	Urgency usually associated with increased daytime frequency (needing to urinate more than 8 times during waking hours in a 24-h period) and nocturia (having to wake up more than once a night to urinate), with or without leakage. A subset of patients with overactive bladder may complain of urge incontinence.[4]	A malfunctioning detrusor muscle. Underlying causes include nerve damage due to abdominal or pelvic trauma or surgery, benign prostatic hyperplasia, bladder stones, drug side effects, neurologic disease (eg, multiple sclerosis, Parkinson's disease, stroke, spinal cord lesions).
Urge incontinence	Leakage associated with an abrupt, strong desire to void that is difficult to defer	Usually idiopathic. May also be caused by stroke and other neurologic disorder or by bladder irritants
Stress incontinence	Leakage associated with coughing, laughing, sneezing, or other physical activity that increases abdominal pressure	Leakage is due to inadequate support of the urethra, severe urethral wall weakness, or rigidity. Also caused by sphincter dysfunction from nerve/muscle damage
Mixed incontinence	Symptoms of both urge and stress incontinence	
Other incontinence	Situational incontinence (eg, the report of incontinence during sexual intercourse). Incontinence associated with chronic retention of urine (formerly known as overflow incontinence[1])	

Fig 1. Age- and sex-specific prevalence of OAB with urge incontinence.



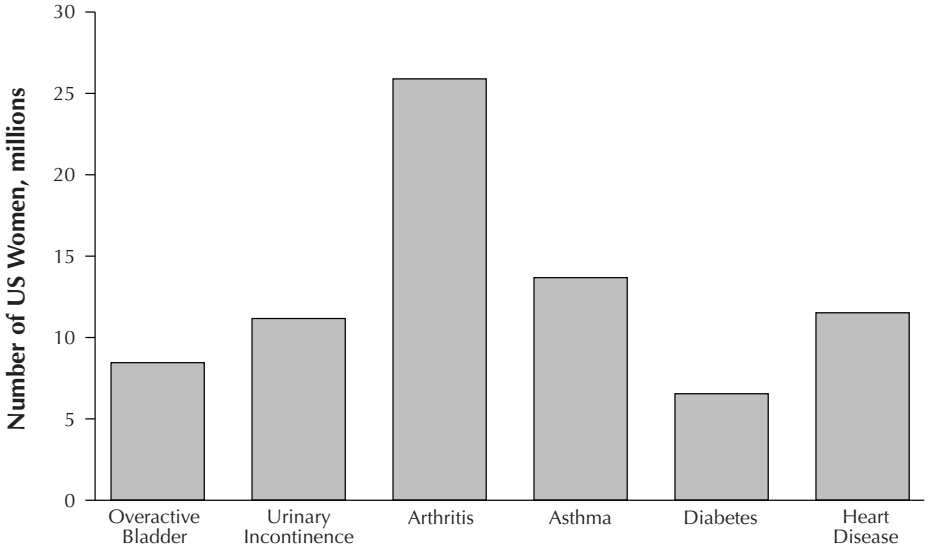
Adapted from Stewart et al (2003).[6]

Fig 2. Relative proportions of stress, urge, and mixed urinary incontinence in women.*



*Proportions of the types of incontinent episodes that occurred over the past 1 to 12 mo for younger (ages 17–44 y) and older (ages 60 y and older) women. Percentages are averages from 3 studies for older women and 2 studies for younger women. Adapted from Thom (1998).[7]

Fig 3. Estimated numbers of women with OAB, UI, and other chronic illnesses in the United States in 2002.*



*Prevalence of OAB (without concomitant urge UI) is from Stewart et al (2003),[6] and prevalence of significant or regular UI in women is based on estimates from Minassian et al (2003).[8] These prevalence rates were applied to the 2002 national female population. Prevalence rates for other chronic diseases were obtained from the National Health Interview Survey, 2002, National Center for Health Statistics, CDC.

The social costs of UI are high because people with this condition may limit their social interactions and may be burdened with psychological problems. Focus groups of older persons with urge incontinence revealed that many spend significant time and psychic energy worrying about incontinent episodes, toilet mapping, and coping with leakage.[15] Even mild symptoms affect social, sexual, interpersonal, and professional function.[16] Loss of self-esteem may result, and dependence on caregivers for activities of daily life increases as incontinence worsens. Consequently, leaving the home, having social interaction with friends and family, and engaging in sexual activity may be restricted or avoided entirely.[17,18]

Behavioral therapy is considered first-line treatment. Pharmacotherapy may be considered, in addition to behavioral therapy.[19] Although no medicine is specifically indicated for stress incontinence in the United States, multiple medications are now available for urge incontinence and OAB, some of which have only recently come onto the market. All of these drugs act by blocking binding of the neurotransmitter acetylcholine to muscarinic receptors in the bladder, but they have different spectra of properties. Selection of the best drug for a patient from among these agents is based on several factors, including the potential for drug interactions and adverse effects, the need for dosing flexibility, costs, and the patient's perception of a drug's effectiveness and tolerability.[20] Optimal therapy with these agents may reduce the economic and social burden of caring for millions of Americans with UI, especially older persons.

COSTS OF UI

Estimates of the costs of managing UI vary widely, depending on the definition of UI and study methods used, but they have been placed as high as $26.3 billion ($3565 per individual with UI, in 1995 dollars).[21] A more recent analysis gives the total (ie, direct and indirect) annual cost of UI as $19.5 billion and that of OAB as $12.6 billion.[5] Most of the total cost involves direct treatment costs (eg, costs of diagnostic tests, inpatient and outpatient care, laundry, labor, medication, behavioral therapy); indirect costs (defined as lost earnings for paid or unpaid caregivers) account for only about 4% of the total cost of UI.[5] Included in the direct costs are those related to the consequences of incontinence because UI and OAB contribute to or are a direct cause of several secondary diagnoses, including skin rashes, urinary tract infections, falls and fractures, and depression.[22] (These cost-of-illness analyses do not include the intangible costs of a reduced quality of life. Patients with OAB are 2 to 3 times more likely than those without OAB to experience frequently disturbed sleep, difficulty concentrating, tiredness, a tendency to overeat, and a lack of self-esteem, according to a 2003 nationwide survey carried out under the auspices of the National Association For Continence.[23])

Cost of UI in Persons Living at Home

The direct cost of UI in community-dwelling persons is about two thirds of the total direct cost of UI (Fig 4).[24] The high cost of UI among persons living at home reflects its prevalence in this setting—as high as 15% to 35% among persons older than 60 years of age who live in the community; 53% of homebound older persons are incontinent, and UI is one of the 10 leading diagnoses among homebound persons.[25]

Contribution of UI to Nursing Home Admissions and Cost

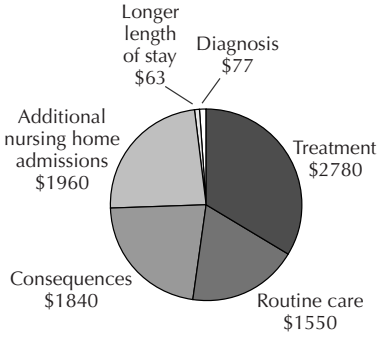
Because of the burden it places on the volunteer caregiver, incontinence increases the risk of institutionalization of aging adults.[26,27] Women with incontinence are twice as likely to be admitted to a nursing home as are women without incontinence; men with incontinence are more than 3 times as likely to be admitted compared with men without incontinence.[2] These findings may reflect a relatively greater difficulty on the part of frail female caregivers to manage incontinent men, although additional research is needed to confirm this.

The proportion of nursing home admissions that is directly attributable to UI has been difficult to estimate because common comorbidities in persons with UI, such as dementia and cardiovascular disease, are themselves reasons for admission. The fraction of nursing home admissions due to UI can be calculated from the relative risk of admission due to UI and adjusted in a multivariate analysis for the presence of comorbidities and demographic factors that may influence nursing home admission independently of UI.[28] On the basis of adjusted relative risks published by Thom et al,[2] it has been calculated that 6% of nursing home admissions among older women and 10% among older men are attributable solely to UI.[28] The cost of these nursing home admissions represents the incremental cost of illness, as defined by Birnbaum et al,[29] for UI admissions (ie, the cost attributable solely to UI). This cost is estimated to be an annualized $6 billion ($3 billion each for elderly men and women in year 2000 dollars).[28] Although the definition of UI ("medically recognized UI"[2]) and the methods by which calculations are derived differ from those supporting the values for OAB and

UI combined in Figure 4 ($1960 + $3950), the total cost is about the same (ie, $6 billion) in both analyses. This cost of nursing home admission represents about 20% of the total direct cost of UI and OAB and the second-largest direct cost expense (after routine care).

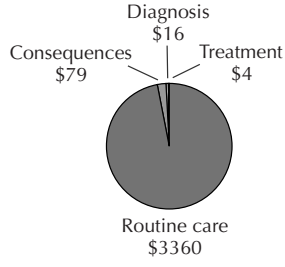
Fig 4. Direct costs of OAB and UI in US$ (millions).*

A. OAB in Community-Dwelling Adults



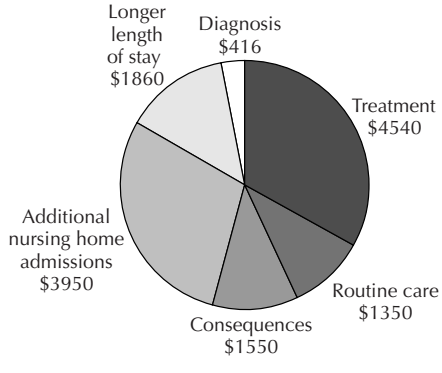
Total $8270

B. OAB in Institutionalized Elderly



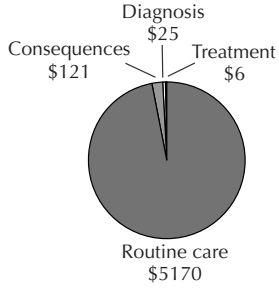
Total $3460

C. UI in Community-Dwelling Adults



Total $13,700

D. UI in Institutionalized Elderly



Total $5330

*Treatment costs of pharmaceuticals, surgical treatments, behavioral therapy, and related procedures. Routine care= costs of routine care products (eg, absorbent pads, laundry). Consequences=costs of health-related consequences of OAB or UI (eg, falls, skin conditions, urinary tract infections). Additional nursing home admissions=costs of admissions due to UI or OAB. Longer length of stay=longer hospitalization periods due to UI. Costs of each category may not add up to total direct costs because of rounding. Because of data limitations, OAB without UI was not distinguished from OAB with UI.

Adapted from Hu et al (2004).[5]

Cost of Care for Nursing Home Residents With UI

A total of 65% of nursing home residents over the age of 65 have incontinence (defined in this instance as difficulty controlling bowels and/or bladder, or the presence of an ostomy or an indwelling catheter),[30] and, every 12 wk, approximately 2 out of 100 nursing home residents develop new UI.[31] Care of residents with UI is costly because it requires additional staff time and training. The impact on staff training requirements alone of Federal Tag 315, issued in 2005 by the Centers for Medicare and Medicaid with the goal of improving the recognition, assessment, treatment, and prevention of UI in nursing homes, has yet to be determined.[32] Consequences of UI, including skin irritation, falls, immobility, and pressure ulcers, may result in hospitalization or other added costs.[25] The direct cost of caring for those with UI in a nursing facility—the costs of routine UI care, treatments, complications, diagnoses, and evaluations—is estimated at $5.3 billion (Fig 4).

Costs of UI for Medicare and Medicaid

Almost half of the costs associated with UI are incurred for medical services paid by Medicare.[33] Medicare covers the costs of diagnosis and evaluation of incontinence, as well as the costs of incontinence supplies for institutionalized persons and those who receive home health services. UI increases the public costs of home care services by about 25%.[34]

The costs of longer nursing home stays are borne predominantly (48%) by state Medicaid programs.[30] Economic models indicate that the overall cost of UI is much higher if the patient enters a nursing home.[5] Considerable savings may result if admission to nursing facilities is delayed or avoided. Appropriate treatment of those with UI who remain in the community may also decrease the cost burden to society.[2,34]

Urinary frequency, nocturia, and rushing to the bathroom to avoid urge incontinence episodes most likely increase the risks of falls and fractures. In a study of more than 6000 community-dwelling women with a mean age of 78.5 y, 8.5% reported fractures over a 3-y period. Weekly or more frequent urge incontinence was associated independently with an increased risk of falls and nonspine, nontraumatic fractures.[35] An increased likelihood of falls related to UI may be costly for Medicare and managed care organizations that accept Medicare recipients. Additional research is required, however, to substantiate the cause-and-effect relationship between incontinence and fractures.

IMPROVED TREATMENT CAN REDUCE THE COST BURDEN OF UI

Demonstrations in Medicaid programs have shown that therapies associated with improved treatment can reduce the cost burden of UI by decreasing the incidence of complications and lowering the need for absorbent pads. More than 30% of California Medicaid (Medi-Cal) women with OAB—a diagnosis that in this case included urge and mixed UI—also had urinary tract infection (22.5%) or skin infection (8%).[22,36] After OAB was diagnosed and patients were treated, the number of services received for urinary tract and skin infections decreased by 40% and 60%, respectively; this was associated with an estimated potential savings to Medi-Cal of $3.3 million.[22,36]

Improved treatment adherence can also reduce the cost burden due to urinary tract infections. In a recent study of the Medi-Cal population, discontinuation of pharmacotherapy for OAB/UI was associated with a subsequent 37% increase in the risk of urinary tract infection.[37] A study of the Illinois Medicaid program showed that adherence to therapy for OAB—again, the diagnosis included urge UI—was linked to cost savings associated with reduced medications and services for urinary tract infections. Total payments per patient were lower for those patients who remained in therapy for 2 y.[22]

Advancements in Medications for OAB/Urge Incontinence

Oxybutynin became the mainstay of drug therapy for OAB/urge incontinence after its introduction to the US market in 1975. It is used to manage symptoms of urinary frequency, urgency, and leakage, as well as nighttime urination associated with OAB. A pooled analysis of 6 placebo-controlled trials indicates that treatment with oxybutynin results in 5 fewer incontinence episodes per week.[38] It is also associated, however, with adverse effects such as dry mouth, dry eyes, blurred vision, constipation, esophageal reflux, drowsiness, dizziness, palpitations, and heat intolerance.[39] Successful management of UI may depend on long-term adherence to drug therapy, and poor tolerability of the adverse effects of oxybutynin has limited patients' ability to continue taking the medication.

Tolterodine was introduced in 1998, followed by extended-release (ER) formulations of both oxybutynin and tolterodine (Table 2).[38,40] Direct comparisons show that the tolterodine immediate-release (IR) formulation is similar to oxybutynin IR in reducing episodes of incontinence, but tolterodine IR is associated with a lower risk of dry mouth or discontinuation of treatment due to adverse effects (Table 2). A comparative trial of oxybutynin ER and tolterodine ER showed that both drugs reduced the number of incontinent episodes similarly, with the approximate number of incontinent episodes per week decreasing from 43 at baseline to 13 at study endpoint.[41] The ER formulation of tolterodine has similar efficacy to its IR counterpart, and the risk of dry mouth was shown in some trials to be lower for the ER formulation.[38]

A transdermal system (TDS) of delivering oxybutynin is also available. In a small trial that compared titrated doses, oxybutynin TDS formulations caused fewer adverse effects such as constipation and dry mouth than were produced by the IR version, while maintaining similar efficacy.[38] The long duration of action of oxybutynin TDS (up to 4 d) reduces the oral medication burden, which may provide a particular advantage for patients who take multiple oral medications or who depend on volunteer caregivers.[42]

Several studies based on pharmacy claims databases have demonstrated improved adherence to therapy with tolterodine and the ER dosage form of oxybutynin. One study found the average duration of continuous therapy with tolterodine to be 143 d, compared with 91 d with oxybutynin IR.[43] A second study found that the proportion of patients who continued therapy for 6 mo was greater for tolterodine (32%) than for oxybutynin IR (22%).[44] Medication possession ratios (the fraction of a given period for which patients have a prescription filled) were also better for patients in the tolterodine group than for those in the oxybutynin IR group (medians, 0.83 and 0.64, respectively). Patients who took oxybutynin discontinued therapy earlier (mean, 45 days) than did those who were taking tolterodine (mean, 59 days), and they were more often switched to another therapy (19% and 14%, respectively).[37]

Table 2. Comparative Efficacy and Tolerability of Agents for the Treatment of Patients With Urge Incontinence*

Agent	Year Introduced	Incontinence Episodes/24 h	Risk of Dry Mouth	Risk of Constipation	Risk of Discontinuation Due to Adverse Events
Oxybutynin	1975	Similar to tolterodine IR	Greater than with tolterodine IR, tolterodine ER, and trospium	Similar to tolterodine IR, tolterodine ER, and trospium	Greater than with tolterodine IR or tolterodine ER
Oxybutynin ER (Ditropan XL®)	1999	Similar to tolterodine ER[41]	Greater than with tolterodine ER[41] Similar to tolterodine IR	Similar to tolterodine IR and tolterodine ER[41]	Similar to tolterodine IR and tolterodine ER[39]
Oxybutynin TDS (Oxytrol®)	2003	Similar to tolterodine ER	Similar to tolterodine ER	Similar to tolterodine ER	Greater than with tolterodine ER
Tolterodine IR (Detrol®)	1998	Similar to oxybutynin IR and tolterodine ER	Less than with oxybutynin IR Tol IR 4 vs Oxy IR 10: RR=0.59 (0.50, 0.71)	Less than with solifenacin Tol IR 4 vs Sol 10: RR=0.34 (0.156, 0.77)	Less than with oxybutynin IR Tol IR 4 vs Oxy IR 15: RR=0.40 (0.24, 0.68)
			Greater than with tolterodine ER Tol IR 4 vs Tol ER 4: RR=1.30 (1.06, 1.60) Similar to oxybutynin ER	Similar to tolterodine ER, oxybutynin IR, and oxybutynin ER	Similar to oxybutynin ER and tolterodine ER
Tolterodine ER (Detrol® LA)	2001	More than with solifenacin Similar to tolterodine IR	Less than with oxybutynin IR, oxybutynin ER, and trospium Tol ER 4 vs Oxy IR 9: RR=0.62 (0.50, 0.77) Tol ER 4 vs Oxy ER 10: RR=0.75 (0.59, 0.95) Similar to oxybutynin TDS	Similar to oxybutynin IR, oxybutynin ER, oxybutynin TDS, and trospium	Less than with oxybutynin IR or oxybutynin TDS Tol ER 4 vs Oxy IR 9: RR=0.32 (0.17, 0.57) Tol ER 4 vs Oxy TDS 3.9: RR=0.15 (0.03, 0.66) Similar to oxybutynin ER

cont'd

Table 2. Comparative Efficacy and Tolerability of Agents for the Treatment of Patients With Urge Incontinence* *cont'd*

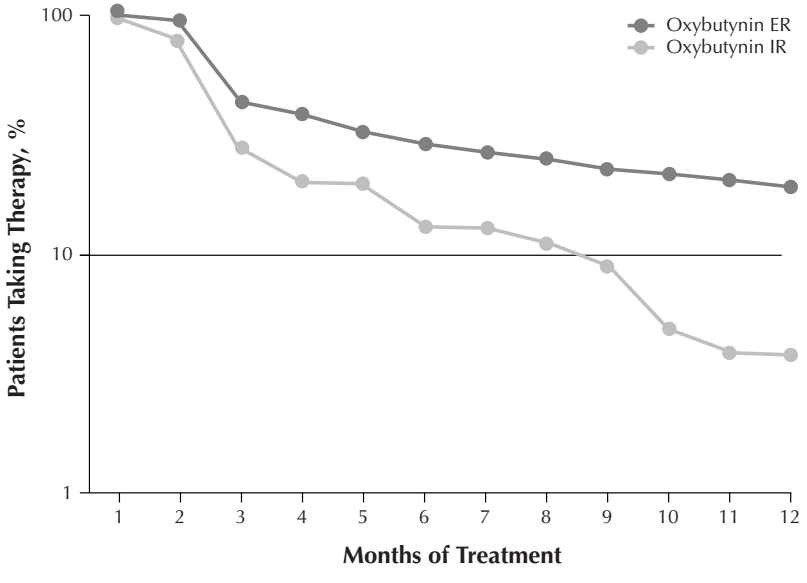
Agent	Year Introduced	Incontinence Episodes/24 h	Risk of Dry Mouth	Risk of Constipation	Risk of Discontinuation Due to Adverse Events
Trospium (Sanctura®)	2004		Less than with oxybutynin IR Oxy IR 10 vs Tro 40: RR=1.53 (1.17, 2.01	Similar to oxybutynin IR	Similar to oxybutynin IR
Darifenacin (Enablex®)	2004				
Solifenacin (VESIcare®)	2004	Fewer than with tolterodine ER Mean baseline to endpoint changes: Sol 5–10 vs Tol ER 4: –1.60 vs –1.11 (P<.01)[40]			

*Summary of data from head-to-head trials with N>200. When several data sets comparing the same drugs existed (ie, same drugs, different doses), data were summarized from trials with subjects who took the highest dosages. The duration of each trial was at least 3 wk. Unless otherwise specified, drug comparisons were adapted from Chapple et al (2005).[38]

TDS=transdermal system.

A third study, which compared 2 formulations of oxybutynin for OAB, found that persistence (the fraction of patients who continued to take the medication after a given time interval) with the new ER formulation was better than with the conventional IR oxybutynin product (Fig 5).[45,46] Finally, a study of the Medi-Cal program that was carried out between 1999 and 2002 found that, when compared with oxybutynin IR, tolterodine and oxybutynin ER were associated with increases in the rate of prescription renewal of 75% and 125%, respectively.[37] It should be noted, however, that, although these studies describe improved adherence with tolterodine and the ER formulation of oxybutynin, the proportion of patients who continue therapy continues to be too low. In the Medi-Cal study, for example, two thirds of all patients treated pharmacologically for OAB/UI filled only a single prescription.[37]

Fig 5. Persistence with IR and ER oxybutynin formulations for OAB.



Adapted from Chui et al (2004)[45] and Noe et al (2004).[46]
ER=extended release; IR=immediate release

Oxybutynin and tolterodine are general antimuscarinics with similar affinities for the muscarinic receptors M1 to M5.[47] (Oxybutynin is called a mixed-action drug because it also has direct muscle-relaxant effects and local anesthetic actions. It is unclear, however, whether these properties are involved in the treatment of patients with incontinence.[48]) The M3 receptor primarily mediates bladder contractions and is thought to be the biologically relevant target of these agents for the treatment of those with OAB/urge incontinence.[49] Cognitive impairments and cardiac effects that may be caused by antimuscarinics are mediated primarily by M1 and M2 receptors, respectively.

Although neither oxybutynin nor tolterodine has been associated with a significant risk of serious adverse cardiac events,[50,51] concern about the potential for these adverse effects led to the development of the second-generation M3-specific agents, solifenacin and darifenacin. Treatment with solifenacin appears to be more effective than therapy with tolterodine IR: it is associated with 5 to 7 fewer urgency episodes per week.[40] The tolerability of solifenacin is similar to that of tolterodine IR, with the exception of a greater risk of constipation (Table 2). Fewer data are available on the clinical features of darifenacin, but a small trial indicates that the efficacy of darifenacin is comparable with that of oxybutynin IR, and that darifenacin is associated with a lower risk of dry mouth.[52]

Similar to oxybutynin and tolterodine, the third new antimuscarinic, trospium, acts nonselectively at muscarinic receptors, although it is distinct among antimuscarinics in 2 respects. First, trospium is not metabolized by the hepatic cytochrome P-450 system and thus does not engage in metabolic competition with other drugs; this is an advantage for patients who take many medications.[53] Second, unlike oxybutynin and tolterodine, trospium contains a quaternary amine. Because of this property, trospium is the least likely of the 3 antimuscarinics to cross the blood-brain barrier and therefore is expected to have fewer central nervous system effects. Quantitative electroencephalographic studies have revealed significant effects on brain activity in patients who take oxybutynin compared with those taking trospium or placebo.[54]

For men with OAB, especially those with BPH, discussion continues among clinicians as to when it is best to prescribe a medication intended to treat patients with OAB. The 2 classes of drugs indicated for the treatment of those with BPH—α blockers, which work by relaxing the smooth muscle in the prostate and bladder neck to improve flow rate, and 5α-reductase inhibitors, which shrink the prostate and arrest its growth to relieve obstruction—are considered to have complementary pharmacologic and clinical properties. These 2 classes of drugs are increasingly being prescribed concomitantly as combination therapy for men with BPH. When considering prescribing medications for men with OAB, clinicians must accurately diagnose the condition, identify the most bothersome symptoms, and select those who would best benefit from this treatment, while taking economic considerations into account.[55]

In a 2004 Internet survey, prescription medications were the most common therapy reported for patients with OAB (used by 44% of respondents), whereas Kegel exercises, behavioral therapy, and nonprescription medications were used by 29%, 7%, and 3% of respondents, respectively; 32% reported no OAB treatment.[56] The antimuscarinics, tolterodine and oxybutynin ER, were the most commonly prescribed medications and together were used by 53% of patients. Prescription medication was rated as the most successful treatment for OAB, with 75% of those taking prescription medications reporting successful treatment, compared with 68% of those prescribed behavioral therapy and 49% of those who performed Kegel exercises. Successful treatment was associated with reduced use of health care resources, including fewer health care visits and less frequent use of incontinence pads.[56]

Although no "breakthrough" drugs have appeared for the treatment of those with UI, the availability of a number of drug options in OAB/urge UI treatment provides physicians and patients with a range of effective products whose different pharmacologic profiles may enable more precise targeting of therapy for individual patients.

These new agents and formulations may reduce the costs of UI for patients in the community, as well as for those living in nursing facilities. Although these therapies are more costly than oxybutynin IR (about $90 to $100/mo vs about $30/mo), their improved profiles may result in overall cost savings. For example, a cost-effectiveness model that compared oxybutynin IR with oxybutynin ER and tolterodine ER found the ER formulations to be cost-effective in the management of urge incontinence.[57] Similarly, despite its higher cost, long-term therapy with tolterodine may be more cost-effective than treatment with oxybutynin IR because of the reduced need for incontinence protection supplies.[58]

FUTURE INNOVATIONS

Advances in our understanding of bladder receptor pharmacology have promoted optimism about the potential for agents with fewer adverse effects and increased efficacy. At least 20 new pharmaceuticals for incontinence or OAB are in development, with the potential to reach the market in a few years.[59] This includes not only product line extensions, such as an ER trospium, but innovative delivery vehicles such as a topical gel. New incontinence applications for existing agents that are currently used for other purposes (eg, botulinum toxin A injected into the bladder wall or sphincter) are also under clinical investigation. Of particular importance is continuing research on agents that selectively target 1 or more muscarinic receptor subtypes in the bladder,[60] as well as treatments that will allow introduction of medication directly into the bladder, thereby avoiding systemic adverse effects.

Medicines available to treat patients with incontinence are antimuscarinics, which are specific to urge incontinence and OAB. Currently, no medicine is approved in the United States for stress incontinence. Duloxetine—a medicine that is currently indicated for depression and diabetic peripheral neuropathic pain—has been investigated for the treatment of those with stress UI. Duloxetine is a dual (serotonin and norepinephrine) reuptake inhibitor that promotes contraction of the urinary sphincter, thus reducing the risk of urine leakage during physical activity. It has been approved for the treatment of patients with stress incontinence in Europe and elsewhere but not in the United States. This does, however, provide hope that pharmacologic therapy will offer an option for stress incontinence in the United States in the future.

CONCLUSIONS

After many years of relatively little progress in the treatment of patients with urge incontinence and OAB, several new pharmaceutical products offer options for more effective management of these common, expensive, and often disabling conditions. This multiplicity of agents allows personalized treatment and an improved quality of life to help the growing population of older people with UI stay active and independent. Improved treatment adherence with these agents has the potential to reduce the cost burden of UI by reducing complications and the need for additional services. Potential cost savings to public and private payers may result if nursing home admissions are reduced or delayed.

Unfortunately, despite the potential for improved treatment, patients with UI frequently do not receive therapy because of reluctance to report this condition, or because

those in whom the condition is diagnosed are undertreated. Education of providers, patients, family members, and policy makers is necessary to promote a greater awareness of the condition and its social, clinical, and economic ramifications. Insurance coverage for these drugs in public and private health plans will encourage the continued development of better agents for UI. Access to these improved therapies by older persons will be greatly facilitated by their inclusion in formularies associated with the new Medicare Part D drug benefit.

Although the new products available for UI may represent important improvements over older medications for individual patients, considerable confusion and misperception abound regarding the nature and value of such incremental pharmaceutical innovations. Incremental improvement in medications for UI has provided considerable benefit to patients. Advantages of the newer agents include fewer and less severe adverse effects; greater ease of use, thereby promoting adherence to prescribed therapy; and the availability of product alternatives that enable personalized treatment. Alternate delivery vehicles and dosage forms (eg, patches, gels, sustained-release formulations) may benefit patients who have difficulty chewing, swallowing, or remembering to take medications.[61]

Advanced technology dosage forms may promote greater independence for older residents in long-term care facilities and may delay institutionalization. These advantages are typical in the evolution of therapies for a variety of conditions.[62] The availability of multiple agents for UI provides physicians with a spectrum of choices with which to personalize treatment for each patient and provides options when a particular agent is ineffective or poorly tolerated. In some cases, use of these innovative products may reduce overall treatment costs.

Despite recent progress in the treatment of patients with UI, significant issues remain to be addressed. Research on agents that affect molecular targets other than muscarinic receptors should be pursued. Because available antimuscarinics are indicated only for the treatment of those with UI associated with OAB (ie, urge or mixed UI), the development of pharmacologic treatments for stress UI is important (eg, to promote contraction of the urethral sphincter muscle by stimulating serotonin and norepinephrine receptors in the central nervous system). Most studies of antimuscarinics have been performed with relatively young subjects, and research into the effects of these agents on the extremely aged and infirm is needed. Finally, studies should be performed to determine whether current medications do, as postulated, delay or prevent the institutionalization of older persons because of UI.

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