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Cost-Effectiveness of New Treatments for Overactive Bladder: The Example of Tolterodine, A New Muscarinic Agent: A Markov Model

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Economic analyses of interventions for chronic diseases require evaluations over a long timeframe to illustrate the benefits and costs of treatments. Clinical trials are generally short and carried out in strictly controlled conditions. They are therefore of limited value for economic evaluation aimed at facilitating decisions about resource allocation. The objective of this study was to develop a simulation model that allows integration of data from different sources to calculate the incremental cost-effectiveness and cost-utility of new treatments for overactive bladder. The model compares tolterodine, a new treatment that aims at alleviating symptoms and improving patients' quality of life, to no treatment. Simulations for Sweden are presented as an example.

The Markov model combines clinical, observational, and economic data. Markov states are defined based on severity of symptoms of overactive bladder (frequency of voids and leaks). Specific costs for drug treatment and use of sanitary protections as well as utilities are assigned for each state. The effectiveness of tolterodine is based on controlled clinical trials and open long-term extensions of these trials. Outcome is measured as quality-adjusted life years (QALYs) and as the number of months spent in a state with no or very limited symptoms.

During the course of 1 year, patients treated with tolterodine spend more time in states with no or limited symptoms compared to those receiving no treatment. Tolterodine-treated patients having a better quality of life during the year. The mean utility of the treated cohort is 0.70, compared to 0.67 in the no-treatment cohort, which is equivalent to the entire cohort moving by one level to a state with less severe symptoms. Mean total costs per patient in the tolterodine arm are SEK8,595 (US $1,131; 1 US$ = 7.6 SEK) compared to SEK3,286 (US$432) in the no-treatment arm. The extra cost due to tolterodine is SEK380 (US$50) per month, which falls within the range of monthly amounts that patients were willing to pay out of pocket for a 25 or 50% improvement of their symptoms in a previous study. The cost for pads is reduced by 23%. The marginal cost per QALY gained with tolterodine is estimated at SEK213,000 (US$28,000).

Based on this simulation model, it appears that treatment of overactive bladder with a well-tolerated pharmacological treatment such as tolterodine is cost-effective. *Neurourol. Urodynam. 17:599–611, 1998.* © 1998 Wiley-Liss, Inc.

Key words: overactive bladder; modeling; cost-utility; cost-effectiveness; tolterodine

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INTRODUCTION

Economic analyses of new interventions for chronic diseases require evaluations over a relatively long timeframe to illustrate the benefits and costs of treatments. Clinical trials are generally rather short and carried out in strictly controlled conditions and in specific patient populations. They are therefore of limited value for economic evaluation aimed at facilitating decisions about resource allocation. This is particularly true at the time new treatments are launched, when information about costs and effectiveness in usual care is still lacking. In such situations, the use of modeling is the only possibility to perform economic evaluations, as this allows the combination of data from different sources (clinical, epidemiological, observational, economic) to illustrate the monetary value of a new treatment and to extrapolate to the longer term [Bloom et al., 1996; Rittenhouse, 1996].

Patients with overactive bladder experience a range of different clinical symptoms such as urgency, frequency of voids, and involuntary leaks. The condition is caused and influenced by a number of different factors. It is not life threatening per se or severely physically handicapping and therefore inaccurately often not considered a very serious condition. However, a number of studies have shown the extensive negative impact that the disease exerts on quality of life, particularly in the emotional and social domains [Herzog et al., 1989; Hunskaar and Visnes, 1991; Wyman, 1990, 1994; Lenderking et al., 1996]. In a willingness-to-pay survey in Sweden [Johannesson et al., 1997], patients with symptoms of overactive bladder were found to score significantly lower ($p < 0.001$) than the normal population in all eight domains of the MOS Short Form 36, a widely used international general health profile [Stewart et al., 1988]. The same result was found with EuroQol, a preference-based health-status instrument [EuroQol Group, 1990]. EuroQol scores were significantly lower than those in an age- and sex-matched normal population ($p < 0.001$) [Kobelt, 1997].

Economic evaluation is a comparative analysis of alternative courses of action in terms of their costs and their consequences [Gold et al.,1996; Johannesson, 1996; Kobelt, 1996; Drummond et al.,1997]. Thus, if effectiveness is expressed as a single generic outcome measure such as quality-adjusted life years (QALYs), cost-effectiveness can be compared to the treatment of other diseases and the importance of investment in the treatment of incontinence highlighted [Mason, 1994; Williams, 1995].

The objective of this study was to develop a simulation model to calculate the incremental cost-effectiveness of new treatments for overactive bladder adaptable to different countries. Treatment alternatives are limited and current drug therapy is hampered by low efficacy or many side effects leading to bad compliance. The standard pharmacotherapy is oxybutynin, an anticholinergic agent with low tolerability and therefore not an option for the majority of patients [Salvatore et al., 1997]. Few outcome studies for oxybutynin are available, but data from the literature suggest that very few patients remain on drug beyond 6–12 months [Kelleher, 1997]. Retrospective data-base analyses show that most patients withdraw from treatment with oxybutynin within the first year. An analysis of claims data from Medicaid the United States shows survival on oxybutynin to be approximately 20% only after 1 year [Pharmacia & Upjohn, 1997, unpublished data]. This was confirmed by an analysis of claims at Medco (United States), which showed that 55% of patients stop oxybutynin treatment within the first month. A similar analysis in France, based on a medical

record data from a network of 300 general practitioners, showed that 25% of patients stopped treatment during the first month and 51% did so during the first year [Pharmacia & Upjohn, unpublished data, 1997]. Thus, for a large majority of patients the relevant choice after failure of the first treatment will be no treatment or a new therapy such as tolterodine.

The model therefore compares tolterodine, a new treatment that aims at alleviating symptoms and improving patients' quality of life, to no treatment. Calculations for Sweden are used to illustrate the model.

MATERIALS AND METHODS

The Markov Model

Markov models are useful when a decision Involves a long-term risk [Sonnenberg and Beck, 1993]. It is assumed that all patients can be classified into a finite number of states, called Markov states. In the case of overactive bladder, states may be defined by the severity of the symptoms. The effect of treatments on symptoms is represented as transitions from more severe to less severe states. The time horizon in Markov models is divided into equal increments of time, referred to as Markov cycles. During each cycle, patients have a certain probability of making a transition from one state to another. Spending one cycle in a particular state is associated with a certain cost and utility, and cumulative costs and utilities are calculated at the end of the Markov process.

Markov States. Our model defines the states according to the severity of symptoms (micturitions/day + leakages/day), and cut-off points between the states were based on data from the willingness-to-pay survey [Johannesson et al., 1997]. In this survey, a symptom score based on the combined measure of frequency of micturitions and episodes of incontinence was correlated with SF36 and EuroQol scores to verify that it did adequately capture the impact of the disease. Quality of life and utility scores derived from the descriptive part of EuroQol (EQ-5D) correlated significantly with this outcome measure, and the symptoms score was thus used to define five Markov states. In addition, there is a state for patients who discontinue treatment (dropout state). Markov models are driven by the transition probabilities during each cycle and have no memory of previous cycles. Individual patients can therefore not return to their own symptom state at baseline, and we assigned the mean cost and utility of the cohort at baseline to the dropout state. However, to account for the fact that utilities and costs may differ among dropouts, depending on the severity of their symptoms at the time they discontinue treatment, an alternative version of the model with one dropout state corresponding to each symptom state was built in for sensitivity analysis. An illustration of the basic Markov model is shown in Fig. 1.

Transition Probabilities. The model runs for 1 year in monthly cycles. Monthly transition probabilities for the first 3 months were calculated from international clinical trial data. The entire patient cohort was distributed into the five states according to symptoms at baseline. Thus, the cohort distributions in the treatment and no-treatment groups are identical at baseline.

In the treatment arm, the transitions to different states were based on the monthly micturition charts in the clinical trial for the first 3 months. No micturition charts were available beyond the trial, but tolterodine appeared to achieve most of its

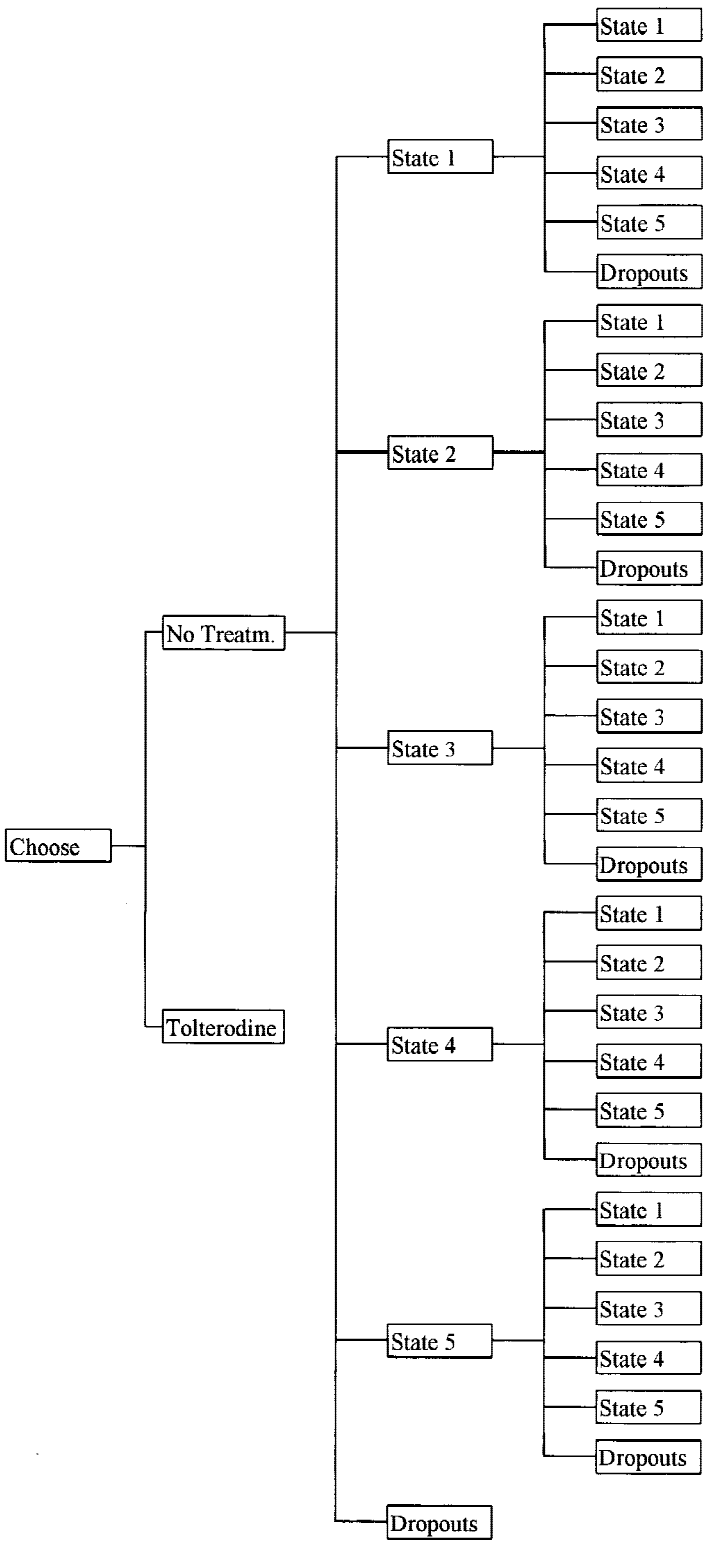

Fig. 1. The Markov model.

clinical efficacy within 12 weeks. We therefore assumed that no further treatment effect, i.e., no further transitions between treatment states, would occur for the remaining 9 months of the model. However, patients would continue to drop out from treatment, and we assumed the dropout probability to be equal in all five treatment states and constant over all cycles.

For the no-treatment arm, we assumed no transitions to other states during 1 year. As overactive bladder symptoms may increase over time, our model may overestimate the quality of life and underestimate the cost in the no-treatment arm. However, there are no published data on progression of symptoms available, and we therefore kept the cohort distribution constant.

Utilities and Costs. In the model, spending time in a state is associated with a certain utility and a certain cost. In this type of economic analysis, utility refers to the preference individuals or society have for a particular health outcome. Preference scores or utility weights on a cardinal scale between 0 (dead) and 1 (perfect health) are attributed to health states and states valued relative to one another relative. A life year spent in a certain health state is thus multiplied by the utility weight of the health state to yield a quality-adjusted life year (QALY). When valuing the effect of treatments, QALYs are particularly useful for interventions that do not prolong life but improve the quality of life, such as treatments for incontinence. Utility weights for the Markov states were obtained by a linear regression analysis of the correlation between urinary symptoms and EQ-5D scores in the Swedish willingness-to-pay survey [Johannesson et al., 1997]. The mid-point of the symptom range in the different states was used to calculate the utility for each state, whereas the mean utility of the cohort at baseline was assigned to the dropout state.

Costs in the treatment states were based on drug costs and pad usage, whereas in the dropout states it was based on pad cost. In the treatment arm, two visits to the general practitioner were added, at treatment start and after 6 months, at a cost of SEK800 (US$105) per visit. No other costs were included, as no detailed data on other resource utilization over 1 year were available either for the treatment group or the group with no pharmacological treatment. Similarly, the costs for an extensive initial medical evaluation were considered sunk costs, as the model assumes that patients had previously been treated and a full evaluation performed at that time. At the time of this analysis, tolterodine was not yet marketed in Sweden, and we therefore set the monthly drug cost at the expected price to public of SEK450 (US$59.20). Pad usage data were collected and mean pad costs calculated for the entire patient population in the international clinical trials. However, patterns of usage may differ in individual countries, and pad costs were therefore adjusted to reflect the usage of the Swedish cohort in the clinical study. In the clinical study, only 67% of patients used protection. The average pad cost in the different states was therefore further adjusted to account for the proportion of patients in each state who did not use any protection. The mean pad cost of the cohort at baseline was assigned to the dropout state.

Table I indicates the symptom scores, utilities, and costs for each state.

Effectiveness of Tolterodine

The effect of tolterodine on symptoms and quality of life is calculated in the treatment arm of the model that incorporates both short- and long-term clinical efficacy and tolerability. Effectiveness is expressed as transition probabilities between

TABLE I. Definition of Markov States and Utilities and Pad Costs (1997 SEK) in the Different States

	Markov states					
	1	2	3	4	5	Dropout
Symptoms	<9	9–<12	12–<15	15–<18	⩾18	—
Utilities	0.742	0.712	0.676	0.640	0.598	0.672
Pad costs (SEK/month)	89	186	248	385	447	274

1 US$ = 7.6 SEK

Markov states and compared to the no-treatment arm where the cohort distribution remains constant.

Effectiveness for the first 3 months was calculated from three identical multinational controlled clinical trials comparing tolterodine to placebo in patients with overactive bladder [Abrams et al., 1997; Appell, 1997; Pharmacia & Upjohn, unpublished data]. The studies included a total of 810 patients in Canada, France, Ireland, the Netherlands, Sweden, the United Kingdom, and the United States. Data on frequency of micturitions and episodes of incontinence were available from 7-day micturition diaries at baseline and at weeks 4, 8, and 12. Patients who remained on treatment during the entire 12 weeks but had missing data at any one of these data points were excluded. Exclusion of patients did not affect the demographics of the groups. Patients who dropped out from treatment were included in our calculation of transition probabilities between treatment states until the last available data point and then used to calculate the probabilities of dropping out.

Effectiveness beyond 3 months was based only on dropout from treatment. Interim clinical results for tolterodine showed that the clinical effect at 3 months was maintained at 12 months. The dropout rate for tolterodine was based on open long-term extensions of the pivotal clinical trials [Pharmacia & Upjohn, unpublished data]. Two hundred twenty-three patients entered the 1-year extension and survival on treatment at 12 months was 70% (152 patients). However, approximately half the patients that dropped out did so for other reasons than medical (protocol violation, consent withdrawal, lost to follow-up); only 36 patients withdrew from treatment because of adverse effects of any kind.

We assumed the same dropout rate for all states and held it constant over all cycles between 3 and 12 months to reach the number of dropouts observed at 1 year. The rate was set at 0.02 to yield 30% total dropouts. A constant rate is consistent with the observations in the open extension study for tolterodine, where dropout rates are fairly constant after the third month.

RESULTS

Cohort Distributions

The clinical effectiveness of tolterodine is illustrated by the increased number of patients in states with limited symptoms (1 and 2) after 3 months. After 12 months, half the patients (51%) are still in states 1 and 2, despite the 30% dropouts. Twenty-eight percent of patients are in state 1, with basically no symptoms, compared to 7% at baseline or in the no-treatment group. Table II shows the cohort distribution during

TABLE II. Cohort Distribution in the Treated Cohort

Cycles	State 1	State 2	State 3	State 4	State 5	Dropout
0 (or no treatment)*	0.0680	0.3196	0.2799	0.1592	0.1733	0.0000
1	0.3448	0.3208	0.1412	0.0519	0.0911	0.0503
2	0.3400	0.2954	0.1230	0.0748	0.0656	0.1012
3	0.3413	0.2855	0.0971	0.0665	0.0662	0.1434
4	0.3337	0.2792	0.0950	0.0650	0.0647	0.1624
5	0.3263	0.2730	0.0928	0.0636	0.0633	0.1810
6	0.3191	0.2670	0.0908	0.0622	0.0619	0.1991
7	0.3120	0.2610	0.0888	0.0608	0.0605	0.2169
8	0.3051	0.2553	0.0868	0.0595	0.0592	0.2342
9	0.2983	0.2496	0.0849	0.0581	0.0579	0.2512
10	0.2917	0.2441	0.0830	0.0569	0.0566	0.2678
11	0.2853	0.2387	0.0812	0.0556	0.0553	0.2840
12	0.2789	0.2334	0.0794	0.0544	0.0541	0.2999

*The untreated cohort will remain in the baseline distribution throughout the year

the year for the treatment arm. The distribution at baseline (cycle 0) corresponds also to the cohort distribution in the no-treatment arm.

Costs

The total cost increase per year and patient in the treatment arm is SEK5,309 (US$699) compared to no treatment. Drug costs during the year alone are SEK4,635 (US$610). Pad costs were reduced by SEK766 (US$100) or 23%. It is likely that these savings are underestimated, as we assume no change in pad usage after 3 months. Patients with overactive bladder are known to develop strong coping mechanisms and one would expect that it would take some time until they would feel confident enough to reduce pad usage. The majority of the costs in the treatment arm are for patients who are receiving treatment, with only 8.5% occurring to dropouts. Average annual costs are different for patients in different states at baseline. As expected, total costs in the more severe states were higher in both arms. However, the difference in costs between treatment and no treatment decreased in the more severe states, making treatment of patients in these states more cost effective (Table III).

Utilities

Total utility in the treated cohort indicates a better quality of life compared to the no-treatment cohort. The mean cumulative utility in the treated cohort is 0.6977 compared to 0.6728 in the no-treatment cohort. This is equal to the entire cohort moving by one level, to a state with less severe symptoms. Table IV shows the cumulative utilities for the different states and the total utility during 1 year.

Economic Evaluation

Cost-Utility Analysis. Total costs per patient for 1 year increase with treatment. However, patients' quality of life (utility) is improved compared to receiving no treatment. The extra cost to achieve an additional QALY with tolterodine compared to receiving no treatment is SEK213,042 (US$28,032). This ratio is within the range of cost per QALY generally accepted as cost effective. In addition, it is possible that our model underestimates the real quality of life improvement and pad usage reduc-

TABLE III. Total Average Costs Over 1 Year for Patients in Different Initial States of Severity, 1997, SEK

Initial state	No treatment	Tolterodine	Difference
Cohort	3,286	8,595	5,309
1	1,071	7,813	6,742
2	2,231	8,166	5,935
3	2,978	8,532	5,554
4	4,626	8,841	4,215
5	5,365	9,570	4,205

1 US$ = 7.6 SEK

TABLE IV. Cumulative Utilities the Two Cohorts Over One Year

Treatment	State 1	State 2	State 3	State 4	State 5	Dropouts	Total
No treatment	0.0505	0.2276	0.1892	0.1019	0.1036	0.0000	0.6728
Tolterodine	0.2770	0.1926	0.0701	0.0417	0.0407	0.1256	0.6977

tion over time, when patients become accustomed to the improvement of their symptoms and abandon some of their coping mechanisms. Table V shows the results of the cost-utility analysis.

Cost-Effectiveness Analysis. Effectiveness can also be defined as the number of months patients spend in a state of being cured or well controlled. We considered months spent in state 1 as controlled or basically normal. The marginal cost for an additional month spent in state 1 when using tolterodine, compared to receiving no treatment, is SEK1,860 (US$215). The results of the cost-effectiveness analysis based on this definition are presented in Table V.

Sensitivity Analysis. We performed sensitivity analyses for different rates of dropout from treatment with tolterodine. The first three cycles were kept constant and the probability for dropping out between cycles 4 and 12 varied, reaching different total dropout rates at the end of 12 months. These rates were adjusted to 20 and 15% to account for patients who were excluded from the analysis of the long-term clinical study with tolterodine because of reasons other than adverse effects. Of the 71 patients who were excluded from the analysis, 16 patients (7.1% of patients enrolled) had violated the protocol or withdrawn consent, six patients (2.7%) performed the last visit either too late or too early, and 13 patients (5.8%) were lost to follow-up. We thus included these patients and lowered the dropout rate. In addition, we also increased the dropout rate to 35, 40, and 50% to account for potentially higher compliance in a clinical trial setting. Cost-utility and cost-effectiveness results for different dropout rates are shown in Table VI.

Overactive bladder is a chronic disease and treatment will last longer than 1 year. As no clinical data for tolterodine are available beyond 1 year, modeling of chronic administration is questionable. However, to verify whether the cost-effectiveness ratio is maintained over a longer period of time, we ran the model for a second year. Dropout rates from the first year stayed constant, and no improvement of utility or decrease in pad costs was assumed. This is again likely to underestimate the beneficial effects of treatment on quality of life and pad costs. As can be seen in Table VII, the cost-effectiveness is maintained over a 2-year period.

The basic model assigns the mean cost and utility of the cohort at baseline to

TABLE V. Cost-utility and Cost-effectiveness Analysis, 30% Treatment Dropout Rate, 1997, SEK

	No treatment	Tolterodine
Cost	3,286	8,595 SEK
Marginal cost		5,309 SEK
Utility	0.67275	0.69766
Marginal utility		0.02492
Marginal cost utility		213,042 SEK
Effect (controlled month)	0.816	3.6709
Marginal effect		2.8549
Marginal cost-effectiveness		1,860 SEK

1 US$ = 7.6 SEK

TABLE VI. Sensitivity Analysis of Dropout Rates for Tolterodine, 1997, in SEK

	Dropouts				
	15%	20%	35%	40%	50%
Cost	8,948 SEK	8,828 SEK	8,469 SEK	8,362 SEK	8,085 SEK
Marginal cost	5,662 SEK	5,542 SEK	5,183 SEK	5,076 SEK	4,799 SEK
Utility	0.69957	0.69895	0.69700	0.69637	0.69488
Marginal utility	0.02682	0.02621	0.02426	0.02363	0.02214
Marginal cost utility	211,111 SEK	211,446 SEK	213,042 SEK	214,812 SEK	216,757 SEK
Effect (controlled month)	3.9488	3.8590	3.5747	3.4828	3.2657
Marginal effect	3.1328	3.0430	2.7587	2.6668	2.4497
Marginal cost-effectiveness	1,807 SEK	1,821 SEK	1,879 SEK	1,903 SEK	1,959 SEK

1 US$ = 7.6 SEK

TABLE VII. Sensitivity Analysis: Extrapolation to 2 years, 1997, in SEK

	No treatment	Tolterodine
Cost	6,571 SEK	15,804 SEK
Marginal cost		9,233 SEK
Utility	1.34549	1.39048
Marginal utility		0.04499
Marginal cost utility		205,233 SEK
Effect (controlled month)	1.632	6.6059
Marginal effect		4.9739
Marginal cost-effectiveness		1,856 SEK

1 US$ = 7.6 SEK

patients who withdraw from treatment. Dropouts had not been followed in the clinical trials, and no data on pad usage and utility after treatment stop were available. We assumed, however, that their symptoms and pad usage would increase again. In the alternative model, there is one dropout state corresponding to each treatment state, and we assumed that patients' pad costs would increase and utility decrease by the difference between each state. Thus, for patients who drop out from state 1, 2, or 3, costs and utilities of states 2, 3, or 4 are used ,respectively, and for patients who drop out of states 4 and 5, cost and utilities of state 5 is used. After dropout, these values remain at the same level for the remainder of the year. Table VIII shows the results of the cost-utility and cost-effectiveness analyses using this model.

TABLE VIII. Sensitivity Analysis: Alternative Model, 1997, in SEK

	No treatment	Tolterodine
Cost	3,286	8,654 SEK
Marginal cost		5,069 SEK
Utility	0.67275	0.69449
Marginal utility		0.02174
Marginal cost utility		233,164 SEK
Effect (controlled month)	0.816	3.6709
Marginal effect		2.8549
Marginal cost-effectiveness		1,761 SEK

1 US$ = 7.6 SEK

DISCUSSION

Patients with overactive bladder have been shown to have significantly lower quality of life than the normal population. The use of quality-of-life weights as an outcome for economic evaluation is therefore justified. However, patients with overactive bladder are generally elderly and very often have one or several comorbidities. Also, incontinence is not life threatening per se and the benefit of treatment will not include extension of the quantity of life, but only of quality of life. The impact of treatments for overactive bladder on QALYs can therefore not be expected to be very great over a limited timeframe and will be difficult to illustrate in short-term clinical trials. Treatment options are limited, particularly as far as pharmacological treatments are concerned, and no data are thus available to show quality-of-life improvements over several years. Analyses based on currently available data may therefore underestimate the effect of treatments.

Economic evaluations provide information that can be used for decisions about resource allocation. Clinical trials provide one part of the data required for economic analysis, but particularly in chronic diseases, trials are usually too short and need to be complemented with data from other sources. We propose a simulation model that allows calculating cost-utility and cost-effectiveness of a new agent for treatment of overactive bladder, tolterodine, over 1 year, compared to no treatment. The model also illustrates treatment effects for different treatments.

The effectiveness of treatment with tolterodine is illustrated by the patient distribution over the different states at the end of 1 year. Twenty-eight percent of patients are in state 1, with basically no symptoms compared to 7% at baseline, whereas much fewer patients are in states with severe symptoms. When using the alternative model in which patients drop by one state in terms of utility and cost when they withdraw from treatment, it can be shown that more than half the patients in states 4 and 5 are dropouts. The model thus follows patients in terms of their symptoms and illustrates treatment effect over the longer term.

Another measure of the treatment effect in the model is the utility of the two cohorts. The mean cumulative utility for patients in the treatment arm during the year is 0.70 compared to 0.67 at baseline or with no treatment. A difference of 0.03 corresponds to the difference of the utility between the states. Thus, the overall health benefit with treatment is equivalent to an improvement by one level of symptom severity or by one state. An analysis of patients' rating of the improvements of symptoms in the clinical trials showed that a reduction of three micturitions or

incontinence episodes (which corresponds to the difference between the states in our model) was considered a significant improvement. Also, as two thirds of patients in the tolterodine arm are in treatment at the end of 1 year, there is a potential for a further increase in the difference of quality of life compared to the no-treatment arm. This can be illustrated by an extrapolation of the model to 2 years, leading to a lower cost-utility ratio. The model is rather insensitive to the change in the dropout rates. Cost-utility ratios are almost unchanged when only those who dropout due to side effects are included (15%) or when the dropout rate is increased to 50%. This is likely to be due to the fact that no costs are included for patients who cannot tolerate the treatment.

In the base case assumption, the marginal cost per QALY of tolterodine compared to no treatment is SEK213,000 (US$28,000). This ratio is within the range generally accepted as cost-effective. However, the model may overestimate this ratio, as the quality of life improvements of patients in treatment for a long time may be underestimated by our extrapolation from 3-month results to 1 year. On the other hand, although utilities were measured in a patient population, they were not controlled for the presence of a potentially higher comorbidity in patients with more severe symptoms. Thus, the real change in utility due to alleviation of symptoms of overactive bladder may be less than in the model. However, only about a third of patients are in states 4 and 5 at baseline, and the effect of comorbidity may therefore be limited, if present at all. This will be a subject for further research. Mean drug costs alone amounted to SEK380 (US$50) per month, which is within the range that patients were willing to pay out of their own pocket for a 25–50% improvement of their symptoms [Johannesson et al., 1997].

CONCLUSIONS

Cost-effectiveness and cost-utility analyses are the most frequently used types of economic evaluation. When comparisons of treatments within the same indication are needed, cost-effectiveness provides adequate information. However, when a disease has a major impact on quality of life or when comparison to other diseases is desirable, cost-utility is required, as it uses the same outcome measure in all cases, QALYs. Particularly in a disease such as overactive bladder, comparison to other diseases is crucial. Incontinence is potentially undertreated, as in many instances it is not considered a severe disease. Cost-utility is a tool that determines whether spending for treatment of overactive bladder is a good investment of scarce resources.

The marginal cost-utility ratio for tolterodine when compared to no treatment is within the range of what is generally accepted as cost-effective in most studies. The ratio is comparable to treatment of borderline hypertension or primary prevention of hyperlipidemia in Sweden, but higher than secondary prevention in hyperlipidemia. However, these preventive interventions increase the quantity rather than the quality of life. Treatments for conditions such as overactive bladder alleviate symptoms and increase the quality of life but have no effect on survival. Cost-utility studies in Sweden for treatments of symptoms only are rare and no comparative studies are available. The cost per QALY of palliative chemotherapy in advanced gastrointestinal cancer was found to be SEK160,000 (US$21,000), but it also included a survival benefit. Treatment of overactive bladder has an immediate effect on symptoms; however, the long-term effect on quality of life has not been measured. Our model

extrapolates utility and costs from 3 to 12 months by keeping them constant, which may not be an accurate representation of the real treatment benefit. Further research over the longer term is needed to confirm our results.

However, based on this simulation model, it appears that treatment of overactive bladder with pharmacological treatment is as cost-effective as other interventions. New treatments with few side effects and therefore better compliance have the potential to improve patients' quality of life and health status in the short and medium term. Tolterodine has been shown to have a tolerability profile that allows more patients to remain in treatment longer, and improvements in quality of life can therefore be expected to be maintained for more than 1 year. However, the model contains a number of assumptions, as tolterodine is still an investigational drug, and more definitive data can only be gathered once the product is on the market.

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