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ORIGINAL RESEARCH ARTICLE

Economic Impact of Mirabegron Versus Antimuscarinics for the Treatment of Overactive Bladder in the UK

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Abstract

Purpose Our objective was to estimate the economic outcomes of using mirabegron versus antimuscarinics in the treatment of patients with overactive bladder (OAB) from a societal perspective in the UK.

Materials and Methods A Markov model was developed using Microsoft Excel®. The time horizon and cycle length are 12 and 1 months, respectively; and the hypothetical cohort size 100 patients. Antimuscarinic comparators are fesoterodine, oxybutynin extended release (ER) and immediate release (IR), solifenacin, tolterodine ER/IR, trospium ER/IR, darifenacin and flavoxate. Model inputs included real-world treatment patterns data, healthcare resource use (e.g. clinic visits) and direct and indirect costs (e.g. drug acquisition and productivity loss). Model outputs included patient disposition, healthcare resource use, drug acquisition costs and other treatment-related costs over a 1-year time horizon. A one-way sensitivity analysis was performed to determine the key drivers of the model.

Results In a hypothetical cohort of 100 patients, total annual costs per patient were lower with mirabegron than with all antimuscarinics (£1270.84 vs. 1321.71–1607.48). Healthcare resource use was lower with mirabegron than with all antimuscarinics (115 vs. 119–123 general practitioner visits; 173 vs. 178–185 specialist visits and 0.0042 vs. 0.0050–0.0060 surgical operations) and fewer work hours were lost (4017 vs. 5114–6990 [all per 100 patients]). Sensitivity analysis showed the model was sensitive to persistence and switching rates, although the impact on the overall results was minimal.

Conclusions In the UK, using mirabegron to treat OAB may improve persistence and lead to reductions in switching treatment, healthcare resource utilization, productivity costs, and overall treatment costs versus antimuscarinics.

Key Points for Decision Makers

Treatment of overactive bladder (OAB) with mirabegron 50 mg in the UK may result in lower healthcare resource utilization, lost productivity costs, and overall treatment costs compared with antimuscarinics.

Further work is needed to confirm these findings in different populations to assess the effects of mirabegron on the costs of treatment in other countries.

Electronic supplementary material The online version of this article (doi:10.1007/s41669-017-0011-x) contains supplementary material, which is available to authorized users.

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1 Introduction

Overactive bladder (OAB) is characterized by urinary urgency, usually with urinary frequency and nocturia, with or without urinary incontinence [1]. OAB affects up to 17% of adults aged ≥40 years in Europe and up to 17% of all adults in the USA [2, 3]. In Europe, a higher proportion (30–40%) of OAB is observed in adults ≥75 years of age [2].

The clinical and economic burden of OAB is significant. Symptoms of OAB have been reported to adversely affect patients' daily activities, sleep, mental health and personal relationships [4, 5]. These symptoms also have a significant impact on productivity in the workplace and healthcare resource use [6]. In the UK, the total direct economic impact (incremental costs) of OAB on the national healthcare system is estimated to be in excess of £1 billion [6].

Following the use of conservative management strategies, treatment with pharmacotherapy can result in symptom improvement. However, bothersome on-treatment adverse events (AEs) from antimuscarinic agents (such as dry mouth and constipation) are common because of a lack of target organ specificity [7]. Side effects observed with antimuscarinics may also have deleterious effects on treatment persistence. A screening survey conducted in the USA identified 6577 patients with one or more antimuscarinic prescriptions for OAB [8]. Of the 1322 patients who reported discontinuing treatment prior to follow-up, 1177 (89%) discontinuations were primarily due to unmet treatment expectations and/or tolerability [8].

Mirabegron is a first-in-class licensed selective oral β_3-adrenoceptor agonist approved in the UK for the treatment of OAB [9]. It promotes bladder relaxation of the detrusor muscle during the storage phase, improving bladder capacity [10]. Mirabegron demonstrated overall efficacy similar to that of antimuscarinic therapies in clinical trials [11] but with an improved overall tolerability profile [11, 12]. Evidence from a recent retrospective analysis of prescription claims in Canada demonstrated that, over a 12-month period, patients with OAB treated with mirabegron have improved persistence compared with those treated with antimuscarinics [13].

A prospective study of women with OAB who received treatment with fesoterodine for 8 weeks also showed that those who adhered to treatment reported significantly

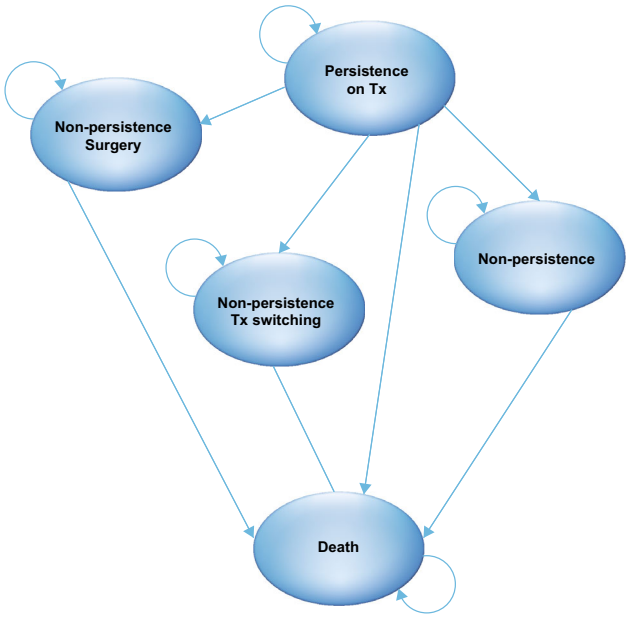
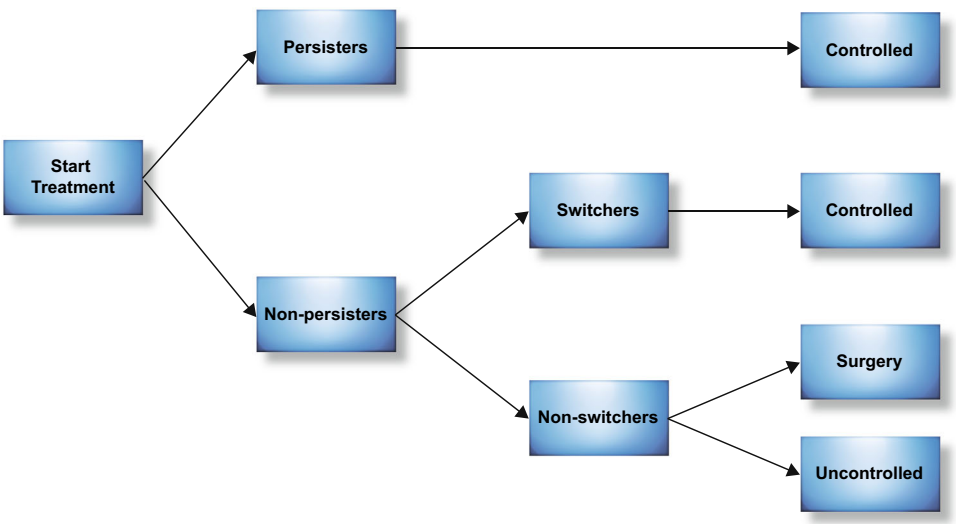


Fig. 1 Markov model structure *tx* treatment

Fig. 2 Treatment pathway



greater improvements in clinical symptoms at the end of the treatment period than those who were non-adherent [14]. In addition, persistence with treatment has been shown to reduce consumption of healthcare resources in OAB [15]. Given the impact of OAB on work absenteeism and productivity [6], persistence and symptom control may be expected to reduce the impact of these factors.

This study aimed to use predominantly real-world evidence to estimate the economic outcomes associated with persistence with mirabegron treatment versus antimuscarinic agents in patients with OAB in the UK.

2 Methods

2.1 Model Overview

This is a Microsoft® Excel-based (version 17.0, Microsoft Corporation, Redmond, WA, USA) Markov model. The time horizon is 12 months, the cycle length is 1 month and the default cohort size is 100 patients. Mirabegron 50 mg/day is compared with the following antimuscarinic treatments (all doses reported are per day): fesoterodine 4/8 mg, oxybutynin extended release (ER) 5 mg, oxybutynin immediate release (IR) 5 mg, solifenacin 5/10 mg,

Table 1 Model assumptions

Non-persisters were assumed to either switch, undergo surgical operations or remain uncontrolled
Switchers and patients having surgical operations were assumed to have controlled symptoms
At treatment initiation (the start of the model), all patients were assumed to incur one visit to a GP and 1.5 visits to a specialist (urologist) [17]
Switchers were assumed to have one GP visit, 1.5 visits to a specialist (urologist) and one urodynamic test [17]
Patients who switched treatment were ascribed a drug acquisition cost, which was weighted by the market share of each treatment. The market share data were provided by Astellas [24]
One total probability of surgical operations was included and costs were applied [19], assuming that 50% of patients had onabotulinumtoxinA injection and 50% had SNS
Only non-persisters with uncontrolled symptoms were assumed to be at risk of co-morbidities (depression and UTI) [25]; the risk was applied in each cycle
Patients who were non-persistent and uncontrolled were assumed to have a 21.1% decrease in hours worked [25]
The persistence at 12 months was assumed to be the same for each treatment irrespective of the dose received [16]
The persistence at 12 months was assumed to be the same for trospium ER and IR formulations, and tolterodine ER and IR [16]

ER extended release, *GP* general practitioner, *IR* immediate release, *SNS* sacral nerve stimulation, *UTI* urinary tract infection

Table 2 Clinical inputs

Variable	Value (%)	Source
Proportion of patients with incontinence	60.00	Nitti et al. [22][a]
Percentage of patients switching treatment	26.06	Nazir et al. [17]
12-month persistence (UK CPRD)		
Mirabegron 50 mg	37.70	Astellas [16]
Fesoterodine 4/8 mg	24.00	Astellas [16]
Oxybutynin ER 5 mg	17.20	Astellas [16]
Oxybutynin IR 5 mg	12.40	Astellas [16]
Solifenacin 5/10 mg	24.80	Astellas [16]
Tolterodine ER 4 mg	20.60	Astellas [16]
Tolterodine IR 4 mg	20.60	Astellas [16]
Trospium ER 60 mg	19.10	Astellas [16]
Trospium IR 40 mg	19.10	Astellas [16]
Darifenacin 7.5 mg	15.90	Astellas [16]
Flavoxate 600 mg	8.30	Astellas [16]
General population mortality	0.97	ONS [18]

CPRD Clinical Practice Research Datalink, *ER* extended release, *IR* immediate release, *ONS* Office for National Statistics

[a] A conservative estimate of 60% was applied to the model based on 65.7% of the total population who were reported to have urgency or mixed incontinence at baseline. All doses reported are the total dose per day

tolterodine ER or IR both 4 mg, trospium ER 60 mg or IR 40 mg, darifenacin 7.5 mg, and flavoxate 600 mg.

The base-case analysis provided a societal perspective of OAB management by accounting for all costs incurred by the UK NHS as well as those associated with lost productivity. Patient disposition, healthcare resource use, direct costs, indirect costs and total costs were all assessed as part of the base-case analysis.

2.2 Treatment Pathway

Patients enter the model in the 'persistence on treatment' health state (Fig. 1) and are assigned to treatment with mirabegron 50 mg (the recommended approved dose in the UK [9]) or an antimuscarinic agent (Fig. 2). At the end of each month, patients either persist with treatment or discontinue. Those who discontinue initial treatment switch to an alternative pharmacological intervention, undergo surgical operations (onabotulinumtoxinA injection or sacral nerve stimulation [SNS]) or discontinue treatment altogether. Patients can transition to other treatment states or death at each cycle. To make the analysis tractable within a 12-month time horizon, the model assumes that switching to a second-line pharmacotherapy and undergoing surgical operations both lead to symptom control (with no option for additional lines of treatment) until the end of the time horizon. Patients who discontinue treatment altogether are assumed to

Table 3 Resource inputs

Parameter	Value or probability	Unit cost	Source
Drug acquisition		Cost per day (£)	
First-line pharmacotherapy	–		
Mirabegron 50 mg	–	0.97	BNF 71 [23]
Fesoterodine 4/8 mg	–	0.92	BNF 71 [23]
Oxybutynin ER 5 mg	–	0.46	BNF 71 [23]
Oxybutynin IR 5 mg	–	0.07	BNF 71 [23]
Solifenacin 5/10 mg[a]	–	1.00	BNF 71 [23]
Tolterodine ER 4 mg	–	0.92	BNF 71 [23]
Tolterodine IR 4 mg	–	0.09	BNF 71 [23]
Trospium ER 60 mg	–	0.82	BNF 71 [23]
Trospium IR 40 mg	–	0.83	BNF 71 [23]
Darifenacin 7.5 mg	–	0.91	BNF 71 [23]
Flavoxate 600 mg	–	0.39	BNF 71 [23]
Second-line pharmacotherapy[b]	–	0.64	BNF 71 [23], Astellas [24]
Surgical operations[c]	0.01%	1242.59	
Visits/test			
GP	1	46.89	Nazir et al. [19]; PSSRU [21]
Urologist	1.5	102.16	Nazir et al. [19]; UK Department of Health
Urodynamic test	1	282.00	Nazir et al. [19]; South Devon Healthcare [30]
Pads		Cost per pad (£)	
On treatment	2.5/day	0.25	Nazir et al. [19]; Incontinence Direct [31]
Off treatment	5.5/day	0.25	Nazir et al. [19]; Incontinence Direct [31]
Co-morbidities			
Depression	19.0%[d]	99.10	Arlandis-Guzman et al. [25]; Irwin et al. [6]
UTI	30.7%[d]	2.79	Arlandis-Guzman et al. [25]; Irwin et al. [6]

All doses reported are the total dose per day

BNF British National Formulary, *ER* extended release, *GP* general practitioner, *IR* immediate release, *OAB* overactive bladder, *UTI* urinary tract infection

[a] Weighted average of solifenacin 5 mg (70%) and 10 mg (30%); unit costs of 30 tablet packs of £27.62 and £35.91, respectively

[b] Weighted cost based on market share of oral therapies for OAB

[c] Weighted cost based on a 50:50 ratio of onabotulinumtoxinA and sacral nerve stimulation

[d] 6-month probability; unit costs based on 2005 monthly costs, converted to 2015 values using the UK forex exchange rate (as of October 2015)

remain uncontrolled. Other model assumptions are reported in Table 1.

2.3 Model Input Parameters

2.3.1 Clinical Inputs

We derived 12-month persistence data (Table 2) from a retrospective database study conducted in the UK [16]. In addition, the treatment switching rate (26.06%) was taken from a previously published cost-effectiveness analysis of mirabegron compared with antimuscarinics for the treatment of adults with OAB in the UK [17]. Mortality for the population with OAB was based on the UK age-standardized general population mortality rate [18] and converted to a 1-month probability (P) using the formula: $P = 1 - e^{-rt}$, where r represents rate and t time.

2.3.2 Healthcare Resource Use

Costs associated with resource use such as general practitioner (GP) and specialist visits were derived from NHS data [19–21]. Unit costs were calculated/estimated for one GP visit and 1.5 referrals to a urologist at treatment initiation and treatment switch (Table 3) [17]. One test by a specialist clinician (e.g. urologist, gynaecologist or other) was performed for each patient who switched to a second-line pharmacotherapy [17]. The proportion of patients with incontinence and requiring pads was estimated to be 60% based on the number of patients with wet OAB [22]. Pad use was estimated to be 2.5 pads per day for patients on treatment (i.e. persisters and switchers) and 5.5 pads per day for those off treatment (i.e. those who underwent surgical operations or discontinued all treatment) [19].

Drug acquisition costs were calculated based on the treatment cost per pack (Table 3) [23] and were correct as of quarter 1, 2016. The cost of second-line pharmacotherapy was based on a weighted average derived from UK market share data [24].

Patients who were uncontrolled were considered to be at risk of two co-morbidities: depression and urinary tract infection (UTI). The 6-month probabilities of depression and UTI were 18.8 and 30.7%, respectively [25], and the monthly probability of surgical operations was 0.01% [17].

The costs for all resources were based on 2015 values, or inflated to 2015 values using the consumer price index (CPI) where applicable. The costs of depression and UTI sourced from Irwin et al. [6] were converted from € to British £ using the UK Forex exchange rate (as of December 2015).

2.3.3 Loss of Productivity

The model accounts for loss of work productivity only in patients who are non-persistent with treatment, have uncontrolled symptoms and are in employment. The base-case analysis assumed that 34.7% of the patients were employed for an average of 40 h per week [25, 26], had uncontrolled OAB and had a 21.1% reduction in the hours worked [25]. The average hourly wage of £12.62 (2011 value) was inflated to £13.94 (2015 value) using the CPI [27].

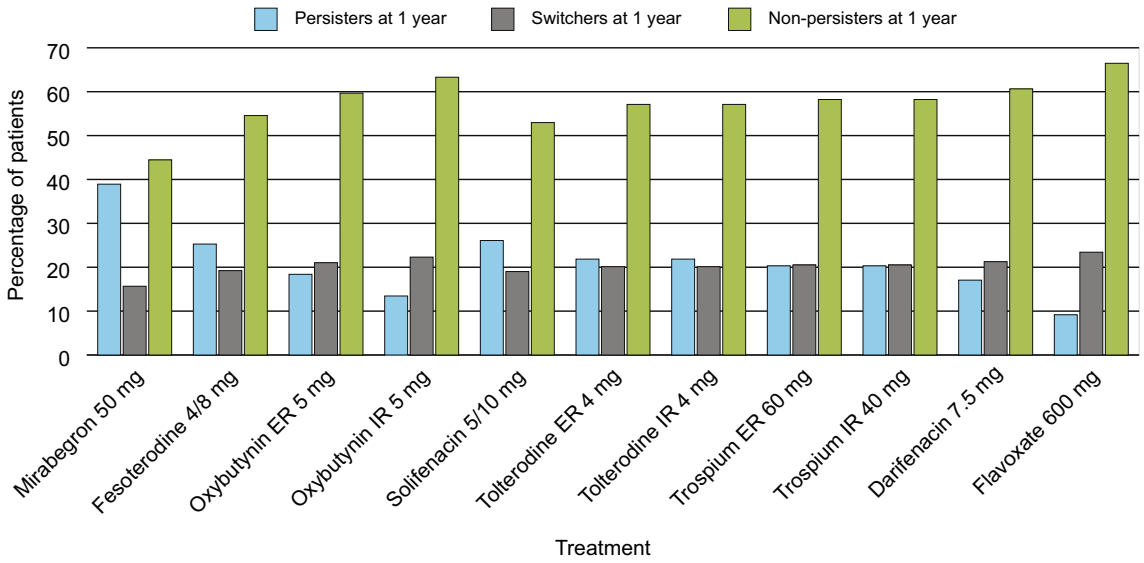


Fig. 3 Summary of patient disposition after 12 months for each treatment. Total disposition may not sum to 100% because of rounding. All doses reported are the total dose per day. *ER* extended release, *IR* immediate release

2.4 Sensitivity Analysis

A one-way univariate deterministic sensitivity analysis (DSA) was performed to assess the uncertainty of chosen parameters [28]. Here, a standard 20% variation in the following model parameters was tested individually and the effects on the incremental costs determined: persistence at 12 months, percentage of patients switching and probability of surgical operations. Mirabegron 50 mg was compared with solifenacin 5/10 mg and oxybutynin IR 5 mg. The results of the DSA were presented as a tornado diagram, with the parameters that had the greatest impact at the top.

3 Results

3.1 Patient Disposition

After 12 months, more patients persisted on treatment with mirabegron 50 mg than with all antimuscarinics (39 vs. 9–26%, respectively [values for all antimuscarinics presented as a range]) (Fig. 3). This resulted in fewer patients either switching treatment (16 vs. 19–23%, respectively) or becoming non-persistent uncontrolled patients (44 vs. 54–66%, respectively).

3.2 Healthcare Resources

Resource use was lower with mirabegron 50 mg than with all antimuscarinics, including GP visits (115 vs. 119–123, respectively, per 100 patients), specialist visits (173 vs. 178–185, respectively, per 100 patients) and number of surgical operations (0.0042 vs. 0.0050–0.0060, respectively, per 100 patients) (Table 4). Total pad use per patient over 12 months was also lower with mirabegron 50 mg than with all antimuscarinics (71,807 vs. 76,531–84,602, respectively, per 100 patients) (Fig. 4).

3.3 Direct Costs

Mirabegron 50 mg had a higher medication cost than all antimuscarinics (£24,744 vs. 4599–22,634 per 100 patients) (Table 5). However, resource use costs, including those for the co-morbidities of depression and UTI, GP visits, specialist visits, surgical operations, urodynamic tests and pads, were lower with mirabegron than with all antimuscarinics (Table 5).

3.4 Indirect Costs

The number of work hours lost (4017 vs. 5114–6990 per 100 patients) and the cost due to work hours lost (£55,983

Table 4 Healthcare resource use over 12 months

Result parameter	Mirabegron 50 mg	Fesoterodine 4/8 mg	Oxybutynin ER 5 mg	Oxybutynin IR 5 mg	Solifenacin 5/10 mg	Tolterodine ER 4 mg	Tolterodine IR 4 mg	Trospium ER 60 mg	Trospium IR 40 mg	Darifenacin 7.5 mg	Flavoxate 600 mg
GP visits	115	119	121	122	119	120	120	120	120	121	123
Specialist visits	173	178	181	183	178	180	180	180	180	182	185
Surgical operations	0.0042	0.0051	0.0055	0.0058	0.0050	0.0053	0.0053	0.0054	0.0054	0.0056	0.0060
Total pad use	71,807	76,853	79,798	82,194	76,531	78,274	78,274	78,932	78,932	80,414	84,602
On treatment	40,123	35,918	33,464	31,467	36,187	34,734	34,734	34,186	34,186	32,950	29,461
Off treatment	31,684	40,934	46,334	50,727	40,334	43,540	43,540	44,747	44,747	47,464	55,142

All doses reported are the total dose per day

ER extended release, *GP* general practitioner, *IR* immediate release

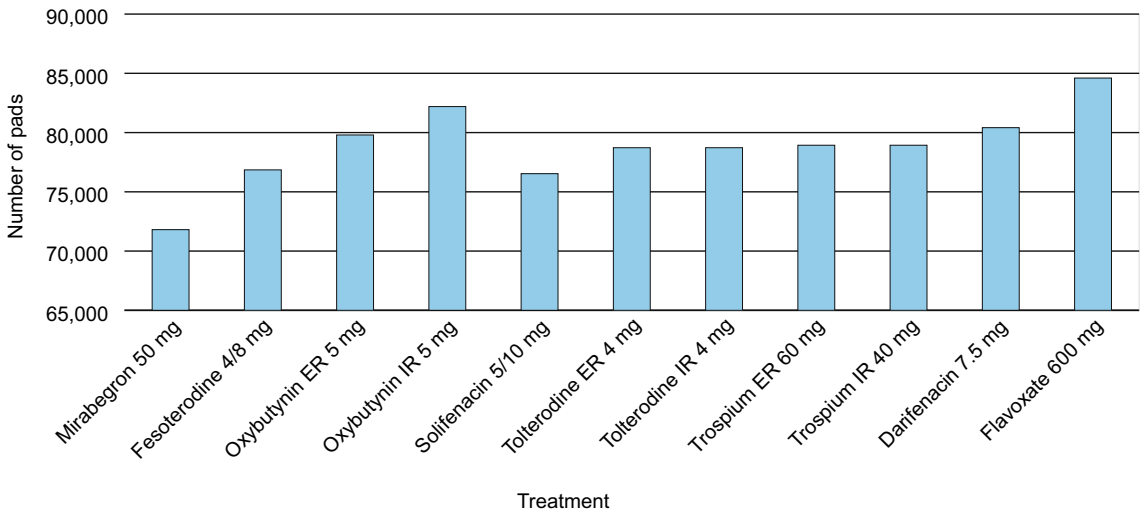


Fig. 4 Total pad use per 100 patients, after 12 months for each treatment. All doses reported are the total dose per day. *ER* extended release, *IR* immediate release

vs. 71,284–97,430 per 100 patients) were both lower with mirabegron 50 mg than with all antimuscarinics (Fig. 5).

3.5 Total Costs

Total costs were lower for mirabegron 50 mg than for all antimuscarinics (£127,084 vs. 132,171–160,748, respectively, per 100 patients) (Fig. 6). This translated into lower respective total costs per patient (£1271 vs. 1322–1607) and per patient per day (£3.48 vs. 3.62–4.40).

3.6 Sensitivity Analysis

For both comparisons, the model was most sensitive to ± 20% changes in persistence rates for either treatment and the percentage of patients switching (Fig. 7). The incremental cost savings per patient per day were −£0.45 in the base-case analysis of mirabegron 50 mg versus solifenacin 5/10 mg and −£0.55 versus oxybutynin IR 5 mg. The overall impact was similar when the incremental cost savings per additional patient persisting on treatment were assessed (Fig. S1 in the Electronic Supplementary Material).

4 Discussion

To our knowledge, this model is the first to estimate the economic impact of using mirabegron 50 mg versus antimuscarinic agents for the treatment of OAB from a societal perspective in the UK, largely employing real-world data (specifically persistence rates).

According to the model, after 12 months, more patients receiving mirabegron 50 mg versus all antimuscarinics persisted with treatment, fewer patients switched treatment and fewer work hours were lost. Although mirabegron 50 mg had higher medication costs over 12 months than did antimuscarinics, these costs were offset by savings attributed to other direct and indirect costs. This was partly attributable to a lower proportion of non-persisters and switchers, who had higher demand for healthcare resources and higher pad use than patients who persisted with treatment. The results suggest that more patients in the UK who receive mirabegron will persist with first-line pharmacological treatment versus antimuscarinics over 12 months, resulting in more patients with likely controlled symptoms. Administration of mirabegron as first-line pharmacotherapy for OAB could have beneficial effects in terms of lower resource use and overall treatment, containment of healthcare costs and societal benefit. Furthermore, while lower healthcare resource use has been cited as a benefit of increased treatment persistence [15], better persistence rates could also be expected to improve patient quality of life (QoL), likely because of increased symptom control and an increased ability to continue daily activities [15]. This model did not include the likely improvements in QoL for those who persist with treatment.

While similar efficacy is observed between mirabegron and antimuscarinics [11], real-world evidence indicates that a higher proportion of patients are likely to be non-persistent with treatment with antimuscarinics versus mirabegron 50 mg [13]. Potential reasons for treatment discontinuation with antimuscarinics include bothersome AEs such as dry mouth and constipation, the most common AEs in these patients [7]. A recent systematic literature review and network meta-analysis of mirabegron 50 mg versus antimuscarinics in 27,309 patients with OAB reported a similar incidence of dry mouth for mirabegron 50 mg and

Table 5 Total direct costs over 12 months for each treatment

Cost (£)	Mirabegron 50 mg	Fesoterodine 4/8 mg	Oxybutynin ER 5 mg	Oxybutynin IR 5 mg	Solifenacin 5/10 mg	Tolterodine ER 4 mg	Tolterodine IR 4 mg	Trospium ER 60 mg	Trospium IR 40 mg	Darifenacin 7.5 mg	Flavoxate 600 mg
All medication	24,744	20,810	11,124	4599	22,634	20,004	4677	17,875	17,907	18,609	9104
First line	22,586	18,022	7969	1145	19,886	17,038	1712	14,827	14,859	15,377	5349
Second line	2158	2788	3155	3455	2748	2965	2965	3047	3047	3232	3755
Co-morbidities	1121	1448	1639	1795	1427	1540	1540	1583	1583	1679	1951
GP visits	5408	5577	5664	5727	5567	5620	5620	5639	5639	5680	5782
Specialist visits	17,674	18,226	18,509	18,715	18,193	18,367	18,367	18,429	18,429	18,565	18,897
Surgical operations	5.19	6.30	6.83	7.18	6.24	6.57	6.57	6.68	6.68	6.93	7.45
Urodynamic tests	4326	5342	5863	6243	5281	5601	5601	5716	5716	5965	6577
Total pad use	17,824	19,076	19,807	20,402	18,996	19,429	19,429	19,592	19,592	19,960	20,999
On treatment	9959	8915	8306	7811	8982	8621	8621	8485	8485	8179	7313
Off treatment	7864	10,161	11,501	12,591	10,014	10,807	10,807	11,107	11,107	11,781	13,687

All doses reported are the total dose per day

ER extended release, *GP* general practitioner, *IR* immediate release

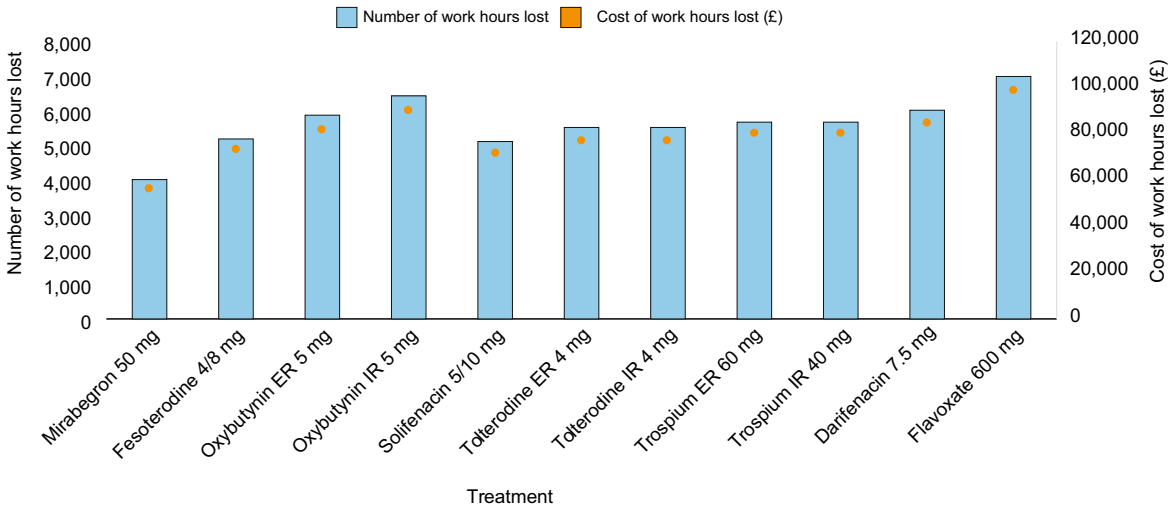


Fig. 5 Total work hours lost over 12 months and associated costs for each treatment per 100 patients. All doses reported are the total dose per day. *ER* extended release, *IR* immediate release

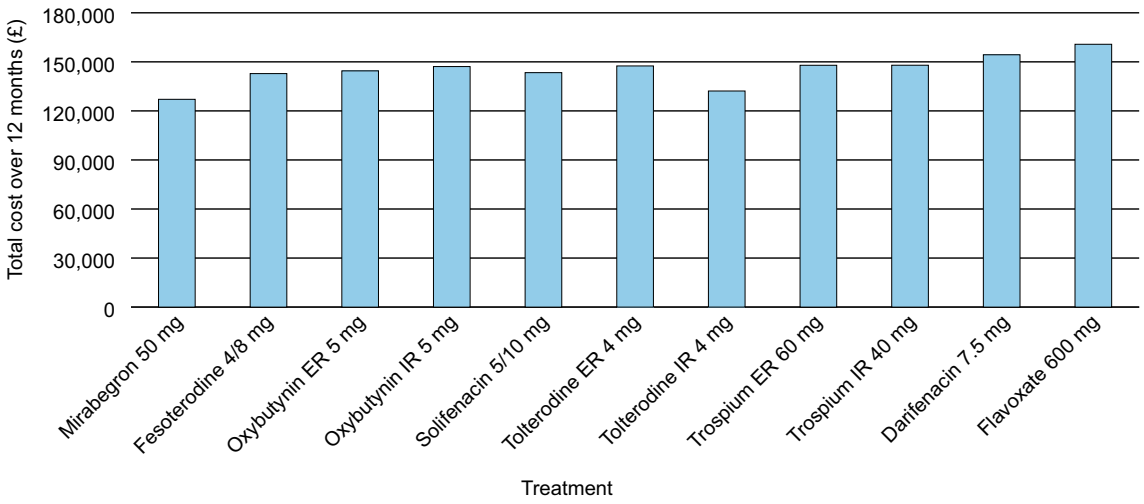


Fig. 6 Total costs (including indirect costs) over 12 months for each treatment per 100 patients. All doses reported are the total dose per day. *ER* extended release, *IR* immediate release

placebo but a lower incidence for mirabegron 50 mg versus all antimuscarinics assessed [11]. These findings may be reflected in the present study, as healthcare resource use was lower for mirabegron 50 mg than for all antimuscarinics, with fewer associated costs. However, it should be noted that treatment discontinuation can be attributed to many factors, and a greater overall focus should be applied to tailoring OAB treatment to the individual.

The primary strengths of this model are that it utilizes real-world data related to treatment of OAB and healthcare resource use in the UK. Therefore, the total costs derived for mirabegron versus antimuscarinics are based on effectiveness rather than efficacy. However, the findings that suggest a benefit of mirabegron (if used as first-line pharmacotherapy for OAB) depend on the several key assumptions made in the model, such as persistence at 12 months being independent of the treatment dose received and persistence not varying between trospium ER and IR and tolterodine ER and IR. Furthermore, all patients who switch treatment or undergo surgical operations are assumed to have controlled symptoms, and this would be variable. Structural edits to the model would be required to account for these factors if additional sensitivity analyses were to be performed. As OAB is a chronic condition, provision of a longer time horizon would be beneficial to accurately estimate the economic benefits of long-term treatment. Another limitation is that no direct clinical data for estimates of efficacy, tolerability or health-related QoL were included; therefore, some patient perspectives were not captured. With respect to the treatment comparators,

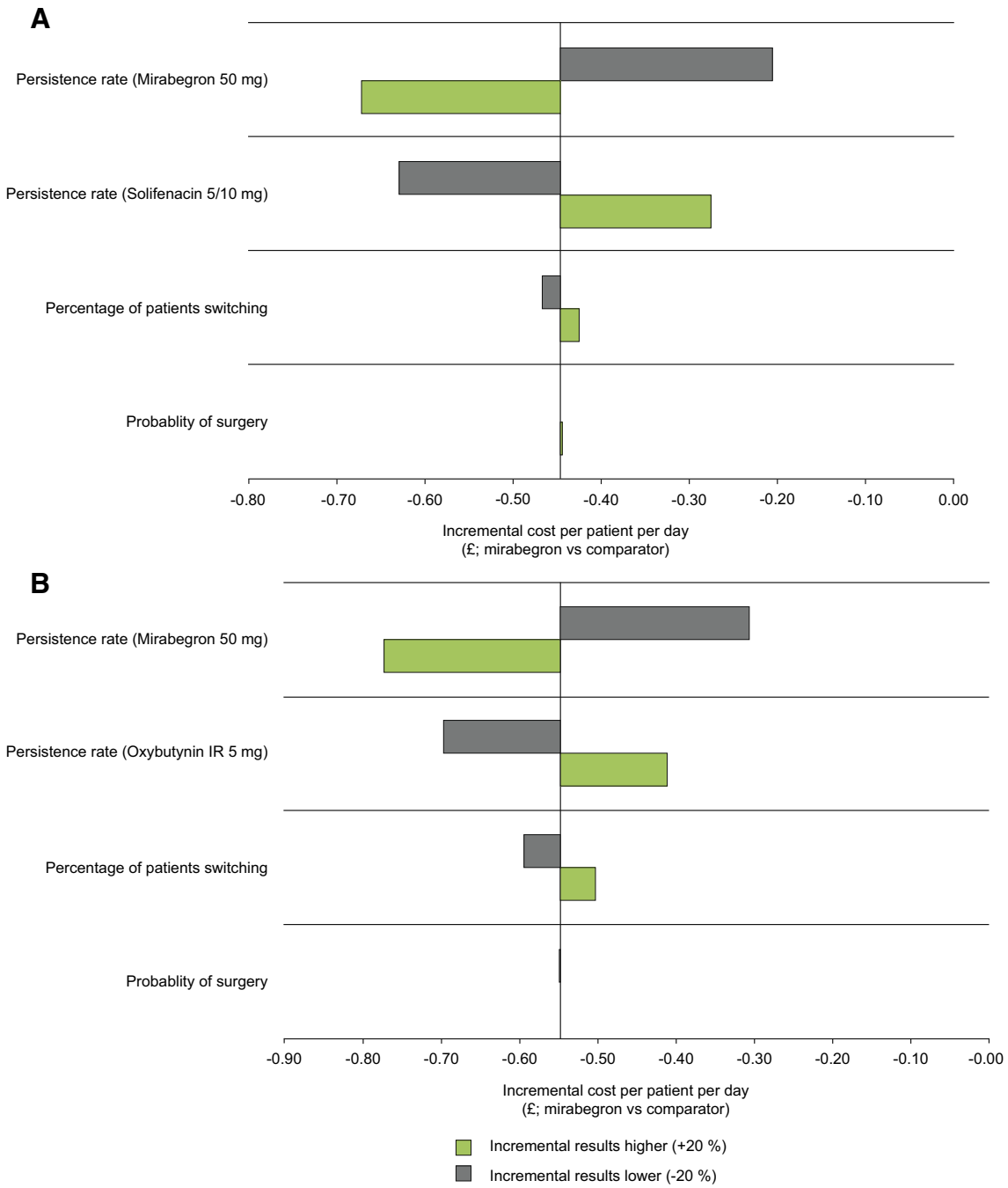


Fig. 7 Results of the deterministic sensitivity analysis for mirabegron 50 mg versus **a** solifenacin 5/10 mg and **b** oxybutynin IR 5 mg (incremental cost per patient per day). All doses reported are the total dose per day. *IR* immediate release

the model includes the most common treatment options for OAB in the UK according to the results of a retrospective analysis of a clinical practice database [16]; this included flavoxate, which is not recommended for use in women with urinary incontinence in the UK [29].

Although the model does not account for persistence in different subgroups of patients, results were largely consistent with the total study population, and few differences in persistence between subgroups were observed in a Canadian study of persistence with mirabegron 50 mg versus antimuscarinics over 12 months (the only notable difference was that patients were more likely to persist as the number of co-existing prescribed medications increased [up to more than eight]) [13]. Whether differences between subgroups would be observed if the model were updated to allow these kinds of analyses is unclear. The persistence data used in the model were taken from a large non-interventional study conducted in the UK [16];

patient demographics in this study were generally well-balanced across treatment groups, although significantly more patients receiving mirabegron were female, treatment-experienced and receiving co-existing medications compared with those receiving the primary comparator treatment (tolterodine ER).

5 Conclusions

This model suggests that treatment of OAB in the UK with mirabegron 50 mg will result in more patients persisting with treatment and lower total costs of treatment versus antimuscarinics. Further work is needed to confirm these findings in different populations to assess the effect of mirabegron on persistence and overall treatment costs in other countries.

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Compliance with Ethical Standards

Conflict of interest AW received research grants from Astellas Pharma Europe Ltd, Pfizer Inc. and the Canadian Urological Association. He also received consulting fees or honoraria from SCA, Astellas Pharma Europe Ltd, Pfizer Inc. and Duchesnay Inc. MB and CMc received consulting fees from Astellas Pharma Europe Ltd for developing the model as part of the PAREXEL team. FF received grant funding from Astellas Pharma Europe Ltd. JN, SB and ZH are employees of Astellas Pharma Europe Ltd. No research involved human participants and/or animals, and no informed consent was required.

Data availability The datasets generated and/or analysed during the current study are not publically available because the model is proprietary. However, all appropriate data generated or analysed during this study are included in this published article and its supplementary information files.

References

1. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology. 2003;61(1):37–49.
2. Milsom I, Abrams P, Cardozo L, Roberts RG, Thüroff J, Wein AJ. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. BJU Int. 2001;87(9):760–6.
3. Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, et al. Prevalence and burden of overactive bladder in the United States. World J Urol. 2003;20(6):327–36.
4. Brown JS, McGhan WF, Chokroverty S. Comorbidities associated with overactive bladder. Am J Manag Care. 2000;6(11 Suppl):S574–9.
5. Abrams P, Kelleher CJ, Kerr LA, Rogers RG. Overactive bladder significantly affects quality of life. Am J Manag Care. 2000;6(11 Suppl):S580–90.
6. Irwin DE, Mungapen L, Milsom I, Kopp Z, Reeves P, Kelleher C. The economic impact of overactive bladder syndrome in six Western countries. BJU Int. 2009;103(2):202–9.
7. Lucas MG, Bedretdinova D, Berghmans, LC, Bosch JLHR, Burkhard FC, Cruz F, et al. Guidelines on urinary incontinence. http://uroweb.org/wp-content/uploads/20-Urinary-Incontinence LR1.pdf/. Accessed 16 May 2016.
8. Benner JS, Nichol MB, Rovner ES, Jumadilova Z, Alvir J, Hussein M. Patient-reported reasons for discontinuing overactive bladder medication. BJU Int. 2010;105(9):1276–82.
9. European Medicines Agency. Betmiga EPAR Product Information. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002388/human_med_001605.jsp&mid=WC0b01ac058001d124/. Accessed 17 Aug 2016.
10. Sacco E, Bientinesi R. Mirabegron: a review of recent data and its prospects in the management of overactive bladder. Ther Adv Urol. 2012;4(6):315–24.
11. Maman K, Aballea S, Nazir J, Desroziers K, Neine ME, Siddiqui E, et al. Comparative efficacy and safety of medical treatments for the management of overactive bladder: a systematic literature review and mixed treatment comparison. Eur Urol. 2014;65(4):755–65.
12. Nitti VW, Chapple CR, Walters C, Blauwet MB, Herschorn S, Milsom I, et al. Safety and tolerability of the beta3-adrenoceptor agonist mirabegron, for the treatment of overactive bladder: results of a prospective pooled analysis of three 12-week randomised Phase III trials and of a 1-year randomised Phase III trial. Int J Clin Pract. 2014;68(8):972–85.
13. Wagg A, Franks B, Ramos B, Berner T. Persistence and adherence with the new beta-3 receptor agonist, mirabegron, versus antimuscarinics in overactive bladder: early experience in Canada. Can Urol Assoc J. 2015;9(9–10):343–50.
14. Andy UU, Arya LA, Smith AL, Propert KJ, Bogner HR, Colavita K, et al. Is self-reported adherence associated with clinical outcomes in women treated with anticholinergic medication for overactive bladder? Neurourol Urodyn. 2015;35(6):738–42.
15. Kim TH, Lee KS. Persistence and compliance with medication management in the treatment of overactive bladder. Investig Clin Urol. 2016;57(2):84–93.
16. Astellas. Mirabegron vs antimuscarinics in OAB: retrospective analysis of a UK general practice prescription database. Data on file. 2016.
17. Nazir J, Maman K, Neine ME, Briquet B, Odeyemi IA, Hakimi Z, et al. Cost-effectiveness of mirabegron compared with

antimuscarinic agents for the treatment of adults with overactive bladder in the United Kingdom. Value Health. 2015;18(6):783–90.
18. Office for National Statistics. Mortality statistics: Deaths registered in the UK by areas of usual residence. http://www.ons.gov.uk/ons/rel/vsob1/deaths-registered-area-usual-residence/2014/index.html/. Accessed 17 May 2016.
19. Nazir J, Posnett J, Walker A, Odeyemi IA, Hakimi Z, Garnham A. Economic evaluation of pharmacological treatments for overactive bladder from the perspective of the UK National Health Service. J Med Econ. 2015;18(5):390–7.
20. National Health Service. NHS reference costs 2014 to 2015. https://www.gov.uk/government/publications/nhs-reference-costs-2014-to-2015/. Accessed 1 July 2016.
21. Personal Social Services Research Unit (PSSRU). Unit costs of health and social care 2014. http://www.pssru.ac.uk/project-pages/unit-costs/2014/. Accessed 1 July 2016.
22. Nitti VW, Khullar V, van Kerrebroeck P, Herschorn S, Cambronero J, Angulo JC, et al. Mirabegron for the treatment of overactive bladder: a prespecified pooled efficacy analysis and pooled safety analysis of three randomised, double-blind, placebo-controlled, phase III studies. Int J Clin Pract. 2013;67(7):619–32.
23. British Medical Association, Royal Pharmaceutical Society. British National Formulary 71st edition. Joint Formulary Committee. London: British Medical Association; 2016.
24. Astellas. Mirabegron. IMS Country Retail Sales Audit from March 2016. UK Market Shares for HEOR. Data on file. 2016.
25. Arlandis-Guzman S, Errando-Smet C, Trocio J, Arumi D, Rejas J. Cost-effectiveness analysis of antimuscarinics in the treatment of patients with overactive bladder in Spain: a decision-tree model. BMC Urol. 2011;11:9.
26. Astellas. Mirabegron. Mirabegron cost-effectiveness model for the UK. Technical report. Data on file. 2016.
27. Office for National Statistics. Earnings (inflation adjusted) have risen by 62% since 1986. http://webarchive.nationalarchives.gov.uk/20160105160709/http:/www.ons.gov.uk/ons/rel/lmac/earnings-in-the-uk-over-the-past-25-years/2012/sty-pay-over-25-years.html/. Accessed 19 Jan 2017
28. Briggs AH, Weinstein MC, Fenwick EA, Karnon J, Sculpher MJ, et al. Model parameter estimation and uncertainty: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–6. Value Health. 2012;15(6):835–42.
29. National Institute for Health and Care Excellence. Urinary incontinence in women: management. Clinical guideline. London: NICE; 11 September 2013. https://www.nice.org.uk/guidance/cg171/resources/urinary-incontinence-in-women-management-35109747194821/. Accessed 1 July 2016.
30. NHS South Devonshire. Private patient and overseas visitor price list, effective from 1st of April-31st March 2016. http://www.torbayandsouthdevon.nhs.uk/uploads/23968.pdf. Accessed 18 May 2016.
31. Incontinence Direct UK: LILIFORM Large Shaped Pads. http://www.incontinencedirect.co.uk/ladies-incontinence-products/disposable-products/LILFORM-Large-Shaped-Pads/. Accessed 1 July 2016.