Pharmacoeconomic evaluation of antimuscarinic agents for the treatment of overactive bladder
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study compared different antimuscarinic agents for the treatment of overactive bladder (OAB). The antimuscarinic agents and doses compared in the analysis were:

- immediate-release (IR) oxybutynin, 5 mg, 3 times daily;
- extended-release (ER) oxybutynin, 10 mg, once daily;
- transdermal (TD) oxybutynin, 3.9-mg patch, every 3 to 4 days, or two patches per week;
- IR tolterodine, 2 mg, twice daily;
- ER tolterodine, 4 mg, once daily;
- trospium, 20 mg, twice daily;
- solifenacin, 5 mg, once daily; and
- darifenacin, 15 mg, once daily.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The population comprised patients with OAB. No further details were provided.

Setting
The setting was outpatient care. The economic evaluation was conducted in the USA.

Dates to which data relate
The main data to feed the model were obtained from articles published from 1998 to 2005. The costs were expressed in 2005 prices.

Source of effectiveness data
The clinical outcomes of taking antimuscarinic agents included therapy continued or discontinued, treatment success or
failure, and OAB-induced co-morbidities. Treatment success was defined as complete continence (e.g. no incontinence episodes, or 7 continuous dry days). The discontinuation rates due to adverse effects, as reported in clinical trials, were used as the discontinuation rates in the model. Co-morbidities included urinary tract infections, bone fractures, depression and skin infections.

**Modelling**
A decision tree with a 3-month time horizon was developed. A full outline of treatment pathways, including adverse events and outcomes, along with a graphical representation of the model, was reported.

**Sources searched to identify primary studies**
The continence rates and adverse event-related discontinuation rates of the drugs were taken from six clinical trials; these were mainly randomised controlled trials (RCTs). Rates of OAB-induced co-morbidities for three risk groups (low, medium and high) were derived from three trials, the designs of which were not specified.

**Methods used to judge relevance and validity, and for extracting data**
The authors stated that they systematically searched MEDLINE for published trials. Articles published and indexed in MEDLINE from January 1990 to January 2006 were eligible for inclusion. The search was limited to publications in the English language and the drug names were used to identify relevant studies. Inclusion criteria were not explicitly stated. The method used to select the parameters was not discussed. For one parameter (rates for ER tolterodine), the authors stated that results from two RCTs were combined and weighted by sample size. Three patient risk groups (low, medium and high) were linked to treatment outcome (success, failure and discontinuation) to enable OAB co-morbidities to be appropriately evaluated within the model.

**Measure of benefits used in the economic analysis**
The summary measure used for the economic analysis was "patient with continued and/or successful treatment". Discounting was not conducted as the time horizon for the analysis was only 3 months.

**Direct costs**
The costs of medications and adverse events were included in the analysis. Medication unit costs were calculated using the lowest average wholesale price per unit from Medi-Span (Indianapolis, IN) as of February 2005 for all drugs, except IR oxybutynin for which a generic was available. For IR oxybutynin, the mean of the average wholesale price per unit was applied. The costs of adverse events per episode were obtained from the literature. These costs were adjusted for inflation to reflect 2005 US dollars by using the Bureau of Labour Statistics Consumer Price Index for all urban consumers for medical care services. No details of the cost categories included in the source study were reported. Discounting was not undertaken as the time horizon for the analysis was only 3 months.

**Statistical analysis of costs**
The data were deterministic.

**Indirect Costs**
Productivity costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
The authors investigated parameter uncertainty within the model by conducting a one-way sensitivity analysis. They used a +/- 20% variation around the point estimate for the discontinuation rate and cost of treating OAB-induced co-morbidity, the highest and lowest average wholesale costs for each antimuscarinic agent, and +/- 50% (or a higher range if reported in the literature) for success rate. No other source of uncertainty was explored.

**Estimated benefits used in the economic analysis**

The solifenacin strategy dominated all others antimuscarinic agents (i.e. it was more effective and less costly than the other options).

The proportion of patients with continuous and successful treatment with solifenacin, the strategy that dominated all others, was 0.491. Incremental effectiveness results were presented for all other strategies with respect to solifenacin.

The side-effects of treatment were included in the model, with a risk of discontinuation because of adverse events.

**Cost results**

The total costs for the different strategies were as follows:

- solifenacin $3,373,
- oxybutynin TD $3,603,
- darifenacin $3,633,
- oxybutynin ER $3,646,
- tolterodine ER $3,659,
- trospium $3,722,
- tolterodine IR $3,750, and
- oxybutynin IR $3,769.

The costs of co-morbidities were included in the analysis.

The incremental costs with respect to solifenacin were as follows:

- oxybutynin TD $230,
- darifenacin $260,
- oxybutynin ER $273,
- tolterodine ER $287,
- trospium $349,
- tolterodine IR $378, and
- oxybutynin IR $396.

**Synthesis of costs and benefits**

The authors stated that they had intended to estimate the average cost-effectiveness ratios as well as the incremental cost-effectiveness ratios. However, as solifenacin dominated all other options, only average ratios were presented.
The average cost-effectiveness ratios were as follows:

- solifenacin $6,863,
- oxybutynin TD $10,346,
- darifenacin $15,462,
- oxybutynin ER $16,704,
- tolterodine ER $17,486,
- trospium $19,434,
- tolterodine IR $18,999, and
- oxybutynin IR $21,685.

The model results were sensitive to the success rate of each product, namely, when the sensitivity analysis was conducted with extreme range values. For example, when the success rate of solifenacin was reduced by 50% to 0.25, TD oxybutynin dominated all comparators.

**Authors’ conclusions**

Amongst the various antimuscarinic agents, solifenacin 5 mg had the lowest cost and highest effectiveness in the treatment of overactive bladder (OAB).

**CRD COMMENTARY - Selection of comparators**

The authors stated that their objective was to compare the cost-effectiveness of currently available antimuscarinic agents for OAB. Thus, the choice of the comparators appears to have represented all those potentially relevant available technologies in the authors' setting. You should decide if these are relevant options in your own setting.

**Validity of estimate of measure of effectiveness**

The model parameters were obtained from published sources. The authors stated that a systematic search of MEDLINE was conducted to identify all published trials. It was unclear whether all the steps for a well-conducted systematic review were followed. Apparently, only one RCT was generally identified for each antimuscarinic agent. The exception was tolterodine ER for which two RCTs were used. These RCTs results were combined and weighted by sample size. The authors reported the sample sizes of the RCTs used to derive data inputs for their model. However, they did not provide any confidence intervals for input estimates (e.g. success rates or discontinuation rates). Overall, it was difficult to fully ascertain the validity of the estimates used in the model.

**Validity of estimate of measure of benefit**

The authors used the proportion of patients with continuous and successful treatment for their cost-effectiveness analysis. The model also allowed for co-morbidities. However, a general measure of quantity and quality of life could potentially have captured the benefits of the interventions more comprehensively. For instance, adverse effects could make individuals opt out of treatment. This was captured within the model using a discontinuation rate. However, a hypothetical situation in which side effects lowered the individual's quality of life, but did not make him or her stop treatment, would not be considered within the authors' analysis. The authors conceded that a cost-utility analysis was a potentially useful approach when discussing the lack of utility data for each comparator in order to incorporate quality of life into the model.

**Validity of estimate of costs**

The authors did not report many details about the costs, other than the fact that they were obtained from the literature.
and were adjusted for inflation. Average wholesale prices were used for drugs, and their doses and frequency of administration were reported. However, no details of the cost components included within the adverse event cost category were presented. This could hinder the generalisability of the results to other settings. The level of reporting around the cost data was very limited.

**Other issues**
The authors compared their findings with those of other studies. Notwithstanding the difficulties arising from the different timeframes used, and differences in the types of costs and comparators, they found that their findings were analogous to previous observations. The authors do not appear to have presented their results selectively and their conclusions were justified by the methods and the results obtained.

The authors acknowledged a number of limitations to their study. First, the economic evaluation did not include a "no treatment" strategy, as the authors were looking at alternatives once treatment was decided. Second, the analysis did not include other drug treatment or no drug treatment, alone or in combination with the comparators. Third, the lack of clinical data did not allow them to consider the possibility of switching therapies or the incorporation of dose titration into the model. Finally, the authors addressed the issue of generalisability, stating that their focus was on outpatient care and, therefore, their results might not be generalisable to hospitals or long-term care facilities.

**Implications of the study**
The authors state that studies that conduct a comprehensive comparison of the treatment alternatives, either alone or in combination, for the long-term management of OAB are needed.

**Source of funding**
None stated.

**Bibliographic details**

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**Other publications of related interest**
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**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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