This overview has been prepared by staff at the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) and is based in part on a study completed by CCOHTA: Cost-Effectiveness and Cost-Utility Analyses of Finasteride Therapy for the Treatment of Benign Prostatic Hyperplasia conducted by Mr. Jean-François Baladi, Research Associate (CCOHTA).

The study has been reviewed and accepted by CCOHTA’s Scientific Advisory Panel. The findings of the study do not necessarily reflect the opinions of the Panel, the Board of CCOHTA or the clinical reviewers.
Additional copies of *Finasteride: Clinical and Economic Impacts* are available from CCOHTA.

Vous pouvez aussi vous procurer la version française à l'OCCETS.

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This overview is based on data obtained in a study completed by CCOHTA entitled *Cost-Effectiveness and Cost-Utility Analyses of Finasteride Therapy for the Treatment of Benign Prostatic Hyperplasia*. It attempts to put these findings into clinical perspective.
CONCLUSIONS

Benign prostatic hypertrophy is a common disorder where several treatment options are available. These include medical (finasteride, alpha blockers), surgery (TURP, open prostatectomy, transurethral incision of the prostate), and watchful waiting. The choice of treatment is dependent upon symptom severity and patient’s perception of the ‘bothersomeness’ of the symptoms. It has been recommended that symptoms are best assessed using the AUA Symptom Index.

This evaluation focused on a new medical treatment, finasteride, and compared it to the two most common treatment options: TURP and watchful waiting. The results indicated that the choice of finasteride is dependent upon two factors: life expectancy (primarily because most of the surgical costs are borne in year one while maintenance medical therapy costs are ongoing) and severity of symptoms (surgical therapy will convert severe symptoms to mild symptoms while medical therapy is only able to reduce symptoms from severe to moderate).

A. Mild Symptoms

Surgical and medical treatments are not required and therefore watchful waiting is the most appropriate treatment option.

B. Moderate Symptoms

1) Life expectancy less than 3 years: Finasteride is cheaper than other options.

2) Life expectancy from 4 to 14 years: Slightly improved quality of life compared to doing nothing but at a cost ranging from $19,000/QALY (quality of life year) at 4 years to $44,000/QALY at 15 years. Finasteride is a cheaper alternative with better results than surgery.

3) Life expectancy over 14 years: Cost/QALY levels off at around $45,000 compared to watchful waiting. Compared to TURP the slightly improved quality of life now begins to cost the health care system but at relatively minor additional cost ($1,000/QALY).

C. Severe Symptoms

1) Life expectancy less than 3 years: Finasteride produces less quality of life but is a less expensive option compared to the two other treatments.

2) Life expectancy from 4 to 14 years: Finasteride produces less quality of life and at more cost than watchful waiting! Compared to surgery, it is less expensive but with poorer results. Because the drug is either more expensive than one of the options or is much less effective than surgery, finasteride would not be considered first line therapy in this group.

3) Life expectancy over 14 years: Finasteride costs more and provides poorer results than either therapy. TURP offers the highest QALY at a relatively low cost of $4,000 to $15,000.

Finally, if one looks at the aggregate impact, the addition of finasteride for only patients classified as moderate (as this analysis suggests would be the population most likely to benefit) would be $2.7 million dollars for every 10,000 men 60 years or older in the general population. However, if one assumes that 30% of mild patients would end up receiving the drug (where watchful waiting is the appropriate therapy) then an additional $2.9 million or $5.6 million in total/10,000 men 60 years or older would be required to fund this therapy in Canada.
INTRODUCTION

Benign prostatic hypertrophy (BPH) is the most common benign neoplasm in males. Even though microscopic evidence of BPH is evident in approximately 50% of men aged 60 and over, only 25% of those will suffer symptoms. By age 85, more than 25% of men will complain of symptoms.

The clinical manifestations of this condition relate to the obstruction of urinary flow and to bladder dysfunction. This includes hesitancy, dribbling, decreased size or force of urine stream, incomplete emptying, urgency, dysuria and straining. The changes tend to occur gradually. Initially, in approximately 42% of men, symptoms will improve without any intervention (referred to as watchful waiting). Long term epidemiological studies are lacking as to how many will require a future medical intervention.

Quantification of symptom severity is recognized as the best diagnostic tool and is the best predictor of the condition. Neither prostate size nor objective measurements such as peak urinary flow rates correlate with symptom severity. The recommended instrument for quantifying symptoms is the American Urological Association (AUA) Symptom Index. The AUA scoring system, based on the classifications of mild (0 to 7 points), moderate (8 to 19 points), or severe (20 to 35 points), can be used to plan and monitor treatment.

The most common treatment options are watchful waiting (i.e., no treatment), surgery (including transurethral resection of the prostate, transurethral incision of the prostate and open prostatectomy) and medical (finasteride and alpha blockers such as terazosin). Other treatments are available but are unproven (e.g., hyperthermia) or ineffective (e.g., balloon dilation). Of the treatment options, the most common are watchful waiting and transurethral resection of the prostate (TURP).

Efficacy

Two randomized controlled trials have compared finasteride versus placebo in men with benign prostatic hypertrophy. Followup was conducted in an open label trial for a further two years. The following conclusions can be derived from these studies:

1) Patients must stay on the drug for a full six months (at a dose of 5 mg daily) to determine if they will respond favourably.
2) Decrease in prostate size, decrease in urinary symptoms and improvement in symptom score can be demonstrated.
3) Approximately 67% of patients improved on the drug as compared to 42% who improved on just watchful waiting during the controlled phase of the trial. In those who responded, improvement was maintained over the 36 months.
4) Almost 50% of men given the choice of continuing therapy (extension study) declined.
5) Although a greater drop in symptom score was demonstrated in those with the most severe form of BPH, the actual percentage improvement of score was similar in all classifications. Most of the patients in the trials were of the mild and moderate classifications.
6) Adverse effects from finasteride therapy were minimal with a slight increase in frequency of decreased libido, ejaculation disorders and impotence compared to the placebo. Of concern is the approximately 50% drop in prostate-specific antigen (PSA) making the diagnosis of prostate cancer more tentative.
In this paper, finasteride will be compared with the two most common treatment options utilizing cost-effectiveness and cost-utility analytical tools. The Guidelines for Economic Evaluation of Pharmaceuticals: Canada were followed in conducting this analysis. The clinical information was derived from randomized control trials of finasteride and Clinical Practice Guidelines published by the Public Health Service Agency for Health Care Policy and Research (AHCPR). Details of the analysis may be obtained through a separate technical document produced by CCOHTA.

PARAMETERS OF THE EVALUATION

a) Product Description

Finasteride (Proscar® - Merck & Co.) approved in Canada for the treatment of benign prostatic hyperplasia (BPH).

b) Target Audience

Provincial/territorial health care systems.

c) Treatment Comparators

Transurethral resection of the prostate (TURP) and watchful waiting.

d) Type of Analysis

Literature evaluation; decision model using results from two randomized control trials; both cost-effectiveness and cost-utility.

e) Outcome of Interest

Symptom improvement using symptom severity scores (based on the AUA Symptom Index) and quality adjusted life years (QALYs).

f) Time Horizon

1 to 15 years.

EFFECTIVENESS

The AUA symptom scoring system was used as the effectiveness tool. The three states (mild, moderate and severe) were taken as distinct classifications. The best one can expect from watchful waiting and finasteride is to decrease symptoms by one level, i.e., from severe to moderate or moderate to mild. Surgical intervention (TURP) may reduce symptoms sufficiently to put all patients into a mild state.

Several other health states are taken into account. Most are as a result of surgery (stress incontinence, impotence, total urinary incontinence or peri-operative death). No improvement was also considered as one of the outcomes.

The probabilities of the following outcomes were taken from the Clinical Practice Guideline publication, Benign Prostatic Hyperplasia: Diagnosis and Treatment, published by the U.S. Department of Health and Human Services (AHCPR).
Financial impact: Clinical and economic impacts

1) **Watchful Waiting**
   - Improvement (42%); no improvement but no further therapy (20%); TURP (38%).

2) **Finasteride**
   - Improvement (67%); no improvement but no further therapy (23%); TURP (10%).

3) **TURP**
   - Improvement (72%); improvement with incontinence or impotence (14%); no improvement (9%); incontinent (1%); intraoperative death (1.5%).

These probabilities were used to develop a decision model for the three interventions. The costs for each probability were determined and summed to produce the total expected costs. The ‘decision trees’ were used for both the cost-effectiveness and cost-utility analyses. Finally, the probabilities of the outcomes were varied, generally using the high and low probabilities and costs, to determine whether the results of the analysis would be impacted by the assumptions and clinical data available.

**COSTS**

Annual direct costs to the health care system were determined for each intervention. The following costs were used for each of the three interventions.

**TABLE 1: Cost Elements and Mean Costs**

<table>
<thead>
<tr>
<th>COST ELEMENTS</th>
<th>TURP 1st yr</th>
<th>TURP Subsequent yr</th>
<th>FINASTERIDE 1st yr</th>
<th>FINASTERIDE Subsequent yr</th>
<th>WATCHFUL WAITING 1st yr</th>
<th>WATCHFUL WAITING Subsequent yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital &amp; OR costs</td>
<td>$4,264</td>
<td>$0</td>
<td>$0</td>
<td>$0</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>Diagnostic procedures &amp; laboratory tests</td>
<td>220</td>
<td>15</td>
<td>38</td>
<td>38</td>
<td>38</td>
<td>38</td>
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<tr>
<td>Professional fees</td>
<td>555</td>
<td>26</td>
<td>209</td>
<td>104</td>
<td>104</td>
<td>104</td>
</tr>
<tr>
<td>Complication costs</td>
<td>369</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Finasteride costs</td>
<td>0</td>
<td>0</td>
<td>679</td>
<td>679</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>$5,408</td>
<td>$41</td>
<td>$926</td>
<td>$821</td>
<td>$142</td>
<td>$142</td>
</tr>
</tbody>
</table>

Table 2 below demonstrates the range of costs for each of the interventions.

**TABLE 2: Provincial Ranges**

<table>
<thead>
<tr>
<th></th>
<th>TURP 1st yr</th>
<th>TURP Subsequent yr</th>
<th>FINASTERIDE 1st yr</th>
<th>FINASTERIDE Subsequent yr</th>
<th>WATCHFUL WAITING 1st yr</th>
<th>WATCHFUL WAITING Subsequent yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>$5,797</td>
<td>$55 (MAN)</td>
<td>$1,036 (B.C.)</td>
<td>$874 (B.C.)</td>
<td>$377 (B.C.)</td>
<td>$357 (B.C.)</td>
</tr>
<tr>
<td></td>
<td>$5,187</td>
<td>$33 (NFLD)</td>
<td>$861 (QUE)</td>
<td>$789 (QUE)</td>
<td>$182 (QUE)</td>
<td>$182 (QUE)</td>
</tr>
<tr>
<td>Low</td>
<td>$5,187</td>
<td>$33 (NFLD)</td>
<td>$861 (QUE)</td>
<td>$789 (QUE)</td>
<td>$182 (QUE)</td>
<td>$182 (QUE)</td>
</tr>
</tbody>
</table>
Health Utilities Index

The Health Utilities Index - Mark II system was chosen as the utility index. This index covers the following attributes: sensation, mobility, emotion, cognition, self-care, pain, and fertility. Each of these attributes is scaled from 0 (death) to 1 (perfect health). There were six health states assessed: the symptom scale of mild, moderate, and severe prostatism as well as the adverse events associated with surgery (TURP): stress incontinence, impotence, and total urinary incontinence. The emotion attribute varied from 0.81 for the incontinence states to 0.989 for mild BPH symptoms. The mobility attribute was assigned a value of 1 for each state except for severe BPH symptoms where a value of 0.97 was assigned. The pain attribute was assigned a value of 1 for each health state except for stress and urinary incontinence where a value of 0.97 was assigned. Finally, the self-care attribute was valued at less than one for stress incontinence (0.97) and total urinary incontinence (0.91).

RESULTS

The following three figures summarize the analysis. Only results in patients suffering from moderate or severe symptoms are shown as the choice of watchful waiting is the most appropriate choice for men complaining of mild symptoms.

FIGURE 1: Finasteride vs Watchful Waiting
Finasteride not only produces more QALYs than surgery, but is also less costly for all men suffering from mild symptoms and whose life expectancy is 14 years or less. For men whose life expectancy exceeds 14 years finasteride still produces higher QALYs but at a higher cost. For men suffering from severe symptoms, surgery produces a better quality of life for all years evaluated but at a higher cost. This cost difference decreases over time until a life expectancy of 14 years or more is anticipated where surgery is actually less costly.

FIGURE 2: Finasteride vs TURP

For a life expectancy of 3 years or less finasteride is more cost effective and produces a better quality of life than watchful waiting in moderate patients. From 3 years on, finasteride produces a better quality of life but at a higher cost. It would cost the health care system $842,000 more to use finasteride over watchful waiting over a 15 year period. However, this assumes that watchful waiting remains successful during that time period. If one were to assume, for example, that all watchful waiting patients would have to be medically treated within a year, then the extra cost would only be $19,000.

Finasteride on moderate patients and life span of 14 years or less
More QALYs
Less Costly

Finasteride on moderate patients and life span more than 14 years
More QALYs
More Costly

Finasteride on severe patients and life span of 14 years or less
Fewer QALYs
Less Costly

Finasteride on severe patients and life span more than 14 years
Fewer QALYs
More Costly

TURP

+ QALYs
- COSTS
- QALYs
+ COSTS
FIGURE 3: TURP vs Watchful Waiting

This figure indicates that watchful waiting is always less costly than TURP. For moderate symptoms watchful waiting also produces a better quality of life but for patients complaining of severe symptoms TURP, as the treatment option, produces a better quality of life at an extra cost.
ENDNOTES


Previous drafts of the technical document Cost-Effectiveness and Cost-Utility Analyses of Finasteride Therapy for the Treatment of Benign Prostatic Hyperplasia were reviewed by the Scientific Advisory Panel of CCOHTA:

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The Wellesley Hospital
Montreal, Quebec
Kirkland, Quebec
Ontario Ministry of Health
Alberta Health

CCOHTA would like to thank the above for their contributions. Staff have incorporated most of the comments received, and take full responsibility for content and form.

The complete report Cost-Effectiveness and Cost-Utility Analyses of Finasteride Therapy for the Treatment of Benign Prostatic Hyperplasia is available by contacting CCOHTA. Please address all enquiries and correspondence to: Publications, CCOHTA, 110-955 Green Valley Crescent, Ottawa, Ontario, Canada, K2C 3V4. Tel.: (613) 226-2553; Fax: (613) 226-5392; Internet: pubs@ccohta.ca.