LETTER TO THE EDITOR

Re: An economic evaluation of doxazosin, finasteride and combination therapy in the treatment of benign prostatic hyperplasia

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To the Editor: McDonald et al[1] conducted a cost-utility analysis to compare the relative merits of alpha-blockers, 5-alpha-reductase inhibitors, and their combination in the treatment of men with moderate to severe BPH. This article is an important contribution to the literature, because the cost-utility of combination pharmacotherapy relative to monotherapy has not been presented previously. This rigorously constructed model extends and improves upon other models, including the model produced by the Canadian Coordinating Office of Health Technology Assessment (CCOHTA).[2] Cost-effectiveness models rely on assumptions and information from the published literature, which have widely-acknowledged limitations.[3]

The method the authors used to assign increments in quality-adjusted life years (QALYs) to pharmaceuticals is different than the method they applied to TURP, the model's alternative for pharmaceutical failure. For pharmaceutical treatments, a one-unit decrease in American Urological Association Symptom Index (AUA-SI) corresponds to an increment in QALY of 0.0138. For example, a patient with a 5-point decrease in the AUA-SI would have an increment in QALY of 0.069 added to baseline Table 1, Example 1. The AUA-SI, a disease-specific health-related quality of life instrument, was not designed to value health states in terms of QALYs; therefore, QALYs were derived. The increment in QALY was derived based on modeling the relationship between QALYS assigned to mild, moderate, and severe symptoms (.99, .90, and .79, respectively)[2] and the change in AUA-SI score following treatment.

The authors assume an increment in QALY due to TURP of 0.0440 Table 1. This was derived from the mean change in preferences elicited directly from patients using the EuroQol,[4] before and after TURP (0.772 and 0.816, respectively).[5] The EuroQol, a generic instrument for describing and valuing health states, measures the health-related quality of life with five dimensions (mobility, self-care, normal activity, pain/discomfort and mood). The response levels in each dimension are weighted to produce a composite utility weight or QALY.

Clinically, TURP is significantly more effective at reducing AUA-SI (10-11 units)[5] than pharmaceuticals (5 to 7 units);[6] however, this is not demonstrated using this model's weighting. For the same decrease in AUA-SI, the treatment QALYs are lower for TURP than pharmaceuticals due to the use of two different algorithms Table 1.

The magnitude of change in the AUA-SI that is perceptible to patients is not well-established and varies by baseline symptom levels.[7] The relationship between AUA-SI and the increment in QALYs may

TABLE 1. **Hypothetical patient profiles**

Example Number	AUA-SI[a] Baseline	AUA-SI[a] Treatment	AUA-SI[a] Change from baseline	QALYs Baseline	QALYs Treatment with pharmaceuticals[b]	QALYs Treatment with TURP[c]	QALYs Difference[d]
1	12	7	5	0.90	0.969	0.944	0.025
2	16	8	8	0.90	1.000	0.944	0.056
3	21	11	10	0.79	0.928	0.834	0.094

[a]AUA-SI severity: 0-7 = mild, 8-19 = moderate, 20-35 = severe
[b]0.0138 increment in QALY per one-unit increase in AUA-SI (derived)
[c]0.044 increment in QALY due to successful TURP from the EuroQol
[d]Difference = QALY for pharmaceuticals minus QALY for TURP

not be linear for the larger changes in AUA-SI. However, the increment in QALY applied to pharmaceuticals in the model may have been overestimated relative to the increment in QALY due to TURP. Using the same algorithm for the increment in QALYs for pharmaceuticals and TURP (0.0138 per one-unit decrease in AUA-SI) might not change the authors' model results appreciably; however, their approach might have a significant effect on the results if pharmaceuticals were compared directly to TURP. The model developed by McDonald and colleagues was rigorously constructed. We wanted to emphasize that deriving the increment in QALYs based on changes in AUA-SI might produce very different results relative to the patient preferences elicited directly from patients using the EuroQol. Therefore, applying a combination of algorithms for the increment in QALYs in the same model might further complicate or confuse the issue. Alternatives to the authors' approach include applying a uniform standard for all treatments (such as 0.0138 per one-unit reduction in AUA-SI), using assumptions similar to the CCOHTA model,[2] or calculating the QALY from the AUA-SI directly.[8] We would be interested to know how the authors' cost-utility results might change if they applied these suggested alternatives.

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1. McDonald H, Hux M, Brisson M, Bernard L, Nickel JC. An economic evaluation of doxazosin, finasteride and combination therapy in the treatment of benign prostatic hyperplasia. *Can J Urol* 2004;11(4):2327-2340.
2. Baladi JF, Menon D, Otten N. An economic evaluation of finasteride for treatment of benign prostatic hyperplasia. *Pharmacoeconomics* 1996;9(5):443-454.
3. Gold MR, Siegel JE, Russell LB, Weinstein MCe. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press, 1996.
4. EuroQol—a new facility for the measurement of health-related quality of life. The EuroQol Group. *Health Policy* 1990;16(3):199-208.
5. Noble SM, Coast J, Brookes S et al. Transurethral prostate resection, noncontact laser therapy or conservative management in men with symptoms of benign prostatic enlargement? An economic evaluation. *J Urol* 2002;168(6):2476-2482.
6. McConnell JD, Roehrborn CG, Bautista OM et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003;349(25):2387-2398.
7. Barry MJ, Williford WO, Chang Y et al. Benign prostatic hyperplasia specific health status measures in clinical research: how much change in the American Urological Association symptom index and the benign prostatic hyperplasia impact index is perceptible to patients? *J Urol* 1995;154(5):1770-1774.
8. Kok ET, McDonnell J, Stolk EA, Stoevelaar HJ, Busschbach JJ. The valuation of the International Prostate Symptom Score (IPSS) for use in economic evaluations. *Eur Urol* 2002;42(5):491-497.

Reply by authors: DiSantostefano et al have thoughtfully reviewed the treatment of utility within our evaluation of finasteride for symptomatic treatment and reduction of prostate size in patients with BPH who choose not to undergo immediate surgery. They note that the utility effects of TURP were derived from a different source than those for pharmaceuticals, and that if the effect on symptom score alone is considered, the utility gain following TURP may have been underestimated.

Our evaluation compared pharmaceutical interventions for patients choosing not to undergo initial surgery. Since utility values derived directly from the relevant populations were not available from the literature, for the baseline health state and for the effect of each of the study comparators (alpha blocker, 5-alpha-reductase inhibitors, and their combination), we transformed symptom scores into QALYs. This seemed appropriate since most utilities and disutilities related to these treatments are correlated with the AUA. Baseline symptom scores for the population under study and improvements in symptom scores shown from the MTOPS study (5 to 7 points) were combined with a common utility decrement due to a change in symptom score (0.0138). This utility decrement was calculated based on utilities reported by Baladi et al[1] for consistency with the CCOHTA evaluation, and the population distribution of severity levels obtained from the MTOPS study.

For surgical intervention following failure of any of the primary treatments, the effect on quality of life and utility measured directly from patients using the Euroqol instrument before and after surgery, was 0.0440 points.[2] DiSantostefano et al note that TURP may have the effect of reducing symptom scores by 10 to 11 points (estimated from this same source).

However, applying their estimated improvement in utility due to TURP (10 points * 0.0138) to a patient with the average baseline utility of 0.8743 would result in a utility greater than one. In addition, a surgical intervention such as TURP has quality of life impacts beyond those resulting from a reduction of symptoms, and assessment directly from patients incorporates all other utilities and disutilities associated with surgery, including psychological impacts and side effects.

The modeling of utility was one of the challenging aspects of this project, and we applied the best estimate of utility available for each type of effect. For surgery, which has impacts beyond symptom score improvements, assessments directly from patients were judged to be the most valid. Sensitivity analyses were also conducted looking at alternative methods of calculating the QALY effects of surgery and symptom point differences, and the trends in cost/QALY for each PSA strata resembled those from the base case analysis.

One such sensitivity analysis may address the concern and alternative approach suggested by DiSantostefano et al. As reported in our paper, one sensitivity analysis incorporated QALY weights, as estimated by clinicians in the CCOHTA analysis for all parameters, including TURP (.0882 increment). In this analysis, the cost-effectiveness ratio of combination therapy relative to doxazosin was moderately higher than those for the base case scenario, ranging from $49,454/QALY for all patients to $44,912/QALY for patients with a PSA > 3.2. It is important to note, however, that the increased cost-effectiveness ratio can be explained by the early treatment failure and consequently more rapid progression of patients to surgery in cohorts treated with doxazosin.

1. Baladi JF, Menon D, Otten N. An economic evaluation of finasteride for treatment of benign prostatic hyperplasia. *Pharmacoeconomics* 1996;9:443-454.

2. Noble SM, Coast J, Brookes S et al. Transurethral prostate resection, noncontact laser therapy or conservative management in men with symptoms of benign prostatic enlargement? An economic evaluation. *The Journal of Urology* 2002;168:2476-2482.