

Finasteride Versus Dutasteride: A Real-world Economic Evaluation

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It is estimated that 24% to 90% of US men older than the age of 40 have enlarged prostate (EP), also known as benign prostatic hyperplasia (BPH).¹ However, the majority of these men are undiagnosed due to the fact that men often seek care for acute medical problems rather than conditions that are chronic or preventive in nature.^{2,3} Even with this lack of formal diagnosis, almost 14% of men will seek care for EP.^{1,4} Although these numbers are certainly promising, a recent study indicated that men aged 50 years or older who initiate treatment for EP have a 19.2% chance of having acute urinary retention (AUR) or prostate surgery within 1 year after treatment initiation.⁴ These high rates of AUR and prostate surgery should not be surprising given that more than 85% of men treated for EP are treated with alpha blocker therapy,⁴ which does not reduce the size of the prostate even though urinary symptoms are improved.⁵ In contrast, the 5-alpha reductase inhibitors (5ARIs), dutasteride and finasteride, have been shown to reduce prostate size, thereby reducing the likelihood of AUR and prostate surgery.⁵⁻⁷

Although the different rationales for initiating alpha blocker or 5ARI therapy are well known, differences within the 2 therapeutic classes may be less clear, especially when comparing dutasteride and finasteride, the only two 5ARIs in the US market. Although both products are classified as 5ARIs, they have different mechanisms of action. Dutasteride blocks both the type-1 and type-2 5-alpha reductase isozymes, whereas finasteride inhibits type-2 5-alpha reductase isozymes only.^{6,7} The dual mechanism of action of dutasteride results in 50% more dihydrotestosterone (DHT) suppression. Additionally, dutasteride has a longer half-life than finasteride. As discussed by Issa et al and Naslund et al in this supplement, in retrospective, real-world outcome studies, patients taking dutasteride had a lower likelihood of AUR and discontinued alpha blocker therapy earlier than finasteride patients. These data suggest that patients who initiate dutasteride rather than finasteride might require less resource utilization. However, no studies have directly compared the economic differences between the 2 drugs. The

Abstract

Objective: The objective of this study was to assess the economic differences between dutasteride and finasteride patients within the first year of initiating treatment.

Methods: A retrospective analysis using the PharMetrics Integrated Medical and Pharmaceutical Database (Watertown, Mass) was conducted to assess economic differences in patients who were initiated on dutasteride or finasteride. The database is nationally representative, encompassing administrative claims from more than 45 million patients within 85 managed healthcare plans.

Male patients aged ≥ 50 years with a diagnosis of benign prostatic hyperplasia who began 5-alpha reductase inhibitor (5ARI) treatment (dutasteride or finasteride) between January 1, 1999, and March 1, 2005, were identified.

Patients eligible for study inclusion were matched (1 dutasteride: 3 finasteride) on 4 variables (measured during the 6-month period before their first 5ARI prescription): age, presence of acute urinary retention, total amount of enlarged prostate (EP)-specific charges (\pm \$1), and the duration of follow-up (measured in months). EP-specific charges were defined as the total amount charged for EP-specific physician visits, inpatient hospitalizations, outpatient hospital care, emergency department visits, and other ancillary services during the follow-up period for each patient, expressed as average monthly costs.

Results: Overall, patients incurred \$121.04 in EP-specific charges per month, with inpatient hospitalizations making up 39.1% (\$47.29) of the total costs of care. Physician office visits constituted 33.6% (\$40.66) of monthly charges. When comparing differences among patients taking the two 5ARIs, patients taking dutasteride incurred \$20.50 less per month in EP-specific charges than patients taking finasteride (\$105.67 vs \$126.17, $P = .0007$). This reduction in overall medical utilization resulted from a lower amount of inpatient hospitalization charges for dutasteride patients.

Conclusion: Patients treated with dutasteride incurred \$20.50 less per month in medical costs than patients treated with finasteride. Healthcare plans should consider the incremental differences in medical costs along with the difference in pharmaceutical expenditures when evaluating these two 5ARIs.

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METHODS

Data Source

The PharMetrics Integrated Medical and Pharmaceutical Database (Watertown, Mass) was used to assess economic differences in patients who were initiated on dutasteride or finasteride. The database is nationally representative, encompassing administrative claims of more than 45 million patients from 85 managed healthcare plans. Data include inpatient and outpatient resource and diagnostic information as identified by *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes,⁸ and procedures as identified by *Current Procedural Terminology 4 (CPT-4)* codes, as well as prescription records. Dates of service and both paid and charged amounts are available for all services rendered.

Sample Selection

Male patients aged ≥ 50 years who began 5ARI treatment (dutasteride or finasteride, excluding dosage forms for male pattern baldness) between January 1, 1999, and March 1, 2005, were identified. The index date for each patient was defined as the first date of the 5ARI prescription within this period. Identified patients were required to have a diagnosis of EP or BPH based on *ICD-9-CM* codes, and to be continuously eligible for medical and pharmacy services for 6 months before and at least 12 months after their index dates. Patients

were excluded if they had an *ICD-9-CM* code for prostate or bladder cancer during the 18-month eligibility period, or did not initiate alpha blocker therapy before 5ARI treatment. **Table 1** lists all relevant inclusion and exclusion *ICD-9-CM* codes.

Comorbidity Assessment. To assess comorbidities across the cohorts, the Charlson Comorbidity Index with Deyo modification was utilized.^{9,10} This index is based on 19 medical conditions, each assigned a weight ranging from 1 to 6. Possible total scores range from 0 to 37, with higher numbers representing a greater burden of comorbidity. Charlson Index scores for this study were derived by evaluating the presence of various *ICD-9-CM* codes in the 6-month period before each patient's index date.

Staging of EP. The Thomson Medstat Disease Staging coding criteria were used to identify the stage of EP before the patient was placed on 5ARI therapy.¹¹ This method is based on electronic screening and identification of a comprehensive map of *ICD-9-CM* diagnosis codes. The proprietary coding criteria, developed by physicians and medical records professionals employed by Thomson Medstat, have been widely used as a classification system for diagnostic categories—1 of 4 systems selected for dissemination with the Healthcare Cost and Utilization Project Nationwide Inpatient Sample. Each patient initiated on 5ARI therapy was placed into 1 of 7 disease stages based on the presence of *ICD-9-CM* codes in the 6-month period before their index dates. The stages and corresponding *ICD-9-CM* codes are presented in **Table 2**.

Patient Matching. Patients eligible for study inclusion were matched (1 dutasteride: 3 finasteride) on 4 variables measured during the 6-month period before their index dates: age (within 4 years), occurrence of AUR, total EP-specific charges (within \$1), and the duration of follow-up after the index date (within 4 months). EP-specific charges were defined as claims submitted with a primary *ICD-9-CM* code of 222.2 or 600.xx.

Analysis of Outcomes. Resource utilization cost was defined as the total amount charged for:

■ **Table 1.** Inclusion and Exclusion *ICD-9* Codes

Inclusion <i>ICD-9</i> codes	
Enlarged prostate	222.2, 600
Exclusion <i>ICD-9</i> codes	
Prostate cancer	185, 198.82, 233.4, 236.5, 239.5, V10.46
Bladder cancer	188, 198.1, 223.3, 233.7, 236.7, 239.4, V10.51

ICD-9 indicates *International Classification of Diseases, Ninth Revision*.

(1) physician visits, (2) inpatient hospitalizations, (3) outpatient hospital care, (4) emergency department visits, and (5) other services. Pharmacy costs were not included in this analysis. Because follow-up times differed from patient to patient, monthly average charges were calculated for each patient and used as the unit of analysis. Statistical differences in monthly charges were determined by a gamma-distributed generalized linear model with a log-link function, controlling for differences in age, the use of urologic specialty care services, Charlson Comorbidity Index score, Thomson Medstat disease severity stage, and pre-period EP-specific charges.

Differences in the demographic characteristics across cohorts were assessed utilizing chi-square tests for categorical variables and *t*-tests for continuous variables. All statistical analyses were conducted using SAS version 9.1.3, with an a priori significance level of *P* = .05.

RESULTS

Demographic Characteristics

Data from 1740 patients (1305 finasteride, 435 dutasteride) were analyzed (Table 3). Overall, patients averaged 61.4 years of age, and were predominantly classified as stage 1.1 (EP without urinary

■ **Table 2.** Thomson Medstat Staging Criteria for Enlarged Prostate

Stage	Description	ICD-9-CM codes
1.1	Benign prostatic hypertrophy	222.2, 600.xx
1.2	with urinary tract infection	Stage 1.1 + 599.0
2.1	with bladder outlet obstruction	Stage 1.1 + 593.5, 596.0, 599.6
2.2	with hydronephrosis	Stage 1.1 + 591.xx
3.1	with renal failure	Stage 1.1 + 584.xx, 586.xx
3.2	with sepsis	Stage 1.1 + 038.xx
3.3	with shock	Stage 1.1 + 785.50, 785.59

ICD-9-CM indicates International Classification of Diseases, Ninth Revision, Clinical Modification. Source: Reference 11.

tract infection, bladder outlet obstruction, or other complications). On average, patients incurred \$8.47 in EP-specific costs per month before index date.

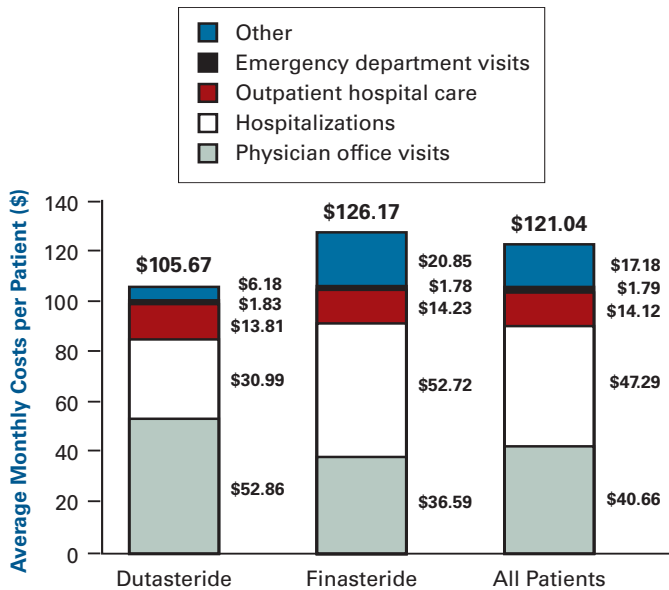
Because patient cohorts were matched on age, EP-specific pre-period medical charges, the presence of AUR, and duration of follow-up, these demographic characteristics did not differ between cohorts. Finasteride patients had a higher level of comorbidity as identified by the Charlson Comorbidity Index, whereas dutasteride patients

■ **Table 3.** Demographic Characteristics

Characteristic	Dutasteride (n = 435)	Finasteride (n = 1305)	Total (N = 1740)
Matched variables			
Mean age ± SD (years)	61.4 ± 7.17	61.4 ± 7.18	61.4 ± 7.17
Presence of AUR	77 (17.70%)	231 (17.70%)	308 (17.70%)
Mean duration of follow-up ± SD (months)	9.50 ± 3.62	9.50 ± 3.61	9.50 ± 3.61
Mean pre-period enlarged prostate costs (\$) ± SD	8.47 ± 42.54	8.47 ± 43.53	8.47 ± 42.52
Specialty care visit in pre-period	190 (43.7%)	533 (40.8%)	723 (41.6%)
Nonmatched variables			
Stage of enlarged prostate			
1	433 (99.54%)	1298 (99.46%)	1731 (99.48%)
2+	2 (0.46%)	7 (0.54%)	9 (0.52%)
Mean Charlson rating ± SD	0.78 ± 1.58	0.93 ± 1.70	0.89 ± 1.67

SD indicates standard deviation; AUR, acute urinary retention.

■ **Figure.** Average Monthly Costs per Patient



were more likely to have specialty care visits; however, these differences were not statistically significant.

Economic Analysis

The total amount charged for EP-specific physician visits, inpatient hospitalizations, outpatient hospital care, emergency department visits, and other ancillary services during the follow-up period for each patient was calculated and expressed as average monthly cost (Figure). Overall, patients incurred \$121.04 in EP-specific medical charges per month, with inpatient hospitalizations making up 39.1% (\$47.29) and physician office visits making up 33.6% (\$40.66) of the total monthly charges. When comparing costs for patients taking the two 5ARIs, those taking dutasteride incurred \$20.50 less per month in EP-specific charges than those taking finasteride (\$105.67 vs \$126.17, $P = .0007$). This reduction in overall medical utilization primarily resulted from lower inpatient hospitalization charges for dutasteride patients.

Discussion

The purpose of this study was to assess the economic differences between patients receiving dutasteride versus finasteride within the first year of initiating treatment. The results indicated that dutasteride patients incurred almost \$21 less in medical resource costs per month than finasteride

patients. These results support the hypothesis that the dual mechanism of action and greater DHT suppression of dutasteride may result in improved outcomes of care, as suggested by Issa et al in this supplement, who found that dutasteride patients had less AUR and tended to have less prostate surgery. Furthermore, in the present study, the cost differences between the 2 groups resulted largely from reduced inpatient charges—possibly reflecting lower AUR and surgery rates.

This is the first published economic study to evaluate cost differences associated with use of the two 5ARIs; however, only resource utilization costs were analyzed. Pharmacy costs were not evaluated in this study, which was conducted before the entry of generic finasteride. If the monthly differences exhibited in this study can be assumed to remain constant over a 1-year period of time, managed care organizations could avoid approximately \$246 in medical charges per year per patient. However, differences in pharmacy costs between dutasteride and finasteride must also be taken into account, especially now that generic finasteride is available. The results of this analysis suggest that when the average monthly difference in pharmaceutical costs to the healthcare plan for dutasteride versus finasteride is less than \$20.50 per month, the use of dutasteride could be cost-saving.

Another observation that should be noted is the average amount of EP-specific charges incurred within 1 year of initiating 5ARI therapy. Previous work indicated that EP patients incurred approximately \$400 in medical resource costs within the first year of treatment.⁴ However, in the current study, patients incurred \$121 per month, or \$1452 per year. This difference in cost may be due to differences in disease severity between the study populations. The previous study identified patients initiating any treatment (predominantly alpha blocker therapy). In contrast, our current study identified patients initiating 5ARIs who had previously been receiving alpha blocker therapy. This may have resulted in our selecting a population with a greater propensity for clinical events, because prior treatment with alpha blocker therapy does not reduce prostate size and therefore does not decrease the long-term risk of AUR and surgery. This raises the question of whether the costs could have been further reduced if 5ARI therapy had been initiated

earlier. Additional studies are needed to address this important issue.

Although the results of this study highlight the potential economic benefits of dutasteride compared with finasteride, interpretation of these results is bound by several limitations. First, this study was retrospective in nature; thus, the exact reason for the reduction in costs is difficult to ascertain, and may be due to a combination of factors, such as improved DHT suppression or lower AUR and surgery rates. Second, the tolerability, safety, and efficacy of the products were not examined in this study and, in any case, one should not conclude superiority of one product over the other in the absence of head-to-head randomized trials. Third, the results of this analysis should not be extrapolated beyond 1 year, because no patients within this analysis were evaluated for longer than that.

Some decision makers may also have concerns about assessing charges in patients with differential follow-up. Earlier work evaluating cost data in patients with differential follow-up utilized survival analysis techniques to evaluate differences in costs. It has been shown that differential follow-up times are correlated with the mean costs incurred by patients, which would bias the results of the analysis.¹² However, in our analysis, follow-up was equivalent in both groups because patients were matched for follow-up duration. Furthermore, we did not use survival analysis techniques, but rather divided the total costs incurred by the patient during the study period by the number of months in the follow-up period for that specific patient, to calculate an average cost per month. This method provides the most realistic cost data for healthcare decision makers, because all patients meeting inclusion criteria are included in the analysis regardless of follow-up time. In more traditional analyses, patients not meeting certain follow-up times are excluded; thus, their costs are not captured. Excluding patients in this manner ignores costs that are actually incurred by the healthcare plan, which may lead to serious type-1 or type-2 errors.

Even with the stated limitations, this study suggests that the use of dutasteride may provide some economic benefit for managed care plans. These

potential differences between the two 5ARIs warrant validation using additional data sources. Future research should continue to assess clinical and economic differences between dutasteride and finasteride in various patient settings, while exploring the relationship between the timing of 5ARI initiation and treatment outcomes.

Conclusions

Patients treated with dutasteride incurred \$20.50 less per month in medical resource costs than patients treated with finasteride. Healthcare plans should consider the incremental differences in medical costs along with differences in pharmaceutical expenditures.

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