Value for Money in Disease Management of Benign Prostatic Hyperplasia

Two articles in this issue of the Journal address the subject of value for money in the treatment of benign prostatic hyperplasia (BPH). Ohsfeldt et al. examine the relative cost-effectiveness of 3 drugs that are in the same pharmacological class, 2 of which are available in generic form. The authors found an incremental cost of $14,609 for tamsulosin (Flomax) to attain the same therapeutic outcome as generic terazosin, using discounted drug prices that would be comparable to actual prices paid by managed care organizations (doxazosin was “dominated” in all scenarios due to its 70% higher cost per unit, $0.80 per unit versus $0.47 per unit for terazosin). The incremental cost was lower, $9,961 per treatment success, when discounted average wholesale prices (AWPs) were used in the pharmacoeconomic model, 80% of AWP for brand tamsulosin and 50% of AWP for generic terazosin and for generic doxazosin.

There is a large effect on the incremental cost-effectiveness ratio for tamsulosin when the α-blockers are used in more than 1 unit per day. Terazosin has flat pricing across all 4 dosage strengths, $0.47 per capsule for 1 mg, 2 mg, 5 mg, and 10 mg, when purchased in a 30-capsule quantity. Doxazosin prices vary slightly by strength, $0.70 per tablet for 1 mg, $0.67 for 2 mg, $0.73 for 4 mg, and $0.80 for 8 mg, when purchased in a 30-tablet quantity. Tamsulosin is available in only 1 strength, 0.4 mg, and is priced at $1.73 per capsule when purchased in a 30-capsule quantity. Dose adjustment with terazosin can be made without an incremental cost per day of therapy. Doxazosin dose adjustment would incur an approximate 15% higher cost in moving to the 8 mg strength from either the 1 mg or 2 mg dose form. By comparison, tamsulosin dose adjustment is expensive, rising by 100% from $1.73 per day of therapy at 0.4 mg to $3.46 per day of therapy at 0.8 mg (since the drug is available only in the 0.4 mg dose form). Ohsfeldt did not investigate this factor except to include the variable in sensitivity analysis, ranging from 5% to 20% of α-blocker use at 2 units per day. For the most likely actual scenario of 15% use of these α-blockers more than once daily, the incremental cost for tamsulosin compared with terazosin increases by 22% from $610 in the base case (0% use of 2 units per day) to $743 at 15% use of 2 units per day, and the ICER increases by 9% from $6,609 to $7,582.

Data from a national pharmacy benefit management (PBM) database suggest that tamsulosin is dosed at 2 units per day in about 15% of patients, the same ratio as terazosin, versus 13% for doxazosin. Weighing only the direct drug cost of these ratios of 2 units per day yields a nearly 3-fold (268%) price premium for tamsulosin ($2.08 per day or $758 per year of therapy) compared with terazosin ($0.56 per day or $206 per year); the tamsulosin price premium is 137% compared with doxazosin ($0.88 per day or $320 per year of therapy).

The U.S. Department of Veterans Affairs (VA) Health System made tamsulosin a nonformulary drug and developed criteria for nonformulary use of the drug early in 2001. Burk et al. found that simple posting of criteria for nonformulary use of tamsulosin had no apparent effect on prescribing behavior for this drug. This is not surprising since there is no assurance that most, or even some, VA physicians actually read the criteria for nonformulary use of tamsulosin. These findings can be used by the VA Health System to develop and implement more effective methods for dissemination and implementation of prescribing guidelines.

From another perspective, one might question the reasonableness of expecting physicians to not prescribe a drug for BPH that is promoted by the manufacturer for this indication while the older drugs, terazosin and doxazosin, are available in generic form and are no longer advertised or promoted to physicians. The drug preference is reduced to the cost factor since tamsulosin has an efficacy profile, as measured by lower urinary tract symptoms (LUTS), in BPH patients similar to that of the older α-blocker drugs and may have an advantage in safety due to its insignificant effect on blood pressure and apparent lower incidence of postural hypotension. Yet, the VA Health System has the capability to turn the cost factor on its head by purchasing drugs at prices that are unattainable except to buyers who can use Federal Supply System prices. The drug cost factor has allegedly been manipulated in other instances by large managed care organizations that have purchased brand drugs at nominal prices that are intended to not trigger Medicaid best-price restrictions.

Multi-tier prices for brand prescription drugs can be understandably confusing to physicians, particularly those who practice in multiple environments. Special prices for brand prescription drugs in the VA Health System would appear to create a larger need to educate physicians about preferred drugs and prescribing guidelines since these special prices may have almost no relationship to the drug prices in the rest of the U.S. market. Certainly, assessing the results of the value-for-money equation becomes more complicated in the presence of wide variability in input prices for the same drug in different U.S. markets.

Who Needs Another Clinical Practice Guideline?

The U.S. Department of Veterans Affairs (VA) Health System has a plethora of clinical practice guidance and other guidelines. There is reliable evidence from the VA Health System that in some cases these guidelines have a significant effect on key intermediate clinical outcomes. For example, a recent cross-sectional patient survey and retrospective review of medical records conducted at 5 VA medical centers and 8 comparable commercial managed care organizations (MCOs) found significantly better clinical outcomes in VA patients with diabetes. In fact, 1,243 VA patients with diabetes compared with 3,154 commercial MCO patients with diabetes had significantly better outcomes on all 9 process measures except...
influenza vaccination; e.g., 93% versus 82% had annual hemoglobin A1c measures (P = 0.006), and 89% versus 74% had an annual eye examination (P = 0.001). The VA patients with diabetes also had better intermediate outcomes; e.g., low-density lipoprotein cholesterol <3.37 mmol/L (<130 mg/dL) for 86% of VA patients versus 75% for MCO patients (P = 0.02), and hemoglobin A1c value less than 8.5% in 84% compared with 65% of the MCO patients with diabetes (P = 0.007). There was no difference between the VA patients and the MCO patients in blood pressure clinical outcome—48% versus 57% had blood pressure controlled to less than 140/90 mm Hg (P = 0.09)—or in patient satisfaction (humanistic-service outcome). It would appear from this example that the VA clinicians and administrators were able to exploit the opportunity presented in this relatively closed system of care to improve upon the process and intermediate outcomes in disease management of diabetes compared with the benchmarks derived from commercial MCOs.

Burk et al. in this issue of the Journal found that making clinicians aware of the existence of (another) guideline was not sufficient to influence prescribing behavior. With the proliferation of “guidelines” and the attendant increase in “noise” and volume of information available to clinicians, this finding would appear self-evident. As noted by Wolff et al. 5 years ago, guidelines on their own change nothing.11

A MEDLINE search of PubMed using the key words “clinical guideline” produced 28,727 literature citations.12 The need for focused attention on guidelines and systems and processes that make it easy to do it right13 is underscored by research in the VA system that found that for patients enrolled in hepatitis C virus treatment clinics, with specific attention to HCV and guidelines for treatment, response to therapy was not systematically measured, even though response (particularly virologic response) is the goal of drug therapy,14 and excessive duration of therapy led to increased costs while exposing patients to the risk of avoidable adverse events.15

Aside from the challenge of attaining physician attention to a given clinical guideline, it would appear obvious that clinical guidelines will vary in quality. The term should probably inform us only that some author(s) determined that their wisdom should be cast as something to acknowledge and follow in the management of a given disease. The term should not be construed to be much more than a proclamation until the details of the guideline can be dissected and evaluated. This process of evaluation should include identification of the sponsorship of the guideline and determination of the methodology used to create the guideline, including the degree of transparency associated with its creation. It would be helpful if creators of clinical guidelines informed us of the sponsor in the title of the guideline, such as “Clinical Practice Recommendations for Disease Management of Asthma Sponsored by XYZ Company.”16 Unfortunately, this does not appear to be standard practice.

Despite the shortcomings, clinical guidelines are important, even necessary. Experts can help us filter the data and help create information from the sometimes large amount of data produced by randomized controlled trials (RCTs) and from other sources. In a structure-process-outcome model of the clinical world, clinical practice guidelines (CPGs) can be viewed as the process component in which the results of RCTs and other data produced from application of the scientific method (the structure) are distilled to the guideline.17 But with the plethora of CPGs, recommendations for clinical practice, and clinical pathways, who needs another guideline? One of the answers comes by way of example.

In early 2004, the National Institute for Clinical Excellence (NICE) published an update18 to the 1997 British Thoracic Society guidelines for treating chronic obstructive pulmonary disease (COPD).19 Included in the NICE guideline for disease management of COPD was the omission of a recommendation to measure the change in forced expiratory volume in 1 second (FEV₁) after inhaled bronchodilator or a short trial of corticosteroids. This may surprise some clinicians. The NICE guideline departs further from conventional wisdom by replacing FEV₁ (a measure of the degree of airflow limitation) with assessment of symptoms to determine and monitor response to therapy. Oxygen therapy is also recommended, consistent with the advice of the Royal College of Physicians.20

A reasonable person might question the need for 3 CPGs for disease management of COPD in less than 2 years. MacNee opined that there is a need for continuous updating of COPD and other treatment guidelines since the evidence is changing rapidly.21 For example, MacNee cited the role of combinations of long-acting bronchodilators and corticosteroids, which was not well defined in the NICE guideline but, in any case, was outdated by new data when the NICE guideline for COPD was published.22 MacNee also observed that the NICE guideline cited the use of mucolytics, drugs which had not been used or licensed for COPD in the United Kingdom, based upon a review of the literature regarding mucolytics, and particularly the mucolytic and antioxidant N-acetylcysteine, which found these agents effective in reducing exacerbations and improving symptoms in patients with chronic bronchitis. Yet, MacNee predicted that this evidence would soon be out of date with the anticipated publication of the RCT of N-acetylcysteine in COPD, including the finding that the drug has no effect on the decline in FEV₁.

With the proliferation of clinical guidelines, we need standardization in their description to help us filter the data. We need a guideline to help us assess the value of guidelines and to guide authors in the creation of clinical guidelines. Just as CPGs help us to filter the RCT and other data, a CPG guideline could be used by CPG authors and CPG users. This CPG guideline might include in the title (a) the date of the
guideline, (b) the sponsoring organization, and (c) the source of the funding used to create the CPG. So, we would have CPGs with titles such as “ABC Organization in 2004: Clinical Practice Recommendations for Disease Management of Fibromyalgia Sponsored by XYZ Company.”

**OTC Omeprazole for Your Heartburn—Enormous Value-for-Money Opportunity**

The 6 prescription proton pump inhibitors (PPIs) collectively account for about 9% to 10% of total drug benefit spending for the average drug plan sponsor in 2004. For the 3-month period ended June 30, 2004, the data from 1 national pharmacy benefit management (PBM) database of small employers showed esomeprazole to account for 3% of total drug plan spending (after subtraction of member cost share), 2.4% for lansoprazole, 1.5% for generic omeprazole, 0.8% each for rabeprazole and pantoprazole, and 0.3% for (brand) omeprazole, a total of 8.8%. Slight drug plans of fewer than 500 covered members could spend as much as 20% of their entire drug budget on these drugs, used primarily for heartburn.

Since December 2002, there has been only 1 supplier of generic omeprazole, and the price has remained high for this “branded-generic.” Coded as a generic (“Y”) drug by Medispan (and similarly by First DataBank), drug plan members pay a generic drug copay. The net cost for the drug plan sponsor, after subtraction of the copayment, can be higher for “generic” omeprazole than for the lowest-cost brand PPI, pantoprazole, depending upon the tier-copayment amounts in the drug benefit design.

The magnitude of spending on drugs for heartburn and the continued high price for “generic” omeprazole has precipitated some creative managed care solutions to the problem. The introduction to the U.S. market of an over-the-counter (OTC) version of omeprazole at a fraction of the price of the prescription PPIs was followed by some unprecedented changes in drug benefit design and health care provider and consumer education to take advantage of the large potential cost savings from the therapeutic substitution of prescription PPIs with OTC omeprazole.

The U.S. Food and Drug Administration (FDA) announced on October 31, 2003, that it had approved omeprazole (Prilosec) for OTC sale in the popular 20 mg strength. The FDA approved the drug for treatment of frequent heartburn, which it defined as heartburn occurring an average of at least 2 days each week. The product became widely available for substitution of prescription PPIs with OTC omeprazole. Education was matched with financial incentives for members and for pharmacy providers. The former 3-tier drug benefit design ($10 copayment per 30-day supply for generic omeprazole, $25 for 3 PPIs, and $50 for 2 other PPIs) was replaced with a very different 3-tier copay design: $5 for a 42-day supply of OTC omeprazole (this became the new tier-1 copay, replacing the former $10 tier-1 copay), $25 for only generic (prescription) omeprazole in the 10 mg capsule form (maximum 30-day supply), and $50 for the 5 other PPIs. Pharmacy reimbursement was increased to $13 per OTC omeprazole claim compared with $2.50 per claim for the other PPIs. This resulted in an increase in average pharmacy reimbursement for professional services of 118.5% ($6.27 per claim in the 2-month postperiod versus $2.87 per claim in the 2-month preperiod), and this average pharmacy reimbursement would rise as OTC omeprazole gained a larger share of PPI prescriptions.
PPIs accounted for 12% of total drug benefit spending in the year prior to the addition of OTC omeprazole to coverage in this state employee health plan. Data from this study by Harris et al. predict a 50% drop in spending for PPIs in the first year of addition of OTC omeprazole to coverage, after accounting for the lower average member cost share and the higher pharmacy reimbursement. Savings for the plan sponsor would be even larger if the addition of OTC omeprazole was implemented coincident to exclusion from coverage of all PPIs except OTC omeprazole. Instead, this program retained coverage of all PPIs, at a cost share of $50 per 30-day supply.

Follow-up data will be of interest—what percent of total PPI prescriptions will be represented by OTC omeprazole when the researchers have 12 months of data after the implementation of this change in drug benefit design and pharmacy reimbursement? What will be the share of utilization, as measured by prescriptions and days of therapy, in this instance, where the member financial incentive is 10 to 1, and pharmacy reimbursement compensates the pharmacist for the additional professional time necessary to participate in this program?

These data will be available early in 2005 and, if the authors are willing, will help us to assess the relative effect of pharmaceutical promotional dollars spent on physicians and direct-to-consumer advertising versus the 10-fold higher point-of-service cost for the member for a PPI other than OTC omeprazole and pharmacy reimbursement designed to obtain continued participation in this therapeutic selection program. Yet, one wonders how much more could be saved under reference pricing, otherwise known as therapeutic maximum allowable cost (or “t-MAC”) in which a drug plan sponsor identifies a reference price of say $0.75 per day for heartburn (or ulcer prophylaxis), and the balance of the drug cost is the member responsibility. Under a t-MAC benefit design for heartburn drugs, the member cost share would be zero ($0) for OTC omeprazole (or ranitidine or famotidine) and more than $100 for esomeprazole, lansoprazole, and rabeprazole and more than $75 for pantoprazole or “generic” omeprazole. This is food for thought for managed care pharmacists pursuing new value-for-money opportunities.

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REFERENCES


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26. Actual price (drug cost plus pharmacy dispensing fee) before copay, standardized to a 30-day supply calculated from a national pharmacy benefits management data warehouse for approximately 500,000 drug plan members.
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Letters to the Editor

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