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James (Jim) Blakeway, founder and CEO of Blakeway Worldwide Panoramas, Inc., has literally taken the art of photography to new heights. He has hung from a helicopter and been suspended 800 feet in the air from a crane to capture the best panoramic shot. The result of his aerobic exploits is an impressive collection of more than 120 panoramic lithographs of U.S. and world cities, historic landmarks, and golf courses. Blakeway’s collection is marketed worldwide through art galleries, framing and art retailers, photography studios, and on the Internet at www.panoramas.com.

When asked how he got his start in such a specialized sector of photography, Blakeway said, “That’s a simple question with a complicated answer. My early career had absolutely nothing to do with photographing and marketing panoramas. In fact, my first job out of college was a sales position with Procter and Gamble. In 1988, I was going through the interview process for sales management positions with several different companies. As I thought back over my life to that point, I realized my most fulfilling experiences were connected to the entrepreneurial ventures I had pursued in college. Several of these had turned out to be quite profitable and were extremely fun and rewarding. I had applied for a tourist visa to Australia several months prior to these interviews, and one day my tourist visa came back approved. So I packed my bags and headed for Australia. I went there to work—to investigate what we had in the United States that might be of interest to the Australians, and what they had that might be marketable in the United States.

“After about 5 months, I met a photographer and a designer who had developed an innovative design for a poster using photographs shot from a helicopter. They had produced a panoramic photo of Sydney Harbor that was phenomenal. Neither knew the first thing about retailing, so I proposed helping them take the poster to the marketplace. I went there to work—to investigate what we had in the United States that might be of interest to the Australians, and what they had that might be marketable in the United States.

“I was impressed with our success in marketing the Sydney poster and immediately began to search for photographers in the United States who could shoot panoramic pictures. I eventually teamed up with a photographer in California who was building his own specialized camera, and we came up with 6 or 7 photographs we thought were quite attractive. I found a house near the beach and a good printing company—and I started shipping posters out of my garage and selling them out of the trunk of my car. That’s basically how the business got started.”

Blakeway says that he hired photographers for about the first 3 years to shoot some of the bigger markets—New York, Chicago, and San Francisco. He decided to move the business to Minneapolis in 1991, and it was then that he met (and eventually hired) Chris Gjevre, a customer of his who had a photography background. Between what Gjevre knew and what Blakeway had learned from being out in the field, they were able to start renting camera equipment and taking some of their own photos. Their first success was a series of shots of the Minneapolis skyline and the Winter Ice Palace that had been constructed for the St. Paul Winter Carnival. These prints hit the market in January 1992, just as the Twin Cities area was hosting the Super Bowl.

Blakeway said, “Once we started shooting our own panoramas, everything changed. This method allowed us to be in control because we didn’t have to rely on hired photographers to shoot a city when the weather was good. Now we could travel around the country to market posters, and on days when the weather was perfect, we could drop everything and start a shoot.”

He added, “We’ve shot double and triple exposures, in different temperatures, summer versus winter, and studied the effects of different angles of the sun. Yet, even with all the variables, a good part of shooting a great panorama is luck…being in the right place at the right time—or maybe just having access to a helicopter when you need it.”

Sheila Macho
JMCP Contributing Editor

COVER CREDIT

SOURCES
Interview with the artist and www.panoramas.com.
**JMCP EDITORIAL POLICY**

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- Subject Reviews
- Formulary Management
- Contemporary Subjects
- Editorials
- Letters

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These are well-referenced articles based on original research that has not been published elsewhere and reflects use of the scientific method. The research is guided by explicit hypotheses that are stated clearly by the authors.

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These are well-referenced, comprehensive reviews of subjects relevant to managed care pharmacy.

**Formulary Management**

These are well-referenced, comprehensive reviews of subjects relevant to formulary management methods or procedures in the conduct of pharmacy and therapeutics (P & T) committees and may include description and interpretation of clinical evidence.

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Editorials should be relevant to managed care pharmacy and address a topic of contemporary interest; these submissions are peer reviewed.

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These submissions may be peer reviewed for accuracy. If the letter addresses a previously published article, an author response may be appropriate.

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Manuscripts should include, in this order, a title page; an abstract of no more than 400 words; text; references; tables, figures, and graphs; and financial disclosures and conflicts of interest (see Submission Checklist for details).

JMCP abstracts should be written narratives that contain the information described for each type of article shown below, where applicable. For descriptions of editorial content, see “JMCP Editorial Policy” in this Journal or at www.amcp.org/jmcp/ep.pdf.

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An abstract is required in the format of:

- Objective
- Methods
- Results

Subject Reviews
An abstract is required, generally in the format of:

- Objective
- Summary
- Keywords

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An abstract is required in the format of Original Research or Subject Reviews, depending upon the subject matter.

Contemporary Subjects
An abstract is required in the format of Original Research or Subject Reviews, depending upon the subject matter.

Editorials
These submissions require no abstract.

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These submissions require no abstract or title page.

Reference Style

References should be prepared following modified AMA style. Shown below are examples of common types of references:

1. Standard journal article
(List all authors when 6 or less, if more than 6, list only the first 3 and add et al.)


2. No author given

3. Journal paginated by issue
Corrigan PW, Luchins DJ, Malan RD, Harris J.

The Journal of Managed Care Pharmacy is indexed by International Pharmaceutical Abstracts (IPA) and Iowa Drug Information Service.


4. Book or monograph by authors

5. Book or monograph with editor, compiler, or chairman as author

6. Chapter in a book

7. Government agency publication

8. Dissertation or thesis

9. Paper (or Poster) presented at a meeting
Reagan ME. Workers’ compensation, managed care, and reform. Paper (poster) presented at: 1995 AMCRA Midyear Managed Care Summit; March 13, 1995; San Diego, CA.

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A paper copy of the manuscript, including originals of figures and tables, should be submitted to the JMCP Peer Review Administrator at the Academy of Managed Care Pharmacy at 100 North Pitt Street, Suite 400, Alexandria, VA 22314. Tel. (800) 827-2627 or (703) 883-8416 or Fax: (703) 883-8417. The paper copy is necessary to ensure proper presentation and placement of text, figures, tables, and graphs. Please send an electronic version of the manuscript, either on a disk or via e-mail, to jmcpreview@amcp.org. All text should be in a word processing program (preferably Microsoft Word). Tabular material also should be in a word processing program using the tab function to create columns, not using “tables” or “cells.” Figures should be saved in Photoshop or Illustrator and may be re-created by us. We cannot accept PowerPoint graphics.

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Before submitting your manuscript to the Journal of Managed Care Pharmacy, please check to see that your package includes the following:

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  - keywords: follows the abstract
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  - tables and figures (generally no more than a total of 6). Submit referenced tables and figures on separate pages with titles (and captions, as necessary); match symbols in tables and figures to explanatory notes, if included.
- Disclosures and conflict of interest: completed and signed author attestation forms (available at www.amcp.org/jmcp/ep.pdf). Clearly indicate source(s) of funding and financial support.

REFERENCE

Effects of a 3-Tier Pharmacy Benefit Design on the Prescription Purchasing Behavior of Individuals With Chronic Disease

KAVITA V. NAIR, PhD; PAMELA WOLFE, MS; ROBERT J. VALUCK, PhD; MARIANNE M. MCCOLLUM, PhD; JULIE M. GANTHER, PhD; and SONYA J. LEWIS, RPh

ABSTRACT

OBJECTIVE: To evaluate the impact of 3-tier (copayment) pharmacy benefit structures on medication utilization behavior.

METHODS: A pretest-posttest quasi-experimental design was employed. Chronic disease sufferers (N=8,132) from a health plan were classified into the following groups: (a) 2-tier copayment moving to a 3-tier structure, (“converting” group), (b) 2-tier staying in a 2-tier structure and, (c) 3-tier staying in a 3-tier structure. The latter 2 were “comparison” groups. Two 7-month time periods were determined: the “preperiod” (June through December 2000) and the “postperiod” (January through July 2001) for a change in pharmacy benefit structure. Pharmacy claims data were used for data collection. Statistical analyses included bivariate tests to evaluate predifferences and postdifferences across study groups. Maximum likelihood estimates from a repeated measures model were used to examine changes in formulary compliance and generic use rates. Discontinuation of nonformulary medications was evaluated using logistic regression.

RESULTS: Controlling for demographics, number of comorbidities, disease state, and pharmacy benefit structure, the formulary compliance rate increased by 5.6% for the converting group. No significant increases were seen for the comparison groups. Generic use rates increased by 6 to 8 absolute percentage points for all groups (3.3% to 4.9% adjusted rates). Converting group members were 1.76 times more likely to discontinue their nonformulary medication than those in the 2-tier comparison group and 1.49 times more likely than those in the 3-tier comparison group.

CONCLUSIONS: These findings suggest that shifting individuals from a 2-tier to a 3-tier drug benefit copayment structure resulted in changes in medication utilization. Decision makers need to balance these changes with the potential dissatisfaction that members may express in paying higher copayments.

KEYWORDS: 3-tier, Cost Sharing, Prescription utilization

J Managed Care Pharm. 2003(9):2:123-133

Editor’s note: “Impact of Multi-tiered Pharmacy Benefits on Attitudes of Plan Members With Chronic Disease States,” by several of the same authors, was published in the November/December 2002 issue of JMCP. That article examined health plan member attitudes regarding the increased cost sharing and experience in 3-tier drug benefit plans. The current article examines actual prescription utilization behavior when individuals move into a 3-tier plan.

Double-digit increases in the cost of pharmaceuticals have prompted managed care plans to identify ways to blunt some of these cost increases while simultaneously trying to maintain a choice of products for beneficiaries. These increasing costs have resulted in beneficiaries participating more in their health care decisions, particularly in their choices for prescription medications. This increased awareness among beneficiaries has supported the relatively new concept in pharmacy benefits known as multi-tiered (copayment) plans. Multi-tiered pharmacy benefits are based on the assumption that drugs within a medication class are relatively interchangeable. Patients have to pay an out-of-pocket difference or a higher copayment for more expensive or nonformulary medications.

An early form of the multi-tiered pharmacy benefit structure was the 2-tier copayment plan. In 2-tier copayment plans, the lower copay tier is used for formulary-based generic medications, and the second copay tier is for formulary-based, brand-name medications. Nonformulary medications typically can be obtained at the brand copayment amount through the health plan’s prior-approval process, if the drug benefit plan required such authorization. Two-tier plans are being rapidly replaced by the 3-tier pharmacy benefit plan. In this structure, as with the 2-tier plans, the lowest copayment tier is for formulary-based generic medications. Formulary brand-name medications constitute the second, or middle, copayment tier, and the highest copayment, or the “third tier,” is usually reserved for nonformulary medications. Medications in the third tier may also include lifestyle or cosmetic drugs (e.g., smoking cessation, weight-loss aids, or antifungal drugs) or higher priced brand-name drugs. In some drug plans, a prior approval may also apply to some brand drugs in either copayment tier in a 3-tier drug design.

In 2002, 3-tier pharmacy benefit plans became a dominant pharmacy benefit structure among prescription drug plans. Managed care decision makers argue that the 3-tier pharmacy benefit structure can help contain the growing cost of pharma-
ceticals by shifting some of the cost of more expensive medications to the beneficiaries who use these products. Three-tier copayment structures can also improve adherence to the health plan’s formulary by using financial (copayment) incentives to encourage beneficiaries to purchase medications assigned to the lower copay tiers.3

The question that begs for evaluation is how beneficiaries respond to the 3-tier pharmacy benefit structures. Proponents of the 3-tier benefit structure suggest that beneficiaries may realize some benefits when managed care plans implement a 3-tier pharmacy benefit structure. For example, a 3-tier pharmacy benefit structure gives beneficiaries a broader choice of medications by extending coverage to products in the third tier that may not have been previously covered.4 In support of this notion, Holdford et al. found that product choice was the most important attribute cited by beneficiaries in selecting a prescription drug plan.4 Three-tier plans could potentially provide more choice to beneficiaries, but at a higher out-of-pocket cost.

Three-tier copayment plans may also reduce the need for other cost-containment mechanisms such as prior authorizations or step therapy that could function as barriers to medication access.4 In a 2-tier pharmacy benefit structure, beneficiaries are given a choice of medications, but the choice may be limited to brand or generic medications. In some 2-tier copayment drug plans, beneficiaries had to get approval from the health plan through mechanisms such as prior authorizations or had to pay out-of-pocket costs for the nonformulary product. Sometimes this prior approval would require beneficiaries to demonstrate that they had failed the lowest-cost formulary alternatives before the health plan would approve the nonformulary medication. A 3-tier plan can eliminate the need for the beneficiary to go through this administrative hurdle by simply paying a higher copayment for the nonformulary medication.

Critics of the 3-tier pharmacy benefit structure may contend that higher copayments for “essential” medications, in particular, may restrict access to certain prescription drugs for persons in vulnerable populations. Essential medications might be defined as those whose withdrawal could have serious effects on health status.4 Individuals on such medications may include those with chronic disease states who often work with their physicians to arrive at the optimal drug or combination therapy after a period of trial and failure. The resulting drug therapies may be less easily interchanged with lower-cost therapeutic alternatives. Vulnerable populations in 3-tier pharmacy benefit structures may have to weigh the increase in copayment between the various tiers with the differences in the perceived benefits of purchasing medications in each tier.4 This multi-tier method of pricing prescription drug benefits likely increases the need for information to assist beneficiaries in making appropriate choices among their prescription options. While beneficiaries may be able to make informed decisions about their drug therapy choices for certain disease states (e.g., impotence), their decision making may be more difficult for chronic disease states such as hypertension, where the decisions may be more complex and involve more directly the clinical assessments and judgment of the prescriber or pharmacist.5

Health plans are adopting 3-tier pharmacy benefit plans as a major cost-containment mechanism and shifting members from their current 2-tier to a 3-tier pharmacy benefit structure to increase formulary compliance and the utilization of lower-cost medications.6 For beneficiaries in a 2-tier pharmacy benefit plan already accustomed to a differential copayment structure, a transition to a 3-tier pharmacy benefit plan is probably fairly comprehensible. Nevertheless, higher copayments for certain drugs may cause beneficiaries to make choices: whether to stay on their current medication by paying more, switch to a formulary or other alternative that has a lower copayment amount, or discontinue the medication. For chronic disease sufferers who have been stabilized on a medication and are accustomed to its effects, these choices may be harder to make and may be followed by a variety of different responses depending on personal financial condition, health status, and perceived health benefits.3,6,10

Past research has shown that moving individuals from a 2-tier copayment plan ($7 generic copayment and $12 brand copayment) to a 3-tier plan ($8/15/$25) plan resulted in lower prescription utilization and expenditures and reduced net plan costs, with no significant differences found in physician office visits, inpatient, or emergency room use rates.11 In the current managed care environment, health plans typically offer a variety of pharmacy benefit structures to their members. There is no standardization among health plans in 3-tier copayment designs; it may involve simply adding a third copayment tier to an existing 2-tier copayment design or lowering or otherwise altering copayments in the first and second tiers and adding a higher copayment tier to the new drug benefit structure.

The primary goal of this study was to examine the effects of a 3-tier pharmacy benefit copayment structure on prescription drug utilization behavior for health plan members with chronic disease states. Of specific interest were the effects of drug benefit design changes on drug utilization measures such as formulary compliance, generic use rates, and discontinuation rates for nonformulary medications for patients with one or more of 5 selected chronic disease states.

Methods

The research design was pretest-posttest quasi-experimental with comparison group to examine enrollees in 2- and 3-tier pharmacy benefit plans of a large managed care plan in the western United States that included health maintenance organization (HMO), preferred provider organization (PPO), and Medicare+Choice members. The goal of sample selection was to obtain a representative group of plan members in 2- and 3-tier pharmacy benefit plans that might be most vulnerable to the changes in cost sharing as a result of their health status.
Five chronic disease states were chosen for prescription medications: hypertension, diabetes, dyslipidemia, gastroesophageal reflux disease (GERD), and arthritis. These 5 categories of medication were selected to minimize the potentially confounding effects of seasonal variation in prescription drug use.

Inclusion Criteria
Pharmacy claims data were used for sample selection. Standard data collected included prescription fill date, days supply, formulary/nonformulary indicator, generic/brand indicator, new prescription or refill indicator, ingredient cost, dispensing and administrative fees, and copayment amount; net plan cost was calculated from these data fields. The type of drug dispensed and its drug class were determined using the generic product identifier (GPI) code (Medspan GPI classification system). Drug classes using the GPI code were used to assign members to one or more of the 5 disease states; i.e., a given member could be assigned to more than one disease category if multiple classes of drugs were utilized.

All 3 drug benefit groups included members from a random sample of 25,008 health plan members who had at least 2 prescriptions filled for any one of the 5 disease states during the 5 months (from January 1 to May 31, 2000) prior to the start of the study period. The observation period for the study was a total of 14 months, 7 months in the preperiod (before a change in pharmacy benefit design) and 7 months in the postperiod (after a change in pharmacy benefit design). The preperiod began on June 1, 2000, and ended on December 31, 2000. On January 1, 2001, pharmacy benefit structures changed, signaling the beginning of the postperiod, which began on January 1, 2001, and ended on July 31, 2001. Additionally, no other changes in health plan design (such as increases in office visit copayments) occurred during the study period.

From this sample of 25,008, 8,132 members were selected based on continuous enrollment during both the preperiods and postperiods and experienced a change from either a 2-tier to a 3-tier benefit structure or no change, remaining in a 2-tier or a 3-tier copay design. These 8,132 health plan members were classified into the following 3 study groups: (a) 2-tier copayment moving to a 3-tier pharmacy benefit structure, referred to as the “converting” group; (b) 2-tier staying in a 2-tier pharmacy benefit structure; and (c) 3-tier staying in a 3-tier pharmacy benefit structure. The latter 2 were the “comparison” groups. For those who remained in a 2- or 3-tier plan during the postperiod, movement within plans (2-tier to another 2-tier or 3-tier to another 3-tier structure) also occurred, and, thus, all 3 study groups experienced some change in their prescription benefit plan.

Study Variables
Study measures obtained from pharmacy claims and membership data included the following: (a) age, (b) gender, (c) disease state (based on the classification of individuals by GPI codes using pharmacy claims data), (d) time period (preintervention versus postintervention period), and (e) outpatient chronic disease indicator based on prescription claims for one year from January 1 to December 31, 2000. The chronic disease indicator (CDI) approximates the number of chronic diseases of each member based on the application to pharmacy claims data of sets of predefined medication classes, which are determined by an expert panel to be indicative of particular chronic disease states.12 Higher CDI scores indicate a greater number of chronic illnesses.

Prescription Medication Utilization and Cost Measures
Medication utilization measures were calculated from pharmacy claims data. Utilization measures included the average number of prescriptions per patient per month and generic use rate, formulary compliance rate; and the medication possession ratio (MPR); a measure of medication compliance. Generic use rate was defined as the number of generic claims (tier 1) divided by the total number of claims (copayment tiers 1, 2, and 3). Formulary compliance rate was defined as the formulary prescription claims (copayment tiers 1 and 2) divided by the total number of claims (copayment tiers 1, 2, and 3). MPR was defined as the total days supply for a medication divided by the total number of days between the first and last prescription for an individual during the study period.13

Prescription cost measures were based on the cost per prescription per patient per month (PPPM) where the cost per prescription was the sum of the ingredient cost, dispensing fee, and administrative fee for each prescription. The 3 prescription cost measures used in the analysis were the median prescription cost per month, median health plan (net) cost per month (determined as ingredient cost + dispensing fee + administrative fee – member copayment), and the median copayment amount PPPM.14

Discontinuation rates for nonformulary medications were examined for individuals in all study groups who had a minimum of 2 claims for one of the medications that were on the formulary during the preperiod and were removed during the postperiod. During the postperiod, more than 70% of the members in the 2-tier comparison groups experienced increases in their copayment amounts either within a different 2-tier structure or in having to assume the full cost of the medication if it was not approved by the health plan. For individuals in the 3-tier comparison group and those in the converting group, the nonformulary medications were removed from the second tier and shifted to the third tier, resulting in increased copayment amounts that these individuals faced for their medications.

Medication classes for nonformulary medications that were examined included calcium channel-blockers, angiotensin II receptor antagonists, angiotensin converting enzyme (ACE) inhibitors, beta-blockers, combination therapies, disease-modifying antirheumatic drugs, nonsteroidal anti-inflammatory medications, bile acid sequestrants, statins, fibrac acid derivatives, and proton pump inhibitors. Prescription claims up to a 34-day equivalent were used to determine discontinuation rates. Treatment termination date was defined as the last observed fill
date for the nonformulary product plus the number of days for which the medication was dispensed in the postperiod. Individuals were classified as “continuing” the nonformulary product in the postperiod if the ratio of their medication possession ratio in the postperiod compared to that in the preperiod for the product was equal to or greater than 0.5. Computing the MPRs in the preperiod and postperiods for the nonformulary product allowed a more accurate evaluation of medication purchasing behavior (as a function of prescription refill data) for each individual by assessing their prescription purchasing behavior after their pharmacy benefits changed relative to their behavior before the change. Thus, if individuals continued to take the nonformulary product in the postperiod with approximately the same regularity as in the preperiod and had a prescription claim for the product that was within 60 days of the end of the postperiod, they were classified as “continuing” the medication.

Individuals who had no claims for the nonformulary product in postperiod or for whom the ratio of post-MPR to pre-MPR was less than 0.5 (i.e., they decreased their use of the medication by more than 50% in the postperiod) or who did not have a termination date for the product that was within 60 days of the end of the postperiod were classified as “discontinuing” the medication.

The difference in the copayment amount for each of the medications examined in this analysis during the preperiod and postperiod was also determined. For example, if an individual in a 2-tier pharmacy benefit plan of $10/$20 in 2000 was taking a formulary brand-name medication, the copayment cost of that medication would be $20. If the individual was now in a 3-tier pharmacy benefit plan of $10/$20/$35 in 2001, and the medication was shifted to the third copayment tier, it would now cost $35 and the copayment difference would be $15. Discontinuation behavior of nonformulary medications at increasing increments of copayment differences was also examined (<$10, $15, $20, $25, $30).

### Statistical Analysis

Bivariate tests of differences across all study groups were based on a chi-square test for independent proportions for categorical variables, and a k-sample median test for continuous variables. Maximum likelihood estimates from a repeated-measures model were used to test for change (preperiod versus postperiod values) in the outcome measures, formulary compliance, and generic use rates. This approach is conceptually the same as multivariate analysis of variance (MANOVA) but avoids the case-wise deletion of subjects with missing assessments (no claim in the preperiod or postperiod data). Discontinuation of nonformulary medications was evaluated using logistic regression. Linearity assumptions were tested and variables recoded where the assumption failed. All statistical analyses were performed in SAS, version 8.1.

### Results

#### Characteristics of the Study Sample

Members in the 2-tier comparison group were older, more likely to be Medicare enrollees, single, and, on average, had more chronic disease states than the other study groups (Table 1). The members in the 2-tier comparison group consumed more medications per month and had higher prescription costs, in accordance with their age demographic. The 3-tier comparison group was similar to the converting group in most respects, but the members were primarily in HMO plans and had, on average, the highest monthly copayment amounts compared to the other groups. The subjects in the converting group were primarily in PPO plans, a greater percentage had family, and they had the lowest number of chronic disease states and lower copayment amounts compared to the other 2 groups. Anti-hypertensive medication was the most common drug category among all 3 of the study groups.

There were various copayment structures among the 2- and 3-tier copayment plans in the sample. In the preperiod, the 2 predominant benefit structures were a $7/$15 2-tier plan and a $15/$25/$40 3-tier plan. More than one third of the sample (34%) was in a $7/$15 2-tier benefit structure, with a $7 copayment for generic medications (tier 1) and a $15 copayment for brand-name medications (tier 2), while 22% were in a $5/$15 plan and 14% were in a $5/$10 2-tier copayment plan. A little more than one quarter of the sample (28%) was in a $15/$25/$40 3-tier pharmacy benefit structure where tier-1 formulary generic medications cost the member $15, tier-2 formulary brand-name medications cost $25, and tier-3 nonformulary medications cost $40. Less than 2% of the sample was in other 2- or 3-tier copayment plans such as $10/$20 or $10/$20/$35 or $5/$15/$30. In the postperiod, only 17% were in the $7/$15 2-tier benefit structure, 45% were now in the $15/$25/$40, 22% in a $10/$20/$35, and 6% in a $5/$15/$30 3-tier pharmacy benefit structure. About 10% of the sample was in other 2- or 3-tier copayment plans such as $5/$10, $9/$18, $10/$20, or $20/$35/$50.

#### Prescription Utilization and Medication Costs for Tiers 1 to 3 in the Preperiod and Postperiod

Overall, it appears that in the postperiod there was a shift from formulary brand-name medications toward generic medications for all 3 study groups and an additional shift away from the use of nonformulary medications for the converting group (Table 2). There appears to be a 6% to 8% absolute increase in the purchase of generic medications for all 3 of the study groups and a 3% to 5% absolute decrease in the use of formulary-based, brand-name medications. As expected, the converting group experienced a decrease (5%) in nonformulary prescription purchases, but it was the only study group to do so.

Overall median monthly prescription utilization, health plan costs, and copayment amounts were examined, and the comparisons were conducted on the median differences rather than mean differences since the data were not normally distributed. All 3 groups had increases in the number of prescription claims for medications in copayment tiers 1 and 2 in the postperiod (Table 3). The
Effects of a 3-Tier Pharmacy Benefit Design on the Prescription Purchasing Behavior of Individuals With Chronic Disease

Table 1: Description of the Continuously Enrolled Population: Demographics, Prescription Utilization, and Cost Measures Before a Change in Pharmacy Benefit Structure

<table>
<thead>
<tr>
<th>Demographic Characteristics*: 2-tier Plan Members</th>
<th>3-tier Plan Members</th>
<th>2-tier Moving to 3-tier</th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N= 8,132) (June 1, 2000 – December 31, 2000)</td>
<td>(n=715)</td>
<td>(n=1,707)</td>
<td>(n=5,710)</td>
</tr>
<tr>
<td>Age Mean (SD)</td>
<td>61.9 (16.3)</td>
<td>48.0 (11.0)</td>
<td>49.4 (11.2)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female N (%)</td>
<td>351 (49.1%)</td>
<td>833 (48.8%)</td>
<td>2670 (46.8%)</td>
</tr>
<tr>
<td>Male N (%)</td>
<td>364 (50.9%)</td>
<td>874 (51.2%)</td>
<td>3040 (53.2%)</td>
</tr>
<tr>
<td>Type of managed care plan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. HMO N (%)</td>
<td>251 (35.1%)</td>
<td>1242 (72.8%)</td>
<td>1704 (29.8%)</td>
</tr>
<tr>
<td>2. PPO N (%)</td>
<td>55 (7.7%)</td>
<td>464 (27.2%)</td>
<td>4006 (70.2%)</td>
</tr>
<tr>
<td>3. Medicare + Choice N (%)</td>
<td>409 (57.2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Family status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Family N (%)</td>
<td>255 (35.9%)</td>
<td>1043 (61.6%)</td>
<td>3615 (65.3%)</td>
</tr>
<tr>
<td>2. Single N (%)</td>
<td>455 (64.1%)</td>
<td>649 (38.4%)</td>
<td>1918 (34.7%)</td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Disease Indicator Score</td>
<td>4.2 (2.7)</td>
<td>3.2 (2.2)</td>
<td>3.1 (2.2)</td>
</tr>
<tr>
<td>Number of individuals in each disease state</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension N (%)</td>
<td>504 (70.5%)</td>
<td>977 (57.2%)</td>
<td>3,157 (55.3%)</td>
</tr>
<tr>
<td>Dyslipidemia N (%)</td>
<td>239 (33.4%)</td>
<td>517 (30.3%)</td>
<td>1,485 (26.0%)</td>
</tr>
<tr>
<td>Arthritis N (%)</td>
<td>212 (29.7%)</td>
<td>495 (29.0%)</td>
<td>1,857 (32.5%)</td>
</tr>
<tr>
<td>Diabetes N (%)</td>
<td>160 (22.4%)</td>
<td>418 (24.5%)</td>
<td>627 (11.0%)</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease N (%)</td>
<td>214 (29.9%)</td>
<td>452 (26.5%)</td>
<td>1,427 (25.0%)</td>
</tr>
<tr>
<td>Prescription utilization:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average number of prescriptions per patient per month (PPPM)</td>
<td>1.8 (1.4)</td>
<td>1.4 (1.2)</td>
<td>1.2 (1.1)</td>
</tr>
<tr>
<td>Formulary compliance rate</td>
<td>0.865 (0.268)</td>
<td>0.856 (0.281)</td>
<td>0.780 (0.346)</td>
</tr>
<tr>
<td>Generic utilization (Rx) ratio</td>
<td>0.386 (0.360)</td>
<td>0.360 (0.393)</td>
<td>0.368 (0.408)</td>
</tr>
<tr>
<td>Prescription expenditures:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average monthly cost per patient</td>
<td>$83.6 ($83.6)</td>
<td>$79.8 ($105.1)</td>
<td>$73.3 ($90.4)</td>
</tr>
<tr>
<td>Mean (SD) [Median]</td>
<td>[$64.6]</td>
<td>[$49.4]</td>
<td>[$45.7]</td>
</tr>
<tr>
<td>Average monthly cost per patient to the health plan</td>
<td>$63.6 ($74.9)</td>
<td>$51.8 ($88.4)</td>
<td>$59.0 ($80.9)</td>
</tr>
<tr>
<td>Mean (SD) [Median]</td>
<td>[$48.0]</td>
<td>[$27.6]</td>
<td>[$34.1]</td>
</tr>
<tr>
<td>Average monthly copayment amount per patient</td>
<td>$20.0 ($16.5)</td>
<td>$28.0 ($25.8)</td>
<td>$14.2 ($16.7)</td>
</tr>
<tr>
<td>Mean (SD) [Median]</td>
<td>[$15.6]</td>
<td>[$21.4]</td>
<td>[$8.7]</td>
</tr>
</tbody>
</table>

* Determined from pharmacy claims in 2000.
† P-value is based on a chi-square test for independent proportions for categorical variables, a 3-sample median test for continuous variables.

The magnitude of overall increase in the median number of prescriptions is consistent with that observed by Motheral et al. (2001) and is consistent with a general increase in the volume of prescriptions in 2001, particularly in the drug classes examined in this study.11,18,19 For both the 2- and 3-tier comparison groups, tier 1 increased the most in the postperiod. For the converting group, tier 1- and tier 2-drugs had similar increases in the postperiod. The greatest change in prescription costs to the health plan was observed for tier-2 medications in all study groups, with the largest absolute increase of 9.4% in the 3-tier comparison group. In the converting group, individuals on tier-2 medications experienced the highest increase in median copayment amount (a 10.4% absolute increase) during the postperiod. Smaller increases in the median copayment amounts were observed for tier-3 prescriptions in all 3 of the study groups.
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### Prescription Utilization for Selected Drug Classes in the Preperiod and Postperiod

The percentage of prescriptions in copayment tiers 1 to 3 for selected drug classes in all 3 of the study groups during both the preperiods and postperiods were also assessed (results not shown). Tier-3 nonformulary use was inconsistent. The H₂ receptor antagonists showed the “expected” behavior in the postperiod for all study groups: an absolute increase in the use for the converting group. For salicylates, bile acid sequestrants, sulfonylureas, ACE inhibitors, and diuretics, nonformulary use during the postperiod for all study groups: an absolute increase in the use of nonformulary products (1% to 2%), and a larger absolute decrease in the use of generics (4% to 10%), a small absolute decrease in the use of formulary products (1% to 2%), and a larger absolute decrease in the use of nonformulary products (4% to 5%), with the largest decrease (9%) in the converting group. A substantial reduction in the use of nonformulary products during the postperiod was observed for the converting group, 11% for calcium channel-blockers and 6% for alpha glucosidase inhibitors (e.g., miglitol, acarbose). On the other hand, the HMG-CoA reductase inhibitor drug class showed little change in prescription claims for all 3 groups during the postperiod. For drug classes such as NSAIDS, fibric acid derivatives, proton pump inhibitors, and beta-blockers, there was little change in the use of nonformulary medications during the postperiod for the converting group. For salicylates, bile acid sequestrants, sulfonylureas, ACE inhibitors, and diuretics, nonformulary use increased for all study groups in the postperiod.

### Formulary Compliance Rates During the Preperiod and Postperiod

Maximum likelihood estimates from a repeated-measures model were used to examine changes in formulary compliance during the postperiod, controlling for demographics (age, gender) number of comorbidities (CDI scores), disease states (one of the 5 diseases being examined), pharmacy benefit structure (2-tier or 3-tier structure), time period (preperiod versus postperiod), and the interaction of the latter 2 terms. All variables that were not significant were eliminated from the saturated model in step-wise fashion to arrive at the final model, which included only those measures that were significantly correlated with the dependent variable. This process eliminated the individual effects of pharmacy benefit structure and time period (the interaction term between the 2 variables was included in the model). The age variable was divided into 3 categories: 18 to 25, 26 to 64, and older than 65 years. The adjusted estimates of formulary compliance for each time period by pharmacy plan type are shown in Table 4. The interaction of time period by pharmacy benefit structure is a significant predictor of formulary compliance. The formulary compliance rates in the comparison groups were similar: 87% for those in the 2-tier and 88% for those in the 3-tier comparison group. However, the converting group had a lower formulary compliance rate during the preperiod (81.31% versus 86.7%), which showed an absolute increase of 5.6% during the postperiod.

The estimates in Table 4 for the different age categories (18 to 25 years and older than 65 years) are the difference in mean compliance rates for those age groups, on average, for the entire study period relative to subjects aged 25 to 64 years. The formulary compliance rate for individuals aged 18 to 25 years was higher (an absolute increase of 7.5%) than for those members aged between 25 and 64 years. Individuals older than 65 years were more formulary compliant than those aged between 25 and 64 years (absolute difference of 4%). The CDI variable is centered, and its coefficient estimates the shift in the mean formulary compliance rate for a one-unit change in CDI (the range is 1 to 10). Although significant, the effect is very small and of no apparent practical significance. Finally, the estimates for the 5 disease states also represent a shift in the mean formulary compliance rate. Thus, diabetics are more formulary compliant than those who were not taking prescription medications for diabetes (absolute difference 6.9%) while individuals with GERD are less formulary compliant than all others (absolute difference 6.3%).

### Generic Use Rates During the Preperiod and Postperiod

Similar to the formulary compliance analysis, maximum likelihood estimates from a repeated-measures model were used to examine changes in generic use rates in the continuously enrolled population controlling for factors outlined in the previous analysis (results not shown). The interaction of the time period (preperiod versus postperiod) and pharmacy benefit structure (2-tier, 3-tier, 2-3 tier) is also a significant predictor of generic use rates. For all 3 of the study groups, the generic use rates increased in the postperiod. The increase in the generic utilization ratio was highest for the converting group (4.9 absolute percent), followed by the 2-tier comparison group.

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**NOTE:** This text is a representation of the document content. The actual context and implications of the data presented may vary based on the complete dataset and analysis. The specific numerical values and conclusions drawn from the data are not fully detailed here for brevity, but they are essential for a comprehensive understanding of the research findings. It is recommended to refer to the original publication for a detailed interpretation of the results.
 Effects of a 3-Tier Pharmacy Benefit Design on the Prescription Purchasing Behavior of Individuals With Chronic Disease

Logistic regression was used to examine the predictors of discontinuation rates for nonformulary medication controlling for the factors outlined previously. As a high level of multicollinearity exists between pharmacy benefit structure and copayment difference for the nonformulary medications (Kendall's tau=0.72), the copayment difference variable was dropped from the analysis. Due to the small sample sizes of members taking an individual nonformulary medication, discontinuation rates are reported by disease state (and not by individual nonformulary medications). The mean copayment difference that members experienced in the preperiod and postperiod for the nonformulary medications was highest for the converting group ($24.21 [+4.6]) and were similar for the 3-tier ($12.53 [+4.1]) and 2-tier comparison group ($12.41 [+11.1]). The overall discontinuation rate was 43.41%, with the highest rate for the converting group (47.2%). The remaining groups had similar discontinuation rates: 40% for the 2-tier and 37% for the 3-tier comparison group. The discontinuation rates for each disease state were also similar (results not shown).

The results of the logistic regression are shown in Table 5. While the model was not very predictive (goodness-of-fit C statistic was 0.57), only pharmacy benefit structure was significantly associated with discontinuation behavior for nonformulary medications. Individuals in the converting group were 1.76 times more likely to discontinue their nonformulary medication during the postperiod than those in the 2-tier comparison group and 1.49 times more likely than those in the 3-tier comparison group. Copayment differences for individual nonformulary drugs in the preperiods and postperiods were not included in the logistic regression model; the discontinuation rates for nonformulary medications with increasing increments of copayment differences is shown in Figure 1. Even though there appears to be an increase in discontinuation rates with higher increments of copayment differences, the actual differences are small (between 1% and 3%) and not statistically significant.

### Table 3: Prescription Utilization and Medication Costs for Copayment Tiers 1-3 in Preperiods and Postperiods*

<table>
<thead>
<tr>
<th></th>
<th>2-Tier Plan Members (n=715)</th>
<th>3-Tier Plan Members (n=1,707)</th>
<th>Converting Group (2-to 3-Tier, n=5,710)</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prescriptions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tier 1</td>
<td>0.29</td>
<td>0.71</td>
<td>0.42</td>
<td>0.14</td>
</tr>
<tr>
<td>Tier 2</td>
<td>0.71</td>
<td>0.86</td>
<td>0.15</td>
<td>0.57</td>
</tr>
<tr>
<td>Tier 3†</td>
<td>0.00</td>
<td>0.10</td>
<td>0.15</td>
<td>0.29</td>
</tr>
<tr>
<td>Total Rxs PPPM†</td>
<td>1.00</td>
<td>1.71</td>
<td>0.71</td>
<td>1.14</td>
</tr>
<tr>
<td><strong>Cost per Member</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tier 1</td>
<td>$0.45</td>
<td>$2.66</td>
<td>$2.21</td>
<td>$0.04</td>
</tr>
<tr>
<td>Tier 2</td>
<td>$31.05</td>
<td>$38.14</td>
<td>$7.09§</td>
<td>$15.11</td>
</tr>
<tr>
<td>Tier 3†</td>
<td>$0.00</td>
<td>$0.10</td>
<td>$0.10</td>
<td>$0.00</td>
</tr>
<tr>
<td>Total health plan cost PPPM§</td>
<td>$31.50</td>
<td>$40.94</td>
<td>$9.44</td>
<td>$15.15</td>
</tr>
<tr>
<td><strong>Copayment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tier 1</td>
<td>$2.14</td>
<td>$5.52</td>
<td>$3.38§</td>
<td>$1.43</td>
</tr>
<tr>
<td>Tier 2</td>
<td>$10.00</td>
<td>$12.86</td>
<td>$2.86§</td>
<td>$13.81</td>
</tr>
<tr>
<td>Tier 3†</td>
<td>$0.00</td>
<td>$1.43</td>
<td>$1.43§</td>
<td>$0.00</td>
</tr>
<tr>
<td>Total copayment PPPM§</td>
<td>$12.14</td>
<td>$19.81</td>
<td>$7.67</td>
<td>$15.24</td>
</tr>
</tbody>
</table>

* Median values are reported because the data are highly skewed.
† Tier-3 copayment drugs represent <15% of all purchases by number of prescriptions (Rxs); the data are organized at the person level, so more than half the participants have no purchases of tier-3 drugs. A median test will pick up changes in the nonzero portion of a distribution, hence the significance even where the median in both preperiod and postperiod is 0.
‡ Not statistically significant at P<0.05, all other changes (preperiod versus postperiod) are statistically significant at P<0.000.
§ Represents a sum of medians across each column for each summary measure. Overall differences are reported in the last column. (e.g., while Rx use in the converting group increased from 0.43 to 0.86, overall Rxs PPPM changed from 1.00 to 1.28 among all study subjects).
Discussion

This study examined the effects of implementation of a 3-tier pharmacy benefit copayment structure on certain medication utilization behaviors. Examining prescription utilization and costs for medications in tiers 1 to 3 showed that the overall generic use ratio increased by a range of 3.3 to 4.9 absolute percent, with smaller decreases observed in brand-name use, and a significant decrease in nonformulary use for the converting group. This finding is consistent with Motheral et al. who found an increase in use of prescription drugs in copayment tiers 1 and 2 and a modest decrease in the use of nonformulary medications (tier 3) when individuals moved from a $7/$12 to a $8/$15/$25 3-tier plan.11 Patterns of use were not uniform among individual drug classes for the converting group; an increase in nonformulary use was found for symptomatic diseases states such as arthritis and GERD, where beneficiaries may (a) be reluctant to switch to lower-cost formulary alternatives for medications that have demonstrated therapeutic effects or (b) not use these medications continuously.

Consistent with Motheral’s findings, prescription costs to the health plan for tier-1 and tier-2 medications also showed an increase for all 3 study groups during the postperiod, with greater increases for tier-2 medications and smaller increases for tier-3 medications.11 It appears that the implementation of a 3-tier plan may cause some shifting of medication costs away from tier-3 to tier-2 medications. As intended by the health plan, member copayments increased by 10% for the converting group and by approximately 3% for both the 2- and 3-tier comparison groups. It therefore appears that a 10% increase in copayments experienced by the converting group did deter

<table>
<thead>
<tr>
<th>Variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period by pharmacy benefit structure interaction term (preperiod)*</td>
</tr>
<tr>
<td>Preperiod: 2-tier interaction (who were in the 2-tier comparison group in the preperiod)</td>
</tr>
<tr>
<td>Preperiod: 3-tier interaction (who were in the 3-tier comparison group in the preperiod)</td>
</tr>
<tr>
<td>Preperiod: 2-tier interaction (who were targeted to convert to a 3-tier pharmacy benefit structure in the postperiod)</td>
</tr>
<tr>
<td>Period by pharmacy benefit structure interaction term (postperiod)*</td>
</tr>
<tr>
<td>Postperiod: 2-tier interaction (who were in the 2-tier comparison group in the postperiod)</td>
</tr>
<tr>
<td>Postperiod: 3-tier interaction (who were in the 3-tier comparison group in the postperiod)</td>
</tr>
<tr>
<td>Postperiod: 3-tier interaction (who converted to a 3-tier pharmacy benefit structure in the postperiod)</td>
</tr>
</tbody>
</table>

Summary of preperiod/postperiod differences for formulary compliance rates

| Variable | Estimate | Standard Error of the Estimate | P value |
|---------------------|
| Preperiod/postperiod difference: 2-tier who stayed in 2-tier | 0.008 | 0.013 | 0.6002 |
| Preperiod/postperiod difference: 3-tier who stayed in 3-tier | 0.01 | 0.008 | 0.2692 |
| Preperiod/postperiod difference: 2-tier who moved to 3-tier | 0.056 | 0.005 | <.0001 |
| 18-25 years† | 0.07534 | 0.015 | <.0001 |
| Over 65 years | 0.04009 | 0.011 | <.0001 |
| CDI‡ | 0.0290 | 0.001 | 0.0094 |
| Diabetes | 0.06930 | 0.006 | <.0001 |
| Arthritis | -0.02832 | 0.005 | <.0001 |
| Hypertension | -0.02549 | 0.005 | <.0001 |
| Gastroesophageal reflux disease (GERD) | -0.06304 | 0.005 | <.0001 |

* Interaction term represents the combined effect of time period and pharmacy benefit structure.
† 26 to 64 years is the reference group.
‡ CDI score is centered in the model.
nonformulary use to a significant extent in the postperiod. Formulary compliance for all 3 of the study groups was high (above 80%) and showed an increase of 5.6% for those in the converting group during the postperiod. The magnitude of the change in formulary compliance for the converting group is no doubt associated with the 5.3% lower formulary compliance rate for this group during the preperiod.

Differences in baseline formulary compliance rates may be a result of other unmeasured factors in addition to the variables included in these analyses. Possible causative or confounding factors may include the differences in prescribing patterns of physicians for the converting group compared to the other groups or consumer demand for nonformulary medications in this group. Differences in formulary compliance rates also differed among disease states, with the diabetics being the most formulary compliant and individuals with GERD being the least formulary compliant. It is possible that for “flare” diseases such as GERD, individuals are reluctant to switch to formulary alternatives, when they have their acid reflux under control. Another explanation could be that a larger percentage of all diabetic drugs have formulary status versus drugs for heartburn (GERD) for which a larger proportion are nonformulary.

Generic use rates increased for all 3 of the study groups, with the largest increase for the converting group (4.9 absolute percent), followed by the 2-tier comparison group (4.8 absolute percent), and then the 3-tier comparison group (3.3 absolute percent; P<0.001). In support of this finding, Motheral et al. also found an increase in the number of generic claims when copayments were increased by $5 for brand-name medications and $2 for generic medications in a particular 2-tier plan.20 Since all 3 of the study groups experienced some increase in their copayment amounts during the postperiod, it appears that members are more likely to purchase generic medications in response to the higher copayments. These increases in the rates of generic use may appear modest but, in fact, represent significant savings to the health plan and to health plan beneficiaries. An absolute increase of 5% in generic utilization ratios can translate into millions of dollars in drug benefit savings for large health plans. These savings that accrue from increases in the ratio of generic prescriptions become larger over time as the cost of brand-name medications continues to increase.

Past research has shown that the removal of a nonformulary product resulted in an increase in the number of prescriptions for its substitutes and other products within other drug classes.21 This suggests that individuals do appear to be sensitive to formulary coverage of their medications and are likely to discontinue use of the nonpreferred drug when coverage no longer exists. Previous findings have reported a decreased rate of continuation with nonformulary medications after the implementation of a formulary (about 27%); the rates of discontinuation in this study were higher, averaging about 40%.22 In support of this finding, Nair et al. found, through a series of focus group examinations, that when beneficiaries are confronted with a decision to pay a higher copayment for their chronic disease medications, their most common response was to switch to a lower-cost formulary alternative after talking to their physician or pharmacist about the alternative medication.10 A linear relationship was not observed between the discontinuation rates of nonformulary medications and increasing increments of copayment differences. However, there was no attempt in this study to determine the cost or availability of medication substitutes (prescription-based or over-the-counter alternatives), making it impossible to draw conclusions about price elasticity for beneficiaries using formulary-based, brand-name medications.

Patient behavior is complex and pharmacy benefit policies intended to change behavior may not always produce the intended effects.23 Formulary compliance rates and generic use rates for the converting groups increased by approximately 5%, while nonformulary use decreased by a similar amount as well. The results of this study appear to support the notion of 3-tier plans where prescription use appears to have shifted to the lower copayment tiers, suggesting that economic disincentives in the form of higher copayments do, in fact, steer individuals to lower cost (copayment) medication alternatives.

There is some evidence to suggest that beneficiaries in 3-tier pharmacy benefit structures are less satisfied with their prescription drug coverage than those in 2-tier pharmacy benefit structures and have expressed intentions to disenroll from their health plan if given the opportunity.24 The challenge for managed care
Effects of a 3-Tier Pharmacy Benefit Design on the Prescription Purchasing Behavior of Individuals With Chronic Disease

decision makers is to balance consumer attitudes about their pharmacy benefit plans, specifically dissatisfaction with increased cost sharing, with the changes observed in their medication utilization behavior, after the implementation of a 3-tier plan.

- Limitations

In the analysis of the discontinuation rates for nonformulary medications, this study did not examine what actions individuals took after they discontinued the medication. These actions could have included (and are not limited to) switching to a brand or generic formulary alternative within the same drug class, switching to a medication in another drug class, discontinuing all drug therapy, purchasing an over-the-counter alternative, or making lifestyle modifications with diet and exercise. Future research can examine the actions of individuals who have discontinued their medication to determine if there are unintended consequences of discontinuation such as stopping drug therapy completely, which may lead to adverse health outcomes.

Several other potential limitations should be noted. The 3 study groups were not homogenous in patient demographic characteristics. Members in the 2-tier comparison group were older, and more than half of them were Medicare+Choice members (57.2%) who are typically higher users of prescription drugs than the employed population. In contrast, subjects in the converting group and those in the 3-tier comparison groups had no Medicare+Choice members. Thus, the results of this study need to be interpreted in light of these differences among these groups. For example, there were no Medicare+Choice members in the 3-tier copayment groups, either converted from 2-tier or remaining in 3-tier copayment benefits, due to the combined effects of our inclusion criteria (i.e., continuous enrollment and membership in one of only 3 comparison groups) and the elimination by the MCO of the 3-tier drug benefit for Medicare+Choice members in 2001, the postperiod of our study.

Individuals in all 3 of the study groups experienced some change in their prescription copayments during the postperiod. Thus, the designated comparison groups also experienced increases in their copayment along with the converting group. While controlling for these differences in copayment in the multivariate models seems an obvious choice, there are problems in doing so. Merely examining differences in copayments would not indicate what actual difference in cost sharing the individual faced for the medications at the various tiers at the time of decision making. In our study, the mean difference in copayment during the preperiod and postperiod for individuals in the converting group was $19.61; for the 2-tier comparison group, it was $12.43; and for the 3-tier comparison group, it was $9.52. Thus, the converting group experienced a 2-fold increase in their copayments during the postperiod.

The study time frame of 14 months (7 months in the preperiod and 7 months in the postperiod) may not capture the full extent of the impact of a 3-tier pharmacy benefit structure on prescription utilization. Members may require some time to understand the changes in their prescription benefits in 2001 and understand how their copayments for prescription medications have changed. On the other hand, this study included only users of chronic medications who would most likely be aware of their pharmacy benefit changes. Earlier research used a 6-month follow-up period with satisfactory results. Our research was encumbered by the business practices of the managed care organization that was implementing additional pharmacy benefit plan changes starting in the fall of 2001, making it necessary to shorten the postimplementation measurement period.

There are inherent limitations in using pharmacy claims. In particular, the use of only pharmacy claims to identify individuals with chronic disease states is not optimal. When prescription claims are used as a proxy for a medical diagnosis, the issue of identifying members who do not have the disease is always a possibility, given the multiplicity of label and off-label purposes for drug products. Although a majority of the drug classes examined in this study are used for one indication primarily, in the case of hypertension, there may be some misclassification of individuals.
Conclusions
The findings of this study reveal that members in a 2-tier pharmacy benefit structure who changed to a 3-tier pharmacy benefit structure experienced an absolute increase of 5.6% in formulary compliance rates relative to members who stayed in their respective 2- or 3-tier pharmacy benefit structure. Generic use increased in all 3 of the study groups, absolute changes in the range of 6 to 8 percent (adjusted changes in the range of 3.3% to 4.9%), and the use of formulary brand-name products increased to a smaller extent (3 to 5 absolute percentage change). Nonformulary use appeared to decrease only for members who changed from a 2- to a 3-tier structure, apparently related to discontinuation of their use of nonformulary medications, compared to those who stayed in their former pharmacy benefit structures.

ACKNOWLEDGMENTS
We would like to acknowledge Steve Teusch and Robin Turpin from Merck and Company for their valuable input and comments.

DISCLOSURES
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REFERENCES
ABSTRACT

OBJECTIVE: To determine the incidence of preventable drug-related morbidity (PDRM) in older adults in a provider-sponsored network and identify risk factors for PDRM.

METHODS: The study was based on a retrospective review of an integrated health care database, using 52 newly developed clinical indicators of PDRM. The incidence of PDRM was determined by identifying individuals in the database who matched an outcome and pattern of care associated with an indicator. Risk factors were determined through a forward inclusion logistic regression model. The subjects in this study were 3,365 older adults enrolled in a hospital-based health care system in Florida in 1997. The principal outcome measure was identification of individuals who matched a PDRM indicator and risk factors for PDRM.

RESULTS: Ninety-seven enrollees who matched one or more of 52 PDRM indicators were found in 3,365 older adults, for an overall incidence rate of 28.8 per 1000. The top 5 indicators of PDRM were responsible for 46.8% of all PDRMs found. Regression analysis identified 5 risk factors: 4 or more recorded diagnoses, 4 or more prescribers, 6 or more prescription medications, antihypertensive drug use, and male gender.

CONCLUSION: This study demonstrated that clinical indicators can be used in a managed care organization to identify seniors who have experienced an ongoing monitoring is a principal cause of PDRM.5,6 Thus, there is a need for a comprehensive study that quantifies the degree of the problem of PDRM in older adults in the managed care setting. Moreover, such a study should examine these multiple causes of PDRM.

As with any epidemic disease, prevention is the most efficient and humane strategy. Reducing PDRM would significantly improve the safety and quality of medical care provided by MCOs, while at the same time reducing average per-patient costs. Risk factors may be used to help allocate scarce health care resources and as potential indicators to identify patients who need interventions. In Tamblyn’s review of the literature of geriatric pharmacotherapy, categories of risk factors for an adverse outcome were identified: the specific drug prescribed, the risks associated with the drug use, and the patient’s condition.7 While risk factors are known for many adverse drug-related outcomes in seniors, such as adverse drug reactions, unfortunately, risk factors that are specific for PDRM in seniors in the managed care setting have not yet been identified. If such risk factors were known, they could be used by MCOs to optimally design interventions that would target high-risk patients.

Identifying the incidence of and risk factors for PDRM may also help MCOs to reduce health care resource utilization.
A recent article in this journal observed that seniors who were prescribed potentially inappropriate medications, when compared to those who were not prescribed such medications, had significantly higher utilization of health care resources (emergency room, inpatient, and outpatient visits) and costs (facility, provider, and overall). Previous research has concluded that those older adults who received sedative-hypnotics with doses exceeding guidelines had increased hospital costs and longer lengths of stay as compared to those who did not receive these drugs or whose dosages did not exceed the guidelines. Bates and colleagues determined that patients with a preventable adverse drug event had an average increase of 4.6 days in length of stay and $5,857 in total cost. Therefore, it appears that there is a significant cost associated with adverse outcomes of drug therapy, and the patients who experience these outcomes consume more health care resources. Of interest to managed care administrators and health care professionals is the relationship of PDRM to health care resource utilization in the managed care setting. At least theoretically, these adverse outcomes, being preventable, can be greatly reduced.

This study used clinical indicators of PDRM, linking both suboptimal patterns of care and outcomes, in a health care database. This database contained administrative and clinical data for older adults who were enrolled in a hospital-based health care system. The objectives of this study were to (1) determine the incidence of PDRM in older adults in this provider-sponsored network and (2) identify risk factors for PDRM.

### Methods

The study was based on a retrospective review of the database of a hospital-based integrated health care system. Ethics approval for the study was obtained from the University of Florida Health Science Center Institutional Review Board.

### Study Population

Our study population was drawn out of a larger pool of enrollees in a hospital-based health care plan in Florida with a Medicare contract. In order to be eligible for the health care plan, the enrollees had to live in one of 3 specific counties in Florida and had to be enrolled in Medicare Part B and continue to pay the Medicare Part B premium. Individuals who elected the Medicare hospice benefit and those with end-stage renal disease were not eligible for enrollment in the health plan. For this study, our inclusion criteria were: (1) individuals who were enrolled in the plan anytime during 1997 and (2) those enrollees who completed the Personal Wellness Profile (PWP) Senior Assessment (approximately 50% of the total plan members). Completion of this instrument was included in our inclusion criteria as the PWP Senior Assessment contained a majority of the variables that were included as possible risk factors for PDRM. The PWP Senior Assessment is an instrument that was given to all plan enrollees to complete upon enrollment. It is an instrument used to identify seniors at high risk for health-related problems. It has been previously used by other health plans and its predictive validity has been verified.

### Study Database

The data used in this study consisted of (1) all claims made in the outpatient and inpatient settings for this population that were already collected as a natural part of the administration of this health plan, (2) data on all prescriptions filled for the plan enrollees in the ambulatory setting provided by the pharmacy benefit manager (PBM), and (3) the PWP Senior Assessment instrument results. All claims processed and surveys completed between January 1 and December 31, 1997, were included in the study. A central database containing these 3 data sets was constructed by a medical artificial intelligence company. This database was completed on April 15, 1998, with approximately 95% of claims from 1997 processed at this time. A unique patient identifier was used to link these 3 data sets. All patient names were masked to protect patient confidentiality.

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**TABLE 1 Hypothesized Risk Factors for PDRM and Their Data Sources**

<table>
<thead>
<tr>
<th>Hypothesized Risk Factor</th>
<th>Data Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin use</td>
<td>PWP additional drug question 1</td>
</tr>
<tr>
<td>Antidepressant drug use</td>
<td>Prescription claims data from the PBM*</td>
</tr>
<tr>
<td>Long-acting benzodiazepine use</td>
<td>Prescription claims data from the PBM</td>
</tr>
<tr>
<td>Antihypertensive drug use</td>
<td>Prescription claims data from the PBM</td>
</tr>
<tr>
<td>Gastrointestinal disorders (ulcers or gastrointestinal bleeding)</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Lung conditions (emphysema, bronchitis or asthma)</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>A history of falling</td>
<td>PWP question 24</td>
</tr>
<tr>
<td>A previous adverse drug</td>
<td>PWP question 3, “Have you had a reaction side effect due to a medication that caused you to stop that medication in the last 6 months?”</td>
</tr>
<tr>
<td>Four or more prescribers</td>
<td>Prescription claims data from the PBM</td>
</tr>
<tr>
<td>Six or more prescription medications</td>
<td>PWP question 24</td>
</tr>
<tr>
<td>Four or more recorded diagnoses</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Self-assessment of poor health status</td>
<td>PWP question 1</td>
</tr>
<tr>
<td>Trouble paying for medicines</td>
<td>PWP question 23, “Do you have trouble paying for your medicines?”</td>
</tr>
<tr>
<td>Difficulty taking medications</td>
<td>PWP question 31</td>
</tr>
<tr>
<td>High alcohol consumption</td>
<td>PWP question 11, “Do you often have more than 1 to 2 alcoholic drinks in a day?”</td>
</tr>
<tr>
<td>Patient belief that they are taking too many medications</td>
<td>PWP additional drug question 4, “How do you feel about the number of medications you are taking?”</td>
</tr>
<tr>
<td>Female gender</td>
<td>Health plan enrollment file data</td>
</tr>
</tbody>
</table>

* PBM=pharmacy benefit manager.
Indicators of Preventable Drug-related Morbidity in Older Adults: 2. Use Within a Managed Care Organization

Incidence of PDRM

In the first phase of this study, 52 clinical indicators of PDRM in older adults were developed. This has been described previously in this Journal.14 The database was searched for patients who had an ICD-9 diagnosis code corresponding to an outcome included in one of the 52 PDRM indicators. Then, for each patient with the outcome, the computerized record was reviewed to determine whether the patient had received care corresponding to the pattern of care associated with the outcome in the indicator. If both the outcome and pattern of care matched the specific indicator, then it was counted as an occurrence of PDRM.

Risk Factors for PDRM

The peer-reviewed medical literature on drug-related morbidity in older adults since 1967 was reviewed for possible risk factors for PDRM. Peer-reviewed medical and pharmacy articles and referenced texts were included in the literature review. Once a possible risk factor was identified, it was determined whether measurement of this risk factor was possible in our study database. Out of this process, 18 possible risk factors for PDRM were selected for inclusion in a forward inclusion logistic regression model to determine which of the 18 hypothesized risk factors were associated significantly with PDRM. The entry level was set at $P=0.05$. These 18 hypothesized risk factors and the data sources for their measurement are contained in Table 1.

Additional logistic regression models were then run, with the risk factors from the first model entered a priori to adjust for their effects on PDRM. Other demographic variables contained in the study database were allowed to enter the model to see if they added significantly to the prediction, based on statistical significance in a forward inclusion logistic regression model to determine which of the 18 hypothesized risk factors were associated significantly with PDRM. The entry level was set at $P=0.05$. These 18 hypothesized risk factors and the data sources for their measurement are contained in Table 1. Due to the large number of variables that were considered, they were dichotomized where possible. Because there was a theoretical basis for including the risk factors from the first model, it was felt that the final model for PDRM must include all of these risk factors, even if it explained less of the variance of PDRM. Thus, this process incorporated both statistical and theoretical criteria for deciding which terms to include in the model and this helped to focus attention on those variables that fit into the conceptual framework and that had the greatest independent effect on PDRM. For the risk factors in the final regression model, the parameter estimate, standard error, and chi-square probability were all calculated. The odds ratios and 95% confidence interval were also determined for each risk factor to provide an estimate of the relative risk of having PDRM given the presence of the risk factor.

Additional Demographic Variable Data Source

<table>
<thead>
<tr>
<th>Additional Demographic Variable</th>
<th>Data Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Bladder/bowel control problems</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Blind/trouble seeing, even with glasses</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Cancer (nonskin)</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Coronary disease</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Angina</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Sciatica</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Deafness or trouble hearing</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Diabetes (high blood sugar)</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Memory problems (more than typical)</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Stroke</td>
<td>PWP question 14</td>
</tr>
<tr>
<td>Self-assessment of much worse health status</td>
<td>PWP question 2</td>
</tr>
<tr>
<td>Smoker</td>
<td>PWP question 11</td>
</tr>
<tr>
<td>Use of 6 or more over-the-counter medications (OTCs)</td>
<td>PWP question 22</td>
</tr>
<tr>
<td>Warfarin use</td>
<td>PWP additional drug question 1</td>
</tr>
<tr>
<td>Theophylline use</td>
<td>PWP additional drug question 1</td>
</tr>
<tr>
<td>Cimetidine use</td>
<td>PWP additional drug question 1</td>
</tr>
<tr>
<td>Phenytoin use</td>
<td>PWP additional drug question 1</td>
</tr>
<tr>
<td>Lives alone</td>
<td>PWP question 16</td>
</tr>
<tr>
<td>Three or more hospitalizations in previous year</td>
<td>PWP question 17</td>
</tr>
<tr>
<td>Three or more ER visits in previous year</td>
<td>PWP question 18</td>
</tr>
<tr>
<td>Five or more MD clinic visits in previous year</td>
<td>PWP question 19</td>
</tr>
<tr>
<td>Nursing home residence</td>
<td>PWP question 20</td>
</tr>
<tr>
<td>Use of durable medical equipment (oxygen, hospital bed, wheelchair, walker)</td>
<td>PWP question 25</td>
</tr>
<tr>
<td>Use of home health services (visiting nurse, physical therapy, homemaker/aide, adult day care)</td>
<td>PWP question 26</td>
</tr>
</tbody>
</table>

Results

Demographics

Enrollment into the health plan began in January 1997, with approximately 7,000 enrollees by December 1997. Approximately 50% of these enrollees completed the PWP Senior Assessment instrument, and 3,365 patients met our inclusion criteria for the study. Table 3 contains the demographic characteristics for the study population.

Incidence of PDRM

When the 52 clinical indicators of PDRM were applied to the study database, 1,005 patients were found who had outcomes consistent with one of the indicators. When each of the 1,005 patient records was searched for the related pattern of care, we...
found 158 events meeting an indicator. This represented 97 patients, as several patients met more than one clinical indicator. The overall incidence of PDRM was 28.8 per 1,000.

**Risk Factors for PDRM**

Through the use of forward inclusion logistic regression with PDRM as the dependent variable and the 18 hypothesized risk factors as independent variables, a 5-variable risk model was produced (Table 4). This model indicates that individuals with 4 or more recorded diagnoses were 2.93 times more likely to have PDRM than those with 3 or fewer diseases (P=0.0001; 95% CI, 1.16-1.47). One other variable, 4 or more prescribers, also placed individuals at a greater risk (1.31 times) for developing a PDRM (P=0.0001; 95% CI, 1.16-1.47). While female gender was included as a hypothesized risk factor for PDRM, the odds ratio for female gender was less than one (0.52) (P=0.0056; 95% CI, 0.823-0.322), meaning that females were at a far lower risk of developing PDRM than males.

The amount of variance explained by the prediction model is quite good. While $R^2$ is not recommended for use in logistic regression, an analogue called $R_L^2$ has been proposed. $R_L^2$ is a measure of the proportional reduction in chi-square, and it varies between 0 and 1 (where 1 is the model predicts the dependent variable perfectly). For this prediction model, the $R_L^2$ is 0.562. The correlation matrix for the final 5 variables in the model suggests that it is free of multicollinearity. Overall, the correlations (pair-wise relationships) between the variables are quite low. Only 2 correlations were greater than ±0.20: 4 or more prescribers and antihypertensive drug use (0.2995) and 4 or more recorded diagnoses and 6 or more prescription medications (0.2965). A backward elimination procedure was also performed, which confirmed the forward inclusion mode results.

It was thought that there might be some additional demographic variables that are risk factors for PDRM. If a variable was significantly associated with PDRM in the bivariate analysis (P<0.05) then it was included in the regression model along with the 5 variables that were identified as risk factors in the original model. A forward inclusion procedure was again used with the entry level set at P=0.05. Further regression models did not greatly increase the amount of explained variance of PDRM so it was decided that the original regression model with the 5 risk factors was the optimal model for predicting PDRM.

**Discussion**

A few specific clinical indicators were responsible for a large percentage of total PDRMs found. Overall, the top 7 indicators of PDRM were responsible for almost half of all PDRMs found (46.8%) (Table 5). The most frequently occurring indicator (outcome=secondary myocardial infarction; pattern of care=history/diagnosis of myocardial infarction, no use of ASA and/or a beta-blocker) was found 24 times (15.2% of all PDRMs). The second most frequently occurring indicator (outcome=ERvisit/hospitalization use to hyperglycemia; pattern of care= use of an oral hypoglycemic agent, hemoglobin A1c level not done at least every 6 months) was found 18 times (11.4% of all PDRMs). As shown in Figure 1, 23 clinical indicators did not occur even once in the study population, while 14 occurred from 1 to 3 times. Figure 2 displays the number of PDRMs experienced by each patient in the study. It appears that just as a small proportion of patients and diseases are responsible for a large proportion of health care costs, a small proportion of indi-

---

**Table 3**

Demographic Characteristics of the Study Population (N=3,365)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Results ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender*</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>1,514 (45.0%)</td>
</tr>
<tr>
<td>female</td>
<td>1,851 (55.0%)</td>
</tr>
<tr>
<td>Age (mean years)*</td>
<td>72.7</td>
</tr>
<tr>
<td>Number of prescribed drugs taken daily†</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>727 (22.0%)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>1,311 (39.7%)</td>
</tr>
<tr>
<td>3 to 5</td>
<td>1,008 (30.5%)</td>
</tr>
<tr>
<td>6 or more</td>
<td>258 (7.8%)</td>
</tr>
<tr>
<td>unknown</td>
<td>61</td>
</tr>
<tr>
<td>Number of over-the-counter drugs taken daily†</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>1,543 (46.3%)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>1,548 (46.4%)</td>
</tr>
<tr>
<td>3 to 5</td>
<td>168 (5.0%)</td>
</tr>
<tr>
<td>6 or more</td>
<td>74 (2.2%)</td>
</tr>
<tr>
<td>unknown</td>
<td>32</td>
</tr>
<tr>
<td>Number of hospitalizations in 12 month period†</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>2,796 (85.6%)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>3,73 (11.4%)</td>
</tr>
<tr>
<td>3 or more</td>
<td>98 (3.0%)</td>
</tr>
<tr>
<td>unknown</td>
<td>98</td>
</tr>
<tr>
<td>Number of emergency room visits in 12 month period†</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>2,724 (82.2%)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>559 (16.9%)</td>
</tr>
<tr>
<td>3 or more</td>
<td>29 (0.9%)</td>
</tr>
<tr>
<td>unknown</td>
<td>53</td>
</tr>
<tr>
<td>Perceived health status†</td>
<td></td>
</tr>
<tr>
<td>excellent</td>
<td>326 (9.8%)</td>
</tr>
<tr>
<td>very good</td>
<td>1,150 (34.6%)</td>
</tr>
<tr>
<td>good</td>
<td>1,323 (39.8%)</td>
</tr>
<tr>
<td>fair</td>
<td>479 (14.4%)</td>
</tr>
<tr>
<td>poor</td>
<td>48 (1.4%)</td>
</tr>
<tr>
<td>unknown</td>
<td>38</td>
</tr>
</tbody>
</table>

* Obtained from health plan enrollment file.
† Obtained from PWP Senior Assessment results.
‡ The percentages in each category do not include the unknown group.

95% CI, 1.16-3.52) as are seniors taking 6 or more prescription medications (1.92 times) (P=0.0266; 95% CI, 1.08-3.42). One other variable, 4 or more prescribers, also placed individuals at a greater risk (1.31 times) for developing a PDRM (P=0.0001; 95% CI, 1.16-1.47). While female gender was included as a hypothesized risk factor for PDRM, the odds ratio for female gender was less than one (0.52) (P=0.0056; 95% CI, 0.823-0.322), meaning that females were at a far lower risk of developing PDRM than males.

The amount of variance explained by the prediction model is quite good. While $R^2$ is not recommended for use in logistic regression, an analogue called $R_L^2$ has been proposed. $R_L^2$ is a measure of the proportional reduction in chi-square, and it varies between 0 and 1 (where 1 is the model predicts the dependent variable perfectly). For this prediction model, the $R_L^2$ is 0.562. The correlation matrix for the final 5 variables in the model suggests that it is free of multicollinearity. Overall, the correlations (pair-wise relationships) between the variables are quite low. Only 2 correlations were greater than ±0.20: 4 or more prescribers and antihypertensive drug use (0.2995) and 4 or more recorded diagnoses and 6 or more prescription medications (0.2965). A backward elimination procedure was also performed, which confirmed the forward inclusion model results.

It was thought that there might be some additional demographic variables that are risk factors for PDRM. If a variable was significantly associated with PDRM in the bivariate analysis (P<0.05) then it was included in the regression model along with the 5 variables that were identified as risk factors in the original model. A forward inclusion procedure was again used with the entry level set at P=0.05. Further regression models did not greatly increase the amount of explained variance of PDRM so it was decided that the original regression model with the 5 risk factors was the optimal model for predicting PDRM.

**Discussion**

A few specific clinical indicators were responsible for a large percentage of total PDRMs found. Overall, the top 7 indicators of PDRM were responsible for almost half of all PDRMs found (46.8%) (Table 5). The most frequently occurring indicator (outcome=secondary myocardial infarction; pattern of care=history/diagnosis of myocardial infarction, no use of ASA and/or a beta-blocker) was found 24 times (15.2% of all PDRMs). The second most frequently occurring indicator (outcome=ERvisit/hospitalization use to hyperglycemia; pattern of care= use of an oral hypoglycemic agent, hemoglobin A1c level not done at least every 6 months) was found 18 times (11.4% of all PDRMs). As shown in Figure 1, 23 clinical indicators did not occur even once in the study population, while 14 occurred from 1 to 3 times. Figure 2 displays the number of PDRMs experienced by each patient in the study. It appears that just as a small proportion of patients and diseases are responsible for a large proportion of health care costs, a small proportion of indi-

---

**Table 3**

Demographic Characteristics of the Study Population (N=3,365)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Results ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender*</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>1,514 (45.0%)</td>
</tr>
<tr>
<td>female</td>
<td>1,851 (55.0%)</td>
</tr>
<tr>
<td>Age (mean years)*</td>
<td>72.7</td>
</tr>
<tr>
<td>Number of prescribed drugs taken daily†</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>727 (22.0%)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>1,311 (39.7%)</td>
</tr>
<tr>
<td>3 to 5</td>
<td>1,008 (30.5%)</td>
</tr>
<tr>
<td>6 or more</td>
<td>258 (7.8%)</td>
</tr>
<tr>
<td>unknown</td>
<td>61</td>
</tr>
<tr>
<td>Number of over-the-counter drugs taken daily†</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>1,543 (46.3%)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>1,548 (46.4%)</td>
</tr>
<tr>
<td>3 to 5</td>
<td>168 (5.0%)</td>
</tr>
<tr>
<td>6 or more</td>
<td>74 (2.2%)</td>
</tr>
<tr>
<td>unknown</td>
<td>32</td>
</tr>
<tr>
<td>Number of hospitalizations in 12 month period†</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>2,796 (85.6%)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>3,73 (11.4%)</td>
</tr>
<tr>
<td>3 or more</td>
<td>98 (3.0%)</td>
</tr>
<tr>
<td>unknown</td>
<td>98</td>
</tr>
<tr>
<td>Number of emergency room visits in 12 month period†</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>2,724 (82.2%)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>559 (16.9%)</td>
</tr>
<tr>
<td>3 or more</td>
<td>29 (0.9%)</td>
</tr>
<tr>
<td>unknown</td>
<td>53</td>
</tr>
<tr>
<td>Perceived health status†</td>
<td></td>
</tr>
<tr>
<td>excellent</td>
<td>326 (9.8%)</td>
</tr>
<tr>
<td>very good</td>
<td>1,150 (34.6%)</td>
</tr>
<tr>
<td>good</td>
<td>1,323 (39.8%)</td>
</tr>
<tr>
<td>fair</td>
<td>479 (14.4%)</td>
</tr>
<tr>
<td>poor</td>
<td>48 (1.4%)</td>
</tr>
<tr>
<td>unknown</td>
<td>38</td>
</tr>
</tbody>
</table>

* Obtained from health plan enrollment file.
† Obtained from PWP Senior Assessment results.
‡ The percentages in each category do not include the unknown group.
cators are responsible for most PDRMs. A majority (62.9%) of the patients who had PDRM matched only one indicator of PDRM. Almost 19% (18.6 percent) of patients with PDRM matched 3 or more indicators and one patient matched 5 indicators. This finding should not be too surprising. There is some evidence that patients who experience an adverse drug event are at higher risk for a second adverse drug event\(^\text{2,18}\) therefore, the same could be true for PDRM. Some patients may suffer from general medical mismanagement. For example, if the patient has multiple prescribers who are not communicating their therapeutic plans to one another, the patient may be taking a dangerous combination of medications, placing that patient at greater risk for a PDRM.

The overall incidence of PDRM, 28.8 per 1,000 (2.9%), is really a lower-bound estimate of the incidence of PDRM since the 52 indicators used in this study do not represent all possible PDRMs that occur in older adults. Further investigations may focus on refining and/or developing additional PDRM indicators in an attempt to identify more patients with PDRM. This would help to increase the sensitivity of using these indicators together as a group to detect PDRM in a population of older adults.

The application of the prediction model for PDRM is beyond the scope of this study, but some general principles may still be stated. Boult and colleagues argue that the first step of any geriatric evaluation and management program is the identification of high risk.\(^{19}\) Patients with multiple risk factors for PDRM could be identified by MCOs or individual physicians and then proactively managed to help prevent PDRM and allocate resources in the most efficient manner. For example, we know that physician-pharmacy-staff communication is a necessity of the medication use system, and, therefore, if a patient has 4 or more prescribers, attempts should be made to improve communication by reducing the number of prescribers or better coordinate therapy. The final PDRM model demonstrates that a wide variety of factors influence PDRM, not just drugs themselves or certain diseases. This supports the idea that the medication use system is influenced by numerous factors. In fact, only one of the 5 risk factors is a drug class (antihypertensive drug use). Other researchers in the future may investigate whether the risk factors identified are truly causal or predictive.

### Limitations

Some potential limitations pertain to the identification of risk factors for PDRM. Only risk factors associated with PDRM in older adults were considered. Risk factors may differ for other populations, and it may differ for PDRMs in older persons that were not investigated in this study. While the list of possible risk factors considered in this study was more thorough than any other study in the peer-reviewed medical literature, there could be additional risk factors that may contribute to the regression models. Some potential risk factors for PDRM, such as an abnormal potassium level, drug interactions, specific dosages of drugs, and a patient belief that the drugs were responsible for hospitalization, have been previously shown to be risk factors for adverse drug events but could not be tested in this study due to limitations of the study database. For example, although the study database listed all laboratory tests performed on any given patient, it did not contain the actual value of the test. Since administrative health claims data were used in this study, the limitations associated with the use of this type of data (not all clinical data present, misclassification bias in ICD-9-CM coding, etc.) apply to this study.

Other limitations pertain to the population used in this study. These clinical indicators of PDRM were applied to a population enrolled in one health care plan and who completed the PWP Senior Assessment tool. Since enrollment in the plan was optional, the study population may not be representative of the geriatric population in general. As well, those older adults who elected to complete the PWP Senior Assessment instrument may be different from those who did not complete the instrument. However, a previous study of Medicare beneficiaries concluded that older persons who participate in screening services (such as completing a risk assessment questionnaire) did not differ significantly in their health behaviors from older persons not participating in the preventive services.\(^{19}\)

A study that included 217 noninstitutionalized older persons in Sweden also concluded that those older persons who do, and do not, participate in health promotion activities do not differ in health status.\(^{20}\) Older persons enrolled in a managed care Medicare-risk health plan may differ demographically and may have different health care resource utilization and outcomes than

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**TABLE 4** Logistic Regression Model Results With Risk Factors for PDRM

<table>
<thead>
<tr>
<th>Variable</th>
<th>Parameter Estimate (b)</th>
<th>Standard Error (SE)</th>
<th>Chi-Square</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Four or more prescribers</td>
<td>0.2683</td>
<td>0.0602</td>
<td>0.0001</td>
<td>1.308</td>
<td>1.162-1.472</td>
</tr>
<tr>
<td>Four or more recorded diagnoses</td>
<td>1.0758</td>
<td>0.2475</td>
<td>0.0001</td>
<td>2.932</td>
<td>1.805-4.763</td>
</tr>
<tr>
<td>Female gender</td>
<td>-0.6633</td>
<td>0.2393</td>
<td>0.0056</td>
<td>0.515</td>
<td>0.823-0.322</td>
</tr>
<tr>
<td>Antihypertensive drug use</td>
<td>0.7023</td>
<td>0.2787</td>
<td>0.0118</td>
<td>2.018</td>
<td>1.156-3.524</td>
</tr>
<tr>
<td>Six or more prescription medications</td>
<td>0.6525</td>
<td>0.2942</td>
<td>0.0266</td>
<td>1.920</td>
<td>1.079-3.418</td>
</tr>
<tr>
<td>Equation constant</td>
<td>-4.6958</td>
<td>0.2758</td>
<td>0.0001</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
those older persons not in these plans. One study that compared older persons with joint or chest pain in traditional Medicare and Medicare-risk health plans found little significant difference, although the patients in the managed care environment had reduced utilization of services and poorer improvement of symptoms in one of 4 outcomes considered. In contrast, another study that compared 10 HMOs with Medicare-risk contracts to 10 traditional fee-for-service plans found that enrollment in an HMO was not significantly associated with functional status or medical visits. There is much controversy surrounding the matter of how much of the measurable effects of managed health care are due to potential enrollment bias.

Future research should replicate this present study, and these indicators will need to be extended to include other, nonsenior, patient populations, validated for positive and negative predictive values via chart review and updated as clinical practice and standards of care progress.

<table>
<thead>
<tr>
<th>PDRM Indicator</th>
<th>Number of Patients Who Matched the PDRM Indicator</th>
<th>Percentage of All PDRM Indicators Found in the Study Population (n=158)</th>
</tr>
</thead>
<tbody>
<tr>
<td>This outcome has occurred after the pattern of care below:</td>
<td>24</td>
<td>15.2%</td>
</tr>
<tr>
<td>Secondary myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This is the pattern of care:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. History/diagnosis of myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. No use of ASA and/or a beta-blocker (e.g.; metoprolol, etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This outcome has occurred after the pattern of care below:</td>
<td>18</td>
<td>11.4%</td>
</tr>
<tr>
<td>ER visit/hospitalization due to hyperglycemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This is the pattern of care:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Use of an oral hypoglycemic agent (e.g.; chlorpropamide, etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Hemoglobin A1c level not done at least every 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This outcome has occurred after the pattern of care below:</td>
<td>12</td>
<td>7.6%</td>
</tr>
<tr>
<td>ER visit/hospitalization due to hypothyroidism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This is the pattern of care:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Use of a thyroid or antithyroid agent (e.g.; levothyroxine, propylthiouracil, etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. T4/TSH not done before therapy starts and at least every 12 months thereafter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This outcome has occurred after the pattern of care below:</td>
<td>10</td>
<td>6.3%</td>
</tr>
<tr>
<td>ER visit/hospitalization due to hypoglycemia or hyperglycemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This is the pattern of care:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Use of insulin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Hemoglobin A1c level not done at least every 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This outcome has occurred after the pattern of care below:</td>
<td>10</td>
<td>6.3%</td>
</tr>
<tr>
<td>Acute renal failure and/or renal insufficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This is the pattern of care:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Use of an ACE inhibitor (e.g.; captopril, enalapril, etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. BUN/serum creatinine not done at initiation of therapy and at least every 3 months thereafter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This outcome has occurred after the pattern of care below:</td>
<td>8</td>
<td>5.1%</td>
</tr>
<tr>
<td>Gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This is the pattern of care:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. NSAID (e.g.; diclofenac, ibuprofen, ketoprofen, etc.) use for at least one month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. No concurrent use of a cytoprotective agent (misoprostol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Hemoglobin/ hematocrit/CBC not done within 30 days of start of therapy or not done at least every 3 months thereafter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This outcome has occurred after the pattern of care below:</td>
<td>8</td>
<td>5.1%</td>
</tr>
<tr>
<td>ER visit/hospitalization due to congestive heart failure and/or fluid overload</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This is the pattern of care:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. History/diagnosis of high blood pressure (over 140/90) and/or congestive heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. NSAID (e.g.; diclofenac, indomethacin, ketoprofen, etc.) use for at least 3 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

Managed care pharmacists and administrators may be able to use the results of this study to reallocate resources in the most effective and efficient way possible. The identification of the significant risk factors for PDRM should support the development of a rational basis for planning and implementing interventions to reduce drug-related morbidity and mortality in older adults. Furthermore, the patterns of care included in the PDRM indicators may be useful as a clinical tool. They could be used to identify patients who should receive prompt, preventive, clinical follow-up. Future studies may be able to use this knowledge to perform pharmaceutical care interventions that will have the potential to deliver the greatest good and test the results of these “targeting” pharmaceutical care interventions.

ACKNOWLEDGMENTS

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DISCLOSURES

No outside funding supported this study. Author Neil J. MacKinnon served as principal author of the study. Study concept and design, analysis and interpretation of data, critical revision of the manuscript, and statistical expertise were contributed by MacKinnon and author Charles D. Hepler. Drafting of the manuscript was primarily the work of MacKinnon.

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The Cost of Treating Osteoporosis in a Managed Health Care Organization

SHETAL S. DESAI, BS, PharmD; BABETTE S. DUNCAN, PharmD, MBA, BCPS; and ALICE S. SLOAN, RPh

ABSTRACT

OBJECTIVE: To measure the differences in direct health care costs and resource utilization among female enrollees in a health maintenance organization who were aged 45 through 65 years and had either osteoporosis or an osteoporosis-related fracture.

METHODS: One year of medical and pharmacy claims (October 1, 1998, to September 30, 1999) from a mixed-model health plan located in the Midwest were evaluated. Diagnoses were determined from medical claims with ICD-9 codes specific to either osteoporosis or osteoporosis-related fracture. Aggregate costs specific to osteoporosis were compared to all costs incurred by the members regardless of the disease status.

RESULTS: We identified 600 women who had consumed a total of $4.6 million in health care resources and $411,684 in direct costs specifically related to osteoporosis. The highest total average disease-specific costs were found for women with a fracture ($939 per patient per year [PPPY]) compared to those with osteoporosis only ($645 PPPY). Outpatient costs accounted for the highest percentage of mean total annual costs of care, representing up to 38% of the total health care resources consumed. Average medical costs for women with a fracture were highest for the 60 to 64 years age category, the oldest age category in the study population ($17,403 PPPY, P=.0379). Estrogen was the most utilized drug for treatment of osteoporosis, accounting for 41% of the total osteoporosis-specific prescription utilization.

CONCLUSION: The costs of care for members with osteoporosis-related fractures were, on average, higher than for women with osteoporosis only. The component costs included outpatient services, inpatient services, and prescription costs. Women not receiving drug therapy for management of osteoporosis incurred slightly higher total health care costs than women who did not receive drug therapy for osteoporosis.

KEYWORDS: Women’s health, Osteoporosis, Pharmacy claims, Health care outcomes, Cost

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OSTEOPOROSIS is a growing public health concern associated with aging and is a major cause of morbidity and mortality in postmenopausal women. Characterized by low bone mass and microarchitectural deterioration of bone tissue, osteoporosis leads to bone fragility and an increased risk of developing a debilitating fracture. According to the National Osteoporosis Foundation, 13% to 18% of postmenopausal white women in the United States have osteoporosis, and an additional 30% to 50% have low bone density at the hip.1 Postmenopausal women are at greatest risk of developing osteoporosis because of the accelerated loss in bone mass associated with the first several years of menopause. An estimated 1 of every 2 white women will experience an osteoporotic fracture at some point in her lifetime.1 The annual health care costs and resource utilization associated with osteoporosis are staggering, estimated to exceed $13 billion.2

Currently, osteoporosis accounts for nearly 1.5 million fractures annually, with nearly 300,000 attributed to fractures of the hip.1 However, as the average life expectancy continues to increase, the frequency of developing fractures and the costs associated with this disease are expected to more than double by 2026.

The consequences of osteoporosis, including fractures of the hip, wrist, and spine, can have devastating consequences on quality of life. One half of all hip-fracture patients will be unable to live independently, and hip fractures have been associated with a 12% to 36% mortality rate within the first year of incident.1 In addition to the personal burden and impact on quality of life, the costs associated with fracture treatment and rehabilitation are enormous. Many countries, such as Australia and Switzerland, have estimated direct costs of osteoporosis for women; however, few cost-of-illness studies have been published in the United States and, thus, a need for such literature exists.3,4 At present, the most thorough estimate of the cost of osteoporosis was published by Ray and colleagues in 1997.2 This study, based on national health care survey data from 1995, estimated national health care expenditures attributable to osteoporosis fractures for persons aged 45 years and older to be $13.8 billion. Approximately 75% of these costs ($10.3 billion) were for the treatment of white women and included direct medical costs associated with inpatient services, nursing home care, and outpatient services. However, studies estimating the average cost of treatment per patient per year (PPPY) or the proportion of women receiving antosteoporotic agents for secondary fracture prevention in a managed health care setting are limited. Quantification of these costs may prove useful in the determination of cost drivers for this disease and in the allo-
cation of limited resources and promotion of preventive health care services within a managed health care population.

The goal of this study was to determine the direct costs of treating osteoporosis and osteoporosis-related fractures and to identify the principal cost drivers and the prevalence of drug therapy utilization among women with either diagnosis. Using medical and pharmacy claims data, we expected to (a) estimate the direct health care expenditures associated with treating osteoporosis and osteoporosis-related fractures, (b) identify the distribution of costs stratified by age and fracture incidence, and (c) identify any cost differences between women receiving drug therapy for osteoporosis management compared to women not receiving drug therapy. Although the exact dollar amounts and percentages may vary among managed care organizations (MCOs), these findings will likely be generalizable to other mixed-model health maintenance organizations (HMOs). The costs described in this study are from the perspective of an MCO, as derived from actual medical and pharmacy claims data.

Data Collection
All corresponding pharmacy and medical administrative claims were collected for members identified for inclusion in the study. For the pharmacy claims, the following information was collected: ingredient cost paid, copayment amount, date filled, days supply, metric decimal quantity, member identification number, new or refill code, patient date of birth and sex, national drug code (NDC), therapeutic class, prescription number, pharmacy identification number, amount paid by health plan, prescriber identification number, and prescriber last name. For the medical claims, the following information was obtained: primary or secondary diagnosis of osteoporosis or osteoporosis-related fracture, member identification number, place and type of service, allowed amount, date of service, admission and discharge date, provider specialty and type, procedure, specialty, and type codes, and patient date of birth and sex.

Cost Calculations
Once all the data were collected, a relational database was constructed in Microsoft Access using the member identification numbers of the patients as grouped by ICD-9 codes (osteoporosis-only versus fracture), and the medical and pharmacy claims were integrated into a single database. Actual costs incurred by the MCO were included in the analysis. To accurately capture costs, the allowed amount for medical claims and ingredient cost paid for pharmacy claims were used. The allowed amount is defined as the amount submitted for payment as the predetermined allowable charge agreed upon by the managed health care payer for the service or procedure rendered. The drug cost paid amount is defined as the amount allowed by the MCO for payment before any patient liability (copayment or member cost share) has been applied and does not include the pharmacy dispensing fee or rebates or other postservice discounts.

The CPT codes were reviewed, determined to be either related or unrelated to osteoporosis as indicated by the corresponding ICD-9 codes, and assigned to resource unit groups (outpatient services, inpatient services, laboratory, radiology, ambulance, emergency room visits, home health, pharmacy, and other). Overall costs to manage osteoporosis or osteoporosis-related fractures were determined, and a mean was used to calculate the cost of treatment ppy. A mean was calculated for drug costs and medical treatment costs, and the associated costs were further categorized into the above-mentioned resource unit groups. The mean costs were then stratified into 4 age groups (45-49, 50-54, 55-59, and 60-64) and fracture incidence. The percentage of patients with osteoporosis or osteoporosis-related fractures receiving drug therapy was also determined. Treatment for osteoporosis was defined as drug therapy that included a pharmacy claim for one or more of the following medications: estrogen, alendronate, raloxifene, and calcitriol. Estrogen products were further broken down to include the following categories: oral estradiol, transdermal estradiol,
conjugated estrogens, conjugated estrogen-progesterone combinations, estropipate, ethinyl estradiol, esterified estrogens, oral estrogen-testosterone combinations. Risedronate claims were not captured in this study because the first approval for risedronate for the treatment of osteoporosis was on April 14, 2000, after the period of the extant study.

Statistical Analysis

Wilcoxon analysis and chi-square analysis were used to describe the differences in costs between patients with osteoporosis and osteoporosis-related fractures and between patients receiving osteoporotic drug therapy and those not receiving any drug therapy. Wilcoxon analysis was also used to determine cost differences by age distribution. All tests were performed using the Statistical Analysis System for Windows (SAS Institute, Cary, NC), version 6.12, on an IBM-compatible personal computer in Microsoft Windows 97 environment. The a priori level of statistical significance was set at 0.05.

Results

A total of 600 women, 516 with osteoporosis and 84 with fractures, were identified, reflecting prevalence rates of 4.3 per 10,000 female members in the age range 45 to 65 years and 0.84 per 10,000 female members, in the age range 45 to 65 years, respectively. These 600 members consumed $4.6 million in total medical resources and $411,684 in direct costs related specifically to osteoporosis. By age category, women aged 55 to 59 years experienced the greatest percentage of fractures, accounting for 33% of the total (Table 1).

Costs by Indication

Total direct health care costs. Costs unrelated to osteoporosis (unrelated claims) plus the osteoporosis costs comprise the total direct health care costs to manage members with osteoporosis or osteoporosis-related fractures (Table 2). The total direct-cost categories are broken down into the various service components, including inpatient, outpatient, emergency room and ambulance services, radiology, laboratory, pharmacy, and other. The group receiving drug treatment for osteoporosis demonstrated lower inpatient costs than the group not receiving treatment for osteoporosis ($1,475 versus $3,872, \( P = .02 \)). A difference was also demonstrated between drug treatment and no-treatment groups for radiology services and pharmacy costs. There was no apparent difference in total direct health care costs between the drug treatment group and no treatment for osteoporosis group (Table 2).

For the fracture group compared to the osteoporosis group, pharmacy costs were significantly higher for the fracture group ($1,765 versus $1,609 PPPY; \( P = .02 \)). There was no difference in total direct health care costs between the osteoporosis group and the fracture group, and pharmacy costs were the only category of component total direct health care costs in which there was a statistically significant difference between the 2 groups.

Disease-specific costs. For costs related to osteoporotic, disease-specific claims, the group of women receiving treatment for osteoporosis was compared to the group of women not taking any prescription drugs for osteoporosis, and the fracture group was compared to the osteoporosis group. Overall, the average pharmacy costs were lower for the fracture group ($176 PPPY) compared to the osteoporosis group ($314 PPPY, \( P = .0001 \)); however, the outpatient and radiology service costs were greater in the fracture group (Table 3). In addition, the group not receiving any treatment for osteoporosis exhibited higher inpatient, emergency room and ambulance, and laboratory service costs than the group taking osteoporosis medication. The group not receiving drug treatment incurred higher inpatient costs ($296 versus $23, \( P = .0092 \)) and total average disease-specific costs ($724 versus $679, \( P = .0001 \)) compared to the group that received drug treatment for osteoporosis (Table 3).

Principal cost drivers. Outpatient costs made up the high-

---

**TABLE 1** Patient Characteristics

<table>
<thead>
<tr>
<th>Age, year (mean +SD)</th>
<th>Osteoporosis (n=516)</th>
<th>Fracture (n=84)</th>
<th>Combined (N=600)</th>
</tr>
</thead>
<tbody>
<tr>
<td>57 + 5</td>
<td>55 + 6</td>
<td>56 + 5</td>
<td></td>
</tr>
</tbody>
</table>

Age category (number, %)

<table>
<thead>
<tr>
<th>Age category</th>
<th>Osteoporosis (n=516)</th>
<th>Fracture (n=84)</th>
<th>Combined (N=600)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-49</td>
<td>64 (12)</td>
<td>17 (20)</td>
<td>81 (14)</td>
</tr>
<tr>
<td>50-54</td>
<td>114 (22)</td>
<td>20 (24)</td>
<td>134 (22)</td>
</tr>
<tr>
<td>55-59</td>
<td>160 (31)</td>
<td>28 (33)</td>
<td>188 (31)</td>
</tr>
<tr>
<td>60-64</td>
<td>178 (35)</td>
<td>19 (23)</td>
<td>197 (33)</td>
</tr>
<tr>
<td>Receiving osteoporosis drug therapy</td>
<td>457 (89)</td>
<td>57 (68)</td>
<td>514 (86)</td>
</tr>
</tbody>
</table>

* Determined from medical claims with a primary or secondary diagnosis code (International Classification of Diseases-ninth revision [ICD-9] for osteoporosis (codes 733, 733.01, 733.02, 733.03, or 733.09), or osteoporosis-related fractures (ICD-9 codes 733.10, 733.11, 733.12, 733.13, 733.14, 733.15, 733.16, or 733.19).
The Cost of Treating Osteoporosis in a Managed Health Care Organization

Table 2: Total Direct Health Care Costs* Per Patient Per Year

<table>
<thead>
<tr>
<th>Service Type</th>
<th>Treatment n=514</th>
<th>No treatment n=86</th>
<th>P value</th>
<th>Fracture n=84</th>
<th>Osteo-only n=516</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Mean (+ SD)</td>
<td>1475 (+ 6,122)</td>
<td>3,872 (+ 11,563)</td>
<td>0.02</td>
<td>2,719 (+ 9,785)</td>
<td>1,672 (+ 6,680)</td>
<td>0.82</td>
</tr>
<tr>
<td>Outpatient Mean (+ SD)</td>
<td>2,692 (+ 4,284)</td>
<td>4,194 (+ 7,061)</td>
<td>0.12</td>
<td>3,749 (+ 5,546)</td>
<td>2,770 (+ 4,664)</td>
<td>0.83</td>
</tr>
<tr>
<td>ER/Ambulance Mean (+ SD)</td>
<td>36 (+ 111)</td>
<td>37 (+ 118)</td>
<td>0.83</td>
<td>51 (+ 123)</td>
<td>33 (+ 110)</td>
<td>0.06</td>
</tr>
<tr>
<td>Radiology Mean (+ SD)</td>
<td>495 (+ 1,262)</td>
<td>958 (+ 3,356)</td>
<td>0.02</td>
<td>852 (+ 3,585)</td>
<td>514 (+ 1,272)</td>
<td>0.13</td>
</tr>
<tr>
<td>Laboratory Mean (+ SD)</td>
<td>666 (+ 1,043)</td>
<td>1,187 (+ 2,943)</td>
<td>0.65</td>
<td>1,042 (+ 1,964)</td>
<td>692 (+ 1,384)</td>
<td>0.70</td>
</tr>
<tr>
<td>Pharmacy Mean (+ SD)</td>
<td>1,674 (+ 1,593)</td>
<td>1,373 (+ 1,665)</td>
<td>0.0006</td>
<td>1,765 (+ 1,844)</td>
<td>1,609 (+ 1,595)</td>
<td>0.04</td>
</tr>
<tr>
<td>Other (DME) Mean (+ SD)</td>
<td>31 (+ 237)</td>
<td>8 (+ 29)</td>
<td>0.13</td>
<td>13 (+ 85)</td>
<td>30 (+ 234)</td>
<td>0.93</td>
</tr>
<tr>
<td>Total Mean (+ SD)</td>
<td>7070 (+ 11,477)</td>
<td>11,628 (+ 21,800)</td>
<td>0.65</td>
<td>10,191 (+ 18,926)</td>
<td>7,322 (+ 12,399)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Includes costs for all health-care-related claims.

Table 3: Disease-specific Direct Health Care Costs* Per Patient Per Year

<table>
<thead>
<tr>
<th>Service Type</th>
<th>Treatment n=514</th>
<th>No treatment n=86</th>
<th>P value</th>
<th>Fracture n=84</th>
<th>Osteo-only n=516</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Mean (+ SD)</td>
<td>23 (+ 284)</td>
<td>296 (+ 1,560)</td>
<td>0.0092</td>
<td>265 (+ 1,544)</td>
<td>29 (+ 318)</td>
<td>0.09</td>
</tr>
<tr>
<td>Outpatient Mean (+ SD)</td>
<td>139 (+ 315)</td>
<td>161 (+ 295)</td>
<td>0.98</td>
<td>225 (+ 456)</td>
<td>129 (+ 281)</td>
<td>0.006</td>
</tr>
<tr>
<td>ER/Ambulance Mean (+ SD)</td>
<td>0.61 (+ 7.2)</td>
<td>2.4 (+ 11.8)</td>
<td>0.01</td>
<td>1 (+ 8)</td>
<td>0.83 (+ 8)</td>
<td>0.48</td>
</tr>
<tr>
<td>Radiology Mean (+ SD)</td>
<td>53 (+ 150)</td>
<td>109 (+ 704)</td>
<td>0.001</td>
<td>103 (+ 710)</td>
<td>55 (+ 152)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Laboratory Mean (+ SD)</td>
<td>119 (+ 200)</td>
<td>154 (+ 371)</td>
<td>0.087</td>
<td>168 (+ 390)</td>
<td>117 (+ 195)</td>
<td>0.98</td>
</tr>
<tr>
<td>Pharmacy Mean (+ SD)</td>
<td>343 (+ 264)</td>
<td>NA</td>
<td>0.0001</td>
<td>176 (+ 205)</td>
<td>314 (+ 277)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Other (DME) Mean (+ SD)</td>
<td>0.76 (+ 10.1)</td>
<td>NA</td>
<td>–</td>
<td>NA</td>
<td>0.76 (+ 10)</td>
<td>–</td>
</tr>
<tr>
<td>Total Mean (+ SD)</td>
<td>679 (+ 706)</td>
<td>724 (+ 2,493)</td>
<td>0.0001</td>
<td>939 (+ 2,523)</td>
<td>645 (+ 697)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* Costs for medical and pharmacy claims related to osteoporosis or fracture.

Table 2 and Table 3 provide a detailed comparison of direct health care costs associated with fracture and osteoporosis for patients receiving treatment versus those not receiving treatment, as well as those with fractures only versus those with osteoporosis only. The data show significant differences in costs across various service types, with pharmacy costs being the highest for both fracture and osteoporosis groups. The findings also highlight the importance of early detection and treatment to minimize long-term costs. For instance, the highest costs were observed for inpatient services, followed by outpatient services and pharmacy costs.

Cost by age category. Average medical costs for women with a fracture were highest for the 60 to 64 years age category ($17,403 PPPY, P=0.0379) (Table 3). The total pharmacy-related costs were highest for women age 55 to 59 years with a fracture ($2,589 PPPY, P=0.0137). The disease-specific costs broken down by age category showed that women with a diagnosis of osteoporosis in the 45 to 49 years and 50 to 54 years age categories had the highest average pharmacy-related costs when compared to women with a fracture diagnosis ($243 and $304 PPPY, respectively; P<0.05). Disease-specific costs for women aged 60 to 64 years with fractures also appeared to be the highest in comparison to the other age categories ($1,991 PPPY), but these apparent differences were not statistically significant (Table 4).

Cost by drug use. A total of 86% (n=514) of women were receiving osteoporosis medication, while 14% (n=86) were not; 32% of women with a history of fractures were not receiving drug therapy, while 11% of women with an osteoporosis diagnosis were not on drug therapy. Women in the 60 to 64 years age category not receiving osteoporosis drug therapy incurred the highest average cost PPPY ($18,592) compared to women not receiving drug therapy ($5,074, P=0.0156). Overall, women not receiving osteoporosis treatment appeared to have slightly higher average total medical costs ($11,628 versus $7,070), but this apparent difference was not statistically significant (Table 2). Women receiving drug treatment for osteoporosis had lower total disease-specific direct health care costs compared to women who did not receive drug treatment for osteoporosis ($724 versus $679, P=0.0001) (Table 4).
Breakdown of osteoporosis drug treatment. Forty-one percent of the patients taking drug therapy for osteoporosis were on estrogen or estrogen combination (i.e., progestin or testosterone combination) alone, followed by alendronate monotherapy (17%), raloxifene monotherapy (4%), and calcitonin monotherapy (6%). Other treatments included combinations of the above 4 drugs and accounted for the remaining 32% of the prescription utilization. Estrogen and alendronate taken in combination comprised 18%, and estrogen and calcitonin taken in combination accounted for 5% of the prescription utilization.

Discussion
This study identified 600 women with osteoporosis or fracture diagnosis who utilized a total of $411,684 in osteoporosis-related health care resources. Approximately 86% (n=514) of women with a diagnosis of osteoporosis or fracture received drug therapy. Torgerson and Dolan found that among fracture patients (hip, wrist, and spine), only those with a diagnosed vertebral fracture had a significantly higher use of drug therapy (39% versus 2%). Furthermore, they found that as many as 59% of fracture patients were not prescribed antiosteoporotic treatment in the year following the fracture. Although the percentage cited in this study is higher than that reported for the general population, it is not known how many women continue to take therapy as directed over a long period of time. Prior research conducted by Ettinger et al. found that as many as 50% to 60% of women initiating hormone therapy discontinue within 3 years.

Another reason for the higher percentage of drug therapy use among this population of women in the extant study is due to the inclusion criteria that included at least one pharmacy claim per calendar quarter. Using this criterion to determine eligibility may have selectively excluded members who chose not to obtain drug therapy during the 1-year observation period. All members with medical coverage were also covered by pharmacy benefits through the same health plan, and it is therefore unlikely that these women were receiving prescriptions from another source not captured by the plans prescription claims.

A more thorough method for determining continuous eligibility would have involved examination of the enrollment database to determine active enrollment. However, this eligibility information was not readily available for analysis in this study.

The mean age of the women in this population was 56.3 years. As expected, older women appeared more likely to incur a fracture attributable to osteoporosis. Women in the 55 to 59 years category experienced the greatest percentage of fractures, accounting for 33% of the total. A limitation of this study was that women aged 65 years and older were not included as part of this analysis and would have offered an interesting look at fracture incidence and costs in a linear relationship to age. Women age 65 and older were excluded from analysis because access to the complete Medicare claims data was not available and reasonable coordination of benefits was not possible, reducing the certainty of capturing all relevant medical claim records for women age 65 older.

On the basis of mean total costs, women taking osteoporosis medications exhibited lower health care resource consum-
tion in inpatient, emergency room and ambulance, and radiology services than those women not taking any drug treatment for osteoporosis. Women with fractures were less likely to be receiving osteoporosis-related drug treatment (68% versus 89%) than their osteoporosis counterparts without diagnoses for fractures. Interestingly, women with fractures incurred lower disease-specific pharmacy costs but had higher general pharmacy costs than women with osteoporosis. The need to manage other disease states that were a consequence of the fracture, such as pain, antithrombotic therapy, and depression, is the obvious explanation for this finding. However, further analysis is warranted to determine the differences in the types of prescription utilization accounting for the overall higher pharmacy costs in women with fracture compared to osteoporosis-only.

When comparing total health-care-related costs between the 2 groups of women, osteoporosis and fracture, pharmacy costs were significantly higher for the fracture group, but only 68% of the patients in the fracture groups were receiving drug therapy to prevent osteoporosis-related fracture. The major cost drivers for both groups included outpatient services (38%), followed by inpatient services (24%) and pharmacy (21%). When disease-specific costs were calculated for both groups, the major cost drivers were found to be pharmacy costs (43%), followed by outpatient (21%), laboratory (18%), and inpatient services (9%). The differences in the identified cost drivers when accounting for only osteoporosis-specific health care utilization may be attributed to the criteria used to identify osteoporosis-related costs. Pharmacy costs were derived from prescriptions for drugs used to treat osteoporosis. With regard to coding practices, not all physician offices code diagnoses in the same manner on medical claims. This practice may result in variations in coding. Finally, members were identified by primary and secondary diagnosis codes. Members with multiple disease states with more than 2 diagnosis codes may not have been captured in the dataset due to the method of patient identification used in this study. The results of our study may have been more representative and reliable if we had expanded our search method to include all diagnoses submitted on the medical claims. This method may have captured more osteoporosis-specific claims. Given these factors, the cost estimates for disease-specific osteoporosis or fracture events may have been underestimated.

Estrogen therapy was the most prevalent drug therapy among women in this study population, followed by alendronate, calcitonin, and raloxifene. In this study, women receiving osteoporosis drug treatment, on average, had lower medical-related health care costs than their non–drug-therapy counterparts. The 60 to 64 years age group not receiving drug therapy had greater than 3 times the average total cost PPPY ($18,592) than women taking osteoporosis drug therapy ($5,074, \( P = .0156 \)). This result may suggest that the use of prescription drugs is associated with lower medical and other health-care-related costs. For osteoporosis-specific medical costs, no statistically significant differences were found between users and nonusers of osteoporosis drug therapy. However, average medical costs were lower for the group utilizing osteoporosis-specific drug therapy. Further investigation is needed to conclusively show that use of an osteoporosis drug may be positively correlated with a decrease in health care costs and resource utilization.

While estrogen replacement therapy (ERT) and opposed estrogen replacement therapy, otherwise known as hormone replacement therapy (HRT), have long been considered to be the most effective for maintenance of bone density and the development of stronger bones, recent studies have suggested

<table>
<thead>
<tr>
<th>TABLE 4</th>
<th>Average Medical and Pharmacy-related Costs Per Patient Per Year by Age Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Group</td>
<td>Average Total Health Care Costs (Mean + SD)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Medical</td>
</tr>
<tr>
<td>45-49 (n=64)</td>
<td>6,632 + 12,657</td>
</tr>
<tr>
<td>50-54 (n=114)</td>
<td>6,506 + 13,688</td>
</tr>
<tr>
<td>55-59 (n=160)</td>
<td>5,435 + 11,973</td>
</tr>
<tr>
<td>60-64 (n=178)</td>
<td>5,125 + 10,005†</td>
</tr>
<tr>
<td>Fracture</td>
<td>Medical</td>
</tr>
<tr>
<td>45-49 (n=17)</td>
<td>3,921 + 4,702</td>
</tr>
<tr>
<td>50-54 (n=20)</td>
<td>5,802 + 9,433</td>
</tr>
<tr>
<td>55-59 (n=28)</td>
<td>6,942 + 11,080</td>
</tr>
<tr>
<td>60-64 (n=19)</td>
<td>17,403 + 33,886†</td>
</tr>
</tbody>
</table>

* Disease specific refers to costs specifically related to osteoporosis or fracture-related costs.
† Statistical significance (\( P < .05 \)) when women in age categories compared between osteoporosis and fracture groups.

Pharmacy costs were compared to pharmacy costs and medical costs were compared to medical costs.
that the risk of harm from prolonged HRT may outweigh its benefits. Combined estrogen/progestin therapy (HRT) has been associated with unwarranted adverse effects such as vaginal bleeding, breast tenderness, increased risk of cardiovascular disease, and breast cancer. Recent findings from the Women's Health Initiative (WHI) study assessed the effects of combined HRT in healthy postmenopausal women with an intact uterus. These findings will most likely decrease the use of postmenopausal hormones for the prevention of osteoporosis. The WHI study was designed to assess major health benefits and risks of the most commonly used combined hormone preparation in the United States. The study showed no benefit for the prevention of coronary heart disease and indicated a small, but significant, increase in the risk of cardiovascular events for women taking the combined HRT. Women on the combined HRT had a 22% increased risk of cardiovascular disease, including a 29% increased risk of coronary heart disease.

The WHI study was also designed to determine the incidence of breast cancer as a primary adverse outcome of combined therapy. The WHI study found a 26% increase in the risk of breast cancer, confirming previously observed findings. It is important to note that while there was a statistically significant increased risk of cardiovascular disease and breast cancer in WHI, the absolute increased risk for individual women was small and estimated to be 7 more coronary heart disease events (37 versus 30) per 10,000 women per year and 8 additional new cases (38 versus 30) per 10,000 women per year, respectively.

Of equal or perhaps greater importance, the WHI study showed positive correlation between use of HRT and the decreased risk of vertebral and other osteoporotic fractures. The rates of hip fracture decreased by 34%, confirming that HRT has beneficial impact on bone mineral density. The WHI study was the first clinical trial to date to demonstrate the protective effect of HRT in the prevention of fractures secondary to osteoporosis.

While the data from the WHI study are suggestive and the findings statistically significant, the results from the study pertain only to women taking continuous conjugated equine estrogen (0.625 mg/day) and medroxyprogesterone acetate (2.5 mg/day), and the conclusions can be applied only to this formulation. Based on the findings from the WHI study, users of HRT seeking protective benefits for osteoporosis prevention may turn to alternative therapies, including the bisphosphonates or selective estrogen receptor modulators. If women also have vasomotor menopausal symptoms, HRT or ERT are of obvious benefit but should be evaluated for risk versus benefit for each individual patient.

Many health plans and employer groups are seeking to develop WHI programs intended to increase awareness of issues surrounding women's health among members and physicians. Possible interventions include identification of candidates who would benefit from bone-strengthening drug therapy. Health plan sponsors may also want to identify women currently on HRT to help physicians assess reasons for use and to evaluate potential benefits versus risks and alternative therapies. The decision to use HRT is patient-specific and requires close examination of the risk versus benefit in each individual. Nondrug interventions include fall-avoidance education, exercise programs, and nutritional supplementation, including calcium and vitamin D. Increase in the use of bisphosphonates and selective estrogen receptor modulators may become more apparent to pharmacy benefit managers and have profound financial impact on costs of the pharmacy benefit as these drugs replace some of the ERT and HRT use.

**Limitations**

This study was based on a 1-year snapshot of retrospective claims data. Using claims experience to study groups for the purpose of making comparisons can be challenging because the data contained within medical and pharmacy claims do not contain laboratory values and other information about the health status of the study population. There may have been population-based differences in demographics between the various groups of women that we studied (osteoporosis versus fracture diagnosis and treatment versus no treatment) that we were not able to account for because we used medical claims data. We were unable to control for demographic differences between the groups. Additionally, we observed a 1-year period of time to study patterns of resource utilization and cost differences among the groups of women. This time period is not long enough to draw definitive conclusions, and therefore, needs to be studied further by others. For example, it is possible that women in the osteoporosis-only group had, in fact, incurred an osteoporosis-related fracture prior to the data capture period if an ICD-9 code for fracture was not identified during the extraction phase. This is one of the limitations of a retrospective claims-based study.

The absence of a control group makes our results suggestive. We are unable to make definitive conclusions regarding the costs of care without a control group. The sample sizes between the groups of women were also not standardized because we did not have control over how many women would be identified by the criteria that we established at the beginning of the study. This is another limitation of using medical and pharmacy claims data. Our results may also be influenced by the characteristics of the patients enrolled in this health plan. Since this health plan serves mostly employer groups, the women enrolled may be younger, healthier, and more active, and women aged 65 years or older were excluded from analysis because we were unable to obtain reliable Medicare medical claims records for them.

Our method of cost analysis attempted to capture direct medical and pharmacy costs to reflect the total direct cost burden, including member cost amounts (e.g., medical visit and prescription copayments). These are discounted direct medical costs obtained through MCO negotiation with hospital, medical, and pharmacy providers.

**Conclusion**

The average direct health care costs were highest for women aged 60 to 64 years presenting with fractures compared to women in
the same age category with osteoporosis only. In order of magnitude, the cost drivers for osteoporosis were outpatient services, inpatient services, and pharmacy costs. Women not receiving drug therapy for osteoporosis treatment incurred slightly higher average total health care costs than women receiving drug therapy. The results in the study are suggestive that treatment with osteoporotic agents may offset use of disease-specific health care resources and costs. Further research in this area is warranted to make a definitive conclusion. Unhealthy patients incur a greater direct cost burden to health plans. The use of preventive health care may offset the long-term consequences of disease and improve health status. One of the primary concerns for MCOs is the allocation of resources for preventive care to maintain or improve health status and thereby offset the long-term cost of treating diseases with avoidable adverse consequences.

ACKNOWLEDGMENTS
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DISCLOSURES
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Modeling the Annual Costs of Postmenopausal Prevention Therapy: Raloxifene, Alendronate, or Estrogen-Progesterone Therapy

C. DANIEL MULLINS, PhD, and ROBERT L. OHSFELDT, PhD

ABSTRACT

OBJECTIVE: To estimate the annual cost and outcome impacts attributable to raloxifene, alendronate, and estrogen-progesterone therapy as prevention therapies among postmenopausal women over the first 7 years of hormone replacement therapy (HRT).

METHODS: A budget-impact model was devised to compare the costs, benefits, and costs per event avoided for various postmenopausal therapies (raloxifene, alendronate, or estrogen-progesterone combination therapy), compared to no intervention, taking into account the persistency rates. Net costs are direct medical costs attributable to treatments relative to no intervention. Net benefits are defined as the number of events avoided as a result of therapy. The main outcome measures are annual total net costs, net benefits, and costs per event avoided compared to no intervention among postmenopausal white women with intact uteri and normal baseline risks for osteoporotic hip or vertebral fractures, fatal or nonfatal myocardial infarction, and breast cancer. Data and model assumptions are based on clinical trial data and published retrospective studies.

RESULTS: The average annual net cost of therapy declines after the first year of therapy for all interventions, primarily due to discontinuation, and continues to decline over time due to savings in medical costs for events avoided. Net events avoided are greater for raloxifene than alendronate, but HRT use results in net harm. The cost per event avoided is lower for raloxifene than alendronate. Improved persistency improves the cost-effectiveness for both interventions. Sensitivity analyses indicate the model results are most sensitive to the assumed impact of raloxifene on coronary heart disease and breast cancer risk. Alendronate as a prevention intervention is dominated by raloxifene under almost all model scenarios.

CONCLUSION: The annual cost of long-term postmenopausal prevention therapy is highest during the first few years of therapy. Long-term prevention does not provide a return on investment in fewer than 3 years, but savings in medical costs partially offset intervention costs after 2 years. For postmenopausal women, pharmacologic interventions with multiple prevention benefits tend to be more cost effective than interventions with a single source of health benefit.

KEYWORDS: Postmenopausal, Prevention, Cost-effectiveness, Osteoporosis

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F or any new pharmacological agent, it is difficult to assess the agent’s economic impact on health care system costs based on clinical trial data alone. In such cases, cost modeling may be particularly useful in estimating the potential economic impact of a new agent. Cost models make use of the best available evidence about the clinical effectiveness of alternative agents and the resource consumption attributable to their use. A cost model can assist decision makers until more definitive information becomes available about outcomes and costs in actual clinical practice. Such analyses can also inform and structure subsequent prospective trials, leading to far better trial designs.

Traditionally, cost-effectiveness or cost-utility analyses of long-term prevention therapies compare the (discounted) lifetime costs of therapy to its lifetime clinical benefits, often summarized as incremental cost per quality-adjusted life-year (QALY) gained. However, this type of cost-effectiveness information often is either not used at all or given little weight in decisions about the formulary status of drugs. A number of possible explanations for this phenomenon exist, but a likely barrier to use of cost-effectiveness analysis is that formulary decision makers often have a shorter planning horizon than that employed in standard cost-effectiveness analyses. The decision to “invest” in prevention may be viewed as a capital budgeting issue, where data for the time-path of costs and benefits over a relevant planning horizon are needed to assess alternative investment options. However, the current standards for reporting results of cost-effectiveness analyses do not require or recommend reporting the time-path of costs and benefits. Thus, cost-effectiveness models that employ net present values for a 30-year or longer time horizon may not be considered relevant for these decision makers.

In contrast to lifetime models, in this paper, a medium-term cost-effectiveness model is developed using the perspective of a payer such as a managed care organization. Specifically, the model provides estimates of the annual costs and outcome impacts attributable to the use of alternative pharmaceutical agents for the primary prevention of osteoporosis compared to no drug therapy, over the first 7 years of therapy. In addition, the model departs from many cost-effectiveness analyses by accounting for the impact of early discontinuation of therapy observed in clinical practice, which provides a more realistic assessment of the potential costs and benefits of an intervention. The objective of this medium-term cost model is to estimate annual cost and outcome impacts attributable to raloxifene, alendronate and estrogen-progesterone therapy as prevention therapies among postmenopausal women over the first 7 years of
therapy. The goal is to provide decision makers in managed care organizations with information needed to anticipate the budgetary impact of alternative prevention strategies, as well as an assessment of their potential benefits, within a time horizon relevant to the decision makers.

Model Design

The model compares osteoporosis prevention strategies using one of 3 prescription drugs or calcium and vitamin D supplementation only (no prescription drug intervention). The 3 prescription drug alternatives considered are (1) conjugated equine estrogens plus medroxyprogesterone acetate [CEE+MPA], a specific example of continuous-combined estrogen-progestin replacement therapy; (2) raloxifene hydrochloride, an agent within the class of drugs called selective estrogen receptor modulators (SERMs); and (3) alendronate, a bisphosphonate. In all cases, the prescription drug interventions include calcium and vitamin D supplementation. The model focuses on 3 main clinical outcomes: hip and vertebral fracture, fatal and nonfatal myocardial infarction (MI), and breast cancer. Direct medical costs and the number of model disease events (fractures, MIs, breast cancers) are estimated for each year for each of the 4 model arms. The differences in direct medical costs in the treatment arms and costs in the no-drug-intervention arm are defined as the net costs of therapy. Similarly, net benefits are defined simply as the number of clinical events avoided as a result of therapy.

The model results reported here focus on women who have not had a hysterectomy who initiate therapy at age 55. As a base case, the populations considered consist of women representing a normal distribution of age-related baseline risks for the 3 outcomes of interest to avoid the complication of incorporating risk-assessment procedures and their costs into the model. However, the impact of “costless” risk stratification is assessed in alternative model scenarios. To simplify the model, a fixed population is analyzed (i.e., no disenrollment or new starts over the 7-year period).

To further simplify the model, the following clinical events are excluded: other osteoporotic fractures (e.g., wrist fractures), non-MI coronary heart disease (CHD) outcomes, uterine cancer, and venous thromboembolic events (VTE). The exclusion of other fracture outcomes biases the model results in favor of no drug intervention but may not bias comparisons across treatment arms significantly unless clinical effectiveness in preventing other fractures differs substantially across agents. Excluding non-MI CHD events (e.g., unstable angina, revascularization procedures not secondary to treatment for MI) may bias model results to the extent that either CEE+MPA or raloxifene affect non-MI CHD events. Excluding uterine cancer may favor CEE+MPA, although the bias should be negligible if, as generally assumed, the impact of CEE+MPA on uterine cancer risk is small. Other potential benefits (e.g., prevention of Alzheimer’s disease) or risks (e.g., ovarian cancer) associated with CEE+MPA use are not accounted for in the model. The exclusion of VTE will bias the model in favor of both CEE+MPA and raloxifene. Since VTE risk increases with age, this bias will be larger in models focused on older postmenopausal women compared to models focused on younger postmenopausal women. For younger women, the exclusion of VTE will have a negligible impact on net costs. (For example, if CEE+MPA or raloxifene increases annual VTE risk from 1/1,000 to 3/1,000, and the expected cost of VTE is $4,000, the impact on net cost is $8 per woman initiating therapy.)

A key determinant of costs and outcomes at the population level is the pattern of persistence of therapy. A prevention therapy that is initiated and then discontinued within a short period of time generates costs with little or no benefit. The medium-term model presented here differs from many traditional cost-effectiveness models of long-term prevention therapies in that the impact of early discontinuation of therapy on costs and outcomes is evaluated.

The general model structure is illustrated in Figure 1. For each of the 4 interventions (including no drug intervention), in each period, every woman faces some risk of an event: fracture (vertebral or hip), MI (fatal or nonfatal), or breast cancer (differentiated by stage at diagnosis). If no event occurs, the woman moves to the next period to face the risks again. If an event occurs, the process ends with an anticipated stream of costs in the current and subsequent years. In each of the prescription drug intervention arms (raloxifene, CEE+MPA, alendronate), annual event risks are altered by therapy. For the intervention arms, the full impact of therapy on event risks over time occurs only if a woman who initiates therapy remains persistent on therapy. If therapy is discontinued, she begins to revert to the event risks associated with no drug therapy.

As with any model, the specific effects of therapy on costs and outcomes are not known with certainty. This is particularly true for a new therapeutic option for which data are limited. A base-case model scenario is specified using reasonable estimates of the potential effectiveness of each therapy. To address uncertainty about the assumptions regarding the effects of therapy, alternative model scenarios are evaluated in sensitivity analyses.
Clinical Effectiveness Assumptions

The clinical effectiveness assumptions, including all efficacy and safety assumptions, are summarized in Table 1. All assumptions about percent risk reduction are rounded to the nearest multiple of 5. The specific components of model assumptions are described in greater detail below.

Vertebral/hip fracture. Evidence of vertebral fracture prevention efficacy for raloxifene arises from the Multiple Outcomes of Raloxifene Evaluation (MORE) study, a placebo-controlled randomized clinical trial (RCT) with vertebral fracture as a primary endpoint.14 Vertebral fracture prevention efficacy assumptions for alendronate are taken from the Fracture Intervention Trials (FIT).5 In addition to these data, estimates of fracture efficacy after one year of therapy have been reported for both raloxifene6 and alendronate.7 These estimates are based on reported clinical vertebral fractures in MORE and FIT, respectively. Osteoporosis trials usually focus on vertebral fractures as a primary endpoint and thus are not powered statistically to detect differences in incident hip fractures between treatment and placebo groups. Nonetheless, in FIT, a statistically significant treatment effect for hip fracture risk reduction was observed for alendronate, but only in women with prior osteoporotic fractures. However, the base-case model scenario assumes the same relative reduction in hip fracture risk applies to women with low bone mass but no prior fractures using alendronate. No statistically significant differences in hip fracture incidence were observed in the MORE study. However, the treatment difference in vertebral bone mineral density (BMD) only accounts for (in statistical terms) about one third of the actual vertebral fracture rate treatment difference observed in MORE.9,10 This fact, together with the fact that raloxifene increases total hip BMD,11 suggests that raloxifene is likely to have some clinical benefit in terms of reducing hip fracture risk. Nonetheless, to be conservative, the base-case model scenario assumes no fracture prevention efficacy for raloxifene at the hip.

Until recently, no evidence for the fracture prevention efficacy of CEE+MPA from a large, placebo-controlled RCT was available. Estimates from observational studies were summarized in a report produced by the National Osteoporosis Foundation.8 However, given the potential for “prevention bias” in observational studies, such estimates may overstate CEE+MPA’s true fracture prevention efficacy. In the model, fracture efficacy assumptions for CEE+MPA are based on data from the recently halted estrogen-progestin therapy RCT conducted as part of the Women’s Health Initiative (WHI), which reported a 33% reduction in both hip and vertebral fracture rates associated with CEE+MPA use over 5 years.12

Fatal/non-fatal MI. The data collected in MORE included CHD events as a secondary endpoint. Since the primary endpoint in MORE was vertebral fracture among women with osteoporosis, women participating in the study represented an approximately normal age-related distribution of CHD risks at baseline. Over the entire sample (N=7,705), use of raloxifene (60 mg) was associated with an 18% reduction in the risk of CHD events (95% CI, 0.56, 1.22) over 4 years. A post-hoc analysis of a subset of 1,035 women at increased risk for cardiovascular disease at baseline found that use of raloxifene was associated with a 33% reduction in the risk of cardiovascular disease events (95% CI, 0.37, 1.19) over 4 years. There was no evidence of an “early” increase in risk in either sample.13

Neither of these point estimates is statistically significant. However, using the impact of raloxifene on serum cholesterol established in RCTs14 and the Coronary Heart Disease Policy Model to estimate the impact of therapy on the risk of a CHD event results in an estimated risk reduction of 14%, which is similar to the 18% point estimate from the full sample in MORE. The literature suggests at least a 1-year lag in modeling the onset of effect of LDL cholesterol reduction on CHD event risk reduction.15 To be conservative, the base-case model scenario assumes a 15% reduction in CHD risk after a 2-year lag in onset of effect for raloxifene.

The WHI study results showed a 29% increase in the risk of CHD events associated with CEE+MPA use over 5 years. Findings reported by year of follow-up indicated point estimates of a 78% increase in risk during the first year of therapy, a 15% increase during the second year, with approximately no difference thereafter. The finding of “early” CHD harm in WHI is consistent with the Heart and Estrogen/Progestin Replacement Study (HERS)16 finding of a statistically significant 50% increase in CHD risk during the first year of therapy. A re-analysis of the HERS data concluded that the use of CEE+MPA was associated with net CHD harm in terms of survival over 5 years.17 Other studies also suggest the potential for an increase in CHD risk associated with the initiation of HRT.18 Thus, the base-case model scenario assumes “early” harm for CEE+MPA during the first 2 years of therapy with no effect thereafter. The model assumes alendronate provides no CHD benefits or risks.

Breast cancer. Breast cancer was another secondary end-

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**TABLE 1** Summary of Base-Case Model Efficacy/Safety Assumptions: Relative Risk Decrease/Increase

<table>
<thead>
<tr>
<th>Fracture (Fx)</th>
<th>CEE+MPA</th>
<th>Raloxifene</th>
<th>Alendronate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip Fx (Y1)</td>
<td>-18%</td>
<td>0</td>
<td>-25%</td>
</tr>
<tr>
<td>(&gt;Y1)</td>
<td>-35%</td>
<td>0</td>
<td>-50%</td>
</tr>
<tr>
<td>Vertebral Fx (Y1)</td>
<td>-45%</td>
<td>-65%</td>
<td>-60%</td>
</tr>
<tr>
<td>(&gt;Y1)</td>
<td>-35%</td>
<td>-50%</td>
<td>-50%</td>
</tr>
<tr>
<td>Breast Cancer (Y1)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(&gt;Y4)</td>
<td>0</td>
<td>-55%</td>
<td>0</td>
</tr>
<tr>
<td>CHD (Y1)</td>
<td>+75%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(Y2)</td>
<td>+15%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(&gt;Y2)</td>
<td>0</td>
<td>-15%</td>
<td>0</td>
</tr>
</tbody>
</table>

---

### Risk Decrease/Increase

<table>
<thead>
<tr>
<th>Fracture (Fx)</th>
<th>CEE+MPA</th>
<th>Raloxifene</th>
<th>Alendronate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertebral Fx (Y1)</td>
<td>-45%</td>
<td>-65%</td>
<td>-60%</td>
</tr>
<tr>
<td>(&gt;Y1)</td>
<td>-35%</td>
<td>-50%</td>
<td>-50%</td>
</tr>
<tr>
<td>Breast Cancer (Y1)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(&gt;Y4)</td>
<td>0</td>
<td>-55%</td>
<td>0</td>
</tr>
<tr>
<td>CHD (Y1)</td>
<td>+75%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(Y2)</td>
<td>+15%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(&gt;Y2)</td>
<td>0</td>
<td>-15%</td>
<td>0</td>
</tr>
</tbody>
</table>
Dollars per Woman Initiating $1,000 difference was not statistically significant. These findings are consistent with a recent re-analysis of data from 51 observational studies, which concluded that each year of postmenopausal HRT increases the risk of breast cancer by 2.3%. This translates into a 17% increase over 7 years of therapy. The base-case model scenario assumes the use of CEE+MPA increases the relative risk of breast cancer risk by 25% after 3 years of therapy. Alendronate is assumed to have no impact on breast cancer risk.

Therapy Persistence Rates

The assumed persistence rates for CEE+MPA are taken from Ettinger et al., extrapolated from 3 to 7 years. About 4 of 5 postmenopausal women who initiated CEE+MPA were found to have discontinued therapy within 3 years. The base-case model scenario assumes persistence rates (i.e., the percentage of women who have not discontinued therapy) across all 3 therapy arms are identical to the rate assumed for CEE+MPA. However, a recent analysis of data from a large managed care organization found that discontinuation rates at one year after initiation were higher for estrogen-progestin therapy compared to raloxifene. The base model assumes that 41% of patients are persistent at the end of the first year and 26%, 19%, 17%, 15%, 14%, and 13% are persistent at the end of the second through seventh year, respectively. Alternative scenarios are used to evaluate the impact of discontinuation rate assumptions.

Costs

The annual cost of each drug therapy is assumed to be the average wholesale price (AWP) as of October 1, 2000, for the recommended daily dosage times 365 plus the cost of one physician visit per year. To assess the costs of managing side effects or treating adverse events of therapy, estimates of resource utilization associated with side effects of HRT, andralonate, and raloxifene are combined with estimates of costs of resources (using Medicare payment rates). Most of the costs of side effects are assumed to occur during the first year of therapy, and all side-effect costs are assumed to end with discontinuation of therapy. Specifically, the side-effect costs used for years 1, 2, and 3 Beyond in the model are $200, $100, and $25 for estrogen-progestin; $100, $0, and $0 for alendronate; and $25, $15, and $0 for raloxifene.

No direct estimates from RCTs of the cost impact of raloxifene or the alternative therapies are available. The model makes use of estimates of event costs in the literature to assess potential costs averted by therapy. Estimated direct medical costs attributable to hip fracture, fatal MI, and nonfatal MI are from the former Congressional Office of Technology Assessment. Estimated direct medical costs of vertebral fractures are from the National Osteoporosis Foundation. Estimated annual direct medical costs of treating breast cancer for 4 years postdiagnosis, by stage at diagnosis, are from Legoretta et al. Costs reported in the literature were converted to 2000-equivalent dollars using the medical care component of the consumer price index. Cumulative costs estimates are not discounted to their present value, though it should be noted that discounting has less impact over the medium-term period addressed in the model compared to a traditional lifetime model.
Results

Net Costs

Net costs are defined as costs attributable to treatments relative to no drug intervention and consist of 3 components: (1) pharmacy costs, (2) cost of managing side effects or minor adverse events attributable to therapy, and (3) savings or costs associated with events (fractures, fatal/nonfatal MIs, or breast cancers) avoided by or attributable to therapy.

The base-case model scenario suggests that annual net costs per woman age 55 initiating raloxifene average about $860 during the first year of therapy, decline to about $330 per woman by the second year, and further decline to about $90 per woman by the seventh year of therapy (Figure 2). Most of this decline is due to early discontinuation of therapy. Annual net costs per woman initiating CEE+MPA are expected to average about $682 during the first year, declining to about $50 by the seventh year. Again, much of this decline is due to early discontinuation. For alendronate, the annual incremental costs per woman initiating therapy are expected to average about $950 during the first year, declining to about $110 by the seventh year. (The U.S. Food and Drug Administration-approved daily dose for alendronate as a prevention therapy is 5 mg, but the fracture prevention efficacy assumptions in the model are from the FIT studies, where the daily dose was primarily 10 mg. Cost estimates are similar for both the 5 mg and 10 mg daily dose.) Again, much of this decline is due to early discontinuation of therapy, as well as reduced side-effect costs associated with “biased” discontinuation. That is, those experiencing side effects resulting in resource utilization are assumed to be more likely than others to discontinue therapy.

Net Benefits

Net benefits are defined as the difference in the number of model events (hip/vertebral fracture, fatal/nonfatal MI, breast cancer) for women initiating each therapy compared to the number of events among women in the no-drug-therapy group (i.e., net events avoided).

Over the first 3 years of raloxifene therapy, the base-case model scenario suggests an expected reduction of about 1.8 events per 1,000 women initiating therapy, increasing to 4.0 events per 1,000 initiating therapy after 7 years (Figure 3). The estimated difference in events after 7 years is about 0.7/1,000 for alendronate. These estimated benefits are modest in large part due to the assumed high rate of early discontinuation of therapy, as well as the 7-year focus of the model. The outcome effect for alendronate is particularly small because (a) it only reflects the risk of hip and vertebral fracture in the model and (b) the risk of hip fracture is quite small over a 7-year period in a cohort of women aged 55 years at initiation of therapy.

In contrast, the high assumed rate of discontinuation exacerbates the “early” CHD harm associated with CEE+MPA use. Women initiating therapy are exposed to these early risks, but too few remain on therapy to attain the benefits of fracture prevention.

Furthermore, the relative few who remain on therapy for more than 4 years face an increase in breast cancer risk. As a result, CEE+MPA is associated with cumulative net harm (negative events avoided) in all 7 years.

Cost-Effectiveness

A cost-effectiveness ratio can be defined as the cumulative net costs of a therapy relative to its cumulative net benefits.

For CEE+MPA, cost-effectiveness is not a relevant issue in the base-case scenario due to estimated net harm. For both raloxifene and alendronate, the costs per event avoided during the first 2 years of therapy are substantial, as few of the benefits of long-term prevention accrue in just 2 years (Figure 4). For raloxifene, the costs per event avoided begin to decline after 2 years as more events are avoided. For alendronate, the decline in cost per event...
TABLE 2  
Sensitivity of Cost/Event-Avoided Estimates to Key Model Assumptions

<table>
<thead>
<tr>
<th>Therapy/Model Scenario</th>
<th>Cost/Event Avoided ($Ks)</th>
<th>Net Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Raloxifene Versus No Therapy (Base Case)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip Fx efficacy = 0.7 x alendronate efficacy</td>
<td>455</td>
<td></td>
</tr>
<tr>
<td>No CHD risk decrease RR=1.0, Y1-7</td>
<td>425</td>
<td></td>
</tr>
<tr>
<td>Higher CHD risk reduction RR=0.5, Y3-7</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>Lower BrCa risk reduction RR=0.75, Y3-7</td>
<td>350</td>
<td></td>
</tr>
<tr>
<td>No BrCa risk reduction RR=1.0</td>
<td>675</td>
<td></td>
</tr>
<tr>
<td>No CHD and no BrCa risk reduction RR=1.0</td>
<td>1,350</td>
<td></td>
</tr>
<tr>
<td>Population x2 normal fracture risk</td>
<td>4,180</td>
<td></td>
</tr>
<tr>
<td>Population x2 normal CHD risk</td>
<td>405</td>
<td></td>
</tr>
<tr>
<td>Population x2 normal breast cancer risk</td>
<td>2,850</td>
<td></td>
</tr>
<tr>
<td>Improved persistence (1.33 x CEE+MPA rate)</td>
<td>2,720</td>
<td></td>
</tr>
<tr>
<td><strong>CEE+MPA Versus No Therapy (Base Case)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No CHD risk increase RR=1.0, Y1-7</td>
<td>3,925</td>
<td></td>
</tr>
<tr>
<td>Pre-WHI presumed CHD benefit RR=0.75, Y3-7</td>
<td>640</td>
<td></td>
</tr>
<tr>
<td>No breast cancer risk increase RR=1.0, Y1-7</td>
<td>net harm</td>
<td></td>
</tr>
<tr>
<td>Population x2 normal fracture risk</td>
<td>net harm</td>
<td></td>
</tr>
<tr>
<td>Population x2 normal CHD risk</td>
<td>net harm</td>
<td></td>
</tr>
<tr>
<td>Population x2 normal breast cancer risk</td>
<td>net harm</td>
<td></td>
</tr>
<tr>
<td><strong>Alendronate Versus No Therapy (Base Case)</strong></td>
<td>2,850</td>
<td></td>
</tr>
<tr>
<td>AWP = risedronate AWP</td>
<td>2,440</td>
<td></td>
</tr>
<tr>
<td>Take 10 mg every other day (efficacy = QD)</td>
<td>1,605</td>
<td></td>
</tr>
<tr>
<td>Higher GI side-effect costs ($600, Y1)</td>
<td>3,705</td>
<td></td>
</tr>
<tr>
<td>Population x2 normal fracture risk</td>
<td>1,440</td>
<td></td>
</tr>
<tr>
<td>Population x3 normal fracture risk</td>
<td>970</td>
<td></td>
</tr>
<tr>
<td>Improved persistence (1.33 x CEE+MPA rate)</td>
<td>2,720</td>
<td></td>
</tr>
</tbody>
</table>

Avoided is not as substantial, since alendronate only reduces the risk of fracture outcomes in the model and is assumed to have no impact on CHD or breast cancer risk.

In the base-case scenario, the cost per event avoided over the first 7 years of therapy for raloxifene is about $455,000 compared to about $2.9 million per event avoided for alendronate. The impact of specific base-case model assumptions is assessed though a series of one-way sensitivity analyses (Table 2).

For raloxifene, the key area of sensitivity in the model relates to the assumed impact of therapy on the risk of breast cancer. In a model scenario where the use of raloxifene has no impact on breast cancer incidence, the cost per event avoided is about 3 times higher than in the base-case scenario. The assumed impact on CHD risk also affects model results. Compared to the base-case, the cost per event avoided increases by 30% if raloxifene does not reduce CHD risk but decreases by 23% if the magnitude of the risk reduction is as large as 35% (similar to the point estimate for the high-risk subgroup in MORE). Improved persistence, as suggested by the results of the Kayser, Ettinger, and Pressman study, would improve cost-effectiveness, but not dramatically so. The population targeted for intervention also has some impact—among women at 2 times the normal age-related risk for breast cancer, the cost per event avoided falls to $266,000 over 7 years.

In contrast, for CEE+MPA, virtually any model scenario with an assumption of significant “early” CHD harm (25% or more relative risk increase during year 1) produces an estimate of cumulative net harm over 7 years of therapy. If CEE+MPA is assumed to neither increase nor decrease CHD risk, the estimated cost per event avoided is $3.9 million. As had been assumed prior to the WHI findings, if CEE+MPA use was associated with a 25% reduction in CHD risk (after a 2-year lag) with no early harm, cost per event avoided would have been $640,000 over 7 years.

For alendronate, an area of sensitivity is drug acquisition costs. If risedronate is considered clinically equivalent to alendronate, using its lower AWP reduces the cost per event avoided for bisphosphonate therapy to $2.4 million. If alendronate 10 mg is administered every other day as a prevention (versus treatment) therapy, with no adverse impact on efficacy, cost per event avoided falls to $1.6 million. If the population targeted for alendronate therapy is at 2 times the normal age-related risk for osteoporotic fracture, its cost-effectiveness improves by 50% to $1.4 million per event avoided, and improves to $970,000 for a population at 3 times the normal fracture risk.

### Discussion

It should be noted that the model presented here was submitted for publication prior to the publication of findings from the estrogen-progestin therapy component of the Women’s Health Initiative. In revising the manuscript for publication, the base-case model assumptions for estrogen-progestin therapy were modified to reflect the WHI findings. The results imply net harm associated with CEE+MPA therapy under almost all scenarios. Thus, CEE+MPA should not be considered as a long-term prevention strategy. This implication is consistent with the recent recommendation by the U.S. Preventive Services Task Force to avoid using estrogen-progestin as a prevention therapy for healthy postmenopausal women.

The analyses undertaken in this study are technically complex and should be interpreted in the context of the assumptions used in the models. The model employed here presents estimates of direct medical costs per “event avoided.” As such, the reported cost-effectiveness estimates are not comparable to the most published cost-effectiveness ratios for long-term prevention therapies. Further, it would be inappropriate to construct a “league table” comparing these “cost per event avoided” measures to the incremental “cost/QALY” measures in the literature. First, the model attempts to account for the practical challenge of persistence on long-term therapy by using therapy discontinuation assumptions based on experience in clinical practice.

Most published models either assume complete persistence or use discontinuation rates from clinical trials. The use of more realistic discontinuation assumptions reduces the cost-effectiveness of all interventions relative to no intervention. Second, as
a “medium-term” model, all future benefits of therapy over the remainder of life are not captured. Finally, given the payer perspective of the study, the model does not account for any indirect cost savings attributable to drug therapy.

Some indication of the differences between the results reported here and results from a more traditional cost-utility analysis (CUA) is provided by reference to a CUA by Armstrong and colleagues38 comparing raloxifene and HRT to no therapy over a life-cycle time horizon. This pre-WHI analysis assumes a 44% reduction in CHD risk for HRT users as a base case, but a “CHD-neutral” scenario also is reported. (The potential for early CHD harm is not addressed.) In a model with HRT assumed to be “CHD neutral,” the incremental cost per QALY over a lifetime horizon for HRT versus no therapy is $8,500, compared to the estimate of $3.9 million per event avoided over 7 years for a CHD-neutral scenario reported here. In addition to the shorter time horizon, our substantially higher cost-effectiveness estimate results from the high rate of discontinuation incorporated into the analysis. (Armstrong and colleagues assume no discontinuation of therapy.) Armstrong and colleagues also report a lifetime incremental cost per QALY of $9,820 for raloxifene versus no therapy in their base-case scenario (normal breast cancer risk). This estimate falls to $4,100/QALY for a population of women at 3 times normal age-related breast cancer risk and $1,900/QALY among women at 6 times normal risk. Bisphosphonates were not considered as a prevention option in the analysis reported by Armstrong and colleagues.

Published economic evaluations of bisphosphonates tend to focus on the treatment of established osteoporosis, not prevention.30 Any broad-based osteoporosis prevention intervention using a prescription drug will tend to have high costs relative to benefits, especially over a 7-year time horizon, if the drug only prevents osteoporosis. Costs per event avoided for both raloxifene and alendronate in “fracture-only” models are estimated at more than $2 million over 7 years. Even in a scenario where CEE+MPA is “CHD neutral” its cost per event avoided also exceeds $2 million.

Indeed, most of the past economic evaluations of HRT as a broad-based postmenopausal prevention strategy that have found incremental costs per QALY less than $25,000 were highly dependent on a presumed substantial CHD risk-reduction benefit.44 Thus, the promise of HRT as a cost-effective, broad-based postmenopausal prevention strategy was reliant on a presumption of a broad spectrum of clinical benefits. Although WHI has not yet evaluated all of the putative clinical benefits of long-term HRT (e.g., prevention of Alzheimer’s disease), one of the most significant presumed benefits from a cost-effectiveness prospective—CHD risk reduction—now appears to be unupportable. On the other hand, if SERMs such as raloxifene or others currently in development provide a spectrum of clinical benefits, as much of the available data suggest, they may prove to be more cost effective as broad-based prevention strategies than drug interventions with a single source of clinical benefit.

Limitations
The outcome measure used in the model is a simple metric of “clinical events avoided.” Although aggregations of occurrences of clinical events with substantially different impacts on health-related quality of life (HR-QOL) are commonly used as primary endpoints in clinical trials (e.g., cardiovascular disease “events” avoided), in this case, vertebral fracture seems unlikely to have an impact on HR-QOL as substantial as hip fracture, fatal or nonfatal MI, or breast cancer. If an arbitrary weight with a value less than unity (e.g., 0.2) is assigned to a vertebral fracture when determining net events avoided, the impact is to decrease estimated net events avoided for both raloxifene and alendronate, thereby further increasing estimated costs per event avoided. However, given the similarity in assumed vertebral fracture prevention across therapies, the estimated differences in cost-effectiveness across therapies are not affected significantly.

As noted, the model incorporates a number of simplifying assumptions, including the exclusion of several potentially relevant clinical considerations. Recently reported data highlight some additional clinical considerations that may warrant greater attention in any future analysis. First, the model reported here does not include stroke as an outcome. However, the WHI data indicated that CEE+MPA therapy was associated with a 41% increase in the incidence of stroke over 5 years. In contrast, data from MORE indicate a potential reduction in stroke risk associated with raloxifene use.14, 41 Second, the WHI data indicated that CEE+MPA therapy was associated with a 37% reduction in risk for colorectal cancer. Incorporating a colorectal cancer benefit into a decision-model-based economic evaluation would partially offset the CHD and stroke harm associated CEE+MPA use. However, CEE+MPA still would be predicted to cause net harm except, perhaps, in a population at well above average risk for colorectal cancer and well below average risk for CHD and stroke.

Conclusion
For a variety of reasons, lifetime cost-effectiveness analyses are seldom used by managed care organizations when making decisions about reimbursement policies for specific pharmaceutical agents. Providing managed care decision makers with information about the time-path of cost and outcome effects of a new pharmaceutical agent may prove to be more useful than a summary of net present values, especially for models with a long time horizon. Such details can assist in assessments of potential budget impact and “pay-back” periods for potential investments in long-term prevention initiatives.

The example of a medium-term model presented in this paper focuses on alternative osteoporosis prevention strategies. Overall, in this example that focuses on alternative osteoporosis prevention strategies, the model results suggest that raloxifene provides greater cost-effectiveness than alendronate for women initiating therapy at age 55 over the first 7 years of therapy, under most model scenarios. The estimated cost-effectiveness for raloxifene is sensitive to assumptions about the magnitude
of breast cancer risk reduction associated with therapy but remains more cost effective than alendronate as long as it provides clinical benefits beyond fracture reduction. In a scenario where the use of raloxifene has no effect on the risk of developing breast cancer and no effect on CHD risk, alendronate provides a lower cost per event avoided than raloxifene. However, at several million dollars per event avoided, prevention with either drug under a “fracture benefit only” scenario generally would be considered cost prohibitive, at least over the time horizon examined. In general, a broad-based prevention intervention using a prescription drug that provides a spectrum of clinical benefits is more likely to be cost effective than a narrow-spectrum prescription drug intervention.

ACKNOWLEDGMENTS

Paula Funk Orsini and Sheila Weiss, from the University of Maryland School of Pharmacy, contributed to the development of an early version of the model used in this analysis.

DISCLOSURES

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REFERENCES

2. Lyles A, Luce BR, Rentz AM. Managed care pharmacy, socioeconomic critical revision of the manuscript, and statistical expertise were contributed by both authors.

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33. Data on file, Eli Lilly and Company.
34. Data on file, Eli Lilly and Company.


Industry’s Perception of Presenting Pharmacoeconomic Models to Managed Care Organizations

BRIDGET M. OLSON, PharmD, MS; EDWARD P. ARMSTRONG, PharmD, BCPS, FASHP; AMY J. GRIZZLE, PharmD; and MARK A. NICHTER, PhD

ABSTRACT

BACKGROUND: Previous research has shown that pharmacoeconomic (PE) data are considered important but may not be optimally utilized by decision makers. No research has compared the effectiveness of different types of PE models.

OBJECTIVES: The purpose of this study was to examine the perceived value and understanding of PE models among decision makers in managed care organizations. The perspective of this study was from research scientists working in the pharmaceutical industry who present PE models to managed care clients. The study objectives were to (1) examine what types of models are best received by decision makers, (2) investigate the barriers to using PE models, and (3) recommend methods for improving PE models.

METHODS: A telephone survey of 20 PE research scientists from various US pharmaceutical and biotechnology companies. Topics addressed included factors contributing to how well PE models are received, barriers to using PE models, and recommendations for improving PE models.

RESULTS: Models have an impact on health policy decision making. Nineteen of 20 respondents had at least one experience where a PE model played a role in optimizing the formulary positioning of a product. No single model format (e.g., decision analytic tools, spreadsheet analyses, Markov models, multivariate regression models) was regarded as the most effective model type. Although 7 of 20 respondents said simple spreadsheet models were most effective, well-designed, scientifically sound regression models were also reported to be very effective.

CONCLUSIONS: The respondents commonly used models to share PE information, which was said to play a role in making health policy decisions by decision makers in managed care. There was no consensus regarding the type of model that was most effective. Study participants indicated that a variety of model designs are effective, ranging from simple spreadsheet models to multivariate regression models. Recommendations for improving PE models include (1) producing scientifically sound models, (2) customizing models where possible, (3) making models transparent, (4) making models user friendly, and (5) involving a nonbiased third party for model development.

KEYWORDS: Pharmacoeconomics, Decision making, Models, Modeling, Managed care, Formulary, Cost

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Industry’s Perception of Presenting Pharmacoeconomic Models to Managed Care Organizations

### APPENDIX A. Contents of the 39-item Questionnaire

<table>
<thead>
<tr>
<th>Items related to demographic characteristic of participants (n=6)</th>
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<tbody>
<tr>
<td>1. What is the title of your position within your company?</td>
</tr>
<tr>
<td>2. How many years experience have you had presenting pharmacoeconomic (PE) models to clients/customers?</td>
</tr>
<tr>
<td>3. What type of pharmacoeconomic training do you have (e.g., on-the-job training, fellowship, continuing education)?</td>
</tr>
<tr>
<td>4. On average, how many times do you present PE models to clients/customers per month? If your experience was in the past, please specify</td>
</tr>
<tr>
<td>5. What type of clients do you serve (e.g., managed care, health plan directors, P&amp;T)?</td>
</tr>
<tr>
<td>6. In what areas of the United States and/or international sites have you presented PE models?</td>
</tr>
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<table>
<thead>
<tr>
<th>Items related to PE models (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Can you describe the type(s) of PE model(s) that you present to clients (e.g., spreadsheet, decision analysis, multivariate [regression])?</td>
</tr>
<tr>
<td>2. What is the specific format in which you present the model (e.g., laptop presentation of the model, slide presentation of the model, article reprint of the model)?</td>
</tr>
<tr>
<td>3. What therapeutic or product areas have you presented models?</td>
</tr>
<tr>
<td>4. In your experience, what therapeutic or product areas are best served by presenting PE models?</td>
</tr>
<tr>
<td>5. What factors contribute to how well the model is received (e.g., user training, model format, presentation format, therapeutic area, level of model complexity, number of assumptions)?</td>
</tr>
<tr>
<td>6. How long do your presentations of PE models typically take?</td>
</tr>
<tr>
<td>7. Do you feel that the length of time needed to present the PE models is adequate? Too long? Too short?</td>
</tr>
<tr>
<td>8. Do you leave an electronic copy of the PE model with the client so that they can evaluate it on their own time? Why? or Why not?</td>
</tr>
<tr>
<td>9. Is the client able to “customize” the PE models you present (e.g., input their own institution and/or patient information, get information from client ahead of time, and incorporate in model)?</td>
</tr>
<tr>
<td>10. If they can customize the model, how do they do this (e.g., extent of allowable variable manipulation, any variables they are not allowed to change)?</td>
</tr>
<tr>
<td>11. What are the most common questions that your clients ask you after presenting them with a decision analysis model?</td>
</tr>
<tr>
<td>12. What are the most common questions that your clients ask you after presenting them with a spreadsheet model?</td>
</tr>
<tr>
<td>13. What are the most common questions that your clients ask you after presenting them with a multivariate (regression) model?</td>
</tr>
<tr>
<td>14. In your opinion, are the decision analysis models that you present well received and understood by your clients?</td>
</tr>
<tr>
<td>15. In your opinion, are the spreadsheet models that you present well received and understood by your clients?</td>
</tr>
<tr>
<td>16. In your opinion, are the multivariate (regression) models that you present well received and understood by your clients?</td>
</tr>
<tr>
<td>17. Do the models that you present include pop-up windows that aid in clarifying these concepts?</td>
</tr>
<tr>
<td>18. Do you think it would be helpful for “refresher” pop-up windows explaining concepts embedded in the computer presentation (e.g., statistics, equations) to be included in the model itself?</td>
</tr>
<tr>
<td>19. If you have pop-up windows, do clients find them helpful? If you do not have pop-up windows, do you think they would be helpful?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Items related to clients’ knowledge of statistics (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Based on your experiences, do you feel that there is a wide range of statistical knowledge among those clients that you present PE models to?</td>
</tr>
<tr>
<td>2. Is it difficult to determine the client’s level of statistical knowledge during your presentation?</td>
</tr>
<tr>
<td>3. When are you typically most able to assess the level of a client’s statistical knowledge (at the beginning, throughout, or following the presentation)?</td>
</tr>
<tr>
<td>4. How do you explain complex concepts in simple terms (e.g., what the model is doing “behind the scenes”)?</td>
</tr>
<tr>
<td>5. How often are you asked to clarify or remind clients about basic concepts that are included in the model (e.g., what a P-value is, what a regression model is)?</td>
</tr>
<tr>
<td>6. What other issues do clients raise in conjunction with the presentation of statistical information?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Items related to effective modeling and communication techniques (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Are you aware of any decisions that were specifically identified as a result of the information presented in your PE model (specify model type)?</td>
</tr>
<tr>
<td>2. How does the effectiveness of the PE models you present compare to that of other forms of presentations or communications with decision makers (e.g., publications, presentations, slides)?</td>
</tr>
<tr>
<td>3. What types or mediums for presenting PE models would be more useful for decision makers (e.g., leaving model behind, small group versus large group versus one-on-one, MDs and RPhs—together or separately more effective)?</td>
</tr>
<tr>
<td>4. How could these models be changed to improve their effectiveness?</td>
</tr>
<tr>
<td>5. What are the most common problems you have experienced in presenting PE models (specify model type)?</td>
</tr>
<tr>
<td>6. What are the most common misinterpretations of the data you present in PE models?</td>
</tr>
<tr>
<td>7. In your opinion, are there any differences in communication patterns based on client age, gender, or professional background (e.g., types of questions asked, receptiveness to different formats)?</td>
</tr>
<tr>
<td>8. Are there any other issues affecting the usefulness of PE models that we did not discuss (e.g., impact of AMCP guidelines)?</td>
</tr>
</tbody>
</table>

### Methods

Approval was obtained from the University of Arizona’s Human Subjects Protection Program Committee for the interview discussion questions and recruitment invitations prior to initiation of the study. Individuals within health outcomes departments of pharmaceutical and biotechnology companies across the United States were contacted. These individuals were known to utilize PE information with customers, and these people were queried to obtain names of professionals within their organizations who would be best qualified to discuss their experiences in presenting PE models. Potential subjects were emailed and telephoned between March and May 2002 to ask if they would participate in a 30-minute interview. Twenty-three industry representatives (e.g., directors, managers, or medical liaisons) were invited to participate. When potential participants agreed to be interviewed, this served as consent to participate in the study.
Subjects did not receive compensation for their participation. All interviews were completed by June 2002.

A survey instrument was created from a review of the literature on the use of PE models. Using this information and expertise in the areas of PE and human behavior (i.e., anthropology), the 4 researchers from the University of Arizona developed a draft questionnaire. The authors had previous experience developing questionnaires regarding the use of PE and the role of PE models in decision making among managed care executives. The questionnaire content was reviewed for face validity by an independent health outcomes researcher at the University of Arizona. A formal pilot test of the questionnaire was not conducted.

The final telephone survey consisted of 39 items, focusing on demographic characteristics of participants; a description of the types of PE models presented; participants’ perceptions of their clients’ knowledge of statistics (i.e., tools, methods, terminology); and techniques for effective demonstration and communication of PE models (Appendix A). The interview questions were primarily open ended, with the purpose of gaining as much information from subjects as possible. This was a qualitative study by design. Because of the open-ended nature of the questions, participants did not have an opportunity to agree or disagree with all issues. Study participants were asked to discuss issues related to all PE models as well as specific types of models, including decision-analytic models, spreadsheet analyses, Markov models, and multivariate regression models.

A series of items was included in order to assess the types of PE models being presented by the pharmaceutical industry and how well these models were received by decision makers. In this context, decision makers were primarily described as those working in various health plans and organizations across the United States who have substantial influence over the medications that are included on drug formularies. The format by which the models are commonly presented (e.g., laptop presentations, slide presentations, article reprints of model) was recorded as were differences in reception by the end user associated with these various presentation designs. Factors contributing to how well the models are received (e.g., audience, user training, model format, presentation format, therapeutic area, level of model complexity) were assessed in order to identify potential barriers to using PE models in decision making. The ability and extent by which clients are able to “customize” the PE models developed by the pharmaceutical company were also discussed with survey participants. Reasons for and against leaving electronic copies of the PE models with clients, commonly asked questions, and participants’ perceptions of client understanding of the PE models were recorded.

Several items focused on the participants’ perceptions of their clients’ knowledge of statistics. The purpose of these ques-

**TABLE 1** Demographic Characteristics of Sample

<table>
<thead>
<tr>
<th>Number of interviews completed</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean interview length (SD), minutes</td>
<td>31.45 (8.73)</td>
</tr>
<tr>
<td>Mean years experience (SD)</td>
<td>4.55 (2.56)</td>
</tr>
<tr>
<td>Number of pharmaceutical companies represented by participants</td>
<td>10</td>
</tr>
<tr>
<td>Titles within companies</td>
<td>Directors (associate, senior) of outcomes, PE, managed care, medical services: 10 Managers (corporate, global): 6 Medical liaison: 4</td>
</tr>
<tr>
<td>Type of pharmacoeconomic training*</td>
<td>On the job: 16 Continuing education program: 3 Short courses/certificate program: 2 U.S. college of pharmacy: 2 Canadian university: 1 Doctor of philosophy: 1 Economics: 1 Pharmacy administration: 1 Psychology: 1</td>
</tr>
<tr>
<td>Master’s degree: 1 Pharmaceutics: 1 Preventive medicine: 1 Fellowship/postdoc: 5</td>
<td></td>
</tr>
<tr>
<td>Mean number of presentations per month (SD): 1.76 (1.34)</td>
<td></td>
</tr>
<tr>
<td>Type of clients*</td>
<td>Managed care organizations: 17 Independent health care organizations: 4 Physician group practices: 5 Long-term care facilities: 2 Public sector administrators (United States and abroad): 3 Pharmacy benefit management companies (PBMs): 2 Group purchasing organizations (GPOs): 1 Hospitals: 2 High-prescribing physicians in community practice: 1 “At risk” medical groups: 1 Individual physicians: 1</td>
</tr>
</tbody>
</table>

* Multiple responses permitted.
† Two subjects noted that presentations post launch are conducted much more frequently than after the launch “rush.”
‡ One respondent could not quantify, noting that PE information is presented “whenever available.”
§ Pharmacy directors, medical directors, pharmacy and therapeutics committees, clinical pharmacists, program administrators.
|| Including reimbursement agencies in Europe, Canada, and Asia.
tions was to identify statistical tools or concepts that were presented in PE models but poorly understood by decision makers in managed care. Participant ability to identify his or her audiences’ level of understanding with respect to statistics and successfully explain complex concepts was assessed. The usefulness of “pop-up” windows (e.g., explanation of concepts and/or definitions embedded in the model) was discussed in the interviews as well. This information was used to develop recommendations for improving the understanding of PE models presented to decision makers.

Finally, a series of items addressed the effectiveness of PE models and potential opportunities for improving their usefulness. Participants’ most common problems in presenting PE models were gathered, including the most common misinterpretations of the data presented. Because of their extensive experience in presenting PE models, participants were also asked to make recommendations for how models could be changed to improve their effectiveness and enhance their usefulness to health care decision makers.

The primary objectives of this study were to identify barriers to using PE models and to make recommendations to improve the utility of these models. The analysis was, therefore, primarily descriptive in nature. Study investigators summarized data gathered from the interviews and outlined the key issues described by study participants. This method was used in order to organize a set of recommendations for improving the usefulness of PE models.

Results

Sample Characteristics
Twenty (87%) of the 23 pharmaceutical representatives invited to participate agreed to be interviewed; 3 of those representatives contacted were unavailable to participate (Table 1). Participants were spread across the United States, representing 10 pharmaceutical and biotechnology companies. The mean interview length was approximately 32 minutes, with a range of 20 to 57 minutes. Participants had mean years of experience presenting models of 4.6 years, with a range of 1 to 10 years of experience. Respondents (15 of 20, 75%) indicated that on-the-job training was the most common method for obtaining PE education or training. All respondents had given presentations involving PE models within the United States, and 4 respondents had presented PE models internationally. On average, PE models were presented between 1 and 2 times each month by survey participants, with managed care organizations (MCOs) being the most common clients of these presenters.

Factors Contributing to How Well Models Are Received
Audience. Most participants preferred small group presentations (18 of 20, 90%) consisting of both pharmacists and physicians (14 of 20, 70%). The combination of these 2 groups was thought to be effective in bringing together multiple viewpoints in the decision-making process and balancing the opinions of each. An overall theme was that physicians and pharmacists view model information differently (i.e., with a different focus). Eleven participants (55%) reported that physicians were more interested in clinical outcomes and the overall model results (or take home messages) than the cost components of the model (e.g., cost-effectiveness, budget impact). Thirteen participants (65%) indicated that pharmacists were more educated in cost issues and tended to focus more on the economic impact demonstrated by PE models as opposed to concentrating on the clinical outcomes.

Respondents noted that because many pharmacists continue to operate in a silo-based environment (i.e., required to focus on the budget constraints of one department rather than the total health care budget impact across multiple departments), it is helpful to have physicians in attendance to represent the broader issues (e.g., impact on overall health care costs). Participants viewed physicians as being less receptive to technical cost issues presented in the models. Therefore, presenting to both groups simultaneously was perceived to be advantageous. In an effort to bring these disciplines together, one participant reported success in assembling decision makers from multiple health plans for presentations. This was found to be an extremely effective means of sharing model information, according to one participant. While presenting to pharmacists and physicians together was preferred by the majority of participants, one respondent had a preference for speaking with pharmacists and physicians separately until they were ready to make a decision.

Two participants commented that younger professionals were more aware of some of the newer tools such as PE models for decision making, perhaps due to more recent training. It was also noted that the best audience to whom to present models is composed of those individuals responsible for decisions affecting total health care costs. However, respondents agreed that PE model effectiveness would be enhanced with supplemental training for decision makers across health care systems.

In addition to audience characteristics, respondents identified several other factors that determine whether a model is well received by decision makers. The most frequently mentioned factors included (1) ease of understanding (i.e., model simplicity and transparency) (19 of 20, 95%); (2) the ability to customize the model to individual practice settings (12 of 20, 60%); (3) presenter credibility and training (9 of 20, 45%); (4) model format and content (6 of 20, 30%); and (5) availability of reprints (i.e., model results have been published) (3 of 20, 15%). The contribution of each of these factors is detailed below.

Ease of understanding. Simplicity (14 of 20, 70%) and transparency (9 of 20, 45%) were the most frequently mentioned factors in determining how well a PE model is received. Transparency describes the ability of the end user to “see through” the design of the model and easily understand how the model reaches its conclusions. Being able to clearly see what is happening “behind the scenes” of the model (e.g., description of the calculations and methods, identification of all of the
assumptions and the data elements that were included) was thought to be of great importance to decision makers.

**Keeping the model simple.** While maintaining scientific quality was a challenge described by participants. One respondent stated that it was more valid and effective to develop a complex model that could be explained well than to oversimplify the disease represented by the model. An overall theme that resonated from these interviews was that even when PE models are well received, they are not necessarily fully understood by clients.

**Ability to customize the model.** Nearly all models presented by study participants (19 of 20, 95%) included the ability to modify variables to tailor for specific customers. The ability to customize models was thought to be important for the purpose of generalizability across practice settings. Although some variables were thought to be inappropriate to alter, several participants (5 of 20, 25%) noted that their models do allow all variables to be modified, regardless of whether the change makes sense. Increased credibility of the model was said to justify these modifications and add to the robustness of the model. Two participants said that for those models that cannot be customized, the use of extensive sensitivity analyses (e.g., tornado diagrams) was an important means by which to compensate for the lack of customization. Although all participants agreed that the ability to customize PE models is helpful, seven participants noted difficulty in actually obtaining customized information from clients. In many cases, participants noted that the required data were unavailable or inaccessible to the clients that typically interact with.

**Presenter credibility and training.** Presenter credibility was also considered to be an important factor in delivering a well-received PE model. The presenter must understand all aspects of the model and be able to effectively answer questions in order to gain the attention and respect of the audience. Understanding what is wanted and needed by decision makers was also described as a key factor in the presentation of a well-received model.

**Model content and format.** Nearly all participants (19 of 20, 95%) said that referencing cost information and citing all sources of information improves the credibility of the model. Three participants noted that the face validity of the model is also an important factor. Similarly, sensitivity analysis was mentioned by 2 participants as important in determining how well a model was received.

There was no consensus regarding which model format was most effective. Seven participants (35%) reported that decision makers prefer spreadsheet and budget impact models most often and regression models least often. However, those respondents with extensive experience presenting regression models (6 of 20, 30%) felt that they were very well received by decision makers. Cost-minimization models, cost-of-illness models, and cost-offset models (3 of 20, 15%) were also included in this category of “best received” formats. Two participants (10%) specifically mentioned that Markov models were not well received because of the lack of understanding associated with this modeling technique.

There were also different opinions regarding the type of model interface that is best received by decision makers. Most participants (18 of 20, 90%) commented that “pop-up” windows that detail source information, definitions, or background information were helpful to both the presenter and the end user. Five participants (25%) indicated that models with a visually pleasing front end (referred to by one respondent as a “glitzy interface”) improved the usefulness of the model because of its user-friendly presentation. Others stated that, in their experience, a “barebones” spreadsheet was best and that a “fancy front” was not well received because of skepticism caused by its apparent “black box.”

Participants reported that results of PE models were shared with decision makers via laptop and slide presentations as well as published articles of the model results. The format by which these presentations were delivered was said to be dependent on the individual product area and the audience to which the model was presented.

**Availability of reprint.** All participants agreed that having a publication of results derived from a PE model available for distribution at the time that the model was presented increases the credibility of the model itself. Four respondents (20%) noted that models were better received compared to publications because of their interactive nature. However, 16 of 20 participants (80%) indicated that the combination of these formats was most effective for demonstrating the validity of the model while allowing decision makers to actively apply the model in their own practice setting.

**Therapeutic area.** There was no consensus regarding which therapeutic areas were best suited for model presentation. Nine participants (45%) noted that models work well for chronic diseases because of their ongoing cost structure and the ability of an intervention to have an impact over time. Individual respondents stated that they thought models were helpful in therapeutic areas with well-accepted end points; very expensive products, where head-to-head comparisons were lacking; and in instances where products are differentiated only by cost. One participant mentioned that for models to be effective, there need to be competitive products available in the market, especially when trying to create awareness or treatment demand for conditions that may be under-treated. For example, practitioners may still view obesity as a “lifestyle” issue rather than a disease that should be treated with medication. In such cases, PE models may only be effective if competing products were being compared.

**Barriers to using pharmacoeconomic models.** Participants identified several barriers to the effective use of models. Model complexity was stated by 8 respondents (40%) as a barrier to full acceptance of the model. Several participants (7 of 20, 35%) identified skepticism surrounding model assumptions as a barrier. Five participants (25%) perceived that their customers felt an industry
bias existed because of industry funding and/or the development of models by pharmaceutical companies. Lack of model transparency was also mentioned as a barrier by 4 participants (20%).

**Leaving the model with the decision maker.** The majority of participants (16 of 20, 80%) stated that electronic copies of the models were not provided to their customers. Reasons for not leaving the model behind included company policy, legal implications, FDA restrictions, competition, and the proprietary nature of the model. Another reason models were not provided was described as a fear that decision makers may misuse the model (via misunderstanding the assumptions or model structure) and make inaccurate conclusions based on their own manipulation of the model. Respondents agreed that decision makers seldom have time to “play” with the model, even when they were left behind. One participant added that this practice (i.e., leaving the model behind) may diminish the role of the presenter of PE information. Pending publication of model results was also described as a reason why PE models may not be distributed to the end users.

Few participants (4 of 20, 20%) offered to leave the company’s model with the customer audience. If a customer requested that a model be provided, they may be asked to sign confidentiality agreements to account for issues associated with competition (e.g., keeping the model out of the competitor’s hands) and avoiding lawsuits by competitors who may feel that their own product was inadequately represented. Even those participants who reported leaving models with their customers to facilitate model utility maintained that the models were unlikely to be used by decision makers in the absence of the presenter (i.e., pharmaceutical company representative).

**Statistical knowledge of decision makers.** Most participants (18 of 20, 90%) agreed that there was wide variation in the statistical knowledge of clients who attend their presentations. Nine participants (45%) noted that, overall, clients did not have a strong understanding of statistical methods. It was agreed that statistical issues (e.g., interpretation of P-values, confidence intervals, and odds ratios) are rarely the focus of the model or the presentation; however, “pop-up” windows were thought to be helpful in some situations where basic statistical concepts could be illustrated. For those presenting regression models, a strong background and explanation of statistics was considered more important.

**Use of Academy of Managed Care Pharmacy (AMCP) formulary guidelines.** Our study was conducted in the fall of 2002. At that time, the AMCP Format for Formulary Submissions had been introduced into the marketplace. When asked about the impact of the recent formulary submission guidelines recommended by AMCP, 11 participants (55%) felt it was too soon to say what kind of impact they will have on managed care organizations or on the pharmaceutical industry. Twelve participants (60%) had no or few requests to follow the AMCP Format for Formulary Submissions to date. These respondents felt the number of requests was growing, particularly in state Medicaid programs and in the northwest region of the United States.

None of the participants discussed the unique benefit of the recommendation in the AMCP Format to build a model specific to a health plan. Five participants (25%) mentioned that the guidelines may be helpful in an ideal world but were contrary to the environment in which the pharmaceutical industry operated. Specifically, AMCP Format expectations for the availability of “quality” PE data at time of launch (or soon after) were said to be unrealistic. Respondents agreed that, although the AMCP Format guidelines have raised awareness of PE models, decision makers were often not equipped to evaluate them, thereby negating their effectiveness in certain settings.

Five respondents (25%) noted that some customers have requested the AMCP Format for Formulary Submissions for aspects other than PE models (i.e., clinical efficacy and safety information). One participant noted that the guidelines were useful for presenting and standardizing information. Two respondents (10%) commented on disadvantages of the guidelines, including the fact that the respondents felt the guidelines did not define what constituted a “good” model. Another participant thought that the guidelines were onerous and questioned their clinical or economic relevance. As the adoption of the AMCP dossier model (AMCP Format for Formulary Submissions) expands, the perceptions of its usefulness in practice should be reevaluated.

From an international perspective, concerns were expressed by respondents that the AMCP Format for Formulary Submissions does not apply to other countries because of the unique managed care environment in the United States. However, one respondent suggested that pharmacoeconomics might be more important in other countries because of limited government health care budgets and a strong interest in balancing health outcomes and cost issues.

**Effectiveness of pharmacoeconomic models.** Nearly all participants (19 of 20, 95%) agreed that PE models have had an impact on decision making for their clients. However, 14 respondents (70%) mentioned that models were just one piece of an entire package necessary for decision making by their customers. These participants mentioned that PE models had contributed either to formulary adoption, priority or preferred formulary status, shifts in tier placement, maintaining formulary listing, or reimbursement without formulary status. There was no consensus regarding the type of model (e.g., spreadsheet, decision analysis, regression models) having the greatest impact on decision making. Instead, a combination of multiple factors discussed above was thought to contribute to the acceptability and effectiveness of the PE models presented. One participant mentioned that although PE models had minimal impact on HIV/AIDS products (i.e., products were routinely added to the formulary regardless of PE information), they had been helpful for estimating budget needs for health plans.

**Recommendations for improvements.** Participants were
asked what changes could be made to improve the effectiveness of the PE models they presented. The most common response (7 of 20, 35%) was to customize the model (i.e., the ability to adapt the model to include data from specific organizations). Further, participants said that models could be improved if clients would routinely provide data for model customization. Outlining the data elements needed from clients in advance of the presentation was recommended. This approach was thought to encourage clients to participate in the customization of PE models in an effort to make information more applicable to their organization.

Six respondents (30%) recommended simplifying the models, making them more user friendly (e.g., easy to manipulate and interpret). Another theme mentioned by 5 respondents (25%) was to make models more transparent to decision makers. Gathering additional data during model development in order to decrease the number of assumptions necessary was also recommended. One participant mentioned that a societal perspective, in which all possible costs and benefits were considered regardless of who the payer is, should be avoided. A more focused payer perspective was thought to be most relevant to the decision makers with whom study participants interact. One participant noted that having head-to-head comparative models, including overall health care costs, would improve their effectiveness. Having the model developed by an academician with whom the decision maker was familiar was also recommended to address issues of industry bias. Survey participants also stated that having a publication to distribute at the time of model presentation would improve the model’s effectiveness. It was also thought to be of value to understand what the customer wants to see in the model prior to developing it.

Discussion

Studies focused on PE research have been conducted by a number of stakeholders. Researchers in academia, industry, managed care organizations, hospitals, and government have each contributed to this literature. In 2000, Hill and colleagues reported on problems associated with interpreting PE analyses.11 These problems were revealed through a comprehensive review of submissions to the Australian Pharmaceutical Benefits Scheme Department of Health and Aged Care (DHAC) between 1994 and 1997.11 These authors concluded that the resources required to fully evaluate PE analyses are beyond the capacity of many organizations and peer-reviewed journals. Looking specifically at PE models, Hill and colleagues found several problems associated with technical aspects of the models (e.g., discounting costs but not benefits, failing to appropriately relate costs and outcomes, and uncertainties arising from extrapolating short-term benefits).11 In addition, unsubstantiated assumptions and cost estimates were criticized by the DHAC evaluators. Hill and colleagues also stated that the models were not transparent in their calculation of cost-effectiveness.

The current study took on a different perspective compared to the study by Hill and colleagues; however, the primary goal of identifying problems associated with PE models was the same. In our study, individuals who presented PE models to clients were asked to self-evaluate the usefulness and effectiveness of that information tool and to offer recommendations for how PE models can be improved. This is an important step in developing future PE models, especially since it is apparent that the use of economic analyses in managed care decision making across the United States is likely to expand. The responsibility to understand and appropriately evaluate these models will fall on health plan decision makers. Developers of these models (e.g., the pharmaceutical industry), however, must also assume responsibility for providing objective and accurate analyses.

Several studies have been conducted evaluating how decision makers are actually using PE data. Previous research reported that it was difficult to locate examples where PE data constituted the primary end point by which drug policy decisions were made (e.g., adding a product to formulary).12,13 In contrast to previous literature, our study suggests that PE models are perceived by pharmaceutical manufacturers to be useful in influencing drug policy decisions.1,3,5,7,9,12-14 This appears to be a growing trend that can be useful to both the industry and health care organizations. Guidelines, such as those recommended by AMCP, are further encouraging the use of modeling techniques for the evaluation of pharmaceuticals and may receive increased attention over the next few years.

Numerous barriers have been suggested as to why PE studies have not played a larger role in drug policy decisions to date.1,3,5,7,9 Limitations of the usefulness of PE information found in this study were similar to those cited in previous literature.5,7,9 The most important barriers were skepticism of a “black box” model design, credibility of model assumptions, and perceived or actual biases in the model results. Since government funding for these types of studies is uncommon, the pharmaceutical industry has funded the majority of this research.9 Participants in this study continued to perceive that leaders in managed care organizations feel uncomfortable with and untrusting of the potential bias that this funding source may introduce. This study supports the idea that model credibility is enhanced with scientific soundness of the model, transparency of model specifications and resource unit costs, the ability to customize the model, and involvement of nonbiased third-party researchers in the development of models. In addition, publication of the model in peer-reviewed journals may enhance credibility.

Issues such as relevance and generalizability of PE studies may be limitations for some health systems. The timeliness of some studies may be a concern as well since much of the PE data collected are not available until after a product has been introduced into the market place. Inadequate understanding of PE methods may also be an important barrier for some decision makers. Participants in this study suggested that educating the end user may be an important step in enhancing the effectiveness of PE information, especially with respect to model-build-
ing. To strengthen the appropriate use of models, many health plans may benefit from enhanced training of staff in developing and evaluating PE models. Significant education and training is needed across a broad range of health care professionals. Although most decision makers have received training to evaluate clinical trials, few are familiar with modeling techniques commonly used in PE research. Decision analysis will likely become more commonly used by health plans given the expansion of software systems that can easily be used on personal computers. Training opportunities will speed the adoption of these evaluation tools within health plans. With the increasing use of databases within managed care organizations, it is also anticipated that multivariate (regression) models will become more important and more prevalent in the future.

More recent studies have demonstrated that although PE data are considered important, this information remains secondary to safety and efficacy data when making drug benefit decisions. Despite this, studies suggest that health plans are desiring additional PE data and that this information is beginning to play a larger role in health policy decision making. The PE model may not be the most important piece of data; however, models have demonstrated utility in combining important data that is useful to decision makers. All participants in our study believed that PE models were effective in promoting informed decision making. The majority of respondents had at least one experience where a PE model played a pivotal role in optimizing the formulary positioning of a product.

By customizing PE models and pursuing collaborations with academia, perhaps some of the perceived industry bias can be avoided and other barriers to using PE information can be overcome. As the role of formulary submission guidelines continue to expand, the usefulness and necessity of quality PE models will likely grow in parallel. Based on the findings of this study, the researchers compiled a list of recommendations for improving the usefulness of PE models (Table 2).

Prior to this study, there was a gap in the literature with respect to the effectiveness and application of specific PE modeling techniques. In our study, there was no single model format (e.g., spreadsheet model, decision analysis, regression analysis) that was regarded as the most effective model type. Although many respondents said simple spreadsheet models are most effective, complex regression models were reported to be very successful with well-trained presenters. Well-designed, scientifically sound regression models were also reported to be very effective by several respondents. It is difficult to compare these results to existing literature, as previous studies have not examined the impact of various model designs.

**Limitations**

The results of our study were derived from a small convenience sample of pharmaceutical company representatives. While the sample was developed to reflect a wide range of companies across the United States, the results are not necessarily generalizable to all people involved in the dissemination of PE research to managed care organizations (MCOs) and other recipients. In addition, there may be a social desirability bias since some respondents may have answered questions in a manner they believed would be preferred or anticipated by the interviewers. Furthermore, health policy decision makers (e.g., from MCOs) may have had different perceptions than the participants in this study. Because of the qualitative study design and open-ended nature of the interview questions, participants did not have an opportunity to agree or disagree with all issues. Comments made by individuals, however, can still be insightful and generate ideas for future research.

**Conclusion**

Research scientists from the pharmaceutical industry who participated in this investigation suggested that PE models are useful in influencing drug policy decisions. Nineteen of the 20 respondents could provide examples where a PE model contributed to a health policy or medication policy decision (e.g., drug coverage, formulary position). No single model type surfaced as the single most effective means by which to communicate PE findings. Additional user training will be an important component for optimizing the usefulness of PE models. This study provides several recommendations for enhancing the effectiveness of PE models such as ensuring that model assumptions and calculations are transparent, creating and encouraging model customization by working directly with managed care decision makers, and incorporating head-to-head comparisons wherever possible. Great opportunities exist for further research in the area of effectiveness and utility of PE models in decision support for drug formulary content, placement, and

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Recommendations for Improving Pharmacoeconomic Models</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Provide more user-friendly, scientifically sound models</td>
<td></td>
</tr>
<tr>
<td>- Ensure that model assumptions and calculations are transparent</td>
<td></td>
</tr>
<tr>
<td>- Create and encourage model customization by working directly with decision makers in the development of PE models</td>
<td></td>
</tr>
<tr>
<td>- Collaborate with academia to avoid perceived industry bias</td>
<td></td>
</tr>
<tr>
<td>- Provide opportunities to educate decision makers on interpreting PE models</td>
<td></td>
</tr>
<tr>
<td>- Include overall health care costs when developing PE models</td>
<td></td>
</tr>
<tr>
<td>- Use real-world data to make PE models more relevant to individual practice settings</td>
<td></td>
</tr>
<tr>
<td>- Incorporate head-to-head comparisons wherever possible</td>
<td></td>
</tr>
<tr>
<td>- Use credible data sources and be prepared to share those sources with clients</td>
<td></td>
</tr>
<tr>
<td>- Consider publishing PE models prior to presenting results to decision makers in the field, then follow up with customizing the model to reflect organization-specific characteristics/data</td>
<td></td>
</tr>
</tbody>
</table>
coverage. The uptake of health plans employing the AMCP Format for Formulary Submissions process may provide the impetus for increased collaboration among academia, the drug industry, and MCOs in maximizing the usefulness of PE models in making formulary coverage and placement decisions.

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DISCLOSURES

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REFERENCES

ABSTRACT

OBJECTIVE: To estimate the incremental change in pharmacy per-member-per-month (PMPM) costs, according to various formulary designs, for a new interferon beta-1a (IB1a2) using administrative claims data.

METHODS: Cross-sectional sex- and age-specific disease prevalence and treatment rates for relapsing, remitting multiple sclerosis (RRMS) patients were measured using integrated medical and pharmacy claims data from a 500,000-member employer group in the southern United States. Migration to IB1a2 from other drugs in the class was based on market-share data for new and existing RRMS patients. Duration of therapy was estimated by analyzing claims for current RRMS therapies. Daily therapy cost was provided by the manufacturer of IB1a2, adjusted for migration from other therapies, and multiplied by estimated volume to predict incremental and total PMPM cost impact. Market-share estimates were used to develop a PMPM cost forecast for the next 2 years. PMPM cost estimates were calculated for preferred (copayment tier 2) and nonpreferred (copayment tier 3) formulary designs with and without prior authorization (PA). One-way sensitivity analysis was performed to assess the influence of product pricing, duration of therapy, and other market factors.

RESULTS: Annual incremental PMPM change was $0.047 for the scenario of third copayment tier with PA. The incremental change was greatest for those aged 55 to 65 years ($0.056 PMPM) and did not vary greatly by benefit design. Duration of therapy had the greatest impact on the PMPM estimate across benefit designs.

CONCLUSION: IB1a2 will not cause a significant change in managed care pharmacy budgets under a variety of formulary conditions, according to this cross-sectional analysis of current care-seeking behavior by RRMS patients. Economic impact may differ if IB1a2 expands RRMS patients’ treatment-seeking behavior.

KEYWORDS: Interferon beta-1a, Multiple sclerosis, Treatment costs

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A new form of interferon beta-1a (IB1a2) was approved in March 2002 for the treatment of relapsing, remitting multiple sclerosis (RRMS). Clinical trial results suggested improved clinical efficacy compared to the previous formulation of interferon beta-1a (IB1a1), leading to an override of the existing product’s orphan-drug-status exclusivity. IB1a2, an injectable, subcutaneous therapy, will be a direct competitor in the RRMS marketplace, which includes IB1a1, interferon beta-1b (IB1b), and glatiramer (Table 1). As a new first-line therapy and expensive biotech product, health plans may need to consider the pharmacy-budget impact of this product.

RRMS is the most common presentation of multiple sclerosis at onset, affecting 65% to 85% of newly diagnosed cases. Although therapies attempt to slow progression, many RRMS patients develop the secondary progressive (SPMS) form of the disease and face significant disability. Some new MS cases may present in the primary progressive form (10%) without relapses or remissions in symptoms over time. Fewer cases (5%) have the primary relapsing form, which is characterized by chronic deterioration and acute episodes. Managed care prevalence of MS in insured populations has been measured at rates of 24/10,000 enrollees for privately insured populations, with higher rates in Medicare (36/10,000) and Medicaid (71/10,000) over 2 years.

This benefit forecast analysis quantifies pharmacy costs from the perspective of the managed care payer, using actual care-seeking behavior as measured in administrative claims. It does not consider literature-based values, such as quality of life or medical-cost offsets, as do traditional cost-effectiveness or cost-utility models that may not reflect actual community practice. The forecasting analysis quantifies the use of therapies in a population and calculates the budget impact based on a simple scenario: unit cost multiplied by volume.

The importance of this approach is that it provides timely data regarding anticipated (pipeline) or recently approved therapies that may concern decision makers because of price, potential adoption as a new standard of care, or the number of patients affected.

Indeed budget impact represents an additional hurdle in the drug uptake process for managed care organizations after consideration of other primary factors, including safety, efficacy, and quality. The proposed technique addresses the pharmacy...
budget impact as it affects administrators determining coverage decisions. Actual value of the therapy in relation to its competitors would need to be measured by cost-effectiveness analysis that incorporates safety and efficacy outcomes. While IB1a2 may be clinically superior to its competitors in clinical trials, a cost-effectiveness analysis would be needed to show long-term benefit in community use. These end points may not be immediately relevant to payer decisions about costs in the short-term, which necessitates budget impact analyses.

When budget impact is small, formulary decision makers can focus on safety and efficacy differences among products. In contrast, when budget impact is high, the situation may be complicated by conflicting consumer, physician, and payer demands. Payers may then want to shift focus to more extensive cost-effectiveness or cost-benefit studies. In these cases, establishing cost offsets on the medical side may be necessary to justify the pharmacy-budget impact.

We conducted this study to estimate the pharmacy-budget cost impact of IB1a2, a new RRMS treatment. The analysis emphasized the following attributes in its design: transparency to the managed care audience, usage estimates based on actual care-seeking behavior in a managed care setting, sensitivity analysis of key uncertainties, a short-term time horizon (1–3 years), and simplicity of relevant metrics for decision-makers using per-member-per-month (PMPM) cost estimates.

### Table 1: Study Drugs

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Abbreviation</th>
<th>Brand Name</th>
<th>Manufacturer</th>
<th>Form</th>
<th>Strength</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon beta-1a</td>
<td>IB1a1</td>
<td>Avonex</td>
<td>Biogen</td>
<td>Powder, injection kit</td>
<td>30 mcg</td>
<td>Once weekly, IM</td>
</tr>
<tr>
<td>Interferon beta-1a</td>
<td>IB1a2</td>
<td>Rebif</td>
<td>Serono SA</td>
<td>Prefilled syringe</td>
<td>22 mcg, 44 mcg</td>
<td>3x weekly, SC</td>
</tr>
<tr>
<td>Interferon beta-1b</td>
<td>IB1b</td>
<td>Betaseron</td>
<td>Berlex</td>
<td>Powder, injection kit</td>
<td>0.25 mg</td>
<td>QOD, SC</td>
</tr>
<tr>
<td>Glatiramer acetate</td>
<td>Glatiramer</td>
<td>Copaxone</td>
<td>Teva Marion</td>
<td>Prefilled syringe and powder; injection kit</td>
<td>20 mg</td>
<td>QD, SC</td>
</tr>
</tbody>
</table>

### Identification of Base-Case Model Population

A 500,000-member, state-employer group in the southern United States was selected as the test plan to define model inputs using integrated medical and pharmacy claims data for calendar year 2000. This plan provided pharmacy coverage for members aged 65 years and older as part of a major medical supplement to Medicare; i.e., these are not Medicare+Choice members. The portion of the population covered under the State Children’s Health Insurance Program (SCHIP) was eliminated from the analysis.

Rates of MS were described separately by sex, and the population was categorized into 3 age groups: 0 to 54 years, 55 to 64 years, and 65 years and older. Age was calculated as a percentage, using eligibility data, and applied to the total member counts for the plan. We defined the care-seeking prevalence of MS by identifying the unique patients with an International Classification of Diseases Code—ninth revision (ICD-9) code 340 during the study period. Rates of disease treatment were measured by assessing how many patients had a pharmacy or medical claim using either national drug code (NDC) numbers or Health Care Procedural Coding System numbers (J-codes) that refer to the injectable treatments of IB1a1 (54569443300, 59627000103, J1825), IB1b (50419052101, 50419052105, 5041905210, 50419052115, J1830), or glatiramer (00088115003).12,13

Patients were further stratified by new or existing patient status, as shown in Figure 1. The initial date of service in 2000 was compared with records from the previous 6 months to see if another diagnosis or treatment code indicating RRMS was present. If there was such a code, the patient was classified as an existing user. If there was no RRMS code, the patient was classified as a new user. The analysis assumed that the pharmacy benefit manager would process 100% of the prescription claims in this therapeutic class.

### Market-Share Projections

The manufacturer of IB1a2 provided us with projections for target markets estimating that IB1a2 use among new MS patients
would be 80%. The manufacturer assumed that a shift to IB1a2 among existing patients would depend on their current therapy, estimated at 65% for IB1a1, 20% for IB1b, and 25% for glatiramer users (Figure 1). The market-share for the base-case plan in 2000 was calculated as an overall percentage of days supply dispensed: 51% for IB1a1, 34% for IB1b, and 16% for glatiramer.

Annual duration of therapy was used to estimate utilization per user. The mean sum of days supply dispensed under the pharmacy benefit in 2000 was calculated for current drug therapies. The resulting 253.13-day estimate (95% CI, 235.89–270.36) was used to model similar duration of use by IB1a2 users.

**Benefit Design**

Four benefit-design scenarios were considered:

- Second formulary tier ($15 copayment) with PA required
- Second formulary tier ($15 copayment) with no PA
- Base case—third formulary tier ($25 copayment) with PA required
- Third formulary tier ($25 copayment) with no PA

The costs associated with administering a PA program were included in the analysis. Criteria for authorization for this drug would include confirming a diagnosis of relapsing multiple sclerosis. We estimated that 80% of PA requests would be approved. Of the denials, 50% would be appealed and processed, and half of the appeals would be approved. PA review costs an estimated $30 and appeals $45. These costs are cumulative such that an initial review plus appeal would total $70. Treatment costs incurred by denied patients, based on the market share of the alternative injectable therapies, were also included, because the plan may have to pay for another treatment that is almost as expensive as IB1a2, and those costs would erode the savings accrued from the PA denial. The eventual acquisition of IB1a2 therapy through a PA override was also estimated at the rate of 14% of all denied patients. The base case assumed that, like the current treatments, the new therapy would be covered 100% under the pharmacy benefit, less the copayment amount.

**Costs of Therapy**

The $35.58 estimated daily cost of therapy for IB1a2 was based on estimated wholesale acquisition cost (WAC) (80% of average wholesale price for 1 month $1,334.13). This cost was then adjusted for migration from other therapies based on their respective market shares within the plan population.

For the base-case plan, we calculated the cost offset by multiplying the daily estimated WAC of each existing drug by its market share: for IB1a1, $29.24 multiplied by 51% (WAC effective January 1, 2002); for IB1b, $30.05 multiplied by 34% (WAC effective January 1, 2002); and for glatiramer, $27.71 multiplied by 16% (WAC effective October 3, 2001). The resulting incremental cost of IB1a2 was $6.02 per day or $1,523 per average course of therapy.

The final cost calculation was based on the total number of patients approved to receive IB1a2 (after the PA process) multiplied by the duration of therapy and the incremental daily cost of therapy. Total costs were adjusted to reflect PA administrative costs, savings from PA denials, eventual acquisition of IB1a2 therapy, and the costs of alternative therapy for patients with PA denials. The costs were expressed using PMPM and per-member-per-year (PMPY) metrics.

**Market-Launch Curve**

Using the 2000 assessment of the total potential user popula-
Results

The demographic description of the study population is shown in Table 2. This plan had 72% of its membership under the age of 55 years; the remaining 28% of members were split equally between the 56 to 64 years and 65 years and older age categories. Sixty percent of the members aged 64 years and younger were female and 40% were male, while 66% of the members age 65 and older were female and 35% were male. The base-case model settings for benefit design and coverage issues are shown in Table 3.

After the claims algorithm was applied (Figure 1), 201 individuals were considered candidates for IB1a2 use. After applying rates of PA application, approval, and appeals, 146 individuals were identified as IB1a2 users. The costs of therapy after a $25 copayment per prescription were $191,498. For the PA simulation, the costs were adjusted for PA administrative costs ($4,980), annual costs of alternative therapies in denials ($104,725) and acquisition by some members receiving a PA override who never entered the PA process ($2,571). The total annual incremental cost for all patients in this 508,066 member plan seeking IB1a2 in a third tier with PA scenario was $285,412.

The estimated incremental impact of IB1a2 on the pharmacy budget for the base-case scenario was $0.047 PMPM ($0.56 PMPY). The per-patient-per-year (PPPY) costs were estimated at $1,954.88 or $162.91 per-patient-per-month (PPPM). This represents the maximum additional drug expenditures after member cost share (i.e., the net additional cost for the drug to the plan sponsor) that could be expected in the RRMS class with the launch of IB1a2, assuming that all projected patients start using the drug. As shown in Figure 2, incremental PMPM was $0.053 for patients aged 0 to 54 years, who comprise 72% of the study population. Although there are equal numbers of members in the remaining 2 categories, incremental PMPM for the 55 to 64 years category was $0.056, compared with only $0.04 for those aged 65 years and older.

The incremental PMPM impact by benefit design, shown in Figure 3, was calculated to be $0.049 when IB1a2 was placed on the second formulary tier and PA was required, compared with $0.046 for tier 2 with no PA. The incremental PMPM is higher for the plan design with required PA due to PA administrative costs and the costs of alternative therapy for denied patients.

Estimated incremental PMPM for tier 3 was $0.047 with PA and $0.043 without PA. These estimates are lower than for tier-2 plan designs, because patients pay a larger share of the cost.

Sensitivity Analysis

One-way sensitivity analysis was performed to assess variation in the outcomes of

- duration of IB1a2 therapy,
- migration of new users to IB1a2, and
- shift of IB1a1 users to IB1a2.

The model was developed as an interactive tool using Microsoft Excel 97 and supplemented with data from claims analysis using Embarcadero RapidSQL version 5.5 or SPSS version 11.0. The spreadsheet can be modified for different health care payers by inserting specific demographics, benefit designs, and the market shares of existing RRMS treatments (IB1a1, IB1b, and glatiramer).

Table 2: Description of Base-Case Population for Pharmacy-Budget Impact Analysis of IB1a2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plan Size*</td>
<td>508,066</td>
</tr>
<tr>
<td>Number of members by age category (years) n (%)</td>
<td></td>
</tr>
<tr>
<td>0-54</td>
<td>369,808 (72)</td>
</tr>
<tr>
<td>55-64</td>
<td>71,129 (14)</td>
</tr>
<tr>
<td>65+</td>
<td>71,129 (14)</td>
</tr>
<tr>
<td>Female members by age category (years): n (%)</td>
<td></td>
</tr>
<tr>
<td>0-54</td>
<td>219,485 (71)</td>
</tr>
<tr>
<td>55-64</td>
<td>42,678 (14)</td>
</tr>
<tr>
<td>65+</td>
<td>46,945 (15)</td>
</tr>
<tr>
<td>Coverage of injectables under pharmacy benefit</td>
<td>100%</td>
</tr>
<tr>
<td>Risk for members over age 65 years</td>
<td>100%</td>
</tr>
<tr>
<td>Calendar Year 2000 market share of existing</td>
<td></td>
</tr>
<tr>
<td>products based on days supply dispensed (%)</td>
<td></td>
</tr>
<tr>
<td>IB1a1</td>
<td>51</td>
</tr>
<tr>
<td>IB1b</td>
<td>34</td>
</tr>
<tr>
<td>Glatiramer</td>
<td>16</td>
</tr>
</tbody>
</table>

*All members eligible for pharmacy benefits as of December 31, 2000, excluding the SCHIP program carrier.
† Counts of member population were based on calculated percentage of age applied to the current eligibility numbers. The 65+ years population includes Medicare enrollees with supplemental coverage through the plan, i.e., does not include Medicare+Choice members.

Table 3: Estimates of Care-Seeking Behavior for MS in Base-Case Health Plan by Age and Sex (N=508,066)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Males (%)</th>
<th>Females (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-54</td>
<td>55-64</td>
</tr>
<tr>
<td>MS diagnosis</td>
<td>0.08</td>
<td>0.14</td>
</tr>
<tr>
<td>Injectable rate</td>
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<tr>
<td>Existing users</td>
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</tr>
<tr>
<td>Total predicted population (n)</td>
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<td>4</td>
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which decreases the health plan’s portion of the cost.

Sensitivity analysis was performed for IB1a2 duration of therapy, IB1a2 market share among new RRMS patients, and existing users’ shift from IB1a1 to IB1a2. As shown in Figure 4, the base-case estimates changed slightly when altering the duration of therapy by 25%. The incremental budget impact was $0.035 for 190 days’ annual duration of therapy and $0.058 for 316 days, compared with the base case of $0.046 for 253 days. The model reacted less sensitively to the assumption that 80% of new users would initiate therapy on IB1a2. Variation from 60% to 100% of the market share among new users caused a shift of only $0.04 to $0.05 in incremental PMPM. Changes in the projected market share from 49% to 81% of existing IB1a1 users to IB1a2 similarly caused minimal fluctuation in the incremental PMPM ($0.044 to $0.049).

While the incremental increase in current drug expenditures for injectable MS therapy was less than $0.05, Figure 5 shows that the estimated total cost for one year, after subtraction of member cost-share, for IB1a2 one year after the market launch is $0.21 PMPM for the base case, only slightly less than the current drug expenditures for IB1a1 ($0.23).

Figure 6 shows the estimated 3-year market-launch curve for each product in the class and IB1a2 uptake extrapolated based on manufacturer targets for market share. The estimated market share in year 3 is IB1a1, 29.8%; IB1a2, 26.2%; IB1b, 9.5%; and glatiramer, 34.4%. The estimated incremental PMPM after the IB1a2 launch is $0.02 after year 1, $0.03 after year 2, and the $0.047 at the end of year 3.

Discussion

This model predicts that IB1a2 will add an additional cost of $0.047 PMPM to the pharmacy budget of a health plan with full injectable coverage and placement on tier 3 with PA required. Estimates of budget impact on the other 3 plan designs did not vary much from the base case after considering administrative fees and alternative therapy costs for PA denials. The predicted impact is considered low, relative to other therapies such as Cox-II inhibitors20 and allows for more flexible benefit design in the MS injectable drug class.

Although the estimates resulting from this study are specific to the age and sex distribution of the test health plan, the age of this population resembles the age distribution reported in the 1996 Medical Expenditure Panel Survey for the total insured population.19 The annual rates of MS prevalence derived from our study population are similar to those reported by Pope et al.,6 using 2 years of claims data. Pope’s prevalence rates were slightly lower for the 55 to 64 years age group (26/10,000 in Pope compared to 32/10,000 here).6 We surmise that an increased percentage of females or a higher concentration of members aged 35 to 54 years would increase estimates of the potential population of users. Accordingly, we would anticipate budget impact to be higher in these scenarios as well.

The most significant driver in the model was duration of IB1a2 therapy. Increasing the average duration of therapy by 25% increased the estimated incremental PMPM to $0.058 ($0.70 PMPY). Since duration of therapy was derived from
Byproduct of these improvements may be increased patient
compliance, which could raise the average duration of therapy
and ultimately affect the incremental cost. However, the pre-
dicted change would be small ($0.047 to $0.058) and poten-
tially offset by medical savings due to improved efficacy.

This analysis used fixed pricing for all of the agents consid-
ered since the price at launch had already been determined.
Additionally, the new agent was already priced at higher cost
than the other agents on the market and would most likely not
stimulate price reduction in the competition. If the incremental
price of the agent was twice what it is today ($12 per day), the
incremental budget impact would be $0.08 PMPM. Ideally,
budget impact analyses should consider price of the agents and
potential changes in the market as competitors react to market
changes. If the price of the competitor agents decreased with-
out a parallel price decrease in lb1a2, the budget impact would
be higher. If the price of the new agent was reduced without a
price shift in the competitors, the impact of the new agent
would be smaller. Inflationary pressures over time would most
likely affect each competitor similarly, and the incremental
impact would remain the same.

The manufacturer had predicted a high percentage—80%—
of lb1a2 market penetration among new users similar to the
addition of pegylated interferon for the treatment of hepatitis-
C.21 We felt this utilization target was high (making it conserva-
tive from a pharmacy budget standpoint) and performed sensi-
tivity analysis around that assumption. However, 20% variation
in this percentage did not greatly affect the PMPM estimate due
to the small number of patients affected by this market-share
estimate.

Our analysis was undertaken to develop a method for esti-
mating budget impact that could be readily customized to indi-
vidual health plan needs. For instance, prevalence of the disease
is an important consideration since it may vary by plan. A dou-
bled the number of patients identified in this scenario would
increase the base-case incremental impact to $0.09 PMPM. A
50% reduction in the number of patients results in an incre-
mental impact of $0.02 PMPM. While these are relatively small
increases, they do reflect the need for health plans to have cus-
tomized information. Administrative claims data can provide a
ready source for such customization.

The model assumes that there would be no additional
growth in the number of diagnosed cases of RRMS, so the num-
ber of patients per year would be relatively static. If new diag-
nostic tests or widespread education about RRMS promotes
more care-seeking behavior, there may be unanticipated growth
in the market. However, any increased incidence would not be
solely attributed to the launch of lb1a2, and the relative mag-
nitude of the impact to the therapeutic class would likely
remain the same. Future drug releases or market shifts could
also impact the market-launch curve as we have predicted it.

This analysis assumes that a health plan is at risk for the
administrative costs associated with conducting PA programs.
While this is true for many health plans, some insurers may
shift that cost to their pharmacy benefit manager (PBM). The
rates of PA denials and appeals were derived from PBM experi-
ence with Cox-2 inhibitors, so actual experience with this new
injectable therapy may differ. However, widespread denial of
this drug to treat a serious, debilitating condition is unlikely.

While claims data may represent a better estimate of the
care-seeking behavior in specific communities, selection bias
and coding errors may affect the results. For instance, a 1-year
cross-sectional analysis of ICD-9 codes may underestimate
chronic conditions that are not relevant with each physician
visit. Also, the use of an employer-group dataset biases the test
population toward healthy workers. It may not be appropriate
to apply this analysis to Medicaid or Medicare populations with

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**FIGURE 5** Comparison of Projected Annual PMPM, Including lb1a2 With Current Market Drug Health Plan Expenditures (After Member Cost-Share)

**FIGURE 6** Market-Launch Curve With Incremental PMPM Shift for 3 Years Postlaunch
higher disease prevalence; accurate results would most likely require different assumptions.

Costs associated with side effects or adverse events that may require other drug therapies are not included in the model. The current clinical trial data do not suggest that IB1a2 would cause a disproportionate number of adverse events that would require additional drug therapy and thereby raise the incremental costs. Conversely, if the side-effect profile is improved with IB1a2, use of the new agent may reduce the impact on the pharmacy budget.

Future development of budget forecast analyses should include a wider range of benefit design options that are increasingly used in health plans, including percentage copayments, 4 or 5 copayment tier placement, and defined contribution plans. Methods should also be developed to validate the findings in specific populations after a forecast analysis has been implemented and a new drug launch can be evaluated. Deficits in the accuracy of models can be addressed in future simulations. While budget impact modeling is necessary and relevant, the technique relies on inexact science of cost calculations and assumptions.

The strength of this pharmacy budget impact approach is that rates of utilization are based on actual community data. The pharmacy-budget payer’s perspective was aided by providing useful metrics. The analysis is a first-line decision tool for benefit design and helps direct the agenda for further pharmacoeconomic research that many include broader medical-cost implications.

■ Conclusion

IB1a2 will have minimal incremental budget impact ($0.047 PMPM for third tier with prior authorization) over the current drug expenditures for the drug plan sponsor (i.e., after member cost-share) for RRMS therapies. This pharmacy-budget impact analysis indicates that health care benefit managers have flexibility when designing coverage for IB1a2 and can emphasize choice and clinical efficacy over cost containment.

ACKNOWLEDGMENT

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Beyond Narcotics for Effective Pain Management

An editorial by Andis Robeznieks titled “Prescription drug abuse deadlier than use of illegal drugs” in American Medical News was but one of many articles and editorials constituting the swelling backlash against abuse of prescription drugs.1-3 Age has its virtues. One of them is perspective. Having been in practice for a quarter of a century, it has been my opportunity to watch many fads come and go in medicine. Sometimes they quietly fade away—dying of inattention and loss of interest. Other times they fade away—dying of adverse outcomes. The current fad of apparent narcotic leniency is an example of the second.

The article by Robeznieks discussed deaths in Florida attributed to drug abuse. Specifically, he detailed that between January and June of 2002, Florida medical examiner reports listed as the cause of death cocaine in 180 deaths, benzodiazepines in 150 deaths, methadone in 133 deaths, heroin in 121 deaths, oxycodone in 112 deaths, and hydrocodone in 61 deaths. In total, prescription-type narcotics accounted for 40% of the deaths. Obviously, this is but the tip of a much larger “iceberg” of narcotic-related misuse problems. Robeznieks stated, “In 2001, the DAWN (Drug Abuse Warning Network) report estimated that 43% of the 1.1 million emergency department drug mentions were a result of abusing legal prescription or non-prescription medications.” Yet, even this is still only a part of the iceberg, since excessive use of narcotics tends not to be mentioned in patients who have a condition that might defend (but doesn’t really) the excess use of the drugs. Other data and national statistics may be obtained online.4 The trend is toward an increasing emphasis on excessive narcotic use by some individuals.

From data of this type, both from the perspective of abuse and the growing backlash in the literature and media exposure, it may be argued that current American policy to narcotic leniency is a fad—a temporary excessive interest that reflects a momentum more than a logic. The current fad to narcotic leniency came about as the result of 2 principal factors: (1) a national recognition of pain as a real issue, requiring attention and (2) the utilities of leniency.

Pain certainly is an important issue. Pain is the single most common complaint leading patients to doctors. Pain may stop function. Pain may create misery. And, we have many medications that may be helpful in the control of pain. So, pain is an important national agenda. On the other hand, pain is not simply a discussion of physical illness (pain as nociception). Discussion of chronic pain heavily centers on issues of anguish in many patients. And, in these latter conditions, the chronic use of pain medications leads to life deterioration. This is the addiction discussion.

When pain medications are used to control a “painful” experience of sensory input (nociception) then people tend to do well, and addiction is largely not an issue. When the pain source stops, the pain medication use also stops. In contrast, when pain medication is used to control anguish (emotionally “painful” experience) then the patient may be encouraged to allow the basic social/psychological problems to continue. The drugs lead to “escape,” but when the drugs wear off, the problems are still present—possibly even worse due to inattention. Using narcotics to control anguish leads to life deterioration, increasing drug dependency, reduced social capacity, and emotional dissolution. This is the problem of addiction.

When patients are suffering from anguish, several mechanisms may lead the patient to the doctor with complaints of physical pain. Stress biology is a major cause of pain syndromes in patients with anguish. Chronic stress causes pain due to increased sensitivity to painful stimuli (via neural sensitization mechanisms), and stress also causes an increase in pain generators such as chronic muscle spasm or stress-induced bowel problems. Anguish also leads to somatization: fear of dysfunction and illness leading to excessive focus on health. Anguish also leads to anxiety and depressive disorders, with excessive worry or excessive pessimism. Anguish also leads to the desire for “escape.”

So, to understand a patient’s pain we must understand many things. When we fail to understand that the complaint of pain is really the derivative of an anguish mechanism, then we may prescribe the very medications that propagate the problem.

America is interested in good control of pain. But, good control of pain does not always mean prescribing more pain pills. This point has been underestimated in the recent fad of narcotic leniency in America.

This leniency has also been promoted by another factor—utility. For a doctor, it is vastly easier to give a prescription for a pain pill than to confront the issues that make doing so unwise. When the patient says, “I have pain,” it is much easier to make the presumption that there is some noiceceptor rather than to explore for anguish. In addition, in a country enamored of the concept that pain is undertreated, the pursuit of a sanguine balance may be less than popular.

So, America has recently been involved in an experiment, the experiment to see what happens when restraint is removed from the use of narcotics. Not surprisingly, the result has included some adverse outcomes. These reveal that overly simplified thinking about the pain issue will not produce a universally good outcome. The pendulum is now forced back more toward center. Another fad begins to end.

We will not treat pain correctly until we understand it. We will not understand pain until we understand both nociception and anguish—both represented by “pain.” In America, we will continue to have problems with narcotics until we learn that we can manage both nociception and anguish. Anyone who believes that narcotics are the problem has simply missed the point. Anguish is the problem. Narcotics are simply not a good way to manage it.

Thus the flurry of articles recognizing the potentially serious outcomes of drug abuse may herald an end to another fad, the fad of excessive narcotic leniency in America. It won’t be the first time that backlash has been required to recenter an imbalanced pendulum. And, it won’t be the last.

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PHARMACEUTICAL INNOVATION & BUDGET IMPACT MODELS
An Analysis of ADHD Treatment in Managed Care

April 9, 2003 · 1:00 – 5:00 pm
Lunch Symposium
Minneapolis Convention Center
Minneapolis, MN

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Executive Vice President
Economic and Outcomes Research
Ingenix · Eden Prairie, Minnesota

Peter Levine, MD
Staff Pediatrician
Co-Chair ADHD Best Practice Committee
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Unraveling the Effects of Tier-Copayment Drug Benefit Designs

More information is needed about the effects of member out-of-pocket copayments on prescription drug utilization and costs. On the one hand, the introduction in the last 2 years of generic versions of several popular drugs reduces dramatically the treatment cost per patient for hypertension, coronary heart disease, community-acquired bacterial infections, depression, gastroesophageal reflux disease (heartburn), and hyperlipidemia. Over-the-counter loratadine (generic Claritin) has added more opportunities for cost-effective drug benefits management and caused many pharmacy benefit managers to reconsider the common coverage exclusion for OTC drugs; competition had reduced the OTC price of loratadine to less than $.50 per day of therapy within a few weeks of OTC availability of loratadine, a discount of about 75% compared to prescription drug alternatives cetirizine, desloratadine, and fexofendadine. Generic versions of therapeutic class leaders such as Mevacor, Prilosec, Augmentin, Zestril, Prinivil, Vasotec, and Prozac make it possible to treat up to 5 times as many patients for the former cost of treating one patient with the brand-name drug.

A generic-only drug benefit plan is becoming increasingly plausible. Clinicians will differ, but the economics are compelling. Short of a generic-only benefit, health plans and employers can push members to generic drugs with low copayments ($5 or less per month of therapy) and higher brand-drug copayments ($20 or more per month of therapy) in 2-tier copayment drug plan designs. Three-tier, 4-tier, and 5-tier copayment designs create more opportunities to influence member behavior. Member satisfaction must always be a measure to consider in designing any health benefit, particularly prescription drugs, the most commonly used health plan benefit. In this issue of the Journal, Nair, Wolfe, Valuck, McCollum, Ganther, and Lewis conclude that drug utilization changes were modest in the measurement of prescription utilization behavior among health plan members who were converted from a 2-tier copayment plan to a 3-tier copayment drug benefit plan. Other observers may find generic drug utilization changes of 6 to 8 absolute percentage points and a 5.6% absolute increase in formulary adherence, from 81% to 87%, to be more than modest. In fact, most managed care pharmacists would find these changes significant and remarkable.

In addition to utilization changes associated with benefit design (copayment) changes, members in the drug plans that “converted” from 2-tier to 3-tier copayment designs had median health plan costs per patient per month (PPPM) that were 60% less than the median health plan costs PPPM for 2-tier plans and 33% less than 3-tier plan members who remained in the 3-tier copay plans. The median copayment for members converted from a 2-tier to a 3-tier plan increased from $3 to $16.83, but this amount was less than the median copayment of $19.81 for 2-tier plan members who remained in 2-tier plans and a median $21.42 copayment for 3-tier plan members who remained in 3-tier copayment drug plans. These collective data appear to suggest that while median copayment changes may be large in relative terms for members converted to a 3-tier copayment plan from a 2-tier copayment plan, these changes produce significant and remarkable changes in drug utilization and significant reductions in net health plan costs.

Yet, the extant work by Nair et al. appears to raise as many questions as it provides answers, similar to published work that preceded this article. These outcomes may be associated with the lack of a common definition of the intervention. Multiple-tier copayment drug benefit plans are a heterogeneous lot. Two-tier plans may or may not be administered with prior authorization requirements (for nonformulary or high-cost drugs), and these PA requirements may be rigorous or lax, the latter amounting to not much more than hassle factors for physicians, pharmacists, and members. The formulary content for 2-tier plans may be small in scope or more comprehensive, and without PA or other restrictions on access, the 2-tier formulary would rely upon voluntary behavior change among members, prescribers, and pharmacists. Three-tier copayment plans may be associated with a small number of formulary drugs or broad in scope. Some 3-tier copayment plans employ the third copayment tier for nonformulary drugs while other 3-tier copayment plans have 2 copayment tiers for formulary drugs. As with 2-tier copayment plans, the amount of the copayments and the magnitude of the difference between the copayment tiers may be small ($5 or less per month) or quite large ($20 or more per month of drug therapy). Controlling for all of the important factors that may have some effect on cost and utilization outcomes in prescription drug benefits is a formidable task, particularly as the content of the drug formulary may change as often as each calendar quarter.

One particularly thoughtful and comprehensive examination of prescription use among persons aged 65 years or older also raised as many questions as it provided answers. Within the long list of findings was the apparent conclusion that 3-tier copayment drug plans for persons aged 65 years or older were associated with higher member cost-share, but this additional cost was offset by plan cost savings greater than the amount of the increase in the average member cost. This finding suggests that financial incentives caused persons aged 65 years or older to use lower-cost brand drugs and more generic drugs, resulting in more value for each drug benefit dollar (with a potential favorable effect on the drug benefit premium). A study published 2 months earlier, in October 2002, found that adding a third copayment of $30 for nonpreferred brand-name drugs to a $10 generic, $20 brand, 2-tier copayment plan reduced overall drug spending by 4% (P<.001), providing additional evidence of the ability of 3-tier copayments to improve value in excess of the simple transfer of costs from health plans to health plan members.

Sophisticated pharmacy benefit managers will note that the work by Nair, Wolfe, Valuck, McCollum, Ganther, and Lewis in this issue of the Journal pertains only to members in health plans with specific chronic disease states. These findings may have little relevance to pharmacy benefit managers and actuaries when estimating future costs and premiums, both of which are calculated...
primarily on the basis of per-member-per-month and per-employee-per-month measures. Similarly, Nair et al. employed measures of the median, rather than the mean, and per-patient rather than per-member, in their investigation of the effects of benefit design on prescription utilization and costs. Use of these alternate measures was made necessary by the nature of their study design, which used inclusion criteria that made their subjects “patients,” chronic users of prescription drugs.

Readers of the article by Nair et al. should also note that the 3 study groups were dissimilar. The authors readily acknowledge this dissimilarity in the study groups. In fact, their Table 1 shows that the only factor that was not dissimilar among the study groups was the proportion of males versus females in each. Medicare+Choice members accounted for 57.2% of the 2-tier copayment plan members who stayed in 2-tier drug plans versus zero members in each of the other 2 study groups. Others have not been as careful or thorough in measuring characteristics of study groups in a longitudinal, preintervention and postintervention design with comparison groups. Nevertheless, the findings of the work by Nair et al. in this issue of the Journal are suggestive and not definitive.

### Preventable Drug-related Morbidity (PDRM)

MacKinnon and Hepler in this issue of the Journal examine the incidence of potential examples of preventable drug-related morbidity (PDRM) in a senior, Medicare-risk population of a hospital-based health system in Florida.7 This study does not tie these identifiable examples of PDRM to actual clinical outcomes. Yet, the work is of interest to those dedicated to continuous quality improvement (CQI) in health care, the reduction of threats to patient safety, and maximization of opportunities to increase the frequency of favorable clinical outcomes. The method used to develop these PDRM indicators was described in a previous article in the Journal.7 Expert panel consensus was reported for several clinical indicators of PDRM that included indicator no. 6, an emergency room (ER) visit or hospitalization due to hyperkalemia subsequent to the use of an ACE (angiotensin converting enzyme) inhibitor, without checking electrolytes and CBC at least every 6 months. By this measure, most of our elderly population on an ACE inhibitor could be at risk of PDRM.8 The distinction between drug-related morbidity (DRM) and preventable DRM (PDRM) is of obvious importance to managed care pharmacists since PDRM, by definition, be reducible.

More than 50% of the patients with identifiable PDRM risk factors in the study by MacKinnon and Hepler were in 3 categories (pertaining to postmyocardial infarction (MI) treatment and diabetes management) that have been addressed specifically by managed care organizations in clinical practice improvement interventions and CQI programs. In fact, significant strides have been made in the past few years to improve the quality of care for patients after MI and in the periodic and scheduled measurement of hemoglobin A1c in diabetic patients. The National Committee for Quality Assurance (NCQA) 2002 report of health care quality measures from 2001 for 271 MCOs representing 71 million members, or about 28% of the U.S. population, found improvement in several key measures. Beta-blocker use increased in 2001 to 93.5% of eligible post-MI patients compared to 89.4% in 2000, 85.0% in 1999, and 62.5% in 1996.9 Hemoglobin A1c testing increased to 81.4% of diabetic enrollees in 2001 compared to 78.4% in 2000 and 75.0% in 1999, and hemoglobin A1c testing among Medicare enrollees was 85.3% in 2000 for NCQA-accredited MCOs versus 78.9% among nonaccredited MCOs. While managed health care systems have made significant and measurable strides in quality improvement in care processes that pertain to at least 3 of the top 5 potential PDRMs suggested by MacKinnon and Hepler, this is a moving target. While there is still opportunity to improve quality, significant improvement has been made.

Examination of data from 149,177 Medicare hospital admissions for MI in 1994 and 1995 showed that the top-ranked cardiology hospitals in U.S. News & World Report’s “America’s Best Hospitals” had lower adjusted 30-day mortality (odds ratio 0.87) compared to other hospitals. Aspirin and beta-blocker use was higher in the top-ranked hospitals compared to other hospitals, 96% versus 89%, and 75% versus 62%, respectively.10

### ERT, HRT,Raloxifene, Calcitonin, or Bisphosphonates for Osteoporosis

The sudden termination of the Women’s Health Initiative (WHI) trial of combination conjugated equine estrogen (CEE) and medroxyprogesterone acetate MPA) on May 31, 2002, precipitated a significant media event in the succeeding months. For most physicians, the “news” that estrogen and progestin in combination (hormone replacement therapy—HRT) were associated with a small increase in risk of breast cancer was not surprising, nor was it surprising that fractures were significantly lower among users of combination estrogen and progestin. Any prior use of HRT was found to be associated with a 11% cases of breast cancer over the average 5.2 years of follow-up, a rate of 1.34%, compared to 102 cases (rate of 1.26%) for women who had never taken HRT.11 This finding combined with the results from the Heart and Estrogen/progestin Replacement Study (HERS) and HERS II suggest that combination estrogen and progestin is associated with (a) a higher risk of breast cancer than estrogen alone,12 and (b) no protection from the risk of coronary heart disease (CHD) in either primary or secondary prevention.13,14 WHI found increases in CHD (22%), MI (29%), stroke (41%), and pulmonary embolism (twice the rate in the placebo group). On the positive side, combination HRT was shown to result in 37% fewer cases of colon cancer, 33% fewer hip fractures, and 24% fewer fractures overall.

Physicians in the United Kingdom reacted to the news of termination of the WHI trial by requesting the continuation of clinical HRT trials.15 British scientists recommended in mid-July 2002 that a major trial of HRT set to involve 22,000 women should continue. The U.K. study, the Women’s International Study of Long-Duration Oestrogen after Menopause (WISDOM), began in 1999 and will be conducted until the end of 2012 to determine if HRT,
specifically estrogen alone or in combination with progesterin, is associated with the risk of MI, breast cancer, osteoporosis, or dementia. Britain’s Medical Research Council said the committee in charge of the WISDOM trial believed there were no strong ethical or scientific reasons to stop. WISDOM has already recruited 5,000 British women. Eventually, more than 16,000 postmenopausal women aged 50 to 69 years in the United Kingdom and 6,000 from Australia and New Zealand will be involved in the study.

Most women do not take estrogen replacement therapy (ERT) or combination HRT to lower lipid levels or for protection from adverse cardiac events, despite the earlier evidence that estrogen had favorable effects on cardiovascular disease, about one third attributable to lipid reduction and two thirds of the favorable effect attributable to direct effects such as vasodilatation and inhibition of the response of blood vessels to injury and development of atherosclerosis. Wyeth reported in mid-July 2002 that 92% of the prescriptions for HRT in 2002 were written for postmenopausal symptoms, compared to 76% in 1999. Osteoporosis accounted for 51% of the reasons for using ERT/HRT in 2002, compared to 80% in 1999. Protection from cardiovascular disease accounted for only 16% of the prescriptions in 2002, down from 68% in 1999.

A comprehensive review of the literature published in early 2002 found that ERT/HRT (a) may not be the best choice for osteoporosis, but it is relatively inexpensive with few side effects; (b) is effective in primary prevention of cardiovascular disease (CVD) but may not be effective in secondary prevention (in women with established CVD); and (c) may help retard memory loss in women and might prevent Alzheimer’s disease (AD). This review also suggested a qualitative point about ERT/HRT and the risk of breast cancer: ERT/HRT might increase the risk of breast cancer, but the cancers associated with ERT/HRT appear to be more benign tumors, possibly explaining the observation of lower breast cancer mortality rates among ERT/HRT users compared to nonusers. The 33% fewer hip fractures and 24% fewer fractures overall found in the WHI study are consistent with previous findings from case-controlled and cohort studies in which HRT was associated with about a 30% reduction in risk of hip fracture;2221 2 placebo-controlled studies in osteoporotic women found a 50% reduction in the risk of fractures of the spine.2223 The effectiveness of ERT in the prevention of osteoporosis may be improved by starting at menopause rather than later in postmenopausal life. Revised labeling for CCE and combination CCE+MPA approved by the FDA in January 2003 included indications for (a) relief of moderate to severe vasomotor symptoms associated with menopause (the primary reason women seek treatment), (b) relief of moderate to severe symptoms of vulvovaginal atrophy associated with menopause, and (c) prevention of postmenopausal osteoporosis in appropriately selected patients.2528

Bisphosphonates are alternative pharmacotherapy for osteoporosis. A study funded by the maker of alendronate found that 0.625 mg CEE plus 5 mg MPA was approximately 2 times as effective as 5 mg of alendronate in preserving or building bone mineral density (BMD) in postmenopausal women.27 There has been controversy surrounding the promotional activities of raloxifene for risk reduction for breast cancer,28 despite FDA-approved labeling that did not permit this claim but did include study findings that raloxifene is associated with a lower rate of breast cancer; 0.52 cases of invasive breast cancer per 1,000 women-years, one third less than the rate among women taking placebo.29

In this issue of the Journal, Mullins and Ohsfeldt present a budget impact model that compared raloxifene to alendronate (risedronate was not compared) and CEE+MPA therapy for postmenopausal prevention; calcitonin was not included in the model. The authors used conservative outcomes from clinical trials in the assumptions in their model. For example, the authors assumed no reduction in risk of hip fractures from raloxifene since the available evidence points to reduction in risk of vertebral fractures only. On the other hand, unlike raloxifene, there is convincing clinical evidence that risedronate reduces hip fractures, by 30% over 3 years, regardless of BMD, 40% for women with low BMD, and 60% for elderly women with prevalent vertebral fractures. In their model, Mullins and Ohsfeldt used estimates of 1-year and 3-year risk reduction for hip fracture of -18% and -35% for CEE+MPA, respectively, and -25% and -50% for alendronate, respectively.

There are both safety and efficacy concerns for the bisphosphonates and safety concerns for ERT. Reports of liver damage with alendronate caused some experts to question the safety of the bisphosphonates in general. The labeling for pamidronate (not FDA-approved for osteoporosis) was changed in late 2002 to warn against the use of doses of greater than 90 mg (the recommended dose) due to the possible risk of deterioration of renal function that may lead to renal failure. A study of the use of alendronate under real-world conditions found about one third of users discontinued use of alendronate within the first 3 months of use, and many upper gastrointestinal (GI) symptoms ascribed to use of alendronate were reported by 32.7% of users. The effects of bisphosphonates on the GI tract appear to contribute to symptoms that many users find intolerable or unacceptable, and a study reported in 2002 found an incidence of gastric ulcers in 6% of 300 patients taking 5 mg per day of risedronate and 12.1% of 297 patients taking alendronate 10 mg per day (P=0.013).

The efficacy data for the bisphosphonates in the prevention and treatment of osteoporosis suggest that better pharmacologic therapies are needed. Alendronate users have been found to experience a 1% incidence of hip fractures versus 2% in untreated patients, which the news media reported in relative terms only, as a 50% reduction in the risk of hip fracture. Risedronate at either 3.5 mg per day or 5.0 mg per day was associated with an incidence of hip fracture of 2.8% versus 3.9% among patients who received placebo (P=0.02), an absolute difference of 1.1% and relative risk reduction of 28%. For the osteoporosis group only, the incidence of hip fracture was 1.9% versus 3.2% for placebo, an absolute risk reduction of 1.3%, meaning that it would require 231 person-years of risedronate to prevent one hip fracture or
about $160,000 of risedronate at discounted pharmacy prices in CY 2000. Also notable was that only 50% of the women completed the full 3 years of treatment with risedronate.

In addition to the bisphosphonates, risedronate and alendronate, calcitonin, ERT/HRT, and parathyroid hormone (PTH), the pharmacologic armamentarium for treatment of osteoporosis includes teriparatide, a PTH segment approved by the FDA on November 26, 2002. Teriparatide, injected daily into the thigh or abdomen, is approved for the treatment of osteoporosis in postmenopausal women who are at high risk for a fracture and to increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk for a fracture. The definition of high risk would include men or women with a history of osteoporosis-related fracture, or who have multiple risk factors for fracture, or who have failed or are intolerant to previous osteoporosis therapy, based upon physician assessment. The inconvenient administration, high cost (about $7,300 per year), black-box label warning of osteosarcoma observed in rat studies, and approval for use only in high-risk osteoporotic persons would tend to suppress widespread use of the drug. However, teriparatide is unique among the agents used to treat osteoporosis by increasing the number and action of the bone-forming osteoblasts. The FDA “Talk Paper” released with the notice of approval of teriparatide noted that this “is the first approved agent for the treatment of osteoporosis that stimulates new bone formation.” Data from 24 clinical trials enrolling more than 2,800 men and postmenopausal women with osteoporosis showed that the drug stimulated new bone formation, lowered the risk of vertebral (spinal) fractures and BMD in postmenopausal women with osteoporosis during an average of 19 months of treatment. Relative risk of spinal fractures was reduced by 65% (9.3% absolute risk reduction), and the relative risk of nonspinal (wrist, ribs, hips, ankle-foot, etc.) by 53% (2.9% absolute risk reduction). BMD increased in 96% of women, compared to baseline; 72% experienced a BMD increase of at least 5% and 44% had a BMD increase of 10% or more.

Osteoporosis disease management should become a primary focus for all managed care organizations for several reasons, not the least of which is the looming cost of preventing fractures with drugs. Hip fracture, the most serious and even life-threatening outcome, has become the accepted measure of the cost of osteoporosis. Hip fracture is a valid measure of the societal cost of osteoporosis because hip fractures (a) are strongly related to low BMD, (b) cost more to repair than other fractures, and (c) cause more disability than any other type of osteoporotic fracture. Hip fracture is a relatively reliable measure of osteoporosis because hip fractures are usually treated in hospitals and therefore more amenable to accurate counting, domestically and internationally. The estimated lifetime risk of hip fracture for white women aged 50 years or older is 17% in the United States compared to only 6% for white men; the risk of vertebral fracture is greater than 30%. The 17% (one-in-six) lifetime risk of hip fracture for white women aged 50 years or older is greater than the one-in-nine lifetime risk of developing breast cancer. Hip fracture is a serious and even life-threatening outcome of osteoporosis, and the prevalence of hip fractures is increasing because the world’s population is aging and because the frequency of hip fractures is increasing by 1% to 3% per year in most areas of the world. More than 300,000 hospital admissions per year are attributable to osteoporotic hip fractures among estrogen-deficient women. Effective osteoporosis disease management includes member education about the importance of diet, particularly adequate calcium and vitamin D intake; weight-bearing exercise; avoidance of risk factors that include cigarette smoking; alcohol and drugs that might contribute to hypotension or impaired motor skills; and even physical protection from the effect of falls.

Desai, Duncan, and Sloan in this issue of the Journal found that only 68% of women with a fracture and a diagnosis of osteoporosis received drug therapy to prevent osteoporosis-related fracture. This percentage is optimistic since the inclusion criteria for their study included at least one pharmacy claim per calendar quarter, thereby selecting a patient population that was not random in the health plan. Their patient identification criteria may have missed some patients with diagnoses of osteoporosis or osteoporosis-related fracture since they captured only the primary or secondary diagnosis on medical claims. Data used to develop the proposed Health Plan Employer Data and Information Set measure for 2004 showed that there was a range of 30% to 41% of women who were on drug treatment for the prevention of fracture at the time of fracture, and two thirds of the prior treatment was HRT. Nevertheless, the study by Desai, Duncan, and Sloan underscores another opportunity for managed care to improve population health. Left to others is determination of the cost-effectiveness of prescription drug therapy to reduce the effects of osteoporosis, an analysis that should include all available alternate therapies for prevention of osteoporosis and real-world estimates of drug cost. The relative cost-effectiveness of alendronate would be increased significantly by the market availability of generic alendronate, a development of great interest to managed care pharmacy and one made contemporary by the decision of the High Court of Justice for England and Wales that found in January 2003 that 2 patents protecting alendronate sodium were invalid.

References


Frederic R. Curtiss, PhD, RPh, CEBS
Editor-in-Chief


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The following poster presentations have been prepared for the Academy of Managed Care Pharmacy’s 15th Annual Meeting & Showcase, April 9–12, 2003, in Minneapolis, Minnesota.

For more information about the studies described below, please contact the corresponding authors, indicated by an asterisk (*), whose addresses are listed in full. The names of individuals who are scheduled to present at the meeting are underlined. Abstracts were edited by Marissa Schlaifer and Mark Brueckl.

DESCRIPTIVE REPORTS

Cost Analysis of Chronic Atrial Fibrillation Patients in a Decentralized Outpatient Pharmacy Anticoagulation Service

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PURPOSE: To determine the total per-member-per-month (PMPM) cost including the cost of an outpatient pharmacy anticoagulation service (OPAS) in chronic atrial fibrillation patients maintained on sodium warfarin therapy in a managed care setting.

METHODS: Data was retrospectively collected from clinical, research, and administrative claims databases. Patient chart reviews were completed to verify hospital discharges, ER visits, and complications. Patient demographic data was stratified to include age, gender, and risk factors for stroke. Inclusion criteria for the study were adult patients (>age 18 years) who were maintained on chronic warfarin sodium therapy with a diagnosis of atrial fibrillation (ICD9 427.31) and continuously enrolled during CY 2000. Cost data included personnel time, laboratory and pharmacy costs, physician visits, hospital and ER claims, as well as indirect costs.

RESULTS: A total of 97 patients on chronic warfarin therapy for atrial fibrillation were identified for cost analysis determination. The demographics for these patients included 71% male, with 32% of the patients over the age of 75 years; 84.5% of these patients had one or more identifiable risk factor for stroke. The vast majority of the patients (94.8%) had nonvalvular disease, with an international normalized ratio (INR) goal between 2 and 3 in 90.7% of the cases. During CY 2000, the overall hospitalization rate for this population was 8.25% (N=8), with no admissions due to thromboembolic disease and one admission due to bleeding. The ER visit rate was also 8.25% (N=8) with 3 visits due to minor bleeding. A majority of the hospital admissions and ER visits (56%) were due to cardiac causes.

The actual total PMPM cost for the chronic atrial fibrillation patients was found to be $636. The PMPM for the high risk valvular disease patients was 44% higher. For those patients with hospitalizations and/or ER visits during CY 2000, the PMPM total cost was $1,422. The PMPM personnel cost for these patients in the OPAS service was calculated to be $18.42 PMPM for “maintenance” patients. The actual costs of sodium warfarin and INR monitoring was $15.61 PMPM.

CONCLUSIONS: The total PMPM cost for this chronic atrial fibrillation population in CY 2000 was $636. The PMPM cost for pharmacist and laboratory monitoring as well as drug product tenance service (OPAS) in chronic atrial fibrillation patients maintained was calculated to be $18.42 PMPM for “maintenance” patients. Effective monitoring to minimize preventable hospitalizations and ER visits is the most cost-effective strategy.

Use of Pain Medication Among Managed Care Organization Patients With and Without Depression

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INTRODUCTION: Little is known about how depression affects use of pain medications by patients with painful physical complaints. Method: Twelve thousand health maintenance organization members were surveyed within one week of a primary care visit. Respondents were divided into 4 groups of those reporting: (1) pain >6 months and no depression, (2) depression plus pain, (3) only depression, and (4) neither pain nor depression. The groups were compared on various instruments to look at major depressive disorder (MDD) and physical symptoms (patient health questionnaire), disability (the Graded Chronic Pain Scale), coping strategies (Catastrophizing subscale of the Coping Strategies Questionnaire), and use of prescribed, over-the-counter (OTC), and overuse of pain medications.

RESULTS: Of the 5,808 respondents (54% of patients meeting eligibility criteria), 45% reported chronic pain and 7.6% had MDD. Among those reporting chronic pain, 11% had MDD; in the MDD group, 67% reported pain. Compared to patients with pain-only, those with depression plus pain reported higher pain-related disability (P<.001). The depression plus pain group scored significantly higher (P<.001) than the pain-only group on the Pain Catastrophizing subscale (effect size=18%). Depressed
patients with pain were more likely than patients with pain-only to report using OTC (P<.05) and prescribed pain medications (P<.001); they reported taking more pain medication than prescribed (P<.001).

CONCLUSIONS: Patients with comorbid pain and depression are more likely to use and overuse pain medications. Patient safety issues may be compromised by this pattern of medication use. Physicians might consider screening depressed patients for pain and developing complementary treatment regimens that address both conditions.

Impact of a Multiple Sclerosis Health Management Program on Persistency and Compliance

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OBJECTIVE: A comparison study of multiple sclerosis (MS) participants enrolled in a health management (HM) program was conducted. The hypothesis tested whether participants in the program had higher drug persistency and compliance over a 12-month period than nonprogram participants.

METHODS: Intervention (n=1,200) and comparison groups (n=4,400) were identified between July 1, 1999, and December 2000, and followed for 12 months to determine program effectiveness at increasing persistency and compliance. Participants were required to have filled one of the 3 drug therapies that treat multiple sclerosis and have been new to therapy based on a 6-month claim history absent of multiple sclerosis therapy. Results were tested using a nonparametric test of means.

RESULTS: 87.3% of program patients were persistent with MS therapy compared to 77.6% of nonprogram participants 12 months post enrollment. The mean duration of therapy was 467 days and 429 days for the program and comparison groups, respectively. Persistency results were statistically significant (P<0.07). Patient compliance (drug on hand) for a 12-month analytic period was 91.4% and 88.1% for program and nonprogram participants, respectively. Results were statistically significant (P<0.03).

CONCLUSIONS: Enrollment in an intervention-based HM program increased both persistency and compliance for participants new to MS therapy. Based on the results of the study, we can conclude that MS program participants continue their therapy for a longer duration and are more likely to have drug on hand than nonprogram participants over a 12-month analytic period.

Cost Analysis of Gastrointestinal Events in Osteoporotic Patients Receiving Bisphosphonate Therapy in a Managed Care Setting


INTRODUCTION: The objective was to compare resource utilization and associated direct medical costs of gastrointestinal (GI)-related events for both alendronate and risedronate patients utilizing an integrated administrative, medical, and pharmacy claims database.

METHODS: A retrospective cohort study was conducted among 3,947 women and men (aged 65+ years) with a new prescription for daily risedronate (5 mg/day), daily alendronate (5 mg/day or 10 mg/day), or weekly alendronate (35 mg/week or 70 mg/week) between November 1, 2000, and August 31, 2001. GI-related medical resource utilization and direct medical costs were assessed for a 4-month period following initiation of the bisphosphonate therapy. GI-related events and/or medications, during a 6-month pre-treatment period, were used to stratify patients by “GI history” or “no GI history.” Utilized resources (pharmacy, outpatient, inpatient, and ER) were valued using 2002 USD.

RESULTS: 16% of selected patients were treated with risedronate daily, 28% were treated with alendronate daily, and 56% were treated with alendronate weekly.

• “No GI history” group: In the first 4 months after initiating bisphosphonate therapy, the average GI-related direct medical per-member-per-month (PMPM) cost was significantly lower for risedronate patients compared to both daily alendronate ($2.52 versus $7.40, P<0.049) and weekly alendronate patients ($2.52 versus $7.50, P<0.01).

• “GI history” group: As would be expected due to ongoing GI problems, patients with a “GI history” incurred notably higher GI-related medical costs than the “no GI history” group. When comparing individual bisphosphonates, however, risedronate patients continued to exhibit lower costs than alendronate patients. The average GI-related direct medical PMPM cost was lower for risedronate patients compared to daily alendronate ($19.66 versus $26.11, P=0.42) and weekly alendronate patients ($19.66 versus $37.65, P=0.03).

CONCLUSIONS: In a patient population aged 65+ years receiving osteoporosis treatment, risedronate was associated with markedly lower GI-related medical costs compared to both daily and weekly alendronate.
INTRODUCTION: The prevalence of chronic pain in the general population has been estimated to be from 2% to 40%, and pain-related annual costs ranging from $80 to $90 billion. As a symptom spanning many diseases, pain has not received the same care management attention as prevalent and costly diseases such as asthma and diabetes. The objective of this national survey of medical directors was to determine whether MCOs have pain management programs in place and to describe the programs’ key features.

METHODS: A survey was mailed to more than 500 of the most senior medical directors within each of the nation’s MCOs. It examined 4 pain management topics: guideline implementation, pharmacy management, program implementation, and concerns. Data analysis was conducted using SAS (version 8).

RESULTS: A total of 118 surveys were received (26% response rate). Two thirds of respondents (n=79) did not have a pain management program in place or development, and most of those MCOs saw pain management as a low priority (78%). Clinical guidelines were used at only 18% of the organizations, but most had formulary controls for pain medications, such as tiered copayments (56%), monthly quantity limits (57%), and prior authorizations (54%). Important factors in making formulary determinations included comparative efficacy (88%), side-effect profile (82%), improvement in patients’ ability to function (76%), and cost (74%).

CONCLUSIONS: Although many MCOs have mechanisms in place for managing pain medications, few have a systematic approach to managing pain. MCOs have further opportunities to reduce costs and improve quality of care, quality of life, and member satisfaction.

Baseline Differences in Clinical Characteristics Among Patients Using Cox-2 Specific Inhibitors and Nonspecific Nonsteroidal Anti-inflammatory Drugs

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OBJECTIVE: The objective of this study was to identify and compare baseline demographic and clinical characteristics of patients newly treated with a Cox-2 specific inhibitor or a nonspecific nonsteroidal anti-inflammatory drug (NSAID).

METHODS: Using integrated pharmacy and medical claims data, members from 2 geographically dispersed health plans were identified with new prescriptions for celecoxib, rofecoxib, or nonspecific NSAIDs from December 1, 1999, to May 31, 2000. Data were analyzed retrospectively for 6 months prior to the initiation of drug treatment. A total of 78,804 patients began treatment on a Cox-2 specific inhibitor (celecoxib: 10,741, rofecoxib: 9,716, or a nonspecific NSAID: 58,347). Univariate analysis using paired t test, chi-square test, and ANOVA were performed to ascertain the statistical differences in baseline characteristics among treatment groups.

RESULTS: Overall, patients prescribed a Cox-2 specific inhibitor were significantly older than patients prescribed nonspecific NSAIDs (celecoxib: 54.3, rofecoxib: 53.5, nonspecific NSAIDs: 43.3 years; P<0.001). A greater percentage of patients on either Cox-2 specific inhibitor had a diagnosis of arthritis (celecoxib: 54.9%, rofecoxib: 54.0%, nonspecific NSAIDs: 22.6%; P<0.001). Prior to the index prescription, patients on either Cox-2 specific inhibitor had significantly higher prevalence rates for each of the 7 identified comorbidities than patients on a nonspecific NSAID: hypertension (19.9% to 20.9% versus 6.7%); cerebrovascular disease (1.4% to 1.7% versus 0.3%), congestive heart failure (1.8% versus 0.4%), myocardial infarction (0.6% versus 0.1%), gastrointestinal disease (12.3% to 13.4% versus 5.6%), edema (3.5% to 3.6% versus 1.0%), and renal insufficiency (0.4% to 0.6% versus 0.2%), P<0.001 for each comorbidity.

CONCLUSIONS: In this cohort, compared to nonspecific NSAIDs, Cox-2 specific inhibitors were prescribed to older patients diagnosed with arthritis, gastrointestinal, cardiovascular and renal comorbid disease. While physician preference and health plan access rules may partially explain the differences in patients receiving Cox-2 specific inhibitors, we found that preexisting cardiovascular and renal disease were also prevalent in this patient population. Clinicians and policy makers need to carefully consider all of the baseline characteristics of their patients when comparing the potential clinical and economic impact of these 2 therapeutic approaches on their patient population.

Achieving the Desired Outcomes of a Physician Incentive Program Without Placing Providers at Financial Risk

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INTRODUCTION: Through collaborative efforts, a pharmacy benefit manager (PBM) and health maintenance organization (HMO) developed a voluntary, gain/share program whose goals were to increase appropriate drug use while reducing costs. Allergy, anti-infective, and gastrointestinal therapeutic categories were chosen for intervention based on high utilization and positive economic and clinical impact projections. An incentive payment, funded by the calculated savings and equal to 40% of the cost avoided, was returned to the intervening primary care providers.

METHODS: Between fourth quarter 1999 and the end of third quarter 2000, baseline measurements were obtained and program specifics were defined, approved, and communicated at key internal HMO and primary-care panel meetings. Program introductory packets were mailed to prospective participants and included evidence-based treatment recommendations, provider profile reports with patient-specific data, and projected cost savings/incentive share. Progress reports and general comments on observed trends, were sent on a quarterly basis. Reports were dis-
cussed with providers upon request. Disbursements were sent to eligible participants at program conclusion.

RESULTS: The measurement period, between fourth quarter 2000 through the end of third quarter 2001, showed a total of more than $670,000 in savings across the 3 targeted therapeutic categories, with a disbursement of 40%, or nearly $270,000, supplied to the 268 participant providers.

CONCLUSIONS: The gain/share structure of the physician incentive program successfully achieved the goals of increased appropriate drug utilization and reduced costs without placing providers at financial risk.

Incidence and Cost of Medically Treated Hypoglycemia in Diabetic Patients Enrolled in Managed Care

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OBJECTIVE: To determine the incidence and cost of medically treated hypoglycemia in diabetic patients and differentiate the cost per treatment setting.

METHODS: Data for calendar year 2000 were extracted from an administrative claims database that includes data from 19 affiliated UnitedHealth Group health plans serving 5 million enrollees. A diabetes diagnosis was based on the presence of 2 claims with a primary or secondary ICD-9-CM code of 250.xx or at least one pharmacy claim for insulin or an oral hypoglycemic agent. The definition of medically treated hypoglycemia was based on the presence of a claim with a primary or secondary ICD-9-CM code of 250.8x or 251.0x. The cost of treatment was based on resource use (office, outpatient clinic, emergency department, hospital, or home health care) and included cost to health plan and enrollee.

RESULTS: A total of 129,844 health plan enrollees met eligibility criteria for diagnosis of diabetes and 3,612 enrollees met the criteria for hypoglycemia. The incidence rate for medically treated hypoglycemia was 2.8/100 enrollees with diabetes. Study subjects were treated for their diabetes with insulin (37%), oral hypoglycemics (30%), combination insulin and oral hypoglycemics (26%). Seven percent of the study subjects did not receive drug therapy for their diabetes. Of the patients in the study, 40% sought medical care for hypoglycemia more than once during the study period. Male patients had a higher incidence of hypoglycemia than female patients. Site-specific resource utilization and cost was available for 2,147 study subjects. Nine hundred twenty-six (43%) subjects sought care in an office setting; average cost $56; 680 (32%) sought care in the emergency department: average cost $328; 309 (14%) sought care in a home health care setting: average cost $1,094; and 245 (11%) received care as hospital inpatients: average cost $5,361. The total number of hypoglycemia-related health care visits was 5,656, with a combined total average cost per episode of hypoglycemia of $641.

CONCLUSIONS: Hypoglycemia has important clinical, humanistic, and economic considerations for enrollees with diabetes. While hypoglycemia may not require accessing the health care system for most episodes, this study shows that there are important direct costs to enrollees and payers that can be identified in medical claims.

Deep-Vein Thrombosis: Prevalence, Inpatient Treatment Costs, and Opportunity for Outpatient Therapy in a Medicare Managed Care Population

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INTRODUCTION: The purpose of this study was to understand the resource utilization and financial impact deep vein thrombosis (DVT) had in a Medicare managed care population. Currently, varying on a state-by-state basis, the Center for Medicare and Medicaid Services reimburses intravenous anticoagulation treatment on an inpatient-basis only.

METHODS: This study was conducted using pharmacy and medical administrative claims data from 5 discounted, fee-for-service, independent practice association (IPA) model health plans serving Medicare enrollees located in the Midwest, Northeast, West, and Southeast regions of the United States. An administrative claims database was used to identify enrollees with a diagnosis of DVT between January 1, 1999, and June 30, 2000.

RESULTS: A total of 5,353 enrollees had a DVT diagnosis that was defined as having a medical claim with a primary or secondary ICD-9-CM code of 451.0x-451.2x, 453.1x-453.3x, 453.8x, 453.9x, or a DRG 128. The prevalence of DVT was 24 per 1,000 Medicare members. The prevalence of DVT increased with age. Age-adjusted prevalence of DVT was 18 per 1,000 for subjects aged 65 to 74 years; 30 per 1,000 for subjects aged 75 to 84 years, and 46 per 1,000 for subjects aged 85 years and older. For the 18-month study period, the rate of DVT-related hospital admissions was 6.0 per 1,000 Medicare members. There was a statistically significant difference between the mean length of stay for subjects with a primary diagnosis of DVT (7 days) compared to subjects with a secondary DVT diagnosis (12 to 14 days). Subjects with a primary diagnosis of DVT had lower mean hospital costs compared to subjects with a circulatory or other primary diagnosis, $4,968, $11,889, and $13,525, respectively. A total of 3,298 (62%) subjects who did not have a claims history of peptic ulcer disease, familial bleeding disorders, pulmonary embolism, or a stroke were considered to have no claims-based contraindications to outpatient therapy. The proportion of subjects who did not have contraindications to outpatient therapy was comparable across age groups and health plans.

CONCLUSION: There are significant inpatient costs associated with DVT. Many patients may benefit from outpatient therapy, although there are reimbursement challenges. Cost savings associated with outpatient therapy have been established. Further research should focus on the potential cost impact of the ambulatory treatment and prophylaxis of DVT.
Effect of Memantine on Costs Associated With Moderate to Severe Alzheimer’s Disease

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OBJECTIVE AND PERSPECTIVE: Alzheimer's disease (AD) is a costly illness. Later stages of the disease are associated with large demands on caregiver time and high rates of institutionalization, 2 major components of the total economic burden of the disease. We assessed the pharmacoeconomic (PE) effects of treatment with memantine, a moderate affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist, during a 28-week, multicenter, double-blind, placebo-controlled study in 252 patients with moderate to severe AD (Global Deterioration Scale [GDS] Stages 5 and 6, Functional Assessment Staging [FAST] scores ≥6a, Mini-Mental Status Exam [MMSE] range 3 to 14).

METHODS: The primary outcomes of the PE analysis were resource utilization, residual status, and costs. Patient and caregiver resource use and patient residual status were tracked using the Resource Utilization in Dementia questionnaire, and an average unit cost was assigned to each relevant resource utilization variable.

RESULTS: According to multivariate analyses of the treated-per-protocol population, which included all patients with no missing values across the study period (N=166), treatment with memantine was associated with a significant reduction in average monthly caregiver time compared with placebo (−31.5 hours, P=0.02). The incidence of institutionalization at week 28 was also significantly lower in the memantine group compared with the placebo group, P=0.04). These reductions in resource utilization were associated with an average drop in both total cost for caregivers ($824/month, P=0.03) and societal costs ($1,234/month, P=0.01). There was also a trend toward lower direct nonmedical costs among patients on memantine, with a between-group difference of $431/month.

CONCLUSION: Thus, the use of memantine in patients with moderate to severe AD appears to significantly reduce costs relative to placebo.

Impact of a Collaborative Care Model for Depression in Primary Care: A Randomized Controlled Trial

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INTRODUCTION: The objective of this investigation was to evaluate the clinical and economic impact of a collaborative care model featuring clinical pharmacists providing medication management, patient education, and treatment follow-up services.

METHODS: Patients were randomized to the investigation immediately after initiation of an antidepressant. The intervention group received medication management and follow-up services from clinical pharmacists through scheduled clinic visits and telephone contacts while the control group was managed by the referring physician (ie., usual care). Medication adherence and resource utilization were determined from the health maintenance organization's (HMOs) electronic medical information system while clinical outcomes and patient satisfaction were compared from surveys mailed 6 months after randomization.

RESULTS: An intent-to-treat analysis of medication adherence (based on HEDIS specifications) revealed that 67% of the intervention group (n=75) and 48% of the control group (n=50) completed the continuation phase of antidepressant treatment (P=0.0375). Switch rates were higher in the intervention group as well (19% versus 4%, P=0.016). Clinical and functional outcomes were similar. Patient satisfaction was greater among the patients receiving collaborative care, specifically with regard to the HMO, overall treatment, personal nature, and access to care (P<0.05 for all measures). Provider satisfaction scores were also favorable. Total resource utilization was similar between groups, but there was a significant decline in primary care visits with the intervention group (39% decrease versus 1% increase, P=0.015).

CONCLUSIONS: Results of this investigation provide further evidence that direct involvement of clinical pharmacists in the management of depressed patients can improve outcomes and patient satisfaction. Studies of this treatment model in different health care settings appear warranted.

Patient/Provider Assessment to Identify Need (PAIN) Indicators: Identifying Candidates for a Pain Management Intervention Program

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OBJECTIVE: Develop Patient/Provider Assessment to Identify Need (PAIN) indicators for identifying noncancer patients with low back pain (LBP) or osteoarthritis (OA) who have evidence of inadequate pain management.

METHODS: Indicators were developed in 3 steps. First, a pain management expert identified indicators indicative of noncancer
LBP/OA patients who were receiving inadequate pain management care that could be identified with claims data. Second, an expert panel scored each indicator on 5 criteria measuring feasibility and utility; indicators with scores above a specified minimum were retained. Third, integrated claims data were used to calculate (a) the number of patients and per-patient costs in each PAIN indicator and (b) between-PAIN indicator correlation and overlap (the same patient in 2 indicators). Data were from Protocare Sciences’ managed care database that contains facility, professional, and pharmacy claims data from more than 3 million lives in more than 20 States.

RESULTS: Fifty-six indicators were initially identified, 26 of which were retained after feasibility and utility scoring. The retained indicators were categorized according to services and diagnoses (n=9), medication use (n=13), and medication safety (n=4). Prevalence in the OA/LBP population ranged from <0.1% to 9.6%, and per-patient monthly costs ranged from $392 to $6,846. Maximum between-indicator correlation was 0.66, and the maximum percentage overlap was 100%. All 26 indicators were retained after reviewing these data.

CONCLUSIONS: Integrated claims data can be used to identify patients receiving inadequate pain management using PAIN indicators. Health plans interested in improving care among this population—as suggested by the AMA, JCAHO, NCQA, and others—can use these indicators to identify patients who would benefit most from an intervention program.

■ Utilization Differences in Concomitant Anxiolytic and Antidepressant Therapy Versus Antidepressant Monotherapy

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INTRODUCTION: Since recent literature suggests that a majority of patients with depression have associated symptoms of anxiety, this study sought to examine the frequency of coprescription of antidepressants and anxiolytics in a “usual-care” setting, as well as to determine the effect of concomitant anxiolytic therapy on antidepressant prescription utilization.

METHODS: A retrospective analysis of pharmacy claims was used to evaluate patients continuously enrolled in a large, geographically diverse pharmacy benefit manager (PBM) who were new to antidepressant therapy and had at least 2 fills of the index antidepressant agent between June 1, 2000, and May 31, 2001. Concomitance was defined as any anxiolytic fill with an overlap of days of supply between 2 fills of the index antidepressant agent, and chronic disease burden was assessed via drug markers, using a modified chronic disease score (CDS). Statistical differences between compliance and medication possession ratio (MPR) means were established using t tests, while persistence and switch rates were compared using the chi-square test.

RESULTS: The total study cohort comprised 371,951 patients, of which 50,124 (13.5%) filled a concomitant anxiolytic prescrip-
tion. Initial antidepressant therapy consisted of SSRI (65.6%), TCA (15.7%), SNRI (5.8%) and new generation antidepressants (12.9%). Compared with patients on antidepressant monotherapy, concomitant anxiolytic patients were generally older (mean=53.4 versus 47.5 years) and had a higher chronic disease burden (mean CDS = 7.4 versus 4.6). Utilization measures for concomitant anxiolytic patients were consistently better than for monotherapy patients: compliance (mean=85.9% versus 73.9%, P<0.0001), MPR (mean=67.5% versus 53.0%, P<0.0001), and 6- and 12-month persistence (68.8% versus 52.6%, P<0.0001, and 52.6% versus 38.1%, P<0.0001). However, concomitant anxiolytic patients had a higher rate of therapy switching (23.0% versus 16.8%, P<0.0001). Utilization rates were similar across SSRI agents between concomitant and antidepressant-only patients.

CONCLUSIONS: While the scope of this study may be limited in that diagnoses were unavailable, patients receiving concomitant anxiolytic and antidepressant therapy appear to have more favorable utilization patterns than monotherapy antidepressant patients. Improved therapy compliance may represent better symptom control, which can translate into cost savings related to increased productivity and decreased frequency of provider visits, as well as improved patient quality of life. The higher rate of antidepressant agent switching observed in the concomitant anxiolytic cohort may reflect more challenging therapeutic needs of this subgroup. This study suggests that further research into symptom-specific treatment options and subsequent patient outcomes may provide useful information to guide policy and coverage decisions and therapy options in the management of depression and anxiety-related disorders.

■ Opportunities for Improved Diabetes Management Within an Advanced Physician Organization

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INTRODUCTION: Given the significant morbidity and mortality associated with diabetes mellitus, the purpose of our study was to identify opportunities to improve care in patients with diabetes within an advanced physician organization.

METHODS: Approximately 3,000 diabetic patients were identified through medical claims (January 1, 2000, to December 31, 2001) and randomly selected for medical chart review. Retrospective chart reviews were conducted to verify diabetes diagnosis and to document fasting blood glucose (FBG), HbA1C, post-prandial blood glucose (PPG), blood pressure (BP), lipid panel, serum creatinine, microalbuminuria, and foot and eye exam. Diabetic pharmacotherapy was also assessed.

RESULTS: Of the 447 randomly selected patients (mean age 63.4 years, 52.8% male) with a confirmed diagnosis of type 1 or type
2 diabetes, FBG and HbA1C was controlled in 32.8% (n=133) and 41.6% (n=151), respectively. Among patients with uncontrolled HbA1c, 13% of patients had controlled FBG. PPG levels were measured in just 2.7% (n=12) of patients. Adequate BP control was found in 15.2% (n=37) of patients according to Americans With Disabilities Act recommendations (BP<130/80 mmHg). Low-density lipoprotein (LDL) levels were less than 100 mg/dL in 29.3% (n=46) of patients with a value recorded. Foot and eye exams were documented in 22.4% and 32.7%, respectively. A microalbuminuria test was collected in 16.6% (n=74) of patients. Additionally, most patients were treated with 1 (41.2%) or 2 (34.2%) antidiabetic agents, with the majority prescribed oral sulfonylureas. (35.1%, n=252).

CONCLUSIONS: Identification and management of glycemic, comorbid disease, and diabetic complication control is not optimal. Additional quality improvement initiatives and treatment strategies are needed to improve the diabetes management.

Hypertension and Diabetes: A Costly Combination

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OBJECTIVE AND PERSPECTIVE: This study compares health care resource use and costs between patients with both hypertension and diabetes and patients with either diabetes or hypertension. The study uses managed care perspective and aims to identify patterns of resource use and cost that may lead to useful health care management intervention measures.

METHODS: The study uses integrated pharmacy and medical claims data from 6 independent practice association-model health plans with an average annual enrollment of 1.8 million members. Hypertension (H) and/or diabetes (D) patients aged 18 years and older with full drug benefits were identified during 1996, and 1 year of prediagnosis and 2 years of postdiagnosis periods were analyzed. Two cohorts of newly diagnosed hypertension-only patients and diabetes-only patients were compared with a third cohort of patients with diagnosis of both hypertension and diabetes (HD). Demographics, comorbidities, and prior use were compared during the preperiod. Hospital, emergency room (ER), and physician visits and costs as well as prescription utilization were compared during the postperiod. Logistic regression on the likelihood of hospital visit and log-linear regression on cost were performed, controlling for baseline characteristics and prior use.

RESULTS: The analysis is based on 13,733 H-only, 1,995 D-only, and 2,930 HD patients. Average age was 55, 50 and 60 years, respectively. Ischemic heart disease, hyperlipidemia, heart failure, and other cardiovascular diseases were 2 to 3 times more prevalent among HD patients compared to H or D patients. During the preperiod, HD patients had more hospital, ER, and office visits and used more prescriptions compared to H or D patients. During the post-eriod, HD patients used significantly more healthcare resources and incurred more cost. HD patients cost an average of $5,978 during the year after diagnosis of both diseases. This compares with $3,670 for H patients and $3,967 for D patients. Hospitalization costs accounted for about 40% of total health care costs in all 3 patient cohorts. The risk of hospitalization was significantly higher among HD patients, with odds ratios of 1.47 relative to H patients (95% CI, 1.33-1.62), and 1.23 relative to D patients (95% CI, 1.06-1.44).

CONCLUSIONS: Hypertensive diabetic patients are much more costly for the health care system and require closer attention. Considering higher rates of comorbidities and resource use, these patients should be more readily identified for disease management, patient education, and other health care interventions.
** Managed Care Health Care Cost Analysis of Allergic Rhinitis Treatment: Budesonide Aqueous Nasal Spray Versus Loratadine

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OBJECTIVE: Intranasal corticosteroids have been shown to be superior to oral H1-receptor antagonists in relieving symptoms of allergic rhinitis. The objective of this study was to compare rhinitis-related health care charges before and after initial rhinitis therapy with budesonide aqueous nasal spray (BANS; Rhinocort Aqua) or loratadine (Claritin) in a managed care population.

METHODS: Patients were selected from several managed care organizations (Source: PHARMetrics Integrated Outcomes database); those who received a new prescription for BANS or loratadine from February 2000 to January 2001 were included in the analysis. Patients also had either an ICD-9-CM code for allergic rhinitis (477.xx) or a second prescription for the initial rhinitis medication within 6 months of the initial prescription. Patients were matched into comparable cohorts by demographic data using the propensity score method. Log-transformed allergic rhinitis charges were compared for 1 year after the initiation of rhinitis treatment with BANS or loratadine using ordinary least squares regression.

RESULTS: There were 1,746 patients in the BANS cohort, matched with 1,746 similar patients in the loratadine group. Patients were similar in terms of age ($P=.5930$), sex ($P=.6828$), and region ($P=.5318$). Rhinitis-related charges in the year after treatment were $387 (SD=499) for the BANS group and $423 (SD=423) for the loratadine group. After adjusting for potential confounders, patients in the loratadine group incurred 17.4% greater rhinitis-related charges in the year after treatment ($\beta=0.174, P<.0001$).

CONCLUSIONS: Patients with allergic rhinitis treated initially with budesonide aqueous nasal spray have lower rhinitis-related health care charges in the year after initiation of therapy when compared with similar patients started on loratadine.

** One-Year Economic Comparison of Intranasal Corticosteroid Prescribing Patterns for the Treatment of Allergic Rhinitis

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OBJECTIVE: Effective treatment of seasonal or perennial allergic rhinitis often requires use of topical intranasal corticosteroids (INSs). Despite differences in recommended starting dosages, the leading INSs are dispensed in 120 metered-dose spray bottles. This analysis was conducted to determine the relative prescribed dosages of the leading INSs and compare economic differences demonstrated by these prescribing behaviors.

METHODS: The IMS National Disease and Therapeutic Index (NDTI) was used to identify prescribing habits for the leading 4 INSs: fluticasone propionate nasal spray (FPNS, Flonase), mometasone furoate aqueous nasal spray (MFNS, Nasonex), triamcinolone acetonide aqueous nasal spray (TANS, Nasacort AQ), and budesonide aqueous nasal spray (BANS, Rhinocort Aqua). The NDTI uses a national, randomly drawn, 2-stage stratified cluster sampling methodology. Physicians are sampled during the first stage, with 2 workdays per month subsampled from each physician in the second stage. Each physician reports on all patient contacts during the 2 consecutive days, offering a continuing compilation of statistical information about patterns and treatment of disease encountered by office-based physicians. In a given month, the NDTI reports on 1,180 unique physicians.

RESULTS: From July 2001 to June 2002, 51% of prescriptions for FPNS were for 4 sprays daily and 34% were for 2 sprays daily, MFNS 46% for 4 sprays and 42% for 2, TANS 57% for 4 sprays and 29% for 2, and BANS 28% for 4 sprays and 60% for 2. These equated to mean-prescribed-daily dosages of 3.44 sprays per day for FPNS, 3.21 for MFNS, 3.52 for TANS, and 2.78 for BANS. Because each INS is dispensed in a 120 metered-dose spray bottle, the differences in prescriptions offer varying days of supply depending on dosage. BANS offered the most days of treatment (43 days), followed by MFNS (37 days) and FPNS and TANS (35 and 34 days, respectively). Cost per day of treatment was calculated by multiplying the prescribed dosage with the average wholesale price of the products. BANS had the lowest cost per day of treatment at $1.49, with each other INS costing at least an additional $0.31 daily (FPNS: $1.86; TANS: $1.81; MFNS: $1.80).

CONCLUSION: Based on physician prescribing patterns of INSs, BANS offers more days of treatment at a lower cost per day than other leading INSs.
Impact of Weight Gain on Health-related Quality of Life (HRQL) of Bipolar Patients
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OBJECTIVE: To determine whether patients with bipolar disorder with weight gain have different HRQL than those without weight gain.

METHODS: In June 2001, 573 persons reported being diagnosed with bipolar disorder on a self-administered questionnaire. Of these, 377 provided information on their weight gains or losses during the past 6 months. A cross-sectional comparison of the HRQL of patients with bipolar disorder who gained weight and those who did not was performed. Weight gain was defined as gaining 6 or more pounds (2.73 Kg) over the past 6 months. HRQL was measured using 2 validated scales, the Psychological General Well-Being scale (PGWB) and the SF-8.

RESULTS: Out of 377 patients included in the analysis, 168 (44.6%) reported weight gain. Patients who reported weight gain had significantly lower mean PGWB scores, 47.4 (SD=21.9) versus 53.2 (SD=23.6), P=0.015 and lower scores on Anxiety, Self-Control, and Vitality subscales compared to those without weight gain. Patients with weight gain had statistically lower scores in the mental health summary scale and the role emotional and mental health domains of the SF-8.

CONCLUSION: Patients with bipolar disorder and weight gain appear to have a lower HRQL compared to patients without weight gain.

Effects of a 3-Tier Pharmacy Benefit Design on the Prescription Purchasing Behavior of Individuals With Chronic Disease*

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INTRODUCTION: Multi-tiered pharmacy benefit plans have important consequences for individuals confronted with purchasing higher-cost medications, particularly those with chronic disease states. The impact of 2- and 3-tiered plans on medication utilization behavior and discontinuation rates for nonformulary medications was evaluated.

METHODS: A pretest-posttest quasi-experimental design was employed. Chronic disease sufferers (N=8,132) from a health plan were classified into the following groups: (a) 2-tier moving to a 3-tier structure (“converting” group), (b) 2-tier staying in a 2-tier structure and (c) 3-tier staying in a 3-tier structure. The latter 2 were “comparison” groups. Two time periods were determined: the “preperiod” before (June to December 2000) and the “postperiod” (January to July 2001) after a change in pharmacy benefit structure. Pharmacy claims data were used for data collection. Statistical analysis included bivariate tests to evaluate predifferences and postdifferences across study groups. Maximum likelihood estimates from a repeated measures model were used to examine changes in formulary compliance and generic use rates. Discontinuation of nonformulary medications was evaluated using logistic regression.

RESULTS: Controlling for demographics, number of comorbidities, disease states, and pharmacy benefit structure, formulary compliance rates increased by 5.6% for the converting group. No significant increases were seen for the comparison groups. Generic use rates increased by 3% to 5% for all groups. Converting-group individuals were 1.76 times more likely to discontinue their nonformulary medication than those in the 2-tier and 1.49 times more likely than those in the 3-tier comparison group.

CONCLUSIONS: Findings suggest that shifting individuals from a 2-tier to a 3-tier structure resulted in a small change in medication utilization. Decision makers need to balance these changes with the potential dissatisfaction that members may express in paying higher copayments.

*Editor's note: The subject of this poster abstract is described in greater detail in an article on page 123 of this Journal. The AMCP process for poster abstracts is independent of the editorial process for JMCP.

Consumer Understanding and Satisfaction Associated With a 3-Tier Prescription Drug Benefit
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PURPOSE: The purpose of this research was to investigate consumer understanding and satisfaction associated with a 3-tier prescription drug benefit and to examine the relationships between tested understanding, satisfaction, prescription drug utilization, and sociodemographic characteristics.

METHODS: A questionnaire was developed to assess the study variables and mailed to 1,500 persons enrolled in an employment-based insurance plan with a 3-tier pharmacy benefit. In addition, prescription drug utilization was obtained from pharmacy claims processed through the plan’s pharmacy benefit management (PBM) company. Multiple linear regression, logistic regression, and negative binomial regression techniques were utilized.

RESULTS: The usable response rate was 35%. With possible scores ranging from zero (none correct) to 6 (all correct), the mean tested understanding score was 2.22±1.54. Experience with purchasing a medication within a particular tier was predictive of correctly answering the item related to that tier’s copayment. Being female (P=0.038) and from a higher income group (P=0.005) were significant predictors of tested understanding in regression analysis. Mean satisfaction with the pharmaceutical benefit was 54.32±19.69, on a scale from zero (least satisfied) to
100 (most satisfied). The relationship between tested understanding and satisfaction was not significant ($r_s=0.077$, $P=0.129$). Increasing age ($P<0.001$), a higher number of comorbidities ($P<0.001$), a higher level of tested understanding ($P=0.025$), and a higher level of satisfaction ($P=0.012$) were significant predictors of increased prescription drug utilization in this investigation. Better self-reported health status was associated with lower prescription drug utilization ($P<0.001$).

CONCLUSIONS: This study documents a substantial knowledge gap regarding prescription drug benefits. The findings provide a basis for the development of consumer-focused educational efforts. Providers of insurance benefits should carefully evaluate the impact of educational or informational programs on member understanding and satisfaction. Such activities create an opportunity for health insurers, PBMs, and academia to work together to enhance understanding of prescription drug benefits with the goal of optimizing drug use and consumer satisfaction.

Effect of a Prior Authorization on the Utilization of Cox-2 Inhibitors in a Staff-Model Managed Care Organization

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PURPOSE: To compare health care resource utilization of the cyclooxygenase-2 (Cox-2) inhibitors and evaluate patient characteristics following initiation and cessation of a prior authorization in a staff-model managed care organization.

METHODS: Medical and pharmacy claims data were analyzed over a 28-month duration to identify and characterize patients receiving a Cox-2 inhibitor. The study was divided into 2 periods of equal duration: period 1 (prior authorization) and period 2 (post-prior authorization). The prior authorization stipulated that Cox-2 inhibitors be considered in patients with a history of GI bleed/ulcer or who were on warfarin or who were aged 65 years or older with significant comorbidities. The health plan utilizes a 3-tiered copayment structure with the Cox-2 inhibitors at the highest third-tier level throughout study duration.

RESULTS: There were 9,071 claims in period 1 ($N=2,725$) as compared to 16,259 claims in period 2 ($N=4,853$) with a mean claims per utilizing member of 3.33 versus 3.35, respectively. Because of the recent release of the Cox-2 inhibitors prior to the beginning of period 1, the pharmacy claims data increased dramatically over the initial 14-month interval. However, utilization rates per month in period 1 peaked at 985 claims and showed little change in the per month utilization over period 2. The average age was significantly higher in period 1 versus period 2 (69 + 13 years versus 64 + 15 years, $P<0.0001$).

CONCLUSION: Although a trend toward increased utilization in younger patients was observed following removal of the prior authorization, this effect did not result in an overall increase in utilization. The fact that these agents were at the highest third-tier copayment may be a better explanation as to why the presence or absence of a prior authorization did not significantly impact Cox-2 inhibitor utilization.

Depressive Disorders and Physical Symptoms: The Relative Impact of Each on Lost Work-Time Costs in the United States Workforce

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INTRODUCTION: We conducted a study of the U.S. workforce to determine if depressive disorders with concomitant physical symptoms had a greater than expected impact on the loss of productive work time.

METHODS: The study was completed as a supplement to the American Productivity Audit, an ongoing weekly health and productivity survey of the U.S. population who work for pay. A random sample of 692 adults responding affirmatively to depression screening questions in the previous 2 weeks completed a supplemental 10-minute interview along with a matched sample of 435 adults responding negatively to those questions. Self-reported data were collected on employment, occupation, symptoms of depression, physical symptoms, and health-related lost productive work time (HRLPT) in the past 2 weeks. Diagnosis of major depression, dysthymia, partial remission of major depression, and minor depression was based on the PRIME-MD Mood Module. The Somatic Symptom Inventory was used to evaluate 26 physical symptoms.

RESULTS: The prevalence of depressive disorders in the U.S. workforce was 6.9%. Among workers with a depressive disorder, 89% reported at least one concomitant physical symptom, and 43% reported 6 or more symptoms. Among those who did not have a depressive disorder, only 10% reported 6 or more symptoms. The cost of HRLPT (including both time absent from work and time lost while at work from reduced performance) among U.S. workers with a depressive disorder was $38.6 billion per year. Almost 60% of this cost ($22.3 billion) was among the 43% of workers with 6 or more physical symptoms. Of the depressive disorders identified, major depression (with and without dysthymia) with 6 or more physical symptoms accounted for 20% of all depression but 34% of the total HRLPT cost in workers with a depressive disorder.

CONCLUSIONS: Physical symptoms commonly co-occur with depressive disorders and substantially impact work ability. Workers with major depression and 6 or more physical symptoms account for a disproportionate share of the cost from lost productive time.
Depression and Fibromyalgia Treatment and Cost When Diagnosed Separately or Concurrently

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INTRODUCTION: This study compared the costs in claims associated with fibromyalgia plus depression, fibromyalgia alone, and depression alone.

METHOD: Using administrative claims data from a national Fortune 100 manufacturer, 3 mutually exclusive cohorts and an overall beneficiary cohort were defined based on diagnostic claims: fibromyalgia only, depression only, fibromyalgia plus depression, and a random sample comprising 10% of the employer's overall beneficiary sample. The cohorts were compared for demographics, comorbid conditions, health care resources used, medication use by therapeutic class, and mean direct costs and imputed indirect costs.

RESULTS: Mean annual costs per patient to the employer were $5,163 for fibromyalgia only, $8,073 for depression only, $11,810 for fibromyalgia plus depression, and $2,486 for patients in the overall sample. Mean incremental employer costs (above overall sample payments) per patient for those with fibromyalgia plus depression were a cost addition of $1,060 when compared with the sum of the incremental costs for those with fibromyalgia only and depression only ((($11,810-$2,486)-(5,163-$2,486)+(8,073-$2,486))). For every dollar spent on fibromyalgia health care costs for employees (medical care plus prescriptions), the employer spent $57 to $143 on additional direct and indirect costs.

CONCLUSIONS: Patients with both fibromyalgia and depression claims are high users of the health care system. Although data are limited to an insured population, they concur with previous literature establishing relationships between depression and painful conditions. When fibromyalgia and depression co-occur, there is more than additive relationship between the incremental costs versus single-syndrome cohorts. Improved management of these patients could result in reduced patient, physician, and employer burdens.

Profile of Prescribing Patterns for COPD in the Managed Care Setting: Impact on Health Care Charges

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INTRODUCTION: Cost-effective chronic obstructive pulmonary disease (COPD) management requires appropriate pharmacologic therapy. A retrospective managed care claims analysis was performed to compare medication prescribing practices against national COPD guidelines and identify opportunities to improve care.

METHODS: A total of 23,596 enrollees with COPD were identified from a managed care research database. Inclusion criteria were defined as 2 claims with a COPD ICD-9-CM diagnosis code, age 45 years or older, and continuous enrollment with prescription benefits between October 1, 2000, and September 30, 2001. COPD patients were further stratified as follows: “Low Utilizers”—no COPD-related ER visits or hospitalizations during the 12-month study period; “Moderate Utilizers”—1 ER visit and/or admission; and “High Utilizers”—2 or more ER visits or hospitalizations. The COPD cohort was analyzed to identify outpatient prescription rates, utilization, and charges.

RESULTS: Overall, only 58.1% of COPD patients received a bronchodilator agent, which is the first-line therapy recommended by the Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) and the American Thoracic Society. Less than one third (32%) of the COPD population received inhaled anticholinergics and less than one half (48%) received inhaled ß-agonist therapy. By utilization status, only 53.8% of Low Utilizers, 73.3% of Moderate Utilizers, and 83.9% of High Utilizers received a bronchodilator agent. Inhaled corticosteroids, which are only recommended for use in selected patients and in combination with bronchodilators, were prescribed for 24% of patients. Contrary to guideline recommendations, corticosteroids were the only agents (i.e., without bronchodilators) prescribed for 10%, 7%, and 5% of Low, Moderate, and High Utilizers, respectively. In assessing the economic impact of adherence to medication guidelines for COPD, we found that total health care charges were 8.5% lower for COPD patients receiving bronchodilator agents compared to those not prescribed bronchodilators. This difference was greater for higher acuity patients, with 32.4% lower total charges for bronchodilator users in the Moderate Utilizer group and 23.6% lower in the High Utilizer group.

CONCLUSIONS: Despite the availability of recent, evidence-based COPD guidelines, there is underuse of medications that have been demonstrated to improve COPD symptoms and reduce health care costs. Furthermore, less-preferred agents are overutilized. Appropriate use of medications may lead to measurable pharmacoeconomic benefits. Opportunities exist to improve the clinical management of patients with COPD.

Impact of Open Access to Second-Generation Antipsychotic Medications on Treatment Decisions for Patients with Bipolar Disorders in the California Medicaid (Medi-Cal) Program

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OBJECTIVE: Document the impact of Medi-Cal's decision to grant open access to second-generation antipsychotic medications on treatment patterns for patients with bipolar disorders.

METHODS: Data for the number of drug therapy episodes initiated per month were plotted over time, broken down by episode type and the class of medication used. Descriptive statistics doc-
RESULTS: The number of patients restarting drug therapy or augmenting existing drug regimens with second-generation antipsychotic drugs increased immediately with open access. These increases were limited to a 6-month period following the formulary expansion. There were no offsetting reductions in the use of other medications, including conventional antipsychotics. For patients restarting drug therapy, this “open-access” response was particularly pronounced for patients with a recent hospitalization, minority patients, patients with a history of alcohol or drug abuse, and prior treatment with an antidepressant. Older patients tended to restart therapy in the first 6 months of open access, though this effect was reversed over time. Open-access patients were less likely to have a prior diagnosis of depression, personality disorders, or schizophrenia and had fewer reported medical comorbidities.

CONCLUSIONS: Open access to new psychotropic medications may induce a temporary increased response by patients restarting drug therapy, thus changing the characteristics of patients being treated. Efforts to estimate the cost impact of open access must take this response into account.

Incidence of Gastrointestinal Events Among Osteoporotic Patients Treated With Bisphosphonates


INTRODUCTION: The purpose of this study is to evaluate the occurrence of gastrointestinal (GI) events for patients taking risedronate, alendronate, 2 oral bisphosphonates for the treatment of osteoporosis, in an observational setting.

METHODS: A retrospective cohort study was conducted among 3,947 women and men (aged 65+ years) initiating bisphosphonate therapy in an integrated medical and pharmaceutical claims database. Patients with a risedronate (5 mg/day) or alendronate (5 mg/day, 10 mg/day, 35 mg/week, or 70 mg/week) prescription between November 1, 2000, and August, 2001, were selected for analysis, and those with a bisphosphonate script in the prior 6 months were excluded. The occurrence of GI events (based on primary ICD-9 diagnosis codes) was assessed for risedronate and alendronate, using a 6-month history preceding the index script (3 month).

RESULTS: The number of patients restarting drug therapy or augmenting existing drug regimens with second-generation antipsychotic drugs increased immediately with open access. These increases were limited to a 6-month period following the formulary expansion. There were no offsetting reductions in the use of other medications, including conventional antipsychotics. For patients restarting drug therapy, this “open-access” response was particularly pronounced for patients with a recent hospitalization, minority patients, patients with a history of alcohol or drug abuse, and prior treatment with an antidepressant. Older patients tended to restart therapy in the first 6 months of open access, though this effect was reversed over time. Open-access patients were less likely to have a prior diagnosis of depression, personality disorders, or schizophrenia and had fewer reported medical comorbidities.

CONCLUSIONS: Open access to new psychotropic medications may induce a temporary increased response by patients restarting drug therapy, thus changing the characteristics of patients being treated. Efforts to estimate the cost impact of open access must take this response into account.
INTRODUCTION: Chronic obstructive pulmonary disease (COPD), affecting an estimated 15 million Americans, is the fourth leading cause of death in the United States, resulting in considerable economic burden. The primary objective of this study was to estimate costs of medical care for patients with COPD versus those without COPD and to determine the attributable costs of treating complications of COPD.

METHODS: This was a case-control study to compare 1-year (2000) costs of medical and pharmacy care in the 18,061 COPD patients and in 18,061 age-, sex-, and geographical region-matched non-COPD control patients. Costs related to COPD and its complications were identified, and the proportion of costs attributable to COPD was calculated. Total medical costs were calculated using the actual amounts requested by the submitting provider, and total pharmacy costs were calculated based on the average wholesale price of each prescription medication. Costs were subdivided into respiratory-related and nonrespiratory-related.

RESULTS: COPD patients incurred higher respiratory ($7,888 versus $315) and nonrespiratory ($12,881 versus $8,085) total health care costs (per patient per year) as compared to matched control patients. Per-person total health care costs for COPD patients were 25 times (respiratory-related) and 1.6 times (nonrespiratory) those for matched control patients. The largest proportion of costs was for acute hospitalization. For COPD patients, respiratory total costs were highest for those <65 years ($8,412), followed by 65 to 74 years ($7,998), 75 to 84 years ($7,775), and 85+ years ($7,359); a similar pattern was observed for nonrespiratory total costs.

CONCLUSIONS: This claims analysis utilizing data from a typical managed care population demonstrates that COPD is a costly condition among managed care patients as indicated by the high per-person costs. Total costs were highest for COPD patients younger than 65 years. Costs for these patients are much higher for respiratory-related charges, with acute hospitalizations accounting for a large proportion of the costs. Nonrespiratory-related charges are also higher among COPD patients, reflecting costs associated with comorbid conditions. Effective pharmacological therapy and disease management programs aimed at preventing COPD complications may potentially reduce total health care costs.

Note: Additional Descriptive Reports abstract is on page 202.
lipoprotein cholesterol (HDL-C). The National Cholesterol Education Program Adult Treatment Panel III defined LDL-C goals for various patients based on different risk categories and redefined the minimum level at which HDL-C is considered to be low from <35 mg/dL to <40 mg/dL. We have devised a simple pharmacoeconomic model to evaluate the cost-effectiveness of statins in terms of their effects on both reducing LDL-C and increasing HDL-C.

**METHODS:** In order to rank the statins and compare their cost-effectiveness, we calculated an “LDL* HDL cost index” that evaluates acquisition cost, LDL-C lowering, and HDL-C rising. We utilized the mean percent reduction of LDL-C and the mean percent increase in HDL-C at each specific dose and/or regimen as reported in the package insert for each statin. Our analysis included both once-daily (qd) as well as twice-daily (bid) regimens. Cost of each statin was based on the wholesale acquisition cost from Medispan, October 2002. For each treatment, the absolute value of the mean percent reduction in LDL-C was multiplied by the mean percent increase in HDL-C to derive a “lipid percent change factor.” The daily cost of each treatment was then divided by its lipid percent change factor to yield the LDL*HDL cost index for each statin treatment. A lower LDL*HDL cost index intuitively represents a more cost-effective treatment since the index is derived by dividing the daily cost of treatment by a composite efficacy calculation (the lipid percent change factor).

**RESULTS:** Based on the calculated LDL*HDL cost indexes, the cost-effectiveness (from most to least) of the statin regimens are ranked as follows: extended-release lovastatin (ERL) 60 mg qd, ERL 40 mg qd, ERL 20 mg qd, simvastatin 10 mg qd, simvastatin 5 mg qd, immediate-release lovastatin (IRL) 10 mg qd, extended-release fluvastatin 80 mg qd, atorvastatin 20 mg qd, generic immediate-release lovastatin (IRL) 20 mg qd, ERL 10 mg qd, IRL 20 mg bid, atorvastatin 10 mg qd, pravastatin 40 mg qd, simvastatin 80 mg qd, simvastatin 40 mg qd, atorvastatin 40 mg qd, atorvastatin 80 mg qd, IRL 40 mg qd, simvastatin 20 mg qd, fluvastatin 40 mg bid, IRL 40 mg bid, fluvastatin 40 mg qd, pravastatin 10 mg qd, fluvastatin 20 mg qd, pravastatin 80 mg qd, and pravastatin 20 mg qd.

**CONCLUSIONS:** The LDL*HDL cost index described in our model considers the effect of treatment on both LDL-C and HDL-C; thus it may serve as an effective and efficient method to measure the cost-effectiveness of statin therapy. Application of this model using efficacy data reported in the package inserts for the statins and cost suggests that once-daily ERL 60 mg offers the most cost-effective regimen in terms of lowering LDL-C and raising HDL-C when compared to the other statin treatments.

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**The Effect of Atypical Antipsychotics on Hyperlipidemia Risk in Schizophrenic Patients**

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**INTRODUCTION:** The newer antipsychotics exhibit an overall superior safety profile compared to conventional agents. Yet case studies suggest an association between olanzapine use and hyperlipidemia. We sought to quantify this association in a large health care database.

**STUDY SETTING:** U.K.-based General Practice Research Database (GPRD) with 3.5 million patients followed from 1987-2000. We identified 20,865 patients with a diagnosis/treatment for schizophrenia.

**DESIGN:** We used a matched case-control design. Conditional logistic regression was used to derive odds ratios adjusted for gender, age, and medications influencing lipid levels. Drug exposure was defined as receipt of at least 30 antipsychotics within 2 months prior to the diabetes diagnosis date.

**RESULTS:** There were 1,268 incident diagnoses of hyperlipidemia, matched to 7,598 controls. Olanzapine use was associated with significantly increased odds of hyperlipidemia compared to nonatypical use (OR=4.65; 95% CI, 2.44-8.83; P<0.001) and conventional use (OR=3.36; 95% CI, 1.77-6.39; P=.0002). In contrast, risperidone use was not associated with increased odds of hyperlipidemia compared to nonuse (OR=1.12; 95% CI, 0.60-2.11; P=.715), or to conventional use (OR=0.81; 95% CI, 0.44-1.52; P=.517).

**CONCLUSIONS:** Our study shows a strong association between olanzapine use and risk of hyperlipidemia in schizophrenic patients. The resultant cardiovascular consequences should be given serious consideration by treating physicians.

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**Number Needed to Treat and Cost-Effectiveness of Ramipril in Preventing Cardiovascular Events in High-Risk Patients**

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**OBJECTIVE AND PERSPECTIVE:** The objective of this study was to assess the number needed to treat (NNT) and cost-effectiveness (CE) of ramipril from a payer perspective.

**METHOD:** A systematic review of all long-term (≥3 months) randomized controlled trials for ramipril published between January 1, 1980, and March 15, 2002, was conducted. Each study was scored for level of evidence (Cook’s criteria) and quality (Jadad scale). The NNT approach (inverse of absolute risk reduction in cardiac mortality) was used to evaluate the CE of ramipril therapy. The mean composite NNT was computed using appropriate weights based on study sample size. CE was defined as the ratio of incremental expected cost of ramipril therapy to life years gained (LYG). LYG was defined as the difference in mortality rates between ramipril and placebo, multiplied by 11.6 years of life.
expectancy, as reported for a similar cohort in the literature. All costs were discounted at 3%.

RESULTS: The mean composite NNT for preventing cardiac mortality for ramipril was 30. The discounted pharmacy cost to treat 30 patients over a 4 year period was $46,572. Based on an average cost of nonfatal CV events of $20,000 and a reduction in event rate of 1.3%, the overall medical cost offset was $7,800. The net incremental cost of $38,772 resulted in a base-case cost per LYG of $3,342. Sensitivity analysis estimates ranged from $3,174 to $3,511 per LYG.

CONCLUSIONS: Ramipril is cost effective in preventing CV events in high-risk patients.

Pharmacy Benefit Forecast for Injectable Teriparatide Using Administrative Claims Data

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OBJECTIVE: To estimate the impact on pharmacy budgets of formulary addition of teriparatide.

METHODS: A retrospective claims analysis was conducted, assuming that teriparatide, an injectable parathyroid hormone for osteoporosis treatment, would be used appropriately in patients over 55 years and would not cause market expansion. Potential teriparatide users were identified using integrated medical and pharmacy claims data from a 230,000-member employer group in the southwestern United States. Patients were identified through osteoporotic fracture diagnosis, concomitant therapy use, and bone-mineral-density test followed by treatment during one year. Off-label use, rates of teriparatide conversion, duration of therapy, and market-launch curves were simulated from products with similar attributes. Daily therapy cost was provided by the manufacturer, adjusted for migration from other therapies, and multiplied by estimated volume to predict incremental and total per-member-per-month (PMPM) costs. PMPM estimates were calculated for 2- and 3-tier benefit design with and without prior authorization (PA) and sensitivity analyses were performed.

RESULTS: Annual incremental PMPM cost was $0.013 for the third tier without PA base-case scenario. The base-case incremental impact was greatest in those older than 85 years ($0.184 PMPM) and did not vary greatly by benefit design. Sensitivity analysis found that maximum impact was $0.09 PMPM at highest estimates of market penetration.

CONCLUSIONS: Teriparatide should not cause significant pharmacy-budget growth according to this administrative claims analysis. Growth may differ if assumptions about the expected use are inaccurate or if the therapy expands the osteoporosis market. Pharmacy-budget analysis can be a useful first-line tool for economic formulary decision support.

Modeling Clinical and Economic Outcomes of Valsartan and Amlodipine in Diabetic Patients

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OBJECTIVE: The objective of this model is to evaluate the long-term consequences and cost-effectiveness of treatment using valsartan or amlodipine in type 2 diabetic patients with microalbuminuria, using Markov modeling.

METHODS: Clinical results and health care utilization from MARVAL, a multicenter, randomized, double-blind, trial of valsartan and amlodipine in type 2 diabetic patients with microalbuminuria, were used as inputs to a Markov model and Monte Carlo analysis, trending results forward 32 quarters. Patients were started at 80 mg/d valsartan or 5 mg/d amlodipine and titrated up to achieve target blood pressure (135/85). Costs from a managed care perspective (Medicare prices for medical services and average wholesale prices for prescription drugs) were applied to services and discounted to present $US2001 at 5%.

RESULTS: MARVAL demonstrated that valsartan was safe and efficacious in reducing BP, albuminuria, and cardiovascular endpoints at a lower total cost ($41,237 versus $49,862, P<0.01) and a corresponding slowing in the progression toward the costly end points of end-stage renal disease and cardiovascular events. Discounted quality adjusted life years (QALYs) were significantly higher with valsartan (27.70 versus 26.68, P<0.01). Discounted total costs were significantly lower with valsartan ($41,237 versus $49,862, P<0.01). Differences in QALYs and costs were not sensitive to differing assumptions regarding trends in clinical outcomes, measurement of resource, prices, or discount rates.

CONCLUSIONS: Treatment of diabetic patients with valsartan is a dominating strategy as compared to amlodipine by yielding a high level of QALYs at lower total costs of therapy and medical care resources.

Acute Bacterial Rhinosinusitis: A Decision Analysis of Antibiotic Strategies

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OBJECTIVE: To predict clinical outcome in acute bacterial rhinosinusitis (ABRS) following different antibiotic treatment strategies under current levels of antimicrobial resistance.

METHODS: We created a decision analytic model of various antibiotic treatment strategies for ABRS. Analysis of pharmacy claims for 9 U.S. managed care organizations in 2000-2001 showed aminopenicillins and macrolides were the most commonly prescribed first-line therapies for ABRS. We compared 2 prescription (Rx) strategies based on this analysis with a new
ketolide, telithromycin. Specifically, we compared 3 strategies of first-, second-, and third-line therapies: Amoxicillin/Azithromycin/Levofloxacin (AMX/AZI/LEV), Azithromycin/Cefuroxime/Levofloxacin (AZI/CEF/LEV), and Telithromycin/Cefuroxime/Levofloxacin (TEL/CEF/LEV). Clinical resolution was due to response to antibiotic or to the organism being inherently nonpersistence and would resolve regardless of treatment. While antibiotic resistance has been strongly linked to treatment failure in otitis media and community-acquired pneumonia, this relationship is not well understood in sinusitis. To gauge the possible impact of antibiotic resistance we considered in vitro resistant bugs to be either 0%, 50%, or 100% susceptible in vivo. We used U.S. surveillance data for 1999-2000 from the PROTEKT study, and employed pharmacokinetic/pharmacodynamic (PK/PD) breakpoints to estimate levels of antimicrobial resistance. The PK/PD breakpoint from 0.5 mg/L to 4.0 mg/L for TEL was used in the sensitivity analysis. Cases of viral origin were excluded since all strategies would be equal in these cases. Distribution of pathogens and rates of spontaneous resolution were based on published literature reviews. Speed of spontaneous resolution was based on placebo arms of published trials. Calibrating the model against trials results produced an estimate of 85% clinical resolution for pathogens susceptible to prescription drugs (Rx). Those failing to improve after 5 days were switched to next-line therapy. We used 3 outcome measures: response at first evaluation, failure rate at end of third round of treatment, and time to completion of therapy.

RESULTS: Assuming in vitro resistance does have impact on clinical outcomes, TEL/CEF/LEV was the superior strategy with 83.7% to 84.0% first-line Rx success, failure rates of 2.0% to 2.2%, and mean time to completion of therapy of 6.5 days. The model predicted the AZI/CEF/LEV strategy would have first-line Rx success of 57.4% to 70.9%, failure rates of 2.4% to 3.7%, and mean time to completion of Rx of 7.9 to 9.3 days. AMX/AZI/LEV was predicted to have a first-line Rx success of 73.3% to 78.8%, failure rate of 2.4% to 3.4%, and a mean time to completion of Rx of 10.4 to 10.9 days. If in vitro resistance were assumed to have no impact on clinical outcomes, then the model would predict that 84.3% would show improvement at first evaluation and only 1.9% would fail treatment. The conclusions were robust to changes in parameter estimates. Varying the breakpoint for TEL from 0.5 mg/L to 4.0 mg/L had impact on the predicted effectiveness, but TEL/CEF/LEV remained the superior strategy.

CONCLUSION: Based on results obtained using this decision analytic model, if antimicrobial resistance has any impact on clinical outcomes, then initial treatment of ABRS with telithromycin may result in fewer treatment failures and reduced time to completion of therapy compared to treatment strategies prevalent in the managed care setting.

Determining the Value Proposition of Contraception With a User-Customizable Pharmacoeconomic Model

OBJECTIVE AND PERSPECTIVE: Develop a pharmacoeconomic model to determine the cost utility of specific contraceptive coverage choices and provide for model updates as new techniques and data become available. The payer perspective was employed in the analysis.

METHODS: A cost-utility Markov model was evaluated by Monte Carlo simulation. Contraceptive methods include oral contraceptives (OCs), transdermal contraceptive (TC), condom, diaphragm, vaginal ring, IUD (copper and levonorgestrel), injectable (both monthly and quarterly), male and female sterilization, withdrawal, and periodic abstinence. Costs, mortality, and utility consequences were modeled for pregnancy and its outcomes, cardiovascular events, gynecologic cancers, menstrual disorders, and sexually transmitted diseases (STDs). Health effects were expressed in quality adjusted life years. (QALYs). Future costs and health effects were discounted at 3% annually. Key assumptions include: each method is modeled for the duration of the simulation, women are in good health and at average risk for medical complications, and a portion of unplanned pregnancies are mistimed rather than truly unwanted. Data sources include the National Study of Family Growth, national databases (National Center for Health Statistics and CDC), and a comprehensive literature search guided by an expert panel. Health utilities were assessed directly using healthy volunteers. Contraceptive cost-effectiveness for individuals or populations were estimated. The model stratifies incurred cost by category (eg., contraceptive method, professional/hospital fees, disease state). Cost data were obtained from product wholesale prices and from the Medstat MarketScan database. Smoking status, age, risk for STDs, and local values for costs and other variables are modifiable by the user.

RESULTS: After 2 years, all methods of contraception result in both net cost savings and improvement in clinical outcomes compared with “no method.” Cost savings over 2 years range from $170 to $3,080 and health gains range from 0.053 to 0.083 QALYs per 25-year-old woman. The vast majority of costs and health effects are due to pregnancy and related outcomes. The most critical variable in sensitivity analysis is the percentage of unplanned pregnancies that are truly unwanted. Comparison of the TC with OCs shows that the magnitude of cost savings depends on the age of the patient. This illustrates the use of the model for comparison of a new contraceptive method with an established method.

CONCLUSIONS: All methods of contraception result in net cost savings and net health gains relative to no method primarily because of reproductive effects. The flexible modeling system provides a novel approach to pharmacoeconomic analysis by
enabling decision makers to tailor the analyses to specific health care settings by customizing relevant parameters.

## INNOVATIVE PROCESSES

### Drug Savings Impact of a Pharmacist-driven Generic Education and Sampling Program

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**OBJECTIVE:** Based on the preliminary success of a pharmacist-driven generic education and sampling program pilot, an analysis was conducted to determine predictors of program success. Through this analysis, we hypothesized that the program could be further refined to maximize results.

**METHODS:** The analysis integrated claims experience of the 1,700 physicians included in the pilot program with details on the specific drug category discussions documented by the 12 participating pharmacists and physician sample-ordering history. SAS procedures (proc mixed and proc logistic) were used to determine predictors of physician order response and of generic prescribing change at the physician and therapeutic category level. Pregeneric and postgeneric utilization and substitution were compared to a representative comparison group.

**RESULTS:** During the first year, the participating physicians had a 1.54% greater increase in generic dispensing rate (GDR) versus the comparison group, resulting in $860,000 of drug-spend savings per pharmacist. Variables that predicted physician-level increases in GDR included the following: physician specialty, number of discussions, baseline generic prescribing, availability of samples to support relevant clinical discussions, and the amount of local press coverage released about generics.

**CONCLUSIONS:** Through the analysis, program enhancements are being made that we estimate will increase generic dispensing rates from 2% to 4%. The enhancements include refinement of physician selection process, expansion of the number of physicians contacted, customization of clinical messages to the physician, and personalization of the sample product offering.

### Impact of National Criteria on Appropriate Use of Tamsulosin in the VA: A Drug-Use Evaluation

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**INTRODUCTION:** Tamsulosin is the newest alpha-adrenergic antagonist used in the treatment of benign prostatic hyperplasia (BPH). The effect of tamsulosin is similar to other alpha-adrenergic antagonists with the exception of its selective alpha-1A activity. The Department of Veterans Affairs PBM/MAP developed national criteria for use to assist in the appropriate therapeutic role of tamsulosin in the VA. A drug-use evaluation (DUE) was performed to determine if tamsulosin was being prescribed appropriately; to evaluate the impact of development of national criteria on prescribing patterns, and to estimate the potential cost avoidance when correcting for inappropriately prescribed patients.

**METHODS:** VA medical centers with utilization approximately twice the national average (high use) as well as those medical centers with utilization less than the national average (low use) were identified. A data collection form for medical record abstraction was designed to capture information on the patient’s diagnosis, reported indication for tamsulosin (indications were identified as appropriate, potentially appropriate, and inappropriate.), history of previous alpha-adrenergic antagonist use, tamsulosin therapy follow-up, and the individual facility's method of criteria implementation. Patients receiving an active prescription for tamsulosin during a 3-month period preceding the posting of national criteria and patients with a first-time prescription for tamsulosin during a 3-month period after national criteria posting were randomly selected by the PBM and assigned for chart review at each site. These patients were identified through the VA National Pharmacy Database, which pulls all VA patient-specific prescription information on a monthly basis.

**RESULTS:** Data on 332 patients were collected from 6 different
sites. Tamsulosin was prescribed for appropriate indications in 66% of patients, potentially appropriate indications in 4% of patients, and inappropriate indications in 30% of patients. Follow-up was conducted in 78% of patients, of which 55% reported effectiveness of tamsulosin, and 6.2% reported side effects attributable to tamsulosin. No meaningful differences in prescribing patterns could be observed between the precriteria and postcriteria groups. Two sites (low-use sites at initiation) had some form of the criteria made available locally, while 4 sites had not implemented the national criteria. Extrapolation of the results to the VA system projected a conservative estimated cost avoidance of $436,668 for third quarter fiscal year 2002 if inappropriate prescribed patients were tried on terazosin, a nationally contracted alpha-adrenergic antagonist instead of tamsulosin for 3 months.

CONCLUSIONS: The large percent of inappropriate tamsulosin use has contributed to the increased utilization of this agent within the VA system. Despite the availability of national criteria, the results reveal that they were not followed in a timely manner to effect improvements in prescribing patterns. The DUE reinforced the need to actively implement/disseminate criteria, when developed, through a formal educational process to decrease inappropriate use of tamsulosin and to attenuate the increasing cost due to this inappropriate use.

Osteoporosis Management Improvement Initiative: Compliance With Daily Calcium Supplements

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OBJECTIVE: The objective of this initiative was to evaluate the self-reported behavior of health maintenance organization members receiving bisphosphonates with respect to calcium supplementation through a collaborative effort between Unity Health Insurance and the University of Wisconsin Hospital and Clinics. Furthermore, the initiative was to encourage the safe and effective use of bisphosphonates with calcium and vitamin D supplements and osteoporosis preventive measures.

METHODS: Calcium with vitamin D supplements, osteoporosis information, and a survey were mailed to 330 plan members with bisphosphonate prescription claims between April 1, 2001, and June 30, 2001. A 6-month postintervention survey was sent to respondents who provided contact information to the initial survey, to determine the effectiveness of the intervention with regard to calcium intake, bisphosphonate administration, and preventive measures. The study coordinator was available by telephone to answer questions regarding the intervention.

RESULTS: Of 330 members, 184 responded to the initial survey and reported compliance of approximately 80% with calcium supplements, 70% with vitamin D, and 80% with exercise. Fewer than 6% smoked. Reasons for noncompliance with calcium supplements included missed doses (10%), the perception that it was unnecessary (5%), and added expense (less than 3%). Bisphosphonates were reportedly administered with water, on an empty stomach, and in an upright position 90 to 97% of the time. Of 66 postintervention surveys sent to respondents of the first survey, 53 were returned, 43 of which provided adequate information for comparison. Calcium supplement utilization in mg per day increased by 9.5%, the number exercising increased by 2%, and smoking was unchanged. The perception of 4 that calcium was unnecessary was changed, and 2 no longer avoided calcium supplements because they considered their dietary intake to be adequate. Bisphosphonates were appropriately administered by 81% to 93% of the 43 members.

CONCLUSIONS: The population studied was motivated with regard to preventive measures for osteoporosis and calcium with vitamin D supplementation. Reported bisphosphonate administration by 81% to 93% remained appropriate. This educational intervention was successful in changing self-reported behavior with regard to calcium intake in members taking bisphosphonates.

Step-Up/Step-Down: An Innovative Approach to Step-Care

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INTRODUCTION/OBJECTIVE: To manage the high expense associated with the proton pump inhibitor (PPI) class of drugs, Blue Care Network (BCN) Pharmacy Services, in cooperation with MedImpact, their pharmacy benefits manager, has implemented a multifaceted approach that includes physicians, members, and pharmacies.

METHODS: In addition to the traditional formulary management approach to cost-containment, BCN has implemented a pilot program with an employer group in its central Michigan region that focuses on the PPIs. A step-therapy requirement for members with mild to moderate gastroesophageal reflux disease (GERD) ensures that members are given a trial with a prescription-strength generic H₂-receptor antagonist prior to receiving a prescription for a proton pump inhibitor (“step-up”). A mechanism is available to override this process for members with more significant disease. If the member advances to treatment with a PPI, a notice to the physician is generated with the first refill. This notice utilizes the MedPreferred program and encourages the physician to reassess the patient. The physician is asked to consider discontinuation of the drug and/or a switch to a less-expensive alternative for symptom control (“step-down”). Before the switch can be implemented, the physician is required to sign and return the agreement. MedImpact forwards the signed agreement with a cover letter to the dispensing pharmacy to initiate the change.

To further the success of this project, the claims processor generates a letter to the member when an initial claim is processed for a PPI. A member educational brochure that encourages members to consider lifestyle changes to improve their symptoms relating to heartburn and GERD is included with this member letter. BCN Pharmacy Services has gained the support of...
INTRODUCTION/OBJECTIVE: Blue Care Network’s (BCN’s) Pharmacy Services Department has developed a reliable, easy-to-use tool to assist its contracted primary care physicians and primary care group administrators with the management of drug therapy for its members.

RESULTS: With the primary care group administrator to assist with the medication management, the new program tool has evolved into a practical system that allows the administrator to generate dozens of possible reports to manage drug therapy. Member-specific issues such as medication compliance, duplicate therapy, and inappropriate drug use can be identified. Additionally, operational issues that face a physician group, such as physician overuse or underuse of a particular agent or class of agents can also be managed through this tool.

CONCLUSION: BCN primary care physician group administrators are now using the new database tool to help manage their pharmacy costs, to ensure medication safety for BCN members, and as an educational device for their primary care physicians.

Trends in Hormone Replacement Therapy Utilization Post-Women’s Health Initiative Trial

INTRODUCTION: The objective of this study was to demonstrate changes in prescription utilization for hormone replacement therapy and osteoporosis prevention postpublication of the conjugated estrogen in combination with medroxyprogesterone arm of the Women’s Health Initiative trial. The trial investigators determined that the increased risk of breast cancer and cardiovascular disease observed in the trial outweighed the benefits of decreased risk for fractures and colon cancer.

METHODS: To study the impact of the results from this trial, published in July of 2002, prescription utilization patterns for second quarter 2002 were compared to third quarter 2002 for females receiving any combination of estrogen with or without a progestin. In addition, second and third quarter 2002 prescriptions for osteoporosis prevention were compared. Prescription utilization from second and third quarter 2001 was used as a baseline comparison.

RESULTS: After adjusting for demographic and seasonal variations, results demonstrate a decline in utilization of estrogen monotherapy. A decline in utilization of combination therapy with an estrogen and progestin was observed. No shift in prescription utilization from oral to transdermal estrogen monotherapy and oral to transdermal combination therapy (estrogen plus progestin) was observed. An additional 7% reduction in estrogen utilization above baseline was observed. Utilization of agents other than estrogen for prevention of osteoporosis did not
increase. Bisphosphonate utilization declined, selective estrogen receptor modulator use declined minimally, and there was no change in utilization of calcitonin.

**CONCLUSIONS:** Overall utilization of estrogen alone and in combination with a progestin declined greater than expected. There was no shift from oral to transdermal delivery of estrogen with or without a progestin. Substitution of alternate therapies to estrogen for prevention of osteoporosis was not apparent in this study. Although there were no early predictors for increased utilization, managed care providers must investigate the possible impact of an increase in utilization of alternate therapies for osteoporosis prevention.

**Utilizing Prescription Patterns to Develop a Cost Model**

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**INTRODUCTION:** Prescribing patterns of long-acting opioids can be examined through descriptive claims analysis. The need for comparing relative analgesic doses of long-acting opioids makes the communication of their results and budgetary impacts challenging.

**PURPOSE:** Develop an analytic tool using established prescribing patterns for decision makers to estimate the budgetary impact of long-acting opioids at comparable doses.

**METHODS:** A model was developed using results from a descriptive claims analysis of long-acting opioids in a California Medicaid population. The recommended initial conversion doses were used to accurately compare opioid costs and strengths. The number of treatment days was identified as the basic unit of analysis. Weighted averages of the mean number of units dispensed daily were generated to precisely approximate treatment patterns within a given population.

**RESULTS:** A customizable user interface that requires input of institution-specific parameters such as indications for use, drug costs, and treatment days. After specifying the model parameters, the user can adjust market share to accurately estimate the potential budgetary impact of changes in utilization.

**CONCLUSION:** The use of previous research and dosing measures allows for the development of an analytic model that can assist decision makers in assessing the economic impact of institution-specific, long-acting opioid utilization.

**Response to the Women’s Health Initiative From a Health Plan Perspective**


**INTRODUCTION:** Women have relied on hormone replacement therapy (HRT) to treat symptoms of menopause and for long-term benefits such as prevention of cardiovascular disease. However, potential therapeutic uses of HRT were challenged by the recent results of the Women’s Health Initiative (WHI). The WHI, the first large-scale, randomized study to evaluate long-term effects of estrogen and progestin therapy, was halted in July 2002 because overall health risks of combined HRT outweighed benefits. As a result, the American College of Obstetricians and Gynecologists (ACOG) released consensus statements on the use of HRT. The objectives of this education initiative were to help network physicians and members understand the implications of the new relevant data and to offer assistance in risk/benefit assessment.

**METHODS:** A core pharmacy workgroup, consisting of an internal medical director (OB/GYN specialist) and 2 pharmacists, developed a strategy for implementing a comprehensive provider and member communication initiative. Based on the new standards of practice for HRT, several areas that required interventions were identified as follows: physician and member education, changes in policies governing the use of agents indicated for osteoporosis, and assessment of current formulary selection of estrogen and progestin products. Pertinent communication materials were reviewed by 2 external OB/GYN specialists prior to the organization’s internal review process. Drug usage guidelines for osteoporosis agents were reviewed and approved by the Pharmacy and Therapeutics Committee.

**RESULTS:** A physician education program was implemented for approximately 18,000 network primary care physicians and OB/GYNs. Packages were mailed out containing cover letters to medical directors of contracted medical groups and the targeted physicians, a summary handout describing the major findings of the study and ACOG’s recommendations on HRT use, a comparison chart for alternative osteoporosis treatment options, and a questions and answers sheet for patient counseling. In addition, the internal member Web site for women was revised to facilitate members in obtaining the most up-to-date information on HRT, menopause, and other associated topics. Drug usage guidelines for osteoporosis agents were also modified to reflect current national guidelines. Lastly, a preliminary assessment of formulary estrogen and progestin products was performed with a plan for a formal evaluation by the Pharmacy and Therapeutics Committee.

**CONCLUSION:** The implementation of this education initiative has provided physicians and members with resources to gain an appropriate understanding of the new significant medical data and to formulate clinically sound treatment plans.

**Impact of a Proactive Prior Authorization Program**

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**INTRODUCTION:** Pharmacy benefit management companies (PBMs) are continually developing efficiencies to improve their ability to provide a high-quality, cost-effective pharmacy benefit. While prior authorization (PA) is a necessary method of formulary management and cost containment for PBMs, it can be a burden for providers, retail pharmacists, and members. The objective of the Proactive Prior Authorization Program is to provide access to nonformulary medications for members who meet PA guide-
lines and who would have received a medication approval had they gone through the regular PA process.

**METHODS:** The program was implemented and tested in one health plan in November 2002. Members who met PA guidelines for long-term coverage of a proton pump inhibitor (PPI) were identified using medical and pharmacy claims data. A PA was proactively entered for each eligible member. The test group was compared to a control group of members of a different health plan that did not have a proactive PA program. Outcomes that were measured preproactive and postproactive PA initiation included PPI utilization, PA statistics (approval rate, denial rate, return on investment), and subsequent gastrointestinal medical encounters.

**CONCLUSIONS:** The Proactive Prior Authorization Program has generated interest as a method of decreasing the burden to providers, retail pharmacists, members, and the health plan by proactively providing access to nonformulary medications for specific eligible members.

**DESCRIPTIVE REPORTS**

**Clinical Outcomes of a Pharmacist-driven Diabetes Disease Management Program**

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**OBJECTIVE:** To evaluate the impact of clinical pharmacists interventions on outcomes relevant to diabetes in a multispecialty physician group practice.

**METHODS:** Medical records of patients (N=316) referred to the diabetes disease management program were retrospectively reviewed from initial referral to the clinical pharmacist through most recent follow-up. Data collection included HgbA1c, LDL, HDL, and TG values as well as patient compliance with ADA guidelines, including annual eye and foot exams, flu shots, and daily aspirin intake. Baseline data were compared with follow-up data to determine the magnitude of change. Continuous variables such as lab values were analyzed using a paired Students *t*-test and compliance with Americans With Disabilities Act guidelines was analyzed using McNemar’s test.

**RESULTS:** The mean reduction in HgbA1c observed was 1.4%, SD 1.94 (*P*<0.001). The percent of patients with HgbA1c less than 7% increased from 14.8% at baseline to 43.2% at follow-up (*P*<0.001). Mean number of days between initial and follow-up HgbA1c values was 144, SD 82. Mean reduction in LDL was 14 mg/dL, SD 41.1 (*P*=0.002) and mean reduction in TG was 42 mg/dL, SD 97.6 (*P*<0.001). HDL values were not significantly affected. The percent of patients with LDL less than 100mg/dL increased from 22% at baseline to 30% at follow-up (*P*=0.143). Percent of patients with TG less than 150mg/dL increased from 36% at baseline to 55% at follow-up (*P*=0.005).
### Membership Application

**Please print or type.**

**Member Information**

- [ ] Mr.  
- [ ] Ms.  
- [ ] Mrs.  
- [ ] Dr.

**FIRST NAME**  
**LAST NAME**

**TITLE**

**ORGANIZATION NAME**

**ORGANIZATION ADDRESS**

**CITY**  
**STATE**  
**ZIP CODE**

**HOME ADDRESS**

**CITY**  
**STATE**  
**ZIP CODE**

Address all mailings to my:  
- [ ] Company Address  
- [ ] Home Address

**WORK TELEPHONE**  
**FAX**

**HOME TELEPHONE**

**E-MAIL ADDRESS (PRIMARY)**

**E-MAIL ADDRESS (SECONDARY)**

Send all e-mail messages to my:  
- [ ] Primary E-Mail  
- [ ] Secondary E-Mail

**REFERRED BY**

**Annual Membership Rates**

- [ ] Active Member  
  (pharmacists who support the mission and goals of AMCP)  
  $225 per year
- [ ] Associate Member  
  (non-pharmacists)  
  $425 per year
- [ ] Student Member  
  $35 per year  
  Required: Graduation date (mo/yr) ____________ School ________________________
- [ ] Resident/Fellow/Graduate Member  
  $75 per year  
  Required: Resident/Fellow/Graduate completion date (mo/yr) ____________  
  Site ________________________

**Method of Payment**

- [ ] Check made payable to AMCP for $ ____________ (in U.S. funds drawn on a U.S. bank)
- [ ] Charge $ ____________ to my credit card  
  - [ ] Visa  
  - [ ] MasterCard  
  - [ ] American Express

**CARD NUMBER**  
**EXP DATE:**  
**CARDHOLDER PRINTED NAME**  
**CARDHOLDER SIGNATURE**

### Demographic Information

**Please tell us:**

I. Are you a pharmacist?  
  - [ ] yes  
  - [ ] no

II. What degrees/designations do you hold?  
- [ ] B.S. Pharmacy  
- [ ] Pharm.D.  
- [ ] M.P.A.  
- [ ] M.P.H.  
- [ ] Ph.D.  
- [ ] J.D.  
- [ ] M.B.A.  
- [ ] R.Ph.  
- [ ] Other ______________________

III. Which of the following best describes your employer?  
(choose one)
- [ ] Association  
- [ ] Health Plan  
- [ ] Medical Group  
- [ ] Integrated System  
- [ ] Hospital  
- [ ] College or University  
- [ ] PBM/Mail Service  
- [ ] Home Care  
- [ ] Long-term Care  
- [ ] Retail Pharmacy  
- [ ] Consulting Firm  
- [ ] Pharmaceutical Manufacturer  
- [ ] Government (VA, PHS, Military, State)  
- [ ] Not Currently Employed  
- [ ] Other ______________________

IV. Which of the following best describes your job function(s)?

- [ ] Director/President  
- [ ] Assistant Director/Vice President  
- [ ] Staff Pharmacist  
- [ ] Clinical Pharmacist  
- [ ] Clinical Coordinator  
- [ ] School/College Faculty  
- [ ] Student  
- [ ] Resident/Fellow/Graduate  
- [ ] Contract/Purchasing  
- [ ] Network Management  
- [ ] Professional Relations  
- [ ] Formulary Management  
- [ ] Distribution/Supply Chain  
- [ ] Customer Service  
- [ ] Consultant  
- [ ] Marketing/Sales  
- [ ] Other (specify) ______________________

V. How many years have you been in your current role?  
  ______ year(s)