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F
ine-art photographer Jason Horowitz is one busy man. During his interview for Cover Impressions in late July, he was in his photography studio in Arlington, Virginia, talking a mile a minute as he fielded calls on both his business phone and cell phone. Horowitz's hectic schedule that week included a photo shoot for The Capital Fringe Festival, an 11-day performing arts extravaganza in Washington, DC. Then he had to finish preparing for a two-week journey to Cartagena, Columbia, to take photos of its people. Horowitz was excited about the opportunity to add some international faces and places to his portfolio because travel-related photography is in great demand by stock-image companies. Many of his photographs can be found on the Web sites of companies such as Getty Images, Alamy Limited, and Panoramic Images.

Horowitz was born in Brooklyn, New York, and lived there until the age of 10, when his family moved to Coral Gables, Florida. After he graduated from high school in 1976, the family relocated to San Francisco. For his postsecondary education, Horowitz decided to attend George Washington University in Washington, DC, where he received a BA in photography. He had originally chosen journalism as his major but changed his mind after taking a photography class at Glen Echo Park near Bethesda, Maryland, during the summer following his freshman year. Glen Echo Park was an amusement park built in the early 20th century that was converted to a national park in 1971. It has been host to a variety of arts, environmental, and history programs since the early 1970s. Horowitz reminisced, “I took the photography class thinking that I would enjoy writing about the experience, but I soon discovered that photography was my true calling. It allowed me to express my creativity in more fulfilling ways.” He completely immersed himself in the artistic atmosphere of Glen Echo Park that summer, listening intently to his photography teacher and mentor, Frank Herrera, as well as the other photographers on staff.

Continuing his education in photography at Virginia Commonwealth University in Richmond, Virginia, Horowitz received an MFA in photography. He said that he likes to explore different types of photography, and he recently began to study digital photography in further detail.

The photographer began his career by taking pictures of landscapes and buildings and progressed to street scenes that incorporated people. In addition to landscapes and cityscapes, Horowitz is currently focusing on people—he considers them to be the most interesting subjects. “People embody so much of what I want to communicate in my work, and they add emotional depth to my photos,” he remarked.

The style of Horowitz's photography has also evolved over the years. Now he prefers a more “painterly” approach. “Most of my work lies somewhere between abstract and representational—I find them equally appealing,” he said. Much of his early work was shot in black and white, but today he shoots almost exclusively in color.

Horowitz fondly recalled that his first composite photograph was taken at dusk in New York's Times Square. “My composite photographs represent the abstraction of time and space. With this method, I can break something apart and then reassemble it,” he explained. “By shooting these scenes at dusk, you can see the darkening of the sky and get a sense of the progression of time.” He said that a good example of his abstraction of space is a composite that he shot of an action-filled volleyball game, showing the movement of the players as their images shift from one frame to another.

Chicago Skyline at Dusk is a compelling composite of multiple photos taken during a 45-minute time span. In this piece, the passing of time is clearly evident—the sky in the center of the work, above the Sears Tower, is quite a bit lighter than the sky on the far right. Chicago Skyline at Dusk could symbolize the tearing down and building up of any major city; but because it depicts Chicago, it is especially poignant in light of the Great Chicago Fire of 1871. Although much of the city was destroyed, the rebuilding that began almost immediately spurred Chicago's development into one of the most populous and economically important American cities.

AMCP is holding its 2006 Educational Conference from October 4-7 in Chicago. If you attend the conference, you will certainly be impressed by the city's skyline at any time of day, but it is especially beautiful in the evening when the lights are reflected on the surface of Lake Michigan. Horowitz has done a wonderful job capturing these enchanting reflections in Chicago Skyline at Dusk.

A seasoned photographer, Horowitz has been in the fine art and commercial photography business for more than two decades. His impressive work can be seen at his photography studio, Mirror Ball Studio, in Arlington, or on his Web site, www.mirrorballstudio.com. Horowitz is also represented by the Jayne H. Baum Gallery in New York City.

Sheila Macho
Cover Editor

COVER CREDIT

SOURCE
Interview with the artist.
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3. Journal paginated by issue

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

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Note: Please do not include author identification in the electronic manuscript document.

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❑ Cover letter
❑ Manuscript: prepared in 12-point type, 1.5 line spacing, including abstract: no more than 650 words keywords: follows the abstract references: cited in numerical order as they appear in the text (use superscript numbers) and prepared following modified AMA style; do not include footnotes in the manuscript 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) at the end of the manuscript, match symbols in tables and figures to explanatory notes, if included. May use 10-point font.
❑ Disclosures and conflict-of-interest forms: completed and signed author attestation forms (available at www.amcp.org); clearly indicate source(s) of funding and financial support.

Note: Please do not include author identification in the electronic manuscript document.

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REFERENCE

Assessing Potentially Inappropriate Prescribing in the Elderly Veterans Affairs Population Using the HEDIS 2006 Quality Measure

MARY JO V. PUGH, PhD; JOSEPH T. HANLON, PharmD, MS; JOHN E. ZEBER, PhD; ARLENE BIERMAN, MD, MS; JOHN CORNELL, PhD; and DAN R. BERLOWITZ, MD, MPH

ABSTRACT

BACKGROUND: Studies have found that 20% to 25% of older patients receive drugs identified as inappropriate by the 1997 Beers criteria. After the addition of 22 new drugs to the 2003 Beers criteria, the National Committee on Quality Assurance convened an expert consensus panel to identify which drugs from the 2003 Beers criteria should always be avoided in the elderly. The resulting list of drugs to avoid was added to the 2006 Health Plan Employer Data and Information Set (HEDIS) to measure the quality of prescribing for the elderly.

OBJECTIVE: To use HEDIS 2006 criteria to determine the rate of potentially inappropriate prescribing in the elderly (PIPE) and to determine if patient risk factors are similar to those found using Beers criteria.

METHODS: This cross-sectional database study identified older patients receiving drugs included in the HEDIS 2006 criteria using national data from the Veterans Health Administration. Patients aged 65 years or older on October 1, 1999, with at least 2 outpatient visit days during fiscal year 2000, ending September 30, or outpatient visits in fiscal years 1999 and 2000 were included (N = 1,096,361). Multivariable logistic regression analyses stratified by gender identified patient characteristics associated with increased risk of HEDIS 2006 drug exposure. Since oral estrogens were considered appropriate at the time of this study, they were excluded from the list of HEDIS 2006 drugs.

RESULTS: Overall, 19.6% of older veterans were exposed to HEDIS 2006 drugs—23.3% of older veteran women and 19.2% of older veteran men. The most commonly prescribed HEDIS 2006 drugs were antihistamines (received by 9.0% of men and 10.7% of women), opioid analgesics (received by 4.6% of men and 5.8% of women), and skeletal muscle relaxants (received by 4.3% of men and 5.3% of women). Propoxyphene was the most commonly used HEDIS 2006 drug, received by 4.5% of men and 5.7% of women, followed by diphenhydramine, received by 3.5% of men and 4.7% of women, and hydroxyzine, received by 3.2% of both men and women. Patients receiving 10 or more medications of any type were at greatest risk of exposure. Men were 8.2 times more likely to receive at least 1 HEDIS 2006 drug than those taking 1 to 3 drugs of any type (95% confidence interval [CI], 8.0-8.4), while women were 9.6 times more likely (95% CI, 8.2-11.2).

CONCLUSIONS: Even though we included a slightly different list of drugs to avoid, results for the HEDIS 2006 measure were similar to those of the 1997 Beers criteria. The HEDIS 2006 drugs are commonly prescribed, and there is a distinct need for direct evidence linking HEDIS 2006 PIPE exposure to adverse patient outcomes. To reduce PIPE, it seems necessary to provide additional evidence for clinicians through the conducting of a well-designed study to assess patient outcomes associated with PIPE exposure as defined by the HEDIS criteria.

KEYWORDS: Geriatrics, Quality of health care, Benchmarking, Pharmacoepidemiology

J Manag Care Pharm. 2006;12(7):537-45

There is a growing concern about the number of older Americans who receive medications offering more potential risks than benefits, or medications that are not consistent with accepted medical practice. Some studies found that approximately 1 in 5 older Americans are exposed to potentially inappropriate prescribing for the elderly (PIPE), based on the 1997 Beers criteria list of generally inappropriate drugs. These studies prompted the 2002 call by the Secretary for Health and Human Services for a national action plan to ensure the appropriate use of therapeutic agents in the elderly population.

About the same time, the National Committee on Quality Assurance convened an expert consensus panel and, using a modified delphi process, developed a quality measure to identify rates of inappropriate prescribing in the elderly based on the most commonly used measure of PIPE—the Beers criteria. This measure includes drugs that should always be avoided in the elderly and is currently being used in the 2006 Health Plan Employer Data and Information Set (HEDIS) in 2006 to assess quality of care for older Americans.

Authors

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Since the quality of prescribing for older patients is now being judged using this quality measure, it is important for managed care plans to understand the magnitude of PIPE exposure and to identify patients most at risk based on these new criteria. This will enable the managed care plans to successfully develop and implement interventions designed to improve prescriptions for older Americans. Because 14 of the drugs included in the HEDIS 2006 criteria (Table 2) were recently added, estimates of PIPE exposure based on these criteria have not yet been published. Accordingly, the objective of this study is to determine if the prevalence and predictors of inappropriate drug use as defined by HEDIS are similar to those for the 1997 Beers criteria for which more information is known. Since oral estrogens were recommended for use in certain women at the time of this study (2000) and prescribing patterns have likely changed since the publication of the Women’s Health Initiative Study findings in 2002, our analysis excludes assessment of estrogens. Because a number of commonly used drugs (e.g., amitriptyline, oxybutynin) were excluded from the HEDIS 2006 criteria, we hypothesized that rates of PIPE using these criteria will be lower than rates reported in studies using the Beers criteria.

### Methods

#### Data Sources and Population

This retrospective cross-sectional study was conducted using administrative data from the National Patient Care Database (NPCD) linked to outpatient pharmacy data for fiscal year (FY) 2000 (i.e., October 1, 1999, through September 30, 2000). The Department of Veterans Affairs (VA) utilizes an all-electronic medical record—the Veterans Health Information Systems Technology and Architecture—which transmits data each night on all patient care received from each VA facility to the national data repository in Austin, Texas. Thus, all inpatient and outpatient care received in the VA health system is documented. Individuals receiving care are identified using encrypted identifiers that are consistent in all VA databases; this allows the linking of individual data components to create a complete administrative record of the care provided to any VA patient. Administrative data include demographic and diagnostic information (International Classification of Diseases, Ninth Revision, codes) for each visit. Pharmacy data include the drug, dose prescribed, directions for use, and days supply for each pharmacy claim record.

Upon receipt of approval by Institutional Review Boards at the Bedford, Massachusetts, and Hines, Illinois, VA hospitals and the University of Texas Health Science Center at San Antonio, we identified regular users of the VA system. To ensure more accurate identification of comorbid conditions, we included only those who were at least 65 years of age at the beginning of FY 2000 and who either had at least 2 outpatient visits on separate days during FY 2000 or outpatient visits in both FY 1999 and FY 2000. Encrypted patient identifiers were linked

### Table 1

<table>
<thead>
<tr>
<th>Measure</th>
<th>Population of Focus</th>
<th>Number of Drugs or Changes to Previous Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beers, 1991†</td>
<td>Nursing-home patients</td>
<td>Expert consensus identifying 19 medications/classes to avoid in the elderly</td>
</tr>
<tr>
<td>Beers, 1997†</td>
<td>Community-dwelling elderly</td>
<td>Expert consensus identifying 28 medications/classes to avoid</td>
</tr>
<tr>
<td>Zhan, 2001†</td>
<td>Community-dwelling elderly</td>
<td>Expert panel classified 1997 Beers Criteria drugs into 3 categories: Always Avoid: should always be avoided Rarely Appropriate: are rarely appropriate but have some indications for appropriate use Some Indications: have some indications for use but most use is thought to be inappropriate</td>
</tr>
<tr>
<td>Beers, 2003†</td>
<td>Community-dwelling elderly</td>
<td>Expert consensus identifying 48 medications/classes to avoid</td>
</tr>
<tr>
<td>HEDIS, 2006</td>
<td>Community-dwelling elderly</td>
<td>Expert panel classified 2003 Beers Criteria drugs into 3 categories: Always Avoid, Rarely Appropriate, and Some Indications: Always Avoid and Rarely Appropriate drugs were included in the 2006 HEDIS measure</td>
</tr>
</tbody>
</table>

HEDIS=Health Plan Employer Data and Information Set.
to the national pharmacy database to identify drug information for each individual. Pharmacy data for HEDIS criteria drugs were extracted over a period of 1 year (FY 2000). Initial analyses found incomplete pharmacy data for 3 VA networks; thus, patients receiving care from these networks during FY 2000 were excluded.4

**Identification of Inappropriate Prescribing**

Initially, patients who received any HEDIS criteria drugs were identified. Table 2 defines the HEDIS 2006 drugs and contrasts them with the full Beers criteria from 1997 and 2003.3,12,25

**Independent Variables Associated with PIPE**

**Demographic characteristics.** Demographic information (age, sex, race/ethnicity) was obtained from inpatient and outpatient administrative data for FY 1998 (October 1, 1997, through September 30, 1998) through FY 2000. In general, VA administrative data on race/ethnicity represent a combination of self-report and provider-identified information. Missing race/ethnicity data were supplemented using self-reported data from the 1999 Large Health Survey of Veterans, a nationally representative survey of VA enrollees (July 1, 1999, through January 1, 2000); these self-reported data have been found to be consistent with VA administrative data.26,27 The VA Office of Quality and Performance (guardians of the Large Health Survey) also uses the same encrypted identifiers found in other VA databases, allowing accurate linking to administrative data.
Patient Characteristics by Gender

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Men (N=1,075,019)</th>
<th>Women (N=21,342)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean [SD])</td>
<td>73.4 [5.6]</td>
<td>75.2 [5.8]</td>
</tr>
<tr>
<td>Race/ethnicity (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>62.9</td>
<td>72.4</td>
</tr>
<tr>
<td>Black</td>
<td>9.3</td>
<td>4.6</td>
</tr>
<tr>
<td>Hispanic</td>
<td>4.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Unknown</td>
<td>22.6</td>
<td>21.1</td>
</tr>
<tr>
<td>Physical comorbidities (mean [SD])</td>
<td>4.1 [2.7]</td>
<td>4.0 [2.7]</td>
</tr>
<tr>
<td>Psychiatric comorbidity (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No psychiatric comorbidity*</td>
<td>79.1</td>
<td>72.7</td>
</tr>
<tr>
<td>SMI†</td>
<td>1.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Other mental illness‡</td>
<td>17.3</td>
<td>21.4</td>
</tr>
<tr>
<td>SMI + other mental illness§</td>
<td>2.4</td>
<td>4.0</td>
</tr>
<tr>
<td>Unique medications (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>12.2</td>
<td>17.0</td>
</tr>
<tr>
<td>1-3</td>
<td>16.6</td>
<td>13.7</td>
</tr>
<tr>
<td>4-6</td>
<td>24.8</td>
<td>21.0</td>
</tr>
<tr>
<td>7-9</td>
<td>20.4</td>
<td>19.0</td>
</tr>
<tr>
<td>&gt;10</td>
<td>26.1</td>
<td>29.3</td>
</tr>
<tr>
<td>Outpatient visits (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>26.9</td>
<td>25.7</td>
</tr>
<tr>
<td>3-4</td>
<td>21.3</td>
<td>19.7</td>
</tr>
<tr>
<td>5-9</td>
<td>26.7</td>
<td>26.1</td>
</tr>
<tr>
<td>&gt;10</td>
<td>25.1</td>
<td>28.6</td>
</tr>
</tbody>
</table>

* No psychiatric diagnosis = no diagnosis of schizophrenia, bipolar disorder, posttraumatic stress disorder, depression, anxiety, or substance abuse.
† Serious mental illness (SMI): schizophrenia, bipolar disorder.
‡ Other mental illness = depression, anxiety, posttraumatic stress disorder, substance abuse.
§ SMI + other mental illness = serious mental illness and other mental health diagnoses.

Disease burden. Using a method adapted from Schneeweiss et al., we used a count of comorbidities and a count of unique medications to assess disease burden.28 For the comorbidity count, we used Selim’s physical and mental health comorbidity indices (CIs) developed for the veteran population to assess comorbid conditions.24 We chose Selim’s CIs rather than the Deyo version of the Charlson Comorbidity Index since the Charlson index was developed to predict mortality, and our purpose was to assess a broader measure of disease burden that may be associated with functional limitations. The physical CI consists of a count of 26 chronic physical diseases, and the psychiatric CI includes 6 mental health conditions. Scores on each CI are associated with health status: high counts of comorbidities are associated with lower scores (lower health status) on all SF-36 scales.29 Moreover, higher counts of comorbidities on each CI are significant predictors of outpatient utilization and mortality.24-31

Because our earlier study published in 2005 identified any mental health condition as increasing the risk for PIPE as defined by the Zhan criteria24 and new drugs added to the HEDIS PIPE criteria are for treatment of psychosis, we categorized the type of psychiatric comorbidity as being either serious mental illness (SMI; psychoses, including bipolar disorder)32 or other mental illness. To accommodate those with both SMI and other mental illness, we developed 4 categories: (a) no psychiatric diagnosis, (b) SMI (schizophrenia, bipolar disorder), (c) other mental illness (depression, anxiety, posttraumatic stress disorder, substance abuse), or (d) both SMI and other mental health diagnoses. To ensure the complete identification of all relevant diagnoses, we assessed comorbidity status for up to 3 years (FY 1998 through FY 2000).

We identified each drug received by its generic name. We then counted the number of unique oral, topical, and injectable medications received by the patient in FY 2000. Drugs with different doses or formulations were counted as a single medication. Initial bivariate analyses found a correlation between the number of physical diagnoses and the number of unique medications ($r = 0.69$). Additional analyses further indicated that the number of unique medications was a better predictor of PIPE and that including the number of physical comorbidities did not add significantly to the model. Thus, our multivariable assessment of disease burden for the present study included psychiatric comorbidity and the number of unique medications.

Opportunities for prescription. Finally, we identified the number of outpatient visits each patient received in a clinic where a prescription may be written. Not only does this measure an opportunity for a prescription, it also provides an underlying measure of disease burden since those patients with more comorbid disease generally receive more care.

### Analysis

The prevalence of PIPE defined by HEDIS was calculated among the entire cohort, while analyses examining patient characteristics associated with use of HEDIS-criteria drugs were conducted only among patients who received at least 1 drug during the year. Multivariable logistic regression analyses were used to identify patient characteristics associated with the increased likelihood of receiving at least 1 HEDIS criteria drug. Because of the small number of women and a number of significant interactions, analyses were stratified by gender. Patient socio-demographic and clinical characteristics described above were included in the model based upon a priori hypotheses, and the Hosmer-Lemeshow and C-statistics were used to assess general model fit.33 The Hosmer-Lemeshow goodness-of-fit statistic measures the difference between the observed and fitted values.
The sample is stratified by deciles based on estimated probabilities; a goodness-of-fit statistic is assessed by computing the Pearson chi-square statistic between the observed and expected frequencies. The C-statistic is a nonparametric measure of the area under the receiver characteristic curve. It is a widely accepted measure of the degree to which the predicted probabilities from a logistic model adequately classify patients with respect to the observed outcome. Model assumptions were also checked by assessing the proportional odds. All analyses were conducted with SAS 8.2 (©1999-2001 SAS Institute, Cary, NC).

### Results

This cohort of older veterans (N=1,096,361) was almost entirely male (98%). Table 3 shows demographic and health status characteristics by gender. Both men and women were predominantly white, with substantial disease burden as measured by the number of chronic diseases, number of unique medications, and number of outpatient visits. Women were older than men (75.2 vs. 73.4 years; *P* ≤ 0.01) and more likely to have mental illness (27.3% vs. 20.9%; *P* < 0.01). From this cohort, 88% (N = 962,049) received medications from the VA and were included in multivariable analyses.

Table 4 shows the use of HEDIS drugs by gender. Overall, 19.6% of the overall cohort received at least 1 drug included in the HEDIS 2006 criteria, and 3.9% received 2 or more HEDIS 2006 drugs. Rates of PIPE varied between women and men; 23.3% of women and 19.2% of men received 1 or more HEDIS drugs. Sedating antihistamines, skeletal muscle relaxants, and certain opioid analgesics were the most commonly used PIPE drugs regardless of gender.

Table 5 shows results from logistic regression analyses predicting use of HEDIS 2006 drugs. The count of unique drugs was the strongest predictor for both men and women: the risk increased dramatically for those receiving 10 or more drugs. Even after controlling for the number of medications, we found that patients who were older (≥85 years) or black were at lower risk regardless of gender. Psychiatric comorbidity was a significant predictor for use of HEDIS 2006 drugs for both men and women. However, the effect for SMI alone did not result in a significant increase in risk for women; only diagnosis with other mental illness (e.g., depression, anxiety) alone or in combination with SMI was associated with higher risk of PIPE for women.

### Discussion

This study demonstrates that when HEDIS 2006 criteria (excluding estrogens) were applied, rates of PIPE (1 in 5) were similar to those reported in previous studies of drug exposure based on 1997 Beers criteria using the same exposure period, the same unit of analysis, and the same measure. Several commonly used drugs from the 1997 Beers criteria were

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**Table 4: Prevalence of Potentially Inappropriate Prescribing in FY 2000* Using the HEDIS 2006 Criteria**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Percentage With HEDIS Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (N = 1,075,019)</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>9.0</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>3.5</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>3.2</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>2.1</td>
</tr>
<tr>
<td>Promethazine</td>
<td>0.7</td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>0.3</td>
</tr>
<tr>
<td>Deschlorpheniramine</td>
<td>0.0</td>
</tr>
<tr>
<td>Tripeledrimine</td>
<td>0.0</td>
</tr>
<tr>
<td>Opioid pain medications</td>
<td>4.6</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>4.5</td>
</tr>
<tr>
<td>Meperidine</td>
<td>0.1</td>
</tr>
<tr>
<td>Pentazocine</td>
<td>0.0</td>
</tr>
<tr>
<td>Skeletal muscle relaxants</td>
<td>4.3</td>
</tr>
<tr>
<td>Methocarbamol</td>
<td>2.2</td>
</tr>
<tr>
<td>Cyclobenzaprine</td>
<td>1.9</td>
</tr>
<tr>
<td>Carisoprodol</td>
<td>0.2</td>
</tr>
<tr>
<td>Chloroxazone</td>
<td>0.2</td>
</tr>
<tr>
<td>Metaxalone</td>
<td>0.0</td>
</tr>
<tr>
<td>Orphenadrine</td>
<td>0.0</td>
</tr>
<tr>
<td>Psychotropic drugs</td>
<td>2.5</td>
</tr>
<tr>
<td>Diazepam</td>
<td>1.5</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>0.4</td>
</tr>
<tr>
<td>Thiuramodiazepoxide</td>
<td>0.2</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>0.1</td>
</tr>
<tr>
<td>Mesoridazine</td>
<td>0.0</td>
</tr>
<tr>
<td>Barbiturates (including phenobarbital)</td>
<td>0.3</td>
</tr>
<tr>
<td>Meprobamate</td>
<td>0.0</td>
</tr>
<tr>
<td>GI drugs</td>
<td>0.7</td>
</tr>
<tr>
<td>Dicyclomine</td>
<td>0.5</td>
</tr>
<tr>
<td>Hyoscyamine</td>
<td>0.1</td>
</tr>
<tr>
<td>Propantheline</td>
<td>0.0</td>
</tr>
<tr>
<td>Trimebuthazamide</td>
<td>0.0</td>
</tr>
<tr>
<td>Belladonna alkaloids</td>
<td>0.0</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>0.4</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>0.4</td>
</tr>
<tr>
<td>Cardiac drugs</td>
<td>0.7</td>
</tr>
<tr>
<td>Dipyridamole (short acting)</td>
<td>0.6</td>
</tr>
<tr>
<td>Nifedipine (short acting)</td>
<td>0.1</td>
</tr>
<tr>
<td>Cyclandate</td>
<td>0.0</td>
</tr>
<tr>
<td>Isoniazide</td>
<td>0.0</td>
</tr>
<tr>
<td>Ergot mesylates</td>
<td>0.0</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td>0.5</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>0.5</td>
</tr>
<tr>
<td>Endocrine drugs‡</td>
<td>0.1</td>
</tr>
<tr>
<td>Methyltestosterone</td>
<td>0.0</td>
</tr>
<tr>
<td>Chlorpropamide</td>
<td>0.1</td>
</tr>
<tr>
<td>Desiccated thyroid</td>
<td>0.0</td>
</tr>
<tr>
<td>Amphetamines and anorexic agents‡</td>
<td>0.0</td>
</tr>
</tbody>
</table>

† Oral estrogen for women is excluded because these medications were recommended for use in certain women at the time of this study.
‡ Dexmethylephedrine, dextroamphetamine, methamphetamine, amphetamine mixtures (Adderall), methylphenidate, pemoline, benztropine, diethylpropion, phenidimetrazine, phenteramine.

HEDIS = Health Plan Employer Data and Information Set.
not included in this HEDIS 2006 measure (e.g., amitriptyline, oxybutynin), but overall exposure remained similar when 15 drugs/drug groups were added from the 2003 Beers criteria. The most commonly used new drugs included nitrofurantoin, nifedipine, chlorpheniramine, and ketorolac, but only chlorpheniramine and nitrofurantoin (in women only) were each used by at least 1% of the population. Thus, the majority of the gender difference in PIPE exposure. Since antihistamines, skeletal muscle relaxants, opiates (predominantly propoxyphene), and psychotropic medications account for most PIPE exposure, this study suggests that research examining why these drugs continue to be so commonly used may be important to the development of successful interventions to reduce PIPE in both women and men. These drugs are often requested by patients, thus a focus on provider and system factors associated with their use may not be adequate. Further exploration of the patient’s role in this decision-making process is needed.

This study also highlighted an increased risk of PIPE in patients with psychiatric comorbidities. Several prior studies suggested that PIPE is more common in patients with depression.\(^\text{10-42}\) Our data suggest that diagnoses such as depression and anxiety are associated with PIPE for all patients, but comorbid SMI adds to this risk, particularly for men. Post hoc analyses found that not only are patients with psychiatric comorbidities at greater risk of receiving psychotropic drugs, but they are also at risk of receiving other classes of drugs. In particular, both men and women with all types of psychiatric comorbidities were also more likely to receive inappropriate antihistamines, and men were also more likely to receive inappropriate antibiotics. Antihistamines may be used specifically to counteract pseudo-Parkinson symptoms associated with the use of older antipsychotic drugs\(^\text{43}\) or to treat anxiety or insomnia in patients for whom benzodiazepines may be problematic (e.g., patients with substance abuse disorders). Patients with multiple mental illnesses may require different medications for each condition to adequately control symptoms, and the polypharmacy itself may lead to a prescribing cascade to deal with resultant side effects.\(^\text{44}\)

Post hoc analyses also indicated that patients with SMI were less likely to receive inappropriate opiate analgesics and skeletal muscle relaxants, while those with mood disorders were more likely. Those with affective disorders may report somatic complaints to a greater degree than those with SMI and thus be more prone to receiving inappropriate drugs to address these complaints.\(^\text{35}\) Alternatively, patients with chronic back and

---

### TABLE 5

**Logistic Regression Model Predicting HEDIS 2006 Drug Use**

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>HEDIS Criteria Drug Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (944,331)</td>
</tr>
<tr>
<td></td>
<td>Women (17,718)</td>
</tr>
</tbody>
</table>

- **Age, years (vs. 28-55 years)**
  - 65-69: 1.3 (1.2-1.3) vs. 1.3 (1.1-1.6)
  - 70-84: 1.1 (1.1-1.1) vs. 1.0 (0.9-1.2)

- **Race/ethnicity (vs. white)**
  - Black: 0.09 (0.0-0.9) vs. 0.8 (0.7-1.0)
  - Hispanic: 1.3 (1.1-1.3) vs. 1.4 (1.1-1.8)
  - Other: 0.9 (0.9-1.0) vs. 1.0 (0.6-1.8)
  - Unknown: 0.8 (0.8-0.9) vs. 0.9 (0.8-0.9)

- **Psychiatric comorbidity (vs. none)**
  - SMIF: 1.7 (1.6-1.8) vs. 1.2 (0.9-1.5)
  - Other mental illness‡: 1.5 (1.3-1.5) vs. 1.1 (1.0-1.2)
  - SMI + other mental illness§: 1.7 (1.6-1.7) vs. 1.3 (1.1-1.5)

- **Unique medications (vs. 1-3)**
  - 4-6: 2.2 (2.1-2.2) vs. 2.3 (1.9-2.7)
  - 7-9: 3.8 (3.8-3.9) vs. 4.3 (3.7-5.1)
  - >10: 8.2 (8.0-8.4) vs. 9.6 (8.2-11.2)

- **Outpatient visits (vs. 2)**
  - 3-4: 1.1 (1.1-1.1) vs. 1.1 (1.0-1.2)
  - 5-9: 1.2 (1.2-1.2) vs. 1.2 (1.1-1.3)
  - >10: 1.4 (1.3-1.4) vs. 1.4 (1.3-1.6)

---

* No psychiatric diagnosis = no diagnosis of schizophrenia, bipolar disorder, posttraumatic stress disorder, depression, anxiety, or substance abuse.
† Serious mental illness (SMI): schizophrenia or bipolar disorder.
‡ Other mental illness: depression, anxiety, or substance abuse.
§ SMI + other mental illness = serious mental illness and other mental health diagnoses.

CI = confidence interval; HEDIS = Health Plan Employer Data and Information Set; SMI = serious mental illness.
other types of pain are at risk for depression, resulting in the relationship between other mental illness and PIPE. These findings suggest that more thorough investigation of the relationship between PIPE and mental illness is needed to better understand this risk, in order to develop ways to improve prescribing to this population.

Another important contribution of this study is that, consistent with some prior studies, the oldest of the elderly were at lower risk of PIPE and the youngest of the elderly were at greater risk. This suggests that providers become increasingly cautious as patients age and physical health deteriorates. This finding also suggests that defining “elderly” as 65 years and older may be arbitrary. The age of 65 was identified as retirement age in 1883 by Otto von Bismarck when the average life span was 47 years. This age was adopted as the age of retirement in the United States when the Social Security program was initiated. Since that time, the life span has increased to 74.5 for males and to 79.9 for females. The elderly population is healthier today than ever before, and it is a highly homogeneous population. For instance, in 1994 the percentage of individuals who reported no disability was 89% for ages 65 to 74 years, 73% for ages 75 to 84 years, and 40% for ages 85 years and older.

Should all drugs from the HEDIS 2006 criteria be avoided by all persons 65 years and older? Should these drugs be restricted to older patients with certain physical conditions or limitations? While these questions have not been adequately examined, the HEDIS criteria are targeted to all patients aged 65 years and older.

Limitations

Our study does have some limitations. First, the medications examined included only those prescribed within the VA health system. This may underestimate exposure, particularly for drugs that can be obtained over the counter (e.g., antihistamines). However, the highest copayment at the time of this study was $2 for a 30-day supply—which is much less than the cost of a 30-day supply of over-the-counter drugs. Since diphenhydramine—which can be obtained over the counter—was the most commonly used antihistamine and antihistamines were the most commonly used group of PIPE drugs, our estimates seem reasonable. Moreover, some VA patients may receive medications through Medicare HMOs. Shen et al. found that 33% of VA patients with Medicare eligibility received care in both systems, and a recent small survey found that 18% of VA patients (not necessarily Medicare-eligible patients) received medications from both VA and private-sector HMOs. As we have no way to identify these patients, the effect on our findings is unknown.

Second, our data included only a small number of women. Since these findings are consistent with findings from other national database analyses of 1997 Beers-criteria drugs and with findings assessing preliminary HEDIS criteria using a sample of 10 managed care organizations, we believe that our findings, which were stratified by gender, may be generalizable. However, further research confirming this finding is warranted.

Third, the data for this study were from services received in 2000—5 years before the final development of the HEDIS 2006 criteria. However, these data provide an accurate picture of the types of patients who received these drugs at that time. More importantly, these data provide a benchmark for assessing change in the prevalence of drug use prior to publication of these criteria. With this data point, assessment of change in practice both before and after publication of the HEDIS 2006 criteria can be more accurately ascertained. However, further evaluation of PIPE exposure for women is needed since we excluded estrogen because results from the Women’s Health Initiative Study were not available at the time these data were obtained. Finally, we restricted this analysis to patients who received at least 2 outpatient visits in the VA health system. This restriction excluded approximately 300,000 patients and may bias the cohort to those with greater disease burden, but we thought it important to improve our ability to identify comorbid conditions. Analyses using the full cohort found lower rates of PIPE (17.5% vs. 19.6% in the restricted sample), but analyses on the full cohort yielded similar findings.

Conclusions

These data suggest that PIPE exposure remains substantial for both men and women. The study produced these findings even though we limited the definition of PIPE to a select group of drugs included in the 2003 Beers criteria. While controversy has surrounded using the Beers criteria to measure PIPE, this HEDIS measure is now used to assess the quality of prescribing for older patients. It is unknown whether this quality measure will stimulate change in prescribing patterns, but implementation of a similar quality measure by the Centers for Medicare and Medicaid Services resulted in only small reductions of PIPE for patients in nursing facilities over a 4-year period, perhaps because of substantial prescribing changes that preceded the study. Nonetheless, Briesacher et al. reported that the changes that did occur in prescribing could not be attributed to implementation of the quality measure. It is likely that a similar situation exists for attempts to change prescribing patterns in community-dwelling elderly. Consequently, it will be important to identify barriers to more appropriate care at all levels, including the patient, provider, and the health care system, before effective interventions to reduce PIPE can be developed and implemented by managed care organizations.

Furthermore, the findings of Stuart et al. that there was little change in the most commonly used drugs, in conjunction with findings from Briesacher at al., suggest that providers may need additional evidence before they change prescribing patterns. The inconsistency in findings from studies evaluating outcomes associated with exposure to Beers-criteria drugs...
based on a dichotomous measure\textsuperscript{17,19-23} may merely be the result of methodological problems, such as failure to use an incident cohort in analyses or poor ascertainment of the temporal relationship between drug exposure and patient outcome.\textsuperscript{65} Thus, an important step in changing prescribing patterns is to provide additional evidence for clinicians by conducting a well-designed study to assess patient outcomes associated with PIPE exposure as defined by the HEDIS criteria. Still, if findings suggest a lack of association between PIPE exposure and negative patient outcomes or findings suggest that PIPE drugs are particularly problematic for the oldest of the elderly but not for the youngest, they will stir additional debate and perhaps encourage the development of a new measure of PIPE.

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DISCLOSURES

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Pugh served as principal author of the study. Study concept and design were contributed primarily by Pugh and Bierman, with input from the coauthors. Data collection was the work of Pugh, with input from Berlowitz; data interpretation was the work of Pugh, Hanlon, and Cornell, with input from Bierman. Writing of the manuscript was primarily the work of Pugh, with input from Zeber, its revision was primarily the work of Pugh, with input from Hanlon, Zeber, and Bierman.

REFERENCES

22. Steel K. The time to act is now. \textit{Arch Intern Med.} 2004;164:1603-04.


Total and Component Health Care Costs in a Non-Medicare HMO Population of Patients With and Without Type 2 Diabetes and With and Without Macrovascular Disease

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ABSTRACT

BACKGROUND: Type 2 diabetes (T2DM) is one of the most prevalent and costly chronic conditions in the United States. Macrovascular disease (MVD) remains a common and costly comorbidity in T2DM. Understanding the impact of MVD on total health care costs in patients with T2DM is of great importance to managed care organizations (MCOs).

OBJECTIVE: To examine from the perspective of an MCO the impact of MVD on health care costs in patients with T2DM and in a matched comparison group of patients without diabetes.

METHODS: This study involved retrospective analysis of administrative claims (eligibility, pharmacy, and medical) using data from a commercial health maintenance organization population of approximately 700,000 members in an East Coast health plan. Patients were included in this study if they (a) had 2 or more claims for T2DM [International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 250.X0 or 250.X2), or (b) had a prescription drug claim for insulin and a diagnosis of T2DM, or (c) had at least 1 pharmacy claim for an oral glycemic-modifying agent during the 12-month period from January 1, 2003, through December 31, 2003. Patients with 2 or more medical claims for type 1 diabetes (ICD-9-CM codes 250.X1 or 250.X3) were excluded from the study. A random group of comparison patients without diabetes (ICD-9 code 250.xx) were matched on age group and sex. Study patients in these 2 groups were subdivided into 4 groups based on the presence of medical claims with diagnosis codes for MVD (acute myocardial infarction, other ischemic heart disease, coronary artery bypass surgery, percutaneous transluminal angioplasty, congestive heart failure, cerebrovascular accident, peripheral vascular disease, cerebrovascular disease, and peripheral vascular disease). Direct medical costs were aggregated for 12 months after the index date for patients in all 4 groups. Bootstrapping technique was used to compare the health care costs between patients with T2DM and those without diabetes, stratified by MVD status.

RESULTS: A total of 9,059 patients with T2DM were identified and were matched by age group and sex to a random group of patients without diabetes. MVD was present in 26.9% (n = 2,441) of patients with T2DM versus 11.3% (n = 1,027) of patients without diabetes. Patients with MVD and T2DM were, on average, a year younger than patients with MVD but without diabetes (54.55 vs. 55.55 years, P <0.001). Patients with T2DM but without MVD were nearly the same age as patients with neither diabetes nor MVD (50.44 vs. 50.59 years, P = 0.092). The T2DM patients with MVD had average 12-month costs more than 3 times the costs for patients with T2DM but without medical claims with diagnosis codes for MVD—$10,450 versus $3,385, respectively. Pharmacy costs accounted for 29.0% and inpatient hospital costs accounted for 43.9% of total medical costs in T2DM patients with MVD versus 55.0% and 17.3%, respectively, in T2DM patients without MVD. Patients with MVD diagnoses and T2DM had total average medical costs that were 1.7 times the total medical costs for MVD patients without T2DM—$10,450 versus $6,090, respectively.

CONCLUSIONS: The results of this analysis suggest that MVD may triple the total medical care costs in patients with T2DM. These economic consequences would appear to support the importance of interventions intended to prevent macrovascular event in patients with T2DM.

KEYWORDS: Macrovascular disease, Type 2 diabetes, Health care costs, Managed care, HMO

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Diabetes has been classified as a global epidemic. The World Health Organization estimated that more than 177 million individuals live with diabetes, and approximately 4 million deaths each year are related to complications from the disease. Globally, the total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million by 2030, largely due to the prevalence of type 2 diabetes (T2DM), which accounts for 95% of all diabetic cases. In the United States, there were approximately 12.1 million cases in 2002, and forecasters predict that this number will increase to approximately 14.5 million by 2010 and 17.4 million by 2020. Over the past decade, the age at diagnosis of T2DM has decreased by an average of 6 years, from 52 to 46 years.

The American Diabetes Association (ADA) estimated the direct costs of diabetes to be $91.8 billion in 2002; associated health care costs and demands of diabetes are increasing along with its prevalence. T2DM is associated with many microvascular and macrovascular complications. Macrovascular disease (MVD) includes coronary disease, cerebrovascular disease, and peripheral vascular disease. Cardiovascular disease (CVD) is the major cause of morbidity and mortality in subjects with T2DM, accounting for approximately 65% of deaths in patients with T2DM in 1999. Several studies have shown that CVD is a major driver of costs in patients with diabetes. The excess costs of T2DM could start as early as 8 years before diagnosis, and CVD is responsible for a significant portion of the prediagnostic costs. When CVD is present in patients with...
T2DM, more costs occur earlier in life as well as earlier in the course of T2DM. However, few data are available in the typically younger, commercially insured population.

Although there are national estimates for aggregate expenditures for CVD and diabetes, there are few published studies estimating the average cost of treatment per patient per year (PPPY) for MVD. Glauber and Brown reported that CVD accounted for at least 24% of total medical care costs among patients with diabetes, compared with 12% of costs for patients without diabetes. While that study included members of a health maintenance organization (HMO) diabetes registry, it did not differentiate between patients with type 1 and type 2 diabetes. Nichols and Brown reported the annual cost of CVD in patients with and without T2DM among members of an HMO diabetes registry. However, nearly half of their study sample was aged 65 years and older. With the increase in T2DM in younger age groups, it is important to quantify the medical costs of T2DM and MVD in this “working age” population.

Given the prevalence of T2DM in the United States, and its impact on health care and budgets, policy makers need up-to-date information about treatment outcomes and costs. Interest in prevention and treatment of MVD in T2DM is increasing. ADA has called for renewed efforts at intensive treatment so that the most serious complications of this disease can be prevented or mitigated. In this article, we detail the economic impact on health care and budgets, policy makers need up-to-date information about treatment outcomes and costs. Interest in prevention and treatment of MVD in T2DM is increasing. ADA has called for renewed efforts at intensive treatment so that the most serious complications of this disease can be prevented or mitigated.

Using a case-control methodology, the analyses allowed for an examination of the direct medical costs associated with T2DM and T2DM with comorbid MVD compared with a “healthy” nondiabetic cohort. Quantification of the medical costs may prove useful in the determination of cost drivers and promotion of preventive health care services within a managed care population. The study therefore provides data that may help managed care decision makers and employers gain a better understanding of the economic impact of T2DM, both alone and accompanied by comorbid MVD.

**Methods**

**Data**

This retrospective analysis was based on a deidentified administrative claims database containing medical and demographic information on approximately 700,000 members enrolled in an East Coast commercial HMO health plan. The database contains paid facility, professional service, and community and mail-service pharmacy claims for inpatient and outpatient care for all enrollees (and their spouses and dependants). Monthly eligibility data were also available for all enrollees. All patient identifiers in the database have been fully encrypted, and the database is fully compliant with the Health Insurance Portability and Accountability Act of 1996. Since study subjects cannot be identified, either directly or through linked identifiers, Institutional Review Board review was not sought for this study.

**Patient Selection**

Study patients were identified during the period January 1, 2003, through December 31, 2003. The index date was the first identified claim for T2DM during the subject identification period. Patients between the ages of 30 and 65 years as of January 1, 2003, who were commercially insured with a pharmacy benefit, were included in this study if they met the following criteria: (1) at least 2 or more claims for T2DM (ICD-9-CM code 250.X0 or 250.X2) with different dates of service, or (2) had at least 1 pharmacy claim for insulin and at least 1 diagnosis code for T2DM, or (3) at least 1 Rx claim for oral glycemic-modifying agent. After enrollment and exclusions n=9,059 (5.2%) MVD Diagnosis n=2,441 T2DM, MVD n=2,441 T2DM, No MVD n=6,618 T2DM, No MVD

ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification; MVD= macrovascular disease; Rx= prescription; T1DM= type 1 diabetes mellitus; T2DM= type 2 diabetes mellitus.
required to have at least 12 months of continuous enrollment prior to the index date and at least 12 months of continuous enrollment following the index date. MVD was identified using ICD-9-CM codes in any position on office visits, emergency room visits, and hospital claims, for cases and controls. The diagnosis codes used for identifying MVD are listed in Table 1.

Exclusion criteria for patients included (1) 2 or more claims for type 1 diabetes (ICD-9-CM codes 250.X1 or 250.X3); (2) 2 or more claims with a diagnosis of neoplasm (ICD-9-CM codes 140-239) on different dates of service (at least 2 claims were required to ensure that patients with rule-out diagnosis [i.e., those thought to have neoplasms but found not to have neoplasms upon further examination] were not captured); and (3) a diagnosis of gestational diabetes (ICD-9-CM codes 648.00, 648.03, or 648.80). Patients with neoplasms typically are heavy users of the health care system and incur high direct medical costs. These patients were excluded because this allowed us to ensure that the costs in both T2DM and comparison groups were not driven by the presence of a high proportion of patients with neoplasms.

Control Group Selection
A random sample was drawn from the same overall patient population to serve as the control group. Sex- and age-matched groups (30-35 years, 36-40 years, 41-45 years, 46-50 years, 51-55 years, 56-60 years, and 61-65 years) of enrollees who used services but did not have any diabetes claims (ICD-9-CM code 250.xx) during the study period were selected on a 1:1 basis. Matched controls were continuously eligible for medical and pharmacy benefits and required to have at least 1 facility or medical claim during the study year. We matched patients on age and sex because these variables often influence treatment patterns. We were unable to match on other patient characteristics such as race/ethnicity, income level, region, etc., since this information was not available in the database.

Comorbidity
Patient comorbidities were identified using ICD-9 codes from medical claims. The comorbidities were selected to represent the conditions expected to be the most common and costly. The comorbidities identified among the 4 groups included nephropathy, neuropathy, retinopathy, obesity, hyperlipidemia, and other metabolic diseases. These comorbid conditions were considered to exist for a patient if there was at least 1 claim with a corresponding ICD-9 code at any time during the study period. Table 1 lists the ICD-9 codes used to identify these conditions.

Cost Calculations
The direct medical costs included inpatient, outpatient, ancillary, and pharmacy costs for each member. Costs were defined from the perspective of the health plan and included total payments made by the health plan to health care providers for inpatient, outpatient, physician, prescription drug services, and other ancillary services (e.g., laboratory tests, procedures). Patient copayments and deductibles were not included in the total direct medical costs. Costs were reported as PPPY costs in 2004 U.S. dollars. The medical care component of the consumer price index was used to adjust the costs to 2004 dollars.

Costs relating to claims for the following primary diagnoses were excluded from the computation of direct costs: (1) injury and poisoning (ICD-9-CM codes 800–999.99); (2) complications of pregnancy, childbirth, and the puerperium (ICD-9-CM codes 630–679.99); (3) potential health hazard related to personal and family history of malignant neoplasm (ICD-9-CM codes V10-V10.99); and (4) persons encountering health care services relating to pregnancy (ICD-9-CM codes V22-V24.99), procreative management (ICD-9-CM codes V26-V26.99), outcome of delivery (ICD-9-CM codes V27-V27.99), and amnestic screening (ICD-9-CM codes V28-V28.99).

Mean annual medical costs were computed for patients with and without T2DM, stratified by MVD status for 12 months after the index date. The goal for the cost analysis was to compare costs for 4 groups of patients: (1) patients with T2DM and MVD, (2) patients with T2DM but without MVD, (3) patients without diabetes but with MVD, and (4) patients without diabetes and MVD.
Statistical Analysis

Descriptive statistics were used to describe the differences in costs among patients with T2DM and MVD, patients with T2DM but without MVD, patients without diabetes but with MVD, and patients without diabetes or MVD. Chi-square analysis was used to detect differences in age distribution (30-35 years, 36-40 years, 41-45 years, 46-50 years, 51-55 years, 56-60 years, and 61-65 years) and sex distribution among the 4 groups. All summary statistics are presented as mean ± standard deviation for continuous variables and as percentages for categorical variables.

Skewed data are often encountered in economic evaluations. Although statistics such as the median are of interest descriptively, economic analysis is fundamentally concerned with mean values. The median is not well suited to allowing policymakers to determine the total cost of treatment for a group of patients. The bootstrapping approach allows a comparison of means while avoiding distributional assumptions. The bootstrapping procedure we used involved random sampling of data, with replacement, to obtain a new sample of equal size. This process was iterated 1,000 times in order to obtain the 95% confidence intervals (CIs) around the costs. SAS Version 8.2 was employed for data management and statistical analyses. The a priori level of significance was set at <0.05.

Results

After the application of the eligibility criteria, 9,059 patients with T2DM were identified (Figure 1). A comparison group of 9,059 patients without diabetes with continuous enrollment for 2 years was created by matching with the T2DM group on age and sex. Table 2 presents the age-group and sex distribution based on 1:1 matching between patients with T2DM and those without diabetes. The Table 2 data show that although patients with T2DM and patients without diabetes were matched by age group and sex, patients with and without MVD within the T2DM group and nondiabetic group were not matched on these variables.

Table 3 displays the characteristics of the groups based on diabetes and MVD status. The mean age ± standard deviation of patients with T2DM was 51.7 ± 8.6 years, whereas the mean age ± standard deviation of patients without diabetes was 51.1 ± 8.5 years. The T2DM group had a higher proportion of male patients (54.7%). Patients with MVD and T2DM were, on average, a year younger than patients with MVD but without diabetes (54.55 ± 6.9 years vs. 55.55 ± 6.6 years, P < 0.001). Patients with T2DM but without MVD were nearly the same age as patients without diabetes or MVD (50.44 ± 8.6 vs. 50.58 ± 8.5 years, P = 0.092). Of the total study population, patients with MVD were significantly older than patients without MVD (54.82 ± 6.9 vs. 50.45 ± 8.4 years, P < 0.001). Nearly half of all members were women (45.3%), but in both groups, patients with MVD were less likely to be women (38.8% of patients with T2DM and 33.8% of the control group).

Table 4 shows that the annual medical cost for patients with T2DM and MVD was significantly (as evidenced by nonover-
Total and Component Health Care Costs in a Non-Medicare HMO Population of Patients With and Without Type 2 Diabetes and With and Without Macrovascular Disease

<table>
<thead>
<tr>
<th>TABLE 3 Characteristics of Patient Groups</th>
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<tbody>
<tr>
<td>Characteristic</td>
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<tr>
<td>N</td>
</tr>
<tr>
<td>Baseline age ± SD*</td>
</tr>
<tr>
<td>Women (%)</td>
</tr>
<tr>
<td>Obesity (%)</td>
</tr>
<tr>
<td>Nephropathy (%)</td>
</tr>
<tr>
<td>Neuropathy (%)</td>
</tr>
<tr>
<td>Retinopathy (%)</td>
</tr>
<tr>
<td>Other metabolic diseases (%)</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
</tr>
</tbody>
</table>

* Age is not significantly different between the cohorts with T2DM and without diabetes; however, within both cohorts, age is significantly different between those who did and did not experience MVD (P < 0.001).

MVD=macrovascular disease; T2DM=type 2 diabetes mellitus.

A retrospective study design using eligibility data and medical and pharmacy claims was used to determine the impact of MVD on the mean annual costs incurred by patients with T2DM and patients with no diabetes. The results show that patients with MVD experience significantly higher annual medical costs. Annual health care costs incurred for patients with both T2DM and MVD were 7.7 times greater than those for patients with neither diabetes nor MVD, 3 times greater than those for patients with T2DM but without MVD, and almost twice those of patients without diabetes but with MVD. When MVD occurs in patients with T2DM, it is more expensive when compared with MVD in patients without diabetes.

MVD remains a common and costly comorbidity in T2DM. Diabetes markedly elevates the risk for MVD, and, according to ADA, diabetes-related cardiovascular disease directly accounts for $500 million yearly in lost productivity. In addition to these indirect costs associated with lost productivity, it is important to have accurate estimates of the direct costs of care for T2DM and MVD. Such cost data allows policymakers and health plans to estimate the savings that might be achieved by investing in early intervention and preventive programs.

The annual cost for patients with T2DM and MVD in 2004 dollars was $10,450 (95% CI, $9,692-$11,279) PPPY for patients with T2DM and MVD compared with $6,090 (95% CI, $5,331-$6,862) PPPY for patients with T2DM and MVD compared with $6,090 (95% CI, $5,331-$6,862) PPPY for patients with T2DM and MVD compared with $6,090 (95% CI, $5,331-$6,862) PPPY for patients with T2DM and MVD compared with $6,090 (95% CI, $5,331-$6,862) PPPY for patients with T2DM and MVD.

The annual cost for patients with T2DM and MVD was significantly (as evidenced by nonoverlapping CIs) higher than for patients without diabetes but with MVD for all categories of costs. The annual cost for patients without diabetes but with MVD was $6,090 (95% CI, $5,331-$6,862) PPPY for patients with T2DM and MVD compared with $7,915; however, there are differences between the 2 studies.

The annual cost for patients without diabetes but with MVD was $6,090 (95% CI, $5,331-$6,862) PPPY for patients with T2DM and MVD compared with $7,915; however, there are differences between the 2 studies. Our estimates are conservative since we excluded costs relating...
Total and Component Health Care Costs in a Non-Medicare HMO Population of Patients With and Without Type 2 Diabetes and With and Without Macrovascular Disease

Table 4: One-Year Health Care Costs in 2004 Dollars by Diabetes and MVD Status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>T2DM Group (95% CI)</th>
<th>Comparison Group Without Diabetes (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVD status</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MVD</td>
<td>No MVD</td>
</tr>
<tr>
<td>N</td>
<td>2,441</td>
<td>6,618</td>
</tr>
<tr>
<td>Pharmacy costs ($)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>3,032 (2,924-3,143)</td>
<td>1,861 (1,813-1,914)</td>
</tr>
<tr>
<td>% of total cost</td>
<td>29.0%</td>
<td>55.0%</td>
</tr>
<tr>
<td>Median</td>
<td>3,031</td>
<td>1,861</td>
</tr>
<tr>
<td>Outpatient costs ($)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>1,730 (1,522-1,984)</td>
<td>533 (495-576)</td>
</tr>
<tr>
<td>% of total cost</td>
<td>16.6%</td>
<td>15.7%</td>
</tr>
<tr>
<td>Median</td>
<td>1,723</td>
<td>532</td>
</tr>
<tr>
<td>Inpatient costs ($)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>4,583 (4,027-5,225)</td>
<td>584 (483-695)</td>
</tr>
<tr>
<td>% of total cost</td>
<td>43.9%</td>
<td>17.3%</td>
</tr>
<tr>
<td>Median</td>
<td>4,572</td>
<td>582</td>
</tr>
<tr>
<td>Ancillary costs ($)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>1,086 (998-1,180)</td>
<td>407 (382-431)</td>
</tr>
<tr>
<td>% of total cost</td>
<td>10.4%</td>
<td>12.0%</td>
</tr>
<tr>
<td>Median</td>
<td>1,085</td>
<td>407</td>
</tr>
<tr>
<td>Total costs ($)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>10,450 (9,692-11,279)</td>
<td>3,385 (3,232-3,546)</td>
</tr>
<tr>
<td>Median</td>
<td>10,432</td>
<td>3,387</td>
</tr>
</tbody>
</table>

CI = confidence interval; MVD=macrovascular disease; T2DM=type 2 diabetes mellitus.

to injuries, pregnancies, neoplasms, etc., whereas the other study did not exclude these costs. Moreover, all of our study sample were aged between 30 to 65 years and represented a younger population. Nearly half of the sample in the study by Nichols and Brown was aged 65 years and above and therefore represented an older population. Since many of the national statistics indicate that the largest burden of illness is in those older than 60 years, our data illustrate the substantial cost of illness associated with T2DM and MVD in a younger, working-age population.

Our findings show that inpatient costs were higher as a proportion of total costs for patients with both T2DM and MVD (44%) compared with patients with T2DM but without MVD (17%). Pharmacy costs represented the largest cost component (55%) in patients with T2DM but without MVD. Although the actual percentages vary, the results are comparable with those of a large Pacific Northwest HMO in which inpatient costs represented 51% of total costs in persons with diabetes and CVD compared with 31% in persons with diabetes but without CVD. Inpatient cost for persons with MVDs ranged from 44% to 49%, whereas those for persons without MVD were in the range of 15% to 17%, regardless of the presence of diabetes. The finding that inpatient costs represent a large proportion of the annual medical costs in patients with MVD is consistent with earlier studies. These studies also suggest that much of the added cost of MVDs results from hospitalizations for heart attacks, heart failure, and other major cardiovascular events.

Patients with MVD tended to be significantly older when compared with those without MVD (55 years versus 51 years) regardless of the presence of diabetes. Therefore, it is possible that the increased costs seen in these patients could be related to patients being older. However, since the HMO population in the present study represented a younger, employed population, and those with MVD were on average only 4 years older when compared with those without MVD, age is not likely to fully explain the large cost differential.

Observations from MCOs suggest that annual management costs for patients with diabetes are 1.5 to 2 times higher than those for patients without diabetes. Glauber and Brown estimated that the HMO spent 4.5 times per person more on CVD care for members with diabetes than for members without diabetes. As diabetes-related complications develop and progress, care management costs increase. Our findings show that direct medical costs for patients with both T2DM and MVD were 3 times higher than the costs incurred for patients with...
T2DM but without MVD. The HMO in the present study spent nearly 2 times more on MVD care in patients with T2DM than in patients without T2DM. The cost differential between patients with T2DM with MVD and without MVD was on the order of $7,065 PPPY ($10,450-$3,385). The large difference in costs between all 4 patient groups (among patients with T2DM and MVD, patients with T2DM but without MVD, patients without T2DM but with MVD, and patients without T2DM and MVD) was an expected result of this study. The magnitude of the cost differential is suggestive of the cost savings potential from initiatives aimed at preventing macrovascular events.

An important consideration in this analysis is that we could not detect undiagnosed T2DM in the control population. If T2DM was undetected in this population, especially among those with MVD, then the estimated costs of MVD might be understated in the T2DM group and overstated in the control group. Although patients with T2DM and patients without diabetes were matched by age group and sex, patients with and without MVD for comparisons within the T2DM population were not matched on age group and sex. Thus, in these data, patients with T2DM but without MVD are more likely to be recently diagnosed diabetic patients with potentially lower costs.

The relative proportion of inpatient hospital costs in patients with T2DM—43.9% for patients with MVD versus 17.3% for patients without MVD—suggests the potential value of disease management interventions to encourage effective prevention and treatment of MVD. Considerable evidence suggests that strategies such as primary and secondary prevention of coronary artery disease, control of blood pressure, and control of lipids provide more clinical benefits at less cost on a population basis. Strategies targeted at preventing the onset of T2DM or delaying the progression of its complications could produce substantial savings to the health care system. The findings from this study may be helpful in framing the context for measuring the economic implications of various interventions, such as disease management programs or newer drug therapies designed to improve glycemic control and other clinical outcomes in diabetic patients with T2DM.

**Limitations**

Patients with both incident and prevalent T2DM and MVD were included in this analysis. This means that at the initial observation point in our analysis, the patients were mixed with respect to duration of their disease. Our findings are, however, a likely reflection of a steady state that one would expect to find within the given population, but the findings are less useful for estimating lifetime disease burden. Also, the patients with the conditions studied may have more health care use than controls simply because of opportunities for contact with the system. This is probably minimized by the requirement that all comparison patients without diabetes had at least 1 outpatient visit. We also note that we were unable to match the comparison group on other patient characteristics, such as race/ethnicity, income level, region, etc., since this information was not available in the database.

This is a descriptive cost analysis only. Outcomes data, such as hemoglobin A1c laboratory values, blood pressure measurements, body weight, and lipid levels, would provide additional value to the study results. Other potentially valuable patient characteristics, such as body mass index and vital signs at office visits, were also unavailable. The descriptive analyses reported in this study do not control for comorbidities among the different groups. Choosing a comparison group based on propensity score matching would allow for a better comparison of costs between the groups, while simultaneously controlling for a variety of factors that may drive costs. However, propensity score matching only controls for known or measurable factors. Although we report the proportion of patients with a claim for obesity as comorbidity, it should be recognized that obesity is quite likely underreported in administrative claims, except in the case of morbid obesity, and therefore may not present a true picture of the prevalence of the condition. Nevertheless, the relative proportion of patients with a diagnosis code for obesity among the 4 patient groups and between the 2 groups with and without T2DM provides some additional indication of comorbidity.

The cost findings in the present study are most likely not generalizable to all patients with T2DM. Treatment patterns for this disease may differ according to individual physician practice styles, health plan guidelines, and geographic region. Any out-of-pocket expenditures that resulted from the use of diabetes- and cardiovascular-related services by the HMO members were not captured by the claims data and therefore were not included in the study, resulting in analyses primarily from the health plan perspective. It is important to note that the analysis focuses exclusively on direct medical costs and hence does not include other costs associated with T2DM and MVD such as productivity costs and caregiver burden.

The results are based on claims data collected for administrative purposes, primarily payment of claims. Due to inaccuracies in the coding of services and diagnoses, some patients and services provided may have been miscoded and/or misclassified. The use of medical claims data also precludes the use of patient assessments, and, as a result, the analysis cannot examine quality of life, functional status, or any other clinical outcomes. Also, because claims data are available only for a limited period of time for each patient, it was not possible to ascertain the length of time since initial diagnosis of T2DM. Thus, the present study is also limited by the inability to control for duration of T2DM.

The results of this study may not be generalizable to other populations. The sample consisted of continuously enrolled members of an East Coast HMO who had a pharmacy benefit. These individuals may not be similar to individuals who are not
employing or have not been continuously enrolled in the same health plan for at least 2 years. The generalizability of the results is also limited by the geographic and demographic characteristics of the study population. For example, it was necessary to set an upper age limit of 65 years to remove the Medicare patient population because their medical benefits are typically different from those of the commercial population, and the coordination of payment between Medicare and supplemental or other private payment hinders the ability to capture all relevant claims data.

Conclusions

Direct medical costs aggregated for HMO members with T2DM and MVD are 1.7 times higher than for HMO members with MVD but without diabetes. This analysis of administrative claims data for HMO members between the ages of 30 and 65 years also suggests that MVD may triple the total medical care costs in patients with T2DM. These economic consequences would appear to support the importance of interventions intended to prevent macrovascular events in patients with T2DM.

DISCLOSURES

No outside funding supported this research. Author Shravanthi R. Gandra discloses that a portion of the work in this article was part of her doctoral dissertation when she was a doctoral candidate at the University of Louisiana at Monroe. The coauthors, Lesa W. Lawrence, Bhash M. Parasuraman, Robert M. Darin, Justin J. Sherman, and Jerry L. Wall disclose no potential bias or conflict of interest relating to this article. Gandra served as principal author of the study. Study concept and design were contributed by all authors. Data collection was the work of Gandra; data interpretation was primarily the work of Gandra, Darin, and Sherman, with input from the coauthors. Writing of the manuscript was the work of Gandra; its revision was the work of Lawrence, Parasuraman, and Wall, with input from the coauthors.

REFERENCES

ABSTRACT

BACKGROUND: Treatment options for the management of rheumatoid arthritis (RA) have expanded from the traditional disease-modifying antirheumatic drugs (DMARDs) to include the biologic DMARDs that inhibit tumor necrosis factor-alpha (TNF-α).

OBJECTIVE: To assess the medical literature for studies of the economic value of biologic DMARDs, specifically the 3 TNF-α inhibitors (adalimumab, etanercept, and infliximab) used for the management of RA, compared with the traditional DMARDs such as sulfasalazine, antimalarials, penicillamine, gold, methotrexate, azathioprine, leflunomide, and cyclophosphamide.

METHODS: A comprehensive search of the MEDLINE and HealthSTAR databases was conducted to identify cost-utility, cost-effectiveness, or cost-utility studies published in the English language (from 1966 through November 2004). The search terms and/or MeSH (medical subject headings) titles were cost-benefit analysis, rheumatoid arthritis, antirheumatic agents, antineoplastic and immunosuppressive agents. Studies were critically reviewed and quality was assessed using the Quality of Health Economic Studies instrument. Most studies evaluated the use of biologics among RA patients resistant to DMARDs. Studies were assessed with regard to comparators evaluated, measures of efficacy, perspectives, model duration, treatment duration, and discount rate.

RESULTS: From 180 titles identified, 155 were excluded for the following reasons: 89 because they did not consider the drugs of interest, 15 because the population was not RA, 19 because of having the wrong drugs and population, 22 because they were review articles, and 10 because they were general articles. Twenty-five abstracts were accepted for further review. Of these, 13 abstracts were subsequently selected for full-text review. One of the authors identified a study not indexed in MEDLINE. Ultimately, 2 cost-effectiveness and 6 cost-utility studies were selected for this critical review. One study over 6 months reported that triple therapy with DMARDs (methotrexate-hydroxychloroquine-sulfasalazine) was cost effective for methotrexate-resistant patients, which is consistent with American College of Rheumatology (ACR) guidelines that support the use of triple therapy prior to biologics. The incremental cost-effectiveness ratio (ICER) was $1,500 per patient to achieve an ACR20 response for this triple therapy compared with no-second-line agent. Overall, biologic therapies cost considerably more than traditional DMARDs but produced more quality-adjusted life-years (QALYs). Despite differences in design and assumptions, published economic models consistently reported ICERS <$50,000 per QALY gained for biologics compared with traditional DMARDs, although ICERS of >$100,000 were reported from sensitivity analyses.

CONCLUSIONS: Clinical guidelines currently recommend the use of biologics as step therapy after failure of traditional DMARDs. Reported ICERS comparing biologics with traditional DMARDs are within a range that is comparable with other accepted medical interventions. The worth of the additional expenditure will ultimately be judged by formulary and policy decision makers because no maximum cost has been defined. Models can be used to inform decision makers, but they must be interpreted and applied carefully. More research is also needed to differentiate the relative economic value of the various biologic agents by therapeutic indication.

KEYWORDS: Cost-effectiveness, Cost-utility, Rheumatoid arthritis, Biologics, DMARDs, Anti-TNF-α

J Manag Care Pharm. 2006;12(7):555-69

Review of Eight Pharmacoeconomic Studies of the Value of Biologic DMARDs (Adalimumab, Etanercept, and Infliximab) in the Management of Rheumatoid Arthritis

QUAN V. DOAN, PharmD; CHIUN-FANG CHIOU, PhD; and ROBERT W. DUBOIS, MD, PhD

Rheumatoid arthritis (RA) is a systemic chronic inflammatory condition that presents with joint swelling, tenderness and inflammation. The prevalence of RA in North America is estimated to be 0.5%-1.0%.1 As joint damage progresses over time, patients experience increasing levels of disability. Consequently, RA imposes a substantial economic burden on society. The direct and indirect medical costs for RA were estimated to be $26 to $32 billion per year in the United States in 1998 dollars.2

The American College of Rheumatology (ACR) established that the goals of managing RA are to prevent or control joint damage, prevent loss of function, and decrease pain.3 Treatment options for RA historically have included nonsteroidal anti-inflammatory drugs, analgesics, corticosteroids, and traditional disease-modifying antirheumatic drugs (DMARDs). Traditional DMARDs include drugs such as sulfasalazine, antimalarials, penicillamine, gold, methotrexate, azathioprine, leflunomide, and cyclophosphamide. Disease activity is evaluated periodically, and the regimen is adjusted based on clinical response.3 The effectiveness of traditional DMARDs may decrease as the disease progresses or when patients experience adverse effects that require switching.

Once patients fail at least 2 standard DMARD therapies, one of which includes methotrexate, they are potential candidates for biologic therapies per the recommendations of the British Society of Rheumatology (BSR) guidelines.4 Since the late 1990s, the most studied class in the drug armamentarium for RA is biologic DMARDs, which inhibit tumor necrosis factor-alpha (TNF-α inhibitors; see Table 1). TNF-α is a cytokine present in the rheumatoid joints and is involved in the abnormal inflammatory and immune responses that occur with RA. Biologics can offer better clinical response compared with...
traditional DMARDs,\,* but they are associated with greater costs (including costs of drugs and of health resource utilization). These costs, when accumulated over the duration of the condition, are of interest to potential payers.

In recent years, a number of evaluations have assessed the economic value of biologics for the management of RA. Several review papers have been published based on this body of literature, which either focused on comparing the underlying methodologies across studies or provided a review of a single biologic.\,*\,* In contrast, the present review aims to provide decision makers with the results of research performed to determine the potential economic value of biologic DMARDs (i.e., TNF-\(\alpha\) inhibitors) and to highlight special considerations when interpreting results for formulary decisions. Specifically, the objective of this article is to provide a comprehensive review of the literature on cost-effectiveness analyses (CEAs) and cost-

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>FDA-Approved Indications for TNF-(\alpha) Inhibitors</th>
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<tbody>
<tr>
<td>TNF-(\alpha) Inhibitor</td>
<td>FDA-Approved Indication</td>
</tr>
</tbody>
</table>
| Infliximab* | Rheumatoid arthritis:  
| | • Infliximab, in combination with methotrexate, is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis.  
| | Crohn's disease:  
| | • Infliximab is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy.  
| | • Infliximab is indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease.  
| | Ankylosing spondylitis:  
| | • Infliximab is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.  
| | Psoriatic arthritis:  
| | • Infliximab is indicated for reducing signs and symptoms of active arthritis in patients with psoriatic arthritis.  
| | Ulcerative colitis:  
| | • Infliximab is indicated for reducing signs and symptoms, achieving clinical remission and mucosal healing, and eliminating corticosteroid use in patients with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy. |
| Etanercept† | Rheumatoid arthritis:  
| | • Etanercept is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis. Etanercept can be initiated in combination with methotrexate or used alone.  
| | Polyarticular-course juvenile rheumatoid arthritis:  
| | • Etanercept is indicated for reducing signs and symptoms of moderately to severely active polyarticular-course juvenile rheumatoid arthritis in patients who have had an inadequate response to one or more DMARDs.  
| | Psoriatic arthritis:  
| | • Etanercept is indicated for reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis.  
| | • Etanercept can be used in combination with methotrexate in patients who do not respond adequately to methotrexate alone.  
| | Ankylosing spondylitis:  
| | • Etanercept is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.  
| | Psoriasis:  
| | • Etanercept is indicated for the treatment of adult patients (18 years or older) with chronic moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. |
| Adalimumab‡ | Rheumatoid arthritis:  
| | • Adalimumab is indicated for reducing signs and symptoms, including major clinical response, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. Adalimumab can be used alone or in combination with methotrexate or other DMARDs.  
| | Psoriatic arthritis:  
| | • Adalimumab is indicated for reducing signs and symptoms of active arthritis in patients with psoriatic arthritis. Adalimumab can be used alone or in combination with DMARDs.  
| | Ankylosing spondylitis:  
| | • Adalimumab is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis. |

DMARDs = disease-modifying antirheumatic drugs; FDA = U.S. Food and Drug Administration; TNF-\(\alpha\) = tumor necrosis factor-alpha.
utility analyses (CUAs) of biologic DMARD treatments for RA, specifically for the 3 TNF-α inhibitors (adalimumab, etanercept, and infliximab).

The TNF-α inhibitors adalimumab, etanercept, and infliximab (the latter only in combination with methotrexate) are recommended as options for the treatment of adults who have both of the following characteristics: (1) continuing clinically active and severe RA as measured by disease activity score (DAS28) >5.1 (i.e., highly active disease)—disease activity should be measured at 2 time points, 1 month apart, confirming ongoing active disease; and (2) have received at least 2 adequate trials of DMARDs, including methotrexate (unless contraindicated).

### TABLE 2  Comparison of Study Characteristics

<table>
<thead>
<tr>
<th>Comparators</th>
<th>Choi et al., 2002&lt;sup&gt;19&lt;/sup&gt;</th>
<th>Choi et al., 2000&lt;sup&gt;18&lt;/sup&gt;</th>
<th>Wong et al., 2002&lt;sup&gt;21&lt;/sup&gt;</th>
<th>Kobelt et al., 2003&lt;sup&gt;23&lt;/sup&gt;</th>
<th>Chiu et al.,† 2004&lt;sup&gt;22&lt;/sup&gt;</th>
<th>Kobelt et al., 2004&lt;sup&gt;24&lt;/sup&gt;</th>
<th>Brennan et al., 2004&lt;sup&gt;28&lt;/sup&gt;</th>
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</table>

* Based on definition of model population or population from the source clinical trial(s) used by the model.
† Unless specified, discount rates for costs and effectiveness are the same.
‡ The study by Chiu et al. was not indexed by MEDLINE.
§ The sponsor of this study was not specified in the publication.
AE = adverse effect; DMARDs = disease-modifying antirheumatic drugs; MTX = methotrexate.
Methods

A comprehensive literature search of the MEDLINE and HealthSTAR databases was conducted using cost-benefit analysis, rheumatoid arthritis, antirheumatic agents, and antineoplastic and immunosuppressive agents as search terms and/or MeSH (medical subject headings) titles (from 1966 through November 2004). Published articles that conducted a formal cost-efficacy, cost-effectiveness, or cost-utility analysis of adalimumab, etanercept, or infliximab in RA were included. Studies were excluded if they were not in the relevant population, did not include the interventions of interest, were not in the English language, did not involve human subjects, or were review articles. After a review of the titles and abstracts, 7 full-text papers were obtained for all relevant studies. One additional study published in a pharmacoeconomics journal that was not indexed in MEDLINE or HealthSTAR was included based on the recommendation of one of the authors (Chiou). Data were collected on the comparators studied, patient characteristics, data sources, model assumptions, costs, effectiveness, and incremental cost-effectiveness ratios (ICERs).

These studies reported costs from different years and in different currencies. To reduce the variation, costs were reported in 2 ways: (1) expressed as the value documented in the year when the analysis was conducted and (2) converted to 2004 U.S. dollars (USD) using the medical care component of the Consumer Price Index (CPI) for studies done in prior years. For studies that expressed costs in currencies other than USD, a currency exchange rate was applied to convert their values into USD, and then the CPI was applied to adjust costs to their 2004 values. In this article, costs represent the values in the base year during which the authors conducted their models and/or analyses. Where indicated, adjusted costs represent values in 2004 USD.

Because the value of a reported ICER depends on which reference comparator was chosen, large differences could be observed across studies that employed different methods of calculation. For this review, 2 methods were used to standardize the reporting of the ICERs. In the first method, comparators were rank ordered from the least to the most costly. Alternatives that were both more costly and less effective than another option (i.e., dominated) were eliminated from consideration. ICERs were calculated and reported among the remaining alternatives. Alternatively, the ICERs were calculated using a common reference comparator; in most instances, the comparator was methotrexate.

Results

From a total of 180 titles identified, 155 were excluded for the following reasons: 89 because they did not consider the drugs of interest, 15 because the population was not RA, 19 because they had the wrong drugs and population, 22 because they were review articles, and 10 because they were general articles. Twenty-five abstracts were accepted for further review. Of these, 13 were subsequently selected for full-text review. Three of the 13 were excluded because the drugs of interest were not included. Another 3 of the 13 were excluded because they were review articles. One of the authors identified a study not indexed in MEDLINE. Ultimately, 2 cost-effectiveness and 6 cost-utility studies were selected for this critical review. Two were CEAs, which defined effectiveness based on ACR criteria. ACR 20 was defined as ≥20% improvement in tender and swollen joint counts and ≥20% improvement in 3 of 5 other core measures: patient’s global assessment, physician’s global assessment, physical disability score, acute-phase reactant value, and patient’s assessment of pain. The remaining studies were CUA, which defined effectiveness as quality-adjusted life-years (QALYs). Table 2 shows distinct variation across studies in terms of comparators evaluated, perspectives, model duration, treatment duration, and discount rate.

Using the QHES instrument, all studies achieved scores of ≥78, and scores ranged from 78 to 92 (Table 3). Studies with lower scores tended to evaluate RA over a time period of <1 year, did not discuss direction and magnitude of potential biases, and/or did not adequately present study limitations.

Cost-Effectiveness Studies:

Cost per Patient Achieving ACR Response

Choi et al. conducted 2 CEAs; one study involved a population naive to methotrexate treatment, and the other involved a population resistant to methotrexate. The ACR and BSR guidelines recommend the use of biologics after failure to respond to traditional DMARDs. Therefore, the results of the study among methotrexate-naive patients should not be given much weight, although we have summarized them here for completeness.
Both analyses used a decision tree to model events that may occur within 6 months of initiation of various therapies (Table 4). Outcomes in the models were based on ACR response and the occurrence of toxicity related to each therapy.

Among a methotrexate-naïve population, Choi et al. compared the cost-effectiveness of etanercept, leflunomide, methotrexate, and sulfasalazine compared with no second-line agent (Table 4). When the effectiveness measure was defined

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**TABLE 3: Quality of Health Economic Studies (QHES)**

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</tbody>
</table>

* + Study met the criterion.
* – All or part of the criterion was not met.
* Sixteen criteria of the Quality of Health Economic Studies (QHES) instrument:
  1. Was the study objective presented in a clear, specific, and measurable manner? (7 points)
  2. Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated? (4 points)
  3. Were variable estimates used in the analysis from the best available source (i.e., Randomized Control Trial—Best, Expert Opinion—Worst)? (8 points)
  4. If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study? (1 point)
  5. Was uncertainty handled by: 1) statistical analysis to address random events; 2) sensitivity analysis to cover a range of assumptions? (9 points)
  6. Was incremental analysis performed between alternatives for resources and costs? (6 points)
  7. Was the methodology for data abstraction (including value health states and other benefits) stated? (5 points)
  8. Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond one year discounted (3%-5%) and justification given for the discount rate? (7 points)
  9. Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described? (8 points)
  10. Were the primary outcome measure(s) for the economic evaluation clearly stated and were the major short term, long term and negative outcomes included? (6 points)
  11. Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used? (7 points)
  12. Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear transparent manner? (8 points)
  13. Were the choice of economic model, main assumptions and limitations of the study stated and justified? (7 points)
  14. Did the author(s) explicitly discuss direction and magnitude of potential biases? (6 points)
  15. Were the conclusions/recommendations of the study justified and based on the study results? (8 points)
  16. Was there a statement disclosing the source of funding for the study? (3 points)
as either the ACR20 or the ACR70 weighted response, methotrexate was the lowest-cost option and etanercept was the highest-cost option. The least effective option was no second-line agent at 0.27, and the most effective option was etanercept at 0.68. Compared with methotrexate, etanercept was associated with an ICER of $40,300 per patient with an ACR20 response ($49,900, 2004 USD) over a 6-month period (Table 5). This is interpreted as the additional cost per patient to achieve an ACR20 response. In 1-way sensitivity analyses, the ICER per patient achieving ACR20 improvement for etanercept was greater than $39,000 unless the cost of etanercept was reduced or the probability of achieving ACR20 response was increased. When the baseline cost of etanercept ($6,600) was reduced by 25% and 50%, the ICERs compared with methotrexate were $28,400 and $15,000, respectively, per ACR20. When the probability of achieving ACR20 (81%) was increased by 20%, the ICER was $17,700 compared with methotrexate.

Among methotrexate-resistant patients, Choi et al. analyzed

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**TABLE 4** Characteristics of Cost-Effectiveness Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Objective</th>
<th>Model Assumptions</th>
<th>Data Source: Costs</th>
<th>Data Source: Effectiveness</th>
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</thead>
<tbody>
<tr>
<td>Methotrexate-naïve patients</td>
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</table>
| Choi et al., 2002<sup>19</sup> | To determine the cost-effectiveness of treatment options including etanercept (25 mg BIW), leflunomide (20 mg QW), MTX (15 mg QW), sulfasalazine (2 gm QW), and no second-line agent for patients naïve to MTX | • Similarities in baseline patient characteristics in the source trials  
• Toxicity probabilities for sulfasalazine were the same as those for MTX  
• Adverse effects associated with leflunomide or etanercept are negligible  
• Monitoring costs for etanercept were the same as those of no second-line agent  
• Linear relationship between work capacity and HAQ score | Monitoring costs: Obtained from published estimates. Where published estimated costs were not available, cost estimates were based on recommendation from the ACR monitoring guidelines lab monitoring components (1999 Clinical Diagnostic Laboratory Fee Schedule of the Health Care Financing Administration).  
Medication costs: AWP average wholesale price from 1999 Redbook  
Inpatient surgical costs: Developed an exponential relationship between HAQ score and inpatient surgery costs  
Indirect costs: Used a HAQ-based indirect cost assignment using the same HAQ efficacy estimates used for estimating surgery costs | • ACR response data for all considered treatment options were taken from source clinical trials |

| Methotrexate-resistant patients | | | | |
| Choi et al., 2000<sup>18</sup> | To determine the cost-effectiveness of treatment options including MTX, etanercept, MTX + etanercept, MTX + cyclosporine, MTX + hydroxychloroquine + sulfasalazine, and no second-line agent) for patients resistant to MTX | • Similarities in baseline patient characteristics in the source trials  
• Combination therapies were associated with no more adverse effects than MTX monotherapy | Monitoring costs: Obtained from published estimates. Where published estimated costs were not available, cost estimates were based on recommendations from the ACR monitoring guidelines. For lab monitoring components (1999 Clinical Diagnostic Laboratory Fee Schedule of the Health Care Financing Administration).  
Medication costs: AWP from 1999 Redbook  
Indirect costs: Used a HAQ-based indirect cost assignment using the same HAQ efficacy estimates used for estimating surgery costs | • Efficacy data based on 3 double-blind, randomized controlled trials and 1 open trial  
• The participants in 3 of the 4 trials were RA patients with inadequate responses to MTX  
• In 1 of the 4 trials, 90% of the participants were categorized as having inadequate response to MTX |

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ACR = American College of Rheumatology, AWP = average wholesale price, BIW = twice per week, HAQ = Health Assessment Questionnaire, MTX = methotrexate, QW = daily, RA = rheumatoid arthritis.

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Review of Eight Pharmacoeconomic Studies of the Value of Biologic DMARDs (Adalimumab, Etanercept, and Infliximab) in the Management of Rheumatoid Arthritis

Efficacy data were based on 3 double-blind randomized controlled trials (RCTs) and 1 open-label trial. ACR response data were collected from the source clinical trials and used to estimate the probabilities of achieving an ACR response for each of the comparators. The authors assumed that patient characteristics in the source trials were similar based on similar RA duration and Health Assessment Questionnaire (HAQ) disability score. HAQ assesses arthritis-related functional disability in activities such as dressing, arising, eating, walking, hygiene, and reaching and gripping. The HAQ score ranges from 0 to 3; a higher score indicates greater disability. Also, combination therapies were assumed to be associated with no more adverse effects than methotrexate monotherapy, which was suggested by findings from individual trials. Defining ACR20 as the effectiveness measure resulted in the “no second-line agent” option being the lowest cost and least cost-effective option, and methotrexate plus etanercept being the highest-cost and most cost-effective option, over the 6-month model duration (Table 5).

Cost-Utility Studies: Cost per QALY Gained
Six studies used QALYs as the effectiveness measure. Of these, 2 were conducted in the United States and 4 were in other countries. These economic models were based on studies that evaluated RA patients who failed at least 1 DMARD and/or who were methotrexate-resistant. Because of inadequate response to previous trial(s) of DMARDs, patients entering these models were considered eligible for biologics.

U.S. Studies
Wong et al. (Table 6) compared methotrexate alone with infliximab plus methotrexate in patients with active, refractory RA. A Markov model was constructed based on pairwise combinations of treatments and disability levels, as measured by the HAQ and death. Two key assumptions were that mortality increased by 1.77-fold for each increase in disability level and that infliximab would be discontinued after 54 weeks of therapy; those patients would then receive methotrexate, but clinical benefit would
### TABLE 6  Characteristics of Cost-Utility Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Objective</th>
<th>Model Specifications and Assumptions</th>
<th>Data Source: Costs</th>
<th>Data Source: Effectiveness</th>
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</table>
| Wong et al., 2002*             | To estimate the cost-effectiveness of infliximab + methotrexate (≥12.5 mg/week) compared with methotrexate (≥12.5 mg/week) alone for patients with active and refractory RA | • Markov model with 21 states of health based on pairwise combination of 3 treatments (MTX + infliximab, MTX + DMARD, MTX + DMARD, and corticosteroid or NSAID)  
  • Four disability levels as measured by the HAQ (no, mild, or advanced impairment, and death)  
  • Treatment according to ATTRACT protocol during 1st year. After, the disability score and current treatment affected the likelihood of whether the disability level improved, worsened, or stayed the same over 6-month periods.  
  • HRQoL was assessed as self-reported global health using a visual analog scale (0 to 100), rescaled so that 0 = death and 100 = perfect health (Year 1 from ATTRACT, >Year 1 from ARAMIS).  
  • Mortality compared with an age-and sex-matched general population was 1.77-fold greater for each increase in disability level.  
  • Infliximab would be discontinued after 54 weeks of therapy and that patients would then receive MTX  
  • Clinical benefits diminished over time, not immediately at discontinuation of infliximab.  
  • Did not consider dose reductions for side effects or discontinuations. | Drug costs: Based on AWP, infusion administration costs, and pretreatment evaluation  
Direct costs: Taken from ATTRACT and included all non–protocol-related medical care costs  
Indirect costs: First year, taken from ATTRACT for the subset of patients who were employed at time of enrollment, remaining years, estimated as 1 or 3 times the direct costs | Year 1: Data from ATTRACT  
Remaining years: Data from ARAMIS. ARAMIS is a Post-Marketing Surveillance Program, which has prospectively enrolled 4,258 patients with RA who were followed for 17,085 patient-years at 8 representative North American clinical practices. |
| Chou et al., 2004**            | To estimate the direct costs and cost-effectiveness of biologic treatments for RA: (1) adalimumab (40 mg QW), (2) anakinra (100 mg QW), (3) etanercept (25 mg BIW), (4) methotrexate (15 mg QW) + adalimumab (40 mg QOW), (5) methotrexate (15 mg QW) + anakinra (100 mg QD), (6) methotrexate (15 mg QW) + etanercept (25 mg BIW), (7) methotrexate (15 mg QW) + infliximab (3 mg/kg QW with a loading dose of 8 doses/year) | • Did not include non–treatment-related adverse events, potential improvement in long-term clinical outcomes, or indirect costs  
• Effectiveness is measured at 6 months and 12 months.  
• Where 12-month effectiveness rates were not available, 6-month and 12-month effectiveness rates were assumed to be equivalent. | Drug costs: U.S. AWP  
2003 Healthcare Resource Costs: Obtained from the 2003 American Medical Association Current Procedural Terminology codebook, the 2003 Medicare Reimbursement Fee Schedule, and the Medstat Diagnosis-Related Group guide | Efficacy data based on 10 double-blind randomized controlled trials with comparable patient characteristics as selected by a panel of experts |
| Brennan et al., 2004**         | To assess the cost-effectiveness of etanercept monotherapy compared with current care consisting of a series of traditional DMARDs (IM gold, leflunomide, methotrexate plus cyclosporine) in accordance with BSR guidelines | • Patients had failed at least 2 DMARDs that included MTX and sulfasalazine. Patients on etanercept monotherapy can receive the traditional DMARD series if occurrence of adverse effects or lack of efficacy  
• Steroids are not modeled because they are low in cost and because normal use is alongside DMARDs rather than as alternatives.  
• Base-case analysis does not include home help, residential nursing home care costs, and worker productivity.  
• Clinical benefits diminished immediately upon discontinuation of etanercept.  
• Cycle length of 6 months | Drug costs: Derived from current list prices reported in the Monthly Index of Medical Specialities (MIMS) [United Kingdom]  
Drug monitoring: Estimated by costing BSR guidelines  
Direct costs: Included general practitioner, outpatient, and hospital  
Other direct costs: Included costs for general practitioner, outpatient services, and hospitalization  
Differences in HAQ scores between comparators were used to model differences in direct costs. | • Baseline characteristics for the population examined are based on the published etanercept monotherapy trial  
• Treatments are based on both the U.K. ERAS, and a commercially available electronic general practice database (DINLINK, Compufile). |

(continued on next page)
Review of Eight Pharmacoeconomic Studies of the Value of Biologic DMARDs (Adalimumab, Etanercept, and Infliximab) in the Management of Rheumatoid Arthritis

**TABLE 6** Characteristics of Cost-Utility Studies (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Objective</th>
<th>Model Specifications and Assumptions</th>
<th>Data Source: Costs</th>
<th>Data Source: Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kobelt et al., 2003</td>
<td>To estimate the cost-utility of infliximab (initial treatment at weeks 0, 2, 6, and 12, then given at either 3 mg/kg or 10 mg/kg dose every 4 or 8 weeks) plus methotrexate (≥12.5 mg QW) compared with methotrexate alone (≥12.5 mg QW) in inadequately controlled RA</td>
<td>• Treatment was stopped after 1 or 2 years, when no further clinical data were available, and no further treatment costs and effects were therefore assumed. &lt;br&gt; • NSAID usage was not included, as most patients used them and usage did not differ significantly between states. &lt;br&gt; • Clinical benefits diminished over time and not immediately at discontinuation of infliximab. &lt;br&gt; • Cycle length of 1 year</td>
<td>Cost of hospitalization: Based on the number of inpatient days in different wards and ward-specific daily costs &lt;br&gt; Surgical intervention: Calculated from the type of intervention and its duration multiplied by the cost per minute of operating theatre use &lt;br&gt; Outpatient care: Based on the number of visits to different health care professionals &lt;br&gt; Drug cost: Calculated from the number of months of use of each drug, associated with the cost of standard drug monitoring protocols in place in the rheumatology departments participating. Unit costs were taken from hospital accounting data and official price lists from National Health Service (U.K.) and University Hospital Lund (Sweden). &lt;br&gt; Indirect costs: Calculated using the human capital approach, in which an individual’s productivity is valued at the market price</td>
<td>Year 1: Data from the ATTRACT trial &lt;br&gt; Beyond year 1: Disease progression was modeled based on changes in HAQ scores from epidemiological cohorts called Lund Cohort Study (Sweden) and ERAS (U.K.).</td>
</tr>
<tr>
<td>Kobelt et al., 2004</td>
<td>To evaluate costs, benefits, and cost-effectiveness of etanercept or infliximab treatment over 1-year period compared with no biologic</td>
<td>• Comparator represented a group with costs and benefits that were established from baseline and were assumed to remain the same throughout the year. That is, comparison with another RA agent was not conducted. &lt;br&gt; • Improvement in utility occurred after 3 months of treatment (base case).</td>
<td>Structured interview: Obtained resource consumption and work capacity data for the year before treatment and the first anti-TNF year &lt;br&gt; Indirect costs: Estimated by human capital method using average annual gross salary; sick days and loss of productivity were included</td>
<td>Data collected from 116 patients recruited from 4 rheumatology centers in Sweden</td>
</tr>
<tr>
<td>Bansback et al., 2004</td>
<td>To conduct a cost-effectiveness analysis of adalimumab relative to different biologic and nonbiologic DMARDs in the treatment of moderate-to-severe RA</td>
<td>• Indirect comparisons were made between biologics because of lack of head-to-head trials. &lt;br&gt; • Investigators assumed that moderate DAS28 response and good DAS28 response correlated well to ACR20 and ACR50, respectively. &lt;br&gt; • Where there are limited data on ACR response rates for DMARDs, they were assumed to be equal to leflunomide. &lt;br&gt; • Clinical benefits diminished immediately upon discontinuation of biologic DMARDs. &lt;br&gt; • Two sets of analyses were conducted based on ACR20 and ACR50 responses.</td>
<td>Sources of cost data were not specified; health care resource utilizations were modeled as a function of HAQ-DI</td>
<td>Response rate: Data came from published articles and conference abstracts. &lt;br&gt; Adverse events: Obtained from observational study. &lt;br&gt; HRQol: HUI-3 was used to measure health utility in all adalimumab trials. Analysis of 2,000 patients from trial data allowed for linear transformation of disability (HAQ) to HRQol (HUI-3).</td>
</tr>
</tbody>
</table>

ACR20 = American College of Rheumatology 20% response criteria; ACR50 = American College of Rheumatology 50% response criteria; ARAMIS = Arthritis, Rheumatism, and Aging Medical Information System; ATTRACT = Anti-TNF Trial in Rheumatoid Arthritis trial; AWP = average wholesale price; BIW = twice weekly; BSR = British Society of Rheumatology; DAS28 = Disease Activity Score (including a 28-joint count); DMARDs = disease-modifying antirheumatic drugs; ERAS = Early Rheumatoid Arthritis Study; HAQ = Health Assessment Questionnaire; HAQ-DI = Health Assessment Questionnaire Disability Index; HRQol = health-related quality of life; HUI-3 = Health Utility Index-3; IM = intramuscular; MTX = methotrexate; NSAID = nonsteroidal anti-inflammatory drug; QD = daily; QOW = every other week; QW = every week; RA = rheumatoid arthritis; TNF = tumor necrosis factor.
Etanercept was deemed cost effective based on a hypothetical population of 10,000 patients in the United Kingdom. A Markov model was constructed with health states for patients not adequately controlled with traditional DMARDs plus methotrexate (Table 7) was both more costly and more effective compared with methotrexate alone, but the gains in QALYs were associated with a favorable cost-effectiveness profile. Results were qualitatively similar in the 1-year and 2-year analyses of biologic treatment.

In the study that was not indexed in MEDLINE, Chiou et al. (Table 6) modeled the cost utilities of various biologic DMARD monotherapies (adalimumab, anakinra, and etanercept) and combination therapies (methotrexate plus adalimumab, methotrexate plus anakinra, methotrexate plus etanercept, and methotrexate plus infliximab) among patients with moderate-to-severe RA. Etanercept was deemed cost effective based on an ICER of $13,387 per QALY gained as monotherapy ($13,985, 2004 USD) and an ICER of $7,925 per QALY gained when used in combination with methotrexate ($8,279, 2004 USD) (Table 7). This study showed that, with the exception of anakinra, treatment with etanercept plus methotrexate had similar cost ($18,954) and efficacy (0.6919 QALYs) as adalimumab plus methotrexate ($18,957 and 0.6608 QALYs). However, when compared with infliximab plus methotrexate ($20,071 and 0.5949 QALYs), etanercept plus methotrexate or adalimumab plus methotrexate were both less costly and more effective. Sensitivity analyses revealed that the cost of biologics and probabilities for achieving ACR response were the main drivers of incremental cost-effectiveness ratios. Because the cost-effectiveness of biologics relative to nonbiologic agents was not compared, the findings from this study cannot be directly compared with those of other studies.

**Swedish and United Kingdom Studies**

Four studies examined the cost-utility of biologics from a non-U.S. perspective. Kobelt et al. presented results from both the Swedish and U.K. perspectives. Brennan et al. provided only a U.K. perspective.

Kobelt et al. (2003) estimated the cost-utility of infliximab plus methotrexate compared with methotrexate alone in RA patients not adequately controlled with traditional DMARDs (Table 6). A Markov model was constructed with health states defined as functional disability levels (as measured by HAQ scores), and a death state. The model distributed patients into different health states based on whether their HAQ scores have improved, remained stable, or worsened, or if the patient died during the cycle. Although the duration of the model was 10 years, the treatment effects of biologics beyond 2 years were not modeled because long-term clinical data were not available. First-year efficacy data were taken from the ATTRACT (Anti-TNF Trial in Rheumatoid Arthritis with Concomitant Therapy) study, and data for years 2 through 10 were based on epidemiological observation of HAQ disability profile from the Swedish Lund Cohort study. The combination of infliximab plus methotrexate (Table 7) was both more costly and more effective compared with methotrexate alone, but the gains in QALYs were associated with a favorable cost-effectiveness profile. Results were qualitatively similar in the 1-year and 2-year analyses of biologic treatment.

In the same study, a separate analysis from the U.K. perspective was presented (Table 6). This model mirrored the Swedish model except that the long-term data beyond year 2 were based on a cohort from the Early RA Study in the United Kingdom. The combination of infliximab plus methotrexate was also found to be more expensive and more efficacious compared with methotrexate alone (Table 7). The ICER was calculated to be £21,600 (British pounds) per QALY gained ($48,710, 2004 USD).

Kobelt et al. (2004) evaluated the cost-effectiveness of etanercept or infliximab compared with routine clinical practice (i.e., without anti-TNF) for the treatment of patients with RA in Sweden (Table 6). Unlike other studies that were model-based analyses, this study collected actual data on direct and indirect costs, health-related quality of life (HRQoL), and HAQ scores from patients who were either resistant or intolerant of at least 2 traditional DMARDs including methotrexate. The authors concluded that the use of etanercept or infliximab in this population was cost effective because the ICER was below the generally accepted 50,000 EUR (Euros) per additional QALY gain threshold. The following yielded ICERs that did not exceed that threshold: sensitivity analyses conducted on the direct cost only, utility improvement after 6 weeks (instead of 3 months), and linear improvement in utility over 1 year. The ICERs surpassed this threshold only when an intent-to-treat analysis (including all dropouts) was conducted or when patients with low disability (HAQ score <1.6) at baseline were considered.

Bansback et al. conducted a lifetime CUA comparing adalimumab, etanercept, and infliximab as monotherapy and as combination therapy with methotrexate, compared with traditional DMARDs, from the perspective of a policy decision maker (Table 6). A hypothetical population of 10,000 patients who had failed to respond to a traditional DMARD and who were eligible for biologics entered the model. After failure with biologics, 3 other DMARDs were tried. Two versions of the model were created and analyzed based on patients achieving an ACR20 response and an ACR50 response, but these responses were translated to DAS28 response criteria. The results for adalimumab were based on the pooled results of 2 trials. HRQoL and costs were modeled as a function of the HAQ disability index. In the ACR50 version of the analysis, single and combination therapies with biologics were more costly but produced more QALYs compared with DMARDs. It is worth noting that the estimated QALY of <3 from this model was low considering that a lifetime analysis was conducted. In the base-case results, the ICERs were comparable across all biologics, but adalimumab plus methotrexate was the lowest at 34,922 EUR.
### TABLE 7 Results From Cost-Utility Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparator</th>
<th>Total Costs*</th>
<th>QALYs</th>
<th>Costs per QALY Gained**†</th>
<th>Costs per QALY Gained**‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate-resistant patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>U.S. studies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wong et al., 2002**1</td>
<td>MTX</td>
<td>$313,200 ($401,660)</td>
<td>9.11</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>MTX + infliximab</td>
<td>$315,800 ($404,994)</td>
<td>9.4</td>
<td>$9,100 ($11,670)</td>
<td>$9,100 ($11,670)</td>
</tr>
<tr>
<td>Chio et al., 2004**2</td>
<td>Anakinra</td>
<td>$17,412 ($18,190)</td>
<td>0.573</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Etanercept</td>
<td>$18,333 ($19,152)</td>
<td>0.6421</td>
<td>$13,387 ($13,985)</td>
<td>$13,387 ($13,985)</td>
</tr>
<tr>
<td></td>
<td>Adalimumab</td>
<td>$18,414 ($19,237)</td>
<td>0.5842</td>
<td>$91,927 ($96,034)</td>
<td>Dominated</td>
</tr>
<tr>
<td></td>
<td>MTX + anakinra</td>
<td>$18,045 ($18,851)</td>
<td>0.5772</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>MTX + etanercept</td>
<td>$18,954 ($19,801)</td>
<td>0.6919</td>
<td>$7,925 ($8,279)</td>
<td>$7,925 ($8,279)</td>
</tr>
<tr>
<td></td>
<td>MTX + adalimumab</td>
<td>$18,957 ($19,804)</td>
<td>0.6608</td>
<td>$10,909 ($11,397)</td>
<td>Dominated</td>
</tr>
<tr>
<td></td>
<td>MTX + infliximab</td>
<td>$20,071 ($20,968)</td>
<td>0.5949</td>
<td>$114,463 ($119,578)</td>
<td>Dominated</td>
</tr>
<tr>
<td><strong>U.K. studies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kobelt et al., 2003 (1-year biologic treatment)**23</td>
<td>MTX</td>
<td>£36,859 ($60,046)</td>
<td>3.731</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>MTX + infliximab</td>
<td>£43,299 ($70,538)</td>
<td>4.029</td>
<td>£21,600 ($35,188)</td>
<td>£21,600 ($35,188)</td>
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<td></td>
<td>MTX</td>
<td>£36,859 ($60,046)</td>
<td>3.731</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>MTX + infliximab</td>
<td>£48,799 ($79,498)</td>
<td>4.131</td>
<td>£29,900 ($48,710)</td>
<td>£29,900 ($48,710)</td>
</tr>
<tr>
<td>Brennan et al., 2004**14</td>
<td>DMARDs</td>
<td>£9,190 (€16,580)</td>
<td>5.88</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Etanercept monotherapy</td>
<td>£36,212 (€65,268)</td>
<td>7.53</td>
<td>£16,330 (€29,433)</td>
<td>£16,330 (€29,433)</td>
</tr>
<tr>
<td></td>
<td>followed by DMARDs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sweden studies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kobelt et al., 2003 (1-year biologic treatment)**23</td>
<td>MTX</td>
<td>1,121,476 SEK ($125,478)</td>
<td>4.384</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>MTX + infliximab</td>
<td>1,129,507 SEK ($126,377)</td>
<td>4.632</td>
<td>£2,000 SEK ($3,580)</td>
<td>£2,000 SEK ($3,580)</td>
</tr>
<tr>
<td></td>
<td>MTX</td>
<td>1,121,476 SEK ($125,478)</td>
<td>4.384</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>MTX + infliximab</td>
<td>1,166,298 SEK ($130,493)</td>
<td>6.83</td>
<td>£150,000 SEK ($16,783)</td>
<td>£150,000 SEK ($16,783)</td>
</tr>
<tr>
<td>Kobelt et al., 2004**25</td>
<td>Standard (nonbiologics)</td>
<td>27,447 EUR ($39,761)</td>
<td>0.21</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Etanercept or infliximab</td>
<td>39,630 EUR ($55,972)</td>
<td>0.49</td>
<td>£43,500 EUR ($61,438)</td>
<td>£43,500 EUR ($61,438)</td>
</tr>
<tr>
<td>Bansback et al., 2004 (ACR50 analysis)**26</td>
<td>DMARD</td>
<td>70,387 EUR ($104,204)</td>
<td>1.182</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Adalimumab</td>
<td>90,058 EUR ($133,326)</td>
<td>1.655</td>
<td>41,561 EUR ($61,529)</td>
<td>41,561 EUR ($61,529)</td>
</tr>
<tr>
<td></td>
<td>Etanercept</td>
<td>102,099 EUR ($151,152)</td>
<td>1.838</td>
<td>48,334 EUR ($71,556)</td>
<td>65,869 EUR ($97,516)</td>
</tr>
<tr>
<td></td>
<td>MTX + etanercept</td>
<td>102,421 EUR ($151,628)</td>
<td>2.049</td>
<td>36,926 EUR ($54,668)</td>
<td>1,523 EUR ($2,254)</td>
</tr>
<tr>
<td></td>
<td>MTX + adalimumab</td>
<td>102,610 EUR ($151,908)</td>
<td>2.105</td>
<td>34,922 EUR ($51,700)</td>
<td>3,423 EUR ($5,068)</td>
</tr>
<tr>
<td></td>
<td>MTX + etanercept</td>
<td>103,129 EUR ($152,677)</td>
<td>2.097</td>
<td>35,760 EUR ($56,924)</td>
<td>Dominated</td>
</tr>
<tr>
<td>Bansback et al., 2004 (ACR20 analysis)**26</td>
<td>DMARD</td>
<td>68,757 EUR ($101,791)</td>
<td>1.704</td>
<td>Reference</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Etanercept</td>
<td>112,351 EUR ($166,329)</td>
<td>2.730</td>
<td>42,480 EUR ($55,383)</td>
<td>27,099 EUR ($35,330)</td>
</tr>
<tr>
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<td>MTX + etanercept</td>
<td>114,462 EUR ($169,454)</td>
<td>2.742</td>
<td>44,019 EUR ($57,388)</td>
<td>22,444 EUR ($29,261)</td>
</tr>
<tr>
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<td>MTX + adalimumab</td>
<td>114,732 EUR ($169,894)</td>
<td>2.412</td>
<td>64,936 EUR ($84,658)</td>
<td>22,001 EUR ($28,683)</td>
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<tr>
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<td>MTX + etanercept</td>
<td>116,442 EUR ($172,386)</td>
<td>2.432</td>
<td>65,501 EUR ($85,595)</td>
<td>36,627 EUR ($47,751)</td>
</tr>
<tr>
<td></td>
<td>MTX + adalimumab</td>
<td>117,580 EUR ($179,772)</td>
<td>2.952</td>
<td>51,974 EUR ($67,760)</td>
<td>36,576 EUR ($47,683)</td>
</tr>
</tbody>
</table>

* Costs are reported in the year of analysis; (costs are adjusted to 2004 U.S. dollars as shown in parentheses).
† ICERs are calculated by comparing each comparator to the reference.
‡ ICERs are calculated by comparing each comparator to the next best nondominated agent.
ACR20=American College of Rheumatology 20% response criteria; ACR50=American College of Rheumatology 50% response criteria.
DMARDs=disease-modifying antirheumatic drugs; ICER=incremental cost-effectiveness ratio; MTX=methotrexate; N/A=not applicable; QALY=quality-adjusted life-year.
Currency: £=British pound; EUR=Euro; SEK=Swedish krona.
**Discussion**

The introduction of biologic DMARDs for the management of RA poses several challenges for health care decision makers, especially in an era when drug expenditures continue to rise and cost containment is common. First, at an average annual drug cost of $17,000 to $18,000, biologic DMARDs are much more costly than traditional DMARDs. The annual cost of methotrexate therapy is approximately $200 (assuming 7.5 mg per week). Moreover, the studies reviewed have consistently shown that the additional costs of biologics are not completely offset by preventing future disability; hence, the clinical benefits of biologic therapy are likely to come with additional costs. These facts cause payers to be concerned about the value for money obtained from the use of biologic therapy. In the process of trying to determine formulary placement of these expensive specialty drugs, benefit designers also need to consider member access and cost sharing.

Second, the demand for biologics from physicians and patients may increase with more data from RCTs indicating that biologics improve ACR response and decrease disability. Managed care organizations must balance the evidence on safety, efficacy, effectiveness, and cost to assess the economic value of biologic therapy. Well-conducted CEAs are potentially helpful here.

The studies reviewed here suggest that the additional benefits of biologics after failing traditional DMARDs may be worth the additional cost compared with DMARD continuation, based on the commonly cited thresholds used in the different countries. These thresholds, also referred to as ICERs, represent the additional amount of money that payers will spend to gain 1 additional QALY (i.e., a year of perfect health) compared with the current gold standard or best therapy option. While no threshold formally exists in the United States, historically an ICER of ≤$50,000 per QALY gained has been cited as a good value for the additional spending. In other words, the drug can be considered cost effective if the ICER is ≤$50,000. However, an ICER approaching $100,000 per QALY gained has also been used to justify additional drug spending.

The ICERs reported in the studies in our review are within or below this range, even after adjusting for inflation and differences in currencies. In the United States, the adjusted ICER from Wong et al. was $11,670 per QALY gained for infliximab plus methotrexate compared with methotrexate alone (Table 7). In the United Kingdom, these adjusted ICERs ranged from $29,433 (for etanercept compared with traditional DMARDs) to $48,710 (for infliximab plus methotrexate compared with methotrexate alone) (Table 7). Studies from the Swedish setting reported adjusted ICERs ranging from $3,500 (for infliximab plus methotrexate compared with methotrexate alone) to $85,395 (for adalimumab compared with DMARDs). Despite the dissimilarity in their methodologies, these studies consistently reported ICERs within the range where payers may accept additional spending for these agents.

Pharmacoeconomic models may aid decision making in several ways. First, primary collection of data on costs and utilization in an RCT is often impractical; models can overcome this limitation because they can synthesize information from disparate sources. Second, a drug is often compared with placebo in an RCT, but decision makers need to know how the drug compares with standard therapy. Third, models can be used to project the long-term costs and consequences for a chronic condition such as RA in the absence of actual data from RCTs. Lastly, the results from a well-designed model can be presented in a useful metric such as cost per QALY gained, so that therapies can be compared within RA and across other conditions.

Policy makers using these models to make decisions will need to inspect how the study was conducted, to verify the face-validity of key assumptions and to determine whether the model was framed in a way that answered the relevant questions. Several questions need to be addressed before applying the results to the payer’s population.

First, are the metrics reported from these studies useful? Modeling the effective measure as a function of ACR response is practical because this outcome is often reported in clinical trials. For example, the 2 studies by Choi et al. reported the incremental cost per additional patient with ACR response. Response rate is useful when decision makers are only concerned with comparing relative efficacies of different agents. However, this metric has limited application for formulary decision making in the context of cost-effectiveness because the results cannot be easily compared with those of other economic
evaluations in RA or even in other medical conditions.

Without a predefined maximum cost that purchasers will pay to achieve additional ACR response, the economic value of biologics is undetermined. Patients who achieved ACR20 outcomes can still suffer from residual symptoms (tender and swollen joints); these patients may continue to endure up to 80% of their original symptoms. Therefore, decision makers should also ask the following important question: Are the partially treated symptoms worth the additional cost to alleviate them? Alternatively, the U.S. Public Health Service Panel on Cost-effectiveness in Health and Medicine has recommended reporting cost per QALY gained because comparisons across different medical conditions and interventions would be easier. QALYs capture the composite effect of treatment on mortality (or survival) and morbidity. For a chronic condition such as RA, emphasis should also be placed on the long-term progression of disability, how biologics can delay disability, and how this benefit translates to QALYs. Models that accounted for these factors (Kobelt et al., Brennan et al., and Bansback et al.) scored highly on the QHES instrument and should be given greater weight during formulary decision or other review processes.

Second, in the absence of data, how do the models relate treatment to long-term consequences? Because RCTs involving RA are short in duration, the need for modeling to understand the long-term clinical benefits from biologics is inevitable. However, projecting these benefits beyond the clinical trial period requires adding assumptions to the pharmacoeconomic model that necessitate careful scrutiny. Kobelt et al. and Wong et al. projected clinical benefits for up to 10 years based on RCTs of only 1 year’s duration that included outcomes for all patients including those that discontinued therapy. The assumption about when clinical benefit from biologics will diminish is essential for assessing the value of biologics. Wong et al. assumed that the clinical benefit from infliximab plus methotrexate would be diminished by one third at 2 years, three fourths by 5 years, and almost completely by 10 years. This base-case scenario was associated with an ICER of $9,100 per QALY gained ($11,670, 2004 USD). However, when it was assumed that the clinical benefit was lost by 5 years, the corresponding ICER increased to $47,000 per QALY gained ($60,274, 2004 USD). In the most extreme scenario of assuming that all of the benefit is lost immediately after stopping infliximab, the ICER increased to $93,000 per QALY gained ($119,265, 2004 USD).

This example illustrates that the cost-utility is very sensitive to the assumption of when the clinical benefit would diminish, and the resulting policy decision could change depending on that assumption. Kobelt et al. modeled costs and benefits beyond the first year by applying the progression of disability (i.e., HAQ) using epidemiological data. Contrary to what Wong et al. observed, the ICER from a scenario when clinical benefit was lost at discontinuation after 1 year of treatment was not substantially different from the base case. Brennan et al. constructed a conservative lifetime model by assuming that upon withdrawal of etanercept, disability as measured by HAQ score would immediately worsen by exactly the amount equivalent to the initial improvement. The resulting ICER was favorable at £16,330 per QALY gained ($29,433, 2004 USD) even with such a conservative assumption. Likewise, Bansback et al. also applied this same conservative assumption in their base-case model.

Third, to what should the cost-effectiveness of biologics be compared? Although most studies used methotrexate as the reference for comparison, other comparators varied. Kobelt et al. calculated the cost-effectiveness ratio based on change to baseline costs and utilities rather than a direct comparison to another RA treatment. Brennan et al. presented a comparison of treatment sequences rather than a pure comparison of one drug versus another. In the management of RA, patients who do not respond to or who cannot tolerate a particular agent will likely switch to alternative agents; therefore, a comparison of competing treatment strategies that accounts for switching and withdrawal would be useful. Likewise, Bansback et al. presented a model of treatment sequences that may have greater appeal to decision makers as it reflects more realistic utilization of biologics and DMARDS and treatment pattern. In the models by Bennan et al. and Bansback et al., patients who do not respond to or cannot tolerate biologics are switched to a traditional DMARD.

Last, how does one differentiate between biologics in value? It will be natural for decision makers to seek the answer to this question in order to guide drug benefit design; however, evidence is lacking. Chiu et al. was the only study that assessed this relative cost-effectiveness. These investigators maintained that patients enrolled in each of the source RCTs were similar; hence, the efficacies from different studies were applied into their model without any adjustment. However, differences in important characteristics, such as disease duration, disability, and methotrexate response, could influence study outcomes. Therefore, clinical trials with head-to-head comparisons of biologics are needed to validate the relative benefits.

The National Institute for Health and Clinical Excellence (NICE) conducted an independent appraisal of the cost-effectiveness of adalimumab, etanercept, and infliximab and posted preliminary recommendations in early 2006. Five models were submitted to NICE for review: 1 from each of the manufacturers of the 3 anti-TNF-α agents, 1 from the BSR, and 1 from the Assessment Group. In general, models sponsored by the manufacturers reported lower ICERs compared with the Assessment Group’s model. Key findings from the Assessment Group's model. Key findings from the Assessment Group’s model.
Review of Eight Pharmacoeconomic Studies of the Value of Biologic DMARDs (Adalimumab, Etanercept, and Infliximab) in the Management of Rheumatoid Arthritis

Group’s model were that (1) using anti-TNF-α as a first-line treatment is not cost effective (ICER ≥£100,000 per QALY gained) and (2) the assumptions relating to HAQ progression have a significant impact on the cost-effectiveness estimates. If the model assumed no progression of disease while responding to treatment (i.e., optimistic scenario), the ICERS (versus no biologic treatment) were £30,000 per QALY gained for etanercept, £58,000 per QALY gained for adalimumab, and £55,000 per QALY gained for infliximab. If disease progression was assumed to occur during biologic treatment (i.e., the conservative base-case scenario), the ICERS (versus no biologic treatment) were £88,300 per QALY gained for etanercept.

After considering all the economic evidence, the NICE Appraisal Committee concluded that “some patients with severe active disease who have failed to respond to at least 2 trials of DMARDs could be identified and managed cost effectively using 1 of the 3 TNF-α inhibitors.” Therefore, the committee did not recommend use of a TNF-α inhibitor in early stages of RA. Furthermore, treatment should be discontinued if response is not maintained, defined as clinical deterioration (i.e., increase of DAS28 score by more than 0.6) at consecutive assessments. The findings from the studies in our review support these preliminary recommendations of the NICE Appraisal committee (i.e., patients should have failed traditional DMARDs prior to use of a TNF-α inhibitor.) In addition, the committee appeared to support a conservative approach that analytic models should show the loss of clinical benefits at treatment withdrawal (i.e., recurrence of disability) rather than assume that benefits can be extended beyond discontinuation.

In addition to our qualitative review of these studies, we found that reporting scores from the QHES instrument can be useful to decision makers, particularly those with limited experience with reviewing pharmacoeconomic data, as a way to differentiate one study from another. Ofman and colleagues reported that “experts” in health economics considered the QHES instrument as moderately valuable, but 54% would still recommend it to others. QHES instrument as moderately valuable, but 54% would still recommend it to others. In settings where economic evaluations are considered when decisions about resource allocation are made, a tool such as the QHES can be useful.

Limitations

Four of the 8 economic evaluations reviewed were sponsored by manufacturers of TNF-α inhibitors, and 1 of the 8 studies was sponsored by a manufacturer and not indexed by MEDLINE. Bell and colleagues noted that published cost-effectiveness studies tend to report favorable incremental cost-effectiveness ratios. Furthermore, Bell et al. found studies funded by industry to be more likely to report ratios below $20,000, $50,000, and $100,000 per QALY gained. However, studies of higher methodological quality and those conducted in Europe or the United States were less likely to report ratios below $20,000 per QALY gained. These observations suggest that decision makers need to consider study sponsorship and inspect such studies more critically for any potential biases. However, industry sponsorship does not necessarily discredit the findings from such studies.

These models relied on efficacy data from source clinical studies in which the patients had failed at least 1 traditional DMARD. Only 3 of the 8 models defined failure to respond to traditional DMARDs as failing at least 2 traditional DMARDs, of which 1 has to be methotrexate (Table 2). This definition of failure is consistent with the recommendation from the BSR guidelines to determine when patients become eligible for biologic therapies. The 3 studies that evaluated cost-effectiveness of infliximab (in combination with methotrexate) focused on patients with inadequate response as methotrexate resistant but not necessarily having failed 2 DMARDs. Arguably, these patients may respond to other less costly traditional DMARD before considering biologic therapies.

A gap exists between clinical practice guidelines and formal indications approved by the U.S. Food and Drug Administration. According to the current prescribing information (Table 1), etanercept and adalimumab can be initiated in combination with methotrexate or used alone. However, patients are rarely prescribed biologics without having tried at least 1 and usually 2 or more traditional DMARDs in the real-world practice setting.

The cost-effectiveness literature assessed the use of biologic therapies across a range of clinical circumstances from multiple treatment failures with DMARDs to 1 study that involved DMARD-naïve patients. The resulting economic outcomes for these diverse clinical scenarios are consistent with the amount paid for other therapeutic interventions. In a circumstance where only specific clinical situations meet cost-effectiveness guidelines, then a narrowed therapeutic use could be defined. However, we found no such limitation in the pharmacoeconomic literature, and the cost-effectiveness literature has not yet addressed step therapy with DMARDs followed by biologics.

Conclusions

Biologic therapies are more costly compared with traditional DMARDs but produce more QALYs. Despite differences in design and assumptions, published economic models consistently reported ICERS ≤£50,000 per QALY gained for biologics compared with traditional DMARDs when used among RA patients who have become resistant to DMARDs, although sensitivity analyses reported ICERS of >£100,000. This implies that the value of biologics is comparable with that of other well-accepted medical interventions. Nonetheless, the formulary and policy decision makers will ultimately have to judge whether the additional expenditure justifies the clinical gain because no...
maximum cost has been defined. Although models can be used to inform decisions, they must be interpreted and applied carefully. Specifically, the assumption that clinical benefit will persist after biologics are discontinued needs to be validated in order to substantiate the long-term economic value of biologics. More research is also needed to determine the relative economic value of the various biologic agents for specific therapeutic indications.

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Doan served as principal author of the study. Study concept and design were contributed by all authors. Data collection was the work of Doan, data interpretation was the work of all authors. Writing of the manuscript and its revision were primarily the work of Doan, with input from Dubois and Chiou.

REFERENCES
Pharmacy Benefit Spending on Oral Chemotherapy Drugs

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ABSTRACT

BACKGROUND: Pharmacy benefits have historically excluded injectable drugs, resulting in coverage of injectable drugs under the medical benefit. High-cost biologics and other new drug therapies are often injectables and therefore have not presented cost threats to pharmacy benefits. The U.S. Food and Drug Administration approval of capecitabine, an oral form of fluorouracil, in 1998, and imatinib mesylate in oral dose form for chronic myeloid leukemia, in 2001, signaled a new period in budget forecasting for pharmacy benefits, particularly for small, self-insured employers for whom a drug with a cost of $25,000 per year of therapy for 1 patient could increase total pharmacy benefit costs by 10% or more.

OBJECTIVE: To quantify the actual relative costs of the oral chemotherapy drugs in pharmacy benefits in 2006 and identify the history of spending on oral chemotherapy drugs relative to total pharmacy benefit spending for small, self-insured employers over the 4.5 years through May 2006.

METHODS: Administrative pharmacy claims from the database of a pharmacy benefits manager (PBM) for approximately 500,000 members of small, self-insured employer plans were used to calculate the net plan cost of oral chemotherapy drugs relative to total drug benefit costs for the period January 1, 2002, through May 31, 2006. Current costs for oral chemotherapy drugs for small employers were compared with an insured health plan of approximately the same number of members for dates of service January 1, 2006, through May 31, 2006.

RESULTS: This descriptive analysis found that oral chemotherapy drugs represented 0.27% of total drug benefit costs, or approximately $0.08 per member per month (PMPM) for small, self-insured employers in 2002, rising linearly to 0.73%, or approximately $0.24 PMPM in the first 5 months of 2006. Members in pharmacy benefit plans sponsored by small employers paid an average 6.9% cost share for oral chemotherapy drugs in 2006, nearly identical to the average 8.5% paid by members of an insured health plan of similar size in total membership, versus 26.9% average cost share for all drugs. Imatinib mesylate accounted for 45% of total spending on oral chemotherapy agents in 2002 versus 40% in 2006.

CONCLUSION: Spending on oral chemotherapy drugs as a proportion of total pharmacy benefit costs has more than doubled, from about 0.3% in 2002 to 0.7% in 2006. For small, self-insured employers, this represents a nearly 3-fold increase in spending, from about $0.06 PMPM in 2002 to about $0.24 PMPM in 2006.

KEYWORDS: Pharmacy benefits, Budget forecasting, Chemotherapy drugs, Drug costs

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The U.S. Food and Drug Administration (FDA) approved lenalidomide (Revlimid), an analogue or derivative of thalidomide, on June 29, 2006, for use in combination with dexamethasone in patients with multiple myeloma who have received 1 prior therapy. Its manufacturer immediately made headline news by announcing that it would price the chemotherapy agent at $6,195 per month, which extrapolates to a drug cost in excess of $74,000 per patient per year of therapy. This was not lenalidomide’s first approval, however. The FDA had approved it on December 27, 2005, for the treatment of transfusion-dependent anemia due to myelodysplastic syndrome (MDS); for that indication, it was dosed at 10 mg per day with downward dose adjustment for patients experiencing thrombocytopenia. The manufacturer’s pricing structure appeared different for the 2 indications.

When the FDA approved the second indication, lenalidomide’s average price per patient per year increased by about 35%, from $55,000 for 12 months of therapy for anemia associated with MDS to $74,000 per patient per year for the second, more common indication, multiple myeloma. While the dose for multiple myeloma is 25 mg per day (two-and-one-half times higher than the starting MDS dose), some Wall Street analysts criticized the pricing of lenalidomide for multiple myeloma because (a) its annual cost far exceeds that of other antineoplastic agents, (b) its production costs should be lower since it is not a biologic agent and is an oral as opposed to an injectable dosage form, and (c) excessive pricing would likely invoke Congressional scrutiny due to its potential financial impact on Medicare and Medicaid programs.

Capecitabine Marks New Era of Oral Antineoplastics

A few oral antineoplastics have been available for decades; most of these have been relatively inexpensive. The new world of high-cost oral chemotherapy began in the United States when the FDA approved capecitabine (Xeloda), an oral form of fluorouracil, on April 30, 1998, for the treatment of advanced breast cancer resistant to paclitaxel in combination with an anthracycline such as doxorubicin (Table 1). Three years later, and despite the fact that “cancer” is a collection of diverse diseases, results from clinical trials of imatinib mesylate triggered hopes that not only was a cure for cancer possible but also that the treatment could be administered by mouth.

Imatinib Mesylate

At the annual meeting of the American Society of Hematology in early 2001, the results from three phase 3 clinical trials were presented for STI571, a tyrosine kinase inhibitor. One clinical
trial involved 500 chronic phase patients with chronic myelogenous leukemia (CML) who had failed to respond to interferon therapy. CML is characterized by translocation of chromosome material from chromosome 9 to chromosome 22 with formation of the so-called Philadelphia chromosome. After 6 months, greater than 90% of STI571-treated patients had white cell counts return to normal range and half had a significant reduction of Philadelphia chromosome-positive cells.

In a second study of 154 CML patients who had received STI571 for at least 1 month, 78% had a hematology response and 14% (22 patients) experienced disease remission. A third trial involving 94 patients in blast crisis (end-stage CML) showed a 47% response rate after 2 months of therapy with STI571. The researchers speculated that the combination of STI571 and cytosine arabinoside (Ara-C) or interferon could one day produce a cure for CML. Stem cell (bone marrow) transplant remains the only known cure for CML.

The manufacturer sought fast-track approval in Europe and the United States, describing STI571 as a “smart” drug that disables only the abnormal protein that causes CML without affecting normal cells. In March 2001, STI571 was expected to be approved by the FDA as early as fall 2001. In fact, the FDA approved STI571 (imatinib mesylate) in May 2001, just 3 months after the fast-track approval request, with a proprietary name change from the already-approved European name Gleevec to Gleevec. The manufacturer marketed imatinib mesylate in June 2001 at an initial $19.68 average wholesale price (AWP) per 100 mg capsule, resulting in an annual cost in the range of $29,000 to $57,500 per patient when dosed in the recommended range of 400 mg to 800 mg per day. Nine months later, the FDA approved imatinib mesylate for the additional indication of inoperable or metastatic malignant gastrointestinal stromal tumors (GIST).

Imatinib mesylate is now approved for the treatment of patients with all 3 stages of CML—myeloid blast crisis, accelerated phase, and chronic phase—either before or after other therapy, and GIST. Its dosage form has been redesigned for patient convenience, and it is now available as 100 mg scored tablets and 400 mg tablets.
Like gefitinib, erlotinib is 19
On November 2,
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On June 17, 2005, the FDA approved new
and sunitinib malate (Sutent) on
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Unlike gefitinib, erlotinib’s
Two large trials involving
Sorafenib, a multikinase inhibitor that
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Sunitinib malate, which inhibits multiple receptor
demonstrated benefit from receipt of the drug.
labeling for gefitinib for use only in patients who have demon-
chemotherapies.
NSCLC after failure of both platinum-based and docetaxel
for treatment of patients with locally advanced or metastatic
manufacturer to relabel gefitinib to restrict it to monotherapy
the findings from these 2 large clinical trials, the FDA asked the
regimen. It is not approved, however, for first-line therapy, since
metastatic NSCLC after failure of at least 1 prior chemotherapy
approved as monotherapy for patients with locally advanced or metastatic

effectiveness had been determined from objective response
Thalidomide is excluded from these data since the drug was not approved for
a cancer indication until May 26, 2006; summary data for claims with dates
of service from January 1, 2002, through May 31, 2006, for more than 2,000
small, self-insured employers.

**Gefitinib**

On May 5, 2003, the FDA approved gefitinib (Iressa) for treat-
ment of non-small cell lung cancer (NSCLC), dosed as a 250 mg
tablet with or without food; higher doses do not improve
response but do increase toxicity.12 Two large trials involving
2,130 chemotherapy-naïve patients with stage III and IV
NSCLC showed that gefitinib failed to improve tumor response
rates, time to progression, or overall survival, when dosed at
either 250 mg or 500 mg per day in combination with platinum-
based chemotherapy regimens. The chemotherapies given in these
first-line trials were gemcitabine and cisplatin (n = 1,093) or
carboplatin and paclitaxel (n = 1,037). Subsequent to the release of
the findings from these 2 large clinical trials, the FDA asked the
manufacturer to relabel gefitinib to restrict it to monotherapy
for treatment of patients with locally advanced or metastatic
NSCLC after failure of both platinum-based and docetaxel
chemotherapies.13 On June 17, 2005, the FDA approved new
labeling for gefitinib for use only in patients who have demonstrat-
ed benefit from receipt of the drug.14 As part of the new
labeling, distribution of gefitinib is restricted under a risk
management plan called the Iressa Access Program. Gefitinib’s
effectiveness had been determined from objective response
rates, and no controlled trials have demonstrated clinical benefit
(e.g., improved disease-related symptoms or increased survival).
Off-label use of gefitinib includes treatment of squamous cell head
and neck cancer.

**Erlotinib**

Erlotinib (Tarceva) was first approved by the FDA on November
18, 2004. Erlotinib inhibits intracellular phosphorylation of
tyrosine kinase associated with the epidermal growth factor
receptor (EGFR), and further work is under way to completely
characterize its mechanism of action.15 Like gefitinib, erlotinib is
approved as monotherapy for patients with locally advanced or
metastatic NSCLC after failure of at least 1 prior chemotherapy
regimen. It is not approved, however, for first-line therapy, since
2 multicenter, placebo-controlled, randomized, phase 3 trials
showed no clinical benefit when erlotinib was combined with
platinum-based chemotherapy (carboplatin and paclitaxel, or
gemcitabine and cisplatin) as first-line treatment of patients
with locally advanced or metastatic NSCLC.16 On November 2,
2005, the FDA approved the second indication for locally
advanced, unresectable, or metastatic pancreatic cancer in
combination with gemcitabine.17 Unlike gefitinib, erlotinib’s
effectiveness has been proven in randomized, controlled trials.18

**Sorafenib and Sunitib Malate**

The FDA approved 2 additional oral agents, sorafenib (Nexavar)
on December 20, 2005,19 and sunitib malate (Sutent) on
January 26, 2006.20 Sorafenib, a multikinase inhibitor that
decreases tumor cell proliferation, was approved for advanced
renal cell carcinoma (RCC). Dose instructions include expected
skin toxicity and consequent dose reductions to 50% or 25% of
the initial recommended dose of 400 mg (two 200 mg tablets)
twice daily.21 Sunitinib malate, which inhibits multiple receptor
tyrosine kinases, was approved for GIST after disease progression
or imatinib mesylate intolerance. Concurrent FDA approval for
the indication RCC was based on partial response rates and
duration of responses since there are no randomized trials of
sunitinib malate demonstrating clinical benefit, such as increased
survival or improvement in disease-related symptoms in RCC.22

**Thalidomide**

On May 26, 2006, the FDA approved thalidomide (Thalomid)
under expedited review for the indication of newly diagnosed
multiple myeloma patients in combination with dexamethasone.23
Despite a preapproval, U.S. market withdrawal decades earlier
for teratogenicity identified in postapproval European markets,
thalidomide had been reintroduced to the U.S. market on July
16, 1998, when the FDA approved an indication for erythema
nodosum leprosum (ENL; a complication of leprosy).24
Thalidomide’s wide range of off-label uses include treatment of
graft-versus-host disease after bone marrow transplantation,
refractory multiple myeloma, primary brain tumors, appetite
stimulant for cachexia in advanced cancer or human immuno-
deficiency virus (HIV)/acquired immunodeficiency syndrome
(AIDS), aphthous ulcers, and prostate cancer in combination
with docetaxel.25

**Dasatinib**

The FDA approved dasatinib (Sprycel) on June 28, 2006, for
use in the treatment of adults with chronic phase, accelerated

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**FIGURE 1** Proportion of Total Pharmacy Benefit Spending for Oral Chemotherapy Drugs

Thalidomide is excluded from these data since the drug was not approved for
a cancer indication until May 26, 2006; summary data for claims with dates
of service from January 1, 2002, through May 31, 2006, for more than 2,000
small, self-insured employers.
phase, or myeloid or lymphoid blast phase CML with resistance or intolerance to prior therapy, including imatinib mesylate. The expedited approval requires additional follow-up data to be converted to regular approval by the FDA. The FDA granted regular approval to dasatinib for use in the treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukemia with resistance or intolerance to prior therapy.

**Lenalidomide**

The first FDA approval of lenalidomide was on December 27, 2005, for myelodysplastic syndrome (MDS), characterized by hyperactive bone marrow but low blood cell counts. While the colony-stimulating factors such as filgrastim are used off-label for MDS, lenalidomide is the only oral drug approved by the FDA for MDS. Other drugs for MDS are injectables such as azacitidine (Vidaza), approved by the FDA on May 19, 2004. The Myelodysplastic Syndromes Foundation, sponsored by the manufacturers of drugs for MDS, includes on its Web site patient information for Medicare Part D and a Web link to find drug formulary coverage for MDS chemotherapy.

### Methods

The present study was precipitated in part by the pharmacoeconomic work by Ramsey et al. who earlier this year found a seemingly small budget impact from the coverage of erlotinib as a formulary drug, for 1 indication, NSCLC. The estimated budget impact of $0.01 per member per month in a hypothetical health plan of 500,000 members could be consequential in a small employer health plan of 500 members, particularly if the pharmacy benefit is self-insured. Second, 5 new FDA approvals for high-cost oral chemotherapy drugs in 7 months through June 30, 2006, creates the need for descriptive, benchmark analysis of the actual direct pharmacy benefit costs for oral chemotherapy drugs.

Data for this study were obtained from 2 sources: the administrative pharmacy claims in the database of a pharmacy benefits manager (PBM) for approximately 500,000 members from more than 2,000 small, self-insured employers and an insured health plan with approximately 520,000 members. The PBM serves members nationwide, and the insured health plan is located in the southern United States. The net plan cost of oral chemotherapy drugs relative to total drug benefit costs was calculated for the period from January 1, 2002, through May 31, 2006, for the small employer drug plans. Current costs in 2006 for oral chemotherapy drugs for small employers were compared with the insured health plan for dates of service from January 1, 2006, through May 31, 2006. These oral chemotherapy drugs were identified by Medi-Span Generic Product Indicator (GPI) starts with 2153 or 9939 or 2130 (except not GPI starts with 213000501 [methotrexate, which has indications such as rheumatoid arthritis and psoriasis in addition to use as an antineoplastic agent]), and all but oral dose forms were excluded.

Drug cost is defined from the payer perspective as the allowed charge less the member cost share (sum of deductibles, benefit maximums, copayments, and coinsurance).
Pharmacy Benefit Spending on Oral Chemotherapy Drugs

On pharmacy claims. The PBM database includes mail-service and community pharmacy claims. During the time period of this study, from January 1, 2002, through May 31, 2006, mail-service pharmacy accounted for 5% to 7% of all pharmacy claims and 15% to 23% of total net plan (payer) cost. Pharmacy claims are aggregated by date of service, and all resource utilization and costs are reported net of claim reversals and adjustments.

■ Results
Oral chemotherapy drugs represented approximately 0.27% of total drug benefit costs in 2002, rising in a nearly linear manner over a 5-year period to 0.73% in 2006 (Figure 1). Net plan cost PMPM, after subtraction of member cost share, was approximately $0.08 in 2002 and approximately $0.24 PMPM in the first 5 months of 2006 (Figure 2). Due to dollar copayments as the predominant structure for member cost sharing in pharmacy benefit plans of small, self-insured employers during this time period and the relatively high cost for oral chemotherapy drugs, the average member cost share for oral chemotherapy drugs was about one third that for all drugs over this 4.5-year period Figure 3). In the first 5 months of 2006, the average member cost share for oral chemotherapy drugs was 6.9% for beneficiaries in pharmacy benefit plans sponsored by small employers versus an average 8.5% for the comparison insured health plan of similar total membership (data not shown). Imatinib mesylate accounted for 45% of total spending on oral chemotherapy agents for small employers in 2002 versus 40% in 2006 (Figure 4). Despite market availability for only a few months in 2006, erlotinib accounted for 18% of the net cost of oral chemotherapy drugs, followed by capecitabine at 14%; among the other oral chemotherapy drugs, each accounted for less than 10% of total spending. The distribution of spending among the oral chemotherapy agents was similar for the insured health plan, with the exception of gefitinib which, unlike the small employers, had some utilization at 3% of total spending (Figure 5), accounting for approximately $0.01 PMPM (Table 2). The actual price of the oral chemotherapy drugs in the first 5 months of 2006 is derived from the average allowed charge per day of therapy multiplied by 30 to obtain a standardized price per 30-day supply, prior to subtraction of the member cost share. Lenalidomide and sunitinib malate had the highest average allowed charge per 30-day supply, approximately $7,000 for each (Figure 6). The average allowed charge per 30-day supply for the 3 highest-expenditure oral chemotherapy drugs was $3,015 for imatinib mesylate, representing approximately 40% of total spending; $2,864 for erlotinib (18% of total spending); and $2,127 for capecitabine (14% of total spending).

■ Discussion
Prior to the market introduction of capecitabine and imatinib, chemotherapy agents were either relatively low-cost oral drugs or injectable drugs. The relatively low-cost oral chemotherapy drugs included mercaptopurine (6-MP, Purinethol), and thioguanine, both approved before 1967. High-cost chemotherapy drugs such as trastuzumab (Herceptin; initially approved by the FDA on September 25, 199731), bevacizumab (Avastin; approved for metastatic colon cancer February 26, 2004), and cetuximab (Erbitux; approved for metastatic colon cancer, February 12, 2004) are available as injectable dosage forms only. All of these have had either indications added to their approved package labeling or will have in the near future.

While the present impact on outpatient pharmacy budgets is still relatively small, oral antineoplastic agents are associated...
with a host of attractive features that guarantee the commitment of research funding and market introduction of more oral agents. Obvious reasons for the preference of oral dose forms over injectable dose forms include ease of administration, patient preference, and lower risk of complications compared with injectable drugs, particularly intravenous administration. Less obvious reasons include the lower cost of administration, (e.g., the direct costs in medical professional time, medical supplies, and intravenous pumps) and the indirect costs associated with travel time to medical facilities and caregiver time. Oral agents may have fewer side effects with the possibility of improved tolerance and adherence to therapy. However, adherence to therapy is not necessarily assured with oral chemotherapy agents, and the cost of production is not necessarily lower.

A drug like erlotinib, with an average charge per year of therapy of approximately $35,000 for 1 patient and a net cost after member cost share of $34,000 or more, can increase net pharmacy benefit costs by more than 15%, or $5.67 PMPM, for a small self-insured employer with 500 enrolled members. The matter of financial budget impact on a large health plan was posed by Ramsey et al. in mid-2006. The authors used a pharmacoeconomic model to predict the budget impact of erlotinib on a hypothetical third-party payer with 500,000 enrolled members. When used according to the FDA-approved label indications as second-line or third-line therapy for NSCLC, they estimated that the incremental cost of placing erlotinib on the drug formulary would be less than $0.01 PMPM. This pharmacoeconomic work suggests a minimal and insignificant budget impact for a 500,000-member health plan. However, the actual cost effects could be different since (a) the assumed reductions in chemotherapy-related infusion costs may or may not be realized, and (b) costs associated with adverse events may be either over- or under-reported in the actual medical and pharmacy claims data.

From a silo-perspective in cost management, a predominant business perspective in 2006, including the focus on quarterly financial results for the enterprise and its individual departments and cost centers, the immediate effect on departmental (benefit) costs is important. This present research suggests that prior to consideration of potential offsetting costs, the direct drug benefit costs for erlotinib in 2006 are approximately $0.04 PMPM, approximately 5 times higher than the cost identified in the research by Ramsey et al. This 5-fold discrepancy suggests a need to validate the pharmacoeconomic modeling with actual health plan data for pharmacy and other medical costs.

The most likely source of the cost discrepancy is the focus by Ramsey et al. on only 1 of erlotinib’s 2 approved indications. In ignoring erlotinib’s approval for first-line treatment of patients with locally advanced, unresectable, or metastatic pancreatic cancer when used in combination with gemcitabine (Gemzar), the budget forecast model is not a budget forecast model for the drug but for the drug for a specific indication.

### TABLE 2: Pharmacy Benefit Costs for Oral Chemotherapy Drugs in 2006*

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Small Employers</th>
<th>Insured Health Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Net Plan Cost PMPM ($)</td>
<td>% Total</td>
</tr>
<tr>
<td>Imatinib mesylate</td>
<td>0.10</td>
<td>40</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>0.04</td>
<td>18</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>0.03</td>
<td>14</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>0.02</td>
<td>9</td>
</tr>
<tr>
<td>Sunitinib</td>
<td>0.02</td>
<td>8</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>0.02</td>
<td>7</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>Mepactopurine</td>
<td>0.01</td>
<td>4</td>
</tr>
<tr>
<td>Purinethol</td>
<td>&lt;0.01</td>
<td>&lt;1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>0.24</td>
<td>0.42</td>
</tr>
</tbody>
</table>

* These drugs are identified by Medi-Span Generic Product Indicator (GPI) beginning with 2153, or 9939 or 2130 (except not GPI beginning with 213000501 [methotrexate], which is standard treatment for several indications, including rheumatoid arthritis and psoriasis, in addition to use as an antineoplastic agent), for dates of service from January 1, 2006, through May 31, 2006. NA=data not available; PMPM=per member per month.
A portion of the cost difference could also be attributable to off-label use, a factor for erlotinib and the other oral chemotherapy agents as it is for all drugs. For erlotinib, off-label use includes treatment of squamous cell head and neck cancer.

**Limitations**

This analysis was intended to be descriptive, focusing on the direct financial effects of oral chemotherapy drugs on pharmacy benefit costs. Cost-benefit analysis was beyond the objective and scope of this research. Analysis of the cost per outcome is information that is needed. For example, one of the 2 clinical trials used to seek FDA approval for the multiple myeloma indication for lenalidomide showed that median time to progression of disease was increased approximately 17 weeks, from 19.9 weeks in the dexamethasone group to 37.1 weeks in the lenalidomide plus dexamethasone group. In addition to the drug cost in excess of $6,000 per month, the cost in terms of side effects was large, with a greater proportion of patients experiencing serious side effects such as febrile neutropenia and deep vein thrombosis (DVT) in the lenalidomide + dexamethasone group compared with the dexamethasone group alone. The incidence of thrombotic events such as DVT, pulmonary embolism (PE), and intracranial venous sinus thrombosis was 12% in the lenalidomide + dexamethasone versus 4% in the dexamethasone group. The “black-box” warning on the label of lenalidomide includes the potential for birth defects; hematologic toxicity, including neutropenia and thrombocytopenia; and DVT and PE. Results in the willingness-to-pay research suggests that patients with NSCLC and healthy subjects are willing to pay a median of $100 CAD per month of therapy with an oral epidermal growth factor receptor tyrosine kinase inhibitor such as erlotinib, less than 5% of the actual price of the drug in the present study.

Others have posed the question of the value of the outcomes obtained for the rapidly escalating cost of chemotherapy regimens. Schrag compared the costs of various drug therapy regimens for metastatic colorectal cancer following FDA approval in February 2004 of the monoclonal antibodies bevacizumab (Avastin, targeting vascular endothelial growth factor) and cetuximab (Erbitux, targeting epithelial growth factor receptor) for use in conjunction with cytotoxic drug regimens. Schrag calculated at 95% of the average wholesale price in May 2004, 8 weeks of the Mayo Clinic regimen of monthly bolus of fluorouracil plus leucovorin cost $63 versus $304 for a weekly bolus of fluorouracil plus leucovorin (Roswell Park regimen) or $263 for biweekly fluorouracil plus leucovorin in a 48-hour infusion (LV5FU2 regimen). Adding either irinotecan (FOLFIRI) or oxaliplatin (FOLFOX) to LV5FU2 increased the initial 8-week cost to $9,381 or $11,889, respectively. The addition of bevacizumab to FOLFIRI or FOLFOX increased the 8-week cost in 2004 dollars to about $21,000, and cetuximab added to either irinotecan or FOLFIRI resulted in an 8-week cost of approximately $30,700. The numerator for the benefit-cost equation is in the context of 8 months median duration of survival without chemotherapy, 12 months with fluorouracil, and 21 months with FOLFIRI or FOLFOX regimens. The addition of either bevacizumab or cetuximab increased the average drug treatment cost to $161,000 per patient, without evidence that median survival would at any additional time extend beyond the 21 months seen with FOLFIRI/FOLFOX.

The present research is representative only of small, self-insured employers. While an insured health plan of similar-size membership had similar distribution of spending on oral chemotherapy drugs in 2006, the PMPM costs were $0.42 versus $0.24 for the group of small employers (PBM), including $0.01 PMPM contributed by gefitinib, which had no utilization in the group of small employers. Health plans that manage pharmacy benefits more closely, such as the use of prior authorization interventions to ensure utilization of these drugs in accordance with FDA-approved indications or other treatment guidelines, will no doubt experience different costs.

**Conclusion**

The FDA approval of 5 oral drugs for chemotherapy indications in the 7-month period ended June 30, 2006, portends increased spending in outpatient pharmacy benefit plans. At mid-year 2006, total spending is in the range of $0.24 to $0.42 PMPM for 2 different pharmacy benefit sponsors, excluding the additional costs of approximately 7% to 8% for member cost share. Imatinib mesylate accounted for 30% to 40% of total spending for oral chemotherapy drugs in the first 5 months of 2006.

**DISCLOSURES**

The author discloses no potential bias or conflict of interest relating to this article.

This article reflects the work of the author and has received the same degree of peer-review scrutiny required of all articles published in the *Journal of Managed Care Pharmacy*. The author acknowledges the assistance of Alice C. Ceacareanu, PhD, University of Tennessee, Memphis, in preparing summary comparison data for an insured health plan in the southern United States, and Jeanette Y. Wick, RPh, MBA, senior clinical research pharmacist, National Cancer Institute, Bethesda, Maryland, for her guidance and review of this article.

**REFERENCES**


PPIs Are Therapeutically Interchangeable and Ideal for a Managed Care Intervention Such as Therapeutic MAC

Mabasa and Ma recently published a pharmacy claims database review on the effect of a therapeutic MAC intervention for proton pump inhibitors (PPIs). A therapeutic MAC program establishes a therapeutic maximum allowable cost for a drug category and, unless medical necessity exists, requires patients to pay the drug cost difference when a nonpreferred agent is dispensed. In their Canadian employer group, rabeprazole 10 mg daily was the preferred agent, costing Can 71¢ daily. They found a 22.1% reduction in drug cost per patient per year (PMPY) in the intervention therapeutic MAC group (from Can $357 to Can $278 PMPY) versus a 4.1% increase in the comparison group (from Can $293 to Can $305 PMPY).

In response to this study, Peter Wahlqvist, an employee of AstraZeneca, the manufacturer of esomeprazole, has written a letter to the editors of JMCP to highlight “a number of fundamental flaws.” He rightfully points out that the quality of care delivered was not measured, a common shortcoming of the use of administrative claims data. As a clinician, such omissions are very concerning and cause me to immediately cast doubt; can such a study be a “priority update” that would cause me to change my present practice?

Fortunately for Wahlqvist, me, and our readers, other investigators have addressed the quality question regarding the impact of managing PPI agents. Not only has JMCP Editor-in-Chief Frederic Curtiss reminded us of the 2005 U.S. government Agency for Healthcare Research and Quality (AHRQ) conclusions regarding the therapeutic equivalency of all PPI medications but also others have examined quality outcomes for managing PPIs and H-2 blockers. The Georgia Medicaid program implemented a prior authorization (PA) intervention for PPIs on February 1, 2002. The PA criteria were based on diagnosis and risk assessment. Prescribers or pharmacists could submit PA requests by telephone (immediate response), fax (24-hour response time), or mail (48-hour response time). The time required to complete PA applications was not reported. The approval rate for PA requests was 95.1%. Per-member-per-month (PMPM) utilization of PPIs dropped 91% in the first month after implementation, and H-2 blocker utilization increased by 223%, (P <0.001 for both). Total spending fell by 70.1%, from $44.1 million in the 12-month preperiod to $13.2 million in the 12-month postperiod, while total spending on H-2 blockers rose from $6.0 million to $13.5 million. PPIs accounted for 88% of total antisecretory spending in the pre-period and 49% in the postperiod. PMPM expenditures fell 49%, from $3.44 to $1.74, representing savings for the state of $23.4 million in one year. These savings were reported after subtraction of the $20 administrative fee per PA request processed by the pharmacy benefits manager (PBM). Regarding clinical outcomes post-PA implementation, no evidence of an increase in the use of gastrointestinal (GI)-related endoscopies from baseline to follow-up was found among PPI users (14.0% vs. 10.9%), H-2 blocker users (8.3% vs. 7.3%), or nonusers of either PPIs or H-2 blockers (8.5% vs. 5.6%).

A group from Kaiser Permanente of Northern California performed a retrospective 2-year study of 13,971 adults who received a new prescription for a PPI or H-2 blocker. No claims for GI-related diagnoses/endoscopies or medications were found in the preceding 6 months. They found no statistically significant difference for patients who initially received PPI therapy versus H-2 blockers, regarding frequency of endoscopy, physician office visits, upper GI imaging, or hospital admission for GI disease. Drug costs were 4.2 times higher (P <.001) for patients who initially received PPI therapy than for patients who initially received H-2 blocker therapy, while nondrug costs (overall or by diagnosis) were equivalent. The importance of managing the initial treatment choice is borne out by the fact that, of patients who initially received H-2 blockers, 87.4% continued this therapy, while 90.9% of patients who initially received PPI therapy continued PPI therapy.

So while we have discovered evidence that quality of care seems equivalent for patients under active formulary management, what is the proof put forward that therapeutic MAC programs for PPIs may adversely affect patients? Wahlqvist cites a position paper posted on www.badgut.com that describes the British Columbia Pharmacare experience with forced therapeutic substitution of the preferred agent for the patient’s current PPI. This report did not provide a quantitative analysis; rather, it relied on anecdotal qualitative case examples. I was reminded of a late-night infomercial after reading the “personal testimony” style of the report. Of note, the therapeutic MAC study by Mabasa did not require forced substitution, making application of the suspect report even more dubious.

Wahlqvist did bring up a reasonable concern regarding the source of drug savings in the Mabasa study, namely two-thirds savings was due to a decline in use of PPIs. He pointed out that many patients could potentially be harmed by reducing their medication; however, this question has been asked and answered. Inodami et al. in 2001 published a trial on the success of step-down therapy for patients taking PPIs. They found that 42% of patients could safely taper down to H-2 blockers or no prescription agents and still control their reflux symptoms. Additionally, on-demand or as-needed use of PPIs is expanding and is consistent with the patient behavior that I have commonly observed in stable patients; it also can successfully and safely reduce PPI consumption.

The concluding point written by Wahlqvist dealt with the “unwarranted” focus of payers on the cost of medication. Citing his own research, published in abstract form only, he asserts that 17% of gastroesophageal reflux disease (GERD)-related costs are due to medications, while the other 83% are due to physician appointment costs, procedures, workers’ compensation, short- and long-term disability, and decreased work productivity.
He states, “These issues are clearly not addressed by a MAC program that focuses on drug costs alone . . . (c) consequently, drug costs for PPIs should probably not be the primary target for interventions from an employer perspective.” Assuming for the moment that the claim of GERD-related drug costs is only 17% of all GERD expenditures, why is focusing on reducing this figure unreasonable? PPIs are typically in the top 5 agents for PBM and health plan drug expenditures and are a modifiable cost. Why not modify what can be modified? I draw an analogy with my cardiac patients: I cannot change their gender, age, or family history, but we can and should improve their blood pressure, cholesterol, sugar, and tobacco use. Aiming at modifiable drug costs for PPIs should be a primary target.

As an aside, it is important to be aware of national dyspepsia guidelines. The U.K. Scottish Intercollegiate Guidelines Network (SIGN) recommends first-line use of H-2 blockers for dyspepsia, while the American Gastroenterology Association (AGA) promotes PPIs. The AGA guideline combined 3 studies and examined 1,267 patients with uninvestigated dyspepsia; they found PPI therapy was more effective than H-2 blockers at achieving complete symptom relief in individual patients (relative risk, 0.64; 95% confidence interval [CI], 0.58-0.72), with a number needed to treat (NNT) of 5 (95% CI, 3-8). Although not all studies cited were blinded, the study comparing lansoprazole 30 mg daily versus ranitidine 150 mg twice daily was double-blind and randomized and found complete relief of night symptoms in 81% versus 65% (P <0.01). The magnitude of these results was representative of the other studies. The AGA recommends PPIs as first-line therapy but, of note, did not cite any cost-effectiveness data to support this decision—only efficacy data.

Perhaps Goeree et al. captured the truth best regarding first-line dyspepsia agents in their long-term management cost-effectiveness/utility study. Although they concluded that the optimal strategy for managing patients with moderate-to-severe heartburn symptoms is to treat with a PPI, followed by maintenance therapy with an H-2 blocker, reality is that “the best way of managing patients with heartburn depends on how much society is willing to pay to achieve health improvements.” Continuous PPIs may offer higher maintenance efficacy (Ferrari Formula 1 equivalent), but H-2 blockers or on-demand PPIs (Ford Mustang) may be a competent substitute to get the job done (transport you to work and home) at more reasonable prices.

In the final analysis, a therapeutic MAC program that can safely and effectively lower high-dollar costs in a class such as PPIs is a welcome “priority update”; if patients buy into pharmaceutical advertising and want a Ferrari when the Ford Mustang suffices, then they may have to pay for that privilege. Although Wahlqvist has raised sincere questions about the Mabasa study, evidence has been presented to assuage concerns. Patient outcomes and quality of care under active management of dyspepsia agents has been measured in other studies and shown to not be harmful. Aiming at dyspepsia drugs costs should be a primary target in our effort to balance costs while helping our patients.

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REFERENCES
3. Wahlqvist P. Employers need to have a wider horizon than drug costs alone when considering the implementation of health care intervention programs [letter]. J Manag Care Pharm. 2006;12(7):581-82.
Editorial


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Pfizer, Inc. discovers, develops, manufactures, and markets leading prescription medicines for humans and animals and many of the world’s best-known consumer brands. We have an unparalleled opportunity for a Pharmacist Clinical Education consultant to join our winning team in Long Beach, CA:

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Employers Need to Have a Wider Horizon Than Drug Costs Alone When Considering the Implementation of Health Care Intervention Programs

To the Editor:

The study of Mabasa and Ma in a previous issue of JMCP reports on the successful utilization and drug cost savings for proton pump inhibitors (PPIs) in a Canadian employer-sponsored drug plan that implemented a therapeutic maximum allowable cost (MAC) program. Any successful health care intervention program aiming to maximize “value for money” is praiseworthy, especially for diseases that are associated with a high prevalence and/or have high treatment costs. From an employer perspective, however, the current study is associated with a number of fundamental flaws that are essential to point out if similar intervention programs are to be planned and implemented.

Firstly, the study methodology does not allow for a valid comparison of trends between the MAC program and the reference group, since no attempts were made to adjust for the effects of the study groups varying considerably during the study period. For example, the number of patients in the reference group increased by more than 40% during the study period compared with a 21% increase in the MAC group (Table 3 in the authors’ article).

Another important oversight was the failure to assess the effect of drug substitution on the quality of treatment (a fundamental aspect of determining the effects of any medical intervention). Indeed, if quality of treatment is decreased as a result of such substitution, this may have negative effects on nondrug health care utilization such as increased number of physician visits, investigations performed, or even hospitalizations. These generate costs that the Canadian community ultimately has to pay for. In a report issued by a Canadian patient organization, for example, the authors claim that PPI substitution programs are ineffective, have a negative impact on quality of patient care, and ultimately lead to increased overall health care costs.

A third limitation of the study is that it assumed that, at the stated doses, the PPIs provide no therapeutic advantage over one another. According to the Canadian patient organization, this ignores the fact that patients respond differently to different PPIs for many reasons, including drug interactions, side effects, variations in metabolism, and inappropriate dosage. Indeed, numerous studies have shown differences in effectiveness between alternative PPI treatments, not only between patient management strategies but also in relation to utilization patterns with regard to which patients receive PPI treatment, which type of PPI, and at which doses.

It is notable that patients in the MAC group who did not wish to switch to the cheapest (reference) PPI had to either pay the difference for their PPI or their physician had to apply for special authorization for full reimbursement (i.e., based on clinical judgment, the nonpreferred product would be beneficial to the patient). These are difficult barriers to overcome from a patient perspective, and it is interesting that around two thirds of drug cost savings in the MAC program were due to patients stopping PPI treatment. Moreover, it is notable that, within the wider Canadian Therapeutic Substitution policy and despite prescription barriers, around 25% of patients who did switch to the cheapest PPI were subsequently switched back to their previous PPI treatment following a special authorization. Although this has not been studied, it is very likely that the MAC program led to a varying degree of increased symptom burden for patients who stopped PPI treatment as well as for patients who were switched.

While the authors do not provide such information, it is highly likely that a significant proportion of PPI use was for the treatment of gastroesophageal reflux disease (GERD). In this regard, a large U.S. database study comparing costs for GERD cases (n = 11,653) versus a control group (n = 259,616) found that only 17% of total costs were for prescription drugs; the remainder was accounted for by direct medical costs such as physician visits and investigations, etc. (65%) and indirect employer costs for sick leave, short- and long-term disability, and workers’ compensation (19%). Consequently, focusing on drug costs alone ignores a significant proportion of health care costs relating to GERD and other acid-related diseases. Moreover, the MAC approach does not capture the largest cost of GERD for employers, namely the impact of GERD symptoms or symptoms of other acid-related disorders on reduced productivity while at work. Indeed, GERD symptoms interfere with work not only through disturbed sleep and daytime tiredness but also because they interrupt physical activity.

A recent systematic review of studies using patient-reported data in general working populations indicates that GERD causes a reduction in productivity while at work of around 10% on average. Considerably higher levels of reduced work productivity have been observed in untreated patients with troublesome GERD symptoms; in those with GERD-related sleep disturbance, for example, the mean reduction in productivity was up to 40%. PPI therapy to resolve GERD symptoms helps to address this burden and improves work productivity. Further, a case-control study using objective measurements of hourly and annual at-work productivity confirms that GERD, indeed, has a significant impact on productivity while at work, which supports validity of patient-reported productivity assessments. Assuming an average reduction in at-work productivity of around 10% in the PPI study population (281,951 + 374 = 282,325) and a 40-hour work week, this would correspond to more than 50 million work hours per year in lost at-work productivity due to GERD. Indeed, even small improvements in work productivity are relevant from an employer perspective, with a 2.5% improvement corresponding to 1 hour per patient over a 40-hour work week. These issues are clearly not addressed by a MAC program that focuses on drug costs alone.

In conclusion, PPI and other drug-switching programs need
to consider the wider horizon of the implications of switching for quality of treatment and effects on costs other than for prescription drugs alone. Consequently, drug costs for PPIs should probably not be the primary target for interventions from an employer perspective.

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REFERENCES

17. Wahlqvist P, Brook RA, Campbell S, et al. Objective measurement of hourly and annual productivity while at work in employees with gastroesophageal reflux disease (GERD) compared with employees without GERD. Gastroenterology. 2006;130(4 suppl 2):AT1005.

The Authors Respond:

We appreciate the opportunity for additional dialogue on the effect of a therapeutic maximum allowable cost (MAC) program on the cost and utilization of proton pump inhibitors (PPIs) in an employer-sponsored drug plan in Canada. Although the letter by Wahlqvist appears well intentioned, his comments misrepresent some of the main points of the MAC program and can be misleading due to the inadequate presentation and interpretation of the evidence on PPIs.

A fundamental concept in the utilization of a MAC program is that the drugs within a drug class be considered therapeutically interchangeable. The main criticism by Wahlqvist concerns the interchangeability between PPIs, and he argues that there are differences in effectiveness between alternative PPI treatments. It is important to highlight that the data cited by Wahlqvist were mainly comparing esomeprazole to other PPIs. These studies may be considered biased toward esomeprazole and lacking in the strength of evidence because these studies were designed to utilize 2- to 4-fold higher equivalent doses of esomeprazole than the comparator drug. Peer-reviewed meta-analysis comparing the efficacy of various PPIs such as by Vergara et al. on triple therapy Helicobacter pylori eradication and by Edwards et al. for the acute treatment of reflux esophagitis, contradict the argument by Wahlqvist. These meta-analyses are considered a higher level of evidence compared with randomized controlled trials.

Furthermore, the Therapeutic Initiatives group of Canada concluded that no trials have demonstrated an intrinsic therapeutic advantage among PPIs at equivalent doses. In addition, the U.S. Food and Drug Administration (FDA), upon review of the evidence on esomeprazole, concluded that

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esomeprazole affords rates of healing that are comparable to other PPIs, including omeprazole, and share the same overall acceptable safety profile.\(^9\)

Other employee benefits providers such as CIGNA HealthCare provide similar coverage of PPIs and consider PPIs to be similar in efficacy and safety.\(^6\) In their coverage position statement, they mentioned that there are only minor pharmacokinetic differences between PPIs, and these differences are not clinically meaningful. They also mentioned that the only clinically significant interaction among all PPIs is with omeprazole and warfarin. These can be easily managed by adjusting the dose of warfarin and monitoring the international normalized ratio (INR).\(^6\) Therefore, based on the best available evidence to date, PPIs can be considered interchangeable, and the evidence supports the use of a therapeutic MAC program.

Wahlqvist suggested that we committed an important oversight by failing to assess the effect of drug substitution on the quality of treatment. However, there is evidence suggesting that this type of program does not have a significant impact on clinical outcomes and provides economical advantages. A recent study of the British Columbia therapeutic substitution policy on PPIs showed that there was no increase in monthly hospitalization rates of gastrointestinal hemorrhage or major peptic ulcer disease (PUD) after patients switched to the reference drug, rabeprazole.\(^7\) Also, the monthly rates of office visits for gastroesophageal reflux disease (GERD), PUD, or gastritis did not significantly change, and total spending on these office visits were similar. This program led to a savings of Can $2.9 million after 6 months from policy change.\(^7\)

One comment by Wahlqvist was on the larger proportionate increase in the number of PPI patients in the non-MAC reference group in year 3 compared with the MAC group. This was caused by larger growth in non-MAC versus MAC employer groups over the 2-year period from the year ending May 31, 2003, compared with the year ending May 31, 2005, and would not affect the primary utilization measures of the number of claims, days of therapy, and allowed drug cost per patient per year.

We agree with Wahlqvist that GERD can significantly impact a person’s quality of life. This was not disputed in our study. We also agree that patient-specific factors need to be considered when selecting an appropriate PPI. In general, when selecting a medication to use for a patient, the clinician needs to consider, in specific order, the medication’s efficacy, safety profile, the ease of use to facilitate compliance, and, finally, the cost of the medication. For PPIs, the efficacy and safety profile of the available products is considered to be similar and all are taken once daily. Therefore, the cost would be considered the deciding factor when choosing a PPI. Since rabeprazole has the lowest drug cost, it would be appropriate to select this alternative first.

In conclusion, according to evidence-based practice, PPIs are an ideal drug class to utilize in a therapeutic MAC program and their use can lead to substantial drug cost savings without evidence of adverse health outcomes. We recommend that other types of drug classes that fit a similar profile be incorporated in a therapeutic MAC program.

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No outside funding supported the study in the referenced article. Johnny Ma is an employee of the pharmacy benefits manager that administered the maximum allowable cost program described in the article. The authors disclose no potential bias or conflict of interest relating to the article.

REFERENCES
ABSTRACTS

Abstracts From Professional Poster Presentations at AMCP’s 2006 Educational Conference

The following poster presentations have been prepared for the Academy of Managed Care Pharmacy’s 2006 Educational Conference, October 4-7, 2006, in Chicago, Illinois. Poster presentations are selected by the Program Planning Committee from proposals that are submitted to AMCP. Authors of posters are responsible for the accuracy and completeness of data presented in the posters and in the abstracts published here.

For more information about the studies described below, please contact the corresponding authors, indicated by an asterisk (*), whose addresses are listed in full; e-mail addresses and telephone numbers have also been provided. The names of individuals who are scheduled to present at the meeting are underlined.

ABILITY OF MEASURES OF FUNCTION AND INFLAMMATION TO PREDICT LONG-TERM PATIENT-REPORTED DISEASE IMPACT AND DISABILITY IN RHEUMATOID ARTHRITIS

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OBJECTIVE: To assess the relationship between measures of function (Health Assessment Questionnaire [HAQ]) and measures of inflammation (C-reactive protein [CRP] and erythrocyte sedimentation rate [ESR]), and determine if these measures predicted long-term patient-reported outcomes in patients with rheumatoid arthritis (RA).

METHODS: Subjects were 123 members of RAPOLO, a longitudinal, observational study of patients who had participated in etanercept clinical trials, for whom data at entry into the clinical trial were available. CRP, ESR, and HAQ were obtained at clinical-trial baseline. Patient-reported outcomes were from the first RAPOLO interview (mean 24.5 months after clinical trial baseline) and the 2-year RAPOLO interview (mean 51.8 months after clinical-trial baseline). Patient-reported outcomes included an SF-36 Physical Component Summary score; ratings of fatigue and pain impact; number of valued life activities affected and of all outcomes from the first interview except ratings of fatigue and pain impact, and of all outcomes from the 2-year interview except ratings of fatigue impact. In contrast, neither clinical-trial baseline CRP nor ESR was significantly associated with any of the patient-reported outcomes at either interview.

RESULTS: At baseline, correlations between HAQ and measures of inflammation were statistically significant (CRP \( r = .28, P = .002 \); ESR \( r = .27, P = .002 \)). Multiple regression analyses, controlling for age, sex, and disease duration, examined the relationship between baseline data and subsequent patient-reported outcomes. Baseline HAQ was a significant predictor of all patient-reported outcomes from the first interview except ratings of fatigue and pain impact, and of all outcomes from the 2-year interview except ratings of fatigue impact. In contrast, neither clinical-trial baseline CRP nor ESR was significantly associated with any of the patient-reported outcomes at either interview.

CONCLUSION: Long-term outcomes of individuals with RA are better predicted with baseline measures of function than with baseline measures of inflammation. The predictive power of early function is noted even after more than 4 years of follow-up, emphasizing the need to minimize functional impairment in RA early in disease since such impairment is a strong predictor of later disease impact and disability.

AGGRESSIVE STEP-THERAPY PROGRAMS REALLY DO SAVE MONEY

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INTRODUCTION: An aggressive step-therapy program that incorporates advertising, pharmacy claims edits, enhanced benefits, and financial incentives can result in cost savings of more than $4.00 per member per month (PMPM).

METHODS: Based on the potential opportunity for cost savings, 3 drug categories were selected for aggressive step-therapy management. These programs, for proton pump inhibitors (PPIs), non-sedating antihistamines (NSAs), and antidepressants, were in addition to several other step-therapy programs already in place. In addition to traditional methods of requiring a specific drug prior to coverage of a more expensive product, new tools were applied. A marketing campaign regarding the new opportunity was launched and described as an enhanced benefit. Coverage was provided for over-the-counter (OTC) products and was expanded to a 42- or 48-day supply, instead of the usual 34-day supply. Reminders to members regarding the enhanced offering were triggered through the prescription claims system. The pharmacy department worked with physicians to facilitate a prescription switch for PPIs, and a financial incentive was offered to physicians who participated. In addition, member copayment was waived for Prilosec OTC. Market share and PMPM cost within the 3 targeted categories was tracked from the implementation date of the program through the present.

RESULTS: The cost savings resulting from these 3 successful programs has totaled $4.47 PMPM, representing a savings of more than 10% of total retail drug costs for the plan. Costs for the PPIs dropped nearly $2.00 PMPM, and market share for omeprazole and Prilosec OTC is now 65%, compared with 10% nationally. Plan costs for the NSAs and antidepressants...
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Decreased by more than $1.50 and $0.90 PMPM, respectively, and cost per prescription dropped by $15.00 and $13.00 for these 2 drug classes.

**CONCLUSION:** A multifaceted approach to step therapy, incorporating different tools based on the program, can result in significant cost savings.

### Assessing Patient-Reported Outcomes of Patients with Psoriatic Arthritis Treated with Etanercept

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**INTRODUCTION:** Patient-reported outcomes (PROs) provide important information about patient experiences that complement other clinical assessments.

**METHODS:** The effect of etanercept (ETN) treatment on PROs was determined in patients with psoriatic arthritis (PsA) in a phase 3, randomized, multicenter study. PROs were assessed at baseline (BL), through the initial 24-week double-blind (DB) phase, and the subsequent 48-week open-label (OL) phase. PRO measures included (a) the Stanford Health Assessment Questionnaire Disability Index (HAQ-DI), (b) the Medical Outcomes Study Short-Form Health Survey (SF-36) physical component summary (PCS), (c) the EQ-5D Feeling Thermometer, and (d) the ACR Patient Pain assessment scale. Results in the DB phase are based on last-observation-carried-forward imputation, and OL results are observed data at each time point.

**RESULTS:** In the DB phase, 205 patients were randomly assigned with 72/104 and 93/101 patients completing placebo (PLA) and ETN (25 mg, BIW), respectively. In the OL phase, 169 patients (82.4%) participated; 70/104 (PLA) and 78/101 (ETN) completed 48 weeks of treatment. After 24 weeks of DB treatment, ETN patients had significantly greater HAQ-DI improvement relative to patients treated with PLA (0.5 vs. 1.0, 53.6% vs. 6.4%; P <0.0001). Importantly, 38% of ETN patients had an HAQ-DI = 0, compared with 7% of PLA patients. The mean percentage change in HAQ-DI was similar in PLA-ETN and ETN-ETN patients (46.9% vs. 52.8%; OL phase). Mean changes relative to BL for all PRO measures were significant in the DB phase (P <0.001), and all showed improvement for PLA-ETN patients subsequent to ETN treatment in the OL phase.

**CONCLUSION:** Extended etanercept treatment in patients with PsA significantly improved PROs, as assessed using 4 different measures.

### Assessing the Impact of Smoking-Cessation Therapies on a Managed Care Organization’s Budget

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**INTRODUCTION:** A variety of smoking-cessation therapies are on the market. History has shown these therapies to have a dramatic uptake upon introduction, which can create significant economic burden to managed care organizations (MCOs) when covered. With new therapies expected, an economic model to quantify budgetary impact of smoking-cessation therapies is important.

**METHODS:** A decision analytic was developed to assess the budgetary impact of cessation therapies. Using national survey data, the number of patients attempting to quit within an MCO population was estimated. The unassisted quit rate and therapy-specific incremental effect of successfully quitting were extracted from published literature. Drug costs were obtained from the Red Book. Drugs were assumed to be dosed and used according to label, and patients attempted 2 quit attempts per year. Prescription drugs were assumed to be covered by tier-2 copayments and require 1 incremental physician visit for dispensing and/or monitoring. Current and future market share were based on national survey and postmarketing sales data.

**RESULTS:** Based on 1 million lives, the introduction of new cessation therapies increases drug costs from $4.2 to $8.1 million, physician visit costs from $768,000 to $1.3 million, and number of patients successfully quitting from 5,554 to 6,137. Per-member-per-month drug costs increased by $0.28 and physician visit costs increased by $0.04. Costs per quitter increased from $756 to $1,320.

**CONCLUSION:** Introduction of new smoking-cessation therapies has a substantial impact on MCO budgets. Thus, careful coverage decision making is recommended.

### Assessment of Patient Satisfaction after Formulary Conversion of Their Glaucoma Medication

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**INTRODUCTION:** Managed care plans have initiated glaucoma formulary changes (Law et al., 2005). We assessed glaucoma patients’ satisfaction after a recent formulary change to their glaucoma medication.

**METHODS:** Patient surveys consisting of 10 questions were distributed by opthalmologists to their glaucoma patients, whose health plan recently had a formulary change in their glaucoma therapy to bimatoprost. The survey was distributed along with their first prescription, and the completed surveys
were mailed in anonymously by the patients. Five questions asked patients about their satisfaction with their glaucoma medication prior to and following the formulary change on a scale of 1 to 5 (1 = Very satisfied, 2 = Satisfied, 3 = Somewhat satisfied, 4 = Somewhat unsatisfied, 5 = Unsatisfied). Five additional questions inquired about general background information relating to the patients’ medication profile and source of copay change information. Descriptive statistics were generated and the Wilcoxon Signed Rank test was used to determine statistical significance between satisfaction scores.

RESULTS: A total of 99 patients from 11 different states, representing various managed care plans, completed the survey. Patients were receiving an average of 2.6 (median = 3.0) glaucoma medications. Approximately 66%, and 22% received one of the other prostaglandin/prostamide agents (latanoprost or travoprost) and a beta-blocker, respectively, prior to the formulary change. On a scale of 1 to 5 (5 indicating highest satisfaction), the surveyed patients scored their previous glaucoma medication an average of 2.4. Following formulary change, the patients scored bimatoprost an average of 3.4, 1.0 point higher than the medication(s) prior to the formulary change (P < 0.001). Approximately 87% (86) of patients intended to continue with the change, 9 respondents were unsure, 1 individual did not intend to continue, and 3 people did not provide an answer.

CONCLUSION: Most patients were already satisfied with their glaucoma medication prior to the formulary change; however, satisfaction increased after the change in this surveyed population.

BUDGET IMPACT ANALYSIS OF BISPHOSPHONATES FOR FRACTURES IN POSTMENOPAUSAL WOMEN

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OBJECTIVE: To estimate from a health plan perspective the budget impact of treating postmenopausal women with bisphosphonates (alendronate, risedronate) to prevent hip and vertebral fractures.

METHODS: The annual budget impact was calculated by estimating annual expenditures for bisphosphate treatment less the cost of hip or vertebral fractures prevented per year from treatment. Data from pivotal clinical trials were used to estimate the number of clinically significant vertebral or hip fractures prevented with bisphosphonates. Cost of a fracture was based on medical claims data for women hospitalized for hip or vertebral fractures from January 1, 2003, to December 31, 2004. Medication costs were based on the average wholesale price for average dosing of bisphosphonates x 365 days, assuming 100% compliance with therapy.

RESULTS: Annual medication costs for treatment were $9.9 million for risedronate and $10.3 million for alendronate per 10,000 women. Annual savings from averted fractures per 10,000 women were $3.1 to $3.8 million for high-risk women and $22,000 to $33,000 for low-risk women. The annual net budget impact was $6.5 to $6.8 million for high-risk women and $9.8 to $10.3 million for low-risk women. Medication costs were about 3 times higher in high-risk women and 375 times higher in low-risk women than costs of hip or vertebral fractures prevented.

CONCLUSIONS: Using ideal assumptions for baseline fracture risk and medication adherence, treatment costs for bisphosphonates far exceed savings resulting from fractures prevented. Postmenopausal women with high fracture risks show the greatest benefits and offsets in treatment costs. These cost considerations should be factored into designing quality improvement programs that identify women who will best benefit from treatment with bisphosphonates.

CHARACTERISTICS OF PATIENTS INITIATING TERIPARATIDE (FORTEO) THERAPY

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OBJECTIVE: To compare the characteristics of patients initiating teriparatide (TPTD) with those of patients initiating bisphosphonates (BIS).

METHODS: Beneficiaries (aged 45 years and older) with at least 1 claim for teriparatide or a bisphosphonate in 2003 or 2004 and continuous enrollment in the previous 12 months and subsequent 6 months were identified in a large (7.6 million covered lives) national commercial and Medicare administrative claims database (MarketScan). Patients initiating TPTD were compared with patients initiating BIS in terms of age, gender, insurance characteristics, region, provider specialty, conditions associated with osteoporosis, prior use of osteoporosis medications, fractures, BMD screening, health status, resource utilization, and costs. Group comparisons were made using chi-square tests for proportions of categorical measures and t tests for means of continuous variables.

RESULTS: TPTD patients were older (mean age 70 years [TPTD] versus 65 years [BIS]; P < 0.0001) and were more likely to be enrolled in a Medicare plan (64% [TPTD] versus 40% [BIS]; P < 0.0001) compared with BIS patients. The TPTD patients had more preexisting fractures (38% [TPTD] vs. 16% [BIS], P < 0.0001) and more comorbidities than BIS patients as demonstrated by higher scores on the Charlson Comorbidity Index (1.27 [TPTD] vs. 0.82 [BIS]; P < 0.0001). TPTD patients were also more likely to have used another osteoporosis medication in the previous 12 months (80% [TPTD] vs. 32% [BIS]; P < 0.0001).

CONCLUSIONS: In this sample of patients enrolled in commercial and Medicare plans, patients selected for teriparatide treatment differed from those initiating bisphosphonates in several important ways. TPTD patients were older, had poorer overall health status, and appeared to have more-severe osteoporosis than patients initiating bisphosphonates.
COMPLICATION AND CARDIOVASCULAR COMORBIDITY RATES OF NEWLY TREATED TYPE 2 DIABETICS

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INTRODUCTION: The purpose of the study was to evaluate the diabetes-related complication and cardiovascular comorbidity rates in newly treated (NT) patients with type 2 diabetes mellitus (T2DM) in order to identify opportunities for improving medical management of these patients.

METHODS: A retrospective study of a large national managed care claims database was performed using data from January 1, 2002, to December 31, 2004. NT patients were identified if they had filled ≥1 prescription for an oral antihyperglycemic (OAH) agent; had no prescriptions for an OAH within the 6 month period before their OAH index date, had ≥1 medical claim with a T2DM diagnosis code, and were ≥ age 18 years. Patients were observed for 12 months post OAH index date.

RESULTS: 6,436 NT patients were identified for study. High rates of diabetes-related complications and cardiovascular comorbidities were observed: 35.0% of NT patients had evidence of diabetes-related neuropathy, 15.7% had retinopathy, 14.6% had nephropathy, 11.1% had peripheral circulatory disorders, and 9.5% had lower limb ulcers; 79.4% of NT patients had comorbid hypertension, 58.9% had evidence of heart disease, and 78.6% had a diagnosis for dyslipidemia. While 78.6% had a dyslipidemia diagnosis, only 50.3% of NT patients received a prescription for a lipid-lowering agent.

CONCLUSIONS: These data suggest that newly treated T2DM patients have a high incidence of diabetes-related complications and cardiovascular comorbidities. Both glycemic and lipid control contribute to overall cardiovascular risk in patients with type 2 diabetes and require intensive management. Considering the prescription burden of these patients, an unmet need exists for a single agent to address more than one cardiovascular risk factor, such as lowering glycosylated hemoglobin (A1C) and low-density lipoprotein cholesterol. Finally, given the rate of diabetes-related complications and cardiovascular comorbidities in newly treated patients, the cost implications to payers with an initial diagnosis of CKD prior to dialysis.

COST BURDEN OF ANEMIA IN A PREDIALYSIS COHORT OF PATIENTS WITH CHRONIC KIDNEY DISEASE

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OBJECTIVE: To quantify the resource impact of anemia in a cohort of chronic kidney disease (CKD) patients.

METHODS: A total of 37,105 CKD patients diagnosed between 2000 and 2005 were selected from the Medstat MarketScan Commercial and Medicare Research Databases. Patients were followed from the first diagnosis of CKD until the onset of dialysis, transplantation, disenrollment, or study end. Twenty-six percent of patients were identified as anemic, with 59% of anemic patients receiving treatment for their anemia. Health care expenditure was reported in 2004 dollars per patient per month (PMPM). Generalized linear models were used to identify those factors that significantly impacted health care expenditures.

RESULTS: Adjusted expenditure for CKD patients was $2,531 PMPM. Anemia had the greatest impact on total expenditure (P < 0.001), increasing total monthly expenditure by 38% ($1,069) due largely to higher rates of inpatient care (63% vs. 39%). Anemic patients also experienced higher rates of emergency room visits, nutritional counseling, and transportation services, as well as more frequent office visits and laboratory tests.

CONCLUSION: Anemia is a major cost driver in the treatment of patients with CKD prior to dialysis.

COST-EFFECTIVENESS OF ALTERNATIVE TREATMENTS FOR OVERACTIVE BLADDER

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INTRODUCTION: An intent-to-treat Markov model was developed to simulate clinical and economic outcomes for primary care management of patients with overactive bladder (OAB)-related incontinence.

METHODS: From a payer's perspective, we modeled the cost-effectiveness of treatment with solifenacin (SOL), tolterodine (TOL), or no therapy (NT) based on published information, including data from the Solifenacin with Tolterodine as an Active Comparator in a Randomized (STAR) trial. OAB management was simulated in a hypothetical health plan based on 3 phases of care. Diagnosis: assumes 15% of prevalent cases seek treatment and evaluation for OAB; cases not seeking treatment (NST) remain in the model. Titration: assumes three 4-week cycles. Treatment-seeking patients receive SOL 5 mg/10 mg or TOL 4 mg or NT. Treated patients with suboptimal results may discontinue therapy, increase dose (SOL-treated...
COST-EFFECTIVENESS OF DISEASE-MODIFYING AGENTS FOR THE TREATMENT OF RELAPSING MULTIPLE SCLEROSIS

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OBJECTIVE: To compare the cost-effectiveness of disease-modifying agents for the treatment of relapsing multiple sclerosis (MS) from a managed care payer perspective, considering the anticipated reentry of natalizumab into the market.

METHODS: A 2-year model was constructed to compare the cost per relapse avoided of disease-modifying agents used for the treatment of MS. Overall cost of therapy included drug costs (First Databank), drug administration/monitoring costs (published private payer fee ranges), and relapse and disability treatment costs (published literature). All costs were reported in 2005 US$. Prevalence, clinical efficacy, and other model assumptions were based on product labels and published literature. Effectiveness was defined as the estimated number of relapses avoided with treatment, calculated as number of relapses for a nontreated population multiplied by relapse rate reduction (interferon beta 1-a [Avonex] 32%, interferon beta 1-b 34%, glatiramer acetate 29%, interferon beta 1-a [Rebif] 32%, and natalizumab 68%). Univariate sensitivity analyses were conducted to determine model inputs with the most influence on model results.

RESULTS: The annual overall cost of therapy per patient was $23,594 (interferon beta 1-a [Avonex]), $24,971 (interferon beta 1-b), $25,310 (glatiramer acetate), $26,768 (interferon beta 1-a [Rebif]), and $32,890 (natalizumab). The cost per relapse avoided was lowest for natalizumab ($50,860), followed by interferon beta 1-b ($77,229), interferon beta 1-a (Avonex) ($77,530), interferon beta 1-a (Rebif), ($87,959), and glatiramer acetate ($91,773). The incremental cost-effectiveness ratios for natalizumab versus the other disease-modifying agents ranged from $17,883 to $27,154. Sensitivity analyses indicated that the model input with the most influence on cost per relapse avoided is relapse-rate reduction and the input with the least influence is cost per relapse.

CONCLUSION: This analysis suggests that the drug acquisition cost of natalizumab may be offset by its clinical effectiveness, resulting in the lowest cost per relapse avoided, from a managed care perspective.

COST-EFFECTIVENESS OF MEMANTINE AS AN ADJUNCT TO DONEPEZIL IN PATIENTS WITH MODERATE-TO-SEVERE ALZHEIMER’S DISEASE

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INTRODUCTION: The efficacy and safety of memantine in patients with moderate-to-severe Alzheimer’s disease (AD) receiving stable donepezil treatment was recently demonstrated in a phase 3 trial; its cost-effectiveness in this use is unknown, however.

METHODS: A Monte Carlo simulation model depicting disease progression and associated clinical and economic outcomes in patients with moderate-to-severe AD was developed. Disease progression was described in terms of decline in cognitive function, as assessed by the Severe Impairment Battery (SIB), and was estimated monthly. Risk of institutionalization was estimated based on predicted SIB score. Expected costs of formal and informal care (2005 US$) and patient utilities were calculated based on predicted SIB score and setting of care. Patients in the model were assumed to receive memantine plus donepezil or donepezil alone. Memantine plus donepezil was assumed to improve cognition (i.e., increase SIB score) compared with donepezil alone. Duration and benefits of therapy for both regimens were assumed to persist for 1 year. Cost-effectiveness was calculated in terms of cost per quality-adjusted life-year (QALY) gained over a lifetime. Future benefits and costs were discounted at 3% annually.

RESULTS: In patients with moderate-to-severe AD receiving stable donepezil treatment (mean SIB at baseline = 78.7), 1 year of adjunct therapy with memantine would increase costs of pharmacotherapy by $1,250 but would reduce costs of formal and informal services by $1,493 over a lifetime as a consequence of reduced need for formal and informal care. Memantine therefore is a dominant treatment strategy versus donepezil alone (i.e., less costly, more effective). However, the cost-effectiveness ratio is sensitive to assumed severity of disease at therapy initiation and is less favorable (i.e., higher) for patients with greater initial severity of disease.
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COST-EFFECTIVENESS OF VACCINATION STRATEGIES TO PREVENT HUMAN PAPILLOMAVIRUS INFECTION IN THE UNITED STATES

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INTRODUCTION: This study evaluated the impact of vaccination, in addition to screening, in preventing human papillomavirus (HPV) infection and related disease in the United States.

METHODS: The Markov model simulated the lifetime impact of HPV natural history and progression in a cohort of 1,988,614 12-year-old females. Three vaccination strategies (with screening) were each compared with no vaccination (screening only): (1) bivalent vaccine against HPV 16/18 only, (2) quadrivalent vaccine against HPV 16/18/6/11, (3) bivalent vaccine against HPV 16/18 with cross-protection against other oncogenic HPV types. Model inputs were based on clinical trial data and published literature. Standard discount rates (3%) were applied. Outcome measures included total costs; cases of cervical cancer, death, cervical intraepithelial neoplasia (CIN), genital warts, abnormal pap smears; life-years saved (LYS); quality-adjusted life-years (QALYs) and incremental costs per LYS and QALY. Sensitivity analyses addressed uncertainties, including vaccine efficacy waning and vaccine costs.

RESULTS: While screening-only was the least-expensive strategy, it had the least impact on clinical outcomes. The bivalent vaccine with cross-protection (with screening) was the second-least-expensive strategy, preventing the most abnormal pap smears, CIN lesions, cervical cancer and deaths, and resulting in more LYS, more QALYs and lower incremental cost per LYS and QALY compared with all other options. Total per-patient costs across screening and vaccination strategies ranged from $1,300 to $1,654 (2005 dollars). The incremental cost-effectiveness of HPV vaccination ranged from $1,300 to $51,379 per QALY. Results were sensitive to assumptions in vaccine efficacy waning and vaccine costs.

CONCLUSION: The model demonstrates that vaccination, combined with screening, is a cost-effective strategy in preventing HPV infection and related disease. Results further suggest that a bivalent vaccine with cross-protection has the greatest impact on cervical cancer and precancerous disease states and is more cost effective compared with alternative vaccination strategies.

DIABETIC RETINOPATHY CLAIMS IN A COMMERCIALALLY INSURED MEDICARE POPULATION

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INTRODUCTION: Patient characteristics, photoagulation procedures, and health care costs were assessed for commercially insured Medicare patients with diabetic retinopathy (DR), a common diabetic microvascular complication and leading cause of vision loss.

METHODS: Patients with diabetes were identified in the MarketScan Medicare coordination of benefits database. Patients included for analysis had a claim for DR or macular edema (ME) between 3Q 1997 and 3Q 2004, continuous enrollment for 6 months prior to analysis and at least 6 months postanalysis. Baseline DR diagnosis was classified as proliferative (PDR), proliferative with macular edema (PME), background (BDR), background with macular edema (BME), or macular edema only (ME). Other diabetes complications, comorbidities, incident photoagulation, and other health care costs were assessed pre-DR/ME diagnosis and post-DR/ME diagnosis.

RESULTS: Among 373,525 Medicare patients with diabetes, 16.0% had a claim for DR/ME, of whom 70.2% met the inclusion criteria (N = 41,992). Mean age was 72.9 and 49.5% were male. DR/ME diagnoses comprised 1% PME, 12.8% PDR, 2.4% BME, 78.1% BDR, and 6.1% ME. Postperiod diabetes complications included diabetic foot (7.4%), neuropathy (7.2%), kidney disease (9.6%), dialysis (4.4%), and acute hyperglycemia (3.9%). Postperiod macrovascular complications included heart disease (82.8%) and stroke (29.2%). On average, patients used 1.69 distinct diabetes medications and 2.01 medical treatments to treat other chronic diseases. Overall, 27.7% had photoagulation in the postperiod, which varied by type of DR/ME: 87.4% of PME, 80.1% of BME, 53.1% of PDE, 48.1% of ME, and 19.1% of BDR. Preperiod DR/ME treatment costs were 20.4% of total costs for patients with photoagulation and 5.6% of total costs for patients without photoagulation. Postperiod DR/ME costs were 8.4% and 1.8% of total costs for the photoagulation and nonphotoagulation patients, respectively.

CONCLUSION: Patients diagnosed with DR/ME have high levels of other diabetes complications. A lower DR/ME costs in the postperiod suggest an increase in costs related to other health conditions.
ECONOMIC BURDEN OF CHRONIC ANGINA TO MANAGED CARE

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OBJECTIVE: To assess the prevalence and direct costs of angina patients in a managed care environment through retrospective analysis of a large managed care organization (MCO) database.

METHODS: Coronary artery disease patients enrolled in a national MCO between 2001 and 2004 for 18 consecutive months were selected using algorithms comprised of multiple coronary artery disease (CAD), International Classification of Diseases, Ninth Revision (ICD-9) diagnosis, procedure and pharmacy codes. CAD patients with and without angina were identified and followed for 1 year to study health care utilization of each group.

RESULTS: There were 140,011 CAD patients without angina and 25,535 with angina that met the selection criteria. Angina patients were more likely to have a CAD-related emergency department visit (27% versus 12%) and to have multiple separate revascularization procedures (16% versus 3%) during the 1 year follow-up period. Angina patients had a higher average number of CAD-related ambulatory visits (5.92 vs. 2.43) and were prescribed lipid-lowering drugs (71% vs. 50%), Beta-blockers (77% vs. 33%), and calcium channel blockers (39% vs. 16%) more often than were CAD patients without angina. Resource use drives high costs for CAD patients in general; however, costs for patients with angina was twice that of CAD patients without angina, on average 21,904 US$ versus 11,531 US$ annually.

CONCLUSIONS: Angina is costly to managed care. Angina patients make extensive use of emergency departments, likely as a result of angina symptoms. Angina patients, even when revascularized and prescribed guideline-appropriate medications, are likely to have multiple additional procedures during the course of year, suggestive of continuing angina attacks even following treatment. A reduction in angina attacks could result in substantial savings in resource utilization in managed care.

EFFICACY AND SAFETY OF 6 MONTHS OF NIGHTLY ESZOPICLONE IN PATIENTS WITH PRIMARY INSOMNIA: A SECOND LONG-TERM PLACEBO-CONTROLLED STUDY

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INTRODUCTION: Eszopiclone is a nonbenzodiazepine insomnia treatment; results of a second long-term study are presented.

METHODS: In this randomized, double-blind study, adults (aged 21-64 years) with a Diagnoistic and Statistical Manual of Mental Disorders, Fourth Edition diagnosis of primary insomnia (sleeping ≤6.5 hours) and/or having sleep latency (≥30 minutes) received nightly placebo (n = 280) or eszopiclone 3 mg (n = 550) for 6 months followed by a 2-week placebo run-out period. Patient-reported end points collected with the Interactive Voice Response System (IVRS) included sleep (latency, total sleep time [TST], wake time after sleep onset [WASO], sleep quality) and daytime function (alertness, daytime sleepiness, ability to function/concentrate, physical well-being). Withdrawal effects (rebound insomnia and central nervous system [CNS] adverse events) were carefully and prospectively assessed after 180 nights of continuous nightly therapy using a 2-week single-blind placebo-substitution run-out phase.

RESULTS: At all monthly assessment points, eszopiclone 3 mg significantly improved sleep latency, WASO, TST, and sleep quality versus placebo (P < 0.0001). Patients taking eszopiclone had average changes from baseline versus placebo of -38.3 versus -21.7, -22.03 versus -7.5, and 79.38 versus 41.6 minutes for latency, WASO, and TST, respectively. Eszopiclone 3 mg also significantly improved all monthly daytime parameters (P < 0.05) at all assessment points versus placebo. Pharmacologic tolerance was not observed. No rebound insomnia was noted because the medians for all sleep parameters remained below baseline during the entire 2-week run-out period. No withdrawal CNS effects were noted (as assessed by spontaneously reported adverse events during the discontinuation phase and the Benzodiazepine Withdrawal Questionnaire). Eszopiclone was well tolerated; the most common adverse event was unpleasant taste.

CONCLUSION: Results from this study are consistent with a previous 6-month study. In this study, nightly use of eszopiclone produced consistent and sustained improvements across all sleep and daytime function parameters and was well tolerated with no pharmacologic tolerance, withdrawal CNS adverse events, or rebound insomnia.

EPIDEMIOLOGY, HEALTH CARE UTILIZATION, AND COST IN SUBJECTS WITH AND WITHOUT ERYTHROPOIETIN-STIMULATING AGENTS IN AN ANEMIC CHRONIC KIDNEY DISEASE POPULATION

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OBJECTIVES: To estimate the incidence and prevalence of anemia in patients with chronic kidney disease (CKD) not on dialysis and to characterize health care utilization and costs in a commercially insured patient population.

METHODS: CKD was identified in enrolled subjects who had 2 or more claims with International Classification of Diseases, Ninth Revision (ICD-9) diagnoses of CKD from January 1, 2001, through December 31, 2003. Anemia was defined by ≥1 claim with ICD-9 code for anemia, or 1+ claim for erythropoietin-stimulating agent (ESA) or intravenous iron. CKD anemic subjects...
with and without ESA treatment were compared for health care utilization (e.g., inpatient, outpatient, ER visits, pharmacy, and lab) and associated costs. Patients were followed until the onset of dialysis, kidney transplantation, disenrollment, or study end.

RESULTS: Over the study period, the incidence and prevalence rates of anemia among CKD patients were 0.34-0.39 and 0.61-0.75, respectively. Of the 28,153 CKD patients, 33.8% had anemia, and only 16% of anemic subjects received an ESA. ESA-treated patients had a greater prevalence of diabetes (47% vs. 37%, \( P < 0.0001 \)) while a greater proportion of those not treated with ESA had a history of myocardial infarction (2.9% vs. 1.5%, \( P = 0.002 \)). Compared with ESA-treated patients, non-ESA patients had a significantly greater frequency of inpatient and ER visits and longer hospital stays (average 19 days vs. 13 days, \( P < 0.0001 \)). While the non-ESA patients had lower pharmacy and outpatient costs, they incurred a significantly higher inpatient cost (69%), which was the largest cost driver for the total monthly costs ($3,155 vs. $2,453, \( P < 0.0001 \)).

CONCLUSION: Approximately 84% of anemic CKD patients did not receive ESA treatment of anemia. However, ESA patients used fewer hospital inpatient resources, resulting in lower overall costs than those who were not treated with an ESA.

EXAMINING TITRATION PATTERNS WITH ROSUVASTATIN AS COMPARED WITH OTHER STATINS IN ROUTINE CLINICAL PRACTICE

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OBJECTIVE: To assess differences in the frequency of titration between rosuvastatin (RSV) and other commonly used statin monotherapy agents in routine clinical practice.

METHODS: Retrospective study using the General Electric Medical Records database was conducted of patients aged 18+ years, who were newly prescribed statin therapy from August 2003-May 2005 (n = 12,041). Excluded patients included those started on the maximum statin dose (8%), those at Adult Treatment Panel (ATP) III low-density lipoprotein cholesterol (LDL-C) goal level at baseline (40%), or those on fluvastatin (least commonly used statin; 3%). Frequency of titration with RSV was compared with other statins. Multivariate regression models adjusted for baseline LDL-C, coronary heart disease (CHD) risk, therapy duration, and LDL-C goal attainment.

RESULTS: Of the 5,954 eligible patients, 7.2% were prescribed RSV, 63.5% atorvastatin (ATV), 15.2% simvastatin (SMV), 7.2% pravastatin (PRV) and 6.9% lovastatin (LOV). The mean age was 63.4 years, 47% were male, and 12% had CHD. The mean starting dose for RSV was 10.7 mg compared with other statins (15.5-32.9 mg). Significantly fewer RSV patients (9.6%) had at least 1 titration as compared with ATV (19.3%), SMV (21.9%), PRV (19.7%), and LOV (24.2%) (\( P < 0.0001 \)). Similarly, after adjusting for covariates, patients on other statins were significantly more likely to be titrated (odds ratios: 2.0-2.8) as compared with RSV patients (\( P \leq 0.0005 \)). After adjusting for covariates, an estimated 10% of RSV patients were titrated at least once as compared with 19% ATV, 22% SMV, 20% PRV, and 25% LOV. In the subgroup of patients attaining ATP III LDL-C goal, an estimated 9% of RSV patients were titrated at least once versus 17% ATV, 21% SMV, 21% PRV, and 24% LOV (\( P < 0.0006 \)).

CONCLUSION: A significantly lower percentage of patients on RSV were titrated compared with other commonly used statins in routine clinical practice. Additionally, a larger percent of RSV patients attain LDL-C goal without titration compared with other statins.

FINANCIAL IMPACT COMPARISON OF MAIL ORDER AND 90-DAY AT RETAIL VERSUS TRADITIONAL 30-DAY RETAIL PRESCRIPTION PROCESSING

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OBJECTIVE: Mail order and 90-day at retail pharmacy benefit designs for maintenance medications are touted as cost-saving alternatives to traditional 30-day retail prescriptions. Since mail order and 90-day at retail normally lack maximum allowable cost (MAC) pricing and require decreased member cost share per prescription compared with traditional 30-day retail prescriptions, the goal of this analysis was to determine the financial impact to the benefit sponsor.

METHODS: The analysis was based on retrospective, maintenance medication mail-order prescription claims (N = 55,887) submitted between January 1, 2005 and December 31, 2005. Claim data included National Drug Code (NDC), drug name, average wholesale price (AWP), quantity dispensed, days supply, ingredient cost, dispensing fee, and copay. Claims were separated into brand (N = 29,343), generic (N = 25,670), and supply (N = 874). Brand medications comprised 52.5% of the claims. AWP discounts were applied to brand and supply prescription claims. For each generic AWP discount, proprietary MAC and federal upper limit MAC (FUL MAC) were applied. If a proprietary MAC or FUL MAC was absent, AWP discounts were applied. A Microsoft Excel-based financial model was built upon variable ranges of network discounts, dispensing fees, and copayments common in the current pharmacy benefit management marketplace. The data by NDC was then modeled as potential prescription cost expenditures—3 scenarios: 30-day retail, mail order, and 90-day retail.

RESULTS: Brand medications at 30-day retail cost less than mail order or 90-day retail when 1 copayment per prescription was applied. Mail order and 90-day retail cost less than 30-day retail for brand medications when 3 copayments were applied for 90-day quantities. Supplies produced similar results. Thirty-day retail...
cost less to the benefit sponsor than mail order or 90-day retail when 1 copayment was applied for generic medications. The application of 3 generic copayments per 90-day supply resulted in less cost (to the sponsor) for mail order when the proprietary MAC or AWP discount was applied for generic medications. For 90-day retail claims, 3 generic copayments resulted in benefit sponsor savings only when the proprietary MAC was applied. Copayment break-even points for mail order and 90-day retail compared with the cost of 30-day retail was established for brands, supplies, and generics over a range of copayments. The break-even point for mail order and 90-day retail at $20 brand copayments was 1.6 and 2, respectively. Alternatively, the break-even point for mail order and 90-day retail at $40 brand copayments was 2.3 and 2.5, respectively. The aggregation of brand, generic, and supply spend for each modeling strategy resulted in 30-day retail providing potential benefit sponsor savings greater than 20% compared with mail order and 90-day retail when one 30-day copayment is required for the 90-day supply. Thirty-day retail prescriptions potentially increased the sponsor cost more than 10% when 3 copayments were required for a 90-day supply.

CONCLUSION: Mail order and 90-day retail prescription claim processing is financially sensitive to MAC pricing and member cost share. Depending on member cost-share level between 2 and 3 copayments for 90-day prescriptions can potentially provide cost savings to the benefit sponsor.

FORMULARY AND STEP CARE ON NONSEDATING ANTIHISTAMINES: IMPACT ON PRESCRIPTION DRUG COSTS

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OBJECTIVE: To evaluate formulary management and step-care clinical programs on prescription costs of nonsedating antihistamines (NSAs)—a high-volume and high-cost drug category.

METHODS: Twenty-four months of prescription data (January 1, 2004, through December 31, 2005) were obtained from a pharmacy benefit manager’s pharmacy claims database. A pre-retrospective and postretrospective cohort study design was used. Four study cohorts were recognized based on the different strategies clients implemented: (1) moving prescription NSAs to nonpreferred status and implementing an NSA step-care program, (2) implementing an NSA step-care program, (3) moving prescription NSAs to nonpreferred status, and (4) maintaining the preferred status of prescription NSAs with no step care (comparison group). The outcome measure was per member per month (PMPM) total cost.

RESULTS: Clients who moved prescription NSAs to nonpreferred status and implemented a step-care program experienced a 46.35% decrease in PMPM costs. Clients who either implemented a NSA step-care program or moved prescription NSAs to non-preferred status experienced a 33.92% and a 24.88% decrease in PMPM costs, respectively. The control clients who maintained the preferred status of prescription NSAs with no step-care program had a decrease of PMPM costs by only 8.84%. By comparison with the control clients, we estimated PMPM cost savings of $0.43 for clients who moved the prescription NSAs to nonpreferred status as well as implemented a step-care program, $0.36 for clients who implemented a step-care program, and $0.14 for clients who moved prescription NSAs to nonpreferred status.

CONCLUSIONS: Formulary management and step-care clinical programs on NSAs reduced prescription drug costs.

HEALTH CARE COSTS ASSOCIATED WITH PHARMACOTHERAPY FOR ALCOHOL-USE DISORDERS IN AN INSURED POPULATION IN THE UNITED STATES


OBJECTIVE: To determine the impact of pharmacotherapy on health care costs in patients with alcohol-use disorders.

METHODS: Data from the Medstat MarketScan Commercial Claims and Encounters Database for 2000-2004 were analyzed for 3 groups: (1) patients with alcohol-related diagnoses treated with oral naltrexone who had ≥1 medical claim with an alcohol-related diagnosis, ≥1 pharmacy claim for naltrexone, no claims for disulfiram or acamprosate, and ≥6 months continuous plan enrollment before and after the earliest naltrexone claim (index date); (2) alcohol controls (patients with alcohol-related diagnoses without naltrexone, disulfiram, or acamprosate pharmacotherapy); and (3) nonalcohol controls (patients with neither alcohol-related diagnoses nor pharmacotherapy). All 3 groups were matched for gender, age, geographic region, relationship to employee, health plan type, and index quarter/year in a 3:1 ratio (3 controls: 1 naltrexone). Alcohol-related, non-alcohol-related, and total health care expenditures were calculated for the 6-month preindex and postindex periods. Univariate and multivariate analyses controlling for potential confounders were used to compare expenditures and provide cost estimates.

RESULTS: Naltrexone patients (n = 1,138; 62% male; mean age 45 ± 11 years) had higher total health care expenditures in the preindex period ($4,829) compared with alcohol controls ($2,503, P < 0.0001) and nonalcohol controls ($1,414, P < 0.0001). In the postindex period, total alcohol-related expenditures increased from the preindex period by $26 for naltrexone patients compared with $762 for alcohol controls (P < 0.0001). Similarly, total non-alcohol-related expenditures increased by $527 for naltrexone patients, compared with $1,259 for alcohol controls (P = 0.0010) and $82 for nonalcohol controls (P = 0.0292). Multivariate analyses showed that, relative to alcohol controls, naltrexone treatment decreased alcohol-related health care costs by $758 (P < 0.0001), non-alcohol-related health care costs by $937
(P <0.0001), and total health care costs by $1,827 (P <0.0001).

CONCLUSION: Patients with alcohol-use disorders had higher health care costs. Naltrexone pharmacotherapy reduced both alcohol-related and non–alcohol-related health care costs in these patients.

HEALTH CARE EXPENDITURES IN ULCERATIVE COLITIS:
THE PERSPECTIVE OF A SELF-INSURED EMPLOYER

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OBJECTIVE: To characterize health care expenditures associated with ulcerative colitis (UC) and better understand their impact on a large, self-insured employer.

METHODS: Claimant records for a retrospective cohort of patients with UC (International Classification of Diseases, Ninth Revision [ICD-9] code 556.x) were analyzed from a database of a self-insured employer, consisting of approximately 500,000 employees, retirees, or dependents from 2002 to 2004. Eighteen months of continuous enrollment was required [6-month preindex date and 12 months postindex date]. A randomly selected age- and gender-matched control group of noncolitis claimants was the comparator group. Multiple linear regression technique was used to determine the predictors of cost, adjusting for Centers for Medicare & Medicaid Services hierarchical condition category (CMS-HCC) scores. A disease severity stratification algorithm classified UC patients into 3 mutually exclusive cohorts: mild (untreated or treated with aminosalicylates or topical therapy only), moderate (additional medical therapies [e.g., oral corticosteroids and/or immunomodulators]), or severe (requiring hospitalization for UC) cohort.

RESULTS: Health care costs were evaluated for 1,057 UC patients. Mean annual unadjusted total costs for all UC patients were $14,486 compared with $6,158 for the control group. The regression model indicated that UC was a predictor of higher costs compared with the control group (coefficient = 5136.37, P <0.005). When stratified by disease severity, the severe UC cohort had a 2-fold increase of mean total cost as compared with the mild and moderate groups ($12,443 vs. $26,875). After adjustment for CMS-HCC scores in the regression analysis, the severe group was a significant predictor of increased cost compared with the mild and moderate patients (coefficient=5847.84, P= 0.03).

CONCLUSIONS: Utilization expenditures for the UC cohort were more than 2 times more costly as compared with the control cohort. Health care costs were highest for patients with severe UC. These results highlight the impact of UC health care expenditures on a self-insured employer. Increased awareness and attention to UC is warranted.

IMPACT OF A MANDATORY 90 PROGRAM ON PRESCRIPTION DRUG UTILIZATION AND EXPENDITURES

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OBJECTIVE: To evaluate the impact of a Mandatory90 program on prescription drug utilization and expenditures.

METHODS: A retrospective pre-post with control group study design was employed. Twenty-four months of prescription data (March 1, 2004, through February 28, 2006) were obtained from a large pharmacy benefit manager. The study group included prescription drug plan members in the state of Illinois where the Mandatory90 was implemented on March 1, 2005, while the control group comprised of the plan members in all other states. Members in Illinois must get a 90-day supply at the third refill. Members were included if they were continuously eligible during the study period. Only maintenance medications were included, and specialty drugs were excluded. Costs per prescription (normalized to 30-day supply) and generic dispensing rates in Mandatory90 and 30-day retail were calculated for the study group. Per-member-per-month (PMPM) total costs and generic utilization were analyzed and compared between the study and control group. PMPM cost savings were calculated by comparing the actual PMPM costs with the expected PMPM costs that were age- and gender-adjusted using the control group.

RESULTS: Within the study group, the average cost per prescription was significantly lower in Mandatory90 than in 30-day retail ($57.63 vs. $80.17, P <0.0001). The generic utilization rate in Mandatory90 was higher than in 30-day retail prescriptions (44.29% vs. 29.71%). As compared with the control group, the study group had lower PMPM total cost trend (6.63 % vs. 7.80%) and a higher rate of increase of the generic utilization (7.88% vs. 6.48%) from the preperiod to the postperiod. It was estimated that Mandatory90 program resulted in total cost savings of $3.48 annually for each member.

CONCLUSION: A Mandatory90 program was found to lead to decreases in PMPM total costs while increasing generic utilization rate on maintenance medications.
IMPACT OF A TIER STATUS CHANGE ON UTILIZATION OF BLOOD GLUCOSE TEST STRIPS

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OBJECTIVE: To evaluate the impact of a change in formulary tier status on utilization of blood glucose test strips.

METHODS: On May 1, 2005, the health plan made a modification to the formulary that resulted in tier changes for several brands of test strips for many of their members. Some brands had a favorable change, moving from Tier 2 or 3 to Tier 1, while others had an unfavorable change, moving from Tier 2 to Tier 3. Using claims data from the 12-month period prior to the tier change, we identified members whose test strips had a favorable or unfavorable change. We also identified a control group with no tier change. Claims during the 6-month period following the change were examined, and utilization was compared between members with a favorable, unfavorable, or no tier change.

RESULTS: A total of 30,633 members were identified: 11,463 had a favorable change, 11,293 had no change, and 7,877 had an unfavorable change in tier status. Most members were between 45 and 64 years, and cohorts were approximately 50% male. The vast majority with a favorable tier change (94.1%) or no tier change (93.0%) continued to use the same brand of strips following the change compared with 52.5% of members with an unfavorable change. Among those remaining on the same brand following the change, members with an unfavorable change had a significant decrease in both the number of prescription fills and quantity of strips filled compared with the other cohorts (P < 0.0001).

CONCLUSION: Members using test strips with an unfavorable change in tier status had a significant drop in utilization compared with the other cohorts, suggesting that such a change can impact the frequency with which patients monitor their blood glucose. This is important, as decreased monitoring could lead to poor glucose control and, subsequently, poor clinical outcomes.

IMPACT OF IMPLEMENTING A GENERIC SAMPLE PROGRAM IN A MANAGED CARE ORGANIZATION

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INTRODUCTION: This managed care plan generally utilizes an open formulary. Methods were evaluated with the goal of increasing the percentage of generic medication utilization and slowing the trend of drug spend. In order to achieve these goals and to increase awareness of generic therapeutic opportunities to physicians and members, the health plan introduced a new program for members starting July 1, 2003, that eliminated a copay/coinsurance for the first fill of select generic medications when filled at retail pharmacies.

METHODS: This generic sample program involves 15 generic medications, including several antidepressants, nonsteroidal anti-inflammatories, and gastrointestinal medications. Two such medications, ranitidine and famotidine, are always adjudicated with a zero copay. Classes were chosen that had high member utilization and in which there were costly branded alternatives. Prior to implementation, several medications, including fluoxetine, had experienced a decrease in utilization. One possible reason for this trend is the lack of samples of generic medications in providers’ offices. The program has been promoted to physicians through direct mailings, quarterly provider newsletters, wallcards, and physician detailing. It has been promoted to members through a member quarterly newsletter, employer/broker meetings, health fairs, and pharmacy handbook language. The pharmacy department worked with sales and marketing, provider relations, broker relations, etc., in order to gain visibility and promote acceptance. Claims were analyzed starting July 1, 2003, through December 31, 2005, in order to determine use of the program, change in generic utilization, and cost savings.

RESULTS: More than 152,000 members (30% of the total health plan members who filled a prescription during the time period) participated in the generic sample program, filling more than 245,700 prescriptions at a zero copay. The health plan’s percentage of generic utilization across all classes increased incrementally, measured each quarter, resulting in a total increase of 10.7% since program inception. This increase of generic utilization is associated with approximately $9 million in cost savings since July 1, 2003. The financial impact to the health plan due to lost copays was approximately $2 million; resulting in a net savings to the plan of $7 million over two and one-half years.

CONCLUSION: Implementing the generic sample program has been a useful tool to remind physicians and members about generic options within therapeutic classes that have branded alternatives. As more generics become available, it may be prudent for health plans to assess the benefit of implementing a similar program and/or generic step therapies within their pharmacy benefit.

IMPACT OF PRESCRIBER EDUCATION ON UTILIZATION OF MEDICATIONS WITH HIGH ABUSE POTENTIAL IN A HIGH-RISK MANAGED CARE PLAN

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OBJECTIVE: To evaluate the impact of an ongoing pharmacy-driven intervention designed to promote safe and appropriate utilization of medications with high abuse potential.

METHODS: This program was implemented in January 2004 in a health insurance plan serving high-risk individuals (risk pool).
Risk pools provide health coverage for individuals unable to purchase commercial health insurance due to preexisting conditions or lack of access. This ongoing pharmacy intervention identifies patients with 15 prescription claims for targeted medications (i.e., narcotics, stimulants, barbiturates, and muscle relaxants) in the last 3 months. Patients with chemotherapy medications were excluded. Prescribers received patient-specific medication profiles which include drug, pharmacy, and prescriber details to identify inappropriate utilization. Patients were included in the analysis if they had complete 1-year follow-up data. Changes in utilization of medications with abuse potential and patient behavior (i.e., polypharmacy and polyprescriber) were measured.

**RESULTS:** To date, a total of 684 physicians for 231 unique Interventions to improve medication adherence were identified. Prescribers received patient-specific medication profiles which include drug, pharmacy, and prescriber details to identify inappropriate utilization. Patients were included in the analysis if they had complete 1-year follow-up data. Changes in utilization of medications with abuse potential and patient behavior (i.e., polypharmacy and polyprescriber) were measured.

**CONCLUSION:** A physician-focused intervention identifying patients who may be receiving inappropriate therapy has been well received and has resulted in a decrease in utilization of medications with high abuse potential.

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**IMPROVING QUALITY INDICATORS THROUGH CLINICAL INTERVENTIONS TO IMPROVE MEDICATION ADHERENCE**

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**OBJECTIVE:** To evaluate the impact of medication adherence interventions on related quality indicators.

**METHODS:** Pharmacy claims data from a managed care organization of 180,000 lives were analyzed to identify patients receiving medications for diabetes, hyperlipidemia, or hypertension. Medication possession ratios (MPRs), defined as actual days supply divided by possible treatment days, for each medication category were used to identify potentially nonadherent patients. Patient-specific reports were sent to primary care physicians, and related educational materials were mailed to the identified population. This process was initiated in 2003. Crude-Mantel-Haenszel chi-square tests were used to assess change between years.

**RESULTS:** Among 6,533 potentially nonadherent patients, positive trends in MPRs were noted in all medication categories. From 2004 to 2005, MPRs associated with oral antidiabetic, anti-hypertensive, and lipid-lowering medications have increased from 0.63 to 0.89, 0.60 to 0.89, and 0.61 to 0.76, respectively. These changes were associated with positive trends in Health Plan Employer Data and Information Set (HEDIS) results with respect to cholesterol, glycemic, and blood pressure control among commercial members. Similar results were seen in Medicaid and Medicare members. Statistically significant trends were noted for glycosylated hemoglobin (A1C) levels >9.5 (43.8% in 2003, 24.1% in 2004, 22.1% in 2005; P <0.0001); low-density lipoprotein cholesterol (LDL-C) <130 in patients with diabetes (55.5% in 2003, 62.5% in 2004, 69.3% in 2005; P <0.0001); and LDL-C <100 in patients with diabetes (32.1% in 2004, 41.6% in 2005; P = 0.005). A positive, but statistically nonsignificant, trend was noted in blood pressure control rates in this cohort.

**CONCLUSION:** Interventions to improve medication adherence patterns have contributed to improved MPRs and positive outcomes-related quality-improvement indicators in this managed care plan.

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**LOSS OF TREATMENT RESPONSE AMONG CROHN’S DISEASE PATIENTS RECEIVING INFlixIMAB MAINTENANCE THERAPY**

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**OBJECTIVE:** To assess the incidence and economic implications of loss of treatment response among patients with Crohn’s disease (CD) treated with infliximab maintenance therapy.

**METHODS:** CD patients with initial response to infliximab maintenance therapy were selected from Integrated Healthcare Information Services (IHIS) managed care database (1999-2005). As a means of determining initial response, patients were excluded if they experienced any failure event prior to their fourth infusion. Failure events included developing a new fistula, initiating a new CD-related drug, needing urgent care or surgery, and requiring infliximab dosage escalation. Loss of response was defined as occurrence of any failure event. Two-year rate of loss-of-treatment response was calculated using Kaplan-Meier analysis. Annual total health care costs and CD-related costs were estimated and adjusted for inflation to 2005 US$. Generalized linear modeling was used to assess the impact of loss of response on costs.

**RESULTS:** The study sample included 262 CD patients on infliximab maintenance therapy with initial response. Within 24 months following therapy initiation, 81% patients had lost response. Among them, 43% had a CD-related emergency or inpatient visit, 13% were diagnosed with a new fistula, 53% received new drugs for CD, 31% had a CD-related surgery, and 46% experienced dosage escalation of infliximab. The annual
total and CD-related costs for patients who lost treatment response in the first year were 35% and 40% higher than those who didn’t lose response. Regression analyses to control for baseline characteristics showed that loss of treatment response was associated with 29% higher annual total treatment costs (P < 0.0001), and 29% higher CD-related costs (P = 0.003) and mental (P < 0.001) and the annualized rate of MS-related and CD-related costs.

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**NATALIZUMAB IMPROVES HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH RELAPSING MULTIPLE SCLEROSIS**


**OBJECTIVE:** To evaluate the effects of natalizumab on health-related quality of life (QoL) in patients with relapsing multiple sclerosis (MS).

**METHODS:** AFFIRM (Natalizumab Safety and Efficacy in Relapsing-Remitting MS) and SENTINEL (Safety and Efficacy of Natalizumab in Combination With Avonex in Patients With Relapsing-Remitting MS) were 2-year, randomized, double-blind, placebo-controlled, multicenter phase 3 clinical trials. These studies evaluated the efficacy and safety of natalizumab (300 mg administered intravenously) as monotherapy (AFFIRM) and as add-on therapy to interferon β-1a (SENTINEL) in patients with relapsing MS. QoL was a predefined end point in both studies and was measured using the Multiple Sclerosis Quality of Life Inventory (MSQOLI). MSQOLI was measured using a visual analogue scale (VAS). The MSQOLI is an MS-specific health-related QoL instrument that includes a widely used generic measure, the Medical Outcomes Study Short Form-36 Health Survey (SF-36), as well as 9 symptom-specific measures; modified fatigue impact scale (MFIS), bowel control scale, bladder control scale, sexual satisfaction scale, mental health inventory, impact of visual impairment scale (IVIS), perceived deficits questionnaire, Medical Outcomes Study Pain Effects Scale (MOS PES), and MOS modified social support survey.

**RESULTS:** In AFFIRM, natalizumab significantly improved scores on both the physical (P = 0.003) and mental (P = 0.011) components of the SF-36 and well-being as measured by the VAS (P = 0.007) over 2 years of treatment compared with placebo. Two-year results from SENTINEL were generally consistent with these findings. In addition, there were trends toward improvement with natalizumab in the fatigue (MFIS) and pain (MOS PES) subscales of the MSQOLI in AFFIRM, with statistically significant improvements on these subscales in the add-on group in SENTINEL. It should be noted that due to safety concerns, it is not recommended that natalizumab be used in combination with available immunomodulatory or immunosuppressive therapies for MS.

**CONCLUSION:** Natalizumab significantly improves health-related QoL in patients with relapsing MS.

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**NATALIZUMAB REDUCES CORTICOSTEROID USE AND HOSPITALIZATIONS AND INCREASES THE PROPORTION OF DISEASE-FREE MULTIPLE SCLEROSIS PATIENTS**


**OBJECTIVE:** To evaluate the effects of natalizumab on corticosteroid use, hospitalizations, and the proportion of operationally defined “disease-free” patients in relapsing multiple sclerosis (MS).

**METHODS:** AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) and SENTINEL (Safety and Efficacy of Natalizumab in Combination With Avonex in Patients With Relapsing-Remitting MS) were 2-year, randomized, double-blind, placebo-controlled, multicenter phase 3 clinical trials that determined the efficacy and safety of natalizumab as monotherapy and as add-on therapy with interferon-β-1a, respectively, in patients with relapsing MS. In AFFIRM, 942 patients received natalizumab 300 mg (n = 627) or placebo (n = 315) intravenously every 4 weeks, in addition to interferon-β-1a, respectively, in patients with relapsing MS. In SENTINEL, 1,171 patients received natalizumab 300 mg (n = 589) or placebo (n = 582) intravenously every 4 weeks, in addition to interferon-β-1a 30 mcg intramuscular once weekly, for up to 116 weeks. Prespecified end points at 2 years included annualized rate of relapses requiring corticosteroid use and annualized rate of hospitalizations due to MS. In addition, a post hoc analysis was conducted to determine the proportion of patients free of disease activity over 2 years. Disease free was defined as clinically stable patients with no relapses and no progression of physical disability and magnetic resonance imaging (MRI) showing no new gadolinium-enhancing lesions, no new T2-hyperintense lesions, and no new T1-hypointense lesions.

**RESULTS:** In AFFIRM, natalizumab reduced the annualized rate of relapses requiring steroid use (0.13 natalizumab vs. 0.43 placebo, P < 0.001) and the annualized rate of MS-related hospitalizations (0.03 natalizumab vs. 0.10 placebo, P < 0.001) over 2 years compared with placebo. Ultimately, natalizumab
significantly increased the proportion of disease-free patients over 2 years compared with placebo; the proportion of disease-free patients was 28% in the natalizumab group and 6% in the placebo group (P <0.001). Results from SENTINEL were consistent with those from AFFIRM.

CONCLUSION: Natalizumab significantly reduced corticosteroid use and hospitalizations due to MS, and increased the proportion of disease-free patients.

**ONCE-MONTHLY DARBEPOETIN ALFA MAINTAINS HEMOGLOBIN LEVELS IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE**

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INTRODUCTION: This analysis investigated the effectiveness of once-monthly (QM) darbepoetin alfa in maintaining hemoglobin (Hb) levels in chronic kidney disease (CKD) subjects aged <65 and ≥65 years who were previously receiving treatment every other week (Q2W).

METHODS: QM darbepoetin alfa has previously been shown to effectively maintain Hb levels in CKD subjects. This is a secondary analysis of the larger study to investigate the effectiveness of QM darbepoetin alfa in maintaining Hb levels specifically in elderly CKD subjects. Enrolled subjects had CKD (not receiving dialysis), were receiving subcutaneous darbepoetin alfa Q2W, and had stable Hb levels. The initial QM dose of darbepoetin alfa was determined by doubling the Q2W dose received prior to enrollment. QM doses were titrated to maintain Hb levels between 10 and 12 g/dL over the 29-week study duration. This analysis was done on subjects aged <65 and ≥65 years.

RESULTS: Ninety-eight subjects were enrolled in this study: 58% were aged ≥65 years, with a mean (SD) age of 74.4 (6.0) years. Mean (SD) Hb (g/dL) levels at baseline and over the evaluation period were 11.1 (0.5) and 11.0 (0.8), respectively, in subjects aged <65 years, and 11.1 (0.6) and 11.0 (0.7), respectively, in subjects aged ≥65 years. Mean (SD) QM darbepoetin alfa dose (mcg/kg) at baseline and over the evaluation period were 1.1 (0.7) and 1.2 (1.2), respectively, for subjects aged <65 years, and 1.1 (0.6) and 1.1 (1.0), respectively, for subjects aged ≥65 years. Eighty percent and 79% of subjects aged <65 and ≥65 years, respectively, successfully maintained their Hb level. QM darbepoetin alfa was well tolerated.

CONCLUSION: These data demonstrate that QM darbepoetin alfa effectively maintained Hb levels in CKD subjects aged ≥65 years (previously receiving Q2W dose) with similar efficacy and dosing requirements as subjects aged <65 years. QM dosing may provide greater benefit to elderly CKD patients by improving treatment compliance.

**POOR SYMPTOM CONTROL AMONG MODERATE-TO-SEVERE ASTHMA PATIENTS**

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INTRODUCTION: We hypothesized that there is an unmet treatment need among moderate-to-severe asthma patients. This analysis assessed and characterized the proportion of these patients who have evidence of poor symptom control even after maximum guideline-driven therapy, according to compliance with their current asthma controller medication.

METHODS: The Ingenix LabRx Medical and Pharmacy Database was used to study patients who were aged 12 to 64 years, had initiated fluticasone/salmeterol 500/50 treatment between July 1, 2003, and June 30, 2004, had one or more asthma diagnosis codes (International Classification of Diseases, Ninth Revision [ICD-9] code: 493.xx) anytime during the study period, and had 12 or more months of continuous eligibility before and after initiating the asthma controller medication. Compliance was measured as the percentage of days on therapy during the 12-month period following initiation of fluticasone/salmeterol 500/50. Poor symptom control was defined as the occurrence of the following: 1 or more asthma hospitalizations or asthma-related emergency department visits, 2 or more oral corticosteroid prescriptions, or 6 or more short-acting beta-agonist prescriptions.

RESULTS: Among all patients, 36.3% had evidence of poor symptom control in the 12 months before initiating fluticasone/salmeterol 500/50. After initiating fluticasone/salmeterol 500/50 therapy, 28.3% of patients had evidence of poor symptom control over the 12-month follow-up period (P <0.001). Only 20% of patients had a fluticasone/salmeterol 500/50 compliance rate of 75% or greater. Among patients with a compliance rate of 75% or greater, 30.1% had evidence of poor symptom control regardless of their compliance rate with the medication. Reductions in the proportion of patients with poor symptom control were modest. Our study results are consistent with the hypothesis that there is substantial unmet need among moderate-to-severe asthma patients despite maximum guideline-driven asthma therapy.
**PREDICTORS OF COMPLIANCE ON COMBINATION ANTIHYPERTENSIVE THERAPY IN A MEDICAID POPULATION**

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**OBJECTIVE:** To identify predictors of compliance on antihypertensive combination pharmacotherapy in a Medicaid population.

**METHODS:** Retrospective medical and pharmacy claims data analysis for Maryland Medicaid patients who were prescribed combinations of angiotensin-converting enzyme inhibitor/hydrochlorothiazide (ACEI/HCTZ) or angiotensin-converting enzyme inhibitor/calculator channel blockers (ACEI/CCBs) during the period of January 1, 2002-December 31, 2004. Inclusion: continuously enrolled patients, 18 years and older, with at least 1 year of follow-up. Exclusion: use of antihypertensive drugs between January 1 and June 30, 2002 (to obtain incident cohort). Compliance was measured by the medication possession ratio with a cut-point of 80%. Multivariate logistic regression was used to predict compliance as a function of age, gender, race, comorbidities (Charlson Comorbidity Index or CCI), and use of either fixed-dose pill or 2 concurrent pill combination therapies.

**RESULTS:** Total of 568 patients, 63.73% females, 68.84% African Americans, median age 52 years, 35.56% on fixed-dose combination therapy, 72.89% started on ACEI/HCTZ, 24.82% complied with therapy. Patients younger than 40 years (odds ratio [OR] = 0.45; P = 0.03, confidence interval [CI], 0.22-0.91), and African Americans (OR = 0.47; P = 0.0006; CI, 0.31-0.73) are less likely to be compliant than patients older than 60 years, and whites, respectively. Those who have a CCI of 1 (OR = 2.03; P = 0.052; CI, 0.99-4.15) and those on fixed-dose combination drugs (OR = 1.55; P = 0.03; CI, 1.03-2.32) are more likely to be compliant than those with higher CCI and those on 2 concurrent pill therapies, respectively.

**CONCLUSION:** Age, race, comorbidities, and drug-simplified regimen are significant predictors of compliance. These results may inform medication therapy management programs.

**PREVALENCE OF BARRIERS TO MEDICATION ADHERENCE FOR PATIENTS WITH ASTHMA OR DEPRESSION**

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**OBJECTIVE:** To evaluate the prevalence of barriers to adherence identified with the ASK-20 (Adherence Starts With Knowledge) survey in a cohort of patients with asthma or depression.

**METHODS:** This analysis is based on a sample of randomly selected patients with depression (n = 202), diabetes (n = 203), or asthma (n = 200) who completed the 20-item Web-based ASK-20 and validating self-report adherence questions. The ASK-20 identifies barriers to adherence in 5 domains: Lifestyle, Attitudes and Beliefs, Help from Others, Talking with Health care Team, and Difficulty Taking Medicines. Predictors of medication nonadherence, defined by a self-report of a missed dose of medicine in the past week, were determined by logistic regression, adjusting for baseline characteristics.

**RESULTS:** Description of patients with asthma or depression: mean age of 48 years and 79% female. Asthma patients were more likely to have missed a dose of medicine in the past week (47% vs. 37%) and had higher total number of barriers (5.1 ± 3.7 vs. 4.4 ± 3.2) than patients with depression, respectively. Depressed patients were more likely to report worrying about how medicine will affect sexual health (30%) and alcohol getting in the way of taking medicines (8%) than those with asthma or diabetes. Adjusted positive predictors of nonadherence for depression were: forgetfulness (P < 0.0001), alcohol getting in the way of taking medicines (P = 0.0004), hard-to-swallow pills (P = 0.0173), taking meds more/less than prescribed (P = 0.0267), skipped/stopped meds because not working (P = 0.0299), and skipped/stopped meds due to cost (P = 0.0018). For asthma, predictors of nonadherence were: forgetfulness (P < 0.0001), problems getting refills on time (P = 0.0163), inconvenience of taking medicine (P = 0.0168), too many medicines/day (P = 0.0100), taking meds more/less than prescribed (P = 0.0069), and skipped/stopped meds due to cost (P = 0.0156).

**CONCLUSIONS:** Barriers in Lifestyle and Difficulty Taking Medicines domains were the most significant predictors of suboptimal adherence for patients with asthma or depression. The ASK-20 may serve an important role in identifying specific actionable barriers that are prevalent and specific to patients with asthma or depression.

**RISK-FACTOR CLUSTERS AND MEDICAL-CARE COSTS IN PERSONS WITH HYPERTENSION**

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**INTRODUCTION:** Hypertension frequently occurs in combination with other major risk factors for cardiovascular disease; little is known, however, about the actual extent in U.S. clinical practice of risk-factor clustering among persons with hypertension and the relationship between such clustering and medical care costs.

**METHODS:** Study subjects were selected from the electronic medical records system of Kaiser Permanente Northwest and included all persons, aged ≥35 years, who had hypertension (identified based on ≥2 diagnoses, ≥2 elevated blood pressure readings, or use of antihypertensive medication) and were free of cardiovascular disease in 1998. Subjects were stratified into 8...
risk-factor clusters, based on whether they also had diabetes, hyperlipidemia, and/or high body mass index (BMI $\geq 30$ kg/m$^2$). Mean cumulative total medical care costs (per person, in 2004 US$) were then estimated for subjects in each risk-factor cluster over the 6-year period, January 1, 1999, to December 31, 2004.

**RESULTS:** A total of 57,573 persons were identified who had hypertension and were free of cardiovascular disease. Fifty-six percent of study subjects had one or more additional risk factors, including diabetes (15%), hyperlipidemia (24%), and/or a high BMI (37%). At the end of 1-year of follow-up, mean cumulative total medical care costs were $5,455 for hypertensive patients without any other risk factors and $7,878 for those with hypertension plus comorbid diabetes, hyperlipidemia, and high BMI. At the end of 3 years, mean cumulative total costs were $16,055 and $25,647; at the end of 6 years, they were $31,721 and $56,489. Among the 3 additional risk factors, diabetes had the largest impact on future medical care costs.

**CONCLUSION:** More than half of persons with hypertension also have other cardiovascular risk factors, which substantially—especially diabetes—increase future medical care costs. Identification and management of other cardiovascular risk factors are thus important components of hypertension treatment.

**VARIATIONS IN PATTERNS OF CARE OF COLONY-STIMULATING FACTORS: IMPLICATIONS FOR THE EFFECTIVENESS OF FILGRASTIM AND PEGFILGRASTIM IN COMMUNITY PRACTICE**

Morrison VA, Wong M, Campos L, Ding B, Malin J.* Amgen, Inc., One Amgen Center Dr., Thousand Oaks, CA 91320; jmalin@amgen.com, (805) 447-5298

**OBJECTIVE:** To describe the patterns of care and outcomes in cancer patients receiving the colony-stimulating factors filgrastim and pegfilgrastim.

**METHODS:** Data was obtained from medical records of a patient cohort (n = 6,148) treated in a random sample of oncology practices (n = 99) in 2001 and 2003 (before and after the U.S. Food and Drug Administration approval of pegfilgrastim in January 2002.) Multivariable logistic regression was used to estimate the odds of developing febrile neutropenia (FN) in patients who received filgrastim as compared with pegfilgrastim, adjusting for patient and chemotherapy treatment characteristics.

**RESULTS:** Patients who received filgrastim in 2003 were more likely to have advanced-stage disease ($P < 0.05$) or comorbid conditions ($P < 0.01$) than patients who received pegfilgrastim in 2003 or filgrastim in 2001 and less likely to receive myelosuppressive chemotherapy (59%, n = 603 vs. 69%, n = 569 with filgrastim in 2001; 73%, n = 1,404 for pegfilgrastim, and 75%, n = 435 for both; $P < 0.001$.) Among patients who received 21-day chemotherapy regimens, filgrastim was started later in the first cycle of therapy in both 2001 (mean [SD] = 7.7 [6.5] days after chemotherapy) and 2003 (9.6 [6.2] days) than pegfilgrastim (2.4 [3.2] days) ($P < 0.0001$), as well as in subsequent cycles ($P < 0.001$). Mean days of filgrastim administration was 5.2 [3.5] in 2001 and 3.7 [2.8] days in 2003 ($P < 0.001$) in the cycle of initiation and 6.0 [3.5] in 2001 and 4.6 [3.2] days in 2003, in subsequent cycles. Compared with patients who received pegfilgrastim, patients treated with filgrastrim were more likely to develop FN (adjusted odds ratio = 1.42; 95% confidence interval,1.03-1.97).

**CONCLUSION:** Filgrastim is often started later in the chemotherapy cycle and used for less than the 10 to 14 days reported in the pivotal trials demonstrating its efficacy. We found that use of filgrastim in community oncology practices was associated with increased odds of febrile neutropenia compared with pegfilgrastim use.
Managed Care Pharmacy Residencies, Fellowships, and Other Programs

The following is a partial list of available managed care pharmacy residency and fellowship programs and other programs compiled as of August 2006. The residencies listed were submitted by AMCP members in response to AMCP’s call for residency program listings. This is not a comprehensive list of all available programs. AMCP provides it solely as a service to its readers. This list does not imply AMCP’s endorsement of any particular program nor does AMCP guarantee the availability of any of the programs listed. AMCP does not assume responsibility for any errors that may appear in these listings. If you are aware of additional residency and fellowship programs not listed here, please contact AMCP at (800) TAP-AMCP.

■ AMERICAN HEALTH CARE
Clinical Therapeutics/Managed Care Pharmacy
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: Open
Starting Date: July 1
Estimated Stipend: $43,000 and up
Onsite Interview: Yes
Educational/Special Requirements: PharmD with California pharmacist license or eligible for license
Fringe Benefits: Medical, dental, vision, holidays, vacation, and attendance at national conference(s)
Special Features: Activities the resident will be involved in include, but are not limited to, P&T committee participation and presentations, formulary management and review, one-on-one physician correspondence on evidence-based medicine with current clinical studies reviewed and presented, focusing on actual patients that may benefit from this information, new drug review and its placement with available therapies, clinical participation and set-up, client summary report write-up and delivery, participation in various education conference and clinical studies.
Contact Information:
Nazly Westernoff
American Health Care
2217 Plaza Dr., Suite 100
Rocklin, CA 95765
(916) 773-7227
(916) 773-7210 (fax)
n.westernoff@americanhealthcare.com

■ BLUE CROSS AND BLUE SHIELD OF ALABAMA
Managed Care Pharmacy Systems
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: January 15
Starting Date: July 1 (flexible)
Estimated Stipend: $34,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD or equivalent experience
Fringe Benefits: Paid vacation, personal holiday leave, health/dental insurance, no on-call responsibilities, no weekends or holidays
Special Features: The program provides the resident with the opportunity to experience a true integrated medical system, including medical and pharmacy claims. The areas of focus will include pharmaceutical care, drug information, formulary management, clinical program management, disease state management and outcome studies, specialty pharmacy, and Medicare Part D. The resident also will complete a research project suitable for publication. This program will incorporate personal, communication, and time management skills.
Contact Information:
Jerry Wong, PharmD, MBA
Residency Director
Blue Cross and Blue Shield of Alabama
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Birmingham, AL 35244
(205) 220-6526
(205) 220-2939 (fax)
jwtong@bcbsal.org

■ BLUE CROSS AND BLUE SHIELD OF NEBRASKA
Managed Care Pharmacy
Accredited: Seeking
Length of Program: 12 Months
Number of Positions: 1
Affiliation: University of Nebraska Medical Center
Application Deadline: January 12
Starting Date: July 1
Estimated Stipend: $38,000
Onsite Interview: Required
Educational/Special Requirements: PharmD degree from an ACPE-accredited college of pharmacy. Licensed pharmacist in the U.S. or eligibility for licensure (successful candidate must be fully licensed at the start of residency). Application requirements
include: application, writing sample, 3 professional letters of recommendation, and on-site interview with short formal presentation.

**Fringe Benefits:** 10 days paid vacation, holidays, health insurance, paid travel and registration to AMCP Educational Conference and Annual Meeting

**Special Features:** The Blue Cross and Blue Shield of Nebraska residency will offer exposure to various aspects of managed care pharmacy through health plan and PBM exposure as well as direct patient care through clinical rotations. The residency will offer participation and exposure to the following areas: pharmacy benefit design, utilization management, formulary management, pharmacy trend management, drug information, health economic/outcomes research, pharmacy benefits management, disease state management quality assurance initiatives. This unique program also allows the resident the option to participate in teaching or didactic coursework through the University of Nebraska Medical Center.

**Contact Information:**
Lee Handke  
Vice President, Pharmacy and Wellness  
Blue Cross and Blue Shield of Nebraska  
7261 Mercy Rd.  
Omaha, NE 68180  
(402) 398-3884  
(402) 548-4683 (fax)  
lee.handke@bcbsne.com

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**BLUE SHIELD OF CALIFORNIA**

**Managed Care Pharmacy Systems**

- **Accredited:** AMCP/ASHP
- **Length of Program:** 12 months
- **Number of Positions:** 1
- **Affiliation:** UCSF
- **Application Deadline:** February 25
- **Starting Date:** July 1
- **Estimated Stipend:** $46,000
- **Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD degree from an accredited school of pharmacy, completion of a pharmacy practice residency or equivalent experience, 3 letters of recommendation, letter of intent, and on-site interview

**Fringe Benefits:** Health/dental/vision benefit; 20 days of paid time off, including professional leave (with travel allowances); and 9 holidays; no on-call responsibilities

**Special Features:** Rotationally based program that includes both on-site and off-site learning experiences

**Contact Information:**
Tara Abrams  
Senior Clinical Pharmacist, Quality Improvement  
Blue Shield of California Pharmacy Services  
50 Beale St., 22nd Fl.  
San Francisco, CA 94105  
(415) 229-6424  
(415) 229-6011 (fax)  
Tara.Abrams@blueshieldca.com

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**CAREMARK**

**Managed Care**

- **Accredited:** AMCP/ASHP
- **Length of Program:** 12 months
- **Number of Positions:** 1 in Texas, 1 in Arizona
- **Affiliation:** University of Arizona
- **Application Deadline:** January 8
- **Starting Date:** July 2
- **Estimated Stipend:** $38,000
- **Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD or equivalent experience

**Fringe Benefits:** 2 weeks vacation, health insurance, free parking, professional meetings, other management, pharmaceutical industry experience

**Special Features:** Rotationally based program that includes both on-site and off-site learning experiences

**Contact Information:**
Melissa Jay  
Caremark  
750 West John Carpenter Fwy.  
Irving, TX 75039  
(469) 524-5832  
(469) 524-5858 (fax)  
melissa.jay@caremark.com

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**CAREMARK, INC.**

**Managed Care Specialty-Analytics and Outcomes**

- **Accredited:** No
- **Length of Program:** 12 months
- **Number of Positions:** 2
- **Affiliation:** University of Illinois at Chicago; Midwestern University–Chicago College of Pharmacy
- **Application Deadline:** January 3
- **Starting Date:** July 3
- **Estimated Stipend:** $38,000
- **Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD with experiential or internship-based experience in managed care/PBM industry
Fringe Benefits: Comprehensive medical, dental and life insurance plan, 2 weeks paid vacation, holidays, employee stock purchase program, flexible spending program, travel budget

Special Features: Caremark is a leading pharmaceutical services company, providing comprehensive drug benefit services to approximately 24 million participants throughout the United States. Caremark’s clients include corporate health plans, managed care organizations, insurance companies, unions, government agencies, and other funded benefit plans. The Analytics and Outcomes Residency will provide the resident a unique opportunity to work on initiatives that foster proactive management of pharmaceutical and overall health care costs. It offers the ability to work with large data sets and perform various pharmaceutical cost analyses such as plan design modeling, formulary analysis, and clinical outcomes. As part of a core sales and account management team, the resident will have the opportunity to interact directly with clients, consultants, and various other benefit providers. While the focus is on analytics, the resident will be exposed to various areas in pharmacy benefits management such as clinical program development and implementation, operations, sales, account management, clinical sales support, marketing and communications, trade relations, pharmaceutical services, and therapeutic services.

Contact Information:
Anita Allemand
Director, Client Analytic Services
Caremark, Inc.
211 Sanders Rd.
Northbrook, IL 60062
(847) 559-3923
(847) 559-5475 (fax)
anita.allemand@caremark.com

Clinical Pharmacology Services, Inc.

Ambulatory Care/Clinical Research
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: February 1
Starting Date: June 1
Estimated Stipend: $34,000
Onsite Interview: Yes
Educational/Special Requirements: Contact program
Fringe Benefits: Sponsorship to professional meeting and Southwestern Residency Conference
Special Features: Contact program
Contact Information:
Daniel Buffington
Director
Clinical Pharmacology Services, Inc.
6285 E. Fowler Ave.
Tampa, FL 33617
(813) 983-1500
(813) 983-1501 (fax)
danbuffington@cpshealth.com
http://www.cpshealth.com

Commonwealth Medicine
Clinical Pharmacy Services

Managed Care Pharmacy Practice
Accredited: Pending
Length of Program: 12 months
Number of Positions: 2
Affiliation: University of Massachusetts Medical School
Application Deadline: January 12
Starting Date: July 2
Estimated Stipend: $37,500
Onsite Interview: Required
Educational/Special Requirements: PharmD degree; eligibility for licensure in Massachusetts; valid driver’s license; letter of intent, including goals; college transcripts; curriculum vitae; 3 letters of recommendation; personal on-site interview
Fringe Benefits: Health, dental, vision, disability, life insurance, earned time accrual for vacation, 13 state/federal holidays, office space with computer, travel/conference allowance (ASHP Midyear Clinical Meeting, Eastern States Residents Conference)
Special Features: After orientation to the department, the resident will begin a series of longitudinal rotations and other activities designed to meet the goals and objectives of the Commonwealth Medicine Managed Care Pharmacy Residency program. The resident will work with multiple program directors and clinical pharmacists in order to gain a thorough understanding of clinical medication management and cost-containment strategies. Activities will include preparing and presenting monographs for medication/class reviews, participating in the planning and roll-out of clinical pharmacy initiatives, and precepting pharmacy students on clinical rotations.

Contact Information:
Jake Nichols
Associate Director of Clinical Affairs
Commonwealth Medicine
Clinical Pharmacy Services
100 Century Dr.
Worcester, MA 01601
(508) 421-6168
(877) 208-7428 (fax)
Jake.Nichols@Umassmed.edu
www.umassmed.edu/commed/clinical/pharmacy_services.cfm
COVENTRY HEALTH CARE OF KANSAS, INC.

Health Plan–Managed Care Pharmacy
Accredited: Seeking
Length of Program: 12 months
Number of Positions: 1
Affiliation: University of Missouri–Kansas City (UMKC)
Application Deadline: January 5
Starting Date: July 1
Estimated Stipend: $38,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD degree from an ACPE-accredited college of pharmacy, licensed pharmacist in the United States or eligibility for licensure (successful candidate must be fully licensed at the start of residency), application, letter of intent, curriculum vitae, writing sample, official transcripts, 3 professional letters of recommendation, on-site interview with short formal presentation in Kansas City

Fringe Benefits: 2 weeks paid vacation; holidays; medical and dental insurance; paid travel and registration to AMCP Educational Conference, AMCP Annual Meeting, ASHP Midyear Meeting, and FMCP pharmacoeconomics training

Special Features: Residency opportunities in all managed care core competencies: pharmacy benefits management, utilization management, formulary management, clinical consultation service, drug information, new technologies assessment, provider network relations, Medicare plan interventions, disease state management, health and wellness initiatives, quality assurance/improvement activities, marketing and sales, contracting, health economics/outcomes, rotations with pharmaceutical industry, teaching experience through UMKC, PharmD experiential rotation oversight

Contact Information:
Shawn Burke
Regional VP, Pharmaceutical Services
Coventry Health Care of Kansas, Inc.
8320 Ward Pkwy.
Kansas City, MO 64114
(866) 795-3995
(866) 795-3992 (fax)
sburke@cvty.com

GROUP HEALTH COOPERATIVE

Managed Care Pharmacy Practice
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: January 10
Starting Date: July 1
Estimated Stipend: $40,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD or equivalent experience

Fringe Benefits: Full medical coverage ($35/month paid by the employee) and dental coverage (cost varies depending on plan chosen by employee) for the resident, 7 days of vacation; paid registration and some fees to attend professional meetings is provided

Special Features: The residents are trained in the role of the pharmacist in the development and implementation of clinical practice guidelines, formulary development and management, and drug use policy development. In addition, residents are trained to function as leaders in implementing pharmaceutical care plans for specific patients in a managed care setting.

Contact Information:
Jim Carlson
Director, Pharmacy Administration
Group Health Cooperative
12400 E. Marginal Way S.
Seattle, WA 98168
(206) 901-4420
(206) 901-4410 (fax)
carlson.j@ghc.org
http://www.ghc.org/about_gh/employ/rxresidency.jhtml

HARVARD VANGUARD MEDICAL ASSOCIATES

Pharmacy Practice With Emphasis in Managed Care
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: Massachusetts College of Pharmacy and Health Sciences
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $32,000
Onsite Interview: Yes

Educational/Special Requirements: BS in pharmacy or PharmD

Fringe Benefits: Comprehensive medical plan, 2 weeks paid vacation

Special Features: Academic appointment: instructor of pharmacy practice

Contact Information:
Kathy Zaiken, PharmD
Massachusetts College of Pharmacy & Health Sciences
179 Longwood Ave.
Boston, MA 02115
(617) 732-2740
(617) 732-2244 (fax)
kathy.zaiken@mcphs.edu
http://www.mcphs.edu
Managed Care Pharmacy Residencies, Fellowships, and Other Programs

■ HEALTH NET PHARMACEUTICAL SERVICES

Managed Care Pharmacy Practice
Accredited: Pursuing joint accreditation by AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: University of the Pacific; University of California at San Francisco
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $45,000
Onsite Interview: Required
Educational/Special Requirements: Graduate of an ACPE-accredited college of pharmacy, licensed pharmacist or eligible for licensure in California, completed application form, letter of intent (not to exceed 500 words) summarizing applicant’s motivation for pursuing a residency in managed care as well as short-term and long-term career goals, current resume or curriculum vitae, 3 letters of recommendation, 1 official transcript sent directly from applicant’s school of pharmacy, and completion of an on-site interview
Fringe Benefits: Competitive residency stipend; full benefits as a Health Net associate, including paid holidays, medical/dental/pharmacy/vision coverage, paid time off, 401K program, health club reimbursement program; and support to attend various professional meetings
Special Features: Health Net Pharmaceutical Services manages the pharmacy benefits, drug spend, and clinical programs for the health plans of Health Net, Inc. The Managed Care Pharmacy Practice resident will gain experience in formulary management, prior authorization, strategic benefit design, and pharmacy operations and will participate in Health Net’s National P&T Committee and Clinical Pharmacy Advisory Committee.
Contact Information:
Cathrine Misquitta
Director, Clinical Pharmacy Services
Health Net Pharmaceutical Services
10540 White Rock Rd., Suite 280
Rancho Cordova, CA 95670
(916) 463-9602
(916) 463-9750 (fax)
cathrine.v.misquitta@healthnet.com

■ HEALTH PLAN OF SAN JOAQUIN

Managed Care Pharmacy Practice
Accredited: No, but will be pursuing
Length of Program: 12 months
Number of Positions: 1
Affiliation: University of the Pacific, San Joaquin General Hospital
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $45,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD from an ACPE-accredited college of pharmacy or equivalent experience, eligibility for California licensure, good academic standing, excellent written and verbal communication skills
Fringe Benefits: Health, dental, vision, life, and disability available; vacation time allotted; professional travel and stipend available; no weekends or holidays; no staffing requirements in a pharmacy
Special Features: The program is unique in providing a balanced exposure to institutional clinical practice, longitudinal ambulatory care practice, as well as the operation of a Medicaid managed care HMO. The primary emphasis is placed on the application of clinical skill on the development and implementation of medication use management initiatives and policies, clinical programs, formulary management, pharmacoeconomic and outcome assessment, drug information and effective communication. The resident will be involved in classroom teaching and precepting clerkship students from the University of the Pacific.
Contact Information:
Allen Shek
Residency Program Director, Health Plan of San Joaquin,
Associate Professor, University of the Pacific
1530 W. Fremont St., Suite 200
Stockton, CA 95203
(209) 461-2209
(209) 461-2409 (fax)
ashek@hpsj.com

■ HEALTH PARTNERS

Managed Care Pharmacy Program
Accredited: Accreditation being pursued
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: Competitive
Onsite Interview: Yes
Educational/Special Requirements: PharmD
Fringe Benefits: Health insurance, vacation, and holidays
Special Features: Travel/registration for 1 national meeting
Contact Information:
Vyvy Vo
Clinical Pharmacy Program Manager
HealthPartners
8170 33rd Ave. South, Mailstop 21111B
Bloomington, MN 55425
(952) 967-5133
(952) 883-5875 (fax)
vyvy.k.vo@healthpartners.com
http://www.healthpartners.com
**HENRY FORD HEALTH SYSTEM**

Managed Care Pharmacy

- Accredited: AMCP/ASHP
- Length of Program: 12 months
- Number of Positions: 1
- Affiliation: None
- Application Deadline: February 15
- Starting Date: July 1
- Estimated Stipend: Competitive
- Onsite Interview: Yes

**Educational/Special Requirements:** PharmD, pharmacy practice residency desirable

**Fringe Benefits:** Health care, 2 weeks paid vacation, travel to 1 meeting

**Special Features:** The resident will design system enhancements and participate in ongoing utilization management, disease management, and compliance intervention programs. The resident will participate in formulary management and design clinical indications of effectiveness for guidelines and will formulate and answer a research question, using scientific principles, with a strong emphasis on outcomes, pharmacoeconomics, and quality-of-life research. Experiences will include exposure to our HMO (Health Alliance Plan) and involvement with the Center for Clinical Effectiveness, health system studies, quality improvement center, and clinical pharmacy services. Direct patient care responsibilities in one of our ambulatory clinics will be ongoing throughout the year.

**Contact Information:**

Vanita Pindolia  
Director, Pharmacy Care Management  
Health Alliance Plan  
2850 W. Grand Blvd., Tower 14, Suite 200  
Attention: Pharmacy  
Detroit, MI 48202  
(248) 443-8849  
(248) 443-8855 (fax)  
vpindoli@hapcorp.org

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**HORIZON NJ HEALTH**

Managed Care Pharmacy

- Accredited: AMCP/ASHP
- Length of Program: 12 months
- Number of Positions: 2
- Affiliation: Horizon BC
- Application Deadline: January 6
- Starting Date: July 1
- Estimated Stipend: $37,000
- Onsite Interview: Yes

**Educational/Special Requirements:** Graduate of an accredited school of pharmacy, PharmD preferred, minimum GPA of 3.2 (on a 4.0 scale), and eligibility for pharmacy licensure

**Fringe Benefits:** Health, dental, 401(k), 3 weeks vacation, 2 floating holidays, relocation allowance, and travel expenses paid for 2 professional meetings

**Special Features:** Humana Inc. has a broad range of programming within the pharmacy management department. The residency will offer exposure to various aspects of managed care pharmacy as well as direct patient care through clinical rotations at the Veterans Affairs hospital. The residency will offer participation in corporate pharmacy and therapeutics committees, manufacturer relations, pharmaceutical contracting and rebating, pharmacy benefit design, consumer relations, legislative and drug policy issues relating to managed care and health benefit design, ePharmacy initiatives, and outcomes analysis.

**Contact Information:**

Jane Stacy  
Clinical Advisor  
Humana Inc.  
500 W. Main St., 16th Fl.  
Louisville, KY 40202  
(502) 580-1591  
(502) 508-1591 (fax)  
jstacy1@humana.com

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**HUMANA INC.**

Managed Care Pharmacy

- Accredited: AMCP/ASHP
- Length of Program: 12 months
- Number of Positions: 2
- Affiliation: None
- Application Deadline: January 6
- Starting Date: July 1
- Estimated Stipend: $37,000
- Onsite Interview: Yes

**Educational/Special Requirements:** Medicaid managed care HMO, unique focus on government programs, pharmacy case management, formulary and disease state management, development of clinical policies, outcomes research, assist with PharmD student oversight, ambulatory care experience, professional development courses, attend at least 1 national conference

**Contact Information:**

Jennifer Gauweiler  
Pharmacy Clinical Manager  
Horizon NJ Health  
210 Silvia St.  
West Trenton, NJ 08628  
(609) 538-0700  
(609) 538-1698 (fax)  
Jennifer_Gauweiler@horizonnjhealth.com

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Special Features: Medicaid managed care HMO, unique focus on government programs, pharmacy case management, formulary and disease state management, development of clinical policies, outcomes research, assist with PharmD student oversight, ambulatory care experience, professional development courses, attend at least 1 national conference
IBA HEALTH PLANS/BLUE CARE NETWORK

Managed Care Pharmacy
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: Ferris State University/Kalamazoo Center for Medical Studies/Pfizer
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $32,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD
Fringe Benefits: Health/dental insurance, 2 weeks vacation, paid holidays
Special Features: Travel and registration reimbursement for 1 national conference and the Great Lakes Pharmacy Resident Conference, no weekend or evening shifts.
Contact Information:
Teresa Klepser
Residency Director
Promed/Ferris State University
7901 Angling Rd.
Portage, MI 49024
(269) 324-8469
(269) 324-8618 (fax)
klepser@ferris.edu

KAISER PERMANENTE COLORADO—SPECIALTY RESIDENCY IN DRUG INFORMATION

Medical Care/Drug Information
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: March 31
Starting Date: July 1
Estimated Stipend: $70,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD, pharmacy practice residency program or equivalent experience, excellent communication skills, eligibility for California licensure, 3 letters of recommendation
Fringe Benefits: Medical, dental, optical insurance; 10 days time off; attendance at 1 pharmacy conference
Special Features: None
Contact Information:
Rachana Patel
Clinical Pharmacy Specialist
Kaiser Permanente
1375 East 20th Ave.
Denver, CO 80205
(303) 764-4479
(303) 861-3668 (fax)
rachana.j.patel@kp.org

KAISER PERMANENTE COLORADO

Palliative Care
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: January 1
Starting Date: July 1
Estimated Stipend: $41,220
Onsite Interview: Yes
Educational/Special Requirements: PharmD, PGY1 residency, and eligibility for licensure in Colorado

Contact Information:
Mirta Millares
Kaiser Permanente
12254 Bellflower Blvd., Suite 106
Downey, CA 90242
(562) 658-3630
(562) 658-3758 (fax)
Fringe Benefits: Health insurance, paid sick and vacation leave, paid holidays, travel support to ASHP Midyear Meeting and Western States Residency Conference, and online library and computer privileges

Special Features: The palliative care specialty residency will focus on the supportive care of patients with a life-limiting illness. Pain and symptom management will be emphasized. Core rotations include home-based palliative care, inpatient palliative care, and geriatrics. Experiences in hospice, oncology, mental health, and other practice areas are available. A research project of publishable quality is required. Teaching opportunities are available.

Contact Information:
Robin Hill
Clinical Pharmacy Specialist
Kaiser Permanente Colorado
2350 S Parker Rd., Suite 400
Aurora, CO 80014
(303) 636-3013
(303) 636-3358
Robin.R.Hill@kp.org
http://www.kaiserpermanente.org

KAISER PERMANENTE MEDICAL CARE PROGRAM—INLAND EMPIRE SERVICE AREA

General Pharmacy Practice
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $43,700
Onsite Interview: Yes

Educational/Special Requirements: Graduate of an accredited college of pharmacy and be licensed or eligible for licensure in California, pharmacy school transcript, 3 letters of recommendation, letter of intent, and curriculum vitae

Fringe Benefits: 2 weeks paid vacation; health benefits, including dental/optical; paid holidays; office space; reimbursement for off-site experiences

Special Features: Kaiser Permanente is the nation’s largest non-profit health plan serving more than 8.4 million members in 9 states. The Inland Empire Service Area consists of 2 medical centers and 14 satellite medical offices for 598,000 members in the San Bernardino and Riverside counties of southern California.

Contact Information:
Patricia Gray
Clinical Operations Manager
Kaiser Permanente—Inland Empire Service Area
9310 Sierra Ave.
Fontana, CA 92335
(909) 427-3838
(909) 427-3830 (fax)
patricia.l.gray@kp.org

KAISER PERMANENTE MEDICAL CARE PROGRAM—LOS ANGELES MEDICAL CENTER

Pharmacy Practice
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: January 10
Starting Date: July 1
Estimated Stipend: $43,700
Onsite Interview: Yes
Educational/Special Requirements: Graduate of an accredited college of pharmacy and be licensed or eligible for licensure in California. Good communication skills required. Resident will develop a project with targeted care outcomes and present at Annual Western States Conference.

Fringe Benefits: Medical, dental, vision insurance; holidays; vacation/sick leave

Special Features: The Kaiser Permanente Los Angeles Medical Center is the tertiary care center for Kaiser Permanente in southern California and provides comprehensive inpatient, outpatient, and ambulatory care services to Kaiser Permanente members. This residency program provides development and training for recently graduated pharmacists, with an emphasis on pharmaceutical care and leadership to a diverse community. It will allow the residents to become familiar with managed care pharmacy practice in an integrated health care program.

Contact Information:
Steve Litsey
Pharmacy Leader–Metro Service Area
Kaiser Permanente Pharmacy Operations Services
1515 N. Vermont Ave., Suite 237
Los Angeles, CA 90027
(323) 783-8306
(323) 783-7609 (fax)
toni.a.rodriguez@kp.org
http://www.kaiserpharmacyresidency.org/

Kaiser Permanente Medical Care Program—Tri-Central Service Area
Managed Care Organization
Accredited: ASHP
Length of Program: 1 year
Number of Positions: 2
Affiliation: None
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $43,700
Onsite Interview: Yes

Educational/Special Requirements: Graduate of an accredited school or college of pharmacy and be eligible for licensure in California. The applicant must submit an application for consideration, current curriculum vitae, 3 letters of recommendation, official school or college of pharmacy transcript, copy of pharmacy intern license, letter of intent, and sample of recent school work (presentation or journal article)

Fringe Benefits: 2 weeks paid vacation; 6 paid holidays; sick leave; health benefits, including dental/optical (also dependent); uniforms; office space; and reimbursement for off-site experiences

Special Features: The program provides the resident with an opportunity to participate in the provision of health care in a large managed care environment. Resident will gain experience in various practice areas: acute care, ambulatory care, physician drug education, drug information, outpatient pharmacy and practice management. Ambulatory care practice includes anticoagulation, heart failure, hypertension, integrated CVD, oncology, etc. Resident completing our program will have a strong foundation for the future pharmacy practice.

Contact Information:
John Sie
Pharmacy Practice Residency Coordinator
Ambulatory Care Clinical Pharmacy Services Supervisor
Kaiser Permanente Medical Care Program Tri-Central Service Area, Pharmacy Operations
KAISER PERMANENTE MEDICAL CARE PROGRAM AT WEST LOS ANGELES

Pharmacy Practice
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $35,000
Onsite Interview: Yes

Educational/Special Requirements: Graduate of an accredited college of pharmacy and be licensed or eligible for licensure in California. Good communication skills required. Resident will develop a project with targeted care outcomes and present at Annual Western States Conference.

Fringe Benefits: Medical, dental, vision insurance; holidays; vacation/sick leave

Special Features: Hospital and ambulatory care experiences in the nation’s largest integrated care organization, preventative and disease state management in an integrated managed care setting; flexible program molded to the resident’s interests

Contact Information:
Michael Cinnamond Pharm. D.
Inpatient Pharmacy Director, Residency Program Director
Kaiser Permanente Medical Care Program at West Los Angeles
6041 Cadillac Ave., B 310
Los Angeles, CA 90034
(323) 857-2044
(323) 857-2870 (fax)
michael.d.cinnamond@kp.org

KAISER PERMANENTE MEDICAL CARE PROGRAM, CALIFORNIA

Pharmacy Practice and Drug Information Practice
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 26
Affiliation: None
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $35,000
Onsite Interview: Yes

Educational/Special Requirements: Graduate of accredited college of pharmacy and be licensed or eligible for licensure in California. Good communication skills required. Resident will develop a project with targeted care outcomes and present at Annual Western States Conference.

Fringe Benefits: Medical, dental, vision insurance; holidays; vacation/sick leave

Special Features: Hospital and ambulatory care experiences in the nation’s largest health maintenance organization, preventative and disease state management in an integrated managed care setting; flexible program molded to the resident’s interests

Contact Information:
Elaine Watanabe
Pharmacy Services Manager, Recruitment
Kaiser Permanente Pharmacy Operations Services, California Division
9521 Dalen St.
Downey, CA 90242
(714) 796-4809
(714) 796-4826 (fax)
elaine.g.watanabe@kp.org

KAISER PERMANENTE MID- ATLANTIC STATES REGION

Managed Care Pharmacy
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $40,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD, pharmacy licensure eligibility in DC, Maryland, or Virginia

Fringe Benefits: Medical benefits, selected holidays, sick and vacation leave, and education leave for Midyear Clinical Meeting and Eastern States conference

Special Features: In addition to helping develop new and innovative programs, the resident will participate on the Pharmacy & Therapeutics Committee, teach patient education classes, provide pharmacy staff continuing education, assist in educating pharmacy students, and complete residency projects and presentations.

Contact Information:
Katrin Fulginiti
Director, Managed Care Pharmacy Practice Residency Program
Kaiser Permanente-Mid Atlantic
12201 Plum Orchard Dr.
Silver Spring, MD 20904
(301) 572-3330
(301) 572-3399 (fax)
katrin.fulginiti@kp.org
Kaiser Permanente Northwest
Pharmacy Practice With Emphasis on Managed Care
Accredited: No
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: January 15
Starting Date: June 24
Estimated Stipend: $41,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD preferred, eligibility for Oregon and Washington licensure
Fringe Benefits: Health benefits, travel support to ASHP MCM and Western States Residency Conference
Special Features: Multidisciplinary collaborative drug therapy management, including cardiovascular risk factor management, hypertension, diabetes, anticoagulation, depression, pain, and asthma; drug information; drug use management; formulary application; academic detailing; P&T committee support; research and teaching opportunities. Other opportunities include inpatient pharmacy, home infusion pharmacy, long-term care pharmacy, and outpatient pharmacies located in our medical offices.
Contact Information:
Nancy Lee
Director of Pharmacy Clinical Services
Kaiser Permanente Northwest
5717 N.E. 138th Ave.
Portland, OR 97230
(503) 261-7570
(503) 261-7537 (fax)
Nancy.Louie.Lee@kp.org

Kaiser Permanente of Georgia
Managed Care Pharmacy Practice
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: January 13
Starting Date: July 1
Estimated Stipend: $34,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD preferred, eligibility for Georgia licensure
Fringe Benefits: Medical/dental/vision benefits, holidays, vacation/sick leave
Special Features: Ambulatory care-focused administrative and clinical responsibilities, collaborations with other UH residents
Contact Information:
Denise Martinez
Pharmacy Administrator of Clinical Services
Kelsey-Seybold Clinic
Pharmacy Administration
8900 Lakes at 610 Dr.
Houston, TX 77054
(713) 442-6248
(713) 442-5253 (fax)
Denise.Martinez@kelsey-seybold.com

Kelsey-Seybold Clinic/University of Houston
Pharmacy Practice With an Emphasis on Managed Care
Accredited: ASHP/AMCP
Length of Program: 1 year
Number of Positions: 2
Affiliation: University of Houston
Application Deadline: January 5
Starting Date: July 1
Estimated Stipend: $30,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD or equivalent experience
Fringe Benefits: State of Texas benefits; 10 days of vacation; support to attend AMCP, ASHP, TSHP, and either Alcalde or Mid-West Residency Conference
Special Features: Ambulatory care-focused administrative and clinical responsibilities, collaborations with other UH residents
Contact Information:
Denise Martinez
Pharmacy Administrator of Clinical Services
Kelsey-Seybold Clinic
Pharmacy Administration
8900 Lakes at 610 Dr.
Houston, TX 77054
(713) 442-6248
(713) 442-5253 (fax)
Denise.Martinez@kelsey-seybold.com

Medco Health Solutions, Inc.
Managed Care Pharmacy
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: January 12
Starting Date: July 2
Estimated Stipend: $39,000
Onsite Interview: Yes
Educational/Special Requirements: BS or PharmD degree, eligibility for New Jersey licensure, managed care rotation or experience preferred, 3 letters of recommendation, curriculum vitae, letter of intent, transcript, and onsite interview
Fringe Benefits: Paid vacation, holidays, sick and personal time; medical, dental, and life insurance; paid travel/registration
to professional meetings; leadership development training/education; paid New Jersey pharmacist licensure

**Special Features:** Medco's residency is an organized postgraduate year-1 (PGY1) managed care pharmacy practice training program that focuses on the development of the knowledge and skills pharmacists need in order to assume leadership roles within a managed care practice setting. In addition to defined clinical, coverage management, and elective rotations, residents attend a national P&T meeting and are exposed to legislative and regulatory aspects of pharmacy as well as innovative pharmacy models, automation, and information technology. The results of the resident's research will be presented at a professional pharmacy conference and submitted for publication in a peer-reviewed journal.

**Contact Information:**
Doris Fishman
Senior Director, Clinical Therapeutics
Medco Health Solutions, Inc.
100 Parsons Pond Dr.
Mail Stop F2-3
Franklin Lakes, NJ 07417
(201) 269-5812
(201) 260-1035 (fax)
MedcoRProg@medcohealth.com
http://www.medcopharmcareers.com

**NOVARTIS PHARMACEUTICALS CORPORATION**

**Health Economics and Outcomes Research Fellowship**

**Accredited:** No
**Length of Program:** 2 years
**Number of Positions:** 3
**Affiliation:** Duke University, Scott & White Health Plan/University of Texas at Austin, Rutgers University

**Application Deadline:** December 31
**Starting Date:** July 1
**Estimated Stipend:** $35,000-$45,000
**Onsite Interview:** Yes

**Educational/Special Requirements:** Advanced degree in health services research, public health, health policy, pharmacy, economics, medicine, or other related areas, with some experience in outcomes research

**Fringe Benefits:** Medical insurance, vacation

**Special Features:** The fellows will gain familiarity with outcomes research principles/application and experience in designing research studies that examine economic, clinical, and humanistic outcomes. The first year is spent at an academic/managed care institution and the second year with Novartis's Health Economics Outcomes Research Department (Rutgers: both years at Novartis).

**Contact Information:**
Jennifer Sung

**OPTIMA HEALTH PLAN/SENTARA HEALTHCARE**

**Managed Care**

**Accredited:** Not at this time
**Length of Program:** 12 months
**Number of Positions:** 1
**Affiliation:** None

**Application Deadline:** February 15
**Starting Date:** July 1
**Estimated Stipend:** $32,000

**Fringe Benefits:** 2 weeks of paid vacation and uninterrupted stipend during minor illness included. A health insurance plan is provided. Travel assistance is provided for continuing education events and other professional activities.

**Special Features:** Resident will have exposure to an integrated health care system and system-wide pharmacy services, including a drug information center. The resident will have the opportunity to precept students from Virginia Commonwealth University and Hampton University schools of pharmacy and work with medical residents from Eastern Virginia Medical School.

**Contact Information:**
Elizabeth Brusig, PharmD
Clinical Pharmacist
Optima Health Plan
4417 Corporation Ln.
Virginia Beach, VA 23464
(757) 552-7519
(757) 552-7516 (fax)
elbrusig@sentara.com
http://www.sentara.com/pharmacy/residency.html

**ORTHO-MCNEIL JANSSEN SCIENTIFIC AFFAIRS, LLC**

**Drug Information**

**Accredited:** No
**Length of Program:** 12 months
**Number of Positions:** 2
**Affiliation:** Rutgers University

**Application Deadline:** December 31
**Starting Date:** July 1
**Estimated Stipend:** Competitive

**Contact Information:**
Jennifer Sung
Managed Care Pharmacy Residencies, Fellowships, and Other Programs

Educational/Special Requirements: Contact program
Fringe Benefits: Contact program
Special Features: Contact program
Contact Information:
Will Zachok
Associate Director, Medical Communications
Ortho-McNeil Janssen Scientific Affairs, LLC
1000 Route 202 S
Raritan, NJ 08869
(908) 218-6283
(908) 722-6402 (fax)
wzachok@ompus.jnj.com

ORTHOMCNEIL JANSSEN SCIENTIFIC AFFAIRS, LLC
Pharmaceutical Industry, Department of Outcomes Research

Accredited: No
Length of Program: 24 months
Number of Positions: 1
Affiliation: Thomas Jefferson University
Application Deadline: December 31
Starting Date: June 2007 (flexible)
Estimated Stipend: Competitive
Onsite Interview: Yes
Educational/Special Requirements: Contact program
Fringe Benefits: Contact program
Special Features: Fellows spend the first year of the program working on outcomes research projects in an academic setting and the second year in the pharmaceutical industry. Fellows have the opportunity to take coursework in biostatistics, epidemiology, economics, and other outcomes-related subjects.

Contact Information:
Julie Locklear, PharmD, MBA
Associate Director, Outcomes Research
Ortho-McNeil Janssen Scientific Affairs, LLC
1125 Trenton-Harbourton Rd.
Titusville, NJ 08560
(609) 730-3664
(609) 730-2556 (fax)
jlockler1@janus.jnj.com

OUTCOMES PHARMACEUTICAL HEALTH CARE
Medication Therapy Management Firm

Accredited: AMCP/ASHP
Length of Program: 1 year
Number of Positions: 1
Affiliation: University of Iowa
Application Deadline: January 5
Starting Date: July 2
Estimated Stipend: $35,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD degree from a school of pharmacy accredited by the American Council on Pharmaceutical Education (ACPE) and eligibility for licensure in Iowa
Fringe Benefits: For additional information, contact the Outcomes office at (515) 237-0001 or info@getoutcomes.com.
Special Features: This managed care pharmacy systems residency program offers a unique learning experience on how pharmacists can impact the quality and rising cost of health care by providing patient-oriented, care-based services. Residency activities include: MTM claims assessment, development and implementation of disease management programs, account management, marketing and communication, and development and administration of research projects. The program is a collaborative offering by the University of Iowa College of Pharmacy and Outcomes Pharmaceutical Health Care.

Contact Information:
Patty Kumbera
Chief Operating Officer
Outcomes Pharmaceutical Health Care
601 E. Locust, Suite 200
Des Moines, IA 50309
(515) 237-0001
(515) 237-0002 (fax)
pkumbera@getoutcomes.com
http://www.getoutcomes.com

PERFORMRX
Managed Care Pharmacy

Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $35,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD degree from an ACPE-accredited college of pharmacy, Pennsylvania pharmacist license or eligibility for licensure, completed application, letter of intent, curriculum vitae, 3 letters of recommendation, official college transcripts, on-site interview (by invitation)
Fringe Benefits: Benefits package including medical, dental, and vision; 2 weeks paid vacation; 5 personal days; paid holidays; funding available for attendance to professional meetings and tuition reimbursement
Special Features: PerformRx is a pharmacy benefits management company dedicated to providing quality, cost-effective care to members of Medicaid and Medicare programs. Through managing this patient population, the resident is provided with an ideal environment to develop expertise in the following areas: prior authorization, drug utilization review, health outcomes and disease management, formulary management, injectable drug management, pharmacy network management, new business
Managed Care Pharmacy Residencies, Fellowships, and Other Programs

implementation, and pharmacy call center services.

Contact Information:
Edward Scott
Director of Clinical Operations
PerformRx
200 Stevens Dr.
Philadelphia, PA 19113
(215) 937-5090
(215) 397-8661 (fax)
edward.scott@performrx.com

■ PHARMACARE

Pharmacy Benefits Management
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: University of Pittsburgh
School of Pharmacy
Application Deadline: January 12
Starting Date: July 2, 2007
Estimated Stipend: $34,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD degree from an ACPF-accredited school or college of pharmacy, minimum GPA of 3.0 on a 4.0 scale, current license or eligibility for pharmacy licensure in Pennsylvania

Fringe Benefits: Comprehensive benefits package, no weekends or holidays, financial support for professional managed care meetings, no staffing requirements in a pharmacy

Special Features: The University of Pittsburgh School of Pharmacy and PharmaCare, one of the nation's largest pharmacy chain-based prescription management firms, offers an opportunity to practice in a dynamic pharmacy benefits management environment and gain a clinical and administrative perspective in the management of pharmacy benefit plans for a wide variety of clients. Multifaceted experience will include: drug utilization review criteria development, clinical intervention activities, P&T activities, clinical systems development, clinical account management, new business development, and proposals. Additionally, as a potential faculty member at the University of Pittsburgh School of Pharmacy, the resident will participate in undergraduate and graduate student instruction as well as in the development of educational programs for the PharmaCare professional staff.

Contact Information:
Julie Legal
Clinical Management Pharmacist
Pharmacare
620 Epsilon Dr.
Pittsburgh, PA 15238
(412) 967-2300, ext. 75492
(412) 968-2704 (fax)
jdlegal@pharmacare.com

■ PHARMACEUTICAL CARE NETWORK

Managed Care Pharmacy Practice
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: January 15
Starting Date: July 1
Estimated Stipend: $37,500
Onsite Interview: Yes

Educational/Special Requirements: Graduate of accredited college of pharmacy and license or eligibility for licensure in California

Fringe Benefits: Paid vacation and sick leave, health/dental/vision benefits, and educational support to attend professional meetings

Special Features: This residency will provide training in formulary management, provider drug therapy education, drug benefit design, outcomes analysis, and prior authorization. The resident will participate in drug utilization review, P&T committee presentations, and interface with pharmacists from a variety of professional fields. The resident will learn to use PCN's MedIntelligence software to identify drug therapy problems and make appropriate interventions. This program includes rotations in direct patient care and drug information and an opportunity to rotate through the California Pharmacists Association.

Contact Information:
Philip Parsatoon
Vice President, Professional Services
Pharmaceutical Care Network
9343 Tech Center Dr., Suite 200
Sacramento, CA 95826-2563
(916) 361-4450
(916) 414-4650 (fax)
resident@pharmcarenet.com

■ PRESCRIPTION SOLUTIONS

Managed Care
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: January 5
Starting Date: July 2
Estimated Stipend: $46,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD, licensed to practice in California, completion of first-year residency or the equivalent

Fringe Benefits: 2 weeks paid vacation and paid holidays, professional leave to attend conferences, reimbursement for expenses for professional meetings

Special Features: Clinical program development, formulary
Managed Care Pharmacy Residencies, Fellowships, and Other Programs

management, health outcomes research, client management, legal and regulatory affairs, industry relations, and specialty pharmacy. Residents will attend the ASHP Midyear Clinical Meeting, CSHP Seminar, AMCP Educational Conference, and Western States Conference.

**Contact Information:**
Heidi Lew  
*Director, Clinical Programs*  
Prescription Solutions  
2300 Main St.  
Mail Stop CS57-404  
Irvine, CA 92614  
(949) 252-4305  
(949) 474-4237 (fax)  
heidi.lew@rxsol.com  
http://www.rxsolutions.com/b/residency/

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**REGENCE RX**

**Managed Care Pharmacy Systems**

Accredited: Seeking  
Length of Program: 12 months  
Number of Positions: 2  
Affiliation: Regence BlueCross BlueShield  
Application Deadline: May 31  
Starting Date: July 1  
Estimated Stipend: $40,000  
Onsite Interview: Yes  

**Educational/Special Requirements:** Potential residents must possess a BS degree in pharmacy or a PharmD degree from an ACPE-accredited college of pharmacy, be licensed or eligible for licensure in Oregon, and have strong motivation to pursue a dynamic career in managed care pharmacy. Completion of a pharmacy practice residency or equivalent experience is desired but not required for consideration. An interview is required.

**Fringe Benefits:** Health, dental, eye care, life, and disability benefits available; vacation time allotted; professional travel and stipend available; no weekends or holidays; no staffing requirements in a pharmacy; commute expense reimbursement is available for public transportation; membership available to 24-hour on-site fitness center

**Special Features:** RegenceRx is an internal pharmacy benefit program for The Regence Group, the largest affiliation of health plans in the Pacific Northwest/Mountain region. Collectively, it includes 6 health plans serving nearly 3 million people in 4 states: Asuris Northwest Health Regence (Washington based), BlueShield of Idaho, Regence BlueCross BlueShield of Oregon, Regence BlueCross BlueShield of Utah, Regence BlueShield (Washington), and Regence Life and Health (Oregon based). This residency will be primarily based in Portland, Oregon, headquarters for The Regence Group. RegenceRx is a not-for-profit program, offering a full array of pharmacy benefits management services. Science-based evidence and effective utilization management are the foundation for RegenceRx. It focuses on identifying and promoting medications that provide the most value, ensuring quality and patient safety, and providing tools and information to consumers and physicians. The RegenceRx clinical review/formulary process was adopted by the Academy of Managed Care Pharmacy and is now known as the AMCP Formulary Submission Process.

**Contact Information:**
Sean Karbowicz, PharmD  
RegenceRx  
PO Box 1071  
M/S 2P  
Portland, OR 97207-1071  
(503) 225-5367  
(888) 437-1510 (fax)  
shkarbo@regence.com

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**RUTGERS UNIVERSITY/HORIZON BLUE CROSS BLUE SHIELD OF NEW JERSEY**

**Managed Care Organization**

Accredited: No  
Length of Program: 12 months  
Number of Positions: 2  
Affiliation: Ernest Marion School of Pharmacy, Rutgers University, State University of New Jersey  
Application Deadline: January 15  
Starting Date: July 1  
Estimated Stipend: $30,000  
Onsite Interview: Yes

**Educational/Special Requirements:** PharmD, eligibility for New Jersey state license

**Fringe Benefits:** Full medical coverage, dental and retirement benefits

**Special Features:** No weekend or staffing requirements; teaching and preceptoring mandatory; graduate courses offered at Rutgers University; industry and pharmacy benefits management perspectives of managed care

**Contact Information:**
Saira A. Jan  
Associate Professor, Rutgers University/  
Associate Director, Pharmacy Management at Horizon BCBSNJ  
Rutgers University/Horizon Blue Cross Blue Shield of NJ  
Three Penn Plaza East  
PP-13Q  
Newark, NJ 07105  
(973) 466-4575  
(973) 466-6266 (fax)  
saira_jan@horizon-bcbsnj.com
SCOTT & WHITE
Pharmacy Practice Managed Care
Accredited: No
Length of Program: 1 year
Number of Positions: 1
Affiliation: University of Texas at Austin
Application Deadline: February 15
Starting Date: July 1
Estimated Stipend: $30,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD, eligibility for Texas state license
Fringe Benefits: Full medical coverage and dental
Special Features: Minimal weekend staffing requirements; teaching and preceptoring, if desired; industry and pharmacy benefits management perspectives of managed care; marketing and sales exposure
Contact Information:
John Jackimiec
Director of Pharmacy Managed Care
Scott & White
2601 Thornton Ln., Suite A
Temple, TX 76502
(254) 742-3144
(254) 742-3109 (fax)
jjackimiec@swmail.sw.org

SECURE PHARMACY PLUS
Managed Care
Accredited: AMCP/ASHP
Length of Program: 1 year
Number of Positions: 1
Affiliation: Various universities
Application Deadline: January 14
Starting Date: July 1
Estimated Stipend: $35,000
Onsite Interview: Yes
Educational/Special Requirements: Graduate of accredited school of pharmacy; must obtain license before residency begins
Fringe Benefits: Stock purchase plan; 401K; full medical, dental, vision; and no night or weekend obligations. We provide training material and guidance for board certification in pharmacotherapy specialty.
Special Features: During your residency, you will be assigned to a client whom you will assist in providing the most cost-effective care.
Contact Information:
Alexander Tunnell
Formulary and Contract Manager
SelectHealth (formerly known as IHC Health Plans)
4646 West Lake Park Blvd., Suite N3
Salt Lake City, UT 84120
(801) 442-7984
(801) 442-3006 (fax)
jeffrey.dunn@selecthealth.org
http://www.selecthealth.org

SOUTHERN ARIZONA VA HEALTH CARE SYSTEM
Pharmacy Practice (PGY1)
Accredited: ASHP since 1982
Length of Program: 12 months
Number of Positions: 8
Affiliation: University of Arizona
Application Deadline: January 16
Starting Date: July 1
Estimated Stipend: $38,257 plus benefits
Onsite Interview: Interview Required, onsite preferred
Educational/Special Requirements: Curriculum vitae, 3 letters of recommendation, college transcripts, 1 sample of writing, U.S. citizenship
Fringe Benefits: Residents accumulate 13 days of paid vacation time during the residency year. Sick leave is accrued at the rate of 4 hours every 2 weeks. Educational leave is provided to
attend the Arizona Society of Health-Systems Pharmacists Annual Meeting, the ASHP Midyear Clinical Meeting, and the Western States Conference for Pharmacy Residents, fellows, and Preceptors; travel funds are available to offset some of the expenses for these educational meetings. Residents have access to the same medical plans that are offered to full-time employees of the VA. These include a wide range of HMO and PPO health plans. Tucson also has a wide range of outdoor activities and excellent weather year round.

**Special Features:** This comprehensive residency includes a balance of inpatient and outpatient clinical pharmacy experiences. Residents work in the areas of internal medicine, cardiology, neurology clinics, primary care, geriatrics, hospice, surgery/nutritional support, mental health, practice management, drug use evaluation, Pharmacy & Therapeutics Committee activities, drug literature evaluation, drug policy development, teaching, research, and enhancing communication abilities. Two months of elective experience are available.

**Contact Information:**
Christie Barreuther, RPh
Southern Arizona VA Health Care System
3601 South Sixth Ave.
Pharmacy Service 5-119
Tucson, AZ 85723
(520) 792-1450, ext. 5388
(520) 629-4700 (fax)
christine.barreuther@va.gov
www.southwest.va.gov/tucson/Pharmacy_Residency_Program1.asp

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**UNITED DRUGS**

**Managed Care**

Accredited: Not at this time  
Length of Program: 1 year  
Number of Positions: 1  
Affiliation: AMCP  
Application Deadline: June 15  
Starting Date: September 1  
Estimated Stipend: $33,000  
Onsite Interview: Yes  
Educational/Special Requirements: Graduate of an accredited pharmacy school, PharmD preferred; ability to work independently

**Fringe Benefits:** Understanding of managed care from the perspective of a pharmacy benefits manager; product development opportunities; and the ability to live in Arizona for a year

**Special Features:** Work hours negotiable

**Contact Information:**
Jean Brown  
Director of Clinical Services  
United Drugs  
7227 North 16th St., Suite 160  
Phoenix, AZ 85020-5256  
(602) 678-1179, ext. 229

(602) 678-0772 (fax)  
brownj@uniteddrugs.com

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**UNIVERSITY AT BUFFALO**

**Ambulatory Care**

Accredited: Pending  
Length of Program: 1 year  
Number of Positions: 2  
Affiliation: University  
Application Deadline: October 1  
Starting Date: January 1  
Estimated Stipend: Contact program  
Onsite Interview: Required

**Educational/Special Requirements:** PharmD or equivalent experience

**Fringe Benefits:** Health, dental, vision, paid vacation, conference travel funds

**Special Features:** Unique experience designed to further refine skills in pharmaceutical care in addition to developing skills in program development and personnel and resource management. Resident is involved in coordination of clinical activities in a high-volume lobby-based pharmacy and a health-clinic-based ambulatory care pharmacy. The resident will participate in medication histories, adherence counseling, and education programs. Development and implementation of disease management initiatives, patient education, medical informatics, and supervision of PharmD students are also significant aspects of the program. This residency will allow ample latitude for resident to explore interests and further develop skills as a practitioner. The resident will also be appointed as a clinical instructor at University of Buffalo, School of Pharmacy and Pharmaceutical Sciences.

**Contact Information:**
Gene Morse, PharmD  
University at Buffalo  
School of Pharmacy and Pharmaceutical Sciences  
311 Hochstetter Hall  
Buffalo, NY 14260  
(716) 645-2828  
(716) 645-2886 (fax)  
emorse@buffalo.edu

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**UNIVERSITY OF ILLINOIS AT CHICAGO AND WALGREENS HEALTH INITIATIVES**

**Fellowship–Outcomes Research**

Accredited: No  
Length of Program: 2 years  
Number of Positions: 1  
Affiliation: University of Illinois and Walgreens Health Initiatives

**Application Deadline:** February 1  
**Starting Date:** July 1
Managed Care Pharmacy Residencies, Fellowships, and Other Programs

Estimated Stipend: $36,000
Onsite Interview: Yes
Educational/Special Requirements: Applicants should have a PharmD or MD (or equivalent) and have completed a pharmacy practice or managed care residency.
Fringe Benefits: Yes, contact program
Special Features: This is a 2-year fellowship jointly offered by Walgreens Health Initiatives and the Center for Pharmaco-economic Research at the University of Illinois at Chicago. The aim of the program is to train clinical pharmacists to conduct research in drug therapy outcomes and pharmacoconomics in the managed care setting. Knowledge and experience will be gained in the use of research tools to evaluate economic, humanistic, and clinical outcomes of drug therapy. Presentation and publication of research findings in peer-reviewed venues is expected. The fellowship is designed to facilitate career opportunities in managed care, health provider organizations, consulting, academia, or pharmaceutical industry.

Contact Information:
Glen Schumock, PharmD, MBA
University of Illinois at Chicago
Center for Pharmaco-economic Research
833 S. Wood St. (MC 886)
Chicago, IL 60612
(312) 996-7961
(312) 996-2754 (fax)
schumock@uic.edu
http://www.uic.edu/pharmacy/research/cpr/

University of Maryland School of Pharmacy
5106 Bonnie Branch Rd.
Ellicott City, MD 21043
(410) 480-5012
catherine.cooke@pfizer.com
http://www.pharmacy.umaryland.edu/pps/residents/

■ UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY/CAREFIRST BLUECROSS BLUESHIELD

Managed Care Pharmacy
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: CareFirst BlueCross BlueShield of Maryland
Application Deadline: January 5
Starting Date: July 1
Estimated Stipend: $31,500
Onsite Interview: Yes
Educational/Special Requirements: Graduate degree in pharmacy
Fringe Benefits: Health insurance, parking, support for national meeting attendance and poster presentation
Special Features: Appointment as a clinical instructor at the University of Maryland School of Pharmacy, ambulatory care clinics at HMO, office with computer/references at managed care organization. The University of Maryland is an AA/EEO/ADA Employer; minorities and women are encouraged to apply.

Contact Information:
Catherine Cooke
Clinical Assistant Professor

■ UNIVERSITY OF TEXAS MEDICAL BRANCH
CORRECTIONAL MANAGED CARE
Postgraduate Year One (PGY1) Pharmacy Residency Program
With An Emphasis in Managed Care
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: UTMB
Application Deadline: February 15
Starting Date: July 1
Estimated Stipend: $35,000
Onsite Interview: Yes
Educational/Special Requirements: Pharmacy degree from accredited college of pharmacy, Texas license or eligibility for Texas licensure
Fringe Benefits: UTMB is an AA/EO employer; closed major holidays and weekends; generous vacation, holiday, and sick leave; competitive benefits
Special Features: Program strengths include automated technology, telemedicine technology, ambulatory care, and managed care

Contact Information:
Stephanie Zepeda
Assistant Director of Pharmacy
UTMB Correctional Managed Care
2400 Ave. I
Huntsville, TX 77340
(936) 437-5363
(936) 437-5311 (fax)
sdzepeda@utmb.edu
http://www.utmb.edu/cmc

■ UPMC HEALTH PLAN
Managed Care
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: UPMC Health System, University of Pittsburgh School of Pharmacy
Application Deadline: January 8
Starting Date: July 1
Estimated Stipend: $32,000
Onsite Interview: Preferred

Educational/Special Requirements: Applicants must have completed a PharmD degree and be eligible for Pennsylvania licensure. A pharmacy practice residency is recommended but not
required for consideration. Please include letter of intent, curriculum vitae, college transcript, list of references (3) with contact information, and 3 letters of recommendation submitted separately.

**Fringe Benefits:** Health, dental, eye care, life and disability benefits are available; vacation time allotted; professional travel and stipend available; no weekends or holidays; no staffing requirements in a pharmacy.

**Special Features:** UPMC Health Plan is the second largest health insurer in western Pennsylvania and covers commercial, medical assistance, and Medicare populations; it has integrated resources from Community Care Behavioral Health, University of Pittsburgh School of Pharmacy, and the UPMC Health System. UPMC Health Plan provides access to the complete health plan members (i.e., inpatient admissions, outpatient laboratory values, diagnosis, etc.). Residency experience will include drug utilization review criteria development and review, clinical intervention activities, P&T monograph development and presentation, formulary management, policy development, disease management protocol development and review, research project for publication, and the development of educational programs for the health plan staff. Residents will have the opportunity to do an off-site pharmacy benefits management rotation. Additionally, as an adjunct instructor at the University of Pittsburgh School of Pharmacy, the resident will participate in undergraduate and graduate student instruction.

**Contact Information:**
Jessica Daw
Clinical Pharmacy Specialist
UPMC Health Plan
One Chatham Center, 3rd Fl.
112 Washington Pl.
Pittsburgh, PA 15219
(412) 454-7822
(412) 454-5293 (fax)
dawjr@upmc.edu

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**VA SAN DIEGO HEALTHCARE SYSTEM**

**Managed Care Pharmacy Systems**

**Accredited:** AMCP/ASHP
**Length of Program:** 12 months
**Number of Positions:** 1
**Affiliation:** University of the Pacific School of Pharmacy

**Application Deadline:** January 15
**Starting Date:** July 1
**Estimated Stipend:** $46,500
**Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD plus first-year residency or equivalent experience, U.S. citizenship, personal statement, curriculum vitae, transcripts, and 3 letters of recommendation

**Fringe Benefits:** 12-13 vacation and sick leave days, 11 federal holidays, health and life insurance, free parking, paid leave, tuition and travel to required events, office with up-to-date computer systems

**Special Features:** This second-year residency will provide the skills necessary for the practical application of pharmacoeconomic principles to formulary management and outcomes research in integrated health care systems. Education will include formal pharmacoeconomics training classes and hands-on application of principles. Work activities will encompass the VASDHS, Veterans Integrated Service Network 22 (VISN 22) Pharmacy, (i.e., Southern California Regional VA), and VA National Formulary tasks. Out-of-state and in-state travel is required. VASDHS is university-affiliated, teaching, integrated health care system with 100% computerized medical records, cutting-edge patient safety, pharmacy-managed clinics, pharmacist specialty practices, and a dedicated Pharmacy Health Outcomes Division with 4 full-time pharmacoeconomists. The pharmacy service has outstanding leadership with a long positive track record for innovation and excellence at the local, state, and national level and a well-trained, well-published staff, most with residencies. This is an exciting opportunity to learn and start your career.

**Contact Information:**
Anthony P. Morreale, PharmD, MBA, BCPS
Chief, Pharmacy Service
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Pharmacy Service (119)
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(858) 552-8585, ext. 3026
(858) 552-4369 (fax)
anthony.morreale@med.va.gov
http://www.san-diego.med.va.gov

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**VETERANS AFFAIRS MEDICAL CENTER, CINCINNATI**

**PGY1**

**Accredited:** ASHP
**Length of Program:** 12 months
**Number of Positions:** 3
**Affiliation:** None
**Application Deadline:** January 10
**Starting Date:** July 1
**Estimated Stipend:** $39,807 plus benefits
**Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD or equivalent experience

**Fringe Benefits:** Vacation, paid holidays, sick days, and administrative time off for selected meetings

**Special Features:** ASHP-accredited pharmacy practice residency providing experience in both acute care and outpatient primary care while allowing for a variety of elective experiences as well.
The pharmacy resident will work under a collaborative practice agreement with a medical team to facilitate achievement of therapeutic goals through evidence-based disease state management. The resident will have learning experiences in critical care, internal medicine, practice management, drug policy development, education, and teaching. Upon completion of this residency program, the pharmacy resident will have achieved advanced practice skills that will enable the graduate to feel confident to function effectively in multiple health care environments and roles. The resident will also receive a teaching certificate from the University of Cincinnati College of Pharmacy.

**Contact Information:**
Jo-Ann Caudill  
Residency Program Director  
Dept. of Veterans Affairs Medical Center  
3200 Vine St.  
Pharmacy 119  
Cincinnati, OH 45220  
(513) 475-6322  
(513) 475-6981 (fax)  
Jo-Ann.Caudill@va.gov

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### WALGREENS HEALTH INITIATIVES

**Pharmacy Benefits Manager**  
**Accredited:** AMCP/ASHP  
**Length of Program:** 12 months  
**Number of Positions:** 2  
**Affiliation:** University of Illinois; Midwestern University–Chicago College of Pharmacy  
**Application Deadline:** January 7  
**Starting Date:** July 1 (flexible)  
**Estimated Stipend:** $37,000  
**Onsite Interview:** Yes  
**Educational/Special Requirements:** PharmD  
**Fringe Benefits:** Medical plan, 2-week vacation, holidays, travel-expense budget  
**Special Features:** This managed care pharmacy residency program is designed to allow the residents to work within the various departments of a pharmacy benefits management firm including, but not limited to, care management, drug use policy, PBM operations, clinical sales, and specialty pharmacy. The residents will gain practical experience and will develop skills related to disease management, health outcomes, medication management strategies, formulary management, drug utilization review, drug information, and other clinical services. Additionally, residents will have the opportunity to gain exposure to the pharmaceutical industry, be involved in professional organizations, and precept pharmacy students.  
**Contact Information:**  
Azzah Jedd

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### WELLPOINT NEXT RX

**Managed Care Pharmacy**  
**Accredited:** AMCP/ASHP  
**Length of Program:** 12 months  
**Number of Positions:** 1  
**Affiliation:** Blue Cross of California, PrecisionRx, University of Southern California  
**Application Deadline:** January 15  
**Starting Date:** July 1  
**Estimated Stipend:** $46,000  
**Onsite Interview:** Yes  
**Educational/Special Requirements:** PharmD from an ACPE-accredited college of pharmacy or equivalent experience, eligibility for California licensure, good academic standing, excellent written and verbal communication skills  
**Fringe Benefits:** Health insurance; 2 weeks paid vacation; paid holiday and sick days; and attendance at the Western States Conference, at a national pharmacy organization meeting, and at a WellPoint Pharmacy Management National P&T meeting  
**Special Features:** The program is designed to provide the resident with an overall managed care experience. The resident rotates through several areas within the pharmacy benefits manager, including drug information, therapy management, senior and state sponsored business, prior authorization centers, mail-order pharmacy, health informatics and policy research, and pharmaceutical contracting and industry relations. The program also includes rotations at Blue Cross of California health plan and the University of Southern California direct-patient-care sites.  
**Contact Information:**  
Krista Yokoyama  
Residency Program Director  
WellPoint Pharmacy Management  
8407 Fallbrook Ave.  
MS CAAF01-0007  
West Hills, CA 91304  
(818) 313-5082  
(818) 313-5110 (fax)  
krista.yokoyama@wellpoint.com
**XCENDA**

**Health Outcomes Research Fellowship**

Accredited: No  
Length of Program: 2 years  
Number of Positions: 1  
Affiliation: University of South Florida, College of Public Health  
Application Deadline: January 2  
Starting Date: July 1  
Estimated Stipend: Contact program  
Onsite Interview: Yes  
Educational/Special Requirements: PharmD or equivalent (residency preferred)  
Fringe Benefits: Competitive salary, health insurance, vacation, 401(k), tuition for required classes, and travel expenses to a national meeting per year  
Special Features: This 2-year, degree-granting fellowship provides a unique research and education experience in an outcomes consulting environment. Research activities include, but are not limited to, quality improvement programs, database analysis, economic modeling, and development of research-based manuscripts. In addition, the fellow will obtain an MSPH or MPH degree from the University of South Florida, College of Public Health.  

Contact Information:  
James H. Jackson IV, PharmD, MPH  
Director  
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http://www.xcenda.com