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All articles, editorials, and commentary in JMCP undergo blinded peer review; articles undergo blinded peer review. Letters may be peer reviewed to ensure accuracy. The fundamental departments for manuscript submission are:

- Research
- Subject Reviews
- Formulary Management
- Contemporary Subjects
- Brief Communications
- Editorials/Commentary
- Letters

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See the following examples of common types of references:

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

2. **No author given**

3. **Journal paginated by issue**

4. **Book or monograph by authors**

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

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7. **Government agency publication**

8. **Paper (or Poster) presented at a meeting**

9. **Newspaper**

10. **Web site**

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Please submit manuscripts electronically at Jmcp.msubmit.net. All text should be in a word processing program (preferably Microsoft Word). Tables should be prepared in a word processing program using the table function. Figures should be saved in Photoshop or Illustrator and may be re-created by us. Figures may also be prepared in a word processing program (preferably Microsoft Word). We can accept PowerPoint graphics. Please identify the format (PC or MAC), all programs used, and all file names. P values should be expressed to no more than 3 decimal points in the format 0.xxx.

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

**Cover letter:** the corresponding (lead) author should include a cover letter with the manuscript, which should:
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  - 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.
- **information indicating what is known about the subject and what your article adds.**
- **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.

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**REFERENCE**

Sail away to San Diego! AMCP is holding its 19th Annual Meeting & Showcase from April 11-14, 2007, in San Diego, California’s second-largest city. If you attend the conference, you’ll be able to enjoy the city’s warm and sunny climate, scenic harbor, and miles of shoreline as well as its many attractions, including the world-famous San Diego Zoo, Coronado Island, Balboa Park’s museums, downtown’s Gaslamp Quarter, and Old Town.

It is from this picturesque area that photographer David Shuler drew his inspiration. He used a Nikon D2X digital camera to capture an idyllic image of San Diego Bay in his San Diego Skyline With Spinnakers photograph. The vertical shapes of the colorful spinnakers’ sails echo those of the towering buildings in the background. Numerous other beautiful marine photographs are in the “Destinations” section of his Yacht Photography Web site (www.yachtphotography.com). Shuler says that he also likes to take pictures of anything related to water. Spectacular photographs of several forms of sea life, fishing, and seascapes can be found on his Web site. Many of his images are available as stock photos.

Born in 1950 in Beaver Falls, Pennsylvania, Shuler spent his early childhood in eastern Pennsylvania and eastern Ohio. When he was 12 years old, his family moved to Miami, Florida. He recalls, “This was the best thing that could have happened to me. My father bought a small boat, and that’s when my love of the water began. We fished, scuba-dived, and water-skied almost every weekend.” After graduating from high school, he lived in Atlanta, Georgia, for two years, and then relocated to Denver, Colorado, where he lived for 12 years.

Shuler says that he was in his early 20s when he picked up his first 35 mm camera on a dare from one of his roommates who was a photography major at a local Denver college. “From the start, my photos were slightly different from everyone else’s. And I would spend hours waiting to get the perfect lighting. Although I loved photography, it was just a hobby for me at that time,” he says.

Shuler spent the next 10 years working at ski resorts in Summit County, Colorado. In his spare time, he took photos of skiing, wildlife, and mountain scenes. Shuler tried selling some of his work, but he was unsuccessful. “The quality just wasn’t there yet. I still have the stack of rejection letters,” he admits.

Colorado’s cold weather finally got the better of Shuler, and he decided to move to San Diego. He started out by working on local sports fishing boats, and then worked in the construction industry. For a couple of years, Shuler spent his time working during the week and taking photographs on weekends. During this period, he also served as a crew member on racing sailboats throughout Southern California, which gave him the opportunity to photograph them.

In fact, Shuler’s first published photo—a racing sailboat—appeared in the June 1994 issue of The Log, a Southern California boating magazine. “From then on, I was hooked on photography. I showed that picture to everyone. This accomplishment got me a press pass to the 1995 America’s Cup [regatta] held in San Diego Bay. It ended up that my photos of the event were sent around the world for press releases,” relates a grateful Shuler.

After his initial taste of success, he began to realize that marine photography was a very competitive field. “There were hundreds of photographers from around the world and only 30 to 40 sailing publications. Some of these guys had been photographing sailboats for more than 20 years! I knew I had to change my approach to marine photography, so I started to concentrate on working for powerboat and yacht manufacturers. The key was being able to shoot the interior of the yachts,” Shuler explains. “I had never done this type of photography before, but I discovered that I had a knack for it. Pretty soon, I was taking photos for 20 different boat builders in California, Washington, and Florida. The best part of these jobs is I get to photograph the exterior of the yachts from a helicopter.”

Photography assignments for marine manufacturers such as Horizon Yachts, Offshore Yachts, Nordhavn, Smrad, and North Sails led to Shuler being placed on retainer for two boating magazines: Sea and Go Boating. In addition, his work has appeared in almost every major powerboat publication in the world, including Power and Motoryacht, Sail, Showboats, Sailing, and Power Cruising magazines.

Shuler’s next two freelance jobs are in tropical locations. The first is in Costa Rica, to shoot sailfish and marlin fishing photos for Penn Reels, a fishing reel manufacturer, and the second is in the Bahamas, to photograph one of Nordhavn’s boats. Other shoots for Nordhavn have taken him to Alaska, Washington, Florida, Mexico, Panama, Antigua, Bermuda, and the Azores islands.

Shuler is one of those fortunate people who has found their niche in life. He declares, “I consider my job to be one of the best I could have. I get to do the two things I love the most: take photos and work on the water—all expenses paid!”

Sheila Macho
Cover Editor

COVER CREDIT

SOURCE
Interview with the artist.
Total Knee Replacement Delayed With Hylan G-F 20 Use in Patients With Grade IV Osteoarthritis

David D. Waddell, MD, and DeWayne C. Bricker, PA-C

ABSTRACT

BACKGROUND: Total knee replacement (TKR), a last resort for treating knee pain due to osteoarthritis (OA), is not always medically indicated or preferred by many patients. Hylan G-F 20 is a cross-linked hyaluronan derivative approved for the treatment of pain due to OA of the knee after other conservative approaches have failed.

OBJECTIVE: The objectives of this study were to (1) determine the effect of hylan G-F 20 on patient need for TKR as measured by time from hylan G-F 20 injection to TKR, and (2) assess patient factors that might influence time from hylan G-F 20 therapy to TKR.

METHODS: This is a retrospective case series review of the medical records of patients seen in 1 orthopedic specialty practice. The incidence and time to TKR in patients who were TKR candidates (100% grade IV OA [severe]) treated with 1 or more courses of intra-articular hylan G-F 20 injections (3 weekly injections per course) were determined from October 1997 to November 2003. Survival analysis was used to evaluate time to TKR and the effects of age, gender, ethnicity, body mass index (BMI), and presence of effusion on this outcome. Logistic regression was also used to assess these covariates.

RESULTS: The incidence of TKR in hylan G-F 20-treated knees (1,187 knees; 863 patients) was 19% (n = 225 knees). The median time to TKR in these patients was 638 days (1.8 years; minimum 7 days, maximum 2,147 days). For patients in whom a TKR had not yet occurred during the observation time, the median time of hylan G-F 20 treatment and patient follow-up was 810 days (2.2 years; minimum of 7 days, maximum of 2,222 days). A total of 1,978 courses of hylan G-F 20 given to 1,187 knees (average 1.67 courses per knee) resulted in an average cost of $1,419.76 per knee to delay TKR by a median of 2.1 years (772 days, minimum 7, maximum 2,222 days), the median time of all knees to either TKR or time of last observation.

Survival analysis showed that 75% of knees had not had a TKR by 1,370 days (3.8 years). Survival analysis and logistic regression indicated that of age, gender, ethnicity, BMI, and presence of effusion, only age significantly affected time to TKR.

CONCLUSION: In patients who are candidates for TKR, the need for TKR can be delayed with hylan G-F 20 when used for the treatment of OA knee pain.

KEYWORDS: Hylan G-F 20, Knee, Osteoarthritis, Pain, Total knee replacement

J Manag Care Pharm. 2007;13(2):113-21
surgery have been reported, including infection, pulmonary embolism, thromboses, fat embolism, hemarthrosis, patellar fracture, heterotopic ossification, stiffness, nerve damage, vascular injuries, and urinary complications. The perioperative mortality rate has been reported at 0.17%-0.46% for primary total knee arthroplasty within 90 days and 0.33%-0.78% for bilateral knee replacements within 30 days.

Hylan G-F 20 (Synvisc) is a cross-linked hyaluronan derivative approved for the treatment of pain due to OA of the knee after other conservative approaches have failed. Three intra-articular hylan G-F 20 injections effectively relieve the pain associated with OA of the knee as demonstrated by studies of various design, including double-blind, placebo-controlled; open-label, prospective with or without an active control; and retrospective. In many instances, either medically or by patient choice, delaying the need for a TKR would be advantageous. Previous reports, including a case-control study, a small uncontrolled study, and a theoretical managed care model, suggest that hylan G-F 20 may help delay patient need for TKR.

The objective of the current study was to investigate the ability of hylan G-F 20 to delay the need for TKR in patients with predominantly severe OA of the knee in our large orthopedic practice over a 6-year period.

### Methods

#### Patients

In our clinical practice, patients diagnosed with OA of the knee who are assessed as clinically suitable candidates for hylan G-F 20 therapy are routinely offered the therapy for OA knee pain relief. We consider a patient with any Kellgren-Lawrence grade of OA without any mechanical problems in the knee (i.e., torn cartilage, severe varus or valgus deformity, or end-stage bone-on-bone disease) as suitable for hylan G-F 20 therapy. We consider a patient a TKR candidate if they have Kellgren-Lawrence OA grade IV (severe joint space greatly impaired with sclerosis of subchondral bone) and score on the visual analogue scale (VAS) for pain of approximately 60 mm or greater (on a 100-mm scale). All patients included in this 6-year retrospective data review were considered TKR candidates when they entered our practice. Instead of being scheduled immediately for knee replacement surgery, all patients received hylan G-F 20. In our practice, patients who are TKR candidates and who are not appropriate for hylan G-F 20 typically undergo surgery within 3 months.

Exclusion criteria for receiving hylan G-F 20 were mechanical symptoms or deformities due to OA, including flexion contracture >20°, valgus malalignment >15°, or varus malalignment >10°. Patients were not treated if they had any contraindications to the therapy, which are known hypersensitivity to hyaluronan preparations, target knee joint infections, or skin diseases or infections in the area of the injection site. Before undergoing intra-articular hylan G-F 20 injections, all patients had been unsuccessfully treated with nonsteroidal anti-inflammatory drugs and analgesics, and most with COX-2 inhibitors once these were commercially available. At some point, most of the patients had received some form of nonpharmacologic therapy (such as physical therapy) or corticosteroid injections for relief of OA knee pain. Unsuccessful previous treatment was typically defined as a score of 50 on a VAS for pain or as a total score on the Western Ontario McMaster Osteoarthritis Index.

#### Database Methodology

Our clinical practice has developed and currently maintains a database of patient information for those receiving hylan G-F 20 for the treatment of OA knee pain. Specific information routinely recorded in the database includes demographic information, osteoarthritic disease characteristics (grade, presence of effusion), prospectively collected data on efficacy measures (e.g., physician VAS for OA knee pain), the occurrence of local adverse events (knee pain and swelling), and the date of any TKR. These prospectively collected data were taken from the records of patients’ initial and follow-up visits or follow-up telephone calls if the patient did not return for an office visit.

For this study, data (including TKR status) from the described patients who initiated treatment and/or received repeat treatment with hylan G-F 20 from October 30, 1997, to November 30, 2003, were retrospectively reviewed to explore the ability of hylan G-F 20 to delay patient need for TKR. If TKR status of the patient was unknown as of November 30, 2003, attempts were made to contact the patient by telephone to obtain his or her TKR status.

This study was reviewed retrospectively by an institutional review board, which approved the research protocol. Before treatment, all hylan G-F 20-treated patients signed a standard consent form, which included consent for their health or medical record to be used as a source of data for research.

#### Treatment With Hylan G-F 20

Each course of therapy involves 1 intra-articular hylan G-F 20 injection (2 mL) per week for 3 weeks using a fluoroscopic technique that confirms accurate needle placement in the joint as we have previously described. The published cost of a course of hylan G-F 20 injections in 2006 was $852, which includes the cost of 3 injections with arthrocentesis and 1 office visit (Medicare reimbursement policy allows only 1 office visit charge despite the need for 3 visits). The additional cost of fluoroscopy, which is not used by all physicians, is $77 per injection or $231 per course of therapy.

Patients may have received more than 1 course of therapy during this observation period (Table 1). While product information states that results of repeat use have not been established, we have published 3 articles on 2 studies indicating the effectiveness and tolerability of repeat courses of hylan G-F 20. In our practice,
we repeat courses of hylan G-F 20 therapy after a patient experiences an initial beneficial response (≥20 mm reduction in physician VAS for OA knee pain) with the treatment. Subsequent courses of therapy are offered to patients if their VAS score worsens to 50% of their initial baseline VAS. In our prospective study of a second course of therapy, the mean time between first and second courses was 19 months.‡

To avoid local adverse events (knee pain and swelling) after injection, we instruct patients to rest the afternoon of the injection, use an ice pack for 2 to 3 hours, and resume normal activities the day after the injection, except for strenuous work or exercise, which should be resumed only after completion of therapy. We also provide patients with a prescription of hydrocodone and acetaminophen, pentazocine hydrochloride and acetaminophen, or tramadol hydrochloride and acetaminophen, to be used only if they experience postinjection pain and swelling.

**Statistical Analysis**
For patients undergoing a TKR during the observation period, median time to TKR was determined. Median time to TKR included treatment time for hylan G-F 20 (2 weeks) and the time up until the TKR was performed. For those patients who did not receive a TKR, median time of patient follow-up was calculated. Median patient follow-up time was defined as the hylan G-F 20 treatment time (2 weeks) plus the time of follow-up after treatment. For patients with known TKR status during the entire observation period, the end of a patient’s follow-up time was the end of the observation period (November 30, 2003). Otherwise, the end of a patient’s follow-up time was the date of the patient’s last office visit if the patient was no longer being seen in our office and could not be contacted by telephone (lost to follow-up). End of follow-up time for deceased patients was their date of death or the date of the last office visit if the patient was no longer being seen in our office and could not be contacted by telephone (lost to follow-up). Otherwise, the end of a patient’s follow-up time was the date of death. If an exact date of the month or year was not available, the first of the indicated month or year was used for the follow-up time calculation.

Because patients with grade IV OA of the knee are considered candidates for TKR in our practice, only patients with grade IV OA of the knee treated with hylan G-F 20 were analyzed. The incidence of TKR in this patient population was calculated. The effects of age, ethnicity, gender, body mass index (BMI), and effusion history at the beginning of hylan G-F 20 treatment on the odds for a TKR were evaluated using logistic regression (the GENMOD procedure in SAS [SAS version 9.1, SAS Institute, Cary, NC]). Age was categorized to 1 of 5 groups: <50 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, and ≥80 years. BMI was also categorized into groups: normal (20-25 kg/m²), overweight (26-30 kg/m²), obese (31-40 kg/m²), and severely obese (≥40 kg/m²). If significant covariate effects were detected (P < 0.05), covariate effects were evaluated by a Wald chi-square test.

Because not all patients had received a TKR during the observation period, survival analysis was used to evaluate (1) time to TKR for the entire patient population and (2) the effects of age, ethnicity, gender, BMI, and effusion history on the beginning of hylan G-F 20 treatment on the time to TKR. The PHREG procedure in SAS was used to test the effects of these covariates on the time to TKR under the assumption of a proportional hazards model. If significant covariate effects were detected (P < 0.05), covariate effects were evaluated by a Wald chi-square test.

**Results**

**Patient Knee Disposition and Patient Demographics**
A total of 1,187 knees (863 patients) with OA grade IV were treated with hylan G-F 20. The disposition of treated knees, with regard to patient status during the observation period, that

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**TABLE 1** Disposition of Knee Population During the Observation Period*

<table>
<thead>
<tr>
<th>Disposition</th>
<th>N (%) of Knees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated hylan G-F 20</td>
<td>1,187</td>
</tr>
<tr>
<td>Known TKR status during entire observation period</td>
<td>749 (63.1)</td>
</tr>
<tr>
<td>TKR</td>
<td>225 (19.0)</td>
</tr>
<tr>
<td>Still being seen in our practice</td>
<td>210 (17.7)</td>
</tr>
<tr>
<td>Telephone follow-up</td>
<td>293 (24.7)</td>
</tr>
<tr>
<td>Deceased†</td>
<td>21 (1.8)</td>
</tr>
<tr>
<td>Unknown TKR status during entire observation period</td>
<td>438 (36.9)</td>
</tr>
<tr>
<td>Lost to follow-up‡</td>
<td>407 (34.3)</td>
</tr>
<tr>
<td>Deceased</td>
<td></td>
</tr>
<tr>
<td>Discontinued due to local adverse event</td>
<td>10 (0.8)</td>
</tr>
<tr>
<td>Discontinued due to other medical reasons</td>
<td>4 (0.3)</td>
</tr>
<tr>
<td>Number of knees treated by course§</td>
<td></td>
</tr>
<tr>
<td>Course 1</td>
<td>1,187 (100)</td>
</tr>
<tr>
<td>Course 2</td>
<td>533 (44.9)</td>
</tr>
<tr>
<td>Course 3</td>
<td>170 (14.3)</td>
</tr>
<tr>
<td>Course 4</td>
<td>48 (4.0)</td>
</tr>
<tr>
<td>Course 5</td>
<td>13 (1.1)</td>
</tr>
<tr>
<td>Course 6</td>
<td>7 (0.6)</td>
</tr>
</tbody>
</table>

* The observation period was from October 1997 to November 2003.  
† TKR status known up until the date of death.  
‡ Lost to follow-up includes patients no longer being seen in our practice and could not be reached by telephone contact.  
|| TKR status unknown from the time of the last office visit until the date of death.  
§ A course is equivalent to 3 weekly injections, at a cost of $852, including 3 injections with arthrocentesis and 1 office visit (in accordance with Medicare reimbursement policy).  
TKR = total knee replacement.
Total Knee Replacement Delayed With Hylan G-F 20 Use in Patients With Grade IV Osteoarthritis

The number of knees receiving from 1 to 6 courses of therapy is also summarized in Table 1. The demographic characteristics and TKR status of patients whose knees were treated with hylan G-F 20 during the observation time did not require a TKR. A total of 225 knees underwent a TKR, for a TKR incidence of 19% of knees in this population of surgical candidates with OA grade IV (Table 1). The incidence of TKR by demographic and disease characteristics is shown in Table 3. Within age categories, the incidence of TKR in knees was highest for patients aged 60 to 69 years, which was more than double the percentage of patients aged <50 or ≥80 years who had a TKR. Knees from patients who were obese had a higher incidence of TKR compared with knees from patients with normal BMI, or from those who were overweight or severely obese. All other incidences for knees having a TKR within other age categories, gender, ethnicity, and effusion history were comparable with the 19% incidence for all knees.

Logistic regression showed that of age, gender, ethnicity, BMI, and effusion history, age was the only significant covariate (P < 0.001). Odds ratios for age-group comparisons are presented in Table 4. Knees from patients aged 60 to 69 years were significantly more likely to have had a TKR compared with knees from patients in age groups <50 years (P = 0.006), 70 to 79 years (P = 0.0082), and ≥80 years (P < 0.001). Patient knees from the <50-year-old group were 57% less likely to have had a TKR than were patient knees from the 60 to 69-year-old group (P = 0.006). Knees of patients in the age groups 50 to 59, 60 to 69, and 70 to 79 years were approximately 2- to 3-fold more likely to have had a TKR than were knees of patients ≥80 years (P < 0.05).

Time to TKR

For knees that underwent TKR during the observation period, the median time to TKR following hylan G-F 20 treatment (including 2 weeks for hylan G-F 20 administration) was 1.8 years (638 days; minimum of 14 days, maximum of 2,147 days). For knees in which a TKR had not yet occurred during the observation period, median time of hylan G-F 20 treatment and patient follow-up was 2.2 years (810 days; minimum of 7 days, maximum of 2,222 days). While this latter calculation included patients lost to follow-up, we further calculated the known time of follow-up for knees of patients no longer being seen in the practice (lost to follow-up): 1.1 years (416 days; minimum 7 days, maximum 2,112 days).

Collectively, the median time of all knees to either TKR or time of last observation was 2.1 years (772 days; minimum 7, maximum 2,222). Based on the current cost of hylan G-F 20 ($852, including 3 injections with arthrocentesis and 1 office visit [in accordance with Medicare reimbursement policy]), we calculated that 1,978 courses of hylan G-F 20 given to 1,187 knees (average 1.67 course per knee) resulted in an average cost of $1,419.76 per knee to delay TKR by a median of 2.1 years (median time for all knees).

Survival analysis of all knees for time to TKR is shown in Figure 1, which indicates that 75% of knees had not had a TKR...
Total Knee Replacement Delayed With Hylan G-F 20 Use in Patients With Grade IV Osteoarthritis

by 3.8 years (1,370 days; 95% confidence interval [CI], 1,215-1,590 days). These analyses included data on those lost to follow-up who had not had a TKR at the time of their last office visit.

**Effect of Demographic Variables on Time to TKR**

Of the covariates tested in the survival analysis (age, gender, ethnicity, BMI, and effusion history), age was the only significant predictor for time to TKR ($P = 0.009$). Figure 2 illustrates the survival analysis for time to TKR by age group. Knees of patients in the age group 60 to 69 years had the shortest amount of time to TKR, while knees of patients aged <50 years had the longest time to TKR, followed by knees of patients aged ≥80 years (Figure 2). Time to TKR was significantly shorter for knees of patients in the 60 to 69 years age group compared with knees of patients aged <50 years ($P = 0.003$) and of patients aged ≥80 years ($P < 0.004$). For patients aged 70 to 79 years, time to TKR was significantly shorter than for patients aged <50 years ($P = 0.004$) and patients aged ≥80 years ($P = 0.047$). No other age comparisons were significantly different.

**Discussion**

This study suggests that the use of 1 or more courses of hylan G-F 20 in orthopedic practice can delay the need for surgery in patients who are candidates for TKR (OA grade IV knees). Delaying TKR can be advantageous for patients who do not want surgery or for whom surgery is not medically desirable. The incidence of TKR in the population of TKR candidates studied here was low, and for knees that underwent TKR, use of hylan G-F 20 had the ability to delay surgery for approximately 1.8 years. In others, the median time of hylan G-F 20 treatment and patient follow-up without having a TKR was 2.2 years.

Previously reported data also show that hylan G-F 20 can delay the need for TKR in patient populations with predominantly advanced OA. In an open-label, multicenter trial, OA knee pain in 86% of patients (n = 60) with advanced OA (75% grade IV) receiving hylan G-F 20 therapy (up to 4 courses) improved sufficiently enough to delay TKR at week 12 of the study. At the end of the 30-month observation period, a total of 59% of treated patients were able to delay TKR. We reported a preliminary, case-control study (110 TKR patients; 1,151 patients without TKR) in which the probability of progression to TKR in a population of predominantly advanced OA (83% grade IV) knee patients was reduced with hylan G-F 20 therapy.

Although TKR has been shown to be an effective therapy for patients ranging in age from <50 years to >80 and 90 years, patients aged <50 years or >80 years may not be the best TKR candidates and are thus less likely to undergo the procedure. Our study reflects this trend because we found that patients aged <50 years and patients aged ≥80 years were significantly less likely to have had a TKR than other age groups. For example, patients aged <50 years were significantly less likely to have had a TKR than 60 to 69-year-olds, and patients aged ≥80 years were significantly less likely to have had a TKR than patients aged 60 to 69 years.
were significantly less likely to have had a TKR than patients aged 50 to 59 years, 60 to 69 years, and 70 to 79 years. Patients in the age group 60 to 69 years had the highest incidence of TKR and the shortest time to TKR compared with the other age groups. Survival analysis also showed that patients aged <50 years and ≥80 years had the longest time to TKR, reflecting inclusion of data for patients lost to follow-up who had not had a TKR as of their last office visit.

In many cases, it may be desirable to delay TKR in younger patients because of the risk of hardware revisions, loosening from the bone, pain from overuse, or to delay or avoid the procedure altogether in older patients or patients with comorbidities who may increase their complication risk with surgery. Therefore, delaying TKR by incorporating hylan G-F 20 into the treatment plans for these patients is advantageous. Avoiding surgical treatment might also prevent complications that can arise from TKR, including, but not limited to, infection, pulmonary embolism, thromboses, fat embolism, hemorrhosis, patellar fracture, heterotropic ossification, stiffness, nerve damage, vascular injuries, urinary complications, and even death for some. In addition, risk for complication in an older patient due to the delay in TKR is dependent on individual patient factors. The most common adverse events that occur with hylan G-F 20 are local knee pain and/or swelling, which have occurred in 2.2% of injections or in 7.2% of patients treated with hylan G-F 20. We have reported a similar low incidence of local adverse events from the same database of this report (1.2% of injections, 5.2% of patients). If local knee pain and swelling do occur with hylan G-F 20, it is transient and clinically manageable and is less serious than most of the surgical complications listed above. No serious systemic adverse events have been observed with hylan G-F 20 in clinical trials.

With the estimated increase in the ≥65-year-old population with OA in years to come, strategies that would help alleviate the economic burden of OA, including TKR, would be appropriate for providers and policymakers. Given that TKRs are the primary cost drivers for OA of the knee, cost savings to any plan would be a function of delaying or avoiding the number of TKRs in their covered patients. With its ability to delay TKR, use of hylan G-F 20 therapy has the potential to reduce costs for OA knee treatment for not only surgery but revision surgery. A theoretical managed care model with a large Medicare population developed to evaluate the potential savings associated with incorporating hylan G-F 20 into the standard treatment regimen for OA knee pain demonstrated cost savings. In this hypothetical cohort of 100,000 patients (3,835 with mild, moderate, or severe OA of the knee) followed for 3 years, significant cost savings were predicted with the use of hylan G-F 20. This cost savings was primarily due to the predicted 808 TKRs that could be avoided with hylan G-F 20 therapy. Over this 3-year period, a total cost savings of $8,810,771 was reported for the plan, with a total cost savings of $4,706 per patient receiving hylan G-F 20.

The results of this theoretical model in conjunction with the clinical reports above and our clinical experience reported here support significant cost savings with hylan G-F 20 for the OA knee patient as well as for insurance and managed care plans. On the basis of the current cost of hylan G-F 20 ($852, including 3 injections with arthroscopy and 1 office visit), we calculated that 1,978 courses of hylan G-F 20 given to 1,187 knees resulted in an average cost of $1,419.76 per knee to delay TKR by a median of 2.1 years, the median time of all knees to either TKR or time of last observation.
Conclusion

This study suggests that hylan G-F 20 can delay patient need for TKR in a population of OA knee patients with advanced disease. The ability of hylan G-F 20 to delay TKR is advantageous for patients for whom TKR is not medically appropriate or for patients who do not want or who fear surgery. In select patients, delaying TKR will also reduce the risk of any potential complications that may accompany the procedure. As long as TKR candidates can maintain a functional lifestyle and good quality of life with an alternative therapy, delaying TKR is beneficial. Further implications may be made with regard to cost savings for patients, policymakers, and managed care and insurance plans.

What is already known about this subject

• In patients failing usual therapy, TKR may be medically contraindicated due to comorbidities, or is not preferred by some patients, as a last-resort treatment for OA of the knee.
• Hylan G-F 20 is approved for the treatment of pain due to OA of the knee.

What this study adds

• One or more courses of hylan G-F 20 for the treatment of grade IV OA of the knee may delay a patient’s need for TKR.

ACKNOWLEDGMENTS

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DISCLOSURES

Funding for manuscript preparation and statistical analysis was provided by Wyeth Pharmaceuticals and Genzyme Biosurgery and was sought by author David Waddell. Waddell was a consultant to Wyeth Pharmaceuticals at the time of this study and is currently a consultant to Genzyme Biosurgery; author DeWayne C. Bricker has participated in Wyeth’s speakers bureau.

Waddell served as principal author of the study. Study concept and design and writing of the manuscript and its revision were the work of Waddell. Data collection was primarily the work of Waddell, with input from Bricker; data interpretation was the work of Waddell.

REFERENCES


Comparison of Mail-Order With Community Pharmacy in Plan Sponsor Cost and Member Cost in Two Large Pharmacy Benefit Plans

Michael Johnsrud, PhD, RPh; Kenneth A. Lawson, PhD, RPh; and Marvin D. Shepherd, PhD, RPh

ABSTRACT

BACKGROUND: Pharmacy benefit managers (PBMs) play a major role in administering prescription drug benefit programs for health plans and employers. PBMs have often encouraged the use of self-owned mail-order pharmacy services with the promise to plan sponsors of lower prescription drug costs compared with those of the community pharmacy network. Some plan sponsors have requested a higher degree of disclosure of contract relationships and transparency in pricing. Unfortunately, little research exists based on empirical data to determine the net plan cost and member cost for mail-order drugs, as opposed to having these drugs dispensed by community pharmacies.

OBJECTIVES: To determine the difference between mail-order and community pharmacy in the (1) payment (cost) per day of drug therapy for the plan sponsor and for the member for the highest expenditure therapeutic classes, (2) generic dispensing ratios for all drugs and for a comparative market basket of drugs, and (3) cost per unit for the top 20 generic drugs dispensed through the mail-order channel.

METHODS: Pharmacy claim records were obtained from 2 publicly financed pharmacy benefit plans in Texas for fiscal year 2004 (September 1, 2003, through August 31, 2004). There were approximately 460,000 members in Plan A and 177,000 members in Plan B. Pharmacy cost per day (product costs plus dispensing fees, divided by days supplied) was calculated for each drug in the 30 highest expenditure therapeutic categories and aggregated for mail-order and community pharmacy channels for each plan. Differences in the mail-order and community pharmacy cost per day were calculated for each drug (adjusted for dosage) in the therapeutic category and weighted by the product’s share of mail-order therapy days within the therapeutic category. A weighted cost per day for each therapeutic category was calculated with a comparison of what the cost would have been for plan cost and member cost if all mail claims had been paid based on the community pharmacy cost per day. Comparison of the cost per day helped control for differences in quantity dispensed per day per product and for product mix within each therapeutic category. Descriptive analyses were conducted to compare generic dispensing ratios between (1) all mail-order and community pharmacy claims, and (2) a market basket of therapeutic categories most commonly found within the mail-order channel. Finally, the difference in price per unit was calculated between mail-order and community pharmacy channels for the top 20 generic drug products.

RESULTS: Mail-order drugs accounted for 34.4% of overall pharmacy benefit spending, including plan cost and member cost, in Plan A and 43.4% for the market basket of drugs compared with 56.0% of overall spending and 63.1% for the market basket in Plan B. When comparing the cost per day for the top therapeutic categories, the authors found the plan sponsor cost was higher for mail-order than for the community pharmacy channel for approximately half of the top therapeutic categories. This result contributed to a 0.5% higher plan cost per day for mail-order ($1.24) than for community pharmacy ($1.23) for Plan A but a 0.4% lower plan cost per day for Plan B ($1.43 for mail-order vs. $1.44 for community pharmacy). The member cost was lower for mail-order than for community pharmacy for almost every therapeutic category, and overall was 29% lower in Plan A ($0.73 per day for mail-order vs. $1.03 for community pharmacy) and 37% lower in Plan B ($0.52 for mail-order vs. $0.82 for community pharmacy). For all claims, the generic dispensing ratios were lower in the mail-order channel than in the community pharmacy channel (37.7% vs. 49.0% for Plan A and 34.7% vs. 45.0% for Plan B). The cost per unit (tablet, capsule, etc.) for the top 20 generic drug products dispensed by mail order was 16.5% lower than community pharmacy for the plan sponsor in Plan A but 18.0% higher in Plan B; member cost was 29.9% lower in Plan A for mail order and 34.0% lower in Plan B. Comparing plan and member costs combined, 9 of 20 (45%) of the generic prices were higher through mail order in Plan A, and 10 of 20 (50%) were higher through mail order in Plan B.

CONCLUSIONS: Overall, savings from lower unit pricing through the mail-order channel benefitted the member and did not translate into significant cost reductions for the plan sponsor. In both pharmacy benefit plans, the plan sponsor either realized small savings or incurred slightly higher costs when paying for drugs in the top therapeutic categories through the mail-order channel. Some generic drug prices are higher through mail-order pharmacy than through community pharmacy, and one of the 2 plans in this study paid higher net costs after member cost share for generic drugs through mail order.

KEYWORDS: Mail-order pharmacy, Community pharmacy, PBM, Pharmacy benefits, Net costs

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In creased coverage and rising expenditures for prescription drugs have led to the increased use of pharmacy benefit managers (PBMs), which contract with employers and health plans to administer their prescription benefit programs. The PBM industry has evolved over the last 3 decades from providers of community pharmacy network coordination and claims administration services to large publicly owned companies marketing an array of services. PBMs now routinely offer clients expanded services such as drug formulary development, manufacturer rebate negotiation and collection, specialty pharmaceutical distribution, and mail-order prescription delivery options.

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As the PBM industry has grown, the largest of these firms have built considerable market leverage with drug manufacturers and community pharmacies by accumulating prescription drug transaction volume. Because of their unique position within the pharmacy marketplace, PBMs have identified and capitalized on revenue streams arising from this transaction volume, resulting in a complex business model. For instance, over the last decade, large PBMs have generated the majority of their gross margin dollars not from administrative fees collected from clients, but from retained rebates collected from manufacturers and margin derived from mail-order pharmacy operations.\(^6\)

The profitability of PBMs has contributed to greater scrutiny of the business model and calls for more transparency in the relationships between PBMs and their contractors, including community pharmacies and pharmaceutical manufacturers.\(^3\) This transparency can include disclosure of all direct and indirect revenue streams that a PBM realizes from representing the plan sponsor in fulfilling the contracted services. A lack of disclosure of additional revenue streams by the PBM may disadvantage the plan sponsor in its negotiation with the PBM to obtain favorable prices. The absence of disclosure and transparency may contribute to suspicion and accentuate the divergence of financial incentives for PBMs versus for pharmacy plan sponsors. It may also create difficulties for the plan sponsor in comparing the value of services between competing PBMs as part of the contracting process.

## The Mail-Order Option

A popular mechanism touted by PBMs to control prescription drug costs is mail-order prescription delivery as an alternative to traditional community pharmacies. The mail-order pharmacy option has become a core component of the business model for PBMs that own their own mail-order pharmacies, since they profit directly from mail-order dispensing. Ownership of mail-order pharmacies has contributed significantly to the profitability of the 3 largest publicly owned PBMs. In presentations to Wall Street analysts, PBMs have highlighted their ability to drive generic drug products through these facilities as a growing contributor to the firms' overall profit margin.\(^4\) Furthermore, because of generic pricing structures negotiated between the PBM and the plan sponsor, PBMs typically realize significantly higher margins on generic drug products dispensed through their mail-order channels than through reimbursement of community pharmacies within the PBM's provider network for similar generic products.\(^5\) A recent study by the Federal Trade Commission acknowledged this additional revenue stream to PBMs as the result of favorable contracting with plan sponsors.\(^6\) The favorable contract terms typically involve maximum allowable cost (MAC) pricing for community pharmacies but not for the mail-order pharmacy owned by the PBM.\(^6\)

Plan sponsors have in some cases implemented the mandatory use of mail-order pharmacy despite the absence of evidence that the mail-order option costs less than the community pharmacy. Carroll, in a recent commentary, highlighted the need for actual claims-based studies that measure the economic impact of mail-order pharmacy services.\(^7\) One of the few published studies found instances where costs borne by the plan were higher for the same market basket of drugs dispensed through mail-order than for the community pharmacy. While the study noted that the analysis was conducted within a small plan (approximately 100,000 enrollees) with fewer than 45,000 mail claims analyzed, the authors suggested that this example might indicate payment patterns found in other plans.\(^8\)

## Purpose and Objectives

We conducted this study because of the lack of published research that investigates use trends and payment patterns for prescription drugs between mail-order and community pharmacy channels of distribution within a pharmacy benefit program. The objectives were to determine differences between mail-order and community pharmacy in (1) the cost per day of drug therapy for the plan sponsor and for the member for the highest expenditure therapeutic classes, (2) generic dispensing ratios for all drugs and for a comparative market basket of drugs, and (3) cost per unit for the top 20 generic drugs dispensed through the mail-order channel.

## Methods

### Data Source and Plan Characteristics

Paid pharmacy claims from 2 state-financed pharmacy benefit programs in Texas (identified as Plan A and Plan B) from state fiscal year 2004 were analyzed to investigate differences in drug use and expenditure patterns between mail-order and community pharmacy channels of drug distribution. These 2 pharmacy benefit plans included high proportions of enrollees who used chronic drug therapies. These chronic (maintenance) therapies are often the types of medications that patients may request through the

---

**FIGURE 1** Data Fields Included in the Prescription Claims File

Data fields included in the prescription claims file:
- Date prescription dispensed (date of service)
- National drug code (ndc) number of product dispensed
- Metric quantity of drug dispensed
- Days supply of drug dispensed
- Mail order or community pharmacy indicator (where product was dispensed)
- Type of product (brand, multi-source, or generic)
- Ingredient cost of product paid by plan (prior to any rebates)
- Dispensing fee paid by plan
- Member deductible paid (if any)
- Member copayment paid

---

**Comparison of Mail-Order With Community Pharmacy in Plan Sponsor Cost and Member Cost in Two Large Pharmacy Benefit Plans**

- Paid pharmacy claims from 2 state-financed pharmacy benefit programs in Texas (identified as Plan A and Plan B) from state fiscal year 2004 were analyzed to investigate differences in drug use and expenditure patterns between mail-order and community pharmacy channels of drug distribution. These 2 pharmacy benefit plans included high proportions of enrollees who used chronic drug therapies. These chronic (maintenance) therapies are often the types of medications that patients may request through the
TABLE 1 Description of Pharmacy Benefits for Plan A and Plan B

<table>
<thead>
<tr>
<th>Copayment Description</th>
<th>Plan A 460,000 Members*</th>
<th>Plan B 177,000 Members*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier 1 community (acute)</td>
<td>10</td>
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</tr>
<tr>
<td>Tier 2 community (acute)</td>
<td>25</td>
<td>25</td>
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<tr>
<td>Tier 3 community (acute)</td>
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<td>40</td>
</tr>
<tr>
<td>Tier 1 community (maintenance)</td>
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<td>N/A†</td>
</tr>
<tr>
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<td>35</td>
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</tr>
<tr>
<td>Tier 3 community (maintenance)</td>
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<td>N/A</td>
</tr>
<tr>
<td>Tier 1 mail order</td>
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<td>20</td>
</tr>
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<td>Tier 2 mail order</td>
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<td>50</td>
</tr>
<tr>
<td>Tier 3 mail order</td>
<td>120</td>
<td>80</td>
</tr>
</tbody>
</table>

* Average membership and copayments in effect during the period for pharmacy claims with dates of service from September 1, 2003, through August 31, 2004. Community pharmacy prescriptions were limited to a maximum 30-day supply and mail-order prescriptions limited to a maximum 90-day supply.
† Plan B had no differentiation in acute versus maintenance drugs obtained from community pharmacies.
N/A = not applicable.

PBM's mail-order channel due to the long-term nature of their use. The high use of mail-order services within these 2 pharmacy benefit plans permitted adequate comparisons over a large number of drug classes.

Paid pharmacy claim records representing 12 months of use history for each plan were supplied to the researchers through a public information request; these files consisted of 5.1 million claims for Plan A and 3.6 million claims for Plan B (September 1, 2003, through August 31, 2004, for both). No personally identifiable medical information was collected as part of these analyses (Figure 1), and Institutional Review Board exemption for this research was obtained.

Plan A had approximately 460,000 members during fiscal year 2004. Plan A had a 3-tier copayment design with different copayment amounts for acute versus maintenance medications in community pharmacy (Table 1). The pharmacy benefit in Plan B had approximately 177,000 members consisting of retirees and their dependents, and also had a 3-tier copayment design but without differentiation of acute versus maintenance medications in community pharmacy. These copayment designs resulted in a 2-to-1 ratio of copayments for mail-order (90-day supply) versus for community pharmacy (30-day supply) for all drugs in Plan B. For Plan A, the copayment ratios for maintenance drugs were 2-to-1 for tier 1 (generic) drugs, 2.14-to-1 for tier 2 (formulary) drugs, and 2.18-to-1 for tier 3 (nonformulary) drugs (Table 1).

Average Payment Per Day Within Therapeutic Categories

The 2 delivery channels were compared with respect to the average payment (cost) per day of drug therapy (product cost plus dispensing fee, divided by days supply) by both plans for the 30 highest expenditure therapeutic categories dispensed within the mail-order channel. We assigned drugs to therapeutic categories based on a classification system used by the Texas Medicaid Vendor Drug Program. This list consisted of 81 therapeutic categories that grouped drugs based on their interchangeability and common uses as determined by clinicians. The payment per day for the top therapeutic categories of prescriptions dispensed within mail-order pharmacy was calculated and compared with the calculated payment per day for community pharmacy prescriptions within the same therapeutic class. To make fair comparisons, 3 levels of controls were used.

One, only the top 30 therapeutic categories (by expenditure) for prescriptions dispensed within the mail-order channel were selected for comparison, for practical purposes. These 30 categories accounted for more than 80% of all mail-order pharmacy payments during the fiscal year in both plans. Two, an adjustment was made to control for differences in daily doses dispensed across each product within each therapeutic category and between mail-order and community pharmacy. This allowed for an “apples-to-apples” comparison between mail-order and community pharmacy channels within the same therapeutic category. For example, with this adjustment, higher daily dosages of a product in one channel (potentially resulting in higher costs) compared with the other channel would not bias the comparison.

Three, the difference in the calculated payment per day between mail-order and community pharmacy channels was weighted by the total mail-order days supply for each product within the therapeutic category. We performed this weighting to allow for a calculation of the differences in payments (by both the plan sponsor and its members) based on the mail-order market share within therapeutic categories. In essence, we calculated the actual payments made by the plan sponsor and members through the mail-order channel, and compared those payments with what the cost per day would have been had those same prescriptions been filled within the network of community pharmacy. Details regarding this procedure can be found in Figure 2. These payment calculations do not include the effects of price concessions that might be negotiated between the PBM and drug manufacturers and paid to the PBM in the form of either mail-order purchase price discounts or in rebates for mail-order or community pharmacy dispensing. However, these data are not publicly available, and it is not known to what degree rebates that translate into mail-order discounts are shared by the PBM with the plan sponsor. It is possible that some of these discounts are reflected in the actual pharmacy claims used in the current analysis. Rebates that
might be shared are not expected to affect the comparison of mail-order with community pharmacy as measured by price per unit or price per day.

**Generic Dispensing Ratios**

Dispensed drug products were categorized by the plan as (1) single-source (patented) brand, (2) multisource (off-patent) brand, or (3) generic. These categories were used to calculate generic dispensing ratios. When comparing generic dispensing ratios between mail-order and community pharmacy networks, we needed to also control for differences in product mix between the 2 delivery channels. This control allowed for a more appropriate comparison, since many acute care drugs dispensed at community pharmacies are not dispensed through the mail-order pharmacy.

To control for product mix differences in the comparisons, we created a “market basket” of products by assigning drugs to one of the therapeutic categories based on the Texas Medicaid Vendor Drug Program classification system described above. Instead of limiting our comparison to the top 30 categories, we included as many therapeutic categories as possible for this analysis. Our essential criterion for inclusion of a therapeutic category was an adequate representation of claims within both mail-order and community pharmacy channels for that category. To limit the effect of products dispensed infrequently, a minimum of 100 mail-order claims within a therapeutic class was required for the class to be included in the comparison. Using this criterion, a total of 58 therapeutic categories in Plan A and 55 categories in Plan B were selected for the generic dispensing ratio analysis. Comparisons were made based on the percentage of generic claims, as well as the percentage of total days supply accounted for by generics to control for differences between the 2 channels in the quantity dispensed per prescription.

**Average Payment Per Unit for Generic Drugs**

On the basis of a report in the press regarding wide variances in unit (tablet, capsule, etc.) pricing for the same generic product dispensed by mail-order versus community pharmacy channels, we were interested to determine if similar patterns would be found in a sample of the top generic products dispensed in both of the plans we studied. Therefore, we conducted a comparison of generic product payments by first aggregating by the generic code number (First DataBank) total payments (product costs plus dispensing fees) to mail-order or community pharmacy for generic products with the same active ingredient(s) and strength. For comparison, community pharmacy claims dispensed as a 30-day supply and mail-order claims dispensed as a 90-day supply for each active ingredient and strength (e.g., fluoxetine 20 mg) were included. Total payments in each channel (mail-order or community) were divided by the total units (tablets or capsules) dispensed by each channel to calculate an average unit payment amount (plan sponsor payment plus member payment) per specific generic product. Additionally, calculations compared the portion of the claim paid by the plan sponsor with the portion paid by the member. Our sample comprised the top 20 mail-order generic drugs separately, based on total mail-order payments during fiscal year 2004 for each plan. The generic product claims included in the samples represented 23.7% of all generic product payments (both channels) for Plan A, and 22.9% of all generic product payments for Plan B.

**Statistical Analyses**

Chi-square analyses were used to compare the proportions of prescriptions dispensed between mail-order and community pharmacy channels. An alpha level of $P \leq 0.001$ was used for statistical significance. Descriptive statistics were reported for other analyses. All analyses were conducted with SPSS software, version 12.0.

**Results**

Table 2 provides a summary of prescription claims analyzed for this study. Comparisons are shown for total pharmacy claims (prescriptions dispensed), total therapy days (days supply), and total payments (product costs plus dispensing fees) for Plan A, and 55 categories in Plan B were selected for the generic dispensing ratio analysis. Comparisons were made based on the percentage of generic claims, as well as the percentage of total days supply accounted for by generics to control for differences between the 2 channels in the quantity dispensed per prescription.

**FIGURE 2 Calculation of Payment per Therapy Day**

\[ Y = B_0 + B_1 x_1 + B_2 x_2 \]

Where,  
- $Y =$ Prescription Claim Payment / Days Supply  
- $B_0 =$ Constant  
- $B_1 =$ Coefficient of Mail-Order Claim  
- $x_1 =$ Mail-Order Claim ($0 =$ no, $1 =$ yes)  
- $B_2 =$ Coefficient of Drug Product Dose  
- $x_2 =$ Drug Product Dose

Regressions were run for each drug in each therapeutic class to derive a mail-order coefficient for each drug. The coefficient represents the dose-adjusted difference in daily payments between mail and community claims for each drug.

To arrive at the weighted payment difference per day the following calculation was conducted within each therapeutic class (with 3 drugs in the class, for example):

\[
\text{Daily difference in drug payment per day for the therapeutic class } = \left( \left( B_1 x_1 \right) \left( \% \text{ of days in therapeutic class accounted for by Drug "a"} \right) + \left( B_1 x_2 \right) \left( \% \text{ of days in therapeutic class accounted for by Drug "b"} \right) + \left( B_1 x_3 \right) \left( \% \text{ of days in therapeutic class accounted for by Drug "c"} \right) \right)
\]

Where,  
- $B_1 x_1 =$ Mail-Order Daily Payment Difference of Drug "a" in class  
- $B_1 x_2 =$ Mail-Order Daily Payment Difference of Drug "b" in class  
- $B_1 x_3 =$ Mail-Order Daily Payment Difference of Drug "c" in class

To achieve this adjustment, a linear regression model was constructed for each product across all therapeutic categories using the calculated payment per day as the dependent variable and daily dose and mail/community indicator as predictor variables. The coefficient calculated for the mail/community indicator provided the difference in daily payment between mail-order and community pharmacy, adjusted for differences in daily doses. A total of 221 regression models were created to produce the coefficients for each product within each of the 30 therapeutic categories found in Plan A. Finally, these coefficients were weighted for each product within each therapeutic category based on the proportion of therapy days accounted for by the product within the mail-order channel.
Comparison of Mail-Order With Community Pharmacy in Plan Sponsor Cost and Member Cost in Two Large Pharmacy Benefit Plans

TABLE 2  Pharmacy Claims Summary: Plan A and Plan B, State Fiscal Year 2004 *

<table>
<thead>
<tr>
<th></th>
<th>Mail Order</th>
<th>Community</th>
<th>Mail Order</th>
<th>Community</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Claims</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Claims</td>
<td>811,884</td>
<td>4,301,173</td>
<td>586,646</td>
<td>1,976,643</td>
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<tr>
<td>15.9%</td>
<td>84.1%</td>
<td>22.3%</td>
<td>77.7%</td>
<td></td>
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<tr>
<td>Total therapy days</td>
<td>68,136,030</td>
<td>102,861,824</td>
<td>50,112,257</td>
<td>57,766,493</td>
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<tr>
<td>39.8%</td>
<td>60.2%</td>
<td>46.5%</td>
<td>53.5%</td>
<td></td>
</tr>
<tr>
<td>Average days supply per claim</td>
<td>83.9 days</td>
<td>23.9 days</td>
<td>85.4 days</td>
<td>29.2 days</td>
</tr>
<tr>
<td>Total $†</td>
<td>121,524,182</td>
<td>231,636,694</td>
<td>97,970,184</td>
<td>127,608,425</td>
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<tr>
<td>34.4%</td>
<td>65.6%</td>
<td>43.4%</td>
<td>56.6%</td>
<td></td>
</tr>
<tr>
<td>Average member cost share</td>
<td>36.4%</td>
<td>41.5%</td>
<td>37.2%</td>
<td>44.7%</td>
</tr>
<tr>
<td><strong>Market-Basket Claims †</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total claims</td>
<td>1,155,884</td>
<td>2,478,165</td>
<td>839,962</td>
<td>1,270,536</td>
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<tr>
<td>31.8%</td>
<td>68.2%</td>
<td>39.8%</td>
<td>60.2%</td>
<td></td>
</tr>
<tr>
<td>Total therapy days</td>
<td>99,157,418</td>
<td>62,043,576</td>
<td>73,693,042</td>
<td>37,630,139</td>
</tr>
<tr>
<td>61.5%</td>
<td>38.5%</td>
<td>66.2%</td>
<td>33.8%</td>
<td></td>
</tr>
<tr>
<td>Average days supply per claim</td>
<td>85.8 days</td>
<td>25.0 days</td>
<td>87.7 days</td>
<td>29.6 days</td>
</tr>
<tr>
<td>Total $†</td>
<td>171,782,096</td>
<td>134,730,648</td>
<td>141,778,540</td>
<td>82,997,889</td>
</tr>
<tr>
<td>56.0%</td>
<td>44.0%</td>
<td>63.1%</td>
<td>36.9%</td>
<td></td>
</tr>
<tr>
<td>Average member cost share</td>
<td>26.3%</td>
<td>35.9%</td>
<td>26.2%</td>
<td>36.8%</td>
</tr>
</tbody>
</table>

* September 1, 2003, through August 31, 2004
† Comprising claims for the top 30 highest expenditure therapeutic categories by total payments in the mail-order channel, as defined by the Texas Medicaid Vendor Drug Program Preferred Drug List Categorization system. Products were assigned and aggregated to each therapeutic category based on a link between the category and the product’s generic code number. These claims formed the sample of claims used in the therapeutic category analysis presented in Tables 3 and 4. After aggregating all mail-order claims to a category, a total of 58 categories were identified for Plan A and 55 categories for Plan B. Generic dispensing ratios were calculated based on this larger sample of therapeutic categories in Tables 5 and 6.
‡ Total dollars includes plan cost and member cost.

those prescriptions. Mail order accounted for approximately $121.5 million of total pharmacy benefit spending of $353 million (34.4%) in Plan A and $171.8 million of $306.5 million (56.0%) in Plan B in the 12-month period ending August 31, 2004. The average days supply per pharmacy claim was 23.9 days at community pharmacy for Plan A and 25.0 days for Plan B. The average days supply per pharmacy claim was 83.9 days at mail order for Plan A and 85.8 days for Plan B.

The cost per day analyses include a comparative market basket of drugs representing the 30 highest expenditure therapeutic categories (based on total mail-order payments). The market basket of drugs accounted for 81% of total mail-order payments in Plan A and 83% of total payments in Plan B.

Plan Cost and Member Cost Share

Average member cost share differed between the 2 pharmacy benefit plans. Overall, members paid an average of 36.4% of total mail-order pharmacy costs and 41.5% of total community pharmacy costs in Plan A, and 26.3% of mail-order costs and 35.9% of community pharmacy costs in Plan B (Table 2). By type of drug and channel of distribution, average member cost share was greater for community pharmacy compared with mail-order pharmacy for brand drugs (39% vs. 35%), for off-patent brand drugs (59% vs. 55%), and for generic drugs (51% vs. 45%) in Plan A (Figure 3). By drug and channel of distribution for Plan B, average member cost share was also greater for community pharmacy compared with mail-order pharmacy for brand drugs (33% vs. 25%), for off-patent brand drugs (57% vs. 30%), and for generic drugs (48% vs. 37%) (Figure 4).

The average total payment (allowed charge) per pharmacy claim was 11.5% lower for community pharmacy generic drugs in Plan B ($18.60, Figure 4) than in Plan A ($21.01, Figure 3). The average total payment per pharmacy claim was 14.6% lower for mail-order generic drugs in Plan B ($54.52, Figure 4) than in Plan A ($58.45, Figure 3). The price differences per pharmacy claim between the two pharmacy benefit plans for brand drugs by channel of distribution were 3% or less, except for off-patent brand drugs.

Average Cost Per Day Within Therapeutic Categories

Tables 3 and 4 show the weighted differences in payment per
day of therapy within the top 30 therapeutic drug categories for the plan sponsor and the member (through copayments) for Plan A and Plan B, respectively. Both plan sponsors had a higher payment per day for prescriptions dispensed through mail order for a majority of the therapeutic categories.

For example, Plan A paid an additional $0.05 per day per lipotropic (statin) drug when dispensed through the mail-order option ($1.94 per day) compared with the community pharmacy option ($1.89 per day) (Table 3). Since more than 5.3 million therapy days of statins were dispensed through the mail-order option, higher payments of more than $265,000 ($0.05/day x 5.3 million days) were paid by the Plan A sponsor for this particular category compared with the community pharmacy channel. As noted earlier, copayment structures lowered the daily costs for enrollees using the mail option, as shown in the lower calculated member payment per day for all therapeutic categories in both plans.

The difference in total cost per day for all categories is provided at the bottom of Tables 3 and 4. These costs were weighted by the total therapy days for each therapeutic category. In both tables, the majority of the calculated lower payments per day between mail-order and community pharmacy claims were realized by the members through lower copayments. In fact, the Plan A sponsor realized a slightly higher payment per day for all claims dispensed through the mail-order channel ($1.24) for these categories compared with community pharmacy claims ($1.23). The Plan B sponsor realized slightly lower payments through the mail-order channel ($1.43) than through the community pharmacy channel ($1.44) (Table 4). While payments per day for the combined components (plan sponsor plus member) were lower for mail-order than for community pharmacy in both plans, nearly all the savings due to pricing differences between the two channels were realized by the member and not the plan sponsor.

### Generic Dispensing Ratios

Tables 5 and 6 show differences in generic dispensing ratios based on prescription claims between mail-order and community pharmacy channels for all products (unadjusted for product mix) and a market basket of similar drug categories (controlling for product mix). In both plans, the generic dispensing ratio for drugs in the market basket was significantly higher (chi-square, P < 0.001) within the community channel than in the mail-order channel (38.1% vs. 28.0% for Plan A, and 32.7% vs. 24.1% for Plan B). The same relationship was found for all prescription claims. The overall generic dispensing ratio for mail-order and community pharmacy combined was higher in Plan A (47.2%) than in Plan B (41.7%).

### Average Payment Per Unit for Generic Drugs

Table 7 presents differences in the payments made per unit for the 20 highest expenditure generic products dispensed through
the mail-order channel for Plan A compared with the payments for the same products dispensed at community pharmacies within Plan A's provider network. For example, preferential unit pricing for the top generic product dispensed via mail order (omeprazole 20 mg) resulted in a lower total unit payment (on average) per prescription if filled by mail-order ($1.66) compared with community pharmacy ($3.02). This preferential pricing resulted in a savings of 45% in the payment per unit for the omeprazole prescriptions dispensed via mail order.

However, for the second-highest generic product ranked by total payments (fluoxetine 20 mg), the unit payment was higher in the mail-order channel ($1.07) than in community pharmacies ($0.53), resulting in a higher payment per unit of more than 100%. For 9 (45%) of the top 20 generic products dispensed through the mail, total payments per unit were higher via mail-order than in the community pharmacy channel.

Furthermore, the total plan sponsor cost per unit (total payment minus member payment) was lower for mail-order than...
Comparison of Mail-Order With Community Pharmacy in Plan Sponsor Cost and Member Cost in Two Large Pharmacy Benefit Plans

Table 8 shows a similar comparison for the top generic mail-order products within Plan B during fiscal year 2004. Of the top 20 generic drugs dispensed through the mail-order channel, unit cost payments were higher via mail order for half (10) of the generic products, compared with community pharmacy. As an example, the top generic product ranked by total payments within the Plan B mail-order channel (fluoxetine 20 mg) had a higher unit cost ($1.07) than did the same prescription filled at a community pharmacy ($0.53 per unit).

Table 4 shows a similar comparison for the top generic mail-order products within Plan B during fiscal year 2004. Of the top 20 generic drugs dispensed through the mail-order channel, unit cost payments were higher via mail order for half (10) of the generic products, compared with community pharmacy. As an example, the top generic product ranked by total payments within the Plan B mail-order channel (fluoxetine 20 mg) had a higher unit cost ($1.07) than did the same prescription filled at a community pharmacy ($0.53 per unit).

Similar to Plan A, the Plan B sponsor's payment per unit for

for community pharmacy in only 6 (30%) of the 20 top generic products dispensed. However, when aggregating total payments for the top 20 generic products, we found plan sponsor total costs for all sample drugs dispensed through the mail-order channel were 16.5% lower than community pharmacy unit pricing. Combining member payments per unit, the total pharmacy benefit payments (plan sponsor plus member) were 21.3% lower.

Table 8 shows a similar comparison for the top generic mail-
Comparison of Mail-Order With Community Pharmacy in Plan Sponsor Cost and Member Cost in Two Large Pharmacy Benefit Plans

The top 20 generic products was lower through mail-order than through community pharmacy for only 6 out of 20 instances. However, the aggregated results were somewhat different from those found in Plan A. In Plan B, generic product unit pricing resulted in an overall 18.0% higher average plan sponsor cost per unit through mail-order than through community pharmacy. The combined payments (plan sponsor plus member) per unit were 3.3% lower for the 20 highest expenditure generic drugs dispensed through the mail-order channel. In Plan B, the member received some benefit from the mail-order pricing, but the plan sponsor incurred higher average cost per unit for generic drugs than in the community pharmacy channel.

Discussion

The purpose of this study was to examine trends in the use of and payments for drug products between mail-order and community pharmacy channels in 2 publicly funded pharmacy benefit programs in Texas. It was important to conduct such analyses because of the lack of published studies investigating the impact of PBM-owned mail-order plans on drug use and ultimately, on drug expenditures. Furthermore, in light of the aggressive marketing of a mail-order pharmacy option to plan sponsors by PBMs, analyses of this sort are helpful in determining the extent to which mail-order pharmacy delivers on its promise to realize cost-effective provision of prescription drugs to both the plan and its enrollees. A summary of the study findings and their implications follow below.

Average Daily Payment Within Therapeutic Categories

Similar to recently published research, both plan sponsors were found to make higher payments per day of drug therapy for prescriptions dispensed via mail order for many therapeutic categories. This could have been the result of copayment structures that created incentives for using mail order, while shifting a higher proportion of the drug costs to the plan. In cases in which the payment per therapy day is higher for mail order, increased use of this channel will result in higher costs of therapy for the plan sponsor as fewer prescriptions are filled at community pharmacies. This cost difference also results from differences in product mix in therapeutic categories for drugs dispensed via mail-order rather than through community pharmacies. Because a larger proportion of generic drugs may be dispensed within a therapeutic category in the community setting, overall therapy costs for both the plan sponsor and the member will be lower due to lower costs per day for generic rather than branded drugs.

Overall, total payments per day were lower across therapeutic classes in the mail-order channel; however, pharmacy plan members enjoyed nearly all the benefit of this discount in pricing, with little or no benefit for the plan sponsors. The overall result from the plans’ perspective for the therapeutic categories that we studied was either slightly higher (0.5%) payments for Plan A or smaller savings (0.4%) for Plan B.

The lack of relative savings for these 2 plan sponsors is similar to the findings reported by Carroll et al. in a study that evaluated payments for drugs dispensed by mail-order versus community pharmacy. In that study, plan sponsor costs for a sample of products was 6.5% higher in mail-order than in community pharmacy. As in our study, Carroll et al. also found that members paid lower costs for mail-order compared with

<table>
<thead>
<tr>
<th>All Claims (%)</th>
<th>Market Basket (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mail Order</td>
<td>Community</td>
</tr>
<tr>
<td>Total Claims</td>
<td></td>
</tr>
<tr>
<td>Patented brand</td>
<td>58.8</td>
</tr>
<tr>
<td>Off-patent brand</td>
<td>3.5</td>
</tr>
<tr>
<td>Generic</td>
<td>37.7</td>
</tr>
<tr>
<td>Total Therapy Days</td>
<td></td>
</tr>
<tr>
<td>Patented brand</td>
<td>58.8</td>
</tr>
<tr>
<td>Off-patent brand</td>
<td>3.4</td>
</tr>
<tr>
<td>Generic</td>
<td>37.8</td>
</tr>
</tbody>
</table>


* Comprising 58 therapeutic categories defined by the Texas Medicaid Preferred Drug List.
† Generic percentage significantly higher for community than mail-order claims (chi-square, P <0.001).
### TABLE 7
Generic Product Cost Comparison: Plan “A” Mail-Order Versus Community Pharmacy

<table>
<thead>
<tr>
<th>Rank</th>
<th>Generic Product</th>
<th>Total Mail Units</th>
<th>Mail-Order Payment per Unit ($)</th>
<th>Community Pharmacy Payment per Unit ($)</th>
<th>% Difference for Mail-Order Compared With Community Pharmacy*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Plan Sponsor</td>
<td>Member</td>
<td>Total</td>
</tr>
<tr>
<td>1</td>
<td>Omeprazole 20-mg capsule</td>
<td>1,189,260</td>
<td>1.32</td>
<td>0.34</td>
<td>1.66</td>
</tr>
<tr>
<td>2</td>
<td>Fluoxetine 20-mg capsule</td>
<td>664,759</td>
<td>0.79</td>
<td>0.28</td>
<td>1.07</td>
</tr>
<tr>
<td>3</td>
<td>Metformin HCl 500-mg tablet</td>
<td>1,378,481</td>
<td>0.15</td>
<td>0.13</td>
<td>0.28</td>
</tr>
<tr>
<td>4</td>
<td>Metformin HCl 1,000-mg tablet</td>
<td>602,221</td>
<td>0.40</td>
<td>0.18</td>
<td>0.58</td>
</tr>
<tr>
<td>5</td>
<td>Gemfibrozil 600-mg tablet</td>
<td>613,980</td>
<td>0.31</td>
<td>0.19</td>
<td>0.50</td>
</tr>
<tr>
<td>6</td>
<td>Lovastatin 40-mg tablet</td>
<td>173,835</td>
<td>1.38</td>
<td>0.32</td>
<td>1.70</td>
</tr>
<tr>
<td>7</td>
<td>Lisinopril 20-mg tablet</td>
<td>679,905</td>
<td>0.14</td>
<td>0.29</td>
<td>0.43</td>
</tr>
<tr>
<td>8</td>
<td>Paroxetine HCl 20-mg tablet</td>
<td>256,861</td>
<td>0.72</td>
<td>0.35</td>
<td>1.07</td>
</tr>
<tr>
<td>9</td>
<td>Fluoxetine 40-mg capsule</td>
<td>124,965</td>
<td>1.80</td>
<td>0.34</td>
<td>2.14</td>
</tr>
<tr>
<td>10</td>
<td>Verapamil 240-mg capsule</td>
<td>369,675</td>
<td>0.36</td>
<td>0.30</td>
<td>0.66</td>
</tr>
<tr>
<td>11</td>
<td>Ranitidine 150-mg tablet</td>
<td>303,024</td>
<td>0.41</td>
<td>0.21</td>
<td>0.62</td>
</tr>
<tr>
<td>12</td>
<td>Tramadol HCl 50-mg tablet</td>
<td>390,020</td>
<td>0.24</td>
<td>0.09</td>
<td>0.33</td>
</tr>
<tr>
<td>13</td>
<td>Metformin HCl ER 500-mg tablet</td>
<td>625,486</td>
<td>0.17</td>
<td>0.12</td>
<td>0.29</td>
</tr>
<tr>
<td>14</td>
<td>Lisinopril 10-mg tablet</td>
<td>464,265</td>
<td>0.09</td>
<td>0.32</td>
<td>0.41</td>
</tr>
<tr>
<td>15</td>
<td>Tamoxifen 20-mg tablet</td>
<td>122,490</td>
<td>1.12</td>
<td>0.39</td>
<td>1.51</td>
</tr>
<tr>
<td>16</td>
<td>Lisinopril 40-mg tablet</td>
<td>281,835</td>
<td>0.31</td>
<td>0.32</td>
<td>0.63</td>
</tr>
<tr>
<td>17</td>
<td>Amiodarone 200-mg tablet</td>
<td>121,254</td>
<td>1.04</td>
<td>0.32</td>
<td>1.36</td>
</tr>
<tr>
<td>18</td>
<td>Lisinopril-HCTZ 20/12.5-mg tablet</td>
<td>296,055</td>
<td>0.19</td>
<td>0.29</td>
<td>0.48</td>
</tr>
<tr>
<td>19</td>
<td>Buspirone HCl 15-mg tablet</td>
<td>165,594</td>
<td>0.64</td>
<td>0.17</td>
<td>0.81</td>
</tr>
<tr>
<td>20</td>
<td>Diltiazem 240-mg capsule</td>
<td>162,900</td>
<td>0.48</td>
<td>0.34</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>Total payments</td>
<td>4,565,678</td>
<td>2,163,585</td>
<td>6,729,161</td>
<td>5,466,474</td>
</tr>
</tbody>
</table>

* A negative percentage reflects a lower payment for the mail-order channel versus the community pharmacy channel. All costs rounded to the nearest cent.

ER=extended release; HCl=hydrochloride; HCTZ=hydrochlorothiazide.
Comparison of Mail-Order With Community Pharmacy in Plan Sponsor Cost and Member Cost in Two Large Pharmacy Benefit Plans

### TABLE 8

<table>
<thead>
<tr>
<th>Rank</th>
<th>Generic Product</th>
<th>Total Mail Units</th>
<th>Mail-Order Payment per Unit ($)</th>
<th>Community Pharmacy Payment per Unit ($)</th>
<th>% Difference for Mail-Order Compared With Community Pharmacy*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Plan Sponsor</td>
<td>Member</td>
<td>Total</td>
</tr>
<tr>
<td>1</td>
<td>Fluoxetine HCl 20-mg capsule</td>
<td>475,709</td>
<td>0.89</td>
<td>0.18</td>
<td>1.07</td>
</tr>
<tr>
<td>2</td>
<td>Metformin HCl 500-mg tablet</td>
<td>1,440,806</td>
<td>0.20</td>
<td>0.09</td>
<td>0.29</td>
</tr>
<tr>
<td>3</td>
<td>Atenolol 50-mg tablet</td>
<td>1,006,288</td>
<td>0.15</td>
<td>0.19</td>
<td>0.34</td>
</tr>
<tr>
<td>4</td>
<td>Lisinopril 20-mg tablet</td>
<td>756,528</td>
<td>0.24</td>
<td>0.19</td>
<td>0.43</td>
</tr>
<tr>
<td>5</td>
<td>Gemfibrozil 600-mg tablet</td>
<td>646,741</td>
<td>0.38</td>
<td>0.12</td>
<td>0.50</td>
</tr>
<tr>
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<td>Metformin HCl 1,000-mg tablet</td>
<td>545,175</td>
<td>0.47</td>
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<td>0.58</td>
</tr>
<tr>
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<td>Amodarone 200-mg tablet</td>
<td>224,698</td>
<td>1.14</td>
<td>0.21</td>
<td>1.35</td>
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<tr>
<td>8</td>
<td>Verapamil 240-mg tablet</td>
<td>464,760</td>
<td>0.46</td>
<td>0.19</td>
<td>0.65</td>
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</table>

* A negative percentage reflects a lower payment for the mail-order channel versus the community pharmacy channel.
All costs rounded to the nearest cent.
ER = extended release; HCl = hydrochloride; HCTZ = hydrochlorothiazide; N/A = not applicable.
community pharmacy. The member savings were estimated to be 48% for mail-order claims, resulting in overall savings of 7.8% for the combined plan sponsor and member payments.\textsuperscript{9}

**Generic Dispensing Ratios**

As expected, even when controlling for differences in drug product mix, we calculated that generic dispensing ratios for both pharmacy plans were higher for claims processed through the community pharmacy channel than through the PBM-owned mail-order channel. A recently published study noted that in a comparison of generic dispensing ratios between mail-order and community pharmacy channels, the analysis should involve a calculation of ratios across comparable therapeutic classes.\textsuperscript{9} In the current study, product mix differences were controlled by comparing only therapeutic classes most common in mail-order dispensing.

Higher generic dispensing ratios help to slow the growth in prescription drug spending due to the more widespread use of lower-priced therapeutic alternatives, slowing the growth in prescription drug spending. The cause of the difference in generic dispensing ratios between community pharmacy and mail order is not entirely clear; however, previously published studies have also reported higher generic dispensing ratios in community pharmacy than in mail order.\textsuperscript{9-11}

**Average Payment per Unit for Generic Drugs**

Higher cost per unit for the same generic drug product dispensed in mail-order than in community pharmacies should be of concern to plan administrators. Intuitively, program administrators should expect the cost per unit for generic drugs dispensed through mail-order pharmacy to be no greater than that made to community pharmacies for the same product. However, evidence of higher payments was found for some of the most commonly dispensed mail-order generic products. For example, for at least half of the top 20 most commonly dispensed mail-order generic products within Plan B, a higher average unit payment was made in the mail-order channel versus the community pharmacy network.

It is likely that the higher payments are the result of a pricing arrangement between the PBM and a plan that does not ensure a lower or at least comparable price for generic products dispensed via mail order. The price that a plan sponsor pays a PBM when a generic product is dispensed through the mail-order channel is typically determined on the basis of a specified percentage discount of Average Wholesale Price (AWP), commonly in the range of 40% to 60%. While this may appear to provide a steep discount that is favorable to the plan, AWP is not a reliable indicator of actual acquisition cost.

PBMs and nearly all state Medicaid programs pay community pharmacies for many generic drugs based on the method of MAC, in which the MAC price for a particular drug is set somewhere between the lowest and the highest estimated acquisition price for products available from multiple generic drug manufacturers. For example, if the AWP for a particular generic drug from manufacturer X is $1.00 per unit and the pharmacy’s actual cost is $0.30 per unit, compared with a $1.30 AWP and a $0.40 actual cost per unit from manufacturer Y, the MAC price might be set at $0.35 per unit. This method serves to decrease incentives for pharmacies to dispense the generic drug from manufacturer Y with the 30% higher AWP. However, the MAC price of $0.35 will result in a plan sponsor payment that is significantly lower than payment based on a 50% discount arrangement that will yield a unit price of $0.50 from manufacturer X or $0.65 from manufacturer Y. If generic prices paid by the plan sponsor for community pharmacy claims are based on MAC pricing while those for mail-order claims are based on an AWP discount, the plan sponsor can end up paying more per unit for the same generic drug dispensed at mail-order than at community pharmacy.

**Implications for Plan Sponsors**

Plan administrators need to understand the nuances in drug pricing for both branded and generic drugs between mail-order and community pharmacy, as well as be aware of the impact that providing incentives for mail-order channel use may have on the plan sponsors’ resulting portion of total payments. We have provided evidence that lower total pricing provided by the mail-order channel may not result in net savings for the plan sponsor. Furthermore, plan sponsors should understand the need to align incentives, especially during negotiation of PBM service contract terms, to avoid creating unintended benefit to the PBM at the expense of higher drug costs for the plan sponsors.

The PBM business model may not be entirely understood by plan sponsors. In the face of heavy promotion of mail-order pharmacy plans by PBMs, especially mandatory mail-order plans, program administrators should be aware of the competing interests that may result when PBMs seek to maximize their profits. Transparency in pharmacy pricing and drug manufacturer rebates would help plan sponsors assess the relative value of the mail-order and community pharmacy channels. The need for transparency increases when the mail-order pharmacy is owned by the PBM.

**Limitations**

First, this study did not investigate potential waste that might result from dispensing larger quantities at mail-order than at community pharmacy for drugs that might not be used as a result of adverse reactions, lack of perceived efficacy, or dose or drug change, or for other reasons. Second, while the value of mail-order pharmacy compared with community pharmacy was small or negative for both plan sponsors in this study, these results may not be generalizable to all plans. We did not measure or report the age distribution of beneficiaries in these 2 drug plans, an important factor in the use of chronic medications. Copayment design will affect the ratio of member cost to plan...
cost, and the absolute amount of the mail-order copayments was at least twice the amount of community pharmacy copayments in these 2 pharmacy benefit plans.

Third, product-level drug rebates and their effects on plan sponsor cost, if any, could not be determined since rebate information was not publicly available. However, the influence of drug manufacturer rebates is not expected to change the relative price comparisons between mail-order and community pharmacy and for the measures used in this study, cost per unit and cost per day of therapy.

Conclusions

In addition to demonstrating that the mail-order distribution channel can have higher net sponsor costs in a pharmacy benefit plan, this paper has presented and described methodologies and calculations for comparing costs per day and cost per unit between mail-order and community pharmacy networks. More published studies of this sort are needed to determine the true value of the mail-order pharmacy distribution channel within pharmacy benefit programs. Studies that appropriately control for differences in product mix, as well as those that investigate the degree to which member financial incentives result in higher costs (either direct or opportunity costs) to the plan sponsor, will greatly benefit decision makers as strategies are proposed to obtain the best value for prescription drugs and pharmacy services.

What is already known about this subject

- Widespread perception of lower prices via mail-order versus community pharmacy has contributed to the growth of mail-order pharmacy use despite a lack of evidence of cost savings for pharmacy benefit sponsors.
- Pharmacy benefit designs that favor mail-order pharmacy result in lower average member cost share.
- Generic dispensing ratios are lower in mail-order than in community pharmacy.

What this study adds

- Using a methodology that estimated the average price per unit and per day of drug therapy for mail-order prescriptions had they been dispensed instead by community pharmacies, one plan sponsor experienced a small financial benefit from mail-order pharmacy while another plan sponsor experienced a slightly higher cost.
- Differences in pricing of generic drugs between mail-order and community pharmacy appear to contribute to higher unit costs for generic drugs via mail order.

REFERENCES

Member Satisfaction Related to Self-Reported Cost Share and Difficulty in Obtaining Prescription Drugs in a University Pharmacy Benefit Plan

David P. Nau, PhD, RPh, CPHQ; Christina Chi, PharmD Student; Usha Mallya, PhD; and Duane M. Kirkling, PhD

ABSTRACT

BACKGROUND: Utilization management tools (e.g., multitier copayment designs, prior authorization, step therapy, quantity limits) are commonly used to optimize the efficiency and appropriateness of drug therapy. However, these tools may also lead to unfavorable humanistic outcomes, including confusion or annoyance for patients. There is also some concern about whether these tools, along with the cost-sharing burden for medications, may cause patients to discontinue using their medications as well as lead to dissatisfaction with pharmacy benefits. Although anecdotal evidence can be collected from customer complaints, few studies have systematically examined the extent to which prescription drug plan enrollees experience difficulties in obtaining medications and whether these difficulties are associated with their satisfaction with the drug plan.

OBJECTIVES: To determine from a member satisfaction survey (1) perception of difficulties experienced by drug plan members when they tried to obtain prescription medications, (2) whether some segments of members experienced more difficulties, and (3) whether self-reported difficulties in acquiring medications were associated with member satisfaction.

METHODS: The analyses were based on a cross-sectional survey using a stratified sample of drug plan members. Four thousand employees or retirees who used the University of Michigan prescription drug plan were sent a survey in 2005 to ascertain their satisfaction with the drug plan as well as their experiences with the plan. Specifically, the analyses focused on how frequently the patients experienced difficulties in obtaining medications because of costs or drug use management interventions (e.g., prior authorization, step therapy). Logistic regression analyses examined the relationship of copayment changes and drug use management interventions on patients’ satisfaction with the drug plan.

RESULTS: Surveys were returned by 2,061 of the potential 3,667 eligible subjects with valid addresses (56.2% response rate). An overwhelming majority (83.7%) of respondents were satisfied with the pharmacy benefit—17.6% reported being somewhat satisfied, 46.5% were satisfied, and 19.6% were very satisfied. Approximately 25% of drug plan members reported at least 1 difficulty in obtaining medication during the preceding year, including 11.4% who reported difficulties related to prior authorization or step therapy; only 2.0% reported that they couldn’t afford their medication, and only 1.3% reported difficulty in paying the combined cost of their medications. Current employees were more likely to report difficulties than were retirees (30.7% vs. 19.1%; chi-square = 34.8; P < 0.01), and users of the mail-service pharmacy were somewhat more likely to experience difficulties than users of community pharmacies (29.1% vs. 22.9%; chi-square = 9.92; P < 0.01). The logistic regression analyses revealed that having difficulty obtaining medications (odds ratio [OR] = 0.27; 95% confidence interval [CI], 0.20-0.35) and experiencing a copayment increase (OR = 0.62; 95% CI, 0.48-0.81) were associated with a lower odds of member satisfaction. However, a high percentage of members were satisfied despite any difficulties or copayment changes: 66.9% for self-reported difficulty in obtaining medications compared with 89.7% (chi-square = 145.4, P < 0.01) and 78.6% for self-reported copayment increase compared with 87.9% (chi-square = 30.2, P < 0.01).

CONCLUSION: Survey respondents were highly satisfied with their pharmacy benefits despite drug use management interventions in this pharmacy benefit plan. Respondents who reported a copayment increase or difficulty in obtaining medication were less likely to be satisfied with the drug plan.

KEYWORDS: Member satisfaction, Drug benefit, Access

J Manag Care Pharm. 2007;13(2):135-41

As prescription drug expenditures have risen in recent years, so have the efforts of managed care organizations to control the use of prescription drugs. Many drug plans have increased their use of utilization management tools such as multitiered copayments, prior authorization, quantity limits, and step therapy. These tools can be effective at shaping the utilization pattern for medications; however, they may also create difficulties for patients in obtaining needed medications. Although studies have examined the impact of specific drug use policies on satisfaction, few reports exist of how a broad range of difficulties experienced by prescription drug plan members may affect satisfaction.

In one of the few reports on the relationship of drug plan attributes and patient satisfaction, Desselle (2000) conducted interviews with 30 patrons of community pharmacies and had them identify the most important attributes of their drug plans. The patrons selected the items related to coverage restrictions as being the most important determinants of their satisfaction. The items in a resulting interval-level scale for satisfaction were then weighted, with the highest weights assigned to the “coverage limitations” items. A related study by Desselle (2001) used this weighted scale and found that drug plan members who perceived their drug coverage as being limited were less likely to be satisfied with their drug plans. However, since Desselle’s multi-item satisfaction measure was most heavily weighted...
they tried to obtain prescription medications, (2) determine whether some determinants of health plan members’ satisfaction with prescription drug benefits were related to patients’ satisfaction. However, because the respondents came from a multitude of plans with differing structures and policies, it was not possible for the authors to fully sort out the various types of coverage restrictions and their potentially different effects on satisfaction.

Although the aforementioned studies indicate a potential relationship between policies for controlling drug use and enrollees’ satisfaction with a drug plan, we do not know the extent to which members within a typical drug plan experience difficulties in obtaining their medications. It is also not clear how various types of difficulties in obtaining medications relate to member satisfaction for a population in a single drug plan (thereby controlling for the potential confounding that stems from differing premiums and copayment structures). Thus, the objectives of this study were to (1) identify the difficulties experienced by drug plan members when they tried to obtain prescription medications, (2) determine whether some segments of members experienced more difficulties, and (3) determine whether difficulties in acquiring medications were associated with enrollee satisfaction.

### Methods

**Description of the Drug Plan**

The University of Michigan (UM) drug plan is a carve-out model in which all employees and retirees of the university, along with eligible dependents, are included in 1 drug plan regardless of their chosen health insurance plan. A mail-services pharmacy option is available to all members as well as an extensive network of community pharmacies. An open formulary is maintained with a 3-tier copayment design and preferred drug list (PDL). This benefit design is supplemented by drug use management interventions such as step therapy, prior authorization, quantity limits, and dose optimization (Table 1). All members have the 3-tier copayment design except for a small number of unionized employees who have a 2-tier copayment and a small number of retirees who have a coinsurance benefit design. The 3-tier copayment amounts were $7, $14, and $24 for tiers 1, 2, and 3, respectively.

Members could obtain a 90-day supply of medication from a community pharmacy (for 3 copays) or from a mail-service pharmacy (for 2 copays). Tier 1 in the formulary included all generic drugs. Tier 2 included brand-name drugs that were considered by the plan to be more cost effective than other drugs within each class (i.e., preferred brand drugs), and tier 3 included brand-name products that were not selected for tier 2 (i.e., nonpreferred drugs). The copayment amounts for each tier did not change from 2003 through 2005, but a small number of drugs changed copayment tiers as new drugs became available or as new evidence regarding the cost-effectiveness or safety of the products became available. For example, Neurontin was removed from the PDL to nonpreferred (tier-3 copayment) when a generic equivalent ( gabapentin) became available.

A pharmacy benefits manager provides claims processing and other benefit management services but with active involvement of a UM committee that determines the policies for drug use management and selects products for the PDL.

**Survey Sample**

The target population for the survey was the users of the UM prescription drug plan (approximately 28,500 persons per calendar quarter). A stratified sample of 4,000 subjects was selected from a list of UM employees and retirees who had more than 1 pharmacy claim for a prescription drug in 2004. A stratified sample was used to ensure adequate representation of key groups of drug plan users, and the sample size was chosen to maintain a sampling error of less than 3% with \( \alpha = 95\% \) for each stratum. The sample size for each stratum was (1) retirees using only community pharmacies (\( n = 1,000 \)), (2) retirees using the mail-service pharmacy (\( n = 500 \)), (3) current employees using only community pharmacies (\( n = 1,500 \)), and (4) current employees using the mail-service pharmacy (\( n = 1,000 \)). Employees on long-term disability were included in the last 2 categories, depending on their source of medication procurement. Mail-service phar-

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Product</th>
<th>Specifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity limit</td>
<td>Sildenafil</td>
<td>Quantity limited to 6 units per month</td>
</tr>
<tr>
<td>Dose optimization</td>
<td>Donepezil</td>
<td>Must use 10-mg dose for 10-mg dose (i.e., 2 x 5-mg tablets not allowed)</td>
</tr>
<tr>
<td>Step therapy</td>
<td>COX-2 inhibitors</td>
<td>Patients younger than 70 years must have tried at least 2 generic NSAIDs before COX-2 drug</td>
</tr>
<tr>
<td>Prior authorization</td>
<td>Methylphenidate</td>
<td>Prior authorization required if patient is aged 18 years and has not previously received drug therapy for attention-deficit/hyperactivity disorder</td>
</tr>
</tbody>
</table>

COX-2 = cyclooxygenase-2; NSAIDs = nonsteroidal anti-inflammatory drugs.
Macy users were oversampled to ensure that their perspective was considered adequately and to permit valid comparisons between the responses from users of the mail-service pharmacy compared with users of community pharmacies.

For sampling purposes, members were included in the mail-service category if they had received more than 1 medication from the mail-service provider. Within the survey, the subjects were asked about their pattern of pharmacy patronage. Those who indicated that they “mostly” or “always” used the mail-service provider were categorized as mail-service users for the analyses.

**Measures**

**Satisfaction**

Satisfaction was assessed on a 6-point Likert scale with options that ranged from “very dissatisfied” to “very satisfied” (Table 2). Because the resulting distribution was highly skewed toward greater satisfaction, a categorical variable was created wherein responses were coded as 1 for subjects who were “somewhat satisfied,” “satisfied,” or “very satisfied,” and all other responses were coded as 0.

In order to evaluate patients’ perception on their drug plan in comparison with other plans, the subjects were asked the following question: “How would you rate the quality of the UM prescription drug plan as compared to other prescription drug plans you have heard about (e.g., from other employers)?” The 5 response options ranged from “A lot better” to “A lot worse.”

**Difficulties in Obtaining Medications**

Subjects were asked if, during the past year, they had difficulty obtaining medications that their doctor prescribed for them. Those who responded affirmatively were asked to indicate the type of difficulty they encountered. A list of common problems was provided with instructions to check the box next to all those encountered. An option of “other” was also provided along with instructions to describe the other types of problems in acquiring medications. If patients checked “other” but described a problem that was clearly related to one of the predefined categories, the “other” response was combined with that category.

---

**TABLE 2**  Beneficiary Survey Instrument (Excerpted)

1. Overall, how satisfied are you with the University of Michigan prescription drug plan?

- Very Dissatisfied
- Dissatisfied
- Somewhat Dissatisfied
- Somewhat Satisfied
- Satisfied
- Very Satisfied

2. How would you rate the quality of the UM prescription drug plan as compared to other prescription drug plans you have heard about (e.g., from other employers)?

- A lot worse
- A little worse
- About the same
- A little better
- A lot better

5. In the past year, have you had difficulty obtaining medication that your doctor prescribed for you?

- Yes
- No

If Yes, what type of difficulty was encountered? (Please check all that apply)

- The pharmacy did not have the medication(s).
- The mail-service pharmacy did not get the medication to me by the day that I needed it.
- I was told that I had to try another medication before I could get the one that my doctor prescribed.
- I could not afford the cost of a specific medication.
- The combined cost of all my medications made it difficult for me to get all of them.
- Other _______________________________________________

6. During the past year, did the copay increase for at least one of your medications (i.e., were you asked to pay more for a medication than you previously paid)?

- Yes
- No

If Yes, what did you do?

- Kept taking the same medication and paid the higher copay.
- Switched to a different medication (either a brand or generic drug).
- Stopped taking the medication and did not start taking a new one.
### Survey Procedures

A written questionnaire and cover letter were mailed to the subjects in early May 2005 (Table 2). A reminder postcard was sent 1 week after the questionnaire. In late June, non-respondents were mailed a second questionnaire and cover letter. Data collection was discontinued on July 29, 2005. Of the 4,000 surveys mailed, 333 were undeliverable because of incorrect addresses or because the subject had died or was physically unable to complete the survey. Thus, there were presumed to be 3,667 eligible subjects.

### Analysis

Descriptive statistics were calculated for all the variables. To estimate the extent of response bias, the satisfaction ratings of the early responders were compared with the late responders (late responders are considered to be most similar to nonresponders) using an independent samples t test ($\alpha = 95\%$).

The association of satisfaction and difficulties in obtaining medications was first assessed using a chi-square test. Additionally, a multivariate logistic regression analysis was conducted with satisfaction as the dependent variable. Independent variables included “difficulty in obtaining medication,” copayment increase, gender, faculty compared with staff, employee compared with retiree, and mail-service compared with community pharmacy patronage. All analyses were conducted using SPSS software, v. 14.0.

### Results

#### Respondents

Surveys were returned by 2,061 of the potential 3,667 eligible subjects (56.2% response rate). The satisfaction ratings for early and late responders were nearly identical. Additionally, the response rates for the 4 strata (i.e., retirees using only community pharmacies, retirees using the mail-service pharmacy, current employees using only community pharmacies, and current employees using the mail-service pharmacy) were similar, and the age and gender distributions of the respondents were similar to the original sample. Thus, there did not appear to be a substantial response bias.

Table 3 shows the characteristics of the respondents. Retirees were more likely to fill more than 12 prescriptions in the last 3 months (21.6% vs. 12.8%, chi-square=49.31, $P < 0.01$); however, there was no difference in use based on faculty status or source of medications (mail-service vs. community pharmacy).

#### Difficulties in Obtaining Medications

Overall, 511 (24.8%) of respondents indicated that during the past year, they had difficulty obtaining prescription medications. The satisfaction ratings for early and late responders were nearly identical. Additionally, the response rates for the 4 strata (i.e., retirees using only community pharmacies, retirees using the mail-service pharmacy, current employees using only community pharmacies, and current employees using the mail-service pharmacy) were similar, and the age and gender distributions of the respondents were similar to the original sample. Thus, there did not appear to be a substantial response bias.

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#### Frequency of Reported Difficulties in Obtaining Medications

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#### Other difficulties

38 1.8

* Table 2, survey item #5.
Member Satisfaction Related to Self-Reported Cost Share and Difficulty in Obtaining Prescription Drugs in a University Pharmacy Benefit Plan

Differences between faculty and nonfaculty employees in experiencing this difficulty:

The most common types of difficulty reported were related to prior authorization or step therapy (Table 4). Other common difficulties included delivery problems from the mail-service pharmacy or the pharmacy not having the medication. Cost-related difficulties were reported by only 3.3% of the 2,061 respondents.

Cost-related difficulties could be exacerbated by increases in copayments for medications. The cost (e.g., copayment) for at least 1 of the medications for 915 of the respondents (44.4%) had increased during the past year (data not reported in tables).

Nearly 85% of those who had experienced an increase in copayment indicated that they continued to take the same medication and paid the higher cost, while 11% switched to a different medication with a lower copayment. Only 40 people (4.4% of those who experienced a copayment increase) responded that they stopped taking the medication and did not start taking a new one. Only 5.1% of respondents who experienced a copayment increase also indicated that the cost of their medications made it difficult for them to obtain their medications.

### Satisfaction With the Pharmacy Benefit Plan

The vast majority of respondents (83.7%) indicated that they were “somewhat satisfied,” “satisfied,” or “very satisfied” with the university’s pharmacy benefit plan (Table 5, survey item #1 in Table 2).

When asked to rate the quality of the university’s pharmacy benefit plan compared with other pharmacy plans that they had heard about, 47.9% of respondents rated the university’s drug plan as better than others. Another 34.8% believed that the university’s plan was about the same as other plans, and 17.8% believed that the university’s drug plan was worse than other drug plans.

There were no significant differences in satisfaction based on employment status (faculty vs. nonfaculty employees), source of medications (mail-service vs. community pharmacy), or volume of prescriptions purchased. However, retirees were more likely to be satisfied with the drug plan than current employees (87.1% vs. 81.0%, chi-square = 13.9, P < 0.01).

### Self-Reported Difficulty in Obtaining Medication and Satisfaction

Respondents who experienced an increase in copayment were less likely to be satisfied with the drug plan (78.6% vs. 87.9%, chi-square = 30.2, P < 0.01). Respondents who experienced difficulties in obtaining medications were less likely to be satisfied with the drug plan (66.9% vs. 89.7%, chi-square = 145.4, P < 0.01).

When multivariate regression analyses were conducted to control for gender, prescription volume, employee versus retiree, mail-service versus community, and faculty versus staff, the patients’ experiences with “difficulty in obtaining medications” and copayment increases were associated with the odds of satisfaction (Table 6). Thus, members who experienced 1 or more difficulties in obtaining medication and members who experienced an increase in copayment were less likely to be satisfied with the drug plan.

### Discussion

Utilization management tools (e.g., multtier copayment designs, prior authorization, step therapy, quantity limits) are commonly used to optimize the efficiency and appropriateness of drug therapy. However, these tools may also lead to unfavorable humanistic outcomes in member confusion, inconvenience, and annoyance. The need to manage use of medications must be weighed against the potentially negative impact of these tools on member and provider satisfaction.

Nearly 25% of respondents to this survey reported some difficulty in obtaining a prescription medication within the past year. The most commonly reported problems pertained to step therapy or prior authorization, while very few respondents (3.3%) reported cost-related difficulties. This is not surprising since the UM prescription drug plan has an open formulary but employs interventions such as step therapy, prior authorization, and a 3-tier copayment drug benefit design to promote appropriate drug use. Most members of the drug plan have a 3-tier copayment structure with copayments of $7, $14, and $24 for generic, preferred brand, and nonpreferred brand drugs. These copayment amounts have remained the same since 2003 and are lower than recent national benchmarks. The relatively low copayments apparently did not create access difficulties for the majority of the members.

A surprising proportion of respondents (44.4%) indicated that the cost (e.g., copayment) for at least 1 of their medications had increased during the past year, despite the copayment amounts for the 3-tier design that did not change from 2003 through 2005. However, several products changed copayment tier from May 2004 through April 2005, the 12 months before the survey. The change in copayment tier that occurred was typically a
TABLE 6 Multivariate Logistic Regression for Explaining Member Satisfaction

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty in obtaining medication?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.27</td>
<td>(0.20-0.35)*</td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Copayment increase?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.62</td>
<td>(0.48-0.81)*</td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Covariates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>1.41</td>
<td>(1.07-1.85)*</td>
</tr>
<tr>
<td>Current</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Faculty</td>
<td>0.96</td>
<td>(0.69-1.85)</td>
</tr>
<tr>
<td>Nonfaculty</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Source of medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mail</td>
<td>1.12</td>
<td>(0.87-1.46)</td>
</tr>
<tr>
<td>Community</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Rx use (in past 3 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;12 Rx</td>
<td>0.90</td>
<td>(0.69-1.17)</td>
</tr>
<tr>
<td>≤12 Rx</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.99</td>
<td>(0.81-1.21)</td>
</tr>
<tr>
<td>Female</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

* P value <0.01.
CI = confidence interval; Rx = prescription.

PDL-listed product (e.g., Diflucan, Glucovance, Neurontin, Wellbutrin SR) that moved from tier-2 copayment to tier-3 copayment when a generic product became available. A small percentage of retirees had a coinsurance benefit for prescriptions, wherein they paid 20% of the cost of medications. Thus, price increases for these products may have led to an increase in coinsurance payment by the enrollee. Yet another potential influence on perceived copayment increases was a benefit change in September 2004 to allow enrollees to obtain a 90-day supply of medications at community pharmacies for the equivalent of 3 monthly copayments. Some individuals may have interpreted this change as an increase in their cost share. Consequently, there are several plausible scenarios in which enrollees could experience an actual, or perceived, increase in their cost share for medications.

Although few respondents indicated that cost made it difficult for them to obtain their medications, those respondents who experienced an increase in the cost of a medication during the past year were more likely to report a cost-related difficulty for obtaining medication. However, only 4.4% of respondents who experienced an increase in out-of-pocket cost indicated that they discontinued taking medication as a result of the increased cost.

The university drug plan was generally well regarded by its members; two thirds of respondents indicated full satisfaction with the plan and nearly one half of respondents rated the UM drug plan as better than competing plans. However, those members who experienced difficulties in obtaining their medications were less likely to be satisfied. This is consistent with the study by Motheral and Heinle (2004), who found that persons who experienced a coverage denial were less likely to be satisfied with the drug plan. If member satisfaction is affected negatively by unexpected restrictions or changes to drug benefits, then one might expect that educating consumers about the rationale for the restriction...
or change may lessen the surprise or confusion involved with various drug plan policies. Although there is evidence that the dissemination of health plan information has a positive effect on patient satisfaction,\textsuperscript{12} the relationship of general knowledge about a plan and member satisfaction is predictably small.\textsuperscript{13,14} Furthermore, there appears to be no relationship between satisfaction and members’ understanding of the details of a plan (e.g., copayment structure, drug use management strategies).\textsuperscript{14}

**Limitations**

The first and foremost limitation of the current study was the absence of analysis of the relationship of actual drug use data with self-reported survey (satisfaction) data. Comparison of self-reported copayment increase to actual drug-use experience may have provided useful insight into the apparent overreporting of a drug copayment increase.

Second, member satisfaction was assessed by only a few survey questions that have face validity but have not otherwise been validated. We did not, for example, ask pharmacy benefit users about their perception of quantity limits or other use management interventions other than the 1 question about perceived difficulty in obtaining medication related to prior authorization or step therapy (“I was told that I had to try another medication before I could get the one that my doctor prescribed”; see survey item #5, Table 2). Third, although there did not appear to be a substantial response bias, it is possible that the persons who responded had different opinions or experiences from non-respondents. Fourth, the study sample was derived from only 1 drug plan, and these results may not be generalizable.

**Conclusion**

Patients who experienced a self-reported increase in the cost of their medication or who experienced self-reported difficulties in obtaining their prescribed medication were less likely to be satisfied with their drug plan. Further study is encouraged, particularly regarding the impact of educating consumers on drug plan policies and pharmacy benefit interventions that may affect access or member out-of-pocket cost.

**What is already known about this subject**

- Members of pharmacy benefit plans who perceive their drug coverage as being limited are less likely to be satisfied with their plans.
- It is not clear how various types of drug use management interventions relate to member satisfaction.

**What this study adds**

- Members were highly satisfied with their pharmacy benefit despite several drug use management interventions.
- Patients who reported an increase in the cost of their medication or difficulty in obtaining their medication were less likely to be satisfied with their pharmacy benefit plan.
Characteristics of Older Adults Who Meet the Annual Prescription Drug Expenditure Threshold for Medicare Medication Therapy Management Programs

Gregory W. Daniel, RPh, MS, MPH, and Daniel C. Malone, RPh, PhD

ABSTRACT

BACKGROUND: The Medicare Modernization Act of 2003 requires drug plan sponsors to provide medication therapy management programs (MTMPs) to beneficiaries with (1) drug expenditures above $4,000, (2) multiple comorbidities, and (3) multiple prescription drugs. The Medical Expenditure Panel Survey (MEPS) is a national probability survey conducted annually by the Agency for Healthcare Research and Quality and the National Center for Health Statistics to provide nationally representative estimates of health care use, expenditures, sources of payments, and insurance coverage for the U.S. civilian noninstitutionalized population. MEPS comprises 3 components, including the household component (HC) in which households and individuals within households are sampled. The medical provider component (MPC) supplements the HC by contacting providers (hospitals, outpatient offices, home health agencies, and pharmacies) reported in the HC, and the insurance component collects data on health insurance plans and is separate from the HC.

OBJECTIVE: The purpose of this study was to estimate from MEPS data for 2002-2003 (1) the proportion of older adults who may have met the $4,000 expenditure component of the MTMP criteria and (2) the patient-specific risk factors associated with meeting the $4,000 expenditure threshold.

METHODS: This study is a cross-sectional analysis of MEPS respondents aged 65 years or older. Data came from both the MEPS-HC and the supplemental MEPS-MPC for 2002 and 2003. Specific data files were pooled and included the Full Year Consolidated files, Prescribed Medicines files, and the Medical Conditions files for both the 2002 and the 2003 MEPS-HC. Variables extracted from the MEPS data files included demographics, socioeconomic status, functional limitations, health status, presence and number of chronic conditions, body mass index, medical and prescription drug insurance, and health care utilization measures. The expenditure threshold of $4,000 was adjusted to $3,810 in 2003 U.S. dollars. Survey-weighted logistic regression identified factors associated with meeting the expenditure threshold. Unbiased population point estimates were obtained by adjusting for survey nonresponse, poststratification, and oversampling of blacks and Hispanics using MEPS person-level weights. In all analyses, standard errors were adjusted for nonindependence of observations due to complex multistage sampling by specifying the strata and primary sampling units for each respondent.

RESULTS: Based on a sample of 8,035 noninstitutionalized persons aged 65 years or older in the United States, representing a population of 36.5 million older adults, MEPS data estimate that approximately 3.3 million (9.2%) incurred annual drug expenditures greater than $3,810, accounting for 35% of $55.3 billion in drug expenditures among all older adults. Older adults meeting the $3,810 prescription expenditure threshold reported an average 10.8 (SE = 0.2) unique medications, 82.2 (SE = 1.8) prescriptions, and 5.2 (SE = 0.1) chronic conditions. Prescription expenditures accounted for 33.9% of total health care expenditures compared with 15.8% for persons who did not meet the $3,810 criterion and an average 19.5% for all persons aged 65 years or older (n = 8,035). Factors that predicted meeting the expenditure threshold included age in 10-year increments (odds ratio [OR] = 0.81; 95% confidence interval [CI], 0.68-0.97), requiring help with activities of daily living (OR = 1.53; 95% CI, 1.19-1.97), having functional limitations (OR = 1.67; 95% CI, 1.30-2.14), having TRICARE (military health care services) benefits (OR = 0.54; 95% CI, 0.33-0.86), and being on Medicaid (OR = 1.36; 95% CI, 1.02-1.81). Other factors that were also predictive of meeting the expenditure threshold included mental health disorders, ulcers, diabetes, dyslipidemia, cardiac disease, chronic obstructive pulmonary disorder, and the number of chronic conditions.

CONCLUSIONS: MEPS survey respondents aged 65 years or older with drug expenditures exceeding the MTMP threshold of $4,000 per year obtain substantially more drugs and have a higher disease burden than those with lower drug expenditures. Characteristics other than drug use, such as having functional limitations or requiring help with activities of daily living, can be used to identify potential MTMP candidates.

KEYWORDS: Medicare Part D, Medication therapy management, Drug prescriptions, Insurance, Pharmaceutical services

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T he Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003 added the opportunity for outpatient prescription drug coverage for its approximately 42 million beneficiaries.1 Under MMA, prescription drug plan (PDP) sponsors are required to establish medication therapy management programs (MTMPs) that are designed to “optimize therapeutic outcomes for targeted beneficiaries by improving medication use and reducing adverse events.”2 According to the MMA legislation and the Centers for Medicare & Medicaid Services regulations, targeted beneficiaries include those who (1) have multiple chronic conditions, (2) take multiple prescription medications, and (3) are likely to exceed $4,000 per year in prescription drug expenditures.2

Authors

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The statutory language of MMA defines MTMP eligibility broadly, giving PDP sponsors flexibility in defining the “targeted beneficiaries.” While all Part D beneficiaries may benefit from the services that MTMPs provide, resource allocation is essential and PDP sponsors are being challenged with the task of determining eligibility within the legislation framework. PDP sponsors face important issues when deciding how many diseases and prescription drugs will be used to identify candidates; if particular diseases and therapeutic areas will be targeted, or if a combination will be used. A comprehensive list of chronic diseases of interest is not specified in the MMA; however, diabetes, asthma, hypertension, hyperlipidemia, and congestive heart failure are mentioned as examples of conditions that may be targeted.  

Finally, the high drug cost threshold introduces different considerations. For example, must a beneficiary incur an average of at least $333 per month in the first few months of the year to qualify for an MTMP based on the greater than $4,000 threshold criterion? In this case, beneficiaries would already be at a very high drug spending level, with a high likelihood of having already experienced adverse drug events or drug misuse, before receiving MTMP services. It has been suggested that the MMA criteria for MTMP candidates might be too limited and that it might be more cost effective for MTMP services to be used to prevent high-severity cases.  

Our primary objectives were to obtain nationally representative estimates of the proportion of adults aged 65 years or older who would likely meet the high drug expenditure threshold and to identify characteristics that might help identify these candidates. We further intended to explore the significance of the $4,000 threshold as it relates to the other 2 criteria (have multiple chronic conditions and take multiple prescription medications) as well as prescription drug and overall health care use. To our knowledge, no studies have examined the explicit criteria of the MTMPs under the MMA legislation in such detail.

### Methods

#### Data

Data used in this study were pooled from the Full Year Consolidated files, Prescribed Medicines files, and the Medical Conditions files for both the 2002 Medical Expenditure Panel Survey (MEPS) and the 2003 MEPS. Data were pooled from both MEPS years to increase the precision of population estimates for the subpopulation of older adults. MEPS-HC (household component) samples from year to year are not completely independent since households are drawn from the same geographic areas and persons may be in the sample for 2 consecutive years. Valid population estimates can, however, be determined when combining multiple MEPS years since each year of the MEPS-HC is designed to be nationally representative.

MEPS is a national probability survey cosponsored by the Agency for Healthcare Research and Quality (AHRQ) and the National Center for Health Statistics. MEPS is designed to provide nationally representative estimates of health care use, expenditures, source of payments, and insurance coverage for the U.S. civilian noninstitutionalized population. Three components constitute each year of MEPS. The first component, the HC, represents the core survey in which households and individuals within households are sampled. Detailed, self-reported data are collected on demographic characteristics, health conditions, health status, income, health insurance coverage, employment, and both use and expenditures for health care services using computer-assisted personal interviewing technology. The HC uses an overlapping panel design in which data are collected over a series of 5 rounds (interviews) over a 2+½-year period for each panel. Data collected, however, cover a complete 2-year period. A new panel is sampled and launched each year. Annual data are then generated by combining the last 3 rounds (3, 4, and 5) of the previous panel and the first 3 rounds (rounds 1, 2, and 3) of the new panel. Since MEPS began in 1996 with panel 1, this study has used data from rounds 3, 4, and 5 of panel 6 and rounds 1, 2, and 3 of panel 7 (2002 MEPS) combined with data from rounds 3, 4, and 5 of panel 7 and rounds 1, 2, and 3 of panel 8 (2003 MEPS).

The second component is the medical provider component (MPC), which supplements and/or replaces information on medical care expenditures reported by the HC by contacting all pharmacies and home health care agencies as well as a subsample of physicians and hospitals reported by the household respondents. The MPC is conducted through telephone interviews and record abstraction. The third component of MEPS is the insurance component (IC), which collects data on health insurance plans and is separate from the HC. Data collected from the MEPS-IC were not used in this study.

Data from the MEPS-HC and the supplemental information from the MEPS-MPC are available for public use in several downloadable data files. The Full Year Consolidated Files for each year are person-level files and contain summary data for each respondent obtained from the MEPS-HC. Any expenditure data obtained from the MEPS-MPC are generally used in place of HC-reported expenditure data. When MPC data are not available, self-reported data from the HC are used. If neither source is available, expenditures are imputed from MPC data obtained for respondents with similar characteristics. The Medical Conditions files for each year are event-level data files that provide detailed information on each medical condition reported by the household respondent. All data in this file are self-reported data.

The Prescribed Medicines files are also event-level files that contain data on all prescribed medicines, including refills, reported by the respondent of the HC, and are supplemented with detailed data (total amount charged by the pharmacy, all payments by source including third-party and out-of-pocket, National Drug Code, strength, and quantity dispensed) from
MPC pharmacies. Data were obtained from MPC pharmacies through telephone interview and computerized printouts from pharmacies if the HC respondent provided written permission to release such data. Imputation methods were used in cases where pharmacy data were not available.

Medication Therapy Management Expenditure Threshold

All expenditure data were adjusted to constant 2003 U.S. dollars using the consumer price index for all items averaged across all U.S. cities. The 2003 U.S. dollar equivalent of $4,000 was determined to be $3,810 in 2006. The main study comparison groups were older adults with annual prescription drug expenditures (from all payment sources) greater than $3,810 and those with prescription expenditures equal to or below this level.

Identification of Risk Factors

We hypothesized that patient characteristics known to relate to medical and prescription drug expenditures would be key risk factors for being in the high-expenditure group. These factors included demographic and socioeconomic characteristics; medical and prescription drug insurance; perceived health and mental health status; requiring assistance with activities of daily living (ADLs); functional, cognitive, or sensory limitations; body mass index (BMI); and both the presence and count of chronic diseases.

Demographic characteristics included age (continuous variable with results reported for 10-year increments), gender, race/ethnicity, and marital status. Socioeconomic factors included education and total annual personal income (2003 U.S. dollars). As described above, each panel contributes 3 rounds of data to each MEPS year (for example, in 2002, panel 6 contributed rounds 3, 4, and 5, while panel 7 contributed rounds 1, 2, and 3), resulting in round-specific variables. Also, because of the overlapping panel design, each round in one panel occurs at the same time as each round in the next panel (for example in 2002, round 3 of panel 6 occurred at the same time as round 1 of panel 7). Consequently, data from overlapping rounds were combined across panels. Unless otherwise noted, annual summary variables were used that reflect respondent status as of December 31 of the corresponding year (as in age and marital status). For each year, 3 round-specific health status variables and 3 round-specific mental health status variables (coded as “excellent,” “very good,” “good,” “fair,” and “poor”) were available. Since these variables could not be pooled into an annual variable, the mode of the round-specific variables was used to create an overall health status variable and an overall mental health status variable. In cases with multiple modes (either due to nonresponse in one of the rounds or a different response in each of the 3 round-specific variables), the response reflecting poorer health status was used. The “excellent” and “very good” responses were combined for both health status variables to increase reliability of the population estimates.

A total of 5 functional limitation variables were extracted, each a binary (yes/no) variable. If a “yes” was reported during any of the 3 rounds, the respondent was included in this analysis as having the corresponding limitation. These variables included (1) requiring assistance with ADLs, e.g., bathing, dressing), (2) requiring assistance with instrumental ADLs (IADLs, e.g., paying bills, doing laundry), (3) having any reported difficulties with walking, lifting, bending, or limitations with housework, (4) having cognitive difficulties, and (5) reporting any vision or hearing problems throughout the year.

Four medical insurance variables were created from self-reported data: Medicare, Medicaid, private health insurance, and TRICARE (military health care services). Each variable was considered present if the respondent indicated having the corresponding insurance during any round. The presence of prescription drug insurance was determined using self-report and sources of payment in the Prescribed Medicines file. If a respondent indicated having private drug insurance during any round or if any third-party payment was recorded in the Prescribed Medicines file, the respondent was considered to have prescription drug insurance at some point during the year. This method has been used in previous studies.

MEPS professional coders assign International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes to each medical condition reported by the household respondent. These codes for conditions as well as ICD-9 procedure codes were aggregated into 260 mutually exclusive, clinically meaningful categories using Clinical Classification software. From these categories, 25 major chronic conditions were identified based on importance and relevance in the older adult population. Medical service use variables included annual counts of office-based visits, outpatient visits, inpatient discharges and nights, emergency department visits, and home health care visits. Annual total medical expenditures and nonpharmacy medical expenditures were also extracted. Annual totals of prescription drug acquisitions and prescription drug expenditures as well as sources of payment were collected from the MEPS HC. Therapeutic class was determined from Multum Lexicon classifications for all drugs reported by the respondent and was provided by MEPS in the Prescribed Medicines files.

Statistical Analysis

Nationally representative estimates were obtained using respondents with a person-level weight, which accounts for survey nonresponse, poststratification, and oversampling of blacks and Hispanics. To preserve the survey design structure and yield valid standard errors, we used the full person-level files when calculating estimates of subpopulations. Standard errors were adjusted for complex survey design with the use of a Taylor-series linearization approach while specifying strata and primary sampling units from which each respondent was sampled. Bivariate comparisons between the 2 prescription
### TABLE 1
Study Population Characteristics by Amount of Prescription Drug Expenditure

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall</th>
<th>Older Adults With Prescription Expenditures ≤$3,810</th>
<th>Older Adults With Prescription Expenditures &gt;$3,810</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size (%)</td>
<td>8,035</td>
<td>7,233 (90.0)</td>
<td>802 (10.0)</td>
<td></td>
</tr>
<tr>
<td>Weighted average population size (per year) (%)</td>
<td>36,477,534</td>
<td>33,135,274 (90.8)</td>
<td>3,342,261 (9.2)</td>
<td></td>
</tr>
<tr>
<td>Age (years), mean (±SE)</td>
<td>74.7 (±0.12)</td>
<td>74.6 (±0.13)</td>
<td>74.8 (±0.28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>65-74, %</td>
<td>51.7</td>
<td>51.6</td>
<td>52.5</td>
<td>0.941</td>
</tr>
<tr>
<td>75-84, %</td>
<td>36.6</td>
<td>36.6</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>85+, %</td>
<td>11.8</td>
<td>11.8</td>
<td>11.6</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male, %</td>
<td>42.8</td>
<td>43.4</td>
<td>36.7</td>
<td></td>
</tr>
<tr>
<td>Female, %</td>
<td>57.2</td>
<td>56.6</td>
<td>63.3</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td>0.193</td>
</tr>
<tr>
<td>White (non-Hispanic), %</td>
<td>82.0</td>
<td>81.9</td>
<td>82.4</td>
<td></td>
</tr>
<tr>
<td>Black (non-Hispanic), %</td>
<td>8.4</td>
<td>8.2</td>
<td>9.9</td>
<td></td>
</tr>
<tr>
<td>Hispanic, %</td>
<td>6.0</td>
<td>6.1</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Other/multiple, %</td>
<td>3.7</td>
<td>3.8</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td>0.021</td>
</tr>
<tr>
<td>Married, %</td>
<td>53.2</td>
<td>53.7</td>
<td>48.1</td>
<td></td>
</tr>
<tr>
<td>Widowed, %</td>
<td>34.1</td>
<td>33.5</td>
<td>39.4</td>
<td></td>
</tr>
<tr>
<td>Divorced, separated, or never married, %</td>
<td>12.7</td>
<td>12.8</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>Years of education, mean (±SE)†</td>
<td>11.8 (±0.1)</td>
<td>11.8 (±0.1)</td>
<td>11.2 (±0.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12 years, %</td>
<td>33.5</td>
<td>34.1</td>
<td>28.0</td>
<td>0.001</td>
</tr>
<tr>
<td>12 years, %</td>
<td>34.2</td>
<td>34.4</td>
<td>31.8</td>
<td></td>
</tr>
<tr>
<td>&lt;12 years, %</td>
<td>32.3</td>
<td>31.5</td>
<td>40.2</td>
<td></td>
</tr>
<tr>
<td>Total income ($, mean ±SE)§</td>
<td>22,809 (±467)</td>
<td>23,221 (±495)</td>
<td>18,733 (±715)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall health§</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Excellent/very good, %</td>
<td>37.5</td>
<td>39.6</td>
<td>17.3</td>
<td></td>
</tr>
<tr>
<td>Good, %</td>
<td>32.9</td>
<td>33.2</td>
<td>30.1</td>
<td></td>
</tr>
<tr>
<td>Fair, %</td>
<td>20.0</td>
<td>18.8</td>
<td>31.6</td>
<td></td>
</tr>
<tr>
<td>Poor, %</td>
<td>9.7</td>
<td>8.5</td>
<td>21.1</td>
<td></td>
</tr>
<tr>
<td>Mental health§</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Excellent/very good, %</td>
<td>51.5</td>
<td>53.1</td>
<td>35.5</td>
<td></td>
</tr>
<tr>
<td>Good, %</td>
<td>33.9</td>
<td>33.4</td>
<td>39.6</td>
<td></td>
</tr>
<tr>
<td>Fair, %</td>
<td>10.6</td>
<td>9.8</td>
<td>18.6</td>
<td></td>
</tr>
<tr>
<td>Poor, %</td>
<td>4.0</td>
<td>3.8</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>Limitations§</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IADL help, %</td>
<td>20.5</td>
<td>18.6</td>
<td>39.3</td>
<td></td>
</tr>
<tr>
<td>ADL help, %</td>
<td>11.8</td>
<td>10.4</td>
<td>24.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical/functional limitations, %</td>
<td>47.9</td>
<td>45.1</td>
<td>75.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cognitive limitation, %</td>
<td>17.0</td>
<td>15.8</td>
<td>29.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vision/hearing problems, %</td>
<td>29.9</td>
<td>28.8</td>
<td>39.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean BMI (±SE)¶</td>
<td>20.6 (±0.1)</td>
<td>24.5 (±0.1)</td>
<td>28.3 (±0.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Underweight or normal (BMI &lt;25), %</td>
<td>40.5</td>
<td>41.6</td>
<td>29.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overweight (BMI 25-29), %</td>
<td>37.9</td>
<td>38.0</td>
<td>36.9</td>
<td></td>
</tr>
<tr>
<td>Obese (≥30), %</td>
<td>20.4</td>
<td>20.4</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>Health insurance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare ever, %</td>
<td>98.8</td>
<td>98.7</td>
<td>99.6</td>
<td>0.035</td>
</tr>
<tr>
<td>Medicaid ever, %</td>
<td>10.2</td>
<td>9.4</td>
<td>18.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Private ever, %</td>
<td>56.9</td>
<td>57.1</td>
<td>54.6</td>
<td>0.268</td>
</tr>
<tr>
<td>TRICARE (military health care services) ever, %</td>
<td>5.4</td>
<td>5.6</td>
<td>3.5</td>
<td>0.016</td>
</tr>
<tr>
<td>Prescription drug coverage</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any coverage, %</td>
<td>69.4</td>
<td>68.3</td>
<td>80.1</td>
<td></td>
</tr>
</tbody>
</table>

* Determined by survey-weighted t tests and chi-square tests for continuous and categorical variables, respectively.
† Responses from 7,925 subjects used in analysis.
§ Responses from 7,952 subjects used in analysis.
¶ Responses from 7,459 subjects used in analysis.

ADL = activities of daily living (e.g., bathing, dressing, etc.); BMI = body mass index; IADL = instrumental activities of daily living (e.g., paying bills, doing laundry, etc.).
Expenditure Threshold for Medicare Medication Therapy Management Programs

More than half (52.7%) of older adults meeting the expenditure threshold reported having fair or poor overall health and tended to also report significantly poorer overall health and mental health than did those not meeting the criterion (P < 0.001). Also, those with high prescription expenditures more frequently reported requiring help with ADLs and IADLs as well as having functional, cognitive, and sensory limitations (all P values <0.001). Those with high prescription expenditures also had a higher BMI (28.3 vs. 24.5, P < 0.001), with the average being in the overweight category, than did those not meeting the expenditure threshold.

Older adults meeting the expenditure threshold had a higher percentage of respondents reporting Medicaid benefits (P < 0.001) or Medicare benefits (P=0.035) at some point over the year and a lower percentage of older adults having TRICARE (P = 0.016) compared with those not meeting the expenditure threshold. Furthermore, 80% of those meeting the criterion were estimated to have prescription drug insurance at any time over the year, compared with 68% of those not meeting the expenditure threshold (P < 0.001).

Estimates of chronic disease prevalence between the 2 groups are displayed in Table 2. Hypertension, osteoarthritis/joint disorders, cardiac disease, and dyslipidemia were the most prevalent conditions reported overall. Hypertension and cardiac disease were reported in more than half of the study population in the high-cost group. Other notable differences were a higher prevalence of diabetes, mental disorders, ulcers, and asthma. Older adults who met the criterion reported an average of 5.2 (±SE = 0.11) chronic conditions (2.3 more conditions than those in the lower-cost group, P <0.001). As illustrated in Figure 1A, more than 60% of older adults meeting the expenditure threshold reported 5 or more chronic conditions, while the majority of those not meeting the criterion reported between 1 and 3 chronic conditions.

Significant predictors of expenditure group membership were evaluated using logistic regression and are shown in Table 3. Risk factors significantly associated with MTMP expenditure threshold included age, requiring help with ADLs, reporting functional limitations, having selected chronic diseases, having a number of diseases, and having TRICARE or Medicaid. Increasing age was associated with a lower risk of meeting the high-expenditure threshold. For every 10-year increment in age (from 65 years), the risk decreases by 19% (odds ratio [OR] = 0.81; 95% confidence index [CI], 0.67-0.97). Chronic conditions that significantly increased the risk of meeting the high-expenditure threshold, while controlling for other covariates, included mental disorders (OR = 1.32; 95% CI, 1.03-1.70), stomach/duodenal ulcers (OR = 1.55; 95% CI, 1.21-2.00), diabetes (OR = 1.88; 95% CI, 1.50-2.35), dyslipidemia (OR = 1.70; 95% CI, 1.37-2.11), cardiac disease (OR = 1.37; 95% CI, 1.10-1.70), and chronic obstructive pulmonary disorder (COPD) (OR = 1.26; 95% CI, 1.04-1.53).

Furthermore, older adults with 6 or more chronic diseases were 6 times more likely to be in the high-cost group than those with fewer than 3 chronic diseases (OR = 6.14; 95% CI, 3.86-9.78).

Table 4 summarizes prescription drug use and overall health care use within the study population. Older adults meeting the expenditure threshold represented 9.2% of the population and accounted for 35.4% of the $55 billion in annual prescription drug expenditures, used significantly more prescriptions annually (82.2 ± 1.76), and obtained more unique medications (10.8 ± 0.2) compared with those not meeting the expenditure threshold (20.3 ± 0.37 prescriptions and 4.6 ± 0.06 unique medications). In addition, the average prescription cost was $28 higher for older adults who met the expenditure threshold than for those not meeting the threshold. Older adults meeting the expenditure threshold incurred approximately $10,000 higher total health care expenditures ($17,271 vs. $6,840, P <0.001) and $5,600 higher nonpharmacy medical expenditures ($11,416 vs. $5,761, P <0.001) than did those not meeting the expenditure threshold. Furthermore, 33.9% of total health care expenditures for older adults meeting the expenditure threshold went to prescription drugs, while 15.8% of total health care expenditures went to prescription drugs for persons who did not meet the...
Characteristics of Older Adults Who Meet the Annual Prescription Drug Expenditure Threshold for Medicare Medication Therapy Management Programs

$3,810 criterion. Those in the high-cost group also incurred higher levels of health care services, including office-based and hospital-based office visits, emergency department visits, inpatient admissions, and home health care visits.

Figure 1B illustrates the distribution of the number of unique medications obtained by the study population. All older adults meeting the expenditure threshold obtained at least 3 unique medications; approximately 68% obtained 9 or more unique medications.

The proportion of total annual drug expenditures accounted for by therapeutic drug classes is displayed in Table 5. Cardiovascular drugs consumed the largest portion for both expenditure groups and was significantly lower for older adults meeting the expenditure threshold than for those not meeting the threshold (20.1% vs. 28.6, *P* <0.05). No significant differences were observed between the expenditure groups with respect to the use of hormones as a group; however, antidiabetic drugs accounted for a larger percentage of total drug expenditures among older adults meeting the expenditure threshold compared with those not meeting the threshold (9.3 vs. 6.1%, *P* <0.001).
Other drug classes that accounted for a significantly higher proportion of the total drug expenditures among older adults meeting the criterion included proton pump inhibitors, psychopharmacologic agents, respiratory agents, and coagulation modifiers.

**Discussion**

Approximately 3.3 million (9.2%) of the 36.5 million civilian noninstitutionalized adults aged 65 years older would have met the high prescription expenditure threshold MTMP under Medicare Part D. Representing less than 10% of the older adult population, they accounted for 35% of the total annual prescription drug expenditures and 29% of the prescriptions obtained.

The estimates of the number of chronic diseases and annual prescription drug costs are generally consistent with those reported from other sources. Data from the 2002 Medicare Current Beneficiary Survey estimated that approximately 90% of Medicare beneficiaries had at least 1 chronic condition.\(^\text{18}\) We estimated that 91% of older adults had at least 1 chronic condition. Reports from the Congressional Budget Office (CBO) and the AARP Public Policy Institute estimate that average per capita drug expenditure for Medicare beneficiaries in 2003 was $2,318\(^\text{19}\) and that Medicare beneficiaries aged 65 years or older averaged $830 in out-of-pocket spending for prescription drugs in 2003.\(^\text{20}\) This study’s estimate for average per capita drug expenditures, $1,517, was lower than that of the CBO; however, this difference may be partially explained by the target population being noninstitutionalized older adults rather than all Medicare beneficiaries. This study also estimated that approximately 54% of annual drug expenditures were paid out of pocket, about $819 on average.

Approximately 97% of the older adults who incurred annual drug expenditures in excess of the MTMP threshold had 2 or more chronic diseases; all had at least 3 unique medications filled during the year. This finding indicates a redundancy in the criteria and suggests that focusing on the high drug expenditure threshold may be an effective approach for identifying MTMP candidates, while still keeping with the 3 general provisions.

Although unadjusted differences in age were not different between older adults meeting the expenditure threshold and those not meeting the expenditure threshold, age was negatively correlated and significant in the regression model when it was adjusted for all other covariates entered. This result may suggest that, after adjusting for important characteristics such as demographics and comorbidity burden, we found that those adults between 65 and 75 years may be more aggressively treated for their conditions and may have higher medical use than those who are older. We did not explore this possibility. Older adults who reported requiring help with ADLs were 53% more likely to meet the expenditure threshold, and those reporting functional limitations were 67% more likely to have annual prescription drug expenditures in excess of $3,810, compared

**FIGURE 1**

Number of Self-Reported Chronic Conditions (A) and Unique Prescription Medications (B) Obtained Over the Year (2002 or 2003) for Older Adults by Amount of Prescription Expenditure

![Table and Figure]

- **A**
  - No. of Chronic Conditions
  - % of Population
  - None | 1 | 2 | 3 | 4 | 5 | ≥6
  - 50 | 45 | 40 | 35 | 30 | 25 | 20
- **B**
  - No. of Unique Medications
  - % of Population
  - None | 1 | 2 | 3 | 4 | 5 | ≥6
  - 50 | 45 | 40 | 35 | 30 | 25 | 20

- **Legend**
  - Older Adults With Prescription Expenditures ≤$3,810
  - Older Adults With Prescription Expenditures >$3,810
Characteristics of Older Adults Who Meet the Annual Prescription Drug Expenditure Threshold for Medicare Medication Therapy Management Programs

with those not reporting either limitation. Unfortunately, self-reported data on ADLs and other functional limitations will not be available from pharmacy claims, making the role of physicians and nurse practitioners significant in identifying MTMP candidates. Chronic diseases that increased the likelihood of having high prescription drug expenditures included mental disorders, stomach/duodenal ulcers, diabetes, dyslipidemia, cardiac disease, and COPD. Drug plans may target beneficiaries with these diseases in conjunction with a raw count, using medical and/or pharmacy claims, in complying with the "multiple chronic diseases" criteria. Compared with older adults with fewer than 2 reported chronic diseases, those with 6 or more diseases were 6 times as likely to have high prescription drug expenditures.

Results from testing medical and prescription drug insurance were noteworthy. Respondents with Medicaid coverage at some point over the year were 36% more likely and those with TRICARE were 54% less likely to meet the expenditure threshold. Independent of medical insurance, having any prescription drug insurance was not a significant predictor of group membership. Furthermore, older adults meeting the expenditure threshold not only used more classes of prescription drugs, but they also obtained more total fills (including refills) and obtained medications that were, on average, $28 per prescription more expensive than older adults in the lower cost group.

The results have substantial implications for PDP sponsors and for Medicare that underscore the importance of effective MTMP. For one, there is a high level of comorbidity burden and prescription drug use among older adults who met the expenditure threshold. The negative consequences of polypharmacy

### Table 3: Adjusted Odds Ratios for Likelihood of Having Prescription Drug Expenditures >$3,810*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (10-year increments)</td>
<td>0.81</td>
<td>0.68-0.97</td>
<td>0.021</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.14</td>
<td>0.94-1.39</td>
<td>0.181</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (non-Hispanic) (reference group)</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black (non-Hispanic)</td>
<td>0.95</td>
<td>0.69-1.32</td>
<td>0.774</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.71</td>
<td>0.48-1.05</td>
<td>0.086</td>
</tr>
<tr>
<td>Other/multiple</td>
<td>0.72</td>
<td>0.41-1.26</td>
<td>0.253</td>
</tr>
<tr>
<td>Income ($10,000 increments)</td>
<td>0.95</td>
<td>0.91-1.00</td>
<td>0.061</td>
</tr>
<tr>
<td>Years of education (4-year increments)</td>
<td>0.97</td>
<td>0.84-1.12</td>
<td>0.682</td>
</tr>
<tr>
<td>Help with ADL</td>
<td>1.53</td>
<td>1.19-1.97</td>
<td>0.001</td>
</tr>
<tr>
<td>Functional limitations (walking, lifting, housework)</td>
<td>1.67</td>
<td>1.30-2.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mental disorders (depression, anxiety, psychoses)</td>
<td>1.32</td>
<td>1.03-1.70</td>
<td>0.03</td>
</tr>
<tr>
<td>Stomach/duodenal ulcers</td>
<td>1.55</td>
<td>1.21-2.00</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.88</td>
<td>1.50-2.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1.70</td>
<td>1.37-2.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>1.37</td>
<td>1.10-1.70</td>
<td>0.005</td>
</tr>
<tr>
<td>COPD</td>
<td>1.26</td>
<td>1.04-1.53</td>
<td>0.021</td>
</tr>
<tr>
<td>Number of chronic conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2 (reference group)</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.03</td>
<td>1.34-3.09</td>
<td>0.001</td>
</tr>
<tr>
<td>4</td>
<td>3.06</td>
<td>2.00-4.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5</td>
<td>4.59</td>
<td>2.87-7.33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥6</td>
<td>6.14</td>
<td>3.86-9.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prescription drug insurance</td>
<td>1.29</td>
<td>0.99-1.69</td>
<td>0.058</td>
</tr>
<tr>
<td>TRICARE (military health care services)</td>
<td>0.54</td>
<td>0.33-0.86</td>
<td>0.01</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1.36</td>
<td>1.02-1.81</td>
<td>0.036</td>
</tr>
</tbody>
</table>

ADL = activities of daily living (e.g., bathing, dressing, etc.); BMI = body mass index.; CI = confidence interval; COPD = chronic obstructive pulmonary disease; IADL = instrumental activities of daily living (e.g., paying bills, doing laundry, etc.).
and inappropriate prescribing among older adults have been well cited.\textsuperscript{21-37} The prevalence of inappropriate drug use among ambulatory older adults is estimated between 17\% and 48\%.\textsuperscript{23-29} Inappropriate drug use is associated with adverse drug reactions (ADRs), drug-related hospital admissions, increased outpatient visits, and decline in functional status among the elderly.\textsuperscript{23,25,27,28,30} Polypharmacy among older adults increases the incidence of inappropriate drug use,\textsuperscript{31,32} ADRs,\textsuperscript{33-35} and drug-drug interactions. The number of potential interactions increases in a logarithmic fashion as the number of medications increases.\textsuperscript{38} Seniors represent the greatest proportion of the population at risk for exposure to a potential clinically significant interaction.\textsuperscript{39}

### TABLE 4: Prescription Drug and Health Care Utilization by Expenditure Threshold\textsuperscript{*}

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall</th>
<th>Older Adults With Prescription Expenditures ≤$3,810</th>
<th>Older Adults With Prescription Expenditures &gt;$3,810</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual prescription use and expenditures (overall)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total expenditures</td>
<td>$55,332,734,269</td>
<td>$35,762,385,406</td>
<td>$19,570,348,862</td>
<td></td>
</tr>
<tr>
<td>% of total expenditures</td>
<td>100</td>
<td>64.6</td>
<td>35.4</td>
<td></td>
</tr>
<tr>
<td>Total prescriptions</td>
<td>946,635,110</td>
<td>671,874,879</td>
<td>274,760,231</td>
<td></td>
</tr>
<tr>
<td>% of total prescriptions</td>
<td>100</td>
<td>71.0</td>
<td>29.0</td>
<td></td>
</tr>
<tr>
<td>Annual prescription use and expenditures (per capita)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of population with fill</td>
<td>90.7</td>
<td>89.8</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>No. of prescriptions per person, mean (±SE)</td>
<td>26.0 (±0.57)</td>
<td>20.3 (±0.37)</td>
<td>82.2 (±1.76)</td>
<td></td>
</tr>
<tr>
<td>No. of unique medications per person, mean (±SE)</td>
<td>5.2 (±0.08)</td>
<td>4.6 (±0.06)</td>
<td>10.8 (±0.2)</td>
<td></td>
</tr>
<tr>
<td>Paid amount per prescription, mean (±SE)</td>
<td>$59.94 (±0.6)</td>
<td>$57.08 (±0.5)</td>
<td>$85.42 (±3.3)</td>
<td></td>
</tr>
<tr>
<td>Expenditures per person, mean (±SE)</td>
<td>$1,517 (±32)</td>
<td>$1,079 (±17)</td>
<td>$5,855 (±107)</td>
<td></td>
</tr>
<tr>
<td>Annual health care use and expenditures (per capita)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total health care expenditures, mean (±SE)</td>
<td>$7,796 (±202)</td>
<td>$6,840 (±186)</td>
<td>$17,271 (±787)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% of prescription expenditure</td>
<td>19.5</td>
<td>15.8</td>
<td>33.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total nonpharmacy medical expenditures per person, mean (±SE)</td>
<td>$6,279 (±191)</td>
<td>$5,761 (±183)</td>
<td>$11,416 (±771)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Office-based visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% with use</td>
<td>90.6</td>
<td>89.8</td>
<td>98.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of visits among users, mean (±SE)</td>
<td>10.9 (±0.22)</td>
<td>10.3 (±0.21)</td>
<td>16.5 (±0.70)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital outpatient visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% with use</td>
<td>37.3</td>
<td>36</td>
<td>50.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of visits among users, mean (±SE)</td>
<td>4.2 (±0.24)</td>
<td>3.9 (±0.22)</td>
<td>5.9 (±0.90)</td>
<td>0.025</td>
</tr>
<tr>
<td>ER visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% with use</td>
<td>20.2</td>
<td>18.9</td>
<td>33.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of visits among users, mean (±SE)</td>
<td>1.5 (±0.03)</td>
<td>1.5 (±0.03)</td>
<td>1.6 (±0.06)</td>
<td>0.148</td>
</tr>
<tr>
<td>Inpatient admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% with use</td>
<td>19.9</td>
<td>18.9</td>
<td>30.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of visits among users, mean (±SE)</td>
<td>1.5 (±0.03)</td>
<td>1.4 (±0.03)</td>
<td>1.9 (±0.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of inpatient days among users, mean (±SE)</td>
<td>9.6 (±0.39)</td>
<td>9.3 (±0.43)</td>
<td>11.4 (±0.84)</td>
<td>0.028</td>
</tr>
<tr>
<td>Home health care visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% with use</td>
<td>10.8</td>
<td>9.3</td>
<td>25.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of visits among users, mean (±SE)</td>
<td>86.0 (±5.51)</td>
<td>80.4 (±5.83)</td>
<td>106.4 (±11.23)</td>
<td>0.028</td>
</tr>
</tbody>
</table>

\textsuperscript{*} Dollars are CPI-U adjusted to 2003; N=8,035 weighted to represent approximately 36.5 million unique persons per year.
\textsuperscript{†} Determined by survey-weighted \( t \) tests of means or proportions.
\textsuperscript{‡} Statistical comparisons between prescription expenditure threshold groups on prescription use and expenditures not performed since group membership was defined by prescription expenditures.

CPI-U=Consumer Price Index for all Urban Consumers; ER=emergency room.
## TABLE 5
Distribution (%) of Total Annual Prescription Expenditures by Therapeutic Class*

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Overall (N=8,035)</th>
<th>Older Adults With Prescription Expenditures ≤$3,810 (N=7,233)</th>
<th>Older Adults With Prescription Expenditures &gt;$3,810 (N=802)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular drugs</td>
<td>25.6</td>
<td>28.6</td>
<td>20.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>5.0</td>
<td>5.6</td>
<td>3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antianginal agents</td>
<td>0.9</td>
<td>0.8</td>
<td>1.2</td>
<td>0.053</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>4.6</td>
<td>5.3</td>
<td>3.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCBs</td>
<td>5.2</td>
<td>5.8</td>
<td>4.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diuretics</td>
<td>1.7</td>
<td>1.8</td>
<td>1.5</td>
<td>0.08</td>
</tr>
<tr>
<td>Combination medications</td>
<td>2.6</td>
<td>3.4</td>
<td>1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ARBs</td>
<td>2.2</td>
<td>2.3</td>
<td>2.0</td>
<td>0.298</td>
</tr>
<tr>
<td>Others</td>
<td>3.4</td>
<td>3.6</td>
<td>3.0</td>
<td>0.193</td>
</tr>
<tr>
<td>Antihyperlipidemics</td>
<td>14.2</td>
<td>14.5</td>
<td>13.7</td>
<td>0.577</td>
</tr>
<tr>
<td>HMG-CoA</td>
<td>13.2</td>
<td>13.4</td>
<td>12.9</td>
<td>0.694</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>0.3</td>
<td>0.3</td>
<td>0.2</td>
<td>0.087</td>
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<tr>
<td>Fibrin acid</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.785</td>
</tr>
<tr>
<td>Bile acid sequestrants</td>
<td>0.1</td>
<td>0.1</td>
<td>0.0</td>
<td>0.031</td>
</tr>
<tr>
<td>Hormones</td>
<td>13.7</td>
<td>13.9</td>
<td>13.3</td>
<td>0.606</td>
</tr>
<tr>
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<td>7.2</td>
<td>6.1</td>
<td>9.3</td>
<td>&lt;0.001</td>
</tr>
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<td>Thyroid drugs</td>
<td>1.2</td>
<td>1.6</td>
<td>0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estrogens</td>
<td>1.2</td>
<td>1.6</td>
<td>0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gastrointestinal agents</td>
<td>8.9</td>
<td>8.0</td>
<td>10.7</td>
<td>0.01</td>
</tr>
<tr>
<td>PPIs</td>
<td>6.7</td>
<td>5.9</td>
<td>8.1</td>
<td>0.016</td>
</tr>
<tr>
<td>H2 antagonists</td>
<td>1.7</td>
<td>1.6</td>
<td>1.8</td>
<td>0.454</td>
</tr>
<tr>
<td>Analgesics</td>
<td>6.7</td>
<td>6.7</td>
<td>6.8</td>
<td>0.865</td>
</tr>
<tr>
<td>COX-2 inhibitors</td>
<td>3.6</td>
<td>3.6</td>
<td>3.6</td>
<td>0.982</td>
</tr>
<tr>
<td>Narcotics</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.944</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>1.3</td>
<td>1.5</td>
<td>1.0</td>
<td>0.011</td>
</tr>
<tr>
<td>Salicylates</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.999</td>
</tr>
<tr>
<td>Psychotherapeutic agents</td>
<td>5.3</td>
<td>4.9</td>
<td>6.2</td>
<td>0.029</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>3.6</td>
<td>3.2</td>
<td>4.2</td>
<td>0.031</td>
</tr>
<tr>
<td>Anxietolitics, sedatives, hypnotics</td>
<td>1.2</td>
<td>1.1</td>
<td>1.3</td>
<td>0.295</td>
</tr>
<tr>
<td>Respiratory agents</td>
<td>5.4</td>
<td>4.5</td>
<td>6.9</td>
<td>0.011</td>
</tr>
<tr>
<td>Bronchodilators</td>
<td>2.8</td>
<td>2.0</td>
<td>4.2</td>
<td>0.003</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>1.4</td>
<td>1.5</td>
<td>1.2</td>
<td>0.23</td>
</tr>
<tr>
<td>Topical agents (including ophthalmics)</td>
<td>3.9</td>
<td>4.3</td>
<td>3.2</td>
<td>0.016</td>
</tr>
<tr>
<td>Nonanalgesic CNS agents</td>
<td>4.3</td>
<td>4.0</td>
<td>4.9</td>
<td>0.144</td>
</tr>
<tr>
<td>Coagulation modifiers</td>
<td>3.8</td>
<td>3.4</td>
<td>4.5</td>
<td>0.026</td>
</tr>
<tr>
<td>Others</td>
<td>8.1</td>
<td>7.2</td>
<td>9.7</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Data are presented as percentage of total annual drug expenditures.
† Determined by survey-weighted t tests of proportions. Null hypothesis: \([\sum \text{expenditures for drug class}/\sum \text{total drug expenditures}] \text{for older adults with expenditures} <$3,810 - [\sum \text{expenditures for drug class}/\sum \text{total drug expenditures}] \text{for older adults with expenditures} >$3,810 = 0.\n
ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers; CCBs = calcium channel blocker; CNS = central nervous system; HMG-CoA = HMG Coenzyme A reductase inhibitor; COX-2 = cyclooxygenase-2; NSAIDs = nonsteroidal anti-inflammatory drugs; PPIs = proton pump inhibitors.
The incidence of adverse drug events (ADEs) resulting from either medication errors or ADRs is estimated at 27% per year among older adults in the ambulatory setting. Approximately 39% of these ADEs were considered ameliorable or preventable and were attributed to poor communication between physician and patient regarding ADE symptoms and prescribing errors, respectively. Both the level of comorbidity burden and the number of medications used have demonstrated dose-response relationships with the risk of ADEs. Furthermore, ADEs among older adults in the ambulatory setting have been associated with $1,310 and $1,983 higher medical costs, respectively, in the 6 weeks post-ADE onset compared with the 6 weeks pre-ADE.

Pharmacists, along with physicians and nurse practitioners, are in unique positions to identify potential candidates for MTMP services. However, identifying potential candidates is only the first step because providers of these services will face substantial challenges. Older adults experience high rates of inappropriate drug use, polypharmacy, and ADEs, and as a more medically complex group, MTMP candidates will represent a special population in which such services can have a significant impact. Community pharmacists may be a logical choice as providers of MTMP services because of their accessibility to beneficiaries and their in-depth training and experience in providing pharmaceutical care. Pharmacists, either as leaders of interventions or as members of a disease management team, have contributed to improvements in outcomes and compliance in patients with hypertension and heart failure.

Community pharmacist-led services can improve patient outcomes and change patient behavior across chronic conditions, including hypertension, hypercholesterolemia, heart failure, and diabetes. Clinical pharmacy services in ambulatory older adults have led to improvements in the quality of drug use, patient adherence, and suboptimal prescribing. In a study of patients from Veterans Affairs medical centers at high risk for drug-related problems, pharmacist interventions resolved 69% of medication-related problems, significantly improved lipid measurements in patients with dyslipidemia, and demonstrated a dose-response relationship between quality of life and the number of pharmacist contacts. Also, despite the increased number of clinic visits and costs of pharmacist interventions, overall health care expenditures were similar for patients randomized to see a clinical pharmacist versus usual medical care. Despite the observed benefits of pharmacist-led interventions, evidence of the extent of their effectiveness has been inconsistent due to small sample sizes, lack of appropriate adjustment for confounding, and variation in the interventions and definitions of pharmaceutical care.

Another implication for Medicare is that older adults who met the prescription expenditure threshold incurred significantly higher total health care and nonpharmacy medical expenditures. This group was also more likely to have outpatient visits, inpatient and emergency department admissions, and home health visits. Medicare spending exceeded $300 billion in 2004, with the costliest 5% of beneficiaries accounting for 43% of total spending. In light of these estimates and the rapid growth in Medicare spending, a push to focus on high-cost Medicare beneficiaries has been advocated. From the perspective of Medicare, these findings highlight that the importance of focusing on beneficiaries who qualify for MTMP services stretches far beyond prescription drug use.

**Limitations**

First, our results should be interpreted in the context that this study relies heavily on self-reported data and has potential for errors in data collection, editing, and imputation. For example, the data used to determine the number of chronic conditions came from the 2002 and 2003 Medical Conditions files and were based on an assigned ICD-9-CM code imputed by MEPS professional coders for each condition reported. The extent that these conditions were truly chronic within the study population was not verified and may have overestimated the level of comorbidity within the study population. Second, although our estimates for the older adult population are consistent with other studies, only 53% of the prescribed medicines from the MPC pharmacies were exactly matched to drug mentions in the HC. Exact matches were based on drug code, medication name, and the round in which the drug was reported. Drug mentions in the HC that were not exactly matched to MPC pharmacy data were statistically matched to the entire MPC pharmacy data by medication name, drug code, type of third-party coverage, health conditions, age, sex, and other characteristics of the individual to obtain expenditure information. Third, because of the significant editing, coding, and accuracy checks that MEPS data incur before being released, there is a 3-year lag between the year released and the data year. Recently, data from 2004 became available from MEPS. Fourth, older adults who chose to have prescription drug insurance might have been more likely to be in the high-expenditure group (either from adverse selection, moral hazard, or a combination of the two). We were unable to measure the extent of these 2 phenomena; however, after controlling for other significant predictors, having any type of insurance coverage for prescription drugs was not significant as a predictor of meeting the expenditure threshold.

**Conclusions**

Approximately 9.2% (3.3 million) adults aged 65 years or older qualified for the prescription expenditure threshold ($4,000 per year) for MTMPs under Medicare Part D on the basis of MEPS data from 2002 and 2003. Older adults who would have qualified had substantially more chronic conditions, were more likely to report requiring help with ADLs, were more likely to report having functional difficulties such as walking, lifting, and performing housework, and were more likely to be on Medicaid.
Within this population, increasing age was associated with a lower likelihood of meeting the expenditure threshold. Among chronic conditions, diabetes, dyslipidemia, and stomach/duodenal ulcers were associated with the highest risk of meeting the medication expenditure threshold. Our results have uncovered a clear redundancy in the 3 qualifying criteria for MTMP. Further analyses also revealed that older adults meeting the prescription drug expenditure threshold accounted for significantly higher nonpharmacy health care expenditures and more office visits, emergency department visits, and hospitalizations. These results suggest that MTMP may also have an important role beyond prescription drug use.

**What is already known about this subject**

- Health care utilization, including prescription drugs, rises with age.
- Older adults with greater disease burden and who have more-severe conditions tend to consume more prescription drugs and are therefore more likely to qualify for Medicare MTMP services.
- Medicare Part D has been in existence for just 1 year, and little research has been conducted that examines the population size and the characteristics of beneficiaries who qualify for MTMP services.

**What this study adds**

- This research estimates that 3.3 million noninstitutionalized older adults in 2002-2003 would have met the $4,000 per-year threshold to qualify for Medicare MTMP services.
- This research quantifies the level of comorbidity burden, prescription drug use, and the overall health care use and expenditures of older adults who met the MTMP drug expenditure threshold experience and estimates the magnitude of the differences observed between older adults who would have met the MTMP expenditure threshold and the older adults who would not have met the MTMP expenditure threshold.
- The present study provides insight into characteristics, other than current drug spending, that PDPs and Medicare Advantage PDPs may use to identify MTMP candidates.

**DISCLOSURES**

No outside funding supported this study. The authors disclose no potential bias or conflict of interest relating to this article. Author Gregory W. Daniel served as principal author of the study. Study concept and design were contributed by Daniel, with input from author Daniel C. Malone. Data collection and interpretation were the work of Daniel. Writing of the manuscript was primarily the work of Daniel, with input from Malone; its revision was the work of both authors.

**REFERENCES**


Characteristics of Older Adults Who Meet the Annual Prescription Drug Expenditure Threshold for Medicare Medication Therapy Management Programs


Examination of Multiple Medication Use Among TRICARE Beneficiaries Aged 65 Years and Older

Andrea Linton, MS; Mathew Garber, PhD; Nancy K. Fagan, DVM, PhD; and Michael R. Peterson, DVM, DrPH

ABSTRACT

BACKGROUND: The simultaneous use of multiple prescription medications has been associated with an increased risk of adverse drug events and other drug-related complications, especially in the elderly.

OBJECTIVE: To quantify the prevalence of use of multiple medications among a sample of Department of Defense (DoD) health care beneficiaries, aged 65 years and older who used their TRICARE (military health care services) benefit to obtain prescription medication.

METHODS: Outpatient pharmacy fill records were analyzed for a 10% random sample of 1.27 million TRICARE beneficiaries aged 65 years and older who used 1 or more prescription medications in the 90-day period from December 1, 2004, through February 28, 2005. The First DataBank generic code number was used to identify drugs and to calculate the mean number of medications obtained and the mean, frequency, and type of American Hospital Formulary System drug therapy categories. Statistical significance for gender and age subgroups was tested via independent t-tests.

RESULTS: There were 1,268,162 users of the TRICARE pharmacy benefit in the 90-day study period from December 1, 2004, through February 28, 2005, approximately 72.7% of 1,744,072 eligible beneficiaries. The 10% sample of these users (n = 126,682) accounted for 1,091,699 pharmacy fill records for 761,043 unique medications, or an average of 6.01 [SD ± 4.01] unique medications per user, distributed across an average of 3.80 [±2.08] therapeutic categories; 8.8% of users received 1 medication, 50.0% received 5 or more medications from an average of 3 therapeutic categories, and 2.8% obtained 16 or more medications from an average of 8 therapeutic categories.

Multiple drug use was more prevalent among women relative to men, with an average of 6.28 [±4.12] medications from 4.03 [±2.11] therapeutic categories for women versus an average of 5.69 [±3.85] medications from an average of 3.80 [±2.08] therapeutic categories for men (P < 0.001). The prevalence of multiple drug use peaked among beneficiaries aged 80 to 84 years. Cardiovascular drugs, central nervous system agents, and hormones and synthetic substitutes were the 3 most common therapeutic categories used by 77%, 48%, and 42% of beneficiaries, respectively.

CONCLUSION: This baseline analysis documented the common use of multiple medications among TRICARE beneficiaries. The DoD faces a challenge similar to that of Medicare Part D drug plans to cost-effectively monitor and optimize pharmacotherapy for its older beneficiaries.

KEYWORDS: Senior drug utilization, TRICARE, Department of Defense

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The simultaneous use of multiple prescription medications has been repeatedly identified as an area of concern, particularly among our nation’s older adults.1 While older adults typically require more medications to manage multiple comorbidities, disease-centric prescribing, reduced organ function, and higher use of over-the-counter products among older adults complicates a prescriber’s or pharmacist’s ability to anticipate how concomitant use of multiple medications is likely to affect the underlying mechanisms by which each functions as prescribed.2,3 While risks associated with use of specific medications or combinations of medications among older patients have been well characterized,4,6 assimilation of this information into prescribing practice is not evident. Perhaps many prescribers simply cannot consider all the medications their patients are already taking when they prescribe a new medication.1 The likelihood of patients becoming confused by or noncompliant with their own drug regimen also increases with the size of their medication list.2 Too often, a critical review of a patient’s medication use is not conducted until after an adverse drug event occurs and has been recognized as such.6

Many of the studies examining multiple medication use by older adults to date have focused on non-U.S. populations, whereas studies on U.S. populations have focused more on inappropriate prescribing and medication-specific risks. Among the available literature, there is general agreement that multiple prescription medication use is more prevalent among older adults, women, and cardiovascular patients, but estimates vary widely and comparison of findings is complicated by the absence of a standard time period over which medication use
No clear standard has emerged regarding the number of tests using SPSS, Base 10.0. A number of studies estimate the percentage of health insurance was used to purchase prescription medication. Among a 10% sample of 1.27 million Department of Defense (DoD) TRICARE (military health care services) beneficiaries, aged 65 years and older, who used their TRICARE benefit to obtain prescription medication. The TRICARE pharmacy benefit is available to all DoD beneficiaries in all locations, including retired service members, their spouses, and other dependents, and dependents of deceased service members (older veterans will be eligible under TRICARE only if they completed a full military career before retiring from service). Beneficiaries need only a valid DoD identification card and a prescription to use the benefit.

At the time of this study, prescriptions could be filled at military pharmacies at no cost or through a mail-order or a network community pharmacy with a $3 copayment for generic or $9 copayment for brand medications. Beneficiaries could also fill prescriptions at a nonnetwork community pharmacy, with the potential for a point-of-service deductible and higher copayment, though this option was not frequently used by beneficiaries aged 65 years and older. TRICARE does not impose premiums, enrollment fees, benefit caps, or plan-wide deductibles that increase the patient’s cost burden beyond the point-of-service copayment amount, or otherwise promote periods of potential noncoverage. Benefits could use their prescription drug benefit without using any other health care services offered under TRICARE, and TRICARE was a secondary payer if other health insurance was used to purchase prescription medication.

The purpose of the current research was to quantify and characterize multiple medication use among the DoD beneficiaries aged 65 years and older with the ultimate goal of assessing the need for additional interventions to mitigate risks posed to older adults by the growing role of pharmaco-therapy in their treatment regimen.

Methods

The DoD maintains an enterprise-wide information system that captures patient demographic and prescription information for each prescription filled by a beneficiary using the TRICARE pharmacy benefit. A fill record is created in real-time when the prescription is filled regardless of whether a military, community, or mail-order pharmacy is used. The fill records are forwarded to a central data repository and processed for data validity and consistency, such as the removal of transactions that have been reversed (e.g., prescriptions that were filled but never picked up) and the coding of a unique patient identifier that enables the matching of patient-level data with other DoD administrative systems.

Since the TRICARE drug benefit allows beneficiaries to obtain a maximum 90-day supply of medication at a time, 90 days was the shortest period of time that allowed us to obtain a snapshot of drug use among the study population while minimizing the impact of 1-time medication fills and changes in medication dosing on our estimates of the number of medications obtained. A census of outpatient pharmacy fill records for beneficiaries aged 65 years and older for a 90-day period (December 1, 2004, through February 28, 2005) was extracted from this central repository in July 2005, resulting in a total of 11,390,888 fill records.

A total of 5.5% of fill records were then excluded from the dataset on the basis of missing data (such as missing person or product identifier), clinician-administered prescriptions, or nondrug items, yielding a net of 10,768,945 fill records. These fill records were aggregated into patient-level records for 1,268,162 unique beneficiaries that included all prescriptions filled for each beneficiary during the study period. In order to reduce the computing resources required for analysis of a population of this size, we selected a 10% random subsample of beneficiaries for analysis. A 10% subsample ensured that our findings were representative of the study population within a 99.5% confidence level. The final dataset included 1,091,699 pharmacy fill records, corresponding to 761,043 unique medications dispensed to 126,682 beneficiaries.

The First DataBank generic code number (GCN) was used to define unique medications, and the level 1 (2-digit) American Hospital Formulary System (AHFS) nomenclature was used to define therapeutic categories. The level 1 therapeutic category represents the highest level of AHFS categorization and comprises a total of 30 categories, one of which is a placeholder category for new medications that have not yet been permanently placed in the AHFS nomenclature (therapeutic category 92, Unclassified Agents). Therapeutic categories were ranked by number and frequency of beneficiary use, and the mean number of medications obtained per beneficiary within each therapeutic category was calculated.

The mean number of medications obtained and therapeutic categories used were calculated by beneficiary gender and age group. The distributions of beneficiaries by the total number of medications obtained and therapeutic categories used within the 90-day study period were constructed and analyzed. The statistical significance of differences between subgroups was assessed using independent t tests using SPSS, Base 10.0.
Results

Overall, 72.7% of eligible TRICARE beneficiaries aged 65 years and older used their TRICARE benefit to obtain prescription medication during the 90-day study period (Table 1). The frequencies of men and women using their pharmacy benefit were 69.3% and 75.9%, respectively. Pharmacy benefit use ranged from 72.5% to 73.9% in the 80 to 84-year age group, but dropped to 66.6% among beneficiaries aged 85 years and older. Approximately 95.5% of TRICARE pharmacy benefit users used other TRICARE health care services in the 9 months preceding the study period, the majority of which (90%) obtained most or all of their care through civilian providers (data not presented). The remaining 4.5% of TRICARE pharmacy beneficiaries who did not use their TRICARE health services benefit either used no services or obtained health care services through another health plan.

The number and percentage of beneficiaries in the sample population who obtained 1 or more medications in each therapeutic category are presented in Table 2. Cardiovascular drugs (24) were used by 77.0% of the beneficiaries aged 65 years and older who filled a prescription during the study period. Most frequently obtained cardiovascular medications were (in descending order) statins, renin-angiotensin system inhibitors, beta-blockers, and calcium channel blockers. Central nervous system agents (28) were obtained by 47.7% of beneficiaries and included primarily anti-inflammatories, pain relief medications, and antidepressants. Hormones and synthetic substitutes (68) were obtained by 41.8% of the sample population and included antidiabetic and thyroid medications. These 3 therapeutic categories were also associated with the highest mean number of medications obtained per beneficiary, 2.27 (±1.31) for cardiovascular medications, 1.93 (±1.34) for central nervous system agents, and 1.54 (±0.83) for hormones and synthetic substitutes.

Approximately 31% of beneficiaries obtained medications in each of the following categories: gastrointestinal drugs (56); anti-infective agents (8); or electrolytic, caloric, and water balance agents (40). A total of 28.6% of beneficiaries obtained unclassified therapeutic agents (92), which are medications that have not been permanently placed in the AHFS nomenclature. This percentage corresponded to 42,205 of the 761,043 (5.5%) of the unique medications obtained by the sample population during the study period and included primarily brand medications for treatment of osteoporosis, enlarged prostate, gout, asthma, and seasonal allergies, as well as anticoagulating agents. Each of the remaining therapeutic categories was used by less than 20% of the beneficiary population.

The mean number of individual medications obtained across all therapeutic categories and the mean number of therapeutic categories used, by gender and age group, are presented in Table 3. Overall, the sample population obtained a mean of 6.01 (±4.01) medications and 3.80 (±2.08) therapeutic categories during the 90-day study period (refills excluded). Both the mean number of medications obtained and the therapeutic categories used were significantly higher among women relative to men within each age group and increased significantly for both men and women with increasing age up to the age of 85 years.

The number, percentage, and cumulative percentage of beneficiaries and the mean number of therapeutic categories used relative to the number of medications obtained during the study period are presented in Table 4. A total of 11,128 examinations of multiple medication use among TRICARE beneficiaries aged 65 years and older.

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**TABLE 1**

Population Characteristics for TRICARE Eligibles, TRICARE Pharmacy Benefit Users, and 10% Study Sample, Aged 65 Years or Older

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TRICARE Eligibles*</th>
<th>TRICARE Pharmacy Benefit Users†</th>
<th>10% Study Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Total</td>
<td>1,744,072</td>
<td>1,268,162</td>
<td>72.7</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>842,218</td>
<td>583,679</td>
<td>69.3</td>
</tr>
<tr>
<td>Women</td>
<td>901,854</td>
<td>684,483</td>
<td>75.9</td>
</tr>
<tr>
<td>Age group, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>532,386</td>
<td>386,100</td>
<td>72.5</td>
</tr>
<tr>
<td>70-74</td>
<td>483,857</td>
<td>357,233</td>
<td>73.8</td>
</tr>
<tr>
<td>75-79</td>
<td>333,003</td>
<td>246,053</td>
<td>73.9</td>
</tr>
<tr>
<td>80-84</td>
<td>253,591</td>
<td>184,763</td>
<td>72.9</td>
</tr>
<tr>
<td>85+</td>
<td>141,235</td>
<td>94,013</td>
<td>66.6</td>
</tr>
</tbody>
</table>

* Total number of beneficiaries aged 65 years or older eligible for the TRICARE (military health care services) pharmacy benefit on January 15, 2005.
† Users of the pharmacy benefit during the 90-day period from December 1, 2004, through February 28, 2005.
Examination of Multiple Medication Use Among TRICARE Beneficiaries Aged 65 Years and Older

beneficiaries (8.8%) in the study population obtained only 1 medication and 3,528 beneficiaries (2.8%) obtained 16 or more medications during the 90-day study period (refills excluded). The median of the distribution occurred at 5 medications and the mode occurred at 4 medications. The mean number of therapeutic categories used ranged from 1.74 (±0.44) for beneficiaries who obtained 2 medications to 8.49 (±1.55) for beneficiaries who obtained 16 or more medications. The distribution of beneficiaries by number of medications obtained during the study period is graphically presented in Figure 1.

The distribution of beneficiaries by number of therapeutic categories used during the study period is graphically presented in Figure 2. A total of 16,533 beneficiaries (13.1%) in the study population used only 1 therapeutic category, and 3,192 beneficiaries (2.5%) used 9 or more therapeutic categories during the 90-day study period. The median and mode of the distribution occurred at 3 therapeutic categories (tabular data not presented).

Discussion

Our findings present a snapshot of the frequency and type of multiple-medication use among a sample of older adults aged 65 years and older. From a 10% sample of the 1.27 million DoD health care beneficiaries who used their TRICARE pharmacy benefit during the 90-day study period, half obtained 5 or more medications concomitantly from a mean of 3 therapeutic categories, and 2.8% obtained 16 or more prescription medications from a mean of 8 therapeutic categories. Prior studies among the elderly found that the risk of an adverse drug event exceeded 50% with the concomitant use of 5 or more medications, suggesting that some form of intervention might be warranted for those beneficiaries at the higher end of the use spectrum.\(^2,13\) We found that medication use generally increased with increasing patient age but peaked among the 80-to-84-year-olds. The rate of increase was gradual because of the relatively high medication use by the youngest age group examined, 65-to-69-year-olds, with means of 5.2 and 6.0 medications and 3.3 and 3.9 therapeutic categories for men and women, respectively. This finding is consistent with other studies that found prescription medication use for many older adults began before age 65.\(^18\) The standard error for the mean number of prescriptions and therapeutic categories used, however, indicates a wide and relatively similar variation in pharmaceutical use within all age groups. We found

<table>
<thead>
<tr>
<th>Level 1 AHFS Therapeutic Category</th>
<th>N(^*)</th>
<th>%</th>
<th>Mean Rx (SE)(^†)</th>
<th>Most Frequently Obtained Types of Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 Cardiovascular</td>
<td>97,551</td>
<td>77.0</td>
<td>2.27 (±1.31)</td>
<td>Statins, renin-angiotensin system inhibitors, beta-adrenergic blocking agents, calcium channel blocking agents</td>
</tr>
<tr>
<td>28 Central nervous system</td>
<td>60,436</td>
<td>47.7</td>
<td>1.93 (±1.34)</td>
<td>Nonsteroidal anti-inflammatory agents, opiate antagonists, antidepressants</td>
</tr>
<tr>
<td>68 Hormones and synthetic</td>
<td>52,973</td>
<td>41.8</td>
<td>1.54 (±0.83)</td>
<td>Antidiabetics, thyroid agents</td>
</tr>
<tr>
<td>56 Gastrointestinal</td>
<td>39,500</td>
<td>31.2</td>
<td>1.20 (±0.50)</td>
<td>Proton pump inhibitors</td>
</tr>
<tr>
<td>08 Anti-infective</td>
<td>39,156</td>
<td>30.9</td>
<td>1.40 (±0.74)</td>
<td>Antibiotics (systemic)</td>
</tr>
<tr>
<td>40 Electrolytic, caloric, water</td>
<td>38,960</td>
<td>30.8</td>
<td>1.30 (±0.56)</td>
<td>Diuretics</td>
</tr>
<tr>
<td>92 Unclassified therapeutic class</td>
<td>36,222</td>
<td>28.6</td>
<td>1.17 (±0.43)</td>
<td>Alendronate sodium, clopidogrel bisulfate, tamsulosin HCl, xanthine oxidase inhibitors</td>
</tr>
<tr>
<td>52 Eye, ear, nose, and throat</td>
<td>24,644</td>
<td>19.5</td>
<td>1.36 (±0.71)</td>
<td>Anti-inflammatory agents, antibiotics</td>
</tr>
<tr>
<td>12 Autonomic drugs</td>
<td>22,578</td>
<td>17.8</td>
<td>1.41 (±0.74)</td>
<td>Sympathomimetic (adrenergic) agents</td>
</tr>
<tr>
<td>84 Skin and mucus membrane</td>
<td>17,868</td>
<td>14.1</td>
<td>1.30 (±0.65)</td>
<td>Anti-inflammatory agents, antifungals</td>
</tr>
<tr>
<td>04 Antihistamines</td>
<td>14,301</td>
<td>11.3</td>
<td>1.07 (±0.28)</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>48 Antitussives, expectorants</td>
<td>10,408</td>
<td>8.2</td>
<td>1.16 (±0.42)</td>
<td>Antitussives</td>
</tr>
<tr>
<td>20 Blood formation and coagulation</td>
<td>10,319</td>
<td>8.1</td>
<td>1.24 (±0.53)</td>
<td>Anticoagulants</td>
</tr>
<tr>
<td>86 Smooth muscle relaxants</td>
<td>6,938</td>
<td>5.5</td>
<td>1.05 (±0.22)</td>
<td>Genitourinary and respiratory smooth muscle relaxants</td>
</tr>
<tr>
<td>88 Vitamins</td>
<td>5,902</td>
<td>4.7</td>
<td>1.07 (±0.27)</td>
<td>Vitamin B complex</td>
</tr>
<tr>
<td>10 Antineoplastic agents</td>
<td>3,633</td>
<td>2.9</td>
<td>1.06 (±0.26)</td>
<td>Antineoplastic agents</td>
</tr>
<tr>
<td>All other therapeutic categories</td>
<td>184</td>
<td>0.1</td>
<td>1.05 (±0.28)</td>
<td></td>
</tr>
</tbody>
</table>

\(^*\) Categories are not mutually exclusive; beneficiaries were counted under each therapeutic category used during the study period.  
\(^†\) Mean and standard error for number of medications, obtained within the level 1 AHFS therapeutic category per beneficiary.
that women, on average, obtained 10% more prescription medications than men. This finding is consistent with other studies that found medication use by women exceeded that of men by 9% to 26%.9,10

Our estimates of the number of prescription medications being used by the study population generally exceeded those of previous studies of U.S. populations, but direct comparison of findings was complicated by the absence of a standard method for assessing medication use. A 1987 chart review of ambulatory patients in Kentucky, aged 60 years and older, found that 32% took 5 or more prescription medications concurrently, with a mean of 3.75 and 4.22 prescription medications for men and women, respectively.10 A 1995 claims-based study of Medicare-eligible beneficiaries aged 65 years and older in Texas found that 23% received 6 or more prescription medications during a 3-month period.20 A 1999 claims-based study of New England veterans reported that a mean of 3.54 prescription medications were used by patients over a 6-month period.21 A 1999 national survey of ambulatory adults reported that 23% of the adults aged 65 years and older used 5 or more prescription medications over a 7-day study period.21

The estimates reported in studies of non-U.S. populations varied as well.2 A 1997 study of long-term prescription drug use (>240 days) in the Netherlands found that 42% of elderly patients used 2 or more medications and 4% used 5 or more medications concomitantly on a long-term basis.23 A survey-based study in Finland found that concomitant use of 6 or more medications increased from 19% of the community-dwelling population aged 64 years or older in 1990-1991 to 25% in 1998-1999.24 A Danish study of prescription data found that two thirds of all prescription medication users older than 70 years used 2 or more prescription medications.25 And a 1998 Canadian study of emergency department patients aged 65 years and older found that 91% of the study population was taking at least 1 medication, and the mean number of medications used simultaneously was 4.2 ± 3.1.8

It is not clear whether our study findings are higher as a result of our methodology, higher use resulting from DoD beneficiaries’ access to a generous drug benefit, or the later time period of our study, following several years of unprecedented growth in sales in the pharmaceutical industry.26 Most likely, all these factors contributed to higher estimates of multiple medication use among the population in the current study.

Consistent with other studies, we found that cardiovascular drugs were the most commonly used medications among older adults, and cardiovascular medication users were the largest overall consumers of medication in the study population.9 Heart failure, for example, has been characterized as a condition that, to be effectively managed, requires multiple medications, but it is also associated with overuse of ineffective medications for concomitant conditions.27,28 In a case study of a patient diagnosed with heart failure, hypertension, diabetes, and several other comorbidities, the conduct of a critical medication review and 2 years of monitoring resulted in a reduction in the patient’s medication list from 11 to 5.28 While this intervention was patient-specific, it highlighted the potential for reducing the size of the medication lists for a cardiovascular patient with multiple comorbidities. Other initiatives cited in the literature reported significant reductions in both the number of medications taken and total monthly prescription costs.29,30

A strong argument might be made that the prescribing patterns implied by our findings may be generalizable to other insured ambulatory populations of older adults who use prescription medication. Both the DoD population of beneficiaries

![Table 3](image-url)

**TABLE 3** Mean Number of Medications Obtained and Therapeutic Categories Used, by Age Group and Gender

<table>
<thead>
<tr>
<th>Age Group, Years</th>
<th>Total Mean (SE) Rx*</th>
<th>Total Mean (SE) Therapeutic Categories†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N = 126,682)</td>
<td>(N = 58,338)</td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>5.65 (±4.01)</td>
<td>5.25 (±3.82)</td>
<td>0.000</td>
</tr>
<tr>
<td>70-74</td>
<td>6.00 (±4.04)</td>
<td>5.68 (±4.02)</td>
<td>0.000</td>
</tr>
<tr>
<td>75-79</td>
<td>6.24 (±3.99)</td>
<td>6.01 (±3.98)</td>
<td>0.000</td>
</tr>
<tr>
<td>80-84</td>
<td>6.34 (±3.97)</td>
<td>6.07 (±4.00)</td>
<td>0.000</td>
</tr>
<tr>
<td>85+</td>
<td>6.25 (±3.90)</td>
<td>6.02 (±4.09)</td>
<td>0.000</td>
</tr>
<tr>
<td>Total</td>
<td>6.01 (±4.01)</td>
<td>5.69 (±3.97)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

* Mean and standard error for number of medications obtained across all level 1, AHFS therapeutic category.
† Mean and standard error for number of level 1 AHFS therapeutic categories used.
AHFS=American Hospital Formulary System; Rx=prescription.
Examination of Multiple Medication Use Among TRICARE Beneficiaries Aged 65 Years and Older

Aged 65 years and older and the prescribers who treated them were geographically distributed and integrated with the non-DoD population. More than 90% of the study beneficiaries received most, if not all, of their health care services through civilian providers who also treated the general population. Furthermore, there are no data to indicate that this older DoD health care beneficiary population would experience the incidence and progression of disease and the associated need for medication differently from other older adults nationwide. While it is possible that the absence of benefit caps or periods of noncoverage and relatively small copayments under TRICARE made compliance with their medication regimen more affordable for the DoD beneficiaries aged 65 years and older compared with those who used other plans (or no plan at all), it is unlikely that prescribers treated older DoD beneficiaries differently from other older adults.

Our findings indicate that approximately 73% of the eligible TRICARE beneficiaries used their TRICARE pharmacy benefit during the study period. Findings from the Third National Health and Nutrition Survey indicated that 74% of the respondents aged 65 years and older confirmed recent use of prescription medication. Despite the congruence of these ratios, it is possible that some of the current study population might have obtained a portion of prescription medications from another health care provider during the study period, the result of which would be an understatement of the total number of medications obtained.

Some safeguards are in place to help protect beneficiaries from the risk posed by multiple drug therapies. In July 2001, DoD implemented an online screening tool that reviews a new prescription against all previous prescriptions filled and alerts the dispensing pharmacist to potentially dangerous drug combinations or therapeutic duplication on the patient’s medication list. This screening process occurs automatically at the time the prescription is filled, and is performed for all fills at military pharmacies, network community pharmacies, and the mail-order pharmacy.

Limitations

Our methodology introduced the potential for both overcounting and undercounting medications obtained by individual beneficiaries over the study period. The use of GCN numbers to count medications represents a potential source of overcounting in the number of medications in this study. By counting unique GCN numbers, we may have counted 1 medication as 2 medications if a beneficiary filled prescriptions for different dosages of the same medication. This potential for overcounting medications is likely offset to some extent by the 90-day study period. Although the TRICARE benefit does not permit dispensing greater than a 90-day supply of medication, it is possible that some beneficiaries obtained additional medications outside the 90-day study period or through a pathway not captured in our dataset.

<table>
<thead>
<tr>
<th>No. Rx*</th>
<th>(N)</th>
<th>(%)</th>
<th>Cumulative (%)</th>
<th>Mean (SE) Therapeutic Categories†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11,128</td>
<td>8.8</td>
<td>8.8</td>
<td>1.00 (±0.00)</td>
</tr>
<tr>
<td>2</td>
<td>13,515</td>
<td>10.7</td>
<td>19.5</td>
<td>1.74 (±0.44)</td>
</tr>
<tr>
<td>3</td>
<td>14,496</td>
<td>11.4</td>
<td>30.9</td>
<td>2.37 (±0.65)</td>
</tr>
<tr>
<td>4</td>
<td>14,597</td>
<td>11.5</td>
<td>42.4</td>
<td>2.98 (±0.79)</td>
</tr>
<tr>
<td>5</td>
<td>13,478</td>
<td>10.6</td>
<td>53.1</td>
<td>3.50 (±0.91)</td>
</tr>
<tr>
<td>6</td>
<td>12,064</td>
<td>9.5</td>
<td>62.6</td>
<td>4.00 (±0.99)</td>
</tr>
<tr>
<td>7</td>
<td>10,334</td>
<td>8.2</td>
<td>70.7</td>
<td>4.50 (±1.09)</td>
</tr>
<tr>
<td>8</td>
<td>8,496</td>
<td>6.7</td>
<td>77.4</td>
<td>4.96 (±1.14)</td>
</tr>
<tr>
<td>9</td>
<td>6,751</td>
<td>5.3</td>
<td>82.8</td>
<td>5.40 (±1.19)</td>
</tr>
<tr>
<td>10</td>
<td>5,346</td>
<td>4.2</td>
<td>87.0</td>
<td>5.82 (±1.25)</td>
</tr>
<tr>
<td>11</td>
<td>4,166</td>
<td>3.3</td>
<td>90.3</td>
<td>6.22 (±1.30)</td>
</tr>
<tr>
<td>12</td>
<td>3,198</td>
<td>2.5</td>
<td>92.8</td>
<td>6.58 (±1.35)</td>
</tr>
<tr>
<td>13</td>
<td>2,453</td>
<td>1.9</td>
<td>94.7</td>
<td>6.97 (±1.37)</td>
</tr>
<tr>
<td>14</td>
<td>1,797</td>
<td>1.4</td>
<td>96.2</td>
<td>7.33 (±1.39)</td>
</tr>
<tr>
<td>15</td>
<td>1,335</td>
<td>1.1</td>
<td>97.2</td>
<td>7.61 (±1.47)</td>
</tr>
<tr>
<td>16+</td>
<td>3,528</td>
<td>2.8</td>
<td>100.0</td>
<td>8.49 (±1.59)</td>
</tr>
<tr>
<td>All</td>
<td>126,682</td>
<td>100.0</td>
<td>100.0</td>
<td>3.80 (±2.08)</td>
</tr>
</tbody>
</table>

* Number of medications obtained across all therapeutic categories by beneficiary during the study period.
† Mean and standard error for number of level 1 AHFS therapeutic categories used.
AHFS=American Hospital Formulary System; Rx=prescription.

Distribution of Beneficiaries by Number of Medications Obtained During the Study Period
Our date-of-service period from December through February might also have been subject to seasonal variation in medication use. These months of the year have higher overall drug use relative to other months, so our findings may tend to overestimate actual medication use if annualized. On the other hand, most of the medications in this population are taken for chronic conditions and therefore are less susceptible to seasonal variation.

The absence of data for use of over-the-counter medications is another study limitation and contributes to a potentially significant underestimate of total medications obtained by the study population. The elderly are generally the heaviest users of over-the-counter medications, including vitamins, minerals, and herbal remedies, whose use is often not reported by patients unless they are specifically asked about it. A thorough medication review must consider all types of medications used by patients.

Finally, retrospective evaluation of prescription fill data has limitations. The study dataset would not include any prescriptions filled by beneficiaries who used other health insurance (without using TRICARE as a second payer) or no insurance to pay for their medication. Furthermore, pharmacy fill data only permit examination of dispensed medications, which may differ from actual medication consumption by beneficiaries. Beneficiary compliance with their medication regimen and the extent to which beneficiaries were using their medications concurrently are potentially important considerations that cannot be addressed through analysis of pharmacy fill or claims data.

**Conclusion**

In a 90-day period from December 1, 2004, through February 28, 2005, 73% of eligible TRICARE beneficiaries aged 65 years and older used the pharmacy benefit and received an average of 6 unique medications per user in an average of 4 therapeutic categories. Almost half of TRICARE pharmacy benefit users received 6 or more unique medications. Most study beneficiaries, however, received their health care services through either one of the large, DoD-contracted, civilian health care companies or another health plan, such as Medicare, which greatly limits the DoD's ability to coordinate care rendered by multiple prescribers. Optimizing medication use among its older beneficiaries represents a significant challenge for the DoD, similar to the one faced by many Medicare Part D drug plans that are required to implement their own medication therapy management programs. This was the first of several studies to aid DoD planners in crafting future pharmacy policy and benefit revisions to promote safer and more effective medication therapy for beneficiaries.

**What is already known about this subject**

- As the number of medications per person increases, so does the risk of an adverse drug event as well as higher likelihood of inappropriate drug use.

**What this study adds**

- 73% of eligible TRICARE beneficiaries aged 65 years and older used the pharmacy benefit in a given 90-day period, and almost half obtained 6 or more unique medications from 4 or more therapeutic categories.

**ACKNOWLEDGMENTS**

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**DISCLOSURES**

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Author Andrea Linton served as principal author of the study. Study concept and design were contributed by Linton, Petersen, and author Nancy K. Fagan. Data collection was the work of Linton, Fagan, and Peterson; data interpretation was the work of Linton and author Mathew Garber. Writing of the manuscript was the work of Linton and Garber; its revision was the work of all authors.

**REFERENCES**


Abstracts From Professional Poster Presentations at AMCP’s 19th Annual Meeting & Showcase

The following poster presentations have been prepared for the Academy of Managed Care Pharmacy’s 19th Annual Meeting & Showcase, April 11-14, 2007, in San Diego, California. 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 the 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 by most authors. The names of individuals who are scheduled to present at the meeting are underlined.

**A DRUG UTILIZATION REVIEW OF ANTIDIABETIC DRUGS IN AN INDIGENT HEALTH CARE PLAN**

**George SV.** Conexus Health, 6285 East Fowler Ave., Tampa, FL 33617

**OBJECTIVES:** Antidiabetic drugs account for more than 20% of the Hillsborough County Health Care Plan’s drug budget. A goal of improving the health care of patients is to achieve glycosylated hemoglobin (A1C) levels as indicated in published practice guidelines. Currently, no published data exists on the utilization and management of diabetes in the indigent patient population. This retrospective drug utilization review was performed to assess utilization patterns of antidiabetic drugs and the corresponding A1C levels in the indigent patient population.

**METHODS:** Patients are identified from the plan’s pharmacy claims system if they had at least 3 consecutive months of a prescription for an antidiabetic drug during 2004. Also, the identified patients had to be enrolled in the plan consecutively for at least 1 year. The physician who prescribed the antidiabetic drug was contacted to schedule a review of the identified patients’ medical records. Data collection focused on concomitant antidiabetic drug medication usage, demographic data, and laboratory A1C levels.

**RESULTS:** A total of 337 patients (194 female, mean age 53.8) met the inclusion criteria, representing 15 different primary care clinics. A total of 204 patients met the American Dietetic Association chart category for severely unhealthy based on height and weight; 318 patients had at least 1 comorbid condition, with the most common being hypertension (n=211). Only 124 patients had low-density-lipoprotein cholesterol (LDL-C) levels <100mg/dL. A total of 330 patients had at least 1 test for A1C level during the year, with 1.7 mean tests per year. The mean A1C level was 8.22, and 237 patients had A1C >7. During the year, 42 patients had referrals to a cardiologist for coronary heart disease-related events. More than 50% of the population was receiving at least 2 different antidiabetic drugs during the review period.

**CONCLUSION:** This retrospective drug utilization review provides much-needed information about the utilization patterns and outcomes of the indigent diabetic patient population.

**A PROCESS MAP: NEGOTIATING URAC ACCREDITATION FOR PHARMACY UTILIZATION MANAGEMENT**

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**BACKGROUND:** URAC, an independent, nonprofit organization, well-known as a leader in promoting health care quality through its accreditation and certification programs, is currently developing standards for the nation's first-ever accreditation programs for pharmacy benefits management (PBM).

**OBJECTIVE:** Since there are currently no URAC-accredited PBMs, this pharmacy care management company’s award of accreditation for its pharmacy prior authorization service should be helpful to PBMs seeking URAC accreditation for the utilization management portion of their application. By examining the process flow for preparation of the application, preparing for the site visit, and establishing ongoing compliance with established quality standards, PBMs will gain a better understanding of how to best prepare their organization to satisfy that portion of the accreditation process.

**METHODS:** This pharmacy care management organization was required to meet core URAC as well as health utilization management (HUM) standards for its prior authorization process. The application has several phases: preparation of the application, desk-top review, desk-top review summary and response, and finally the site visit. The poster graphically illustrates and details all stages of the application process. This process map outlines requirements similar to those required for the critically important drug use management module of the PBM standards.

**RESULTS:** It would be oversimplification to suggest that the result was full accreditation from URAC on the first try. More significant was the recognition of how instrumental URAC is in allowing an organization to achieve its full quality potential.

**CONCLUSIONS:** At the time this organization was awarded URAC accreditation for HUM, it was unique among URAC-accredited organizations in providing pharmacy prior authorization. Now URAC will soon accredit the full spectrum of PBM services.
thus offering payers the option of buy or build for URAC-accredited HUM programs for prior authorization.

**Achieving Efficient Interaction Between MCOS, SPPs, and Providers: A Distribution Activity Analysis**

**Baker II**, Pierce CA, McClard C. 2253 County Rd. 2390, Pickton, TX 75471; jbakera@consultresourcegroup.com, (903) 866-3614

**INTRODUCTION:** The purpose of this analysis is to promote more efficient interaction between managed care organizations (MCOs), specialty pharmacy providers (SPPs), and physician providers. The activity analysis traces multiple drug and biologic workflow processes involved in distribution to MCO physician providers and develops a pilot workflow model to serve as a benchmark for future study.

**METHODS:** The project utilizes a contingency theory framework in a dimension categorized as changing systems so they perform better technically. The study design for this activity analysis performed in a rheumatology practice incorporated process mapping and interviews to identify and trace applicable business activities. An MCO physician practice provider with advanced administrative management skills was selected for the pilot project, and an MCO drug distribution workflow model was developed using the activity analysis inputs.

**RESULTS:** The practice managed 7 plans utilizing 5 SPPs, of which 2 were nearby and 3 were out of state. All 5 SPPs used the advance delivery method (rather than the drug replacement method) and all 5 collected copays. Only 1 SPP delivered drugs in person; the other 4 shipped by overnight courier. Ordering involved 4 steps, and predelivery involved 2 steps. SPP ordering and distribution paperwork procedures were generally uniform, while procedures for emergencies and patient no-shows exhibited some variance. The degree of recurring distribution problems also varied among the SPPs.

**CONCLUSIONS:** Better technical performance of drug and biologic distribution processes results in more efficient interactive processes between plans, their specialty pharmacies, and physician providers. MCO decision makers should be aware of the potential impact on their provider processes when developing and contracting for an SPP program. Future expansion of this activity analysis may yield a generalizable SPP distribution model.

**Administration of Intravenous Therapies in Metastatic Breast Cancer: A Cost Analysis**

**Krusel GB, Amonkar MM**, Skonieczny D, Smith GL. GlaxoSmithKline, 1250 S. Collegeville, Rd., Collegeville, PA 19426; mayor.m.amonkar@gsk.com, (610) 917-7957

**INTRODUCTION:** There are significant costs associated with intravenous (IV) administration of cancer drugs. This study assessed the cost components of providing IV therapy to women with metastatic breast cancer (MBC).

**METHODS:** Claims and remittance data from >60 multispecialty medical practices/clinics covering more than 45,000 breast cancer patients was used. Women diagnosed with MBC (International Classification of Diseases, Ninth Revision [ICD-9] codes 174 plus 196-198) between January 1, 2003, and May 31, 2006, and receiving IV monotherapy were identified. Costs were estimated using the allowable amount for a claim, which closely represents the actual payments to providers. Costs were measured using 2 approaches: cost per IV administration visit and cost per patient per month (PPPM). Published literature was used to categorize the various components qualified for billing.

**RESULTS:** 828 patients receiving any of 11 IV breast cancer drugs were identified. The cost breakdown by category across all 11 drugs and for the 2 most commonly used drugs is presented in the table on page 205.

**CONCLUSIONS:** Excluding drug costs, costs associated with administration of the IV therapy and other visit-related services are >40% of total costs, which represents a significant cost burden to payers. The increasing availability and use of oral therapies for MBC could help offset some of these costs.

**Angiotensin Receptor Blocker (ARB) and Brand Angiotensin-Converting Enzyme Inhibitor (ACEI) Step-Therapy Program Outcomes**

**Gleason PP, Tran T**, Tiberg K, West B, Walters C, Lassen D. BlueCross BlueShield of Texas, 901 S. Central Expy., Richardson, TX 75080; tom_tran@bcbsmtx.com, (972) 766-8910

**INTRODUCTION:** A brand angiotensin-converting enzyme inhibitor/angiotensin receptor blocker ACEI/ARB step-therapy program requiring members to first try an ACEI is a common pharmacy benefit utilization management program; however, savings outcomes from this type of program have not been assessed.

**METHODS:** A BlueCross BlueShield population with an average of 65,524 members per month implemented an automated program, with grandfathering, on May 1, 2005. Members attempting to fill a brand ACEI/ARB claim who had either the identical drug or an ACEI claim in the prior 90 days were electronically authorized; all others were rejected plan coverage. All ACEI/ARB rejected claim members during the period from May 1, 2005-April 30, 2006, were evaluated for at least 4 months post their reject date. Cost avoidance was calculated using utilization and plan paid per claim (PPPC) for plan member groupings of average brand ACEIs/ARBs, generic ACEIs, and all other antihypertensive agents.

**RESULTS:** During the 12 month analysis period, members utilizing a brand ACEI/ARB averaged 5.6 claims at $36.52 PPC. Among the 65,524 members, 1,894 members initially had a rejected brand ACEI/ARB claim; 1,894 x 5.6 claims x $36.52 PPC = $387,346 estimated cost avoidance. 1,042 (55.0%) members
had an ACEI/ARB authorization; estimated 1,042 x 5.6 claims x $36.52 PPPC = $213,102 net cost. 376 (19.9%) members had a generic ACEI claim at an average PPPC of $10.58 x 5.6 claims x 376 members = $22,277 net cost, and 309 (16.3%) had an alternative antihypertensive claim at an average PPPC of $36.37 x 5.6 claims x 309 members = $62,935 net cost. 167 (8.8%) members had no antihypertensive claims found but could have received antihypertensive therapy through samples. Cost avoidance less the sum of net costs equals an $89,032 annual net plan paid savings, or $0.11 plan paid per member per month.

CONCLUSIONS: A brand ACEI/ARB step-therapy program resulted in the intended reduction in the utilization of ARBs and brand ACEIs with anticipated savings.

### ANTIPSYCHOTIC TREATMENT ADHERE NCE AND ASSOCIATED MENTAL HEALTH CARE USE AMONG PATIENTS WITH BIPOLAR DISORDER

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OBJECTIVE: To evaluate the association between adherence to antipsychotic treatment and mental health care use among patients with bipolar disorder with predominantly manic/mixed or depressive episodes.

METHODS: Claims data for 13,921 antipsychotic treatment episodes in commercially insured patients with bipolar or manic disorder (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes) were examined. Adherence was measured by intensity (medication possession ratio [MPR]) and treatment duration. The impact on health care use during subsequent stages of antipsychotic treatment was evaluated using multiple regression analysis.

RESULTS: There were 6,153 treatment episodes for patients with predominantly manic/mixed symptoms and 2,597 episodes for patients with depressive symptoms. For both groups, a higher MPR was associated with reduced total and outpatient mental health expenditures at various stages over 15 months after treatment initiation (P ≤ 0.05). The trend was generally less pronounced in predominantly depressed patients. Higher MPRs were associated with a lower likelihood for emergent mental health care in subsequent months but were unrelated to the number of mental health inpatient days. In both groups, a longer duration of treatment was associated with lower mental health care expenditures following termination of treatment (P ≤ 0.01). A longer duration of treatment was also associated with a lower likelihood of switching to another antipsychotic or remaining on or switching to other psychotropic medications (P ≤ 0.05).

CONCLUSIONS: For bipolar disorder, improved treatment adherence with antipsychotics is inversely correlated with subsequent total and outpatient mental health care expenditures. This trend was less pronounced in patients with predominantly depressive episodes compared with patients with predominantly manic/ mixed episodes.
ASSESSING DOSING PATTERNS OF TNF ANTAGONISTS AND ASSOCIATED COSTS FOR RHEUMATOID ARTHRITIS PATIENTS TREATED IN ROUTINE CLINICAL PRACTICE

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BACKGROUND: There is limited evidence on how etanercept and adalimumab, commonly prescribed biologics for rheumatoid arthritis (RA), are being used in routine clinical practice.

OBJECTIVE: To assess the dosing patterns of etanercept and adalimumab (approved December 2002) and associated costs from a payer perspective.

METHODS: Claims data from 2002 to 2004 was used to identify biologic-naïve RA patients. Patients with ≥2 claims for the same biologic were followed for 12 months following their index prescription. Patients who switched biologics or had Crohn's disease, psoriasis, psoriatic arthritis, or ankylosing spondylitis were excluded. Initial doses were evaluated for both drugs. Weekly doses of subsequent prescriptions were compared with index prescriptions, and dose escalation was based on ≥2 instances of increased dose. Costs were net payment for all claims, including pharmacy, inpatient, and outpatient.

RESULTS: Etanercept patients (n = 1,369) were younger than adalimumab patients (n = 461); (mean 49 vs. 51 years, P=0.001). 9.8% of adalimumab patients started with high dose (≥40 mg/week) compared with 2.2% of etanercept patients (≥75 mg/week). Cumulatively, 15.2% of adalimumab patients and 6.8% of etanercept patients had dose escalation (P < 0.0001). Rate of dose escalation was similar during early weeks, and starting week 16 to the end, adalimumab patients were twice as likely to be on an escalated dose as compared with etanercept patients. The average annual total cost per patient for adalimumab patients and etanercept patients was $16,812.56 and $15,267.60, respectively (P=0.001). Results from breakdown analysis indicated that the difference in total cost may be attributable mainly to the difference in cost associated with the dosing of the 2 biologics.

CONCLUSIONS: Adalimumab patients started at a high dose more frequently and experienced a significantly higher rate of dose escalations compared with etanercept patients. With similar average wholesale pricing, the differential total cost between adalimumab and etanercept patients was due to the increased dose.

ASSESSING THE IMPACT OF SMOKING CESSATION THERAPIES ON A MANAGED CARE ORGANIZATION’S BUDGET USING CENSUS REGION AND STATE-SPECIFIC SMOKING ESTIMATES

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BACKGROUND: A variety of smoking cessation therapies are on the market. History has shown that these therapies, when first introduced, result in a dramatic increase in usage and, when covered, can create a significant economic burden for managed care organizations (MCOs).

PURPOSE: Since the prevalence of smoking varies within the United States and new therapies are being introduced, an economic model to quantify the budgetary impact of smoking cessation therapies within U.S. regions is important.

METHODS: A decision-analytic model was developed to assess the budgetary impact of cessation therapies. Using national survey data (with region-specific and state-specific estimates), the number of patients attempting to quit smoking within an MCO population was estimated. The unassisted quit rate and therapy-specific incremental effect of successfully quitting were extracted from published literature. Drugs were assumed to be dosed and used according to label, with patients attempting 2 quit attempts per year. Over-the-counter drugs were assumed to be paid for by the patient. Prescription drugs were assumed to be covered with average 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. U.S. region-specific and state-specific per-member-per-month (PMPM) costs are reported.

RESULTS: The introduction of new cessation therapies increases PMPM drug costs by $0.22 to $0.30 when smoking status is analyzed at region-specific levels and $0.14 to $0.36 when analyzed at state-specific levels. Increases in PMPM physician visit costs ranged from $0.03 to $0.05 and $0.02 to $0.05 at region-specific and state-specific levels, respectively.

CONCLUSIONS: When modeling diseases or addiction behaviors with varying prevalence, it is important to analyze budgetary impact considering MCO population-specific prevalence values. Without micro-prevalence estimates, costs could be under- or overestimated. The introduction of new cessation therapies has a substantial impact on MCO budgets regardless of the area analyzed; however, the impact can vary in magnitude. Careful coverage decision making is recommended.
ASSESSMENT OF THE CLINICAL RISK FACTORS FOR CARDIOMETABOLIC RISK IN A NATIONAL PRIMARY CARE ELECTRONIC MEDICAL RECORD (EMR) DATABASE

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OBJECTIVE: This study examines the prevalence of various cardiometabolic risk (CMR) factors that may contribute to metabolic syndrome in a primary care setting. These risk factors were accessed with use of a national electronic medical record database.

METHODS: Ambulatory electronic health record data for 3,301,897 patients included demographics, vitals, labs, drugs, and payment types from the GE Centricity EMR research database. The study period was January 1, 2003, to December 31, 2004. Patients aged 18 to 64 years with any indicator of CMR were identified by clinical (biometrics), diagnosis (International Classification of Diseases, Ninth Revision [ICD-9] codes), or treatment (prescriptions) information.

RESULTS: The study population consisted of 475,651 patients with information on indicators of CMR, excluding patients with bariatric surgery or a body mass index (BMI) >35 kg/m². Of these, 72,593 (15.3%) and 55,928 (11.8%) had metabolic syndrome according to the National Cholesterol Education Program (NCEP) and International Diabetes Federation (IDF) criteria, respectively. In addition, 162,521 (34.2%) had BMI ≥27 kg/m² as a risk factor. High blood pressure was identified as a risk factor in 266,371 patients (56.0%). High triglycerides were identified as a risk factor in 1,230,897 patients (56.0%). High triglycerides were identified as a risk factor in 266,371 patients (56.0%). High triglycerides were identified as a risk factor in 266,371 patients (56.0%).

CONCLUSION: The distribution of CMR factors in a primary care database is similar to that established by prospective national health surveys. A key source of identification of risk factors is clinical outcomes, including BMI and lab values. Definition of patients at risk in managed care databases need to link clinically based information with more readily available treatment and diagnosis information.

ATOMOXETINE (STRATTERA) AND STIMULANT UTILIZATION MANAGEMENT OPPORTUNITIES ON CHILDREN: ASSESSMENT OF MEDICAL DIAGNOSES AND SWITCH RATES TO THE ALTERNATIVE AGENT

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INTRODUCTION: Atomoxetine has a black-box warning for increased risk of suicidal ideation in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) and has been associated with liver injury. Head-to-head clinical trials suggest atomoxetine may be less effective compared with stimulants in treating ADHD. Due to these concerns, we conducted analyses to evaluate utilization management opportunities.

METHODS: Medical and pharmacy claims data from a 1.8 million member BlueCross/BlueShield plan were analyzed. Continuously enrolled children 1Q (first quarter) 2004-3Q2005 with a stimulant (e.g., Adderall, Ritalin, Concerta) or atomoxetine drug claim during 4Q2004 had their medical claims evaluated for the presence of an ADHD, depression, anxiety, schizophrenia, bipolar, or insomnia (narcolepsy) diagnosis. Children newly initiating atomoxetine or stimulants were identified to evaluate the prevalence of a switch or addition of the alternative agent (e.g., stimulant claim after initiation with atomoxetine) during 180 days of follow-up. Newly initiated therapy was defined as a child without a stimulant or atomoxetine claim within 120 days prior to their first 4Q2004 claim. The chi-square test was used for statistical comparisons.

RESULTS: During 4Q2004, 1,538 children newly initiated therapy, with 1,230 of 1,538 (80.0%) using a stimulant and 308 (20%) using atomoxetine. ADHD was the most common diagnosis. During 180 days of follow-up, 54 of 308 (17.5%) children utilizing atomoxetine therapy had a stimulant claim and 52 of 1,230 (4.2%) children utilizing stimulant therapy had an atomoxetine claim, P<0.001.

CONCLUSIONS: ADHD diagnosis was present in approximately 4 of 5 children, with no difference between stimulant and atomoxetine utilizers. The significant 4.2 times higher rate of atomoxetine utilizers switching to or adding therapy indicates that atomoxetine is potentially less effective. The unique atomoxetine safety concern and potentially lower effectiveness suggests that a pharmacy benefit step-therapy program requiring a trial of stimulant before atomoxetine is a reasonable management strategy.

(See table on page 205.)
AVERAGE SALES PRICE METHODOLOGY, RESULTS, AND RELEVANCE TO MCOs

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INTRODUCTION: This study details average sales price (ASP) methodology, explores current results, and discusses relevance to managed care organizations (MCOs).

METHODS: The study design contains 3 parts: (a) develop a summary of the legislatively mandated ASP requirements; (b) create a methodological model of Centers for Medicare & Medicaid Services (CMS) computations and current results; and (c) derive implications about MCO relevance pertaining to individual aspects of the methods and results. Study sources included government legislative and regulatory materials, interviews, and peer-reviewed published articles.

RESULTS: The study's summary of legislative mandates set out restrictive boundaries. The methodological model identified 7 steps in required ASP data reporting to CMS by manufacturers, 5 steps in CMS release of quarterly payment data to providers, and 4 sequential steps in the CMS computation of ASP payment. The computation process, when deconstructed, revealed the following: (1) ASP is legislatively required to be calculated as the manufacturer's sales to all purchasers in the United States for that particular 11-digit National Drug Code, divided by the total number of units sold by the manufacturer in that quarter. Certain provisions apply. (2) Sales exempt from the Medicaid best-price calculation must be excluded. (3) Five types of transactions and items must be deducted, including: volume discounts, prompt-pay discounts, cash discounts, free goods that are contingent on any purchase requirement, and chargebacks and rebates other than rebates under the Medicaid drug rebate program. The resulting CMS payment is computed as ASP plus a percentage (106% in 2006; 105% proposed for 2007). Primary relevance to MCOs is within 3 areas: contracting impacts, adoption of the payment method, and use as a benchmark.

CONCLUSIONS: This study found that current ASP methods and results have 3 primary areas of relevance to MCOs. MCO decision makers should be aware of such implications and any potential impact on their processes, programs, and benefit designs.

CHOLESTEROL REDUCTION AND IMPROVED MEDICATION ADherence ASSOCIATED WITH A CARDIOVASCULAR EDUCATION PROGRAM

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PURPOSE: To measure the effects of a cardiovascular (CV) education program on cholesterol levels and medication adherence.

METHODS: An optional cardiovascular educational program (Counting Cholesterol Down [CCD]) was offered to a total of 895 members during the period of April-September of 2001; 331 patients joined the program. Baseline cholesterol levels (total cholesterol, low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], and triglycerides) were measured prior to enrollment in the program. To measure the impact of the CCD educational program, cholesterol measurements were evaluated in 2005 for 155 of 331 original participating members. An analysis was also performed to determine whether or not the CCD program would affect cardiovascular medication adherence rates.

RESULTS: Significant positive changes were seen for those members who participated in the CCD CV education program. Total cholesterol decreased by 5.7%, LDL-C decreased by 5.2%, triglycerides decreased by 7%, and HDL-C increased by 1.8%. Most of these changes were statistically significant. A positive change was also seen in medication possession ratio (MPR). The baseline MPR was 0.65, with a corresponding average LDL-C of 101 mg/dL. 180 days after the CCD program, members had an MPR of 0.97, with a corresponding LDL-C of 95.7 mg/dL. When members were stratified into LDL-C subcategories, significant changes were also evident. For example, the percentage of members with LDL-C levels between 70 and 100 mg/dL increased from 23.4% to 42%.

CONCLUSIONS: The CCD CV educational program showed positive results for those members who participated. Continued educational programs should be offered to plan members in order to continue to prevent and manage CV disease.

CMS COMPETITIVE DRUG ACQUISITION PROGRAM: LESSONS LEARNED FOR MANAGED CARE PHARMACISTS AND MCOs

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INTRODUCTION: The Centers for Medicare & Medicaid Services (CMS) Competitive Drug Acquisition Program (CAP) implemented in 2006 met resistance from physicians and attracted minimal enrollment. Managed care pharmacists and managed care organizations (MCOs) should compare and contrast
provider's points of resistance to benefit from the CMS experience.

OBJECTIVE: The primary objective of the review was to identify program processes most likely to create provider problems. Sources included government publications and Web sites, vendor telecasts, and physician interviews. A matrix was built to reveal primary drivers for reported problem areas.

METHODS: Program processes were categorized into 4 types: contractual, supply, administrative, and patient access: (1) Primary contractual problems were “as written” requirements for any use outside the CAP list. (Participating CAP physicians must receive all CAP drugs from the approved CAP vendor.) (2) Primary supply problems involved maintaining separate CAP inventory and prediction of exact drug quantity to be used. If greater dosage or emergency use is required, must defend use to obtain restocking of physician’s inventory. Also, drug delivery must be to actual site of administration, causing problems for practices with multiple offices. (3) Primary administrative problems were disconnects with payer on drug and administrative procedure, especially as to prior authorization requirements. In addition, billing must occur within 14 days of administration date, regardless of the office billing cycle. (4) Patient access issues revolved around the CAP vendor’s coinsurance collections and the vendor’s right to cut off a patient’s drug supply if timely payment is not received. The time frame allowed for patient assistance approval is also short, leading to physician concerns about how they can continue to treat the patient under these circumstances.

CONCLUSIONS: CAP stipulates a series of mandatory processes for participating physician providers. This review isolates specific points of resistance that should allow comparison by managed care pharmacists and MCOs in order to benefit from the CMS experience.

II. COMPARATIVE ANALYSIS OF MULTIPLE SCLEROSIS COST-EFFECTIVENESS MODELS: FOCUS ON THE MANAGED CARE PERSPECTIVE

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PURPOSE: To assess medical literature and scientific proceedings for studies evaluating the comparative economic value of 5 disease-modifying drugs (DMDs) used to manage relapsing forms of multiple sclerosis (MS).

METHODS: A comprehensive search of the MEDLINE database, as well as International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and the Academy of Managed Care Pharmacy meeting proceedings was conducted to identify cost-effectiveness (CE) analysis studies published or presented from January 2004 through October 2006. Studies were critically reviewed with regard to evaluated comparators, primary endpoints, measures of relapse reduction, perspective, time frame, and cost of therapy.

RESULTS: Recently presented data have used CE models to compare available DMDs from a payer perspective. Although both analyses utilized cost per relapse avoided as the primary endpoint, the results varied significantly in terms of CE ratios and relative DMD rankings. The primary determinant of these variations was the methodology used to calculate relapse reduction from the data reported in randomized placebo-controlled trials. While the same clinical trials were employed by both models, the number of avoided relapses was based on absolute reduction in the case of Goldberg et al. and on relative reduction in the case of Chiao et al., an important scientific and clinical distinction. In addition, the models used different assumptions with respect to time frame, treatment adherence, monitoring costs, occurrence of progressive multifocal leukoencephalopathy, contractual discounts, and member copayments. Due to the limitations inherent in the relative event reduction methodology, the model developed by Chiao et al. was highly sensitive to the variation in the average relapse rate prior to treatment.

CONCLUSIONS: The choice of methodology used to calculate therapeutic impact on relapse reduction can significantly influence the outcome of CE analyses. Considering significant heterogeneity in baseline disease severity among clinical trials in MS, use of absolute reduction in relapse rate is more appropriate because it more accurately reflects the net clinical benefit. (See table on page 206.)

III. COMPARING OVERALL TREATMENT COSTS OF OROS MPH AND IMMEDIATE-RELEASE MPH IN THE TREATMENT OF CHILDREN WITH ADHD

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BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD) studies in children suggest that more patients achieve remission of ADHD symptoms and have better adherence with OROS methylphenidate (OROS-MPH) than immediate-release methylphenidate (IR-MPH). However, the economic impact of these clinical benefits remains unclear.

PURPOSE: To compare ADHD treatment costs of OROS-MPH and IR-MPH in children.

METHODS: A decision-analytic model was developed from a payer’s perspective in 2005 U.S. dollars comparing per-patient overall treatment costs over 1 year (excluding discounting) between OROS-MPH and IR-MPH in 6-to-12-year-old children with ADHD. Overall treatment costs included ADHD drug costs and non-drug resource utilization costs. All model parameter estimates came from published literature. Incorporating remission rates, dose escalation, and adherence information, the model calculated first-line ADHD drug treatment costs based on...
average wholesale price (AWP), with nonremission patients having a second-line therapy add/switch option. Non-drug resource utilization applied in the model included physician visits (general, specialist, and pediatrician), hospitalization, and emergency room visits. Non-drug resource utilization costs were obtained from Medicare fee schedules and other published literature. Sensitivity analyses were performed on all key clinical and economic variables.

RESULTS: The annual overall cost of ADHD treatment per patient in children taking OROS-MPH was $340 less than children taking IR-MPH ($2,062 vs. $2,402). ADHD drug costs alone were higher with OROS-MPH ($751 vs. $359), but these costs were offset by lower non-drug resource utilization costs ($1,311 vs. $2,042). Increased rates of hospitalization and emergency room visits were the most significant drivers contributing to the excess direct medical costs associated with IR-MPH. These results were stable across a broad range of sensitivity analyses.

CONCLUSIONS: OROS-MPH has lower overall treatment costs compared with IR-MPH. When making ADHD medication decisions for children, resource utilization beyond drug acquisition costs should be considered. Further economic studies are needed to confirm these findings.

COMPARING THE COST-EFFECTIVENESS (CE) OF THE DISEASE-MODIFYING DRUGS (DMDS) UTILIZED IN THE MANAGEMENT OF RELAPSING FORMS OF MULTIPLE SCLEROSIS (MS): A MODEL EVALUATING THE CLINICAL AND ECONOMIC IMPACT OF CURRENT TREATMENT OPTIONS

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OBJECTIVE AND PERSPECTIVE: To compare the relative cost-effectiveness (CE) of the 5 disease-modifying drugs (DMDs) indicated for the management of relapsing forms of multiple sclerosis (MS) from the health system perspective.

METHODS: A 4-year CE model previously developed to compare the relative cost components of relapses, disability progression, and DMDs in the treatment of MS with self-injected DMDs was extended to dynamically model the impact of infusion-based natalizumab utilization and switching between these agents. Drug effectiveness with respect to the absolute risk reduction in relapses and disability progression was based on the published level 1 clinical trials. Data from previously published research was used to model the cost of these key clinical events. The cost of therapy was based on wholesale acquisition cost, contractual discounts, patient copays, and the cost of monitoring. The primary endpoint was the cost of therapy per relapse avoided. Multifactor sensitivity analyses were conducted.

RESULTS: In a typical managed care population, with an estimated prevalence of MS of 0.2%, 50% of patients being treated, an average self-injected DMD compliance of 80%, and an average natalizumab compliance of 90%, the projected impact of MS treatment was $2.04 per member per month. Monthly cost of therapy for glatiramer acetate, interferon beta-1a intramuscular (IM), interferon beta-1a subcutaneous (SC), interferon beta-1b, and natalizumab was $1,448, $1,577, $1,745, $1,578, and $3,081, respectively. Based on the cost of therapy per relapse avoided, DMDs were ranked in the order of decreasing cost-effectiveness (from greatest to lowest): interferon beta-1a SC ($58,561), interferon beta-1b ($59,169), glatiramer acetate ($82,450), natalizumab ($95,532), interferon beta-1a IM ($146,678). Increasing utilization of interferon beta-1a SC resulted in reduced overall therapy cost per relapse avoided with no significant increase in combined costs of drug and medical treatment.

CONCLUSION: Modeling absolute risk reduction in relapse rate and disability progression indicates that interferon beta-1a SC injection is the most cost-effective DMD.

COMPARISON OF ASTHMA-RELATED HEALTH CARE UTILIZATION AND ASSOCIATED COSTS AMONG PATIENTS ON DIFFERENT ASTHMATIC TREATMENTS IN A LARGE MANAGED CARE POPULATION

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BACKGROUND: Asthma is a respiratory disease associated with substantial morbidities and its treatment can result in a considerable financial burden to the health care system. Health Plan Employer Data and Information Set (HEDIS) measures provide specifications to categorize patients according to asthma severity to evaluate the appropriateness of prescribed treatment in an effort to improve outcomes and lower cost.

PURPOSE: To evaluate differences in health care utilization, treatment-related adverse effects (AEs), and associated costs among patients on different asthmatic treatments.

METHODS: A retrospective cohort analysis of the Integrated Healthcare Information Services (IHCIS) administrative database evaluated patients aged ≥5 years with ≥2 prescriptions of asthma medication. Patients were classified as persistent asthmatics, using HEDIS specifications, and were followed while receiving their index medication: inhaled corticosteroids (ICSs) (n = 12,394), leukotriene modifiers (LMs) (n = 23,770), long-acting beta-agonists (LABAs) (n = 2,208), and ICS+LABA (n = 1,361), until censored at time of switch, discontinuation, or augmentation. Health care utilization before censoring was considered and adjusted for 1 year; costs were adjusted for the 2005 dollar values, using various price indexes.

RESULTS: Hospitalizations and emergency room visits were more frequent in the ICS+LABA group (0.63%, 1.77%, respectively) than ICS (0.48%, 1.44%), LABA (0.45%, 0.91%), or LM
(0.46%, 1.54%) (all P <0.001). More ICS patients had ≥10 outpatient visits (19.5%) than ICS+LABA (16.3%), LABA (8.3%), or LM (9.4%) patients (P <0.001). Treatment costs were higher for ICS+LABA patients ($1,076) than LABA ($977), LM ($972), or ICS ($666). Total costs of care, including treatment-related AE costs, were ICS+LABA ($1,178), LABA ($1,190), LM ($1,060), and ICS ($760). The main cost influencers were medication class (relative risk [RR], 1.33-1.49 vs. ICS; 95% confidence interval [CI],1.31-1.53), hospitalization (RR, 2.09; 95% CI, 1.92-2.27), emergency room (RR, 1.57; 95% CI,1.49-1.53), and >3 outpatient (RR, 2.01; 95% CI,1.95-2.07) visits.

CONCLUSIONS: Treatment with ICS resulted in the lowest total cost of care for asthma patients after adjusting for asthma severity. Nonetheless, costs of care remain high, particularly when treatment-related AE costs were considered.

## COMPARISON OF HEALTH CARE COSTS IN PATIENTS WITH ANKYLOSING SPONDYLITIS WHO RECEIVED ETANERCEPT OR INFliximAB THERAPY

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**OBJECTIVE:** To evaluate all-cause health care costs among patients with ankylosing spondylitis (AS) who received etanercept (ETA) or infliximab (INF) therapy.

**METHODS:** A retrospective study using the PharMetrics database, compiled from managed care plans throughout the United States, from January 1, 2000, through June 30, 2005, was conducted. Patients continuously enrolled for 6 months prediagnosis and 12 months postdiagnosis and having 2 distinct claims of AS were included in the study. A 6-month period prior to the index diagnosis date was used to establish anti-tumor necrosis factor (TNF) treatment, naive patients, and to identify new AS patients. Per-patient-per-month (PPPM) costs were compared for patients during their treatment period. The cost of adverse events could not be identified separately in this analysis. A generalized linear model, with log transformation of costs, was used to adjust for covariates including age, gender, number of medical visits, Charlson Comorbidity Index score, and preperiod health care costs.

**RESULTS:** 688 patients with RA were included in this analysis. More than two thirds of the patients were females and the mean age was 46 years. Total PPPM costs were higher among patients who received etanercept (ETA) alone ($12,026) compared with ETA plus MTX ($2,782) or infliximab (INF) plus MTX ($2,064). Differences in total health care costs persisted after adjustment for covariates. Patients who received INF and MTX had lower total health care costs when compared with patients who received ETA and MTX (P <0.002) and patients receiving ETA alone (P <0.0001). Overall, the variables of male gender and higher preindex health care cost were associated with higher total health care costs in the ETA patient population.

**CONCLUSIONS:** This study indicates that INF plus MTX was associated with lower total all-cause health care costs compared with ETA alone or ETA plus MTX in the treatment of RA. The choice of a biologic treatment and its impact on health care costs should be considered when evaluating treatment strategies.
COMPARISON OF HEALTH STATUS AND FUNCTIONAL LIMITATIONS IN PATIENTS WITH DEPRESSION AND PATIENTS WITH OTHER CHRONIC ILLNESSES IN A NATIONAL SAMPLE OF U.S. ADULTS

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BACKGROUND: Depression impacts quality of life and is also the leading cause of disability; it is estimated to cause $83.1 billion annually in the United States, with 31% from direct medical costs and 62% from work productivity loss.

OBJECTIVE: To compare the perceived health and mental status, physical, work, and social limitations in patients with depression and patients with other chronic illnesses, using the 2003 Medical Expenditure Panel Survey (MEPS) data.

METHODS: Data from the Household Component of MEPS, a nationally representative sample of the U.S. noninstitutionalized, civilian population were analyzed. Five mutually exclusive groups of subjects, aged between 50 and 70 years, with the following most prevalent medical conditions, were identified through the International Classification of Diseases, Ninth Revision (ICD-9) codes. The study sample size, using weights provided via population estimates, was 2.3, 6.1, 0.9, 1.6, and 8.9 million patients for depression, arthritis/rheumatism, asthma/chronic obstructive pulmonary disease (COPD), diabetes, and hypertension, respectively. Descriptive statistics and analysis of covariance adjusting for age, gender, race, and the number of comorbid conditions were conducted.

RESULTS: On a 5-point scale with 1 = “excellent” and 5 = “poor” perceived mental health status, depressed patients rated themselves the worst compared with the other groups (adjusted mean ± SE: depression 2.80 ± 0.06, arthritis/rheumatism 2.05 ± 0.04, asthma/COPD 2.33 ± 0.10, diabetes 2.28 ± 0.08, and hypertension 2.06 ± 0.03). Depressed patients also tended to report more social limitations (14.8% vs. 8.6%, 9.0% 6.2%, and 3.6%, respectively). Surprisingly, depressed patients rated themselves worse (2.73 ± 0.07) than patients with arthritis/rheumatism or hypertension (both 2.48 ± 0.04) in perceived health status and reported similar work and physical limitations compared with the other chronic illnesses.

CONCLUSIONS: The results substantiate the evidence that depression impacts patients mentally and socially and also has a detrimental effect on their physical health status and functioning as do other chronic illnesses. Interventions designed to manage depression effectively may help to improve health status and functional ability in patients with depression.

COMPARISON OF MEDICAL AND PRESCRIPTION COSTS FOR MEDICAID PATIENTS WITH COPD BY INITIAL MEDICATION REGIMEN

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BACKGROUND: Chronic obstructive pulmonary disease (COPD) is an important cause of increased health care utilization and costs. Initial maintenance pharmacotherapy is often used to control symptoms and to prevent acute exacerbations. However, limited information is available about their relative benefits on treatment costs in the Medicaid population.

OBJECTIVE: To compare various initial maintenance therapies on COPD-related and all-cause costs.

METHODS: Retrospective observational analysis using linked medical and pharmacy claims from the Texas Medicaid database. Patients aged 40 to 65 years, with COPD-related medical costs (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] = 491, 492, 496), 24 months continuous enrollment (12 months pre and post), and at least 1 prescription claim (index) for ipratropium (IPR), inhaled corticosteroids (ICSs), salmeterol (SAL) or fluticasone propionate/salmeterol (FSC) between September 1, 2000, and December 31, 2003, were included. Outcomes of interest were COPD-related and all-cause medical, prescription, and total costs during the 12 months postindex period. A 2-part model with (1) logistic regression and (2) generalized linear model (GLM) were used to adjust for baseline characteristics and preindex utilization and costs.

RESULTS: A total of 6,793 patients were identified; IPR (n = 4,213), ICS (n = 968), SAL (n = 401), and FSC (n = 1,211). Compared with IPR (referent), SAL and FSC had significantly higher pharmacy costs (COPD-related and all-cause) but significantly lower medical costs (COPD-related and all-cause). Total COPD-related costs were similar in FSC and ICS, and reduced by $108 (P <0.05) in SAL compared with IPR. However, for all-cause total costs, significant reductions were observed in FSC ($792, P <0.05) and SAL ($1,226, P <0.05) but not in ICS compared with IPR.

CONCLUSIONS: FSC and SAL cohorts had reduced all-cause treatment costs in COPD patients. For these cohorts, the reduction in medical costs more than offset the increase in prescription costs, resulting in an overall total cost savings compared with IPR.
**CONSISTENCY IN DOSING WITH INFlixIMAB FOR RHEUMATOID ARTHRITIS USING A COHORT ANALYSIS**

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**INTRODUCTION:** The stability of administered doses of infliximab was examined for Medicare beneficiaries for their first year of treatment following titration.

**METHODS:** Infliximab should be titrated for rheumatoid arthritis (RA) patients to determine their appropriate dose. We hypothesized that with more prescribing experience with infliximab, there may be reductions in the frequency and magnitude of changes in dosage. Using Medicare claims from the 2001 through 2004 5% Standard Analytic Files (SAFs), we analyzed cohorts of Medicare beneficiaries with RA who received infliximab. We examined (1) what proportion kept a constant dosage in the first year after titration and (2) if this proportion changed over time. We created 10 cohorts based on treatment starting date and the presence of 6 continuous quarters of treatment. Our 10 cohorts included 954 beneficiaries, representing an estimated 19,000 beneficiaries.

**RESULTS:** In the year of treatment following titration, 55% of beneficiaries had no increase in dosage between earlier and later cohorts. Between the first and last quarter following titration, across all the cohorts, the average dose increased by 38.5 mg—equivalent to less than half a vial of infliximab. This change is less than 20% of the average dose. Of the minority of patients who increased dosage (39%), the average increase was just over 1 vial of infliximab (118 mg) —just over one third of an average dose.

**CONCLUSIONS:** More than 60% of beneficiaries had no increase in their dosage in the year following titration. The average dose over the year adjusts by a relatively modest amount. This dosing stability may facilitate accurate forecasts of resource utilization associated with treatment in the managed care environment.

**COPD EXACERBATIONS IN A MANAGED CARE POPULATION: ASSOCIATION OF COPD MEDICATION USE WITH COPD EXACERBATION**

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**INTRODUCTION:** Chronic obstructive pulmonary disease (COPD) exacerbations are associated with significant clinical and economic consequences due to hospitalization, ER visits, or additional medication. A retrospective cohort study was conducted to examine the association between the use of inhaled COPD medications and the total number of COPD exacerbations.

**METHODS:** Integrated medical and pharmacy administrative claims data from a proprietary, representative managed care database were used to identify patients with continuous eligibility for ≥2 years between 01/2001 and 12/2004, who were aged ≥40 years, newly diagnosed with COPD (International Classification of Diseases, Ninth Revision [ICD-9] codes 491, 492, and 496), and received ≥2 prescriptions for inhaled corticosteroids (ICSs) alone, long-acting β2-agonists (LABA) alone, anticholinergics (ACs) alone, or a combination of LABA and ICS (LABA/ICS). COPD exacerbations were defined as hospitalizations or emergency room (ER) visits with a primary diagnosis for respiratory conditions or outpatient visits requiring oral steroids or antibiotics for respiratory conditions within 14 days of the visit. Negative binomial regression analysis evaluated the frequency of COPD exacerbations during the 12 months following the initiation of medication adjusting for age, gender, SABA (short-acting β2-agonist) use, comorbidities, and exacerbations in the 12-month history period.

**RESULTS:** The analysis included 2,923 COPD patients: ICS = 561 (19.2%); LABA = 272 (9.3%); AC = 1,220 (42.7%); LABA/ICS = 870 (29.8%). 35% of patients had a total of 1,517 COPD exacerbations. The majority of exacerbations were managed in an outpatient setting (n = 1,258; 82.9%) rather than requiring hospitalization (n = 224; 14.8%) or ER visit (n = 35; 2.3%). COPD exacerbation rates were significantly lower for LABA/ICS (relative risk [RR], 0.65; 95% confidence interval [CI], 0.55-0.76), LABA (RR, 0.68; 95% CI, 0.55-0.84), or AC (RR, 0.72; 95% CI, 0.60-0.83) compared with ICS.

**CONCLUSION:** Use of bronchodilators, with or without ICS, was seen to decrease the risk of COPD exacerbations compared with ICS alone. Although exacerbations were most frequently treated in an outpatient setting, a significant proportion resulted in hospitalization, an outcome with considerably increased cost.

**COST COMPARISONS BETWEEN INFlixIMAB AND ETANERCEPT ANTI-TUMOR NECROSIS FACTOR THERAPY IN PATIENTS WITH PSORIASIS**

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**PURPOSE:** To evaluate the annual costs of anti-tumor necrosis factor (anti-TNF) therapies in the treatment of psoriasis.

**METHOD:** A decision-model was created using TreeAge software with clinical trial data and average wholesale price for drug costs. Two treatment strategies were compared, either etanercept first then switching to infliximab or infliximab first then switching to etanercept. We assumed patients who failed to achieve 50% improvement on the Psoriasis Area Severity Index
(PASI-50) would switch to the other biologic after 24 weeks, and the efficacy rates after switch were the same as the first-line treatment. A sensitivity analysis changing the efficacy rates after switching, to 10% to 30% less than that of the initial treatment, was conducted. The cost of adverse events was not included in the model. Infusion fees ($203/infusion) were included for infliximab. The overall efficacy rate was calculated based on the combination of the efficacy from each treatment group.

RESULTS: With infliximab, 90% of patients achieved PASI-50 at week-24 and continued receiving infliximab. Patients (10%) who failed to achieve PASI-50 were switched to etanercept. With etanercept, 77% of patients achieved PASI-50 at week-24 and continued etanercept treatment. Patients (23%) who failed to achieve PASI-50 were switched to infliximab. The etanercept-first strategy costs $23,047 annually and results in an overall efficacy rate of 78.5%, which yields a cost efficacy (CE) of $29,361. The infliximab-first strategy costs $25,427 annually and results in an 89.4% efficacy rate, which yields a CE of $28,458. Compared with etanercept, the infliximab-first strategy costs $903 less per successfully treated patient. The incremental cost-efficacy ratio per PASI-50 was $21,927, which indicates that infliximab is cost effective. The sensitivity analysis indicated that the results are robust and in the same direction as the initial assumption.

CONCLUSION: Developing a preferred biologic therapy strategy may help reduce overall costs. Analyses using real-world data may demonstrate further cost savings of biological therapy.

■ COST COMPARISONS FOR SPECIALTY MEDICATIONS COVERED UNDER MEDICAL AND PHARMACY BENEFIT PLANS

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BACKGROUND: Most specialty medications are biological preparations that are either injection or infusion therapies and require special handling or administration. Insurance companies cover a majority of the specialty medications under their medical as well as under pharmacy benefits plans. Since such medications are prepared and administered by health care providers, these could be charged differently under medical benefit plans than if they were covered through pharmacy benefit plans.

INTRODUCTION: The purpose of this study was to investigate and compare average per-unit drug cost charged for specialty medications, using medical and pharmacy claims. We hypothesized that the per-unit drug cost charged under pharmacy plans would be lower than the amounts charged by health care providers through medical benefit plans.

METHODS: This study was conducted using retrospective medical and pharmacy claims databases. All claims for single-dose specialty medications adjudicated from January through December 2005, were included in the study. Average medical and pharmacy amounts charged per syringe for the study medications were computed and compared by independent sample t tests.

RESULTS: A total of 25 specialty medications from various therapeutic areas were included in the study. Average per-unit drug cost for specialty medications in the pharmacy and medical benefit plans were about 17.6% and 12.2% lower than the average wholesale price, respectively. Amounts charged per syringe for 24 of 25 medications were found to be lower in the pharmacy plans as compared with medical plans, and such differences were found to be statistically significant (alpha = 0.05). Overall, per-unit drug costs for specialty medications were found to be about 6% lower in the pharmacy plans than in the medical benefit plans.

CONCLUSION: The study findings suggest that there may be greater opportunities for payers to achieve potential cost savings if specialty medications were covered through pharmacy instead of medical benefit plans.

■ COST ESTIMATES OF CHRONIC CONSTIPATION IN CALIFORNIA MEDICAID (MEDI-CAL) PATIENTS

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INTRODUCTION: To characterize the health care expenditures associated with chronic constipation (CC), using a Medicaid database.

METHODS: Pharmacy and medical claims were retrospectively analyzed for California Medicaid (Medi-Cal) patients using the 20% sample from 1995 to 2003. CC was defined as 2 or more diagnoses of constipation (International Classification of Diseases, Ninth Revision [ICD-9] codes 564.0, 564.00, 564.01, 564.09) or a diagnosis and a constipation-related prescription more than 30 days after the diagnosis date. The annual prevalence of CC was calculated for the beneficiaries who were eligible for a whole year. Itemized and total costs were calculated for beneficiaries with eligibility 24 months prior to the observed initial diagnosis of constipation and 12 months after the diagnosis. Prescriptions and available over-the-counter agents (Rx/OTCs), outpatient care, inpatient care, and long-term care costs were compared before and after the diagnosis.

RESULTS: The annual CC prevalence rate was estimated as 1.27% to 2.23% in 1995 to 2003, with increasing trends over time in the number of patients and rate. The population also decreased in age (from 64.8 to 55.7 years) and percentage female (from 66% to 60%) over the study period. Average monthly costs for the CC cohort (n = 7,463) by category before diagnosis and after diagnosis were: Rx/OTCs $173 versus $255, a 47% increase; outpatient $349 versus $508, a 46% increase; inpatient $293 versus $392, a 34% increase; and long-term care $72 versus $113, a 57% increase. There was a 43% increase in total costs after diagnosis, from $887 to $1,269. All before-and-
after differences were significant at P <0.01. Outpatient costs represented the largest absolute increase.

**CONCLUSION:** There is a significant burden of chronic constipation in the Medi-Cal population. Prevalence may be underreported by ICD-9 coding, thereby underestimating costs. Increases in outpatient costs are a primary driver of total constipation costs.

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**COST REDUCTIONS ATTAINED FROM AN EVIDENCE-BASED PREFERRED-DRUG-LIST POLICY ON HMG-COA REDUCTASE INHIBITORS IN A MEDICAID POPULATION**

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**INTRODUCTION:** On June 8, 2005, the Arkansas Medicaid program implemented a prior-approval policy whereby all HMG-CoA reductase inhibitors (statins), except simvastatin, required prior approval to be reimbursed.

**PURPOSE:** The objective of this study was to estimate the impact of this policy on statin costs and utilization as well as utilization of nonstatin antihyperlipemic drugs.

**METHODS:** This study utilized a time series panel design to evaluate the impact of the policy, using Arkansas Medicaid administrative claims data obtained from January 2003 through May 2006. Auto-Regressive Integrated Moving Average (ARIMA) time series models were specified, using monthly prescription expenditures and utilization in the prepolicy period (January 2003 through May 2005) to forecast expenditures and utilization in the postpolicy period. Differences between postpolicy forecasts and actual expenditures were calculated to estimate cost reductions. The Medicaid payer perspective was used, and all prescription costs were calculated based on the amount paid for each claim adjusted for product-specific Centers for Medicare & Medicaid Services rebates.

**RESULTS:** Annual statin forecast expenditures for June 2005 through May 2006 were $6,939,193, and observed expenditures were $4,437,322, indicating that the prior-approval policy was associated with a 36% reduction in statin expenditures, or $2,501,872 (95% confidence interval [CI], $2,235,607-$2,768,136) in annual cost reductions. Smaller monthly cost reductions occurred after the Medicare Part D implementation. The policy was associated with a 6% (95% CI, 3%-10%) reduction in total LSA utilization. Prescription utilization of nonstatin anti-hyperlipemic drugs increased 10% (95% CI, 5%-15%) over trend forecasts, translating to annual increase in costs of $157,674 (95% CI, $105,095-$210,252). The nonstatin-increased utilization consisted mostly of ezetimibe; however, the increase in nonstatin antihyperlipemic drugs did not fully offset the decrease in statin utilization.

**CONCLUSIONS:** The statin prior-approval policy resulted in substantial antihyperlipidemic cost reductions to Arkansas Medicaid of approximately $195,000 per month. Further study is necessary to determine if the policy affected persistence and adherence with antihyperlipidemic therapy.

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**COST REDUCTIONS ATTAINED FROM AN EVIDENCE-BASED PREFERRED-DRUG-LIST POLICY ON LESS-SEDATING ANTIHISTAMINES IN A MEDICAID POPULATION**

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**INTRODUCTION:** On March 25, 2005, the Arkansas Medicaid program implemented a prior-approval policy whereby all less-sedating antihistamines (LSAs) except loratidine required prior approval to be reimbursed.

**PURPOSE:** The objective of this study was to estimate the impact of this policy on LSA costs and utilization as well as utilization of possible substitute drugs: leukotriene inhibitors, nasal steroids, and other antihistamines.

**METHODS:** This study utilized a time series panel design to evaluate the impact of the policy using Arkansas Medicaid administrative claims data obtained from January 2003 through May 2006. Auto-Regressive Integrated Moving Average (ARIMA) time series models were specified, using monthly prescription expenditures and utilization in the prepolicy period (January 2003-February 2005) to forecast expenditures and utilization in the postpolicy period. Differences between postpolicy forecasts and actual expenditures were calculated to estimate cost reductions. The Medicaid payer perspective was used, and all prescription costs were calculated based on the amount paid for each claim adjusted for product-specific Centers for Medicare & Medicaid Services rebates.

**RESULTS:** Annual LSA forecast expenditures for April 2005-March 2006 were $6,650,590 and observed expenditures were $1,954,280, indicating that the prior-approval policy was associated with a 71% reduction in LSA expenditures, or $4,696,310 (95% confidence interval [CI], $3,546,819-$5,845,801) in annual savings. The policy was associated with a 29% (95% CI, 14%-45%) reduction in total LSA utilization. The proportion of nonpreferred LSA utilization was reduced from 98% to 18% after the policy was instituted. There were no significant changes observed for leukotriene inhibitors, other antihistamines, and nasal steroid utilization through December 2005.

**CONCLUSIONS:** The prior-approval policy for LSA resulted in substantial cost reductions to Arkansas Medicaid—of approximately $400,000 per month—without increasing the utilization of leukotriene inhibitors, other antihistamines, or nasal steroids.
**COST-EFFECTIVENESS OF MEETING HEDIS MEASURES FOR SMOKING-CESSATION PHARMACOTHERAPY**


**BACKGROUND:** The Health Plan Employer Data and Information Set (HEDIS) medical assistance with smoking cessation (MSC) measures recommend that smokers be given cessation advice, drug information, or medications. Purpose: To analyze the effects of improving performance on HEDIS measures for MSC using the Archimedes model.

**METHODS:** The Archimedes model is a detailed simulation model using object-oriented programming. The model includes a set of differential equations representing the physiological pathways of diseases and complications.

The model was used to conduct a cost-effectiveness analysis comparing the impact of spontaneous smoking cessation rates and compliance with HEDIS MSC measures across the entire U.S. population. The simulated population was extracted from the Third National Health and Nutrition Examination Survey (NHANES III) data on smokers aged 18 years and older.

The status quo arm assumed that smokers quit spontaneously at age- and sex-specific rates from NHANES III. For the 100% compliance arm—advice, smokers quit at an additional 5.86% in year 1, tapering to 0.586% in year 30; for 100% compliance—medications, the additional quit rate was estimated to be 10.5% in year 1, tapering to 1.05% in year 30.

The total cost of delivering the interventions and potential savings from preventing outcomes were calculated using data from a large health plan. Discount rates for costs and quality-adjusted life-years (QALYs) were 3%. The cost of pharmacotherapy included a nicotine patch ($150) and bupropion ($120) plus an office visit for counseling ($80).

**RESULTS:** 100% compliance with HEDIS MSC including pharmacotherapy reduced the number of myocardial infarctions, strokes, and coronary heart disease deaths at all time points. The total cost of 100% compliance was greater than the cost of the status quo. After 10 years, the cost per QALY for advice and for pharmacotherapy was less than $40,000.

**CONCLUSION:** When physicians counsel patients about smoking cessation, including recommendations and prescriptions for pharmacotherapy, outcomes are improved and the intervention is cost effective. (See table on page 207.)

**COSTS AND OUTCOMES IN ORTHOPAEDIC PATIENTS WHO RECEIVED THROMBOPROPHYLAXIS WITH DALTEPARIN, ENOXOPARIN, FONDAPARINUX, OR UNFRACTIONATED HEPARIN**

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**INTRODUCTION:** Limited information is available on treatment cost differences between the various venous thromboembolism (VTE) prophylaxis regimens. The objective of this analysis was to compare the effect of various anticoagulant regimens used as VTE prophylaxis on costs in orthopaedic patients.

**METHODS:** Retrospective observational claims data analysis using the Premier Inpatient Database, which contains inpatient medical, pharmacy, and billing data for >500 hospitals located throughout the United States. Patients aged ≥18 years, with a primary or secondary diagnosis of orthopaedic surgery (hip fracture, hip replacement, and knee replacement surgery) according to International Classification of Diseases, Ninth Revision [ICD-9] codes and Current Procedural Terminology [CPT] codes, between January 2003 and March 2005 were eligible for inclusion. VTE events and total inpatient costs (pharmacy, medical, and lab) associated with the index surgery and any subsequent hospitalization within 60 days post discharge were assessed. Charges were converted to costs using Medicare regional cost-to-charge ratios. Subjects given unfractionated heparin (UFH), enoxaparin, dalteparin, or fondaparinux during the index inpatient stay were compared. Analysis was based on intent to treat, with logistic regression used to compare VTE event rates, and gamma-distributed, generalized linear model with a log link function was used to compare inpatient costs between the cohorts. All analyses were adjusted for differences in the cohorts.

**RESULTS:** 144,806 patients were included in the analysis: 97,827 with enoxaparin, 18,338 with UFH, 16,109 with dalteparin, and 12,532 with fondaparinux. After adjusting for baseline covariates, fondaparinux-treated patients had a reduced risk of a VTE event compared with dalteparin (adjusted odds ratio [OR]=1.2; 95% confidence interval [CI], 1.01-1.46), enoxaparin (OR=1.4; 95% CI, 1.19-1.62), and UFH (OR=2.0; 95% CI, 1.67-2.34). Adjusted total inpatient costs for fondaparinux ($1,252) was significantly lower than the costs of dalteparin ($1,331, P=0.0026), enoxaparin ($1,288, P <0.0001), and UFH ($1,437, P<0.0001) for all encounters over the study time frame.

**CONCLUSIONS:** Patients receiving fondaparinux were associated with a lower risk of VTE and significantly lower total costs when compared with patients receiving other VTE prophylaxis while patients using UFH were associated with the highest inpatient costs.
DIRECT AND INDIRECT COSTS ASSOCIATED WITH INSOMNIA AND ITS BURDEN TO THE EMPLOYER

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INTRODUCTION: Studies evaluating the overall burden of insomnia from the U.S. payer and employer's perspective are lacking. The purpose of this study is to evaluate direct and indirect cost burden of insomnia patients, using a large national managed care database.

METHODS: Subjects were identified as those with a diagnosis of insomnia and/or prescription(s) for traditional insomnia agents during the study period (05/01/01 to 11/30/03); a control group of noninsomnia patients without such an indicator was also identified during the same study period. Direct medical and indirect absenteeism costs, defined as work hours lost due to illness and short-term disability, times a uniform wage rate were calculated in terms of per-patient-per-year costs. One-year follow-up costs were compared between the 2 groups after adjusting for demographics and baseline comorbidities using regression techniques.

RESULTS: Patients with insomnia (n = 4,764) were similar in age compared with the control group (n = 14,365) with mean age 42.5 versus 42.9 years, respectively. Insomnia patients were more likely to be females, compared with the control group (46.7% vs. 31.5%, respectively, P <0.001), and more chronically ill (Deyo-Charlson 0.317 vs. 0.175, P <0.001). Insomnia patients incurred higher direct medical costs ($6,716 vs. $3,218, P <0.001) and were absent from work nearly twice as often as control patients for illness or disability reasons (53.81 vs. 26.09 hours, P <0.001), equating to $1,024 and $496, in indirect costs. After controlling for baseline differences between groups, insomnia patients continued to have higher total direct and indirect costs compared with control patients ($6,525 vs. $4,119, P <0.001).

CONCLUSIONS: Overall, the direct and indirect economic burden of insomnia for insomnia patients is significant compared with noninsomnia control patients. The results indicate that insomnia presents a substantial burden to the payer as well as the employer in terms of significantly greater direct medical costs and lost productivity through lost work hours.

DIRECT COSTS BY POINT OF SERVICE FOR PERSONS WITH AND WITHOUT CONSTIPATION: AN EMPLOYER PERSPECTIVE

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INTRODUCTION: To compare direct health care costs by point of service (POS) for persons with and without constipation during the sixth months postdiagnosis.

METHODS: An employer database containing medical claims, payroll, and demographic data for approximately 510,000 U.S. employees from 1/1/01 to 6/30/06 was retrospectively analyzed. Semiannual health care costs were captured based on claims from doctors’ offices, inpatient hospitals, outpatient hospitals or clinic, emergency departments (EDs), laboratories, other locations, and pharmacies. International Classification of Diseases, Ninth Revision [ICD-9] codes 564.0 (constipation), 564.00 (unspecified), 564.01 (slow transit), and 564.09 (other) were used to distinguish employees with constipation from the nonconstipation cohort. The index date in the constipation cohort was defined as the date of first diagnosis during 2001 or later; the average constipation index date was used in the nonconstipation cohort. For analysis, propensity scores based on age, gender, marital status, race, salary and other job-related variables, geographic region, existence of a medical cost, and the Charlson Comorbidity Index score were used to match 24 nonconstipation employees to each constipation cohort employee. Per-member-per-month (PMPM) costs were compared for each POS category. All costs were adjusted to 2006 dollars.

RESULTS: Data were available for 1,015 persons with constipation and 24,360 propensity-score-matched nonconstipation controls. Both cohorts were an average age of 41 years and were 73% female. The constipation cohort incurred $349 additional PMPM total costs (P <0.0001). Significant (P <0.001) cost differences by category for the constipation versus nonconstipation cohorts were: outpatient hospital or clinic ($264 vs. $118), doctor’ office ($128 vs. $94), ED ($17 vs. $7), and laboratory ($4 vs. $2). Prescription drug costs also were significantly higher for the constipation cohort ($98 vs. $75, P <0.0001). Findings for inpatient hospital ($228 vs. $106, P = 0.092) and other locations ($18 vs. $6, P = 0.096) were not significant.

CONCLUSION: Patients with constipation incur greater costs throughout the health care system.

DRUG UTILIZATION AND COST CONSIDERATIONS OF ERYTHROPOIETIC-STIMULATING AGENTS IN ELDERLY CANCER PATIENTS IN THE MEDICARE POPULATION

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BACKGROUND: As the involvement of managed care organizations (MCOs) in the treatment of the Medicare population intensifies, resource utilization of erythropoietic-stimulating agents (ESAs) in cancer patients is becoming an increasingly important consideration. To understand current ESA utilization patterns, this study examined real-world epoetin alfa (EPO) and darbepoetin alfa (DARB) dosing patterns, dose ratio, and ESA cost considerations in the Medicare population.

METHODS: A medical claims analysis of cancer patients from 1/2003-12/2004 using the Medicare 5% sample database.
ECONOMIC ANALYSIS OF SHORT-COURSE LEVOFLOXACIN VERSUS AMOXICILLIN/CLAVULANATE IN TREATING ACUTE BACTERIAL EXACERBATIONS OF CHRONIC BRONCHITIS

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BACKGROUND: Standard care for treating adult outpatients with complicated acute bacterial exacerbation of chronic bronchitis (ABECB) is administration of a 10-day course of amoxicillin/clavulanate (amox/clav). Treatment with therapy that is just as effective and has a similar impact on patient resource use/cost with shortened therapy duration can be advantageous.

PURPOSE: An intent-to-treat (ITT) analysis was performed to assess resource use/cost of treating patients with amox/clav and short-course levofloxacin from a U.S. health care payer perspective.

METHODS: A randomized, multicenter, blinded, parallel-group, clinical trial compared efficacy, safety, and prospectively collected resource use in complicated ABECB patients. Patients were randomized to high-dose, short-course levofloxacin 750 mg tablets daily for 5 days (n = 164) or amoxicillin 875 mg/clavulanate 125 mg tablets twice daily for 10 days (n = 171) and were followed up to 45 days. The trial was powered to examine clinical endpoints. Unit costs from U.S. standard costing sources were applied to resource use (hospitalizations, medications, etc).

RESULTS: Levofloxacin and amox/clav showed similar efficacy and safety. Per-patient cost differences were highest for hospitalizations as mean cost for levofloxacin patients was $231.28 and $369.69 for amox/clav; a difference of 138.41 (95% confidence interval [CI], -$513.74 to $167.51). Overall costs per levofloxacin patient were $638.84 and $811.96 for amox/clav; a difference of $173.11 per patient (95% CI, -$513.74 to $676.51). Although not powered to detect cost differences, costs were applied to resource use in an ITT population. No significant differences in costs were found when comparing 5-day course of levofloxacin and 10-day course of amox/clav. Further research is needed to assess cost differences between these treatments.

CONCLUSIONS: This study of 8,351 Medicare cancer patients reported a dose ratio of 266:1 (units EPO: mcg DARB) and 37% DARB price premium. These utilization and cost findings are consistent with other observational studies in the managed care setting.

ECONOMIC BURDEN OF BREAST CANCER IN A MANAGED CARE POPULATION IN THE UNITED STATES

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BACKGROUND: Breast cancer is the most commonly diagnosed non-skin cancer and second leading cause of cancer deaths among women in the United States.

INTRODUCTION: This study assessed health care resource utilization and costs in women with breast cancer in a managed care population.

METHODS: 2,004 prevalent breast cancer cases among women ≥18 years were identified from administrative claims databases of 5 U.S. health plans using International Classification of Diseases, Ninth Revision [ICD-9] code(s) of 174.xx or 233.0x. Treatment included surgical intervention, radiation therapy, chemotherapy, hormonal therapy, and targeted treatment (i.e., trastuzumab). A matched control group of women without cancer was randomly selected between 1/1/2004 and 12/31/2004. Health care costs were determined using per-patient-per-month (PPPM) costs (total costs per patient within 2004 calendar year/months of eligibility).

RESULTS: A total of 10,697 women (mean age 55 years) with breast cancer were identified (prevalence of 250 per 100,000). Approximately 62% of patients received surgical intervention; 41% received radiation therapy. Most common intravenous (IV) chemotherapies were cyclophosphamide (24.4%), doxorubicin (22.4%), docetaxel (12.9%), and paclitaxel (11.5%); capecitabine was the most commonly used oral chemotherapy (4.9%); 6.4% received trastuzumab. Mean breast-cancer-attributable PPPM total costs were $2,896, with hospitalization costs accounting for $1,340. Mean IV chemotherapy PPPM costs were $516, of which 30% were attributable to infusion administration and visit-related costs. Mean all-cause PPPM total costs were $4,421 compared with $3,352 (P <0.0001), with hospitalization costs being $1,576 versus $213 (P <0.0001), for the cases and control groups, respectively. Also, the mean number...
of in-patient admissions were 0.05 versus 0.01 (P <0.0001) and office visits were 1.52 versus 0.34 (P<0.0001), for the cases and control groups, respectively.

CONCLUSIONS: This study demonstrates that treatment of breast cancer is associated with substantial health care costs, driven mainly by hospitalizations. Projected annual costs for a breast cancer patient would be $12,828 higher than for women without breast cancer.

EFFECT OF COST-SHARING CHANGE FROM COPAYMENT TO COINSURANCE ON DRUG EXPENDITURES AND UTILIZATION

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INTRODUCTION: The impact of a copayment to coinsurance drug benefit change on prescription drug expenditures and utilization in 3 essential medication categories was determined through a retrospective cohort study.

METHODS: Expenditures and utilization of beneficiaries, continuously enrolled in 2 privately insured groups, were compared before and after a benefit design change in one of the groups. For the 12 months prior to the benefit design change, both groups employed a 3-tier fixed dollar copayment structure with identical cost sharing. On September 1, 2005, the intervention group implemented a 4-tier coinsurance benefit design, while the control group maintained the same 3-tier benefit in the preperiod and postperiod. A difference-in-difference analysis was used to estimate the effect of the benefit design change on the expenditures and utilization of persistent users of 3 classes of essential medications. The drug classes examined were anti-hypertensives, statins, and selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs).

RESULTS: The average increase in the patient out-of-pocket costs for all drugs from the preperiod to the postperiod was $0.08 more per user per month (PUPM) in the intervention group (n=11,917) than in the control group (n=1,792) (P=0.03) The incremental increase in costs for the employer group were $2.81 PUPM (P=0.06) less than the control. Similarly, the incremental increase in total cost of prescription drugs was $2.73 PUPM (P <0.01) less than the control. Overall, utilization increased in both the intervention and control groups, however, the increase in utilization in the intervention group was 0.05 claims (P<0.01) less than in the control group.

CONCLUSIONS: Switching to a coinsurance design slowed the growth of drug spending without decreasing overall utilization. The coinsurance design may provide a better means of controlling prescription utilization and spending for certain medication classes.

EFFECT OF COST-SHARING CHANGE FROM COPAYMENT TO COINSURANCE ON MULTIPLE SCLEROSIS SPECIALTY DRUG EXPENDITURES AND UTILIZATION

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INTRODUCTION: The impact of a copayment to coinsurance drug benefit change on multiple sclerosis (MS) specialty drug expenditures and utilization was determined through a retrospective cohort study.

METHODS: Expenditures and utilization of beneficiaries, continuously enrolled in 2 privately insured groups, were compared before and after a benefit design change in one of the groups.

RESULTS: The average increase in the patient out-of-pocket costs for the MS drug class from the preperiod to the postperiod was $60.10 more per user per month (PUPM) in the intervention group (n = 84) than in the control group (n = 19) (P < 0.01). Employer group and total expenditures decreased for the intervention group and increased for the control group. The DD for the employer groups costs was -$297 PUPM (P <0.01), and the DD for total expenditures was -$237 PUPM (P = 0.01). Utilization decreased in the intervention group by 0.08 PUPM and increased in the control group by 0.12 PUPM. The utilization DD was -0.21 (P = 0.01).

CONCLUSIONS: Switching to a coinsurance-design decreased MS injectable drug spending, however, resulted in decreasing utilization. The consumer share of the cost of the medication, in this case, was increased significantly. More research is needed to determine if this cost-share change negatively impacted the health of these patients.
EFFECT OF PRESCRIPTION COPAY ON TREATMENT FAILURE WITH ORAL ANTIDIABETIC MEDICATIONS

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BACKGROUND: Previous studies have shown that an increase in patient cost sharing for medications results in reduced medication use.

INTRODUCTION: The purpose of this study was to determine if the amount of member copay predicted oral antidiabetic treatment failure in a managed care population.

METHODS: Health plan members aged ≥18 years diagnosed with type 2 diabetes mellitus and newly initiated on an oral antidiabetic drug (OAD) between January 1, 2002, and January 31, 2006, were identified from a U.S. managed care population totaling approximately 12 million lives. Members were excluded if they did not have continuous eligibility for at least 6 months before and 12 months after the index prescription. Members were placed into 4 treatment groups based upon class of OAD initiated and were followed for 1 year. Treatment failures were defined as discontinuation or therapy switch of index OAD. Time on index OAD was measured until treatment failure or censoring of data. Copays were identified for every prescription, and amount per 30 days of treatment was calculated. Cox proportional hazards models were used to ascertain the impact of copay on treatment failure, using copay as a continuous time-varying covariate, adjusting for differences in member characteristics.

RESULTS: A total of 18,658 members met study criteria, with 8,437 on metformin, 4,938 on a sulfonylurea, 4,754 on thiazolidinediones, and 529 on meglitinide or nateglinide. A total of 13,091 (70%) failed initial treatment (sulfonylureas [72%], metformin [69%], thiazolidinediones [69%], and meglitinide/nateglinide [86%]). Mean OAD treatment time was 189 days. For every $10 increase in copay, members were 25.6% (95% confidence interval, 25.2-25.9) more likely to fail OAD treatment (P < 0.0001).

DISCUSSION: Higher member copays were a significant predictor of treatment failure. With more and more health plans increasing member cost sharing, the impact on treatment persistence for chronic conditions will require ongoing evaluation.

Efficacy and Medication Cost in a Managed Care Organization (MCO) When Using Three Oral Antidiabetic Medications Versus Metformin Plus Insulin, After Failing Two Oral Antidiabetic Medications

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INTRODUCTION/BACKGROUND: Controlling hyperglycemia reduces the risk of microvascular disease and alleviates the classic symptoms of diabetes mellitus including, but not limited to, polydipsia, polyphagia, and polyuria. As part of an integrated health system, health care providers work together to ensure that cost-effective treatment is part of a care process model for diabetic members. Member-specific data needs to be evaluated often in order to guarantee the best service possible is being provided to health plan members.

OBJECTIVE: The primary objective of this study was to evaluate glycemic control, by glycosylated hemoglobin (A1C) values, in type 2 diabetic members who failed 2 oral diabetic medications. The health plan compared members who took 3 oral antidiabetic medications with members using a mixed insulin (70% aspart protamine/30% aspart) plus oral metformin therapy.

METHODS: The health system’s electronic medical record system was used to identify and evaluate a subset of type 2 diabetic members who were using 3 oral antidiabetic medications or metformin plus insulin during a 12-month period; the time period evaluated was October 1, 2005, through September 30, 2006. To be included in the analysis, members needed to have filled 2 oral antidiabetic medications for at least a 90-day period during the prior year. Members also recorded a preintervention and postintervention A1C. Members were assigned to 2 groups according to their medication regimen. The first group consisted of all members taking 3 different oral antidiabetic medications. Members of this group needed to have at least 180 days of concomitant triple oral therapy throughout the year. A combination medication (i.e., glyburide/metformin 2.5/500 mg), counted as 2 different medications. The second group consisted of all members using a mixed insulin (70% aspart protamine/30% aspart) plus oral metformin therapy. Members in this group were required to have at least 180 days of metformin therapy and at least 180 days of concomitant insulin therapy. A1C values were retrieved from the electronic medical record system and were reviewed and evaluated by 3 pharmacists and 1 computer data analyst. Pharmacy and medical claims were analyzed to determine the associated costs of pharmaceutical therapy as well as overall and diabetic associated medial expense between groups.

RESULTS: The oral group (members taking 3 oral medications) contained 73 members. The insulin/metformin group contained 13 members. The A1C values showed noninferiority between groups. The oral group’s average A1C value was 7.64%, while
The metformin/insulin group's average A1C value was 8.00% (P = 0.37 between groups). Throughout the evaluated year, the average allowed spend on diabetic medications in the oral group was $4,841/member. The spend for the metformin/insurance group was $2,760.

CONCLUSION: In this retrospective analysis, hyperglycemic control was similar between groups, but the overall spend on diabetic medications was less expensive in the metformin/insurance group.

Efficacy and Tolerability of Interferon Beta Products for Relapsing-Remitting Multiple Sclerosis: The Quality Assessment in Multiple Sclerosis Therapy Study

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BACKGROUND: Comparing clinical efficacy from phase 3 studies of interferon (IFN) beta products used to treat multiple sclerosis (MS) is difficult because of differences in study design, outcomes, and population. There is conflicting evidence from several open-label postmarketing studies regarding efficacy among interferon beta products.

OBJECTIVE: The purpose of the Quality Assessment in Multiple Sclerosis Therapy (QUASIMS) study was to compare the efficacy and tolerability of IFN beta products and dosing regimens used to treat MS.

METHODS: An open-label, retrospective, observational study conducted in 14 countries. Patients with clinically definite MS who had received 2 years of uninterrupted therapy with IFN beta as initial therapy (IT) or follow-up therapy (FT) were included. Study endpoints were change in Expanded Disability Status Scale (EDSS) score, proportion of patients with sustained disease progression, (≥1.0 point increase in EDSS score over 2 years), annualized relapse rate, and reasons for therapy change.

RESULTS: 7,159 patients were included in the analyses. There were no significant differences among IFNs in mean EDSS scores at baseline, after 1 year, and after 2 years of treatment. The percentage of progression-free patients over 2 years in the IT group was significantly lower for Rebif 44 mcg (57.5%, P = 0.0001) and Betaseron (52.7%, P < 0.0001) compared with Avonex (66%). With the exception of Betaseron (52%), approximately 60% of patients in the FT groups were progression-free at 2 years. There were no differences among IFNs in annualized relapse rates over 2 years, although rates in FT patients were generally higher than those of IT patients. The most common reason for therapy change was perceived lack of efficacy. In this study, switching to a higher dose or more frequent administration of IFN did not improve outcomes.

CONCLUSIONS: In general, the IFN beta products have similar efficacy and are most beneficial when used as initial therapy.

Erythropoietic-Stimulating Agent Utilization and Costs in Chronic Kidney Disease Patients Not on Dialysis in the Managed Care Setting

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INTRODUCTION: Epoetin alfa (EPO) and darbepoetin alfa (DARB) are 2 erythropoietic-stimulating agents approved for the treatment of anemia in patients with chronic kidney disease (CKD).

OBJECTIVE: To compare recent dosing patterns and associated drug costs of EPO and DARB in CKD patients not on dialysis in managed care organizations from January 2004 through December 2005.

METHODS: This retrospective analysis was conducted using medical claims data from approximately 35 health plans nationwide. Eligible patients were aged ≥18 years, newly initiated on EPO or DARB, and had ≥2 doses from January 2004 through December 2005 for anemia of predialysis CKD. If a patient was undergoing renal dialysis, data were collected and censored 30 days before the first dialysis date. Patients diagnosed with cancer or who had undergone chemotherapy in the time period from 90 days prior to treatment initiation or during treatment were excluded. Mean weekly doses weighted by treatment duration were used to calculate drug costs based on September 2006 wholesale acquisition costs (WAC—EPO: $0.01217/unit, DARB: $4.446/mcg).

RESULTS: 860 patients (532 EPO, 328 DARB) met the entry criteria and formed the study population. EPO patients were slightly older (65.9 vs. 62.7 years, P = 0.003), with similar gender distribution between groups. Use of extended dosing regimens (≥ every 2 weeks [Q2W]) was observed in the majority of patients in both groups (EPO: 69%, DARB 92%). The mean (SD) dose per injection was 24,775 (17,950) units for EPO and 112.9 (109.9) mcg for DARB. The weighted average (SD) weekly dose was 13,776 (11,699) units for EPO and 50.0 (47.9) mcg for DARB, corresponding to an average weekly erythropoietic drug cost of $168 for EPO and $222 for DARB (P < 0.0001).

CONCLUSION: Use of extended dosing (≥Q2W) was observed in both EPO and DARB patients. DARB costs were 32% higher than EPO.
■ EVALUATION OF AN APPROPRIATE ANTIBIOTIC USE PROGRAM WITHIN AN INDEPENDENT PRACTICE ORGANIZATION

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BACKGROUND: The Centers for Disease Control and Prevention reports that up to 50% of the antibiotics prescribed in the nation are unnecessary; therefore, there is a need for programs that promote the appropriate use of antibiotics.

OBJECTIVE: To evaluate the impact of an appropriate antibiotic use intervention involving viral kits on antibiotic prescribing patterns of providers within the group.

METHODS: Hill Physicians Medical Group led a comprehensive campaign that included presentations at physician meetings, antibiotic prescribing profiles, and educational materials. In addition, viral kits promoting supportive care treatments were distributed to 52 randomly selected primary care providers (PCPs) and pediatricians to offer their patients an alternative to an antibiotic prescription. Another 52 physicians who did not receive the viral kits were randomly selected to serve as a control group.

RESULTS: Overall antibiotic prescribing rates increased in both groups. However, the control group experienced an increase of 8.8% (342 vs. 372 prescriptions/1,000 members/year) compared with a 4.7% increase in the intervention group (467 vs. 489 prescriptions/1,000 members/year) from the 2004-2005 to the 2005-2006 flu seasons. Therefore, approximately 50% fewer antibiotics were prescribed in the intervention group versus the control group.

CONCLUSION: Although both groups experienced an increase in antibiotic utilization during the 2005-2006 flu season, the use of viral kits as an appropriate antibiotic utilization program may have helped to reduce the percentage of antibiotic prescribed.

■ EVALUATION OF ESZOPICLONE AND ESCITALOPRAM OXALATE COTHERAPY IN PATIENTS WITH GENERALIZED ANXIETY DISORDER AND INSOMNIA


INTRODUCTION: Generalized Anxiety Disorder (GAD) may occur with comorbid insomnia.

OBJECTIVE: To evaluate the efficacy of eszopiclone (ESZ) and concurrent escitalopram oxalate (EO) in patients with insomnia and comorbid GAD.

METHODS: Patients meeting Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria for GAD and insomnia received 10 weeks of EO 10 mg and were randomized to nightly cotherapy with either ESZ 3 mg (n=294) or placebo (PBO) (n=301) for the first 8 weeks. For the last 2 weeks, ESZ was replaced with single-blind PBO to evaluate discontinuation effects. Sleep, daytime functioning, and anxiety measures along with adverse events (AEs) were captured during the study.

RESULTS: Compared with PBO+EO, ESZ+EO improved sleep and daytime functioning at each week and the average of the double-blind period (P <0.05). At week 8, significantly more ESZ+EO patients had no clinically meaningful insomnia based on Insomnia Severity Index (ISI) ≤7. Significant improvements with ESZ+EO were observed in Hamilton Anxiety Rating Scale (HAM-A) total scores each week and at weeks 4-10, excluding the insomnia item. Clinical Global Impression, Improvement Scale (CGI-I) was improved with ESZ+EO at every time point (P <0.02), while CGI-S was not different between treatments after week 1. Median time to anxiolytic response was reduced with ESZ+EO based on HAM-A and CGI-I. HAM-A response and remission rates at week 8 were higher with ESZ+EO, and HAM-D17 scores were improved at all time points (P <0.004).

At week 10, after eszopiclone discontinuation, there was no evidence of rebound insomnia, and there were no treatment differences in sleep or daytime function measures. Significant treatment differences in anxiety and mood were maintained at week 10. Overall rates of AEs were similar in the 2 treatment groups (78% for ESZ+EO vs. 68% for PBO+EO).

CONCLUSION: In this study, ESZ+EO was well tolerated and associated with improved sleep and daytime function without evidence of tolerance. Improvements in anxiety and mood were observed with ESZ+EO compared with PBO+EO in patients with GAD and insomnia.

■ EVALUATION OF PRESCRIPTION REFILL PATTERNS BASED ON DAILY DOSING REGIMEN AND PILL LOAD FOR CALCIUM CHANNEL BLOCKERS

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BACKGROUND: There is a paucity of data that exists concerning refill rate behavior (persistence and adherence) with different daily dosing regimens in an ambulatory setting.

OBJECTIVE: This study analyzed the prescription refill rates of different calcium channel blockers formulated for different daily dosing regimens, after controlling for patient copay.

METHODOLOGY: This retrospective cohort study used records of health service reimbursement from U.S. health plans within the MedStat MarketScan database. Study subjects were patients with a physician-visit for essential hypertension (International Classification of Diseases, Ninth Revision, Clinical Modification...
BACKGROUND: The health plan's Hypertension Disease Management Program identifies hypertensive members and provides case manager interaction as well as educational material about management, evaluation, and treatment of hypertension. Case managers educate members about lifestyle modifications such as diet and exercise and provide members with blood pressure monitors and instructions to follow-up with their health care provider as needed.

OBJECTIVE: The objective of this study was to assess blood pressure control and compliance with The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines among members in the health plan’s Hypertension Disease Management Program compared with hypertensive members not enrolled in the program.

METHODS: The health plan’s electronic medical records were used to identify all members with a diagnosis of hypertension, continuous enrollment in health plan for the 13-month study period, and at least 1 outpatient visit to a provider for hypertension. Two random samples of hypertensive members were identified; a general sample of all hypertensive members (n = 348 patients) and a sample of members enrolled in the Disease Management Program (n = 253 patients). For each sample, medical claims data was used to identify specific comorbidities per JNC 7 guidelines, such as diabetes, ischemic heart disease, and/or heart failure. Pharmacy claims data was used to assess medication treatment patterns. Medical chart reviews were conducted to confirm a diagnosis of hypertension, document blood pressure, describe demographic characteristics, and measure the prevalence of cardiovascular risk factors and target organ damage.

RESULTS: Members in the disease-managed sample had lower average blood pressures and achieved a blood pressure goal of <130/80 mm Hg (<120/70 mm Hg with diabetes) more often than those in the general hypertensive sample. There was no difference in compliance with JNC 7 guidelines in the presence of comorbid conditions and appropriate medication selection. Key results are summarized in the table on page 208. Treatment patterns and switching data were also assessed and will be presented later.

CONCLUSION: The health plan’s Hypertension Disease Management Program significantly improves the percentage of members who achieve their recommended blood pressure goals as defined by JNC 7.

FENTANYL PATCH QUANTITY PER CLAIM DISPENSING PATTERNS AND PATIENTS’ MEDICAL DIAGNOSES: UTILIZATION MANAGEMENT OPPORTUNITY ASSESSMENT

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INTRODUCTION: Fentanyl patch therapy is indicated for management of persistent, moderate-severe chronic pain requiring continuous around-the-clock opioid administration that cannot be managed by other means. The analyses estimate a savings opportunity from off-label and high quantity fentanyl patch prescribing.

METHODS: Medical and pharmacy claims data from a 1.8 million member BlueCross/BlueShield plan were analyzed. Members with a fentanyl patch claim during second quarter (2Q) 2005 had their medical claims from third quarter 2004-2Q2005 evaluated for the presence of a cancer, AIDS, fracture, burn, crush injury, neuropathic pain, or localized pain diagnosis. Off-label use was defined as a localized pain diagnosis only. Fentanyl patches deliver drugs for 72 hours; 10 patches should provide a 30-day supply.

RESULTS: During 2Q2005, 2,167 members had 6,171 claims (85.2% generic) at a total plan paid $1,087,093, and an average $176 plan paid per claim. Per-member-per-month (PMPM) plan paid was $0.20. The most common diagnosis was localized pain. Claims with a quantity dispensed of 1 to 15 represented 5,899 of 6,171 (95.6%) at an average $156 plan paid per claim. There were 272 (4.4%) claims with a quantity >15 at an average $622 plan paid. A 15-patch quantity limit per claim could have potentially saved 272 claims x ($622-$156) = $126,752.
per quarter or $0.02 plan paid PMPM. A prior-authorization program that would limit fentanyl use to members with a U.S. Food and Drug Administration-approved indication could reduce use among the 898 (41.4%) members with a localized pain diagnosis, potentially saving $0.414 x 6,171 claims x $176 plan paid per claim = $449,644 per quarter or $0.08 plan paid PMPM, although some savings would go to other pain therapies.

CONCLUSIONS: A fentanyl patch prior authorization or a quantity limit program may reduce off-label or large-quantity prescribing and plan expenditures by $0.02 to $0.08 PMPM.

(See table on page 208.)

FORMULARY MANAGEMENT OF ANTILIPIDEMIC DRUGS IN THE DEPARTMENT OF DEFENSE

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BACKGROUND: The Department of Defense (DoD) pharmacy benefit provides prescription services to more than 9 million beneficiaries across the Military Health System. The benefit is delivered through 3 different points of services, each with different pricing structures, copay structures, and the ability of patients to move freely across each point of service (POS).

INTRODUCTION: The DoD provides the pharmacy benefit through a single uniform formulary (UF) review process. This review process will be outlined for the antilipidemic agents taking into account clinical and cost-effectiveness.

METHODS: The drug class members were divided into 2 categories, low-to-moderate versus intensive-dose cholesterol-lowering drugs. The low-to-moderate category was defined as antilipidemic agents with a potential to reduce low-density lipoprotein cholesterol (LDL-C) by more than 45%, while the intensive agents reduced LDL-C by more than 45%. An evidence-based clinical effectiveness review included a comprehensive literature evaluation of meta-analyses, clinical trials, and retrospective claims database studies. Efficacy was assessed in primary and secondary prevention of coronary heart disease and acute coronary syndromes. The safety assessment evaluated differences in elevated liver transaminases, proteinuria, and myotoxicity associated with the class. Tolerability and other factors, including special populations, were discussed to differentiate the members of the drug class. Providers, including cardiologists, were also surveyed to obtain expert opinion regarding relative differences between agents. Finally, clinical factors were incorporated into 4 pharmacoeconomic models to complete the cost-effectiveness review across all 3 POSs.

CONCLUSION: Taking into consideration the conclusions from the relative clinical and cost-effectiveness determinations of the antilipidemic agents, other relevant factors, the DoD Pharmacy & Therapeutics Committee recommended across all 3 POSs that atorvastatin, fluvastatin immediate and extended release, pravastatin, simvastatin, lovastatin immediate and extended release, lovastatin/niacin, ezetimibe/simvastatin, niacin immediate and extended release, and ezetimibe be maintained as formulary on the UF and that rosuvastatin and atorvastatin/amiodipine be classified as nonformulary under the UF.

HAWAIIAN STUDY OF LIVER DISEASE

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BACKGROUND: Ursodiol tablets and capsules can be used in a variety of chronic liver conditions. Williams et al., demonstrated significant bioavailability differences between 2 dosage forms of ursodiol—capsule and tablet. However, no studies in patients with active disease have been conducted examining the differences on liver function tests (LFTs). As part of a formulary review process, the health plan (HMSA Hawaii) conducted a drug utilization review of local hepatologists’ medical records to assess if a pharmacodynamic difference existed between the 2 different dosage forms.

OBJECTIVE: To determine if the bioavailability differences between ursodiol tablets and capsules translate into pharmacodynamic changes in LFTs in patients with diagnosed liver disease.

METHODS: The cohort of patients had at least 1 office visit during 2004 for 1 of the following chronic liver conditions: nonalcoholic fatty liver disease, primary biliary cirrhosis, infectious hepatitis, or chronic liver disease and cirrhosis. Analysis of variance (ANOVA) was conducted to assess any observed differences in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels in patients using the 2 different dosage forms.

RESULTS: 71 medical records were identified from the medical claims report as meeting 1 of the diagnosis criteria and receiving at least 1 prescription for ursodiol. The patient population comprised 43 female patients, and the 2 largest ethnicities represented were Asian (n = 37) and white (n = 16). A total of 40 patients received ursodiol capsules at a mean daily dose of 825 mg, and 31 patients received ursodiol capsules at a mean daily dose of 1,016 mg. Among the ursodiol-capsule-treated patients, the percentage reduction in ALT and AST was 38% and 35%, respectively. This compares with a reduction in ALT and AST for the ursodiol capsule group of 27% and 13%. Ursodiol tablets produced a significantly greater reduction in ALT and AST than the capsule formulation (P <0.05; ANOVA).

CONCLUSIONS: In this retrospective review, we observed that ursodiol tablets were associated with a greater reduction in LFTs compared with ursodiol capsules. This drug utilization review confirms the results demonstrated in an in vivo bioavailability study involving healthy volunteers by Williams et al. The pharmacodynamic differences could be important as clinicians and formulary decision makers examine the various products, but further research is needed in more stringent controlled studies.
HEALTH CARE COSTS AND RESOURCE UTILIZATION OF PATIENTS WITH MULTIPLE SCLEROSIS IN A COMMERCIAL MANAGED CARE ENVIRONMENT

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BACKGROUND: Multiple sclerosis (MS) is a chronic disease of the central nervous system (CNS) associated with significant costs to health care plans.

OBJECTIVE: The purpose of the MS Benchmarks study was to observe how demographic, administrative, and clinical variables affect MS costs and utilization patterns and to examine the economic impact of treating MS with interferon (IFN) beta.

METHODS: A retrospective, claims-based observational study based on a database of 45 million managed care members and more than 80 health care plans was conducted. Inclusion criteria were enrollment in the CNS (Episode Treatment Group codes 149 or 150) and a diagnosis of MS (International Classification of Diseases, Ninth Revision code 340). Resource utilization across all health care service categories (inpatient, outpatient, emergency room, and pharmacy) was calculated to determine total episode costs. For MS, an episode was defined as a period of 1 year.

RESULTS: Over the 3-year study period, 41,425 patient-episodes were analyzed, with 10,099 patients analyzed for 2004. Mean patient age was 47 years, and the majority (77%) were female. The average cost of an MS episode for patients on immunomodulatory therapy was $18,944. Intramuscular (IM) IFN beta-1a demonstrated the lowest total episode cost compared with the other IFN beta products. Patients on IM IFN were more likely to refill their IFN prescription (average 10.4/year vs. 8.7/year for other IFNs) and were less likely to use antidepressants, anti-convulsants, antihistamines, oral antispastics, narcolepsy agents, narcotic analgesics, and overactive bladder agents. Furthermore, these patients required the least neutralizing antibody testing and were least likely to experience injection complications among all patients treated with IFN beta products.

CONCLUSIONS: Costs associated with treating patients on IM IFN beta-1a were lower than those of patients treated with other IFN beta products. Data presented here provide a unique method for determining costs associated with MS care.

(See table on page 208.)

HEMOPHILIA CASE MANAGEMENT PROGRAM

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BACKGROUND: Hemophilia is a rare disease that affects about 20,000 people in the United States. Treatment involves the infusion of procoagulation factor products. For payers, the cost of care for even a small number of hemophilia patients is significant. Intensive, coordinated case management can improve clinical and financial outcomes.

INTRODUCTION: The outcomes of a Hemophilia Case Management Program for 2 Medicaid plans, which included 65 hemophilia patients, demonstrated an improvement in the delivery of medical care and quality of life as well as significant reductions in medical and pharmacy costs.

METHODS: The Hemophilia Case Management Program delivered individualized care for each hemophilia patient through the coordinated efforts of the patient, their nurse case manager, utilization management pharmacist, family/caregiver, physician, and the distribution pharmacy. Patients were identified for the program using International Classification of Diseases, Ninth Revision codes from medical claims data and from prior-authorization requests for factor products. Voluntary enrollment consents were obtained. Member risk was stratified based on disease severity. Nurse case manager interventions, including patient education and home visits, were based on the patient’s risk, medical needs, and ability to manage their disease. Clinical outcome measures were assessed regularly. The program required close oversight of factor product distribution and aggressive vendor contracting.

RESULTS: Over a 3-year period, the number of emergency room visits decreased by 63% and in-patient visits decreased by 57%. The total cost savings on factor products exceeded $10.5 million.

CONCLUSIONS: A coordinated Hemophilia Case Management Program has a positive impact on the delivery of medical care, education of patients, and clinical outcomes and results in a reduction in the use of medical resources.

HOSPITAL EXPENDITURES AND PREVALENCE BY TREATMENT PATTERN IN ULCERATIVE COLITIS: THE PERSPECTIVE OF A SELF-INSURED EMPLOYER

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OBJECTIVE: To characterize hospital expenditures and relationships associated with ulcerative colitis (UC) and enhance awareness of their impact on a large, self-insured employer.

METHODS: A retrospective analysis of claims data from 2002 to 2004 for patients with UC (International Classification of Diseases, Ninth Revision code 556.x) were analyzed from a database of a self-insured employer, consisting of approximately 500,000 employees, retirees, or dependents. Eighteen months of continuous enrollment was required (6 months preindex and 12 months postindex date). A randomly selected age-and-gender-matched group of noncolitis claimants was the comparator group. 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 (hospitalized for UC) cohort.

**RESULTS:** Inpatient costs were evaluated for 1,057 UC patients and 4,228 comparators. Total inpatient costs were higher for UC patients than controls ($3,185 vs. $728) and highest for UC patients with severe disease as compared with those with mild and moderate disease ($10,172 vs. $2,028 and $1,849). Inpatient costs comprised 45% to 46% of total costs for severe UC patients. Hospitalizations were most prevalent among UC patients having no treatment (14.5%) or who were treated with corticosteroids, whether alone (10.4%) or in combination (15.5%). Treatment that included immunosuppressive, intravenous, and/or methotrexate without corticosteroids accounted for fewest hospitalizations (7.8%) apart from those treated only with topical agents (4.8%).

**CONCLUSIONS:** Inpatient costs were higher for patients with UC than controls, especially those patients with severe disease. Hospitalizations were most prevalent for UC patients not receiving treatment or receiving corticosteroids. Those receiving topical agents only had the lowest prevalence of hospitalization but were also likely to have more mild disease. Results indicate that treating severe UC with immunosuppressive, intravenous, or methotrexate therapy will reduce prevalence of hospitalizations, a key driver to higher costs.

### IMPACT OF ADHERENCE TO ORAL ANTIHYPERGLYCEMIC AGENTS ON GLYCEMIC CONTROL

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**INTRODUCTION:** Nonadherence to medication may decrease the effectiveness of treatment. This study assessed the relationship between adherence to oral antihyperglycemic agents (OHA) and glycemic control for patients with type 2 diabetes.

**METHODS:** Medical claims, pharmacy claims, and the electronic medical record of a primary care-based network of clinics were used to identify patients aged ≥18 years who had initiated OHA therapy between 01/01/01 and 12/31/04, had 1 or more diabetes diagnosis codes (International Classification of Diseases, Ninth Revision 250.x), and were continuously enrolled for at least 6 months during the study period. Subjects were followed for up to 24 months (or until 06/30/05) from the date of first prescription fill (index date). Adherence was calculated as the sum of days supply from the index date to the last prescription fill date, divided by the duration of therapy. Glycemic control was assessed based on most recent glycosylated hemoglobin (A1C) measurement within the study period, collected at least 60 days following the index date.

**RESULTS:** A total of 481 subjects were identified: mean age 55 ± 12 years, 59% female. Mean baseline A1C was 8% (range, 4%-14%) and mean adherence was 82% (SD = 21). Sixty-five percent of subjects had good adherence (280%). Approximately 61% achieved glycemic control (A1C <7%). Mean adherence was higher among patients achieving glycemic control (84 vs. 78, P = 0.07). An inverse relationship existed between OHA adherence and A1C such that when controlling for baseline A1C levels, each 10% increase in OHA adherence was associated with a 0.1% A1C decrease (P <0.01).

**CONCLUSIONS:** Adherence to OHA agents was strongly associated with glycemic control. Patients with good adherence were more likely to achieve glycemic control compared with those with fair or poor adherence. Greater efforts are needed to facilitate diabetes self-management behaviors to improve patient outcomes and prevent costly complications.

### IMPACT OF ANTIHYPTERTENSIVE THERAPY MODIFICATIONS ON HYPERTENSION AND CARDIOVASCULAR-RELATED COSTS

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**PURPOSE:** Hypertension affects approximately 65 million Americans, costing nearly $60 billion. Study objectives were to evaluate the impact of treatment modifications on hypertension and cardiovascular-related costs.

**METHODS:** Administrative claims data from January 2000 to February 2005 from an integrated health care system were utilized to retrospectively identify antihypertensive-naive patients initiated on therapy with angiotensin-converting enzyme inhibitors (ACEIs), beta-blockers, diuretics, calcium channel blockers (CCBs), ACEI/diuretics, fixed-dose ACEI/CCBs, and ACEI+CCBs (free combination). Patients were evaluated 12 months postinitiation date for treatment modifications, health care resource utilization, and costs. Therapeutic modifications evaluated were augmentation, dropped drug (for those on multiple antihypertensive agents), switch between classes, switch within class, dose increase, and dose decrease. Multivariate analyses were conducted to evaluate outcomes adjusting for age, gender, geographic region, comorbidities, baseline utilization, and index medication.

**RESULTS:** A total of 141,646 patients were identified. Mean patient age was 54 ± 13 years; 49.5% were male. The most common comorbidities identified 12 month preindex baseline period were dyslipidemia (30%) and diabetes (12.5%). The mean number of distinct medications filled per patient in the 12 month preindex baseline period was 4.2. The most frequent therapeutic modification was increased dose (51.2%), augmentation (37.4%) and switch between classes (32.1%). Both hypertension-related costs and cardiovascular-related costs significantly increased incrementally with number of treatment
modifications. Cost ratios associated with ≥5 modifications were 2.77 (P <0.001) and 3.03 (P <0.001) for hypertension-related and cardiovascular-related costs, respectively.

CONCLUSIONS: Study findings underscore the impact of therapeutic modifications on health care costs and highlight the need to minimize changes in pharmacologic therapy over time. Incremental benefits gained with optimizing initial antihypertensive treatment may offset impact on health care costs and warrant further research. 

(See table on page 209.)

IMPACT OF CHANGES IN EXERCISE CAPACITY ON CLINICAL WORSENING AND RELATED COSTS AMONG PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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INTRODUCTION: Exercise capacity evaluated using the 6-minute walk distance (6MWD) is the standard endpoint in studies of new therapies for pulmonary arterial hypertension (PAH). To translate these results into economic consequences, one must understand how changes in 6MWD affect clinically relevant outcomes. This study examines this impact.

METHODS: Endothelin receptor antagonists have emerged as first-line treatment for PAH. To assess the economic impact of these therapies, a model was developed that implements equations predicting clinical worsening (PAH-related hospitalization, lung transplant, atrial septostomy, add/switch treatment, or death) as a function of 6MWD and baseline age. These equations were derived from the ambrisentan and placebo data of the ARIES-I and ARIES-II clinical trials (n = 356), as were patient characteristics. Direct costs were obtained from U.S. discharge databases and are reported in 2006 USD.

RESULTS: Current 6MWD and mean age at the start of treatment emerged as significant predictors of clinical worsening; based on an average annual base hazard of 27.3 per 100 patients. In 1,000 patients with a mean baseline age of 50.2 years and 6MWD of 250 meters, 91.2 clinical worsening events are predicted to occur in a month, at an average cost of $2,105 per member per month. As 6MWD improves, events are less frequent and costs decrease, but nonlinearily. For example, a 35-meter improvement from a 6MWD of 250 results in a reduction of 36.6 events per 1,000 patients in a month, at a cost of $846 per patient relative to 17.8 events at a cost of $411 when the 35 meter improvement was starting from 300 meters.

CONCLUSIONS: Improvement in exercise capacity is predicted to decrease the number of events and, in turn, the cost per member per month. The largest impact is observed in patients with the poorest physical functioning.

IMPACT OF LOWERING MEMBERS’ OUT-OF-POCKET COSTS FOR STATIN MEDICATIONS ON ADHERENCE

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OBJECTIVE: To evaluate the impact of lowering members’ out-of-pocket costs for statin medications on adherence.

METHODS: On February 1, 2006, the employer changed the reimbursement rate for atorvastatin, lovastatin, pravastatin, rosvuastatin, and simvastatin from coinsurance to a flat dollar copay. The average coinsurance for a 90-day supply of these medications had been approximately $90 and was lowered to $6 for generics and $8 for brands. To control net cost, members were required to participate in a half-tablet program to receive the reduced copay. Members were educated about the half-tablet program through a letter campaign that explained a higher dose of medication was needed for appropriate care and that included a coupon for a free tablet splitter. An exception was made for members who required the highest dose of their statin medication to receive the reduced copay. Claims were collected for members who received these medications in February and tracked through September in 2004, 2005, and 2006; adherence and cost data were analyzed for each 8-month period.

RESULTS: The incidence of complete adherence—a possession ratio of 1 or greater—increased by 16.8% in members who received an impacted statin medication in February 2006 compared with February 2005. The financial impact of this increase in adherence was a net cost per member increase of 3.3% for the employer and a decrease of 24.1% for the member. These figures were improved when compared with change in experience of February 2005 to February 2004. Only a 2.7% increase in complete adherence was achieved, while employer and member costs increased at a rate of 2.5% during this period.

CONCLUSION: Lowering members’ costs for statin medications while implementing a half-tablet program increases the rate of adherence and limits an employer’s financial risk.

IMPACT OF PERSISTENCE TO ANTI-TUMOR NECROSIS FACTOR THERAPY ON RHEUMATOID ARTHRITIS-RELATED HEALTH CARE COSTS

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OBJECTIVE: To evaluate the impact of persistence with anti-tumor necrosis factor (anti-TNF) treatment on rheumatoid arthritis (RA)-related health care costs among RA patients, utilizing a managed care database.

METHODS: A retrospective study utilizing the PharMerics managed care administrative claims database was conducted. The first anti-TNF (infliximab, etanercept, or adalimumab) encounter
Relapses in multiple sclerosis (MS) are a major risk for recurrent hospitalization, physician visits, and other medical service costs. CONCLUSIONS: Patients who were persistent had a slightly lower disease severity compared with the lower-persistency cohort. Also, patients who were receiving a repeat rituximab course after week 24 had costs similar to those of patients with 1 relapse only at index relapse at days 0-30 ($21,350 vs. $21,015), monthly costs were higher for patients with ≥2 relapses at days 31-90 ($3,792 vs. $2,712) and remained higher at days 271-360 ($3,636 vs. $1,676). Monthly costs were generally higher for previously diagnosed patients, with the exception of the acute phase of relapse (days 0-30) in the ≥2 relapses subset. CONCLUSION: Recurrent relapses are associated with increased costs, both in the acute phase of managing a relapse and during the follow-up year in both newly diagnosed and previously diagnosed patients.

IMPACT OF RITUXIMAB ON JOINT STRUCTURAL DAMAGE IS INDEPENDENT OF CLINICAL RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS (REFLEX STUDY)


INTRODUCTION: Rheumatoid arthritis patients were treated with methotrexate with or without rituximab to investigate the effects of therapy on joint structural damage and its possible association with clinical response. METHODS: Patients who had experienced an inadequate response to ≥1 tumor necrosis factor (TNF) inhibitors and who were receiving methotrexate were randomized to receive rituximab (2 x 1-g infusions with a 2-week interval) or placebo, with eligible patients receiving a repeat rituximab course after week 24, if necessary. An independent central reading site evaluated radiographs of hands and feet obtained at baseline, week 24, and week 56, using the Genant-Sharp method, blinded to sequence and number. Preliminary analyses of data from week 56 and a subgroup analysis of patients who were ACR20 (American College of Rheumatology, 20% response criteria) nonresponders at week 24 are presented here. RESULTS: Significant differences were observed between the rituximab and placebo arms with respect to mean change in total Genant-Sharp score and mean changes in erosion and joint space narrowing (JSN) scores. ACR20 nonresponding patients at week 24 treated with rituximab had significantly less total progression than had those who received placebo. CONCLUSIONS: Rituximab can prevent joint structural damage in a patient population previously unresponsive to treatment with ≥1 TNF inhibitors, independent of ACR20 response to treatment. (See table on page 209.)
IMPACT OF THE BP DOWNSHIFT PROGRAM ON BLOOD PRESSURE CONTROL AMONG COMMERCIAL DRIVER’S LICENSE EMPLOYEES: A MANAGED CARE PERSPECTIVE

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INTRODUCTION: Rising health care costs to large, self-insured employers in the United States have prompted interest in programs to help manage and prevent chronic conditions. The BP DownShift Program was designed to improve blood pressure (BP) outcomes among commercial driver’s license (CDL) employees in light of recent changes in the Department of Transportation’s (DOT) Hypertension Guidelines for CDL recertification.

OBJECTIVE: To assess the impact of the BP DownShift Program on BP outcomes among CDL employees at a large southeastern U.S. utility company.

METHODS: This study evaluated the DOT Medical Examination Report for Commercial Drivers Fitness Determination prior to and after the BP DownShift Program for a random sample of CDL employees. The program consists of various educational materials for use by employers, employees, and physicians. Clinical data included BP measurement, body mass index (BMI), and patient-reported medical history. Guidelines issued by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure were used to classify employees’ hypertensive status.

RESULTS: A total of 501 CDL employees were assessed; all were male, most (66%) were aged 40 years or older, and mean BMI was 30 kg/m². Compared with baseline, fewer employees were hypertensive (Stage 1 or 2) following the program (25% vs. 18%, P <0.01). Among employees taking antihypertensive medication, a greater number were considered normal in the follow-up period compared with baseline (13% vs. 8%). In addition, a significantly smaller percentage had Stage 1 or 2 hypertension (42% vs. 26%, P <0.05).

CONCLUSIONS: The BP DownShift program was associated with a significant reduction in the number of CDL employees with hypertension. Further investigation is warranted to assess the long-term impact of BP DownShift and associated financial implications.

IMPLEMENTATION OF A WEB-BASED CONSUMERISM HEALTH AND COST MANAGEMENT TOOL: DIRECTINFORM

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BACKGROUND: DirectInform was implemented in a large self-funded employer group starting January 1, 2006.

OBJECTIVE: To describe the implementation of a Web-based consumerism health and cost management tool (DirectInform).

METHODS: During the first 2 quarters of 2006, individualized health and cost-savings recommendations were identified monthly for approximately 50,000 members using a proprietary business and clinical rules engine that queried outpatient pharmacy and medical claims data. Eleven disease modules were implemented in 2 phases: diabetes, asthma, gastrointestinal disease, chronic obstructive pulmonary disease, heart failure, cardiovascular disease (January 2006), and osteoporosis, migraine, hypertension, depression, and smoking cessation (May 2006). Health recommendations were classified into 8 groups: assessments, education, immunizations, laboratory monitoring, self-management, therapy recommendations, exams, and drug-drug interactions. Examples of some of the groups for hypertension included a health survey (assessments), normal blood pressure levels and lifestyle modification (education), home blood pressure monitoring (self-management), and electrocardiogram (exams). Patients were notified of findings via the Web-based tool and detailed mailings.

RESULTS: Thirty percent of members received a recommendation, with an average of 5.3 recommendations per member. The largest number of health recommendations was for education (29.5%), followed by assessments (11.8%), therapy recommendations (10.2%), exams (9.5%), and self-management (8.4%). Significant recommendations for cost savings were with conversion of retail prescriptions to mail order (10.7%), utilization of generics (8.1%), and switch from nonpreferred to preferred brand (1.9%). The annual member savings that could be achieved from all cost-savings recommendations was $782,517. The disease modules with the greatest number of health recommendations were hypertension (11,222 recommendations), diabetes mellitus (7,276), osteoporosis (7,133), gastrointestinal disease (6,111), and asthma (3,153).

CONCLUSION: DirectInform is a health and cost management tool that provides members with actionable information and assists them in taking an active role in their health care.
IMPLICATIONS OF THE NCEP ATP III UPDATE ON LDL-C GOAL ATTAINMENT AMONG MODERATE TO VERY HIGH RISK PATIENTS IN A MANAGED CARE SETTING

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BACKGROUND: The National Cholesterol Education Program Adult Treatment Panel (ATP) III Update (Update 2004) introduced optional low-density lipoprotein cholesterol (LDL-C) goals of <70 mg/dL and <100 mg/dL for patients at very high and moderately high coronary heart disease (CHD) risk, respectively.

OBJECTIVE: Based on the Update, this retrospective analysis used managed care administrative data to examine LDL-C goal attainment among patients on statin monotherapy who were classified by CHD risk (moderate, moderately high, high, and very high).

METHODS: Patients had to be above LDL-C goal and newly initiated on statin monotherapy between August 1, 2004, and May 31, 2005 (with no pharmacy claims for any lipid-lowering medications within 6 months prior to initiation of statin monotherapy). The proportion of patients at LDL-C goal was evaluated between 3 and 6 months after initiation of therapy.

RESULTS: Of the 3,504 patients, slightly more than one third were prescribed high-efficacy or intensive statin therapy (providing expected reduction in LDL-C ≥40.0%). Less than two thirds of patients attained LDL-C goal on the starting dose of statin monotherapy. Approximately one quarter of very high-risk patients and a little more than one half of high-risk and moderately high-risk patients attained goal. Among patients who did not attain goal on the starting dose of statin and who had follow-up LDL-C values available (n = 567), 12.4% were titrated to a higher dose of statin. Of these patients, only 40.0% attained LDL-C goal.

CONCLUSION: Even with the recommendations of the ATP III Update, LDL-C goal attainment remained low among these moderate to very high-risk patients in this managed care setting. The use of high-efficacy therapy was low and titration as a treatment strategy was seldom initiated and appeared to have limited effectiveness. These results suggest an opportunity to put these patients on intensive therapy from the start to further improve LDL-C goal attainment.

(See table on page 209.)

IMPROVED SIX-MONTH PERSISTENCE SEEN IN WOMEN TREATED WITH MONTHLY IBANDRONATE EARLY POSTLAUNCH VERSUS WEEKLY BISPHOSPHONATES

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BACKGROUND: Managed care claim databases are useful for evaluating patient persistence with osteoporosis treatments. These databases provide access to real-world information, enable noninvasive determination of persistence, and allow data collection from large patient populations over long periods of time.

OBJECTIVE: To compare 6-month persistence in women aged ≥45 years who were newly treated with once-monthly ibandronate versus once-weekly alendronate or risedronate.

METHODS: A retrospective health plan administrative claims database covering approximately 16 million lives was used to identify female patients aged ≥45 years who filled new prescriptions for monthly ibandronate or weekly risedronate or alendronate from April 1, 2005, through September 30, 2005. Persistence was measured as the proportion of patients who stayed on therapy with no refill gaps exceeding defined grace periods. A Cox proportional hazards model was employed to control for the effects of confounding factors commonly observed in such nonrandomized, observational database studies.

RESULTS: There were 1,025 women prescribed monthly ibandronate and 9,501 prescribed weekly bisphosphonates included in this analysis. Patients receiving monthly therapy were slightly younger, had slightly higher comorbidity counts, and had significant higher mean and median copays. After adjusting for age, copay, and comorbidities, ibandronate users were 21.7% more likely to continue with therapy than were weekly bisphosphonate users at 6 months (hazard ratio=0.783, P<0.0001).

CONCLUSION: At 6 months, monthly therapy users were more likely to remain on treatment compared with patients receiving weekly therapy. These data suggest an improvement in patient persistence with once-monthly osteoporosis medication administration.

INCIDENCE AND COST OF ADVERSE EFFECTS ASSOCIATED WITH ASTHMA MEDICATIONS: A MANAGED CARE PERSPECTIVE

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BACKGROUND: Medication-related adverse effects (AEs) have been observed in asthmatic subjects receiving treatment in clinical trials.
OBJECTIVE: To evaluate the incidence and cost of AEs associated with classes of medication indicated for treatment of asthma in a managed care database.

METHODS: A retrospective cohort analysis of the Integrated Health Care Information Services administrative database evaluated patients aged ≥ 5 years with ≥ 2 prescriptions of asthma medication. Patients were classified as persistent asthmatics, using 2006 Health Plan Employer Data and Information Set specifications, and were followed while receiving their index medications: inhaled corticosteroids (ICSs, n = 12,394), leukotriene modifiers (LMs) (n = 23,770), long-acting beta-agonists (LABAs, n=2,208), and ICS + LABA combinations (n=14,361) to switch, discontinuation, or augmentation. Chi-square test was used to determine statistical differences in use of medical services between study groups, and Cox-proportional hazard model was used to identify AE risk factors, with adjustment for age and gender.

RESULTS: LM patients (12.4%) experienced more AEs than ICS + LABA (8.1%, P < 0.001), LABA (4.1%, P < 0.001), or ICS (6.7%, P < 0.001) patients after controlling for baseline clinical characteristics. Acute pharyngitis and oral candidiasis (OC) were the most common problems with inhaled medications: ICS + LABA 5.7% and 2.0%, respectively; LABA 2.6% and 1.3%, respectively; and ICS 5.6% and 0.8%, respectively. Cost of AEs treatment per patient was higher for LABA ($30) than for ICS ($14), for CS ($13), or for LM ($11) (P < 0.001). LM patients (12.4%) experienced more AEs than ICS + LABA (8.1%, P < 0.001), LABA (4.1%, P < 0.001), or ICS (6.7%, P < 0.001) patients after controlling for baseline clinical characteristics. Acute pharyngitis and oral candidiasis (OC) were the most common problems with inhaled medications: ICS + LABA 5.7% and 2.0%, respectively; LABA 2.6% and 1.3%, respectively; and ICS 5.6% and 0.8%, respectively. Cost of AEs treatment per patient was higher for LABA ($30) than for ICS ($14), for CS ($13), or for LM ($11) (P < 0.001). OC was most costly per event (ICS $56, ICS + LABA $59, LABA $61). Adults had fewer AEs compared with children (relative risk [RR], 0.5; 95% confidence interval [CI], 0.5-0.6); women had more AEs than men (RR, 1.4; 95% CI, 1.3-1.5).

CONCLUSIONS: Medications commonly used for chronic treatment of asthma are associated with AEs that range in severity. Management of AEs incurred additional costs to the treatment of asthma and increased the total cost of care. Further studies are needed to elucidate the impact of these AEs on compliance and asthma-related outcomes.

INFLIXIMAB (REMYCARE) UTILIZATION MANAGEMENT OPPORTUNITIES: INTEGRATED MEDICAL AND PHARMACY BENEFIT ANALYSIS

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INTRODUCTION: Infliximab and etanercept or adalimumab have similar U.S. Food and Drug Administration-approved indications, with the notable exception that infliximab has an indication for inflammatory bowel diseases (IBDs). Clinical data support equivalence of infliximab compared with etanercept or adalimumab, with the exception of treating IBD. This study assessed a combined medical and pharmacy benefit infliximab step-therapy opportunity.

METHODS: Medical and pharmacy claims data from a 1.8 million-member BlueCross/BlueShield plan were analyzed. Continuously enrolled members from 3Q (quarter) 2005 to 2Q2006 with an infliximab drug claim during 1Q2006 to 2Q2006 had their medical claims evaluated for the presence of an IBD, rheumatoid arthritis (RA), psoriasis, or ankylosing spondylitis diagnosis. Infliximab utilizers with a non-IBD diagnosis were analyzed to identify those newly initiating therapy (defined as members without an infliximab claim within 180 days prior to their first 1Q2006 to 2Q2006 claim). Members with an etanercept or adalimumab pharmacy claim in the 180 days prior to their initial infliximab claim were identified. Savings were estimated using average wholesale prices and the usual dose to treat RA.

RESULTS: Of 1,542,978 continuously enrolled members, 874 had an infliximab claim during 1Q2006 to 2Q2006. 136 of 874 (15.6%) members newly initiated infliximab therapy. Of the 136 members, their diagnoses were 58 (42.6%) RA, 59 (43.4%) RA without IBD diagnosis, and 19 (14%) all others. For the 78 non-IBD members, the average infliximab dose was 440 mg, and 14 (17.9%) had a prior etanercept or adalimumab claim. Infliximab 440 mg x $69.89 per 10 mg x 9 doses per year = $27,676 per year; etanercept 50 mg per week for 52 weeks x $401.33 per 50 mg = $20,869 per year.

CONCLUSION: More than 4 of 5 members initiating infliximab for a non-IBD indication have not tried etanercept or adalimumab. A step-therapy program requiring etanercept prior to infliximab could save $6,807 per member, with an estimated 5 members per 100,000 lives affected.

INTRANASAL FORMULATIONS OF ALLERGIC RHINITIS MEDICATIONS: PATIENT PERCEPTIONS OF EFFICACY AND TOLERABILITY AND PATIENT ADHERENCE TO THERAPY

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INTRODUCTION: Patient perceptions of the efficacy and tolerability of allergic rhinitis (AR) medications and their relationship to patient adherence to therapy were examined.

METHODS: Allergies in America: A Landmark Survey of Nasal Allergy Sufferers included 2,500 adults diagnosed with AR. Participants were interviewed about the effectiveness and side effects of their AR medications and their adherence to therapy.

RESULTS: The majority of patients reported that intranasal corticosteroids (INCcs) either did not provide 24-hour symptom relief (48%) or lost effectiveness over time (54%). Loss of effectiveness caused 37% of patients to change their allergy medications. The most common side effects of allergy medications included nose bleeds (78%), a drying feeling (47%), dripping down the throat (41%), bad taste (32%), and burning (17%). Approximately 18% to 59% of AR patients said that these side effects were moderately or extremely bothersome. Furthermore, 25% of patients discontinued treatment
because of bothersome side effects. The effectiveness and tolerability of INCSs are dependent on specific characteristics of the formulation, which may include spray volume, taste, and smell; relative osmotic pressure (tonicity); and the presence of preservatives. It is clear that although a lack of sustained effect (improvement in AR symptoms) is the most important reason patients change INCSs therapy, a significant number of patients are bothered by side effects that may reflect differences in INCS formulations.

CONCLUSIONS: Patients do not perceive their INCSs as providing 24-hour relief of allergy symptoms. Allergy medications are also perceived as conferring unpleasant side effects. Improvement in the formulation characteristics of AR medications may improve efficacy and tolerability and increase patient adherence to therapy.

MANAGED CARE PHARMACY MEETS ONCOLOGY MANAGEMENT: RESULTS FROM A NATIONAL STUDY

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BACKGROUND: The Zitter Group reports on payer and oncologist data incorporating America’s largest ongoing primary quantitative research on managed care practices toward specialty therapies.

INTRODUCTION: With management of cancer drugs increasing in payer priority, this national study reviewed current and projected management of oncology therapies based on quantitative research with more than 100 managed care organization (MCO) decision makers, the majority of them pharmacy directors.

METHODS: A nationwide sample of more than 100 top decision makers in national and regional MCOs participated in a Web-based survey on oncology management, including access and reimbursement policies. Reported information was combined with prior research spanning 4 years and analyzed using SPSS statistical software; textual data were assessed with standard qualitative techniques. As earlier research signified payer intention to tighten oncology management, particular attention was paid to Medicare average sales price (ASP) reimbursement issues, use rates for specialty pharmacy, and cancer management objectives.

RESULTS: Adoption of ASP-based reimbursement is slow, with only 26.0% of payers reporting use in 2006, an increase from 20.8% in 2005. Most MCOs (82.1%) apply the same ASP rate to all specialties, though only 18.8% consider this rate when setting payment levels for office-administered products. Tumor necrosis factor (TNF)-α inhibitors and human growth hormones are top current payer management priorities; oncology remains a topic for future discussion. Few health plans look to specialty pharmacy vendors (SPPs) in managing oncology as a category (36.5% currently do so), with large nationals expecting to use SPPs sooner for controlling oncology spending.

CONCLUSIONS: Because of the wide range of dosing, mode of administration options, and targets, oncology does not lend itself to easy management using traditional pharmacy-type management techniques. While many predict increasing overall use of specialty pharmacy, health plans will first focus on bulk purchasing and utilization management through SPPs. ASP adoption appears to be broad across all specialties or not at all, and payers express reservations about punitive reimbursement strategies, including the competitive acquisitive program.

MANAGED-CARE BUDGET IMPACT OF RITUXIMAB FOR RHEUMATOID ARTHRITIS

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INTRODUCTION: Rituxan (rituximab) is approved for reducing signs and symptoms of moderately to severely active rheumatoid arthritis (RA) in patients with inadequate responses (IRs) to anti-tumor necrosis factor (anti-TNF) therapies. We modeled rituximab’s impact on a managed care plan’s budget.

METHODS: We estimated the budget impact of rituximab using a before-and-after comparison. In the base year, patients with IRs to anti-TNF agents could continue with anti-TNF agents despite IR or discontinue anti-TNF therapy and take oral disease-modifying antirheumatic drugs (DMARDs) only. In the comparison year, patients with IRs could switch to rituximab or abatacept. The table on page 210 shows how RA patients on rituximab were drawn from a hypothetical plan. 37% of patients on anti-TNF agents had IRs measured by ACR20 (American College of Rheumatology, 20% response criteria). We assumed that 15% of these would continue DMARDS and 85% would continue anti-TNFs despite IR. We assumed that 5% of those who discontinued anti-TNF agents and 13% of those who continued despite IR would switch to rituximab. Costs included drugs, administration, and physician visits. We assumed 3 dosing intervals for rituximab: 4, 8, and 12 months. Doses of anti-TNF agents were based on prescribing information. Impact of key model parameters on the budget was assessed in sensitivity analyses.

RESULTS: Total annual costs for treating anti-TNF IRs for a 1 million-member plan before rituximab were estimated at $8,285,423 and after rituximab at $8,218,515. Per-member-per-month cost did not change significantly, ranging from $0.78 to $0.65, depending on the rituximab dosing interval. Results were most sensitive to rituximab retreatment interval length and proportion of patients choosing rituximab.

CONCLUSION: Rituximab offers an alternative to anti-TNF agents in patients with IRs. Treatment intervals, price of biologics, and the proportion of patients switching to rituximab were among key parameters affecting rituximab budget impact. The real-world budget impact will be evaluated in the future using claims data.
MEDICAL RESOURCE UTILIZATION AND COSTS AMONG PEDIATRIC PATIENTS WITH TRAUMATIC INJURY IN A MANAGED CARE POPULATION

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INTRODUCTION: Health care utilization and associated charges among pediatric patients with traumatic injury were estimated in a managed care organization (MCO) population.

METHODS: Retrospective claims from the Ingenix MCO database (January 1, 2003, to February 1, 2005) were analyzed for 2,226 pediatric patients (aged <18 years) hospitalized for traumatic injury, excluding patients with isolated burns. Study subjects had ≥6 months of health plan enrollment prior to and following initial injury. Three cohorts were identified: isolated traumatic brain injury (TBI), other trauma with TBI (combination trauma), and other trauma without TBI. Per-patient charges for all health care resources utilized were assessed over a 6-month period following initial injury. Charges were stratified by initial hospitalization and postdischarge medical encounters.

RESULTS: Among those with isolated TBI (n = 879, mean age = 10.0, mean Injury Severity Score [ISS] = 10.3), mean charges incurred during postdischarge encounters were $24,724; mean charges for the index hospitalization were $24,724; mean charges incurred during postdischarge encounters were $1,197 for subsequent hospitalizations, $185 for outpatient pharmaceuticals, and $3,499 for outpatient and other ancillary care. Among those with combination trauma (n = 498, mean age = 12.3, mean ISS = 17.7), these mean charges were $90,102, $1,973, $222, and $8,329, respectively. Among those with other trauma but without TBI (n = 849, mean age = 12.3, mean ISS = 10.3), these mean charges were $34,357, $1,587, $276, and $4,265, respectively.

CONCLUSIONS: Pediatric trauma is costly for third-party payers, especially for patients with combined TBI and other trauma. Combination trauma resulted in a 264% increase in index hospitalization charges compared with isolated TBI and a 162% increase compared with trauma without TBI. The primary cost driver of postdischarge expenditures was outpatient and other ancillary care, which was 138% higher among patients with combination trauma compared with those with isolated TBI, and 95% higher compared with trauma patients without TBI. MCOs should be aware of these heightened charges when negotiating reimbursement rates with trauma systems and outpatient providers.

MEDICARE PART D PAYER BENEFIT DESIGNS AND THEIR EFFECT ON PATIENT DECISIONS

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BACKGROUND: Wolters Kluwer Health Source dynamic claims data was used to conduct this study.

PURPOSE: The purpose of the study was to show the impact of top Medicare payers’ commercial and Medicare benefit designs for 2006 on patient decisions.

METHODS: The study used approximately 40% of all pharmacy retail claim transactions to analyze claim rejection rates and reasons, patient reversals, and the corresponding drug substitutions or missed therapies. These data enable an analysis to contrast the impact of Medicare payers’ benefit designs on what the patient ultimately fills at the pharmacy by line of business. They also show how often a prescription is not filled and provide insight into the impact of these missed therapies.

RESULTS: Medicare payers utilize 1 of 3 methods for their Medicare benefit designs versus commercial payers: (1) treat lines of business completely different, (2) keep same pharmacy benefit controls for both lines of business, or (3) invoke specific changes by therapeutic class. Which method a payer selects is influenced by financial benefit, impact to the plan members (patients), and, in some cases, the product usage. The accessibility and financial impact to the patient can be significant.

CONCLUSIONS: Medicare benefit designs differ significantly from commercial benefit designs for some payers. These differences influence decisions by Medicare patients on what ultimately gets dispensed at the pharmacy. Drug utilization review, prior authorization, products rejected for drugs not covered, patient price sensitivity, and other controls drive patients’ drug decisions. In some cases, the impact is solely financial. In other cases, a patient’s actual access to the therapy is influenced. The table on page 210 gives a glimpse of market shares by payers in the cholesterol-reducer therapeutic class. A complete analysis, including results and conclusions, will be completed after December 2006 so the entire year can be assessed. This is important because the Medicare Part D benefit is unique in a number of ways, especially within the standard benefit. The benefit is utilized differently at various points in the year, particularly with regard to the donut hole phase of the standard benefit. The full-year view will provide baseline insights for the 2007 benefit year.
**MEDICARE PAYMENTS FOR DIALYSIS PATIENTS IS LOWER WHEN PERCENTAGE OF PATIENTS ON PERITONEAL DIALYSIS IS HIGHER: A STATE-LEVEL ANALYSIS**

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**INTRODUCTION:** Total 2003 Medicare spending on renal dialysis in the United States was nearly $15 billion and is expected to grow as rates of obesity and diabetes skyrocket.

**OBJECTIVE:** To analyze the factors that impact total Medicare payments for dialysis therapy.

**METHODS:** Data sources include the U.S. Renal Data Systems’ 2005 Annual Data Report, the 2004 National Survey of Nurses, the 2005 Dialysis Facility Report, and data from the U.S. Department of Commerce. The analysis was conducted at the state level for calendar year 2003. The dependent variable is the weighted annual per-patient Medicare payments for all dialysis modalities combined. Independent variables include dialysis facility data, end-stage renal disease (ESRD) hospital and mortality ratios, state per capita income, registered nurse population, and dialysis modality type.

**RESULTS:** The adjusted $R^2$ for the estimated equation was 0.885. Several variables were statistically significant ($P <0.05$) and positively associated with annual per-person Medicare payments, including the number of hemodialysis (HD) stations per facility, the average use capacity of the facilities, the hospitalization and mortality rates, per capita income, and the number of registered nurses per 100,000 population. Several variables were negatively associated with Medicare payments, including the percentage of dialysis patients on peritoneal dialysis (PD) ($P <0.001$), and the number of HD patients per facility ($P <0.05$).

**CONCLUSIONS:** It was found that total Medicare payments for dialysis vary according to the mix of PD and HD therapies. Total Medicare payments for dialysis are higher when the percentage of dialysis patients on HD is higher but lower when the percentage of dialysis patients on PD is higher. In addition, as more HD stations are added per facility, the per-patient payment increases. These results imply that if ESRD costs are to be controlled, policymakers need to focus on micro- and macrolevel variables.

**MEDICARE TO MEDICARE PART D: ARE WE MAKING THE GRADE OR FAILING OUR SENIORS?**

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**INTRODUCTION:** Since the inception of the legislation that brought about the most robust change to Medicare since 1965, it has been debated whether this program has improved access to outpatient prescription drugs for seniors.

**OBJECTIVE:** To determine which beneficiaries have seen drug cost savings from Medicare Part D and to draw conclusions on which subsets of Medicare-eligible seniors will benefit from Medicare Part D in the future.

**METHODS:** By separating Medicare beneficiaries’ claim history into high, moderate, and low drug benefit utilizers, we compared the effects of the various benefit designs leading up to and including the 2006 Medicare Part D plan on member drug spending (sum of monthly premium and other member financial responsibilities).

**RESULTS:** The majority of seniors have seen a reduction in drug spending as a result of Part D. The moderate and high drug utilizers have received benefits from the Part D design with the addition of catastrophic coverage and greater plan and governmental contributions toward members’ drug expenses. The low utilizers have not seen the same level of value from Part D enrollment. At this time, savings for participating in the Part D plans for this subsection cannot be clearly defined since late-enrollment penalties have not been finalized and future drug utilization for this group is yet to be determined.

**CONCLUSIONS:** Overall Medicare Part D plans have improved access to outpatient medications by reducing member costs. Even with the changes in the 2007 design, these savings continue to be realized by most beneficiaries.

**MEDICATION ADHERENCE AND THE HEALTH ECONOMIC IMPACT OF ANTIDIABETIC THERAPY CONVERSION TO AN INSULIN ANALOG PEN DEVICE AMONG TYPE 2 DIABETES PATIENTS**

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**INTRODUCTION:** Recent studies have shown that adherence to insulin therapy is suboptimal among patients with type 2 diabetes, resulting in poor health outcomes and increased resource utilization and economic burden.

**OBJECTIVE:** To assess the impact of conversion from insulin treatment with vial/syringe to administration with an insulin analog pen device on medication adherence and associated health economic outcomes among patients with type 2 diabetes.

**METHODS:** Adult patients with type 2 diabetes undergoing insulin therapy with vial/syringe were retrospectively identified from the PharMetrics integrated medical and pharmacy claims database, which included data from 57 managed care health plans in the United States. Patients who initiated insulin therapy with the FlexPen (insulin aspart or biphasic insulin aspart) between January 1, 2002, and December 31, 2002, with no prior FlexPen prescription in the preceding year were the focus of this assessment. Endpoints included medication adherence in the 6 months prior to and the 2 years following the conversion to
FlexPen (using the medication possession ratio [MPR]), follow-up time-adjusted odds ratio (OR) of hypoglycemic events, association between adherence and hypoglycemic events in a Poisson multivariate context, and diabetes-attributable (DA), total management, and hypoglycemia-attributable (HA) costs.

**RESULTS:** Data from 1,156 type 2 patients newly converted to FlexPen were identified and analyzed (mean age 45.4 + 13.7 years; 51.5% previously on human insulin vials). Postconversion, MPR was significantly improved (69% vs. 62%; P <0.01), regardless of previous type of insulin vial use. A significant reduction in the likelihood of experiencing a hypoglycemic event was also observed (odds ratio [OR] = 0.50; confidence interval [CI], 0.37-0.68; P <0.05), and such events requiring either emergency department visits or physician visits decreased by 56% (OR = 0.44; CI, 0.21-0.92) and 61% (OR = 0.39; CI, 0.24-0.64), respectively (both P <0.05). The incidence of hypoglycemic events in subjects with MPR ≥80% dropped by nearly two thirds (OR = 0.35; CI, 0.11-0.81; P <0.05). The correlation between optimal MPR and reduced hypoglycemia was confirmed by a Poisson multivariate analysis. Total annual HA costs fell 56% ($8,827 vs. $8,227; P <0.01), and total DA costs fell 7% ($8,827 vs. $8,227; P <0.01).

**CONCLUSIONS:** Medication adherence to insulin therapy based on MPR was significantly improved following the initiation of an insulin analog pen device among type 2 diabetes patients. Further analyses on these patients should aim to evaluate the specific impact of variances in cost sharing or managed care benefit design plans.

### Metabolic Monitoring in Medicaid Patients Receiving Atypical Antipsychotics

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**INTRODUCTION:** In February 2004, the American Diabetes Association and American Psychiatric Association (ADA/APA) Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes recommended that patients receiving atypical antipsychotic receive routine lipid and glucose monitoring.

**OBJECTIVE:** To assess whether members taking these medications were tested for lipid and glucose levels during the prior 12 months.

**METHODS:** Lab claims were extracted from the behavioral health managed care organization (BH-MCO) for the participating counties with service dates between April 1, 2004, and June 30, 2005. Claims were sent to the appropriate physical health plan in accordance with HIPAA (Health Insurance Portability and Accountability Act) guidelines. The physical health plan extracted the same lab claims data during that quarter and merged it with the BH-MCO file for completeness. Medicaid pharmacy claims data were analyzed from April 1 through June 30, 2005, to identify patients receiving an atypical antipsychotic (including Symbyax). These members were merged with the lab claims to identify if metabolic testing was performed. The prescribing physicians of members who were identified as not having testing were notified via fax. A summary letter of the findings was sent to all network physicians.

**RESULTS:** 9,388 unique members were identified in Allegheny County as having a paid prescription for an atypical antipsychotic (including Symbyax) during the period April 1 through June 30, 2005. 14.43% (n = 1,355) of those members were identified as having glucose and/or a lipid lab test during the prior 12 months. In Berks, York, and Adams counties, of the 2,408 unique members who were identified as receiving an antipsychotic, 7.27% (n = 175) had received a lab test.

**CONCLUSION:** On the basis of ADA/APA guideline recommendations, patients undergoing atypical antipsychotic therapy did not receive adequate lipid and glucose monitoring. Effective efforts to promote awareness and adherence with monitoring recommendations are needed.

### Missouri Medicaid’s Disease Management Program: A Comprehensive Care Management Model Using Physician and Pharmacist Care Teams

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**BACKGROUND:** Missouri Medicaid implemented a disease management (DM) program during the first quarter of 2003, covering its fee-for-service population.

**OBJECTIVE:** To determine how a DM model that included physician-pharmacist care teams would affect pharmacy and medical costs.

**METHODS:** In the first quarter of 2003, fee-for-service Medicaid patients who had a history of targeted diseases (e.g., asthma, depression, diabetes, and heart failure) were eligible and were invited to participate in the program via mail and select a physician and pharmacist DM care team. Providers were required to be registered as DM providers by Medicaid. Pharmacists were also required to complete an ACPE (Accreditation Council for Pharmacy Education)-accredited continuing education course. Providers received an automated severity and risk assessment, patient profiles with identified drug therapy problems, care plans, patient educational brochures, and listing of patients assigned to them, within 30 days of patient enrollment and every quarter thereafter. Both physicians and pharmacists were reimbursed for providing DM services.

**RESULTS:** Of the approximately 40,000 Medicaid fee-for-service patients eligible for the program, 1,604 were enrolled as of June 2005. Of those, 98 patients were enrolled for at least 1 year. For those 98 patients, the total amount paid per targeted member...
per month for pharmacy and medical utilization increased 18% and 54% for the targeted and comparison group, respectively. Pharmacy costs increased 24% per month in the targeted group and 71% in the comparison group. Medical utilization costs increased 12% and 40% in the targeted and comparison groups, respectively. The actual total savings by the end of June 2005 was $305 per targeted patient per month.

CONCLUSION: A comprehensive care management model using physician and pharmacist care teams effectively managed increases in overall, pharmacy, and medical costs in a Medicaid fee-for-service population.

MODELING ANALYSIS OF THE CLINICAL AND ECONOMIC OUTCOMES OF ONCE-DAILY VERSUS TWICE-DAILY TACROLIMUS IN RENAL TRANSPLANTATION


BACKGROUND: Nonadherence to medication is a common problem in the United States, where it is estimated to result in direct annual costs of $100 billion to our health care system. Simplification of dosing regimens has proved a cost-effective way to improve patient adherence to chronic medications. Extended release tacrolimus is the first once-daily primary immunosuppressant available for transplantation. The economic impact of once-daily tacrolimus will differ for public and private payers because of differing payments for end-stage renal disease care.

OBJECTIVE: To estimate 5-year clinical and economic outcomes for patients on once-daily versus twice-daily tacrolimus from the perspectives of both Medicare and private health insurers.

METHODS: We developed stochastic state-transition models to analyze the cost-effectiveness of once-daily tacrolimus compared with twice-daily tacrolimus in renal transplant recipients over a 5-year treatment horizon. Health states analyzed included acute rejection, graft loss and return to dialysis, retransplantation, and death. Transitional probabilities were taken from the United Network for Organ Sharing, United States Renal Data System (USRDS), and literature reviews. Cost data were obtained from Medstat, USRDS, and Medicare. Once-daily tacrolimus was assumed to have the same daily cost as twice-daily tacrolimus. Sensitivity analyses were conducted around key model inputs.

RESULTS: Treatment with once-daily tacrolimus increased original 5-year graft survival from 63.0% to 69.1%. This improvement in patient outcomes resulted in treatment cost savings of $8,997 per patient (5-year discounted) from the perspective of Medicare and $15,644 per patient from the perspective of a private health insurer. Since once-daily tacrolimus led to both improved outcomes and lower costs, it dominated twice-daily tacrolimus in our analysis. Our findings remained stable under a wide range of input variables.

CONCLUSION: Improved graft survival on once-daily extended release tacrolimus, achieved through increased adherence, projects to result in sizeable cost savings to both Medicare and private health insurers. These savings are amplified for private health insurers in large part because of the relatively higher costs they incur for end-stage renal disease care.

(See table on page 211.)

MONITORING GLUCOSE REGULATION PARAMETERS IN VETERANS LIVING WITH SCHIZOPHRENIA-RELATED DISORDERS AND SWITCHED FROM ONE SECOND-GENERATION ANTIPSYCHOTIC TO ANOTHER

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BACKGROUND: Glucose dysregulation in schizophrenia patients is linked to second-generation antipsychotic (SGA) medications.

INTRODUCTION: It is crucial that patients living with schizophrenia receive baseline glucose screening and routine monitoring.

OBJECTIVES: To (1) describe the proportion of veterans with schizophrenia-related disorders monitored and (2) examine the influences of social-demographic characteristics, hypoglycemic drug treatment, and prior monitoring on the occurrence of monitoring glucose regulation after switching SGAs.

METHODS: We abstracted automated medical, prescription, and administrative data from veterans (n = 1,826) who switched SGAs and were diagnosed with schizophrenia-related disorders. Outcome variables were fasting blood glucose (FBG) and glycosylated hemoglobin (A1C). Cumulative monitoring was calculated in 3-month increments, 180 days prior and 365 days after the index date. Predictors of glucose monitoring 1 year after switching were analyzed using multivariate logistic regression models.

RESULTS: Most veterans were male (92%) and averaged 51.6 ± 10.6 years. The majority was white (55%), followed by black (25%), unspecified (10%), Hispanic (9%), and Asian and American Indian (<1%). Within 1 year after switching, 81% had a laboratory result for FBG or A1C. The 1-year postswitch cumulative monitoring FBG and A1C was 80% and 31%, respectively. FBG was more likely to be monitored 1 year post-SGA switch if the veteran was monitored prior to the switch (odds ratio [OR] = 3.21, P < 0.01). A1C was more likely to be monitored if the veteran was monitored prior to the switch (OR = 7.71, P < 0.01) or was monitored beforehand (OR = 6.51, P < 0.01), was ≥50 years (OR = 1.60, P < 0.01), or was nonwhite (OR = 1.39, P = 0.01).

CONCLUSIONS: Most veterans with schizophrenia-related disorders were monitored for glucose dysregulation within 1 year of switching SGAs. Veterans ≥50 years and receiving hypo-
glycemic drug treatment were most likely to be monitored after switching SGAs. Switching SGAs should trigger monitoring to allow detection of changes in glucose regulation. (See figure on page 211.)

**ONE HEALTH INSURER’S PERSPECTIVE ON MAXIMIZING BRAND TO GENERIC CONVERSION**

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**INTRODUCTION:** We offered financial incentives (6 months of $0 copay) to members on select targeted brand name drugs if they switched therapy to a preferred generic alternative.

**METHODS:** The health plan created a list of targeted brand drugs and their generic alternatives based on sound clinical literature and evidence-based practice guidelines. A pilot program targeting certain drugs in the proton pump inhibitor class was rolled out in the state of New Jersey effective April 1, 2006, for a limited group of members. Monthly letters were sent to members using the targeted drugs, informing them of the potential savings available under the program if they switched to a preferred generic. Physicians of these members were informed of the program separately by mail and newsletters. Changes in brand and generic drug use were tracked and financial impact was recorded.

**RESULTS:** Through August 31, 2006, out of 9,253 members obtaining a subsequent prescription after receiving our letter, a total of 398 unique members elected to switch therapy to the preferred generic drug, the pilot program resulted in savings for both members and plans.

**CONCLUSION:** Though only a small percentage of members elected to switch to the preferred generic drug, the pilot program resulted in savings for both members and plans.

**PATTERNS OF ANTIPSYCHOTIC MEDICATION USE AMONG MEDICAID PATIENTS WITH BIPOLAR DISORDER AND ASSOCIATED HEALTH CARE COSTS**


**BACKGROUND:** Treatment patterns for patients with bipolar disorder (BPD) are changing with the advent of atypical antipsychotics.

**OBJECTIVE:** To examine antipsychotic medication utilization patterns such as polypharmacy, switching, and nonadherence among patients with BPD and to investigate predictors of these utilization patterns and associated health care costs.

**METHODS:** We did a retrospective cohort study using deidentified Medicaid claims data of patients with BPD (identified according to International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 296.00-296.19, 296.40-296.89) with at least 2 antipsychotic prescriptions filled between January 1, 1999, and December 31, 2001. Patients were classified into prespecified treatment cohorts (polypharmacy, switching, nonadherent, and adherent) based on antipsychotic prescription refills during a 12-month follow-up period. Total and mental health-related costs from 12 months before until 12 months after the index prescription were analyzed. Multinomial logistic regression was used to determine factors associated with patterns of antipsychotic medication use.

**RESULTS:** Of the 832 patients with BPD identified, 58% were nonadherent to antipsychotic medication therapy. Alcohol and substance abuse and initiation on conventional antipsychotics were significantly associated with polypharmacy, switching, and nonadherence (odds ratios [ORs] of these associations ranged from 1.1 to 3.4, \( P < 0.05 \)). In contrast, both preindex mood stabilizer (“traditional” mood stabilizers such as lithium and divalproex) and antipsychotic medication use, and a psychiatrist as the prescriber were significantly associated with adherent therapy (ORs of 1.4, 1.1, and 1.2, respectively, \( P < 0.05 \)). Total and mental health care costs (US$) over the 12-month follow-up were significantly lower for the adherent therapy group ($18,383 ± $30,283 and $11,134 ± $21,501) compared with the nonadherent ($20,486 ± $21,513 and $17,890 ± $18,330), switching ($20,104 ± $23,116 and $12,758 ± $15,133) and polypharmacy ($26,972 ± $32,885 and $16,470 ± $15,258) groups.

**CONCLUSIONS:** Patients with BPD receiving antipsychotics demonstrated high rates of nonadherence to treatment. Alcohol and substance abuse and typical antipsychotic medication use were more likely to affect adherence. The impact on health care costs underscores the need to improve treatment adherence.

**PILOT OF A MEDICARE PART D MEDICATION THERAPY MANAGEMENT PROGRAM IN A MANAGED CARE AMBULATORY SETTING**

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**OBJECTIVES:** The objectives of the medication therapy management (MTM) program pilot were to (1) assess barriers to implementation of scheduled pharmacist/patient interactions, (2) improve medication use in the Medicare-defined population, and (3) use the pilot information to improve the program and design future MTM program bids with the Centers for Medicare & Medicaid Services.

**BACKGROUND:** Health care plans providing a Medicare Part D
drug benefit are required to provide an MTM program for specific patients with multiple chronic disease states, multiple Part D drugs, and high annual drug costs. Prior to implementation of the official program, Group Health conducted a pilot of this new program for ambulatory patients in staff model clinics.

METHODS: Eligible patients were identified and invited to participate in a single scheduled phone appointment with a pharmacist who would review all their medications, develop up to 3 drug-related recommendations, and create a current, reconciled medication list for the patient. Recommendations were reviewed and implemented collaboratively with the patient’s personal physician in a managed care setting. The pilot was carried out over a 3-month period in 208 eligible ambulatory patients in 18 primary care medical centers where pharmacists work collaboratively with the patients’ primary care physicians. Data elements collected included program participation numbers, type/number of drug-related problems, type/number of recommendations, percentage of recommendations implemented, pharmacist time spent, effect on Group Health drug costs, and patient satisfaction scores via survey.

RESULTS: Out of 208 eligible patients, 57 (29%) completed the pilot program. Patients, on average, were aged 80 years, were female, had 6 chronic diseases, and had approximately 17 total prescription and over-the-counter/herbal medications. Pharmacists identified 209 drug-related problems that resulted in 172 implemented recommendations. The most frequent drug-related problems included patient education needs (31), inappropriate dose/frequency/route (25), indicated drugs not prescribed (21), and potentially ineffective therapy (17). Group Health drug savings were $98.19 per patient per year, and patient cost shares were reduced by $33.06 per patient per year. 95% of patients agreed or strongly agreed that pharmacists provided quality clinical interventions on a scale of 1-5 (1 = poor, 5 = excellent), 72% of patients rated their discussion with the pharmacist a 5, 42% of patients rated the invitation letter a 4, and 51% of patients rated the overall program a 4 or 5. 88% of patients would recommend the program to family or friends. Average time per patient appointment was 3.23 hours.

CONCLUSIONS: The pilot showed positive clinical and quality pharmacy interventions, with a small but positive impact on drug costs and patient cost shares. Patient satisfaction was very high, though the time per patient must be reduced for the program to be successful over the long term. Further studies should be conducted to assess the impact of the program on clinical outcomes.

### POTENTIALLY INAPPROPRIATE MEDICATION USE IN OLDER ADULTS IN A STATE MEDICAID POPULATION

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**INTRODUCTION:** The use of poorly tolerated medications by older adults is common. Potentially inappropriate medications (PIMs) were identified by Beers and colleagues in 1997 and have been generally accepted by the medical community and expert opinion as the criteria to use to prevent adverse drug events in adults aged 65 years and older.

**OBJECTIVE:** To assess the utilization of PIMs in members aged 65 years and older.

**METHODS:** A retrospective analysis of a Medicaid pharmacy claims database between January 2005 and December 2005 was performed. All patients aged 65 through 89 years were included and the analysis focused on utilization of PIMs, as identified in the Beers criteria, and patient demographics.

**RESULTS:** The analysis included 14,211 members: 75% were female, and the mean age for all members was 74.9 ± 7 years. More than 89% of members were aged 65-85 years. Propoxyphene was the most widely prescribed PIM, representing 13% of all prescriptions, followed by naproxen (8%), cyclobenzaprine (4%), amitriptyline (3%), and fluoxetine (3%). Overall prevalence of prescribing with 1 or more PIMs was 44%, represented by 35.1% of all older females and 9.1% of all older males on a PIM. The prevalence of members prescribed 2 or more agents was 7.1%. The most common types of drug classes prescribed were analgesics (25%), non-cyclooxygenase-selective nonsteroidal anti-inflammatory drugs (21%), antidepressants (17%), and antihistamines (11%). More than 45% of the population was prescribed a PIM over a duration of at least 2 months, and 11% was prescribed a PIM for 9 to 12 months or longer.

**CONCLUSIONS:** These data confirm that there is significant prescription volume of PIMs among this population, but how this utilization translates to adverse drug reactions and other avoidable health encounters is still unknown. Logical next steps include examination of medical claims to evaluate consequences of this PIM utilization and determination of the value of potential pharmacy edits to prevent inappropriate use.

### PRESCRIPTION COVERAGE DONUT HOLE UNDER MEDICARE PART D—ITS IMPACT ON BENEFICIARIES’ PHARMACY UTILIZATION

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**BACKGROUND:** The standard Medicare Part D benefit includes a gap in coverage from $2,250 to $5,100, commonly known as...
the “donut hole.” A beneficiary who falls into the donut hole is responsible for the total costs of the drugs.

**OBJECTIVE:** To evaluate the impact of the prescription coverage donut hole on medication utilizations and expenditures.

**METHODS:** Using pharmacy claims data from prescription drug plans, we conducted a retrospective study using a pre/post (preperiod: January 1-February 28; postperiod: April 1-May 31) with control group study approach. The study group comprised beneficiaries who reached the donut hole in March 2006, and the control group comprised those who did not. Beneficiaries were included if they did not have prescription coverage in the donut hole, were aged 65 years or older, and were continuously enrolled in the prescription drug plans. Per-beneficiary-per-month (PBPM) prescriptions were utilized, and PBPM total and out-of-pocket costs were analyzed and compared.

**RESULTS:** Beneficiaries in the study group were older (76.22 vs. 75.43 years), sicker (6.10 vs. 2.96 disease conditions), and paid much higher out-of-pocket expenses ($1,318.30 vs. $260.98) than those in the control group. From the preperiod to the postperiod in the study group, the number of utilizing beneficiaries, the PBPM prescriptions, and the PBPM total costs decreased by 1.51%, 8.17%, and 8.64%, respectively, but the PBPM out-of-pocket costs increased by 77.83% (from $357.75 to $636.18). However, in the control group, the number of utilizing beneficiaries, the PBPM prescriptions, the PBPM total costs, and the PBPM out-of-pocket costs increased by 8.31%, 6.19%, 7.55%, and 5.57%, respectively.

**CONCLUSION:** Regular Medicare Part D beneficiaries were found to have reduced utilization of their medications after they reached the coverage gap, which raises the concerns that those beneficiaries may face increased risks of adverse events.

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**PREDomination of Comorbidities and Their Correlation With Blood Pressure Control in U.S. Hypertensive Patients, 1999-2002**


**OBJECTIVE:** To examine the prevalence of comorbidities among patients with hypertension (HTN) and its correlation with blood pressure (BP) control among the U.S. adult population.

**METHOD:** This population-based study used the data from the National Health and Nutrition Examination Survey (1999-2002), representing a national sample of the noninstitutionalized civilian U.S. population. Patients with HTN were identified if they had elevated BP (systolic blood pressure [SBP] ≥140 mm Hg or diastolic blood pressure [DBP] ≥90 mm Hg), were taking antihypertensive medications, or were told ≥2 times by a physician that they had HTN. Diagnosed HTN patients were defined as those who were told that they had HTN, and treated patients as those who were taking antihypertensive medications. Controlled BP was defined as SBP <140 mm Hg and DBP <90 mm Hg for HTN patients, and BP <130/80 mm Hg for those with diabetes. Logistic regression was used to estimate the odds ratios (ORs) of uncontrolled BP after adjusting for comorbidities, including 8 cardiovascular-related diseases, diabetes, asthma, and elevated body mass index (BMI). All analyses were performed using SAS and SUDS statistical software.

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**PREvalence and Cost Impact of Noncompliance with Antiepilepsy Drugs in a Managed Care Population**

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**INTRODUCTION/OBJECTIVE:** This study assessed the extent of noncompliance with antiepilepsy drugs (AEDs) and the associated impact on health care costs in a managed care population.

**METHODS:** Retrospective claims from the PharMetrics database were analyzed. Inclusion criteria were epilepsy diagnosis between January 1, 2000, and December 31, 2005, ≥2 AED prescriptions, and continuous health plan enrollment for ≥6 months prior to and ≥12 months following AED initiation. Compliance was evaluated using the medication possession ratio (MPR), defined as the ratio of the sum of total AED days supply to the number of days between the first and last refill date. Patients with an MPR <0.8 were classified as noncompliant. Linear regression was used to assess the incremental effect of noncompliance on annualized cost outcomes. Additional regression covariates included patient demographics, Charlson Comorbidity Index (CCI), follow-up duration (≥12 months), and AED monotherapy initiation.

**RESULTS:** Among patients meeting all inclusion criteria (n = 16,455), 54.8% were female, mean age was 32.6 years (SD = 19.2 years), mean CCI was 0.7 (SD = 1.6), mean follow-up duration was 27.6 months (SD = 12.9 months), and 92.6% initiated monotherapy. Mean MPR was 0.78 (SD = 0.26) and 38.5% of patients were noncompliant. Noncompliance was associated with increased annual inpatient and emergency department costs of $1,034 (P = 0.017) and $191 (P <0.001) per patient, respectively. Excluding costs for AED prescriptions, overall annual health care costs were $1,085 higher (P = 0.047) among noncompliant patients. This increase was moderately offset by a $692 reduction (P <0.001) in annual AED costs due to noncompliance, leaving a net increase of $393 per patient. Outpatient and other ancillary care costs were not significantly affected by noncompliance (-$57 [P = 0.271] and -$0.87 [P = 0.995], respectively).

**CONCLUSIONS:** Compliance with AEDs among epilepsy patients is suboptimal and noncompliance appears to be associated with increased health care costs in these patients. Efforts to promote AED compliance may lead to cost savings for managed care systems.
RESULTS: The number of adult patients (aged ≥18 years) with HTN in the United States was estimated to be 63.3 million, representing an age-adjusted prevalence of 31.4%. Almost all (99%) HTN patients had at least 1 comorbidity/risk condition (35% had 1-2, 28% had 3, and 36% had ≥4). The most common comorbidity/risk condition was elevated BMI (41%), followed by dyslipidemia (32%), metabolic syndrome (21%), and diabetes (14%). Overall, 73% of HTN patients were diagnosed, 55% of HTN patients were treated (74% of diagnosed HTN), and 53% of treated HTN patients had their BP controlled. Fifty-two percent of diabetic HTN patients had their BP controlled, but the BP control rate dropped to 48% if additional comorbidities were present. Patients were significantly less likely to achieve BP control if they were older (OR = 4.7 for ≥75 years, 2.9 for 65-74 years vs. <54 years), black (OR = 1.6 vs. white) or black smoker (OR = 2.4 vs. white smoker) after adjusting for comorbidities.

CONCLUSION: HTN is a highly prevalent medical condition in U.S. adults, with nearly all patients having at least 1 comorbidity. Approximately half of HTN patients received treatments, but only half of the treated patients achieved BP control. This study highlights the continuing need to treat and control HTN, especially in patients with comorbidities who may be at increased risk of having uncontrolled BP.

PREVALENCE OF METABOLIC SYNDROME IN AN URBAN HYPERTENSIVE POPULATION
Shaya FT*, Gu A. University of Maryland School of Pharmacy, 220 Arch St., Baltimore, MD 21201; fshaya@rx.umd.edu, (410) 706-5392

BACKGROUND: The metabolic syndrome is characterized by a group of metabolic risk factors in one person. People with the metabolic syndrome are at higher risk of cardiovascular diseases (CVDs) and type 2 diabetes. The metabolic syndrome has become increasingly common in the United States. With the increase in CVD morbidity and mortality among U.S. adult populations, particularly African Americans, it becomes urgent to monitor and control metabolic syndrome and subsequently conduct effective prevention programs for CVDs.

OBJECTIVE: To assess the prevalence of metabolic syndrome in an urban, predominantly African-American hypertensive population.

METHODS: Risk factors for the metabolic syndrome were assessed at baseline. According to diagnostic criteria recommended by American Diabetic Association, risk factors include abdominal obesity (body mass index [BMI] ≥30), high triglycerides (triglycerides ≥150 mg/dL), low high-density lipoprotein cholesterol (HDL-C <40 mg/dL in men or HDL-C <50 mg/dL in women), elevated blood pressure (BP ≥130/85 mm Hg), and elevated fasting glucose (blood glucose ≥100 mg/dL). We assessed the number of patients with risk factors for metabolic syndrome present by racial (black vs. white patients) and gender groups. We also compared average values of the above indexes with metabolic syndrome criteria and across racial and gender groups.

RESULTS: Data of 321 patients were analyzed for the study. The numbers of white men, black women, and black men were 17, 17, 191 and 96, respectively. By racial and gender groups, 4 white women (23.5%), 7 white men (±1.2%), 33 black women (17.3%), and 28 black men (29.2%) had 3 or more risk factors for metabolic syndrome. On average, study subjects were higher in BMI, blood glucose level, blood pressures, and HDL-C and lower in triglyceride level when compared with metabolic syndrome criteria. Black patients were higher in BMI, systolic blood pressure, and HDL-C and lower in triglyceride levels than their white counterparts, while blood glucose levels were higher among whites. Between genders, women were higher in BMI and HDL-C and lower in blood glucose and triglyceride levels than men. The differences are statistically significant (P < 0.05).

CONCLUSIONS: Risk factors for metabolic syndrome are prevalent in this patient sample. Based on average values of each of the 5 indexes, there do not seem to be significant differences with regard to severity of metabolic syndrome across racial and gender groups.

PREVALENCE OF POTENTIAL MISDIAGNOSIS OF BIPOLAR DISORDER IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER IN A COMMERCIALLY INSURED POPULATION
Kamat SA*, Rajagopalan K, Pethick N, Willey V, Bullano MF. HealthCore, Inc., 800 Delaware Ave., 5th Fl., Wilmington, DE 19801; skamat@healthcore.com, (302) 230-2177


METHODS: Claims data (January 1, 2000, through March 31, 2004) from patients with MDD were evaluated. An age-, gender-, and region-stratified random sample of patients with ≥2 medical claims for MDD (none for BD) were targeted for a telephone survey, which included demographic and comorbidity questions, the Mood Disorder Questionnaire (MDQ), the Medical Outcomes 12-item Short Form, and the Sheehan Disability Scale.

RESULTS: In a survey of 1,360 patients screened using the MDQ, 94 patients (6.9%) screened positive for BD. Prevalence of these screen positives was highest in males aged 18 to 35 years (12.3%) compared with females (7.1%). More patients screening positive reported obsessive compulsive disorder (24% vs.
CONCLUSION: Angina recurs in nearly half of revascularized patients in the year following a percutaneous or surgical coronary procedure. A third of patients experiencing angina postprocedure have a second procedure after experiencing recurrent angina. Angina patients, even when revascularized and prescribed guideline-appropriate medications, are still experiencing recurrent angina at a cost of both suffering for the patient and higher expenses for managed care.

■ RETROSPECTIVE EVALUATION OF HMG-COA REDUCTASE INHIBITOR UTILIZATION RELATIVE TO RISK STRATIFICATION

Fee KA,* Godley PJ, Ershoff DH, Wilson JP. The University of Texas at Austin, College of Pharmacy, 1 University Station A1930, Austin, TX 78712; kellyfee@mail.utexas.edu, (862) 778-7686

PURPOSE: To determine prescribing patterns of statin therapies relative to the target National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III low-density lipoprotein cholesterol (LDL-C) goal.

METHODS: From a 186,000-member southwestern health plan, prescribing patterns for patients starting a statin (monotherapy or in a fixed-dose combination) between December 2004 and June 2005 were examined. Patients were either naive to statins or switched statins within a 6-month history. Using a disproportionate random sample, 1,490 patients (991 naïve patients and 499 switchers) were included with a baseline lipid panel. Patient demographics, risk status (including 2004 NCEP ATP III updated optional guidelines), appropriateness of agent, and dose prescribed to meet the target LDL-C goal were estimated using electronic medical records.

RESULTS: On average, patients were aged 62 years; 55% were female with an average baseline LDL-C of 133 mg/dL for naïve patients and 110 mg/dL for switch patients. A total of 74% of new starts and 83% of switch patients were at high or very high risk based on 2004 updated optional guidelines. When we used 2004 NCEP ATP III updated optional guidelines and efficacy of the statin agent based on the U.S. Food and Drug Administration package insert information, for new starts, 25% of patients were already at LDL-C goal when prescribed the agent, 57% of patients were receiving a statin and dose adequate for goal attainment, and 18% received a statin or dose too low to achieve goal. For patients who switched agents, the corresponding percentages were 38%, 57%, and 5%.

CONCLUSIONS: In this population, a large majority of new starts and switchers were prescribed doses sufficient to achieve/maintain target LDL-C values. Future research should focus on assessing the appropriateness of statin prescribing based on real-world effectiveness of statins.
SUCCESSFUL HIV ADHERENCE SUPPORT PROGRAM THROUGH UNIQUE COLLABORATION OF A HOSPITAL-BASED INFECTIOUS DISEASE CLINICAL SERVICE AND SPECIALTY PHARMACY

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BACKGROUND: Today, the most critical barrier to successfully managing HIV disease is suboptimal patient adherence to antiretroviral therapy (Zabinski RA. Evidence-based health benefits management: strategies to optimize antiretroviral medication adherence and outcomes in HIV/AIDS. J Manag Care Pharm. 2006;27(7(suppl S-5)):S12-S16). A state-supported grant to provide adherence monitoring and interventions was awarded in spring 2005 to a Massachusetts-based infectious disease clinical service. As part of the grant program, a specialty pharmacy was subcontracted with to provide support and expertise.

OBJECTIVE: To evaluate the impact of an HIV Adherence Support Grant Program through collaboration of community infectious disease clinical services and a specialty pharmacy.

METHODS: Criteria for enrolling patients in the program included reported adherence levels less than 80% (self- and/or refill tracking). This subset of patients received more intensive case management, adherence monitoring, and interventions based on in-depth patient interviews and home environment assessments. Monthly team meetings were conducted to discuss progress by individual case, intervention and therapy revision plans, and program challenges. A specialty pharmacist provided refill and adherence reports, additional feedback from patients, as well as recommendations for interventions. Monthly refill dates determined the number of days a prescription was ordered early or late, for adherence monitoring.

RESULTS: Of the 25 patients enrolled in the program for an average age of 10 months (range: 4-20 months), 21 (84%) achieved a program adherence rate of ≥90%; 24 of 25 patients (96%) achieved a program adherence rate of ≥80%. 230 of 265 (87%) doses determined the number of days a prescription was ordered early or late, for adherence monitoring.

CONCLUSIONS: Collaboration between a community infectious disease clinical service and a specialty pharmacy can have a substantial impact on patient adherence to drug therapy. Patients with a previous record of low adherence can be motivated and trained to improve levels of compliance to HIV drug regimens.

TREATMENT PATTERNS AND BLOOD PRESSURE CONTROL FOLLOWING RELEASE OF THE JNC 7 GUIDELINES

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INTRODUCTION: This study compared treatment patterns and blood pressure (BP) control rates for patients with hypertension (HTN) before and after publication of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines.

METHODS: This national observational HTN study included patients aged ≥18 years from 26 managed care and physician organizations. From data collected June 1998 to May 2006, 2 cohorts were defined; pre-JNC 7 (June 1998 to March 2003) and post-JNC 7 (December 2003 to May 2006). The HTN population, identified via claims data, was verified during chart review of 19,359 randomly selected patients (15,359 patients pre-JNC 7 and 4,000 patients post-JNC 7). Variables studied included demographics, comorbidities, treatment patterns, and BP control defined by JNC 7. Statistical analysis included chi-square testing.

RESULTS: Mean age pre-JNC 7 was 61.5 years versus 62.3 post-JNC 7, and the majority of patients were female (56.2% for pre-JNC 7 and 59.8% for post-JNC 7). Common comorbidities pre- and post-JNC 7 were hyperlipidemia (52.4% and 66.2%, P <0.0001) and diabetes (22.1% and 37.0%, P <0.0001). An increase (P <0.0001) in the proportion of patients prescribed ≥2 antihypertensive medications was noted during the post-JNC 7 time frame, as demonstrated by no treatment (21.4% vs. 6.2%), monotherapy (45.8% vs. 34.2%), dual therapy (23.2% vs. 35.8%), and ≥3 agents (9.6% vs. 23.9%). Highly utilized antihypertensives during the same time frame were diuretics (24.8% vs. 38.1%, P <0.0001), beta-blockers (22.0% vs. 33.5%, P <0.0001), angiotensin-converting enzyme inhibitors (21.9% vs. 30.7%, P <0.0001), calcium channel blockers (20.9% vs. 24.2%, P <0.0001) and angiotensin-receptor blockers (4.9% vs. 12.7%, P <0.0001). Fixed-dose combination agents demonstrated the single-highest increase of all antihypertensive classes (10.1% vs. 19.6%, P <0.0001). Blood pressure (BP) control improved 10.0% in the overall population (39.3% to 49.3%, P <0.0001).

CONCLUSIONS: The percentage of patients prescribed ≥2 HTN agents post-JNC 7 significantly increased in parallel with improvements in BP control. JNC 7 guidelines may have helped improve BP control among patients with HTN by promoting more aggressive pharmacotherapy.
**TREATMENT PATTERNS, HEALTH CARE RESOURCE UTILIZATION, AND COSTS ASSOCIATED WITH THE USE OF COMBINATION ANTIHYPERTENSIVE REGIMENS IN HYPERTENSION**

Makin C, Barron J*, Daniel G, Preblick R, Lau H. Health Core, 800 Delaware Ave., Fifth Fl., Wilmington, DE 19801; jbarron@healthcore.com, (302) 230-2113

**INTRODUCTION:** Many people with hypertension require 2 or more antihypertensive medications to control their blood pressure levels.

**OBJECTIVES:** To evaluate treatment patterns, health care resource utilization, and costs associated with initiated combination antihypertensive treatment regimens in hypertension.

**METHODS:** Administrative claims data from January 2000 to February 2005 from an integrated health care system were utilized to retrospectively identify antihypertensive-naïve patients initiated on combination therapy with angiotensin-converting enzyme inhibitors (ACEIs) and calcium channel blockers (CCBs) as fixed-dose combination therapy (FDC-ACEI/CCB) or as separate agents (ACEI + CCB). Patients were evaluated 12 months following initiation date for treatment modifications, health care resource utilization, and costs. Multivariate analyses were conducted to evaluate outcomes adjusting for age, gender, geographic region, comorbidities, baseline utilization, and index medication.

**RESULTS:** A total of 5,625 patients were identified (FDC-ACEI/CCB [n = 4,530] and ACEI + CCBs [n = 1,095]). Mean patient age was 53 years and 60.7% were male. ACEI + CCB was associated with more treatment modifications such as switching, dose adjustments, or augmentations to antihypertensive medication compared with FDC-ACEI/CCB (odds ratio = 4.95; P <0.001). FDC-ACEI/CCB had significantly fewer antihypertensive fills (P <0.001) and inpatient hospitalizations (P <0.001) compared with ACEI + CCB. Similar differences were also observed for cardiovascular-related and all-cause utilization. Adjusted mean hypertension-related costs were significantly lower per patient with FDC-ACEI/CCB than for ACEI + CCB ($1,352 vs. $1,831, P = 0.006). Similarly, adjusted mean cardiovascular-related costs were also significantly lower for FDC-ACEI/CCB than for ACEI + CCB ($1,913 vs. $2,893, P <0.001).

**CONCLUSIONS:** Initial selection of combination antihypertensive therapy regimens were associated with differentiated outcomes. Fewer treatment modifications and lower health care utilization and costs were associated with FDC-ACEI/CCB compared with ACEIs and CCBs as separate agents. Further research is warranted to better understand the incremental benefits associated with interventions that may optimize clinical outcomes, health care utilization, and costs.

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**TRENDS IN OUT-OF-POCKET COST BURDEN FOR PATIENTS WITH CHRONIC CONDITIONS**

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**BACKGROUND:** Recently, coinsurance has become a common cost-sharing feature of benefit plans.

**PURPOSE:** To study annual trends in out-of-pocket (OOP) costs, and to compare OOP costs for patients with chronic conditions with and without benefit plans requiring coinsurance.

**METHODS:** Inpatient, outpatient, and prescription utilization and expenditure data from 2002 through 2004 were obtained from the Medstat commercial claims database. Benefit design information was available for 5.9 million adults with claims. Adult patients eligible for both medical and drug coverage with at least 1 inpatient or 2 outpatient diagnoses of chronic kidney disease, multiple sclerosis, rheumatoid arthritis, or diabetes were selected. Average monthly OOP costs for each patient was the sum of copayments, coinsurance, and deductibles divided by the number of months the patient accessed medical or pharmacy benefits. Monthly OOP costs were multiplied by 12 to obtain annualized OOP costs. We compared annualized OOP costs for patients whose benefit plans required medical and/or pharmacy coinsurance inside the network with patients whose plans did not have any coinsurance requirements.

**RESULTS:** A total of 32,513 patients with no coinsurance and 293,907 with coinsurance met all other selection criteria. Annualized increase in OOP costs from 2002 to 2004 was much greater for patients with each of the 4 diseases studied (10%-24%), compared with the medical care consumer price index (4%) during the same years. Average OOP costs for patients in coinsurance plans were 2 to 3 times greater than those for patients not in coinsurance plans.

**CONCLUSIONS:** Out-of-pocket expenses have increased over time and are much higher for patients with insurance plans requiring payment of coinsurance. The trend toward coinsurance requirements may limit the affordability of necessary treatments for many patients with serious and chronic conditions. (See table on page 211.)

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**USE OF DARBEPOETIN ALFA AND EPOETIN ALFA FOR CANCER-RELATED ANEMIA IN CLINICAL PRACTICE**

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**BACKGROUND:** Patients with cancer-related anemia often receive erythropoiesis-stimulating agents (ESAs), such as darbepoetin alfa (DA) or epoetin alfa (EA). With differing doses and regimens, typical mean weekly doses are not well understood.

**OBJECTIVE:** To estimate average weekly dose of DA and EA in clinical practice.

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METHODS: Using a large U.S. health insurance database (~10 million subjects), we identified all cancer patients receiving ESAs (n = 6,673) between January 2005 and June 2005. Episodes of care (EOCs) with DA or EA were identified using dates of first and last administration. To account for differences in serum half-life between DA and EA, we added an assumed duration of therapeutic benefit to the last administration in each EOC based on dose. ESA weekly dose was calculated as a ratio of total ESA dose to EOC duration. Multivariate regression was used to compare mean weekly doses of DA and EA, controlling for differences in patient characteristics.

RESULTS: There were 2,685 unique DA EOCs and 4,602 EA EOCs; 614 patients had multiple episodes. DA patients were younger, had higher Charlson comorbidity scores, and were more likely to be female, to have had metastases, and to have received chemotherapy than were EA patients. Mean (± SD) number of administrations within EOCs was 3.6 (± 3.2) for DA and 4.8 (± 5.0) for EA. Mean EOC duration was 52.0 (± 42.4) days for DA and 45.1 (± 46.6) days for EA. Mean dose per administration was 221 (± 89) mcg for DA and 43,332 (± 21,302) units for EA. In multivariate regression, estimated mean weekly dose (95% confidence interval) was 107 (106, 108) mcg for DA and 39,198 (38,496, 39,913) units for EA.

CONCLUSION: Among cancer patients receiving ESAs, mean weekly dose during EOCs was 39,198 units for EA and 107 mcg for DA.
**ADMINISTRATION OF INTRAVENOUS THERAPIES IN METASTATIC BREAST CANCER: A COST ANALYSIS**

*See abstract on page 164.*

<table>
<thead>
<tr>
<th>Total</th>
<th>Study Drug</th>
<th>IV Administration</th>
<th>Other Visit-Related Services*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average Costs ($)</td>
<td>%</td>
<td>Average Costs ($)</td>
</tr>
<tr>
<td><strong>Costs/visit</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>All study drugs</td>
<td>2,477.32</td>
<td>100.0</td>
<td>1,462.80</td>
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<tr>
<td>Paclitaxel</td>
<td>2,803.64</td>
<td>100.0</td>
<td>1,213.84</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>2,526.41</td>
<td>100.0</td>
<td>1,976.27</td>
</tr>
<tr>
<td><strong>Costs/PPPM</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>All study drugs</td>
<td>4,965.97</td>
<td>100.0</td>
<td>2,800.31</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>6,323.25</td>
<td>100.0</td>
<td>2,944.86</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>5,256.34</td>
<td>100.0</td>
<td>4,089.50</td>
</tr>
</tbody>
</table>

* Includes other IV or specially administered oral drugs, supplies and equipment, evaluation and management services.

PPPM = per patient per month.

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**ATOMOXETINE (STRATTERA) AND STIMULANT UTILIZATION MANAGEMENT OPPORTUNITIES ON CHILDREN: ASSESSMENT OF MEDICAL DIAGNOSES AND SWITCH RATES TO THE ALTERNATIVE AGENT**

*See abstract on page 167.*

**Medical Claims Diagnoses From January 2004 Through September 2005**

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Children Newly Initiated on Atomoxetine (N = 308) (%)</th>
<th>Children Newly Initiated on a Stimulant (N = 1,230) (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD with or without another defined diagnosis*</td>
<td>250 (81.2)</td>
<td>986 (80.0)</td>
<td>0.75</td>
</tr>
<tr>
<td>Any other defined diagnosis* excluding ADHD</td>
<td>25 (8.1)</td>
<td>114 (7.0)</td>
<td>0.58</td>
</tr>
<tr>
<td>None of the defined diagnoses*</td>
<td>33 (10.7)</td>
<td>160 (13.0)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

* Defined diagnoses were: ADHD, depression, anxiety, schizophrenia, bipolar, drug abuse, or insomnia (narcolepsy) in any medical claim diagnostic field. ADHD = attention-deficit/hyperactivity disorder.
### COMPARATIVE ANALYSIS OF MULTIPLE SCLEROSIS
### COST-EFFECTIVENESS MODELS: FOCUS ON THE MANAGED CARE PERSPECTIVE

See abstract on page 169.

**Results From Disease-Modifying Drug Cost-Effectiveness Studies**

<table>
<thead>
<tr>
<th>Disease-Modifying Drug</th>
<th>Baseline Disease Severity Reported in the Original Trial</th>
<th>Goldberg et al. Model</th>
<th>Chiao et al. Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glatiramer acetate, 20 mcg SC daily</td>
<td>≥2 in 2 years</td>
<td>0.49</td>
<td>26,650</td>
</tr>
<tr>
<td>Interferon beta-1a, 30 mcg IM weekly</td>
<td>≥2 in 3 years</td>
<td>0.30</td>
<td>26,664</td>
</tr>
<tr>
<td>Interferon beta-1a, 44 mcg SC, 3 times weekly</td>
<td>≥2 in 2 years</td>
<td>0.83</td>
<td>30,818</td>
</tr>
<tr>
<td>Interferon beta-1b, 8 MIU-SC every other day</td>
<td>≥2 in 2 years</td>
<td>0.81</td>
<td>29,149</td>
</tr>
<tr>
<td>Natalizumab, 300 mg IV every 4 weeks</td>
<td>≥1 in 1 year</td>
<td>0.90</td>
<td>59,462</td>
</tr>
</tbody>
</table>

*Note that for the calculation of the 2-year relapse reduction rate in patients treated with interferon beta-1a IM injection Chiao et al. used the annual relapse rate instead of the 2-year relapse rate reported by Jacobs et al.*

*IM=intramuscular; IV=intravenous; MIU=millions international units; SC=subcutaneous.*
COST-EFFECTIVENESS OF MEETING HEDIS MEASURES FOR SMOKING-CESSATION PHARMACOTHERAPY

See abstract on page 176.

Effects of Compliance with HEDIS MSC on Outcomes

<table>
<thead>
<tr>
<th>Outcome Scenario</th>
<th>Year 10</th>
<th>Year 20</th>
<th>Year 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI – total number</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Status quo</td>
<td>5,058</td>
<td>11,207</td>
<td>17,906</td>
</tr>
<tr>
<td>100% performance - advice</td>
<td>4,493</td>
<td>9,714</td>
<td>15,657</td>
</tr>
<tr>
<td>100% performance - medications</td>
<td>4,159</td>
<td>8,956</td>
<td>14,687</td>
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<tr>
<td>Stroke – total number</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Status quo</td>
<td>2,888</td>
<td>6,433</td>
<td>10,414</td>
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<tr>
<td>100% performance - advice</td>
<td>2,653</td>
<td>5,792</td>
<td>9,510</td>
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<tr>
<td>100% performance - medications</td>
<td>2,497</td>
<td>5,525</td>
<td>9,101</td>
</tr>
<tr>
<td>CHD – deaths</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Status quo</td>
<td>1,853</td>
<td>4,319</td>
<td>7,170</td>
</tr>
<tr>
<td>100% performance - advice</td>
<td>1,638</td>
<td>3,787</td>
<td>6,329</td>
</tr>
<tr>
<td>100% performance - medications</td>
<td>1,539</td>
<td>3,477</td>
<td>5,782</td>
</tr>
<tr>
<td>Total medical costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Status quo</td>
<td>$746,618,775</td>
<td>$1,673,677,717</td>
<td>$2,782,996,535</td>
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<tr>
<td>100% performance - advice</td>
<td>$779,111,883</td>
<td>$1,762,820,678</td>
<td>$2,933,931,289</td>
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<tr>
<td>100% performance - medications</td>
<td>$803,501,968</td>
<td>$1,809,463,836</td>
<td>$3,015,871,713</td>
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<tr>
<td>Cost per QALY for 100% performance</td>
<td>$34,337</td>
<td>$15,601</td>
<td>$11,952</td>
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<tr>
<td>100% performance - advice</td>
<td>$38,678</td>
<td>$16,503</td>
<td>$12,588</td>
</tr>
<tr>
<td>100% performance - medications</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CHD = coronary heart disease; HEDIS MSC = Health Plan Employer Data and Information Set Medicare assistance with smoking cessation; MI = myocardial infarction; QALY = quality-adjusted life-year.

ECONOMIC ANALYSIS OF SHORT-COURSE LEVOFLOXACIN VERSUS AMOXICILLIN/CLAVULANATE IN TREATING ACUTE BACTERIAL EXACERBATIONS OF CHRONIC BRONCHITIS

See abstract on page 178.

<table>
<thead>
<tr>
<th>Resource Use</th>
<th>Mean Cost Difference ($) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study medication</td>
<td>-17.37 (fixed; no variation)</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>-138.41 (-447.26, 170.44)</td>
</tr>
<tr>
<td>Unscheduled health care visits</td>
<td>-3.63 (-11.85, 4.59)</td>
</tr>
<tr>
<td>Additional antibiotics</td>
<td>-3.71 (-15.19, 7.76)</td>
</tr>
<tr>
<td>Concomitant pulmonary medications</td>
<td>-11.56 (-88.04, 64.93)</td>
</tr>
<tr>
<td>Related medical procedures</td>
<td>1.56 (-4.75, 7.87)</td>
</tr>
<tr>
<td>Totals</td>
<td>-173.11 (-513.74, 167.51)</td>
</tr>
</tbody>
</table>

CI = confidence interval.
### EVALUATION OF PRESCRIPTION REFILL PATTERNS BASED ON DAILY DOSING REGIMEN AND PILL LOAD FOR CALCIUM CHANNEL BLOCKERS

See abstract on page 182.

<table>
<thead>
<tr>
<th>Drug and Dosing Regimen</th>
<th>Mean Pills Per Day</th>
<th>Persistence at 1 Year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem (various n = 12,526)</td>
<td>1.2</td>
<td>37.20</td>
</tr>
<tr>
<td>Isradipine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynacirc CR (n = 817)</td>
<td>1.1</td>
<td>43.2</td>
</tr>
<tr>
<td>Nifedipine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procardia XL (n = 1,972)</td>
<td>1.6</td>
<td>45.9</td>
</tr>
<tr>
<td>Verapamil (various n = 3,227)</td>
<td>1.4</td>
<td>47.22</td>
</tr>
<tr>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicardipine</td>
<td>1.8</td>
<td>58.2</td>
</tr>
<tr>
<td>Cardene SR (n = 122)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isradipine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynacirc (n = 714)</td>
<td>1.6</td>
<td>44.8</td>
</tr>
<tr>
<td>TID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicardipine</td>
<td>2.4</td>
<td>51.9</td>
</tr>
<tr>
<td>Cardene (n = 27)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BID= twice a day; QD= once a day; TID= three times a day.

### EVALUATION OF THE IMPACT OF A HEALTH PLAN’S DISEASE MANAGEMENT PROGRAM ON BLOOD PRESSURE CONTROL AND COMPLIANCE WITH JNC 7 GUIDELINES FOR THE TREATMENT OF HYPERTENSION

See abstract on page 183.

<table>
<thead>
<tr>
<th>General Hypertensive Sample N = 348</th>
<th>Disease-Managed Sample N = 253</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean blood pressure</td>
<td></td>
</tr>
<tr>
<td>133/82 mm Hg</td>
<td>130/77 mm Hg</td>
</tr>
<tr>
<td>Members achieving their goal of &lt;140/90 mm Hg</td>
<td>59%</td>
</tr>
<tr>
<td>Members with diabetes or chronic kidney disease achieving their goal of &lt;130/80 mm Hg</td>
<td>24%</td>
</tr>
<tr>
<td>Total blood pressure control (members achieving their respective goal of &lt;140/90 or &lt;130/80)</td>
<td>50%</td>
</tr>
<tr>
<td>Members &gt;20 mm Hg above goal</td>
<td>10%</td>
</tr>
<tr>
<td>Antihypertensive Rx PMPY</td>
<td>$433.99</td>
</tr>
<tr>
<td>All Rx PMPY</td>
<td>$3,248.40</td>
</tr>
<tr>
<td>Medical PMPY (cardiovascular-related)</td>
<td>$6,294.85</td>
</tr>
</tbody>
</table>

* P < 0.05 compared with the general hypertensive sample.

PMPY = per member per year; Rx = prescription.

### FENTANYL PATCH QUANTITY PER CLAIM DISPENSING PATTERNS AND PATIENTS’ MEDICAL DIAGNOSES: UTILIZATION MANAGEMENT OPPORTUNITY ASSESSMENT

See abstract on page 183.

### MEDICAL CLAIMS DIAGNOSES FROM JUly 2004 THROUGH JUNE 2005

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Members With a Fentanyl Patch Claim During 2Q2005, N = 2,167 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer or AIDS diagnosis with or without another diagnosis</td>
<td>434 (20.0)</td>
</tr>
<tr>
<td>Fracture, burn, crush injury or neuropathic pain diagnosis excluding cancer or AIDS diagnosis</td>
<td>641 (29.6)</td>
</tr>
<tr>
<td>Localized pain diagnosis only</td>
<td>898 (41.4)</td>
</tr>
<tr>
<td>None of the defined diagnoses*</td>
<td>194 (9.0)</td>
</tr>
</tbody>
</table>

* Cancer, AIDS, fracture, burn, crush injury, neuropathic pain, or localized pain diagnosis in any medical claim diagnostic field.

### HEALTH CARE COSTS AND RESOURCE UTILIZATION OF PATIENTS WITH MULTIPLE SCLEROSIS IN A COMMERCIAL MANAGED CARE ENVIRONMENT

See abstract on page 185.

<table>
<thead>
<tr>
<th>Service Category</th>
<th>IM IFN Beta-1a ($)</th>
<th>SC IFN Beta-1a ($)</th>
<th>IFN Beta-1b ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient</td>
<td>854.79</td>
<td>1,216.97</td>
<td>1,972.76</td>
</tr>
<tr>
<td>Outpatient</td>
<td>3,080.34</td>
<td>5,171.93</td>
<td>3,457.47</td>
</tr>
<tr>
<td>Emergency room</td>
<td>99.69</td>
<td>270.39</td>
<td>90.46</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>14,917.39</td>
<td>1,7327.25</td>
<td>14,374.19</td>
</tr>
<tr>
<td>Class-specific</td>
<td>13,380.58</td>
<td>15,296.73</td>
<td>13,304.21</td>
</tr>
<tr>
<td>All other pharmacy</td>
<td>1,526.81</td>
<td>2,030.52</td>
<td>1,069.97</td>
</tr>
<tr>
<td>Total episode cost</td>
<td>18,952.21</td>
<td>23,986.54</td>
<td>19,894.88</td>
</tr>
</tbody>
</table>

IM = interferon, IM = intramuscular, SC = subcutaneous.
**IMPACT OF ANTIHYPERTENSIVE THERAPY MODIFICATIONS ON HYPERTENSION AND CARDIOVASCULAR-RELATED COSTS**

See abstract on page 186.

<table>
<thead>
<tr>
<th>Number of Treatment Modifications</th>
<th>Hypertension-Related Costs ($)</th>
<th>Cardiovascular-Related Costs ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>836</td>
<td>1,386</td>
</tr>
<tr>
<td>1</td>
<td>1,267</td>
<td>2,106</td>
</tr>
<tr>
<td>2</td>
<td>1,421</td>
<td>2,385</td>
</tr>
<tr>
<td>3</td>
<td>1,747</td>
<td>2,952</td>
</tr>
<tr>
<td>4</td>
<td>2,190</td>
<td>3,401</td>
</tr>
<tr>
<td>≥5</td>
<td>2,316</td>
<td>4,196</td>
</tr>
</tbody>
</table>

**IMPACT OF RITUXIMAB ON JOINT STRUCTURAL DAMAGE IS INDEPENDENT OF CLINICAL RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS (REFLEX STUDY)**

See abstract on page 188.

<table>
<thead>
<tr>
<th></th>
<th>Placebo + Methotrexate</th>
<th>Rituximab + Methotrexate</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (Week 56) n = 184</td>
<td>n = 272</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change in total Genant-Sharp score (SD)</td>
<td>2.31 (5.28)</td>
<td>1.00 (2.76)</td>
<td>0.0043</td>
</tr>
<tr>
<td>Mean change in erosion score (SD)</td>
<td>1.32 (3.16)</td>
<td>0.59 (1.85)</td>
<td>0.0106</td>
</tr>
<tr>
<td>Mean change in JSN score (SD)</td>
<td>0.99 (2.57)</td>
<td>0.41 (1.33)</td>
<td>0.0007</td>
</tr>
<tr>
<td>ACR20 nonresponders (Week 24) n = 151</td>
<td>n = 125</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change in total Genant-Sharp score (SD)</td>
<td>2.39 (4.56)</td>
<td>0.93 (2.46)</td>
<td>0.0271</td>
</tr>
<tr>
<td>Mean change in erosion score (SD)</td>
<td>1.46 (3.06)</td>
<td>0.49 (1.35)</td>
<td>0.0396</td>
</tr>
<tr>
<td>Mean change in JSN score (SD)</td>
<td>0.93 (1.88)</td>
<td>0.44 (1.43)</td>
<td>0.0126</td>
</tr>
</tbody>
</table>

JSN = joint space narrowing.

**IMPLICATIONS OF THE NCEP ATP III UPDATE ON LDL-C GOAL ATTAINMENT AMONG MODERATE TO VERY HIGH RISK PATIENTS IN A MANAGED CARE SETTING**

See abstract on page 190.

<table>
<thead>
<tr>
<th>LDL-C Goal Attainment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Very high risk</td>
</tr>
<tr>
<td>High risk</td>
</tr>
<tr>
<td>Moderately high risk</td>
</tr>
<tr>
<td>Moderate risk</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

* P <0.0001.
† P <0.0001.

LDL-C = low-density lipoprotein cholesterol.
Selection of Rituxan Candidates from Hypothetical Million-Member Plan

<table>
<thead>
<tr>
<th>Population Subset</th>
<th>N (%) of Each Subset</th>
<th>Percentage of Patients Who Switch Biologic Therapy N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults with RA</td>
<td>8,000 (1)</td>
<td></td>
</tr>
<tr>
<td>Adults with moderately to severely active RA</td>
<td>6,000 (75)</td>
<td></td>
</tr>
<tr>
<td>Adults with moderately to severely active RA on anti-TNFs</td>
<td>1,500 (25)</td>
<td></td>
</tr>
<tr>
<td>Anti-TNF IR patients – Rituxan candidates</td>
<td>555 (37)</td>
<td></td>
</tr>
<tr>
<td>Anti-TNF IR patients who discontinue anti-TNF therapy (receive DMARDs only)</td>
<td>83 (15)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Anti-TNF IR patients who continue anti-TNF therapy</td>
<td>472 (85)</td>
<td>71 (15)</td>
</tr>
</tbody>
</table>

* 1,000,000 for total plan.
DMARDs = disease-modifying antirheumatic drugs; IR = inadequate response; RA = rheumatoid arthritis; TNF = tumor necrosis factor.
MODELING ANALYSIS OF THE CLINICAL AND ECONOMIC OUTCOMES OF ONCE-DAILY VERSUS TWICE-DAILY TACROLIMUS IN RENAL TRANSPLANTATION

See abstract on page 196.

Five-Year Discounted Average Patient Treatment Costs*

<table>
<thead>
<tr>
<th></th>
<th>Medicare</th>
<th></th>
<th>Private Health Insurer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Once-Daily</td>
<td>Twice-Daily</td>
<td>Once-Daily</td>
</tr>
<tr>
<td>Transplantation†</td>
<td>113,031</td>
<td>114,781</td>
<td>169,742</td>
</tr>
<tr>
<td>Primary immunosuppressant</td>
<td>35,371</td>
<td>34,683</td>
<td>35,371</td>
</tr>
<tr>
<td>Adjunctive immunosuppressant (MMF)</td>
<td>20,360</td>
<td>19,977</td>
<td>20,360</td>
</tr>
<tr>
<td>Antibody rejection treatment</td>
<td>721</td>
<td>780</td>
<td>2,019</td>
</tr>
<tr>
<td>Graft loss costs in excess of dialysis</td>
<td>$10,043</td>
<td>$11,991</td>
<td>$10,043</td>
</tr>
<tr>
<td>Dialysis costs</td>
<td>$14,562</td>
<td>$20,274</td>
<td>$28,998</td>
</tr>
<tr>
<td>Mortality costs</td>
<td>$13,499</td>
<td>$14,097</td>
<td>$13,499</td>
</tr>
<tr>
<td>Total</td>
<td>$207,586</td>
<td>$216,583</td>
<td>$280,033</td>
</tr>
<tr>
<td>Cost savings</td>
<td>($8,997)</td>
<td>($15,644)</td>
<td></td>
</tr>
</tbody>
</table>

* All costs are 2006 US$, future costs discounted at a 5% annual rate.
† Includes retransplantations.
MMF = mycophenolate mofetil.

MONITORING GLUCOSE REGULATION PARAMETERS IN VETERANS LIVING WITH SCHIZOPHRENIA-RELATED DISORDERS AND SWITCHED FROM ONE SECOND-GENERATION ANTIPSYCHOTIC TO ANOTHER

See abstract on page 196.

TRENDS IN OUT-OF-POCKET COST BURDEN FOR PATIENTS WITH CHRONIC CONDITIONS

See abstract on page 203.

Mean Patient Annual OOP Costs by Coinsurance Benefit Design (2002-2004)

<table>
<thead>
<tr>
<th>Chronic kidney disease</th>
<th>No Coinsurance ($)</th>
<th>Coinsurance in Network ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple sclerosis</td>
<td>692</td>
<td>1,856</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>616</td>
<td>1,586</td>
</tr>
<tr>
<td>Diabetes</td>
<td>532</td>
<td>1,384</td>
</tr>
</tbody>
</table>

OOP = out of pocket.

AIC = glycosylated hemoglobin; FBG = fasting blood glucose.