Abstracts from Professional Poster Presentations at AMCP's 24th Annual Meeting & Expo

The following poster presentations have been prepared for the Academy of Managed Care Pharmacy's 24th Annual Meeting & Expo, April 18-20, 2012, in San Francisco, California. Poster presentations are selected by the Program Planning and Development Committee from proposals that are submitted to the 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. The names of the individuals who are scheduled to present at the meeting are shown in bold.

■ 12-Month A1c and Weight Outcomes by Drug Class in Treatment Naïve Patients with Type 2 Diabetes

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BACKGROUND: Antidiabetic-associated weight gain may be considered a necessary trade-off to achieve glycemic control. However, excess weight and obesity increase risk of poor cardiovascular outcomes. Diabetes treatment guidelines recognize the importance of weight management and recommend treatments that are weight neutral or promote weight loss. Few studies have simultaneously considered antidiabetic therapy-related weight and glycemic outcomes in the real-world setting.

OBJECTIVE: To identify weight and glycemic control outcomes at 12 months in patients with type 2 diabetes (T2DM) initiating antidiabetic treatment.

METHODS: Adult, treatment naïve patients with T2DM in the General Electric Centricity Electronic Medical Record (EMR) database with a first-time prescription (index date) for monotherapy metformin (MET), sulfonylurea (SU), thiazolidinedione (TZD), DPP-4 inhibitor (DPP-4), or GLP-1 agonist (GLP-1) between January 1, 2000, and June 30, 2010, were included. Patients had weight and A1c values at index date (± 45 days) and at 365 days (± 45 days) post-index date. Chi-square tests were used to compare the proportion of patients with follow-up A1c at goal ($< 7.0\%$) and separately for weight change, categorized as weight gain at least 3%, weight neutral (change $< 3\%$), or weight loss at least 3%, by drug class. The proportion at A1c goal in each weight change group was compared overall and stratified by individual drug classes. Chi-square tests were used to test differences in proportion at goal by weight change group, and a Cochran-Mantel-Haenszel test was used to control for drug class. Multivariable logistic regression models were used to identify the associations between drug class and A1c goal achievement and weight loss (vs. weight neutral/weight gain) while adjusting for other variables.

RESULTS: A total of 28,290 patients were included in the study. Mean (SD) age was 61 (11.8) years; 53.6% were female. The largest proportion was treated with MET (64.8%) followed by SU (22.2%), TZD (10.5%), DPP-4 (1.6%), and GLP-1 (0.9%). At follow-up, 68.7% were at A1c goal. Overall, 18.1% of patients experienced weight gain, 47.1% were weight neutral, and 34.8% had weight loss. The proportions achieving A1c goal differed significantly between patients with weight gain (60.8%), weight neutral (63.7%), and weight loss (79.7%; $P < 0.001$). In each drug class, follow-up A1c goal attainment was significantly higher in those who lost weight ($P = 0.029$). There was a significant difference in the proportion of patients with goal A1c in each weight group controlling for drug class ($P < 0.001$). Relative to SU, patients receiving MET, DPP-4, or GLP-1 were more likely to have weight loss ($P = 0.009$), and those receiving TZD were less likely to have weight loss ($P = 0.002$). Relative to SU, patients receiving MET or TZD were more likely to obtain goal A1c ($P = 0.001$), and there was no significant difference for those receiving DPP-4 or GLP-1.

CONCLUSIONS: More patients who lost weight achieved goal A1c. MET, as first-line therapy, was associated with both better weight and A1c outcomes relative to SU. Since diabetes is a progressive disease, the weight-effect properties of add-on drugs should also be considered. Newer agents with improved weight-effect profiles may be more expensive than existing therapies; thus, it is important to consider outcomes associated with both improved weight and glycemic control when making formulary decisions.

SPONSORSHIP: This research was funded by Bristol-Myers Squibb, Wallingford, CT.

■ Adherence and Medical Cost Patterns of Treatment with RAS Inhibitor/Amlodipine Combinations

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BACKGROUND: Association between use of renin-angiotensin system (RAS) inhibitor/amlodipine fixed-dose combinations (FDCs) and adherence relative to equivalent loose-dose combinations (LDCs) is documented; however, the literature on associated long-term medical costs is sparse.

OBJECTIVE: To examine adherence and medical costs of treatment with RAS/amlodipine FDC and LDC combinations.

METHODS: Commercial enrollees aged 18 years or older with hypertension and index claim for FDC olmesartan/amlodipine (FDC-OA), FDC benazepril/amlodipine (FDC-BA), or LDC angiotensin receptor blocker and amlodipine (LDC-AA) were identified during September 2007 to December 2008. Absence of study drug 6 months prior to index claim and continuous enrollment for at least 12 months post-index were required. Outcomes included follow-up therapy adherence measured as proportion of days covered (PDC) and all-cause medical costs (inpatient, outpatient, and other nondrug costs). Descriptive and multivariate analyses compared FDC-BA and LDC-AA cohorts versus FDC-OA, separately. Multivariate models for likelihood of PDC ≥ 0.80 (logistic regression) and medical costs (generalized linear models) were performed, adjusting for baseline demographic and clinical characteristics and propensity for assignment to study drug (propensity score subclassification).

RESULTS: A total of 4,864 individuals were identified on FDC-OA, 12,051 on FDC-BA, and 7,748 on LDC-AA. Mean follow-up duration was 543, 625, and 585 days, respectively. Mean PDC was higher in FDC-OA (0.63) cohort compared with FDC-BA (0.55, $P < 0.001$) and LDC-AA cohorts (0.34, $P < 0.001$). Mean follow-up per-member-per-month medical costs were lower in FDC-OA cohort ($501.86) compared with FDC-BA ($574.61, $P = 0.003$) and LDC-AA cohorts ($1,048.67, $P < 0.001$). Multivariate results suggested that subjects in FDC-BA (adjusted odds ratio [OR] = 0.758, 95% CI = 0.635-0.906, $P = 0.002$) and

LDC-AA cohorts (OR=0.242, 95% CI=0.205-0.287, $P<0.001$) were significantly less likely than FDC-OA to have PDC≥0.80. Subjects in FDC-BA (adjusted cost ratio [CR]=1.235, 95% CI=1.128-1.352, $P<0.001$) and LDC-AA cohorts (CR=1.412, 95% CI=1.285-1.551, $P<0.001$) had significantly higher follow-up predicted medical costs than FDC-OA.

CONCLUSIONS: Among RAS/amlodipine combinations studied in this sample of hypertensive subjects from a large nationally representative managed care database, subjects on FDC-OA were more likely to have PDC≥0.80 and lower follow-up medical costs than individuals on FDC-BA and LDC-AA. Limitations include the inability to verify patient medication-taking behavior and potential selection bias due to treatment assignment; propensity score adjustment attempted to adjust for the latter.

■ Advantages of an Integrated System in Changing Proton Pump Inhibitor Prescribing Patterns

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BACKGROUND: Denver Health Medical Plan, Inc. (DHMP) partners with Denver Health and Hospital Authority (DHHA) to provide integrated care through DHHA's clinics and internal pharmacies with access to 340B pricing. In January 2010, esomeprazole was the top prescribed drug for DHMP Medicare Advantage enrollees and identified as an opportunity to modify prescribing patterns that would generate significant cost savings. A proton pump inhibitor (PPI) task force was created in 2010 to develop prescriber guidelines and patient education materials. In second quarter 2010 auto-substitution from esomeprazole to generic omeprazole began at the DHHA pharmacies, and in 2011 a PPI quantity limit of 90 per 365 days was instituted.

OBJECTIVE: To evaluate the impact of multiple intervention strategies on the use of esomeprazole and generic omeprazole among approximately 3,000 DHMP Medicare Advantage enrollees.

METHODS: Claims data were used to identify DHMP Medicare Advantage enrollees who filled a PPI from January 2010 through September 2011 (n=1,904). PPI claims were identified using the American Hospital Formulary Service code 562836.

RESULTS: In first quarter 2010, 3,050 PPI claims from 762 utilizers accounted for a PPI cost of approximately $356,400. 1,874 of these claims were for esomeprazole, and 1,145 were for generic omeprazole. After the initiation of the auto-substitution, 760 utilizers produced 3,183 claims in second quarter 2010, with 607 esomeprazole claims and 2,533 generic omeprazole claims. Due to the shift to generic omeprazole, the total cost of PPIs dropped to approximately $170,800 by second quarter 2010, generating a total savings of approximately $185,600. A decreasing trend was seen in claims and total PPI cost after second quarter 2010 with 2,434 and 1,713 claims costing approximately $102,100 and $71,900 in the last 2 quarters of 2010, respectively. Utilizers peaked at 778 during third quarter 2010 and declined to 770 during fourth quarter 2010, while claims for generic omeprazole remained constant, making up approximately 85% of the total PPI claims in 2010. 2011 started with 1,701 claims and a total PPI cost around $72,400 and dropped to 1,400 claims, costing approximately $59,000 in the second quarter due to the new quantity limit. In the third quarter claims rose to 1,489, but regardless of this increase in claims, total cost declined to approxi-

mately $31,350 for third quarter 2011 due to increasing use of generic omeprazole. While unique utilizers varied in 2010, there was a steady decline in 2011 from 769 to 701 from first to third quarter. In total, these interventions produced a savings of approximately $1,630,800 over the course of 21 months.

CONCLUSIONS: A number of unique programs were implemented in an integrated system that may not be available in other settings. Auto-substitution resulted in a rapid switch from brand to generic PPIs with significant cost savings. Patient and prescriber education seemed to coincide with a decrease in claims and unique utilizers. However, the largest drop in claims and unique utilizers occurred with the institution of the formulary quantity restriction.

■ An Empirical Approach to Measure and Predict Treatment Persistence Among Insulin Glargine-Treated Patients with Type 2 Diabetes

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BACKGROUND: For insulin-treated patients with type 2 diabetes mellitus (T2DM), treatment persistence is critical in maintaining glycemic control. However, evaluating persistence with insulin treatment using health plan claims data is challenging mainly due to its nonfixed dose schedule, and there are limited real-world data on the factors predicting patients being persistent with their insulin treatments.

OBJECTIVE: To use health plan claims databases to measure treatment persistence among U.S. T2DM patients treated with insulin glargine and use different patient populations to identify common factors predicting patients being persistent with their insulin glargine treatments.

METHODS: This is a retrospective cohort database study using 2 claims databases consisting of 3 different populations to confirm robustness of the findings: (a) Thomson Reuters MarketScan database—Commercial ("MC," aged <65) and Medicare populations ("MM," aged ≥65)—and (b) the Integrated Healthcare Information Services multiplan national managed care database ("IH," all ages). T2DM patients were included if they were treated with insulin glargine between 2007 and 2010, aged at least 18 years, had at least 2 vial glargine prescriptions before switching to disposable pen or continuing on vial (index event), and had continuous health plan coverage for 6 months before (baseline) and 1 year after the index event (follow-up). Propensity score matching (1:1) was used to remove the potential selection bias between the pen switchers and vial continuers by matching their baseline demographic, clinical, and health care characteristics. Treatment persistence was defined as remaining on insulin glargine treatment without discontinuation during the 1-year follow-up. Rather than relying on days of supply in the claims data, the actual refill dates of insulin glargine prescriptions were examined, and insulin glargine treatment was considered discontinued if the prescription was not refilled within the expected time of medication coverage, defined as the 90th percentile of the time, measured by the metric quantity supplied, between first and second fills among patients with at least 1 refill. Logistic regression analysis was then conducted to identify baseline factors predicting 1-year treatment persistence.

RESULTS: A total of 8,984 matched patients were included (n=5,782, 1,996, and 1,206; mean age 51, 73, and 53 years; female 50%, 49%, and 42%; in MC, MM, and IH, respectively). In all 3 populations, 1-year treatment persistence rates were significantly higher in pen switchers than vial continuers (70.0% vs. 55.6%, 65.3% vs. 56.8%, and 65.3% vs.

49.8%, in MC, MM, and IH, respectively, all $P < 0.001$). The multivariate analysis showed that disposable pen usage (MC, MM, IH), older age (MC, MM), use of rapid-acting insulin via pen (MC, MM, IH), higher baseline daily average consumption of insulin (MC, MM, IH), and higher adjusted medication possession ratio (IH, MC) were associated with significantly higher persistence rate, but endocrinologist visit (MC, MM) and diagnosis of mental illness (IH, MM) were instead associated with lower persistence rate.

CONCLUSIONS: This real-world study showed that it is feasible to use health plan claims data to study insulin treatment persistence among T2DM patients, and certain baseline clinical and demographic characteristics can be used to predict treatment persistence. These results may have the potential to assist with treatment decisions and help optimize management of T2DM.

■ Analysis and Financial Impact of Maximum Pay Edits Within an Integrated Managed Care Organization

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BACKGROUND: As an administrative edit, the goal of a maximum pay edit is to prospectively manage situations in which pharmacies may be creating inadvertent billing errors related to submission of incorrect quantities or days' supply. The edit will ultimately generate cost savings through the prevention of claim processing for excessive quantities and reduction of administrative burden for the retrospective collection of these funds. Additional benefits include (a) safe drug use considerations; (b) retrospective analysis upon extrinsic claims for possible misuse, waste, or abuse; (c) quality assurance for plan sponsors not subscribing to quantity limit benefits; and (d) discovery and development of future quantity limit utilization management (UM) programs.

OBJECTIVE: To use databases of an integrated health care management system to examine adjudicated claims for drug use patterns, analyze results, apply clinical/financial management, and determine financial impact of an administrative maximum pay UM program.

METHODS: A maximum pay default limit of $750 per prescription was implemented in May 2010. Pre-established monetary restrictions above the default were customized for certain therapeutic categories. However, exceptions to these limits must be routinely identified. Monthly committee reviews are conducted using adjudication data and cost analysis from the entire commercial book of business. Edit exceptions are methodically identified, and higher dollar threshold set on the drug entity when necessary based on changes in average wholesale price (AWP), new FDA indications/clinical considerations, or new dosage forms are launched to market. Additional exceptions are identified by the formulary management team when new drug launches exceed the monetary limit. All recommended changes are approved via an oversight workgroup prior to implementation.

RESULTS: Approximately 4,000 claims per quarter were projected to hit the edit during the first year of implementation (2010), and total claims value was estimated at $23 million for commercial business. Expected cost savings was approximately 1% of the total claims value. These estimates held true after implementation of the edit, and the planned savings goal of $0.03 per member per month for 2011 has been exceeded with year-to-date (YTD) savings of $0.11, and $0.07 incremental savings YTD over the same time period in 2010.

CONCLUSIONS: There are many opportunities for errors in the adjudication process. A well-managed maximum pay UM program can improve the adjudication process, potentially reduce billing errors, and promote safe use of drugs as well as cost avoidance to the plan.

■ Anticoagulants for Stroke Prophylaxis in a Commercially Insured Atrial Fibrillation Population

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BACKGROUND: Roughly 2.3 million people in the United States have atrial fibrillation (AF); this number will likely double by 2050. The morbidity and mortality associated with AF are due largely to the increased risk of cardioembolic stroke. Stroke prevention in AF is particularly important, since AF-related strokes are frequently associated with severe neurologic deficits. Chronic oral anticoagulant prophylaxis is underused, reflecting both physician and patient fear of bleeding and uncertainty about benefit. Current medical guidelines for stroke prevention recommend that all AF patients at high risk of stroke receive anticoagulant prophylaxis unless contraindicated. Dose-adjusted warfarin prophylaxis reduces the risk of ischemic stroke by more than 60%.

OBJECTIVE: To identify gaps in care between current anticoagulation guidelines and practice patterns for AF management as recorded in a national commercial database.

METHODS: This analysis was performed using the Anticoagulant Quality Improvement Analyzer, software designed to analyze health plan data. Data were obtained from a 10% random sample of PharMetrics Integrated Database. Patients were included if they had a primary or secondary diagnosis of AF (ICD-9-CM code 427.31), aged 18 years or older, and were in the database between June 2008 to July 2010. A 1-year follow-up period was used. A CHADS2 score (0 = low risk, 1 = moderate risk, ≥ 2 = high risk) was used to determine stroke risk level for each patient using demographic and clinical characteristics. Demographics, stroke risk level, anticoagulant use, and inpatient stroke hospitalizations were analyzed.

RESULTS: 25,710 AF patients were identified. Their mean age was 71.3 (SD 14.4) years, and 58% (n = 14,929) were male. Stroke risk factors based on CHADS2 were common in these patients; 64% (n = 16,390) had hypertension; 44% (n = 11,559) were aged 75 years or older; 27% (n = 7,015) were diabetic; and 25% (n = 6,457) had heart failure. Stroke risk levels by CHADS2 were as follows: 56% (n = 14,350) high risk, 27% (n = 6,973) moderate risk, and 17% (n = 4,387) low risk. Of all AF patients, 65% (n = 16,617) did not receive an anticoagulant; 61% (n = 8,822 of the 14,350) of the high-risk stroke patients did not receive anticoagulant prophylaxis. Among the patients receiving anticoagulants, the mean time to first gap of at least 60 days of anticoagulant therapy was 167 days of the AF patients; 2% (n = 542) had an inpatient stroke hospitalization, and of these, 70% did not receive anticoagulants for secondary prevention in the outpatient setting.

CONCLUSIONS: Our findings using condition-specific data-analyzer software yielded practice pattern and health care quality information of critical importance for health plan decision makers. Approximately 61% of AF patients at high risk of stroke and 70% of AF patients hospitalized with stroke did not receive outpatient anticoagulant prophylaxis. Increased use of guideline-recommended prophylactic anticoagulation could significantly decrease stroke events, fatalities, and related health care costs in the study population. Increased use of the analyzer and

similar software may support enhanced education efforts for providers and patients, as well as long-term monitoring of practice patterns and quality of care.

Application of Novel Handwriting Recognition Technology for Analyzing Prescription Orders in an Oncology Specialty Pharmacy: A Pilot Study

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BACKGROUND: The National Academy of Sciences estimates that at least 1.5 million Americans are sickened, injured, or killed each year by errors in prescribing, dispensing, and administering of medications. Illegible orders are a widely notable source of medication errors. Health care systems, health professional organizations, and regulatory agencies are urging the implementation of novel approaches to increase pharmaceutical safety and reduce medication-related errors. One emerging solution is the development of patient-centered medical homes (PCMH), which integrate electronic medical record (EMR) systems and e-prescribing to promote continuous care. However, many physicians' practices continue to use handwritten prescriptions in various practice settings, including oncology. This pilot study investigates the use of a novel handwriting recognition technology to analyze prescription orders sent by physicians' offices to an oncology specialty pharmacy for processing. By digitizing handwritten prescriptions, the information can be integrated into EMRs for a comprehensive patient record within a PCMH.

OBJECTIVE: To (a) assess the accuracy of handwriting recognition technology in deciphering handwritten oncology prescriptions and medication orders and (b) identify and implement strategies to improve rate of accuracy of the recognition technology.

METHODS: Seventeen oncology medication orders were randomly selected to be analyzed by the handwriting recognition technology. The medication orders were de-identified for HIPAA compliance. A lexicon with the list of commonly prescribed chemotherapy regimens was sent with the de-identified prescription orders to the University at Buffalo Center for Unified Biometrics and Sensors for analysis. The state-of-the-art equipment extracted relevant words by using automatic line separation and noise removal. The algorithm generated a ranked list of probable drug names, using the lexicon as reference. A summary of the performance was generated based on the rate of the identification of the true drug name as the top choice.

RESULTS: A total of 17 documents were supplied, which included 64 medication names. The lexicon consisted of 52 drug names. In this preliminary study, the correct drug name was recognized as the top choice in 56 of 64 word images that were submitted. This equates to a top-choice accuracy rate of 87.5%. The remaining 12.5% involved drug choices that were ranked second or lower.

CONCLUSIONS: A challenge to this pilot study was the range in quality of the prescription images provided attributable to poor binarization as a result of the de-identification process. By improving the quality of images processed by the handwriting recognition technology, we expect to see an increased rate of recognition accuracy so that these medication orders may be digitized into an EMR. Our aim is to achieve the seamless flow of accurate information among health care providers utilizing EMR systems in a patient-centered medical home model.

Application of Pharmacogenomics Screening into a Specialty Drug Management Program

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BACKGROUND: Pharmacogenomics refers to drug treatment that is specific to individuals based on their DNA. Use of genetic testing and analysis provides key information to allow for a more personalized approach to drug treatment and ensures that patient are receiving the medication that will work for them. The presence of certain biologic markers allows physicians and patients to select an optimal therapy the first time, avoid the frustration of "trial-and-error" prescribing, and set a plan for monitoring and prevention. Due to strong evidence that biologic markers are associated with improved response to treatment and avoidance of side effects, pharmacogenomic information is contained in approximately 10% of the product labels of drugs approved by the FDA.

OBJECTIVE: To evaluate the impact of integrating pharmacogenomics screening criteria to a specialty drug management program in targeted self-funded employer groups.

METHODS: As part of an overall specialty drug management program, a collaborative approach was developed between self-insured employer groups and a pharmacy benefit manager to assist with the management and ensure appropriate utilization of specialty drug products. Prior authorization was utilized as part of an overall management strategy for specialty drug products. Prior authorization was continued and additional screening criteria was implemented that required pharmacogenomics testing as part of the utilization management program for 14 identified specialty products. Prescription drug claims and prior authorization records were evaluated retrospectively to compare a baseline period with the intervention period and quantify the impact of the new pharmacogenomics criteria.

RESULTS: There was an overall savings for the self-insured employer groups through an increase in medication cost avoidance due to the incorporation of pharmacogenomics criteria into the specialty management program. There was an increase in the number of patients who did not meet the specified pharmacogenomics criteria, and these patients avoided unnecessary therapy and the related financial burden.

CONCLUSIONS: Application of pharmacogenomics screening criteria into an existing specialty drug management program demonstrated an approximate 10% increase in prior authorization requests not meeting established criteria and a subsequent increase in cost avoidance. It also provided plan sponsor specialty savings of 2% and avoided unnecessary medication regimens.

Assessing the Impact of Medicare Part D Three Years After Its Implementation: Trends in Prescription and Medical Expenditures for Medicare-Age Adults with Arthritis

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BACKGROUND: Several studies have investigated the effect of Medicare Part D using pharmacy claims data or patient-reported surveys. While a decrease in out-of-pocket drug expenditures has been observed after the

implementation of Part D in 2006, changes in other expenditures have been found to vary depending on the disease or population. Limited evidence is available on the impact of Part D on patients with arthritis, who often face high medical expenditures and economic burden.

OBJECTIVE: To evaluate the impact of Medicare Part D on out-of-pocket (OOP) drug expenditures, total drug expenditures, OOP medical expenditures, medical expenditures paid by Medicare, and total medical expenditures for patients with arthritis.

METHODS: This was a retrospective study using a sample of Medicare-eligible beneficiaries with arthritis from the pooled Medical Expenditure Panel Survey 2005 to 2008 data. For each 2-year panel, the first year of medical data was used to identify arthritis-related diagnoses (ICD-9-CM codes 710-716, 719-721, and 725-728), and the following expenses were estimated in the second year: (a) OOP drug expenditures, (b) total drug expenditures, (c) OOP medical expenditures, (d) medical expenditures paid by Medicare, and (e) total medical expenditures. Medical expenditures included payments for inpatient care, outpatient care, prescription drugs, and other medical services. For each expenditure variable, the 50th, 75th, and 95th percentiles were estimated using quantile regression, adjusting for age, age squared, gender, race/ethnicity, marital status, education, income, metropolitan statistical area, and Charlson Comorbidity Index. All expenditures were inflation adjusted to 2008 dollars.

RESULTS: The sample included 2,484 patients with arthritis aged 65 years or older, with a mean (SD) age of 75.4 (6.3). From 2005 to 2008, the quantile regression showed reductions in OOP drug expenditures across the 50th (–$151 [–25.2%], $P<0.001$), 75th (–$413 [–27.8%], $P<0.001$), and 90th (–$829 [–31.1%], $P<0.001$) percentiles, as well as reductions in OOP medical expenditures across the 50th (–$197 [–17.3%], $P=0.029$), 75th (–$568 [–23.2%], $P=0.001$), and 90th (–$736 [–18.5%], $P=0.023$) percentiles, adjusting for the covariates. In contrast, increases in total drug expenditures were found at the 75th ($844 [25.3%], $P<0.001$) and 90th ($1,194 [22.0%], $P=0.006$) percentiles but not at the median ($214 [10.3%], $P=0.079$). Medical expenditures paid by Medicare increased at the median ($896 [39.5%], $P<0.001$) but not at the 75th ($13 [0.2%], $P=0.989$) or 90th (–$2,929 [–13.86%], $P=0.220$) percentiles. No statistically significant differences were found between 2005 and 2008 in overall medical expenditures (50th percentile: –$181 [–2.8%], $P=0.714$; 75th percentile: –$1,575 [–10.4%], $P=0.300$; 90th percentile: –$3,212 [–10.3%], $P=0.281$).

CONCLUSIONS: Medicare Part D resulted in significant reductions in OOP prescription and OOP medical expenditures among beneficiaries with arthritis 3 years after its implementation. Total drug expenditures increased for those whose expenditures were at the 75th and 90th percentiles, while payments from Medicare for overall medical expenditures increased at the median. Part D was not associated with significant differences in total medical spending. Further research is needed to examine the effect of Part D on health outcomes in Medicare beneficiaries with arthritis.

■ **Association Between Adherence to Oral Bisphosphonate Osteoporosis Medications, Fracture Rates, and Expenditures**

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BACKGROUND: From a payer perspective, nonadherence, specifically with oral bisphosphonates, and how it affects fracture rates and expenditures in osteoporotic women has been studied in large datasets. Translating this to a mid-size health plan has not been done.

OBJECTIVE: To examine the association between adherence for oral bisphosphonate therapy on fractures rates and expenditures using claims data from a mid-size health plan.

METHODS: A retrospective analysis using the claims data between 2005-2010. Women with a new diagnosis for osteoporosis and continuous eligibility for 18 months after the index diagnosis date were identified. The baseline period was for 6 months after the index diagnosis date for osteoporosis. The follow-up period was 12 months after the end of the baseline period. The primary outcome was the presence of osteoporotic fractures, overall and individually by hip and nonhip fractures. Adherence, measured by medication possession ratio (MPR) for the bisphosphonate dosage form they started and stayed on for the study period, and all-cause medical and pharmacy expenditures in the follow-up period was assessed in patients with and without fractures. Logistic regression was used to adjust fracture rates by MPR category—0-19%, 20-49%, 50-79%, and at least 80%—measured prior to any fracture event in the study period, controlling for age, chronic condition index, baseline fracture event, use of steroids, and frequency of bisphosphonate treatment (weekly, monthly, quarterly). Expenditures were estimated by MPR category using generalized linear models. All analyses were conducted in Stata/MP 11.2.

RESULTS: We had 1,622 patients whose mean age was 71 years, with 96% on a weekly regimen, 3.7% on a monthly regimen, and less than 1% on either a quarterly or daily regimen. About 48% of the study sample had adherence rates between 20-49%; 33% had adherence rates between 0-19%; 16% had adherence rates between 50-79% while less than 3% had adherence rates >80%. In comparing those with the lowest adherence to those with the highest adherence for illustrative purposes, those with adherence between 0-19% were 2.74 times more likely ($P<0.005$) to experience a hip fracture compared with those with >80% adherence in the 12-month follow-up period. Similarly, those with adherence rates between 0-19% were 11.68 times more likely ($P<0.005$) to experience a nonhip fracture compared with those with >80% adherence. Finally, those with adherence rates between 0-19% were 6.28 times more likely ($P<0.005$) to experience any fracture compared with those with >80% adherence. The incremental impact of adherence on annual medical expenditures for the lowest level of adherence (0-19%) was $1,711 ($P<0.005$) per patient compared with those with >80% adherence. A similar relationship between adherence and other fracture types and between adherence and expenditures was also observed.

CONCLUSIONS: The association between medication adherence, fractures rates, and expenditures demonstrates increased medical expenditure with poorer therapeutic adherence. The implication of treatment choice on medication adherence and the cost-consequences of poorer adherence is important to understand.

■ **Association Between Osteoporosis and Total Health Care Costs in Members with High-Cost Chronic Diseases in a Managed Care Setting**

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BACKGROUND: Highly prevalent or costly diseases such as chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD),

diabetes mellitus (DM), and depression (DEP) are of significant interest to payers. Little is known about newly diagnosed osteoporosis (OP) in members with these prevalent chronic diseases and the impact on health care costs.

OBJECTIVE: To examine the association between new OP diagnosis and total health care costs among members previously diagnosed with the chronic diseases COPD, CVD, DM, or DEP.

METHODS: This was a retrospective cohort study of commercial and Medicare Advantage (MAPD) members aged 50 years or older in a large U.S. health plan identified with COPD, CVD, DM, or DEP and/or new OP between January 2007 and October 31, 2009. All members were required to have continuous enrollment in the health plan during the 2-year pre-index and 1-year post-index periods with evidence of their chronic diseases and no evidence of OP in the pre-index period. Evidence of new OP was defined as at least 1 medical claim with ICD-9-CM diagnosis code for OP, at least 2 OP medication fills, or at least 1 medical claim for fragility fracture in the index period. Members with Paget's disease of bone diagnosis or medications, hypercalcemia, osteogenesis imperfecta, human immunodeficiency virus, preventive treatment for breast cancer risk, or actively treated cancer were excluded. Members were assigned to a cohort of a single or multiple (MULT) prevalent chronic disease with or without OP. For OP members, an index date was set as the first claim with evidence of OP. Index dates for members without evidence of OP were selected randomly from 1 of their service dates on medical claims during this period. Baseline characteristics were assessed during the 1-year pre-index period. Each chronic disease cohort with OP was compared with its counterpart without OP. Total all-cause health care costs in a 12-month post-index period were examined for the 10 cohorts. A generalized linear model with a log link and a gamma distribution, controlling for covariates, was used to assess the association between OP and total health care costs.

RESULTS: A total of 393,509 members were identified. The chronic disease cohorts with new OP comprised 11.2% of the sample; members with COPD and CVD comprised the smallest and largest cohorts, respectively. Each chronic disease cohort with OP had higher mean unadjusted costs at 12 months compared with their respective cohorts without OP (COPD $20,624 vs. $11,065; CVD $15,941 vs. $8,365; DM $18,195 vs. $8,532; DEP $19,695 vs. $9,414; MULT $23,926 vs. $12,777; all $P < 0.001$). A statistically significant association between OP and total health care costs was found in each of the comparison cohorts after controlling for baseline covariates including age category, gender, business line, region, Quan-Charlson comorbidity score, top ten Agency for Healthcare Research and Quality (AHRQ) comorbid conditions, and baseline logged costs. Predicted mean costs remained higher than their comparison cohorts' predicted costs (COPD $17,748 vs. $11,299; CVD $14,575 vs. $8,431; DM $16,190 vs. $8,516; DEP $16,554 vs. $9,607; MULT $21,218 vs. $12,957; all $P < 0.001$).

CONCLUSIONS: After controlling for covariates, members with a chronic disease and new OP had significantly higher total direct health care costs than members with only chronic disease. The predicted cost ranged from 57.1% to 90.1% greater than costs for subjects with chronic disease alone. New OP appears to be associated with higher health care costs in patients with multiple diseases, and in this population should be managed to improve the quality of care and reduce cost.

SPONSORSHIP: This research was funded by Amgen Inc., Thousand Oaks, CA.

■ Association Between Use of Mealtime Insulin Pens Versus Vials and Health Care Charges in Patients with Type 2 Diabetes

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BACKGROUND: Among patients with type 2 diabetes, outcomes may be affected by the delivery method of antidiabetic therapy.

OBJECTIVE: To compare total direct health care charges and diabetes-related total direct health care charges among adults with type 2 diabetes mellitus (T2DM) who initiate therapy with mealtime insulin disposable pens or vials.

METHODS: Data for this study were obtained from the i3 inVision database over the time period from January 1, 2006, through June 30, 2010. Patients with T2DM who initiated mealtime analog insulin via vial or disposable pen were included in the study, with first such use identified as the index date. Patients were excluded from the analyses if they switched method of delivery or used cartridge mealtime insulin, 3 ml vials of mealtime insulin, inhaled insulin, or an insulin pump. Additionally, patients were required to not be diagnosed with type 1, secondary, or gestational diabetes. Finally, patients were required to have continuous insurance coverage from 6 months prior to the index date through 12 months post-index date and to be at least aged 18 years. Generalized linear models with a gamma distribution and log link were used to estimate the effect of using mealtime insulin pens versus vials on total direct health care charges, diabetes-related total direct health care charges, and key components of such charges, while controlling for a wide range of other factors that may be associated with health care charges, including patient demographic and clinical characteristics. Charges are reported for the 12-month period following mealtime insulin initiation.

RESULTS: There were 8,374 individuals who fit the study criteria (4,429 initiated on pens and 3,945 on vials). After controlling for patient characteristics, general health, and amount of copayment associated with medication of interest, insulin therapy initiation on disposable pens, compared with vials, was associated with significantly lower total direct health care charges ($42,150 vs. $53,340; $P < 0.001$) as well as significantly lower diabetes-related total direct health care charges ($12,722 vs. $14,540; $P < 0.001$). While the use of disposable pens was associated with both higher total drug charges ($8,695 vs. $8,300; $P < 0.001$) and diabetes-related drug charges ($3,593 vs. $2,755; $P < 0.001$), this difference was offset by significantly lower inpatient ($11,960 vs. $19,922; $P < 0.001$), outpatient ($20,746 vs. $25,667; $P < 0.001$), diabetes-related inpatient ($4,352 vs. $6,451; $P < 0.001$), and diabetes-related outpatient ($4,660 vs. $5,340; $P < 0.001$) charges.

CONCLUSIONS: Results from this retrospective study indicate that the use of mealtime insulin via disposable pens, compared with vials, was associated with a significant reduction in both total direct and diabetes-related total direct health care charges despite the higher drug charges associated with the use of disposable pens.

SPONSORSHIP: This research was conducted by Eli Lilly and Company, Indianapolis, IN.

■ Atypical Antipsychotics Versus Non-Antipsychotics: Comparative Treatment Patterns, Resource Utilization, and Costs in Stimulant-Treated Adolescents with ADHD Who Require Subsequent Pharmacotherapy

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BACKGROUND: Although not indicated for attention deficit hyperactivity disorder (ADHD), atypical antipsychotics (AAPs) are sometimes prescribed for patients with ADHD. The treatment patterns, resource utilization, and costs associated with AAP use relative to non-antipsychotic medication (stimulants, guanfacine, atomoxetine, and clonidine) have not been evaluated for adolescents with ADHD.

OBJECTIVE: To compare treatment patterns, resource utilization, and costs to U.S. third-party payers between stimulant-treated adolescent ADHD patients who switch to, or augment their stimulant treatment with, AAPs versus non-antipsychotic medications.

METHODS: Patients aged 13-17 with an ADHD diagnosis (ICD-9 CM codes 314.0x) and having at least 1 stimulant medication claim between January 1, 2005, and December 31, 2009, were identified from a large U.S. commercial medical/pharmacy claims database. Patients were classified into the AAP or non-antipsychotic treatment group based on whether they had a subsequent claim for an AAP or non-antipsychotic medication, respectively. Patients with a psychiatric diagnosis for which AAPs are indicated were excluded. Patients in the AAP group were matched 1:1 to patients in the non-antipsychotic group using a propensity score generated from a logistic regression including demographics, treatments, resource utilization, and comorbidities during the 6 months prior to treatment initiation. All outcomes were measured during the 12-month post-treatment initiation. Treatment patterns were compared using Kaplan-Meier estimates and Cox proportional hazards models. Annual resource utilization was compared using Poisson regression. Costs to third-party payers were adjusted to 2010 dollars using the Consumer Price Index and compared using Wilcoxon signed-rank tests.

RESULTS: A total of 849 patients were included in each of the matched cohorts. The baseline characteristics were well balanced between the 2 cohorts. Patients in the AAP group had a significantly higher rate of medication augmentation (27.7% vs. 15.5%; hazard ratio [HR] = 2.56; $P < 0.001$), and a numerically higher rate of medication switching (11.6% vs. 9.7%; HR = 1.40; $P = 0.14$) compared with non-antipsychotic patients. AAP patients also had significantly higher incidences of inpatient admissions (0.13 vs. 0.05; incidence rate ratio [IRR] = 2.45; $P < 0.001$), emergency room visits (0.39 vs. 0.31; IRR = 1.27; $P = 0.004$), and outpatient visits (14.82 vs. 13.19; IRR = 1.12; $P < 0.001$) and incurred significantly higher mean medical ($3,622 vs. $3,311; $P = 0.002$), drug ($4,314 vs. $2,884; $P < 0.001$), and total health care ($7,936 vs. $6,195; $P < 0.001$) costs.

CONCLUSIONS: Stimulant-treated adolescents with ADHD who switched to or augmented with AAPs versus non-antipsychotics had significantly greater subsequent drug augmentation, health care resource utilization (inpatient, outpatient, and ER), and costs (medical, drug, and total).

■ Budget Impact Modeling of Vemurafenib for Treatment of Metastatic Melanoma

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BACKGROUND: Vemurafenib is a BRAF inhibitor designed to target and inhibit the V600E mutated form of the BRAF protein. The FDA approved vemurafenib in August 2011 for patients with BRAF V600E mutation-positive unresectable or metastatic melanoma.

OBJECTIVE: To develop a tool that can be used by health care plans to assess the budgetary impact of covering vemurafenib.

METHODS: We developed a spreadsheet-based budget impact model using a 1-year time frame and conducted from the perspective of a health care plan. The age distribution of a hypothetical plan with enrollment of 500,000 was based on U.S. Census Bureau data. The SEER Registry was used to determine age and gender stratified incidence estimates of Stage III and IV melanoma. We estimated that 50% of Stage IIIc patients would be classified as unresectable. We based the duration of treatment for vemurafenib on the Phase III pivotal trial (the BRIM-3 trial). Dosing for other treatments (ipilimumab, dacarbazine, temozolomide) were based on randomized control trials published in the literature. We included treatment costs for Grade 3 or Grade 4 adverse events with an incidence rate of 5% or greater. We conducted 1-way sensitivity analyses on all model parameters.

RESULTS: The expected number of patients with unresectable or metastatic melanoma for a health plan of 500,000 enrollees was approximately 7, and the health plan cost of treatment without vemurafenib as a treatment option was $1,215,800 per year versus $978,100 per year with vemurafenib, a projected savings of $237,700 per year. This represents a decreased cost of $0.40 per member per month (PMPM). Sensitivity analyses showed that 3 factors had the greatest impact on results: proportion and cost of receiving ipilimumab, the proportion who received vemurafenib, and the patients who are positive for V600E mutation. The addition of vemurafenib was cost neutral or cost saving in all scenarios. Limitations include the following: only approved treatment options were evaluated, and patients who had a recurrence greater than 5 years after their initial diagnosis were not included.

CONCLUSIONS: Overall, vemurafenib therapy has a relatively small budget impact on a health care plan and may be cost saving in consideration of other currently available therapies.

| TABLE | Comparison of Resource Utilization and Costs Between the Atypical Antipsychotic and Non-Antipsychotic ADHD Groups |

Health Care Resource Utilization	Antipsychotic Users	Non-Antipsychotic Users	Incidence Rate Ratio	P Value
	Incidence Rate	Incidence Rate		
Inpatient admissions	0.13	0.05	2.45	< 0.001
Emergency room visits	0.39	0.31	1.27	0.004
Outpatient visits	14.82	13.19	1.12	< 0.001

Annual Cost	Antipsychotic Users	Non-Antipsychotic Users	Cost Difference ($)	P Value
	Mean Cost ($)	Mean Cost ($)		
Medical	3,622	3,311	311	0.002
Drug	4,314	2,884	1,430	< 0.001
Total	7,936	6,195	1,741	< 0.001

ADHD = attention deficit hyperactivity disorder.

■ Calculation of Annual Biologic Treatment Costs in Rheumatoid Arthritis: A Comparison of Methods and Relationship to Adherence

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BACKGROUND: Several biologic therapies are available to treat patients diagnosed with moderate to severe rheumatoid arthritis (RA). Those that have been available for the longest time include adalimumab (ADA), etanercept (ETA), and infliximab (IFX). Often the reported costs associated with treatment by these agents are calculated based on wholesale acquisition costs (WAC) rather than the actual amounts reimbursed by the health plan and patient out-of-pocket (OOP) costs.

OBJECTIVE: To compare annual WAC-based cost calculations versus actual reimbursed costs in conjunction with adherence to prescribed treatment regimens.

METHODS: Data analyzed were from the Thomson Reuters MarketScan database. Inclusion criteria were patients aged older than 18 years; at least 2 claims for ETA and ADA; at least 4 claims for IFX between January 1, 2003, and June 30, 2008; continuous enrollment for 12 months prior and at least 12 months following index date; at least 2 claims for RA (ICD-9-CM codes 714.0x); no gap in therapy 180 days or greater; and a claim for index biologic at least 12 months after the index date. Exclusion criteria were any biologic claim 6 months prior to index date, switched therapy during the 12-month follow-up, or a diagnosis of other inflammatory diseases. Treatment adherence is defined as excess gaps in days supply for ETA and ADA and number of days between infusion dates for consecutive IFX claims beyond the expected 8 weeks. Drug costs were based on the April 2010 WAC. Costs were calculated using the cumulative dose multiplied by the WAC. Amounts paid by the health plan and by the patient were also measured. All costs were inflated to 2010 dollars using the medical component of the Consumer Price Index.

RESULTS: 3,417, 4,898, and 2,226 patients treated with ADA, ETA, and IFX, respectively, met the inclusion criteria. The average gap (SD) in excess of days supply over the 12 months of follow-up was 9.8 (15.3) for ADA-treated patients and 11.5 (17.7) for ETA-treated patients. The gap in therapy for the first 5 fills was greater than 7 days for over 20% of patients treated with ADA and ETA. The average (SD) interval between maintenance infusions for IFX was 55.2 (13.3). The mean (SD) biologic drug cost of ADA, ETA, and IFX for real-world utilization post-index using WAC-based calculations was $21,394 ($5,702), $19,392 ($4,694), and $22,338 ($10,787), respectively. The health plan reimbursed amount (SD) for ADA, ETA, and IFX treatment was $17,167 ($4,816), $15,586 ($4,171), and $19,054 ($9,205), respectively. The OOP (deductible, co-insurance, and patient copay) (SD) for patients undergoing treatment with ADA, ETA, and IFX were $436 ($754), $421 ($809), and $676 ($1,168), respectively.

CONCLUSIONS: WAC-based cost calculations are significantly higher than health plan reimbursed amounts. The lower costs associated with the more frequently dosed subcutaneous agents (ETA and ADA) compared with IFX may be partially accounted for by underadherence with ETA and ADA treatment. When health plans are assessing real-world biologic treatment costs for their members, the actual reimbursed amounts plus patient share of costs should be the basis of the calculations rather than WAC pricing. Underadherence to therapy should be factored into the understanding of biologic cost.

■ Change in Patient-Reported Adherence with Participation in a Comprehensive Medication Review and Receiving a Personalized Medication List and Medication Action Plan

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BACKGROUND: Medication adherence is recognized as a universal problem with pharmaceutical management of patients. With the advent of medication therapy management (MTM) programs, a collective effort has been established to improve adherence. In providing telephonic comprehensive medication reviews (CMRs) and sending patients the resulting Personalized Medication List (PML), and where applicable a Medication Action Plan (MAP), programs seek to improve patient adherence. Adherence measurement tools have been utilized in providing MTM services previously; however, the impact of providing MTM services and the resultant change in adherence due to services rendered and utilization of the measurement tool has not been documented. In providing telephonic MTM services to Florida Medicaid patients, the University of Florida MTM Call Center included a 30- to 60-day follow-up review following a CMR to capture any changes in patient-reported adherence.

OBJECTIVE: To evaluate if participating in a CMR and receiving a PML and/or MAP changed patient perceived adherence.

METHODS: A pilot study was performed on patients who participated in a CMR and completed a 30- to 60-day follow-up review following the CMR. Patients were asked 8 adherence questions utilizing the validated 8-Item Morisky Medication Adherence Scale (8-MMAS) and then 30- to 60-days following the CMR were re-asked the 8-MMAS questions after receiving a PML and MAP (if applicable) via mail. A summary score was calculated from the 8-MMAS ranging from 0 to 8 (high to low adherence).

RESULTS: Of the 66 patients that completed a CMR and 30- to 60-day follow-up review, 56.1% were females with a mean age of 53.3 years (SD = 8.2), taking an average of 10.7 chronic medications and had an average of 5.5 comorbidities. At the time of the CMR, the average summary score was 1.3, and at the 30- to 60-day follow-up review, the average summary score was 2.1. Data revealed that 12.1% (n = 8) of patients had a decline in their 8-MMAS summary scores, ranging from a 1- to 3-point decline across the 8 patients. 40.9% (n = 27) of patients had no change in their 8-MMAS summary scores, and 47.0% (n = 31) patients had an increase in their 8-MMAS summary scores. Literature cites that a change in the summary score of at least 2 points over time represents a real change in adherence; accordingly, 27.3% (n = 18) of patients had a reported improvement in adherence due to participation in the CMR and receiving a PML and MAP.

CONCLUSIONS: Participating in a CMR and receiving a PML and MAP may positively affect patient-reported medication adherence.

■ Characteristics of Rheumatoid Arthritis Patients Who Initiate Anti-TNF Therapy and Switch to Abatacept or a Second Anti-TNF Agent

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BACKGROUND: A proportion of patients with rheumatoid arthritis (RA) who initiate anti-tumor necrosis factor (anti-TNF) therapy switch

to a second, alternative biologic agent. We have previously shown that the majority of these switches are to a second anti-TNF but a number of patients will receive abatacept. The reason for the selection of this agent over a second anti-TNF agent is not completely understood: 1 hypothesis is that it may be related to the characteristics of the patient at baseline.

OBJECTIVE: To compare baseline characteristics of RA patients who initiated anti-TNF therapy and switched to another anti-TNF agent or intravenous (IV) abatacept.

METHODS: This observational, retrospective study utilized administrative medical and pharmacy claims of the PharMetrics Integrated Database for the period from January 1, 2004, through March 31, 2010, for RA patients who were newly initiated on an anti-TNF (adalimumab, etanercept, or infliximab). Patients were followed forward for 2 years to identify the first claim (index date) for IV abatacept or 1 of the study anti-TNFs that deviated from their initial anti-TNF. Patients were required to have 6 months of continuous eligibility before and 12 months after the biological disease-modifying antirheumatic drug (bDMARD) switch. Baseline characteristics were collected in the 6-month pre-index period, prior to the bDMARD switch. Baseline costs were defined as health care (inpatient, outpatient, and pharmacy) costs incurred in the 6 months prior to switch.

RESULTS: Of 3,077 switch patients identified, 2,478 (80.5%) switched from 1 anti-TNF to another and 599 (19.5%) from anti-TNF to abatacept over 2 years. At baseline, those patients who switched to abatacept had a significantly higher mean age and significantly greater mean comorbidity scores than patients who switched to an anti-TNF (see table). In addition, patients who switched to abatacept had significantly higher overall and RA-related mean baseline health care costs.

CONCLUSIONS: Our study demonstrates that patients who switched to IV abatacept rather than a second anti-TNF agent were older and had more comorbidity and severity of RA at baseline. Further research is required to better understand how specific pre-existing conditions, severity of RA, and other patient characteristics influence physician selection of a second biologic therapy.

SPONSORSHIP: This research was conducted by Bristol-Myers Squibb, Plainsboro, NJ.

■ Communication Intervention for Influencing Physician-Prescribing Behavior

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BACKGROUND: Since 2005, the FDA has communicated to health care professionals and patients with asthma that use of long-acting beta-agonists (LABAs) as monotherapy has been associated with possible increased risk of worsening wheezing and an increased risk of asthma-related death. In 2009, Horizon Blue Cross Blue Shield of New Jersey (Horizon) conducted a 6-month, retrospective drug utilization evaluation (DUE) of physicians with patients on LABA monotherapy for asthma. On November 1, 2009, Horizon mailed a drug safety letter, patient list, and claims data to each physician with 1 or more patients on LABA monotherapy.

OBJECTIVE: To determine the benefit of Horizon's patient-specific intervention on reduction in LABA monotherapy utilization.

METHODS: This study utilized longitudinal prescription data for 97 Horizon members during the period 2009-2010. A medication possession ratio (MPR) statistic was used to estimate treatment timelines. Prior to November 1, 2009, a slow decline in the LABA monotherapy utilization rate was observed, so the study compared the pre- and post-intervention rates of decline. A linear regression method was used to compute slope estimates and slope differences. To ensure a robust analysis, *P* values for the differences between the pre- and post-intervention rates of decline were computed for a grid of MPR values (i.e., 0.45 to 0.95) and multiple post-intervention time periods (i.e., 3 months to 6 months).

RESULTS: For the MPR value of 0.53, 72 patients were on LABA monotherapy by November 1, 2009, while 22 remained on LABA monotherapy 6 months after the drug safety letter was mailed. For each MPR value and time period evaluated, LABA monotherapy utilization declined during the post-intervention period more rapidly than in the pre-intervention period (e.g., maximum *P* value of 0.023 and minimum *P* value of 0.004).

CONCLUSIONS: There was a statistically significant reduction in LABA monotherapy following release of the November 1, 2009, Horizon drug safety letter. Horizon's patient-specific communications to providers regarding safety concerns successfully altered prescribing behavior, providing an effective tool for providers to act on specific information with targeted interventions and resulting in desirable outcomes sooner and with less resource involvement.

TABLE	Comparison of Baseline Characteristics of Anti-TNF to Anti-TNF Versus Anti-TNF to Abatacept Switchers		
Baseline Characteristics	**Anti-TNF to Anti-TNF n = 2,478**	**Anti-TNF to Abatacept n = 599**	**P Value**
Age, mean [SD]	52 [12]	57 [13]	< 0.001
Men, % (n)	23.6 (584)	20.2 (121)	
Women, % (n)	76.4 (1,894)	79.8 (478)	0.078
Charlson Comorbidity Index, % (n)	1.3 (0.9)	1.6 (1.0)	< 0.001
Hospitalization, % (n)	8.6 (214)	8.5 (51)	0.924
Hospitalization with RA diagnosis, % (n)	4.5 (111)	6.5 (39)	0.038
Pre-index costs, mean [SD] $	1,907 [1,779]	2,243 [2,233]	< 0.001
Pre-index RA costs, mean [SD] $	1,132 [936]	1,424 [1,459]	< 0.001

RA = rheumatoid arthritis; SD = standard deviation; TNF = tumor necrosis factor.

TABLE	P Value of Intervention Over Time			
	Number of Months After Intervention			
MPR	**3**	**4**	**5**	**6**
0.45	0.021	0.006	0.006	0.004
0.53[a]	0.023	0.007	0.004	0.002
0.65	0.014	0.008	0.004	0.003
0.75	0.007	0.004	0.004	0.003
0.85	0.005	0.005	0.004	0.005
0.95	0.005	0.005	0.006	0.011

[a]Benchmark MPR = 0.53 selected from Castro et al. Healthcare utilization in a severe asthma population despite use of high dose ICS/LABA. Poster #4217, Session #A30. Annual Meeting of the American Thoracic Society. May 17, 2009, San Diego, CA.
MPR = medication possession ratio.

■ Community Pharmacy: A Preferred Channel to Fill 90-Day Prescriptions for Chronic Medications

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BACKGROUND: Most pharmacy benefit management companies (PBMs) promote mail order programs that typically dispense 90-day fills as 1 of the key cost containment strategies for plan sponsors to manage rising prescription drug expenditures, and many plan sponsors incent mail with favorable cost sharing. Community pharmacies have also introduced 90-day programs that provide similar cost advantages compared with mail order.

OBJECTIVE: To investigate the distribution channel that beneficiaries choose to fill their 90-day maintenance medication prescriptions when the plans do not incent one distribution channel over another. The study also compared the costs for plan sponsors that allowed both mail and community pharmacy choices at equivalent copayments versus those that only offered 90-day fills at mail order.

METHODS: A retrospective, cross-sectional investigation was conducted using pharmacy claims and eligibility data from employer group clients of a large PBM from January 2008 through September 2010. All employers offered 30-day prescription fills. Employers that offered only mail order fills of 90-day prescriptions were classified as "Two Channel." Employers that allowed 90-day fills either through mail order or community pharmacy were classified as "Three Channel." For inclusion in the study, employers and beneficiaries were required to have a minimum of 6 months of eligibility per calendar year. For both groups, relevant costs and utilization were standardized to per eligible member per month (PMPM) values, and differences were compared with t-tests for statistical significance.

RESULTS: A total of 72 employers covering about 566,000 beneficiaries were included in the Three Channel group, while the Two Channel comparison group included 55 employers with about 265,000 beneficiaries. After adjusting for age, gender, condition, and random variations between individual employer years, regression analysis demonstrated that beneficiaries who are offered the choice of channel prefer a community pharmacy by more than 3 to 1 (4.41 scripts per beneficiary per year in community 90-day versus 1.29 scripts per beneficiary per year in mail order). When a 90-day supply at a community pharmacy is offered as an equal benefit choice, higher community pharmacy utilization is a result of shifts from both 30-day (5.94 to 5.04 scripts per beneficiary per year) and mail (4.55 to 1.29 scripts per beneficiary per year) fills. Because of lower use of 30-day scripts, plan sponsors that offer 90-day community fills bear no additional costs (Three Channel plan paid PMPM $39.11 vs. Two Channel $41.04, P < 0.05).

CONCLUSIONS: This study suggests that beneficiaries value choice of channel for filling maintenance drug prescriptions, preferring community pharmacies offering 90-day supply over mail order. Study findings imply that plan sponsors could enhance employee satisfaction, benefit from face-to-face pharmacist interaction with patients, and not incur higher cost by allowing patients to obtain maintenance medications at community pharmacies.

■ Comorbidity and Cost Burden of Patients Prior to Initiating First-Line Biologic Therapy for the Treatment of Rheumatoid Arthritis

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BACKGROUND: Patients with rheumatoid arthritis (RA) often have significant comorbidity that, along with underlying RA severity, may impact both choice and response to treatment. We have previously shown that patients initiating first-line intravenous (IV) abatacept had higher baseline RA-related and overall health care costs and higher comorbidity scores than those patients initiating first-line infliximab. However, it is not known how the characteristics of these patients compare with those prescribed other commonly used first-line biologic agents.

OBJECTIVE: To compare degree of comorbidity, disease severity, and baseline health care costs in RA patients prior to initiating first-line treatment with abatacept, adalimumab, etanercept, or infliximab.

METHODS: Utilizing a large managed care plan claims database, an analysis was conducted in adult RA patients during the 6 months prior to initiating first-line biologic treatment with abatacept, adalimumab, etanercept, or infliximab. The identification period was January 1, 2006, through June 15, 2010. Severity of overall comorbidity was described using Charlson Comorbidity Index (CCI) and all-cause health care costs, while RA-related health care costs were used as a proxy measure of disease severity.

RESULTS: A total of 10,436 RA patients were identified who initiated treatment with 1 of the study agents as first-line biologic therapy. Baseline CCI and total all-cause health care costs were significantly higher for abatacept-treated patients (P < 0.001; see table). Baseline RA-related health care costs for abatacept-treated patients were significantly higher than those of patients treated with adalimumab, etanercept, or infliximab.

CONCLUSIONS: In a commercially insured population, patients initiating IV abatacept as first-line treatment demonstrated more comorbidity and greater baseline severity of RA than those who received adalimumab, etanercept, or infliximab. Further research is required to better understand how pre-existing conditions and severity of RA impact selection of biologic therapy and subsequent response in this patient population.

TABLE Comorbidity and Health Care Costs Prior to Initiating First-Line Biologic Treatment[a]

	Abatacept (n = 654)	Adalimumab (n = 3,464)	Etanercept (n = 4,597)	Infliximab (n = 1,721)
	Mean [SD]	Mean [SD]	Mean [SD]	Mean [SD]
Baseline Charlson Comorbidity Index	1.62 [1.17]	1.36 [0.90]	1.37 [0.91]	1.44 [0.97]
Baseline RA-related health care costs, $	3,686 [9,060]	1,888 [5,713]	1,821 [5,177]	2,192 [5,813]
Baseline all-cause health care costs, $	9,382 [14,646]	5,717 [9,747]	5,815 [10,856]	6,651 [11,925]

[a]P < 0.001 for all treatment values compared with abatacept values.
RA = rheumatoid arthritis; SD = standard deviation.

■ Comparison of Different Measures to Calculate Adherence with Fingolimod

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BACKGROUND: Adherence to standard first-line disease-modifying therapies (DMTs) in the treatment of multiple sclerosis (MS) remains suboptimal, and poor adherence impacts patient outcomes. Fingolimod is a single pill, once-a-day formulation to treat patients with relapsing forms of MS. Different methods of calculating adherence and persistence can generate varied results.

OBJECTIVE: To compare different measures used to calculate adherence with fingolimod using specialty pharmacy refill data.

METHODS: Retrospective analysis of specialty pharmacy refill data for patients initiating fingolimod between October 1, 2010, and February 12, 2011, was conducted. The index date was the date of the first prescription fill of fingolimod during the identification period, and patients were followed for 180 days post-index date. Adherence was measured using 4 different definitions of the medication possession ratio (MPR1-MPR4) based on review of practice and literature. MPR1 was calculated by summing the total days of supply from the first to the last prescription and dividing by the time between the first and last prescription date plus the days supply of the last prescription. This definition was modified by subtracting the last prescription fill from both the denominator and the numerator (MPR2); if the actual last prescription date was before the estimated date then excess days' supply was subtracted from the numerator (MPR3). MPR4 used the total days supply in the numerator divided by the difference between the end of the study follow-up period and the first prescription fill date. Persistence was defined as time in days from the index date until the earlier of a minimum of 60 days gap in therapy or the last claim of the drug during the follow-up period. Descriptive statistics were reported, and bivariate analyses were conducted by age groups (<25, 25-64, 65+, ANOVA test) and gender (t-test).

RESULTS: The values for the MPR using different calculations ranged from 87.9% to 92.0%. Mean time to discontinuation was 176 days. Most patients (80.8%) were persistent to fingolimod at the end of the study period. Adherence and persistence did not differ by gender. There was a trend towards a marginally lower adherence for patients younger than 25 years of age.

CONCLUSIONS: Adherence to fingolimod was high irrespective of the method used to assess MPR. Few patients dropped out during the 6-month follow-up period.

■ Compliance with Warfarin Treatment for Venous Thromboembolism in High-Risk Patients and Its Association with Recurrent Events

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BACKGROUND: Warfarin is a frequently used oral anticoagulant for the prevention of recurrent venous thromboembolism (VTE) events. However, its long-term use is complicated by the need to manage the drug within a narrow therapeutic range and by possible food and drug interactions.

OBJECTIVE: To examine the association between compliance with warfarin treatment for VTE and recurrent events among patients at high risk.

METHODS: Medical and pharmacy claims from enrollees with commercial or Medicare supplemental insurance in the Thomson Reuters MarketScan database were analyzed. Adult patients with medical claims with an associated VTE diagnosis between January 1, 2006, and March 31, 2008, were identified. The index date was the date of the first observed VTE claim or the date of discharge if the index event was a hospital stay. High-risk patients (patients with cancer or noncancer patients who did not have reversible risk factors during the 3-month period prior to the index date) who filled a warfarin prescription within 2 weeks of the index date were included. Compliance was measured by the proportion of days covered (PDC, calculated as the total number of days covered with warfarin supply divided by 365 days) over a 1-year period with a result of <0.8, defined as low compliance. Recurrent VTE events were identified as hospitalizations with VTE as the primary diagnosis after a 1-year assessment period until loss of follow-up. The association between compliance with warfarin and recurrent VTE events was evaluated descriptively via Kaplan-Meier curves and a Cox proportional hazard model, adjusted for patient demographic and clinical characteristics. A similar analysis using the medication possession ratio (MPR, calculated as the number of days covered with warfarin supply before the last observed prescription divided by the number of days between the first and last prescription refill during the specified 1-year assessment period) as a measure of compliance was also performed in a subset of patients who had at least filled 2 warfarin prescriptions.

RESULTS: The study included 8,040 high-risk VTE patients (mean age 61; 59.4% male) of whom 76.9% were not compliant with preventive warfarin treatment based on PDC. Kaplan-Meier curves showed those with low compliance had a higher risk of recurrent VTE events ($P<0.001$). In the regression model, those with low compliance also had a higher risk of recurrent VTE events (hazard ratio [HR] = 3.012; 95% CI = 1.823-4.974). The analysis using MPR included 7,612 patients, of whom 32.3% were not compliant. Both the Kaplan-Meier curves ($P=0.003$) and the regression model showed a higher risk of recurrent VTE events associated with low compliance (HR = 1.596; 95% CI = 1.179-2.160).

CONCLUSIONS: Using the 2 measures of compliance, PDC and MPR, three-quarters and one-third of high-risk VTE patients, respectively, were not compliant with a complete year of recommended therapy, even though long-term therapy should be considered in this population. A lower level of compliance was associated with a higher risk of recurrent VTE events in all of the patients in this study. Strategies to improve compliance with appropriate anticoagulation therapy may potentially reduce recurrent VTE events.

■ Consumer-Directed Health Plans: Impact on Member Adherence to Chronic Condition Medications

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BACKGROUND: Consumer-directed health plans (CDHP) are gaining traction as a means to provide consumer satisfaction and rein in rising health care costs. According to Mercer's 2010 employer survey, 11% of employees are enrolled in some kind of a CDHP (Mercer's National Survey of Employer Sponsored Health Plans [2010]). As this number is set to increase in the near future, understanding member choices regarding utilization in CDHPs will help optimize the plan designs for the best

health outcomes. Preventative therapy option (PTO) excludes drugs for chronic conditions from the member deductible and typically offers lower member cost share under a CDHP. Having a PTO may be a means to achieve better health outcomes and value for the CDHP by increasing member access to necessary chronic medication.

OBJECTIVE: To evaluate the adherence outcomes of CDHPs that offered PTO and no PTO and compare them with traditional plans that do not have deductibles.

METHODS: A retrospective study using data from an integrated database of administrative pharmacy claims was performed for claims spanning the year 2010. Claims of members of over 70 employers that offered both CDHPs and traditional plans covering the pharmacy benefit were analyzed. Metrics including member adherence to chronic medication were compared among the groups and tested for statistical significance.

RESULTS: Over 1.2 million members were covered under CDHPs, and 2.1 million members in the traditional plans were analyzed. Around 320,000 members enrolled in the CDHPs had PTO. Preliminary results show that members enrolled in CDHPs have significantly lower utilization of prescriptions than those enrolled in traditional plans. The overall member cost share for prescriptions is greater among the CDHPs than the traditional plans, but the PTO does considerably defray member cost share. Members enrolled in a CDHP with PTO are more adherent to chronic condition medication, including hypertension, high cholesterol, and diabetes drugs. On an average, CDHPs with PTO have over 7% more adherent population than the non-PTO plans and 3% more than traditional plans.

CONCLUSIONS: By focusing on the common chronic therapies, the CDHPs with PTO are able to keep members adherent to necessary medication that prevent exacerbation of the chronic condition. Studies have shown up to $3,756 in annual health care savings due to member adherence chronic medication (Roebuck MC, et al. Medication adherence leads to lower health care use and costs despite increased drug spending. *Health Aff.* 2011;30(1):91-99). The results of this study demonstrate the financial and clinical value offered by the CDHPs with the PTO.

SPONSORSHIP: This research was conducted by CVS Caremark, Northbrook, IL, without external funding.

■ Cost and Utilization Outcomes of Opioid Dependence Treatments

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BACKGROUND: Approximately 2 million Americans are opioid dependent, with 80% now dependent on prescription opioids. Most of the opioid dependent population remains untreated due to problems with access and reimbursement, poor motivation and adherence, and rejection of current treatment options.

OBJECTIVE: To evaluate the health care costs associated with treatment of opioid dependence with medications versus no medication and between the 4 agents approved by the FDA.

METHODS: In this retrospective claims database analysis, commercially insured adults with opioid dependence were identified from a large U.S. health plan and the PharMetrics Integrated Database. Matching with instrumental variable analysis was applied using baseline demographic, clinical, and health care utilization variables for 13,316 patients; one-half of these patients had used an FDA-approved medication for opioid dependence and half had not. A similar comparison was performed among 10,513 patients treated with once-monthly injectable extended-release naltrexone (XR-NTX; VIVITROL; n=156) prior to its FDA

approval for opioid dependence or with a medication approved at the time: oral naltrexone (NTX-PO; n=845), buprenorphine (SUBOXONE and SUBUTEX; n=7,596), or methadone (n=1,916). Over 6 months, including time on and off medication, analyses calculated persistence, utilization, and paid claims for all medications, specialty and general inpatient admissions, outpatient services, and total costs.

RESULTS: Despite higher costs for medications, total health care costs over 6 months, including inpatient, outpatient, and pharmacy costs, were 29% lower with medication for opioid dependence versus without (P<0.001). Medication was associated with fewer inpatient admissions of all types (P<0.001). Despite higher costs for XR-NTX itself, total health care costs were not significantly different from NTX-PO or buprenorphine and were 49% lower than with methadone (P<0.001). XR-NTX-treated patients had fewer opioid-related and nonopioid-related hospitalizations than patients receiving either of the 3 oral medications (all comparisons P<0.05).

CONCLUSIONS: Limitations of this approach include its retrospective nature, lack of randomization, focus on commercially insured adults, and baseline differences requiring instrumental variable case-mix adjustment. Results are that opioid-dependent patients who received medication for this disorder had lower total costs and hospital utilization than patients who did not. Among the 4 medications, the group receiving XR-NTX had no higher or less total costs than those receiving oral medications but had less hospital utilization.

SPONSORSHIP: This research was conducted by Alkermes, Inc., Waltham, MA.

■ Cost-Effectiveness of Emerging Antiretroviral Regimens in Human Immunodeficiency Virus Disease: An Analysis of Lopinavir/ Ritonavir and Darunavir Plus Ritonavir in Treatment-Naïve Patients

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BACKGROUND: Much has evolved in the 2 decades of economic evaluation of antiretroviral therapy (ART) in terms of management, guidelines, and economic assessment. This study compared 2 protease inhibitors (PI) in first-line ART for human immunodeficiency virus (HIV)-infected patients using state-of-the-art health economic modeling.

OBJECTIVE: To perform a cost-effectiveness analysis of lopinavir/ ritonavir (LPV/r) versus darunavir plus ritonavir (DRV+RTV) for HIV-infected, treatment-naïve patients.

METHODS: A "third generation" economic model (discrete event simulation) was created to realistically represent ART management and HIV outcomes. Prognosis was determined by the impact of initial treatment on baseline CD4 cell count and viral load, adherence, virologic suppression/failure/rebound, acquired resistance mutations, and ensuing treatment changes based on ARTEMIS trial data and the clinical literature. Treatment-naïve individuals similar to those in the ARTEMIS trial were modeled over a lifetime and compared based on first-line therapy: LPV/r versus DRV+RTV. Up to 3 regimen changes were permitted. Clinical measures included acquired immune deficiency syndrome (AIDS) events, adverse events (AEs), time on sequential therapies, expected life years lost due to HIV disease, and cardiovascular events. Cardiovascular risk prediction did not factor the impact of lipid-lowering medications applied to the patient populations. Outcomes were lifetime cost savings and quality adjusted life years (QALYs; discounted at 3% per annum) analyzed from the U.S. health care system perspective. Wholesale acquisition cost (WAC) was referenced for drug pricing.

RESULTS: Choice of LPV/r over DRV+RTV resulted in $13,200-$34,500 per patient savings over a lifetime with longer life expectancy (+0.06 years; +0.05 QALYs), respectively. Similar rates of death, AIDS events, non-AIDS cancer, infection, lipoatrophy, and lipodystrophy were obtained for both groups. Lifetime cost of coronary heart disease was $262 per patient less in the LPV/r arm. LPV/r remained cost saving and more cost-effective across multiple sensitivity and scenario analyses.

CONCLUSIONS: A comprehensive simulation of lifetime ART management demonstrated that initiating HIV-infected, treatment-naïve patients on LPV/r is cost saving and provides more QALYs compared with DRV+RTV. Limitations of the analysis include the uncertainty of long-term outcomes projections driven by short-term clinical trial endpoints and the imprecise estimates of acquired resistance mutations. Sensitivity analyses provide confidence around these uncertainties.

■ **Cost-Effectiveness of Select First-Line Chemotherapy Regimens in the Treatment of Nonsquamous Non-Small Cell Lung Cancer Patients in the Outpatient Setting**

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BACKGROUND: Therapy with cytotoxic doublet and triplet (cytotoxics+antibody) regimens may offer improved clinical outcomes for advanced nonsquamous non-small cell lung cancer (n-sqNSCLC) patients. Data from community practices provides the opportunity to evaluate real-world outcomes of specific regimens.

OBJECTIVE: To evaluate cost-effectiveness of pemetrexed/platinum (Pe/P) chemotherapy relative to other common first-line regimens for advanced n-sqNSCLC.

METHODS: Patients with advanced n-sqNSCLC initiating first-line therapy with Pe/P, carboplatin/paclitaxel+bevacizumab (C/Pa+B), or carboplatin/paclitaxel (C/Pa) from 2006 to 2009 were identified in an electronic medical record (EMR) database of 20 large U.S. community oncology practices. Using a 1:1 ratio, patients receiving C/Pa+B or C/Pa were matched with Pe/P patients on cancer stage, ECOG performance status (PS), gender, age, and index year. Patients were followed for 1 year post-treatment initiation to assess progression, death, and costs. Progression-free survival (PFS)/overall survival (OS) were calculated from treatment initiation to the earliest of the following: progression (for PFS), death, or end of study. The association between treatment and PFS/OS was assessed using Kaplan-Meier and Cox regression analyses. Costs included charges for chemotherapy, supportive care, and physician/nursing services. To evaluate cost-effectiveness, differences in costs/survival were calculated, and bootstrapping was used to calculate 95% CIs for mean differences and the probability of falling within quadrants of the cost-effectiveness plane.

RESULTS: For each comparison, 300 matched pairs were identified. Pe/P patient mean age was 67.6 years; 56.0% were male; and 71.0% had PS=0/1 at therapy initiation. Comparison cohorts had similar characteristics. Mean number of cycles for Pe/P patients was 4.12 (median=4.00), 6.62 cycles (median=5.00) for C/Pa+B patients, and 5.04 cycles (median=5.00) for C/Pa patients. Pe/P patients had a median PFS of 134 days compared with 126 days for C/Pa+B patients (hazard ratio [HR] 0.68, $P<0.001$) and 106 days for C/Pa patients (HR 0.67, $P<0.001$). Patients treated with Pe/P had a median OS of 298 days compared with 271 days for C/Pa+B patients (HR 0.93, $P=0.31$) and 218 days for C/Pa patients (HR 0.88, $P=0.08$). See table for results of the cost-effectiveness analysis.

TABLE	Results of Cost-Effectiveness Analysis	
	Pe/P Versus C/Pa+B	**Pe/P Versus C/Pa**
Overall Survival		
Mean survival (95% CI)	27 days (−23.9 to 87.6)	58 days (−4.6 to 121.1)
Mean cost, $ (95% CI)	−19,946 (−33,874 to −6,074)	19,137 (9,562 to 28,642)
Probability that Pe/P is:		
less costly, more effective, %	85.00	0.00
more costly, more effective, %	0.16	96.30
Progression-Free Survival		
Mean survival (95% CI)	11 days (−33.8 to 70.4)	33 days (−15.4 to 89.4)
Mean cost, $ (95% CI)	−15,160 (−27,547 to −2,817)	21,841 (11,921 to 32,052)
Probability that Pe/P is:		
less costly, more effective, %	69.50	0.00
more costly, more effective, %	0.50	90.10

C/Pa = carboplatin/paclitaxel; C/Pa+B = carboplatin/paclitaxel+bevacizumab; CI = confidence interval; Pe/P = pemetrexed/platinum.

CONCLUSIONS: Patients treated with Pe/P experienced a significant PFS benefit compared with C/Pa+B and C/Pa patients. A trend for longer OS existed in the Pe/P versus C/Pa comparison. Compared with C/Pa+B, Pe/P yielded greater effectiveness with less cost. Depending on a payer's or society's willingness to pay, Pe/P may be considered cost-effective compared with C/Pa given that Pe/P demonstrated greater effectiveness at a higher cost.

■ **Defining and Measuring Primary Medication Nonadherence**

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BACKGROUND: Medication nonadherence contributes an estimated $290 billion of costs to the public health care system in the United States. Many measures of nonadherence are derived from prescription drug claims; however, these measures do not capture the phenomenon of primary medication nonadherence (PMN), which refers to patients not obtaining a first fill of a prescribed medication. The growth of e-prescribing creates the opportunity to identify new prescriptions that were never received by the patient and to better quantify the extent of medication nonadherence.

OBJECTIVE: To develop a consensus-based definition of PMN as well as standardized measures of PMN that could be used by managed care organizations and/or pharmacies.

METHODS: The initiative was led by the Pharmacy Quality Alliance (PQA) with assistance from the National Association of Chain Drug Stores (NACDS) Foundation. It began with an extensive review and synthesis of the literature regarding PMN and related terms such as initial prescription abandonment. A panel of 15 experts was convened to evaluate the literature and build consensus on a definition of PMN. Once consensus was reached on the definitions, the panel considered various methods for measurement of PMN and achieved consensus

on several draft measures of PMN. A public comment period ensued, and the comments were considered by the panel when making its final recommendations.

RESULTS: Twenty-four articles from 1991-2011 met study criteria. Definitions and measures of PMN and related terms varied widely. The expert panel reached consensus on the following definition of PMN: PMN occurs when a new medication is prescribed for a patient, but the patient does not obtain the medication, or appropriate alternative, within an acceptable period of time after it was prescribed. Following the public comment period, the panel also recommended adoption of a draft measure of PMN. The PMN rate includes the following denominator: all e-prescriptions for newly initiated drug therapy during the measurement period. The numerator is the e-prescribing transactions in the denominator for which there was no pharmacy claim that matched the patient and the prescribed drug (or appropriate alternative drug) with a date of service within 30 days of the e-prescribing transaction. PQA has developed detailed technical specifications for the PMN measure, and these technical specifications are being tested by 2 organizations with real-world data.

CONCLUSIONS: It is becoming increasingly evident that the public health problem of PMN is widespread; however, the lack of standardized definitions and measures inhibits our ability to establish the true incidence of this problem or to track changes in PMN rates over time. The PQA effort to develop a consensus-based, standardized definition and measures of PMN is a first step towards consistent measurement of this phenomenon. As e-prescribing becomes the standard mode of prescription transmission, it will be important to have standardized methods for tracking PMN and to study the effectiveness of interventions to reduce nonadherence.

SPONSORSHIP: This research was funded by Pfizer Inc., New York, NY, and GlaxoSmithKline, Philadelphia, PA.

■ Disease-Specific Costs and Resource Utilization Associated with the Initiation of Insulin Therapy Within a Type 2 Diabetes Mellitus Population

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BACKGROUND: Oral antidiabetics such as biguanides, sulfonylureas, thiazolidinediones, and dipeptidyl peptidase-4 inhibitors remain the mainstay treatment for type 2 diabetes mellitus (T2DM), along with lifestyle modification. However, about one-third of T2DM patients may require insulin due to oral treatment failure. Insulin therapy requires close monitoring of blood glucose levels and may increase physician involvement to ensure optimum disease management, thus leading to increased outpatient visits and diabetic supplies. Although these aspects are understood by clinicians and health plans, there is little evidence quantifying the economic impact of insulin use in T2DM patients within a managed care population.

OBJECTIVE: To estimate the costs and resource utilization associated with initiating insulin therapy among patients with T2DM receiving noninsulin antidiabetic (NIAD) therapy.

METHODS: This retrospective, observational study used a large health insurance claims database. Adults with a T2DM diagnosis (ICD-9-CM codes 250.x0 or 250.x2) between July 1, 2003, and March 31, 2008, were identified. Women with evidence of pregnancy/gestational diabetes were excluded. Patient's first receipt of NIAD therapy was deemed the index prescription date, with treatment patterns assessed thereafter to determine cohorts. NIAD users who received combination oral therapy

TABLE — Monthly Disease-Specific Utilization and Costs

	Matched Cohort	
	NIAD Only	NIAD + Insulin
Number of patients	1,050	350
Time period in days for outcomes assessment, mean [SD]	462 [217]	469 [191]
Resource utilization, mean [SD]		
Hospitalizations	0.001 [0.015]	0.002 [0.033]
ER visits	0.006 [0.079]	0.005 [0.020]
MD visits[a]	0.259 [0.291]	0.324 [0.253]
Outpatient visits[a]	0.074 [0.123]	0.105 [0.205]
Costs, mean [SD]		
Total overall, $[a]	171 [409]	221 [177]
Medical, $[a]	57 [154]	76 [134]
Pharmacy, $[a]	114 [381]	145 [109]

[a]$P < 0.05.$
ER = emergency room; MD = physician; NIAD = noninsulin antidiabetic; SD = standard deviation.

but never received insulin therapy were placed in the "NIAD only" cohort. NIAD users who received insulin therapy for greater than 60 days were placed in the "NIAD+insulin" cohort. For each cohort, the time between T2DM diagnosis date and date of switch/add-on therapy was deemed the peri-period. Patients were matched in a 3:1 (NIAD only: NIAD+insulin) ratio based on peri-period costs (±$100), time to treatment switch/add-on (±1 day), proportion of patients with a hospitalization/emergency room (ER) visit during the peri-period, and propensity score (±0.001 units). Disease-specific resource utilization and costs were computed on a monthly basis starting from the end of peri-period through the 24-month period post-diagnosis date. Resource utilization and costs were compared across cohorts using paired t-tests or Wilcoxon signed rank tests.

RESULTS: 1,400 patients were identified (42% female; mean age 56 years). The NIAD+insulin cohort had a $50 per patient per month increase in total costs compared with the NIAD only cohort ($221 per month vs. $171 per month; P<0.001). Drivers of the cost difference were more physician and outpatient visits and higher pharmacy costs (see table). Similarly, the NIAD+insulin cohort on average utilized more health care resources (physician and outpatient visits) compared with the NIAD only cohort.

CONCLUSIONS: Results of this study suggest that initiation of insulin therapy is associated with greater utilization of health care services and higher medical and pharmacy costs.

SPONSORSHIP: This research was funded by Bristol-Myers Squibb, Plainsboro, NJ.

■ Dosing Patterns of Infliximab in Rheumatoid Arthritis Patients Enrolled in a Mid-Atlantic Commercial Health Plan

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BACKGROUND: Infliximab is FDA approved for administration at weeks 0, 2, 6 then every 8 weeks starting at 3 mg per kg with flexible dosing to 10 mg per kg and/or every 4 weeks based on clinical response in patients

with rheumatoid arthritis (RA). Dosing research often focuses only on administrative claims data without confirmation from patient charts.

OBJECTIVE: To evaluate real-world dosing trends of infliximab in RA patients enrolled in a Mid-Atlantic commercial health plan.

METHODS: Patients with at least 2 diagnoses of RA (ICD-9-CM codes 714.xx), aged 18 years or older, and treated with infliximab were identified through a Mid-Atlantic commercial health plan during January 2006 through August 2011. Patients were excluded if there was evidence of terminal illness, thought disorder, organic brain disorder, or pregnancy during the study period as is consistent with other studies of this type. A total of 60 rheumatology offices with a high volume of these patients were contacted and asked to participate in a medical chart review study with a goal of completing 100 chart extractions; 6 (10%) offices agreed to participate. Inclusion criteria were confirmed based on information in the charts prior to extraction. Data extracted from the charts included patient demographics, medical history, rheumatologist visit data, and details of infliximab dosing.

RESULTS: Data were extracted from 103 medical charts. Mean (SD) age was 56 (11) years, and 75% were female. Mean (SD) patient weight was 89 (1.5) kg across the study period, which is greater than reported in other studies of RA patients. Across all patients and infusions, the most commonly prescribed dose (mode) was 5 mg per kg. The mean (SD) dose was 5.2 (0.3) mg per kg with a range of 0.7 mg per kg. The mean (SD) quantity of infliximab administered was 450 (21) mg with a range of 41 mg. Across all patients and maintenance infusions, the mean (SD) maintenance interval was 51 (14) days with a range of 34 days. Patient-level descriptive statistics indicated no evidence of systematic dose increases in this sample across infusions.

CONCLUSIONS: These data demonstrate that dosing and administration schedule of infliximab are consistent with FDA-approved prescribing information and remain relatively stable across the observation period with no systematic dose increases across users during the study period.

SPONSORSHIP: This research was conducted by Janssen Scientific Affairs, LLC, Horsham, PA.

■ Drug Characteristics Associated with Medication Adherence Across 8 Disease States

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BACKGROUND: Adherence to prescribed medications is a widespread problem, and determinants of medication nonadherence have been previously described as health system, social/economic, therapy-related, condition-related, and patient-related factors. Medication nonadherence clearly represents a multifaceted challenge among patients and health care providers. The impact of drug characteristics on medication adherence has not been studied across disease states.

OBJECTIVE: To describe medication adherence by drug characteristics across multiple disease states to identify drug-specific factors that may serve as targets for future intervention to improve medication adherence.

METHODS: We conducted a retrospective analysis of patients with a single diagnosis and oral medication using medical claims and pharmacy utilization data for the following conditions of interest: asthma/chronic obstructive pulmonary disease (COPD), cancer, depression, diabetes, hypercholesterolemia, hypertension, multiple sclerosis (MS), or osteoporosis identified between January 1, 2007, and March 31, 2009. Adherence was calculated using the medication possession ratio

for each patient based on prescription fills occurring within a 12-month window.

RESULTS: Analysis of members with 1 diagnosis and 1 prescribed medication (n = 14,875) found the majority female (61%) and Caucasian (83%). The 3 most commonly occurring conditions were hypertension (n = 5,505), depression (n = 4,349), and hyperlipidemia (n = 2,744). Generic utilization rates varied widely by diagnosis (0-91.6%) as did copayment costs. Binary adherence (>80%) rates varied significantly by diagnosis, drug class (within condition), generic use, and copayment costs. Regression analysis showed significant adherence variations within condition for brand and generic use and copayment costs.

CONCLUSIONS: We ascertained adherence varies by disease state, drug class within disease states, and drug characteristics. Next steps include an interventional study that will use this data to target specific populations by drug-related characteristics.

SPONSORSHIP: This research was funded by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

■ Economic Burden of Treatment Failure in Medicaid Patients with Irritable Bowel Syndrome with Constipation

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BACKGROUND: Irritable bowel syndrome with constipation (IBS-C) is a gastrointestinal disorder characterized by abdominal pain or discomfort in addition to constipation symptoms. Treatment of IBS-C usually involves lifestyle modifications and pharmacologic therapy with over-the-counter (OTC) laxatives, bulking agents, stool softeners, and a limited choice of prescription (Rx) drugs. These treatments are associated with a low satisfaction reported by patients, presumably because of low efficacy and poor tolerability profiles, often causing patients to switch therapies, discontinue treatments, or add concomitant therapies.

OBJECTIVE: To estimate the economic burden of treatment failure with constipation treatments (OTC or Rx) in patients with IBS-C.

METHODS: Data from the Missouri Medicaid program covering medical services and Rx and OTC medications (1997-2010) were used to compare healthcare resource utilization (HRU) and costs of IBS-C patients with and without treatment failure. Adult patients (≥18 years) living in the community, who had ≥1 diagnosis for IBS (ICD-9 code 564.1x), ≥2 diagnoses for constipation (ICD-9 code 564.0x), ≥1 constipation-treatment claim within 1 year of an IBS diagnosis, and no diarrhea-diagnosis claim (ICD-9 CM code 564.5x) or anti-diarrheal claim during the 6 month period prior to treatment index date were selected for this study. Treatment failure, HRU, and costs were observed during the 1-year period following the treatment index date, i.e., the first constipation-treatment claim within 1 year of an IBS diagnosis. Patients were classified as having a treatment failure if any of these occurred while receiving constipation treatment: (1) switch or addition of new constipation therapy, (2) IBS- or constipation-related inpatient (IP) or emergency room (ER) admission, (3) megacolon diagnosis, (4) a constipation-related medical procedure, or (5) use of colchicine, misoprostol or rifaximin. HRU was measured using incidence rate ratios (IRR). Incremental HRU and healthcare costs (USD 2010; measured from a public payer perspective) were compared between study cohorts using multivariate generalized linear regression models (GLM) with a log link and a negative binomial distribution for HRU and a gamma distribution for healthcare costs. Multivariate analyses controlled for baseline patient characteristics including demographics, comorbidities, and HRU.

RESULTS: A total of 2,830 patients with IBS-C were identified; 46.3% of them experienced a treatment failure during the study period. The average age in both cohorts was 51 years and most patients were female (85.7% vs. 87.5% in patients with vs. without treatment failure, respectively). After adjusting for baseline differences, patients with treatment failure exhibited more HRU, especially in the number of IP days (IRR = 1.75; $P<0.001$). Treatment failure was associated with $4,268 in incremental total annual healthcare costs ($P<0.001$) compared to patients without treatment failure. The cost difference was mainly driven by IP ($2,183 vs. $999; $P<0.001$) and pharmacy ($7,821 vs. $6,425; $P<0.001$) costs.

CONCLUSIONS: Treatment failure with constipation treatments presents a significant economic burden for payers and patients suffering from IBS-C.

KEYWORDS: IBS, Constipation, Economic burden, Resource utilization, Medicaid.

■ Economic Implications of New Onset Depression in Newly Diagnosed Multiple Sclerosis Patients: Implications for Managed Care Pharmacy Practice

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BACKGROUND: Cheng et al. (2010) defined a series of quality indicators to guide medical decision making specific to patients with multiple sclerosis (MS). Assessment and treatment of depression for patients with MS was deemed to be an important quality indicator in this patient population. More specifically, these investigators emphasized the importance of early assessment and treatment of depression in MS patients. To date, little evidence exists related to the timing of incident depression in newly diagnosed MS patients or the economic implications of these co-occurring conditions to payers. The study below addresses this gap in the literature.

OBJECTIVE: To examine variations in the incidence of depression and all health care resource utilization for newly diagnosed MS patients.

METHODS: Patients who had been continuously enrolled with a large national insurance company for 30 months without a diagnosis of depression or claim for an antidepressant 6 months prior to the index MS diagnosis were eligible for study inclusion. Index MS diagnosis was assumed to occur with the presence of 2 MS diagnosis codes on the claims for an individual patient. Univariate and multivariate techniques were used to evaluate differences, if any, in the clinical and economic characteristics of newly diagnosed patients with and without incident depression. Time to incident depression was also assessed after patients had been initiated on disease-modifying therapies.

RESULTS: Approximately 30% to 40% of all newly diagnosed MS patients will be diagnosed with incident depression within 4 to 5 months of their initial MS diagnosis. Patients treated with disease-modifying therapies had a more rapid onset to incident depression compared with untreated patients. Across all categories of resource utilization, newly diagnosed MS patients with incident depression incurred 25% greater annual expenditures compared with the same cohort without incident depression ($P<0.001$). The greatest incremental costs were observed in more physician visits (34%; $P<0.001$), home visits (46%; $P=0.005$), other outpatient services (41%; $P<0.001$), and prescription drugs (96%; $P<0.001$).

CONCLUSIONS: Incident depression in newly diagnosed MS patients occurs within months of the initial diagnosis and imposes a significant economic burden on payers. Managed care pharmacy strategies such as prior authorizations and step therapy provide an excellent venue for managed care pharmacists to stimulate provider action related to the assessment and treatment of incident depression in newly diagnosed MS patients. Through implementation of these strategies, managed care pharmacists are in a unique position to improve care for patients with MS as physicians will be prompted to (a) initiate candid discussions with patients about depression once diagnosed with MS; (b) encourage prudent prescribing of disease-modifying agents not known to increase a patient's risk of depression and/or suicidal ideation; and (3) encourage early initiation of antidepressant therapy when depression is suspected to have occurred.

■ Effect of Cost Sharing on Patients' Likelihood of Receiving Disease-Modifying Therapies for Multiple Sclerosis

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BACKGROUND: Benefit designs that increase patient financial burden may negatively impact patients' decisions to receiving disease-modifying therapies (DMTs) to manage multiple sclerosis (MS).

OBJECTIVE: To evaluate the probability of receiving DMTs among MS patients facing various levels of cost sharing for DMTs.

METHODS: Thomson Reuters MarketScan Commercial and Medicare databases were used to identify adult patients with MS (ICD-9-CM diagnosis code 340) from January 1, 2004, through December 31, 2009. Patients were classified as treated or untreated based on presence of any nonintravenous DMTs during 2004-2009 (before or after the first observed MS diagnosis). The first DMT prescription was used to set the index date for the treated cohort. For the untreated, an index date was assigned randomly based on the distribution of time between first observed MS diagnosis and DMT for the treated cohort. Patients were required to have 12 months continuous enrollment before and after the index date, Cost sharing for DMTs was assessed at the plan level in which the patients were enrolled, representing the financial burden patients would have faced when deciding on receiving DMTs. Median cost sharing ($29.08) for DMTs was used as the cutoff to assign patients with an eligible non-zero plan-level cost sharing into low and high cost-sharing cohorts. Logistic regression was employed to assess the probability of receiving DMTs in the high cost-sharing cohort compared with the low cost-sharing cohort. Sensitivity analysis was conducted to examine same outcome for patients with cost sharing of ≤$100, $101-$200, and >$200.

RESULTS: A total of 14,497 treated (low cost sharing [n = 6,954, 48.0%]; high cost sharing [n = 7,543, 52.0%]) and 10,200 untreated patients (low cost sharing [n = 4,957, 48.6%]; high cost sharing [n = 5,243, 51.4%]) were identified. The majority were female (76%), and mean age was 48.9 years. The unadjusted probability of receiving DMTs was similar between the low and high cost-sharing cohort (odds ratio [OR] = 1.03, 95% CI = 0.98-1.08, $P=0.330$). After multivariate adjustment, the odds of receiving DMTs for the high cost-sharing cohort were 21% lower than for the low cost-sharing cohort (OR = 0.79, 95% CI = 0.74-0.84, $P<0.001$). The large adjustment effect was due to age, region, and health plan type, resulting in the lower odds of receiving DMTs for the high cost-sharing cohort. In the sensitivity analysis, compared with patients with cost sharing ≤$100, the odds of receiving DMTs was 37% (OR = 0.63,

95% CI=0.54-0.74, $P<0.001$) and 14% (OR=0.86, 95% CI=0.76-0.97, $P=0.013$) lower for patients with cost sharing >$200 and $101-$200, respectively.

CONCLUSIONS: MS patients are sensitive to the financial costs associated with DMTs and may forgo treatment when facing high out-of-pocket costs. Manufacturer copay assistance programs designed to reduce patient financial burden were not considered in this analysis. Therefore, these results may underestimate the effects of benefit design on the probability of receiving DMTs.

■ Effect of Daily Antiretroviral Pill Burden on Hospitalizations in U.S. Medicaid Enrollees with HIV: An Analysis of Hospital Characteristics and Costs

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BACKGROUND: Previous studies show that antiretroviral therapy (ART) as a once-daily single-tablet regimen (STR) significantly improves patient adherence and virologic outcomes.

OBJECTIVE: To explore whether the adherence effect of STR is associated with fewer hospitalizations and lower costs in patients receiving ART as a STR versus 2+tablets per day (2+TPD).

METHODS: Medicaid claims from multiple states were retrospectively analyzed. Patients diagnosed with human immunodeficiency virus (HIV) from January 1, 2005, through December 31, 2009, receiving complete ART (2 nucleoside reverse transcriptase inhibitors [NRTIs] plus a nonnucleoside reverse transcriptase inhibitor [NNRTI], protease inhibitor, CCR5 antagonist, or integrase inhibitor) for at least 60 days as an STR or 2+TPD were selected. Hospitalizations and ART adherence based on refill timing were observed from regimen initiation until discontinuation or database end. Primary inpatient diagnosis and hospital, pharmacy, and total costs per patient per month (PPPM) were assessed. A multiple-event Cox model was estimated to assess hospitalization risk, including covariates for daily tablet burden (STR vs. 2+TPD), demographics, comorbidities, and prior ART experience. Subgroup analyses were conducted for treatment-naïve patients.

RESULTS: 7,783 patients were included (1,838 STR and 5,945 2+TPD). STR patients were significantly more likely to reach a 95% adherence threshold versus 2+TPD patients. Among patients achieving <95% adherence, 2+TPD patients were followed for mean [SD] 426.9 [345.3] days, received an incomplete regimen for 28.9 [52.2] days, and received no ART medications for 57.5 [61.5] days. The most common primary inpatient diagnoses were for infectious and parasitic diseases, followed by respiratory system diseases. Mean [SD] hospital, pharmacy, and total costs PPPM were $840 [$4,521], $1,590 [$1,097], and $2,961 [$4,996], respectively among STR patients, and $1,171 [$5,158], $1,762 [$1,276], and $3,547 [$5,745], respectively among 2+TPD patients. The STR effect on costs was unchanged for treatment-naïve versus experienced patients. STR patients had a 25% lower hospitalization risk versus 2+TPD (hazard ratio=0.753; $P<0.001$).

CONCLUSIONS: While STR patients were expected to have lower pharmacy costs, STR patients also had fewer hospitalizations and lower hospital costs versus patients receiving 2+TPD. Nonadherence among patients receiving 2+TPD was composed of both partial and complete nonadherence, while partial adherence is not possible by design in STRs.

■ Effect of Medicare Part D Coverage on Adherence with Disease-Modifying Drug Therapy for Multiple Sclerosis

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BACKGROUND: High out-of-pocket (OOP) burden with disease-modifying drugs (DMDs) has been shown to impact adherence among commercially insured patients with multiple sclerosis (MS). The varying levels of low-income subsidy (LIS) and the 3 different benefit coverage phases in the Medicare Part D program provide an opportunity to further examine the effect of coverage on adherence with DMDs among MS patients.

OBJECTIVE: To assess the impact of the Medicare Part D coverage levels on medication utilization behaviors among beneficiaries taking DMDs for the treatment of MS.

METHODS: A retrospective cohort study was conducted using a 5% national sample of Medicare beneficiaries for 2008. Inclusion criteria were ambulatory patients diagnosed with MS, stand-alone Part D coverage, and taking at least 1 DMD. Adherence was measured using proportion of days covered (PDC). Patients were classified as discontinuing therapy if their last day of possession was more than 60 days before the end of the year. OOP burden was classified into 3 groups based on level of LIS provided: full or 15% copayment, reduced copayment (varying levels of premium subsidy with low or high fixed copayments), and no copayment (fully subsidized).

RESULTS: Medicare beneficiaries with MS and covered by stand-alone Part D plans were more than 3 times as likely to be eligible for coverage due to disability than were non-MS beneficiaries (68% vs. 21%, $P<0.001$) and were significantly less likely to be paying full or 15% copayment levels than were non-MS beneficiaries (33% vs. 56%, $P<0.001$). A total of 4,180 beneficiaries were identified as having MS and coverage through a stand-alone Part D provider. The percentage of MS beneficiaries treated with DMDs was significantly related to age: 62% for <45 years of age, 42% for age 45-64, 25% for age 65-74, and 8% for age 75-84 ($P<0.001$). Copayment level was significantly related to likelihood of beneficiary reaching the coverage gap and catastrophic benefit phases: 63% of full/15% copayment beneficiaries reached the coverage gap, and 57% reached catastrophic coverage compared with 89% and 84% for the reduced copayment group and 90% and 82% for the no copayment group ($P<0.001$). OOP burden was significantly related to lower rates of adherence ($P<0.001$) during pre-gap phase and higher rates of nonpersistency ($P<0.001$). Among the 277 beneficiaries not reaching the coverage gap, 27% discontinued therapy, and the average PDC for those on therapy was 73%. This compares with only 7% of beneficiaries who reached the catastrophic phase (n=1,242) discontinuing therapy and average PDCs of 85% in pre-gap and 90% in the gap and catastrophic phases for this group. The highest rate of discontinuation of therapy (72%) occurred among beneficiaries who reached the coverage gap but not the catastrophic phase (n=82).

CONCLUSIONS: OOP burden appears to be associated with an adverse impact on both adherence and persistency behaviors, even for patients with reduced copayment LIS.

■ Employees Living with Human Immunodeficiency Virus: Impact of Disease and Antiretroviral Therapies on Health Care Costs and Productivity

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BACKGROUND: The introduction of highly active antiretroviral therapy (HAART) has transformed the course of human immunodeficiency virus (HIV) infection from an acute to a chronic condition thereby improving morbidity/mortality. Patients treated with HAART can maintain normal functional status, including the capability to contribute in the workplace. Published information regarding the impact of HIV and HAART on employee function and health care burden would enable employers, as payers of health care, to better manage the health benefits for HIV treatment.

OBJECTIVE: To quantify the health care costs and absenteeism of employees living with HIV and the comparative impact of 3 study anchor HAARTs: lopinavir/ritonavir (LPV/r), atazanavir (ATV), and efavirenz (EFV).

METHODS: Health care claims from the HCMS database (2001-2010), representing more than 800,000 employees, were extracted for a pre/post-index analysis of health care utilization, costs, and absenteeism. Inclusion criteria: aged older than 18 years, at least 3 months baseline (pre-index), and at least 3 months follow-up (post-index) enrollment in the database. HIV treatment cohorts: employees initiating (index date) study anchors (LPV/r, EFV, or ATV) with no claims for any other study anchor use pre-index; multiple anchors were excluded. Non-HIV cohort: employees without any HIV diagnosis (ICD-9-CM codes 042.xx) and without any HAART claims of any kind. Calculated index date for non-HIV cohort was the mean index date for treatment cohorts. Monthly health care costs, utilization, and absenteeism (sick leave, short-term disability) were estimated using multivariate 2-part regression models controlling for demographics (age, gender, race, exempt full-time employment, annual salary, geographical region), baseline comorbidities and AIDS events, use of nonstudy-anchor ART in baseline, index-year, and follow-up duration. Costs were inflation adjusted to 2010 $US using the Consumer Price Index. Total monthly health care costs included all inpatient/outpatient services, laboratory, and prescriptions. Reported results include comparison of non-HIV cohort to a combined treatment cohort of the 3 study anchor HAARTs as well as comparison between study anchor HAART cohorts.

RESULTS: In follow-up, average monthly total health care costs for the combined treatment cohort of all study anchor HAARTs (n = 394) were $2,149 but only $287 for the non-HIV cohort (n = 195,956), a difference of $1,862 ($P < 0.001$). For individual study anchor HAARTs, LPV/r cohort (n = 102) had approximately twice the rate of AIDS events at baseline than EFV (n = 218) or ATV (n = 74) cohorts. Post-index, total monthly health care costs were similar ($P > 0.05$) between LPV/r ($1,799) and EFV ($1,674) cohorts but significantly greater in the ATV cohort ($2,322), with differences of $524 and $648, respectively (both $P = 0.01$). Post-index, ATV cohort used significantly more non-ART prescriptions ($431) than the LPV/r ($163) and the EFV ($154) cohorts (both $P < 0.001$). Total absenteeism was similar between LPV/r and EFV cohorts ($P > 0.05$).

CONCLUSIONS: Employees living with HIV and treated with study HAART incur considerably greater health care burden than non-HIV afflicted employees. LPV/r treated employees incur health care burden similar to those treated with EFV but less than those treated with ATV. Limitations include the following: claims data may be inaccurately coded contributing to uncertainty; follow-up period analysis may be limited by database enrollment; however, time of follow-up was controlled in multivariate analyses; and the number of employees treated with study-anchor HAARTs were limited in this database.

■ Enrollment Data from Custom Medication Therapy Management (MTM) Eligibility Criteria and Service Delivery Methods for the Provision of MTM Services to an HIV-Infected Population

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BACKGROUND: Medication therapy management (MTM) services are desired to improve clinical outcomes in many specialty areas beyond the core chronic conditions identified by the Centers for Medicare & Medicaid Services (CMS) for Part D programs. A centralized MTM solution for the Oregon AIDS Drug Assistance Program (ADAP), known as CAREAssist for human immunodeficiency virus (HIV)-infected patients, was implemented utilizing customized entry criteria and service methodologies to meet its unique needs.

OBJECTIVE: To report on a current effort to develop a service model and eligibility criteria for MTM services that meets the unique clinical needs of an HIV-infected population.

METHODS: Oregon CAREAssist (ADAP service provider) has contracted with Ramsell Pharmacy Solutions (RPS) for use of the Ramsell Care Continuum (RCC) MTM solution for the delivery of MTM services to a subset of their HIV-infected clients. Claims data and limited clinical HIV disease measures were available for screening. Standard CMS enrollment criteria were not appropriate for this HIV-infected population; therefore, modified criteria were created. Patients had to meet the following criteria to receive services: adherence (medication possession ratio [MPR]) <80%; history of claims for antiretroviral (ARV) medications in the previous 45 days. Patients were prioritized when the following were present: diagnosis of mental health issue (other than depression) or substance abuse; claims for tipranavir, valganciclovir, or enfuvirtide; or a medical provider referral. MTM services were based on the 2010 CMS criteria of a baseline comprehensive medication review (CMR) and a targeted medication review (TMR) every 12 weeks. Additional interactions were allowed in specific instances. Patients were enrolled in an opt-out manner. MTM services were provided by in-house pharmacists with HIV experience. Specific modifications to the RCC web-based system were made to accommodate the specific clinical data capture needs for this patient population. Enrollment outreach was customized to include an initial enrollment letter followed by pharmacist telephone outreach at 14 and 30 days post-letter mailing. Total enrollment was capped at 250 patients. Phased enrollment is underway with 50 patients being enrolled in October 2011, 100 patients in November 2011, and 100 in December 2011.

RESULTS: Initial enrollment runs identified 437 of 2,876 total enrollees (15.2%) as eligible for MTM services with 22 (0.8%) patients meeting prioritized criteria. Enrolled patients had an average adherence by MPR of 63.46%; prioritized patients had an MPR of 63%. Demographics of current enrollees are 388 male (88.8%), 47 female (10.8%), and 3 transgender (0.7%); Caucasian 324 (74.1%)(%), African American 45 (10.3%), Asian 4 (0.9%), Native American/Hawaiian 11 (2.5%), and unknown or other 24 (5.5%). 223 (51%) of enrollees reside in the city of Portland. The enrollment demographics approximated the overall demographic

make-up of the overall program. The current rate of nonresponse to letters and calls is 23%. The current opt out rate is 34.8% and declining over time. Net participation rate is 65.2% of all patients identified and contacted to date. Interventions (CMR primarily) have been performed on 28.8% of all enrolled patients and 65.2% of all contacted patients to date. Enrollment outreach is ongoing.

CONCLUSIONS: Custom enrollment criteria and methodologies allow the RCC centralized MTM solution to tailor service to the HIV patients enrolled in Oregon CAREAssist and to deliver quality MTM services to meet their unique clinical needs. Opt out rates are better than reported Part D norms and are currently declining.

SPONSORSHIP: This research was conducted by Ramsell Pharmacy Solutions, Oakland, CA.

■ Evaluation of a Pharmacist-Led Medication Reconciliation Program in Post-Discharge Patients: A Phase II Study

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BACKGROUND: To recognize and avoid potential medication errors during the transition of care, a medication reconciliation program which compared the medications being used at home and prescribed during the time of hospital discharge was implemented in a managed care organization. In a phase I pilot study, all patients who were discharged from a hospital had their medications reviewed by a clinical pharmacist. The phase I pilot study showed that 30% of all medications required a clinical pharmacist intervention. Using the key learnings obtained from the phase I pilot, the phase II component of the program narrowed the scope of the medication reconciliation program to targeted medical conditions and/or drug therapy with the intent to measure its impact on hospital admission and readmission rates.

OBJECTIVE: To evaluate the impact of a pharmacist-led medication reconciliation program on hospital admission rates in patients discharged from inpatient settings.

METHODS: This was a prospective observational study conducted at 2 community hospitals in California. Patients were referred to the pharmacy department for intervention if they were discharged from either hospital between May 2010 and June 2011, with at least 1 of the following conditions: diagnosed with pneumonia or renal failure upon hospital discharge; had been diagnosed with chronic COPD, CHF, dementia, atrial fibrillation; or had received warfarin within the past 3 years. A doctor of pharmacy candidate contacted patients by telephone and reviewed the patient's preadmission medications, discharge summary of medications, and current self-reported medications. Discrepancies were reviewed with the supervising clinical pharmacist to develop an action plan. A comparison cohort (control group) was selected retrospectively based upon the same criteria. The index date was defined as the date when patients received medication reconciliation for the intervention group, while it was defined as hospital discharge date for the control group. The time frame to measure hospital admission was 7 and 30 days. Hospital preadmission rates (pre) and readmission rates (post) before and after the index date were calculated and compared between groups.

RESULTS: A total of 276 patients were referred to the intervention program, and a total of 4,051 patients were selected for the control group. In the intervention group, the 7-day hospital admission rate was 7.7% pre- versus 4.0% post-index date compared with the control group which was 5.0% pre- versus 5.4% post-index date. The mean admission rate dropped significantly from pre to post in the intervention group (–3.7%;

$P=0.051$), while increasing in the control group (0.5%; $P=0.228$). The net change was –4.2% ($P=0.022$). The 30-day hospital admission rate was 19.0% pre- versus 14.7% post-index date in the intervention group compared with 16.7% pre versus 17.6% post in the control group. The mean admission rate dropped from pre to post in the intervention group (–4.3%; $P=0.206$), while increasing in the control group (0.9%; $P=0.207$). The net change was –5.2% ($P=0.121$).

CONCLUSIONS: The pharmacist-led medication reconciliation program showed a benefit in reducing both 7-day and 30-day hospital readmissions in this managed care organization. Further study is warranted.

SPONSORSHIP: This research was funded by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

■ Evaluation of Right Heart Catheterization Results for Members Prescribed Pulmonary Arterial Hypertension Medication

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BACKGROUND: Medications for pulmonary arterial hypertension (PAH) are FDA approved for use only in World Health Organization (WHO) group 1 PAH. Current American College of Cardiology/ American Heart Association guidelines state that a diagnosis of WHO group 1 PAH requires confirmation via a right heart catheterization (RHC). Three hemodynamic values obtained from a RHC are used to evaluate a PAH diagnosis: mean pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP), and pulmonary vascular resistance (PVR). A diagnosis of WHO Group I PAH is defined as a mPAP greater than 25 mmHg, a PCWP less than or equal to 15 mmHg, and a PVR greater than 3 Wood units. RHC values outside of the guideline definitions indicate that the patient has a different type of pulmonary hypertension (WHO Groups 2-5) where use of a PAH medication is generally not appropriate.

OBJECTIVE: To evaluate members prescribed a PAH medication for (a) documentation that the diagnosis of PAH was confirmed via a RHC and (b) congruence of available RHC results with guideline recommendations for diagnosis of WHO group 1 PAH.

METHODS: Members with at least 1 paid pharmacy or medical claim for a PAH medication between July 1, 2010, and July 31, 2011, were identified. For each member, prior authorization case documentation and medical claims were reviewed to identify whether a RHC was performed and what the specific hemodynamic values were and where available. For members with no RHC results available, a letter was sent to the prescriber of the PAH medication to request the results.

RESULTS: A total of 104 unique members were identified as being prescribed a PAH medication. Documentation of a RHC was available for 82 (79%) members; all 3 hemodynamic values were available in 73 (70%) members. Of the members who had all 3 hemodynamic values available (n=73), 41 members met guideline criteria for a diagnosis of WHO group 1 PAH, and 32 members had a least 1 RHC value that was not consistent with the guideline criteria. PAH medication was prescribed by an internal medicine/family practice physician for 19 of the members; 16 of the members where an internal medicine/family practice physician was prescribing had either no RHC results on file, incomplete RHC result available, or results not consistent with the definition of PAH.

CONCLUSIONS: This study suggests that a subset of members who are receiving a PAH medication may not have been evaluated via a documented RHC. Furthermore, a subset of members who have had a RHC performed have results that are not consistent with a diagnosis of WHO group 1 PAH and may indicate off-label use for other types of pulmonary

hypertension. There is an opportunity to reduce potential inappropriate use of PAH medications by requiring documentation of RHC procedure and hemodynamic values prior to approval of these products. There may also be an opportunity for referral of members to cardiology or pulmonology specialists to improve the quality of patient care.

SPONSORSHIP: This research was conducted by UPMC Health Plan, Pittsburgh, PA, without external funding.

■ Factors Associated with Unclaimed Prescriptions in the Electronic Prescription Era

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BACKGROUND: Implementation of an electronic medical record system with electronic prescription submission provides significant process efficiency but has been associated with an increase in the rate of unclaimed prescriptions in the pharmacy. Prior to implementation of electronic prescription submission in an integrated health care delivery system, new prescriptions were brought to the pharmacy by patients as written paper prescriptions or submitted via telephone call from the physician offices. After the implementation of the electronic process, prescribers enter prescription orders in the patient's electronic medical record, and the orders were transmitted directly to the pharmacy to be filled. The pharmacy could then get the prescriptions ready for patients to pick up on arrival. Bypassing the step which waited for a patient to present with a request to have the prescription filled resulted in a marked increase in unclaimed prescriptions in the pharmacy, with significant resources used to ready and then return the unclaimed prescriptions to stock.

OBJECTIVE: To estimate the rate and factors associated with unclaimed prescriptions in an integrated health care delivery system.

METHODS: All prescriptions filled in 2009 by the 95 outpatient pharmacies operated by the integrated health care delivery system were included in the study. Unclaimed prescriptions were defined as prescriptions that were returned to stock and never picked up by the patients. We excluded mail order prescriptions and over-the-counter products. Possible factors related to unclaimed prescriptions included patient factors (e.g., age, gender, copayment), medication factors (e.g., brand, new start, acute vs. chronic, medication class, day supply), and pharmacy factors (e.g., location, daily volume, and wait time). Descriptive statistics were used to summarize the data. Bivariate and multivariate analyses were used to assess how prescription level covariables were associated with the rate of unclaimed prescriptions.

TABLE Factors Related to Unclaimed Prescriptions	
	Odds Ratio (95% CI) for Unclaimed Prescriptions
Female	1.115 (1.112-1.119)
Age 0-12 (reference age 46-64)	1.591 (1.579-1.602)
Age 13-25 (reference age 46-64)	1.715 (1.705-1.725)
Age 26-45 (reference age 46-64)	1.513 (1.507-1.520)
Age ≥65 (reference age 46-64)	0.792 (0.788-0.795)
Copayment $1-$5 (reference copayment $0)	1.236 (1.229-1.244)
Copayment $6-$10 (reference copayment $0)	1.459 (1.450-1.468)
Copayment $11-$24 (reference copayment $0)	1.875 (1.862-1.887)
Copayment ≥$25 (reference copayment $0)	2.542 (2.525-2.559)
Pharmacy in rural area	0.841 (0.834-0.848)
Nonformulary drugs	1.436 (1.405-1.466)
Acute (e.g., antibiotics, pain)	0.816 (0.810-0.822)
CI = confidence interval.	

RESULTS: From January through December 2009, there were a total 20,720,572 prescriptions included in the study. Of these, 1,816,268 (8.8%) were unclaimed. We found that younger patients and females were more likely to have unclaimed prescriptions (see table). In addition, prescriptions with higher copayments were more likely to be unclaimed. Pharmacies located in rural areas had a lower rate of unclaimed prescriptions.

CONCLUSIONS: The rate of unclaimed prescriptions was 8.8%. A younger patient age, nonformulary status, and higher copayment were predictors of unclaimed prescriptions.

SPONSORSHIP: This research was conducted by Kaiser Permanente, Oakland, CA, without external funding.

■ Filgrastim (Neupogen) and Pegfilgrastim (Neulasta): Cost Analysis and Utilization Management Opportunity Assessment

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BACKGROUND: Filgrastim (Neupogen) and pegfilgrastim (Neulasta) are both used to prevent chemotherapy-induced neutropenia (CIN) and febrile neutropenia (FN). Pegfilgrastim is a longer-acting pegylated formulation allowing a single injection to last 14 days, and filgrastim use requires daily injections. In clinical trials, equivalent CIN and FN treatment efficacy and safety was seen with single dose pegfilgrastim compared with a filgrastim median duration therapy of 10 or 11 days. Filgrastim therapy of less than 7 days has been associated with increased hospitalization risk.

OBJECTIVE: To compare filgrastim and pegfilgrastim utilization and daily drug costs using integrated medical and pharmacy claims data for a utilization management opportunity assessment.

METHODS: Filgrastim and pegfilgrastim pharmacy and medically processed claims data were queried among 1.2 million commercially insured members from January 1, 2010, to December 31, 2010. Members with both a filgrastim and pegfilgrastim claim were excluded. Days supply was defined for each pegfilgrastim 6 mg claim as 14 days and for filgrastim 300 mcg or 480 mcg claim as 1-day supply. Each member's cumulative days supply and total paid for filgrastim or pegfilgrastim was calculated. Total paid was the sum of plan and member paid. Cost per day was calculated by summing all filgrastim or pegfilgrastim expenditures and dividing by the respective cumulative total days supply. Average cost per day was statistically compared using the Student's T-test. Medical claims for the filgrastim and pegfilgrastim utilizers were queried to identify members with a malignant cancer diagnosis (ICD-9-CM codes 140xx-209xx).

RESULTS: During 2010, 963 (80 per 100,000) members were found to have utilized filgrastim or pegfilgrastim with a cumulative 4,671 pharmacy and medical benefit claims at a total days supply of 40,297 days with a total paid of $9,567,637 ($0.66 per member per month [PMPM]). Pegfilgrastim accounted for $7,855,809 (82.1%) of total paid, and 92.2% of pegfilgrastim expenditures were processed via the medical benefit. Filgrastim accounted for $1,711,827 of total paid, and 41.2% of filgrastim expenditures were processed via the medical benefit. 92 members (9.6%) utilized both filgrastim and pegfilgrastim at a total days supply of 5,200 days with a total paid of $937,915 and were excluded from this analysis. 612 (63.6%) members utilized pegfilgrastim only with a total paid of $6,917,895; cumulative total days supply was 31,212 averaging $222 total paid per day. Pegfilgrastim average total paid per member was $11,304 with a median 42 days supply per member. Filgrastim only was utilized by 259 (26.9%) members with a total paid of $1,440,810;

cumulative total days supply was 3,885 averaging $371 total paid per day. Filgrastim average total paid per member was $5,563 with a median 8 days supply per member. Pegfilgrastim cost per day was $149 less than filgrastim, $P < 0.001$. Among filgrastim utilizers, 116 (44.8%) had less than 7 cumulative days supply. A malignant cancer diagnosis was identified in 89.4% of pegfilgrastim utilizers with a medical claim and 81.8% of filgrastim utilizers with a medical claim.

CONCLUSIONS: Analysis of medical claims for both filgrastim and pegfilgrastim utilizers found more than 4 of 5 members with a medical claim had a malignant cancer diagnosis. While members utilizing pegfilgrastim had a median total days therapy 6 times longer at twice the average total cost per member than filgrastim utilizers, pegfilgrastim cost per day was significantly less. Almost half of filgrastim utilizers received a potentially inadequate days supply of therapy. Utilization management encouraging filgrastim prior to pegfilgrastim may place individuals at risk for inadequate therapy and induce higher costs per therapy day.

Health Resource Utilization and Costs Associated with the Infusion and Monitoring of Zoledronic Acid in Female Health Plan Members with Osteoporosis

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BACKGROUND: Oral bisphosphonates (BPs) are the primary osteoporosis (OP) treatment despite research demonstrating poor adherence. Zoledronic acid (ZA), administered annually via intravenous infusion, provides an option to more frequent oral BP dosing. For payers, additional costs associated with ZA include direct infusion-related costs and may also include pre-administration monitoring costs (e.g., to confirm appropriate creatinine clearance) and post-administration costs for management of ZA-related acute phase reactions (APRs).

OBJECTIVE: To quantify the costs associated with administering and monitoring ZA in women with OP.

METHODS: This retrospective analysis used administrative claims data (medical and pharmacy claims data, enrollment information) from a large national U.S. health plan. Subjects were female commercial (CO) and Medicare Advantage (MA) health plan members aged 45 and older with a ZA infusion for OP between January 1, 2007, and October 31, 2008. The first claim for ZA defined the index date; continuous enrollment was required for 1 year pre- and 15 months post-index date. Members with claims for ZA for oncology use or with other conditions treated with BPs were excluded. Outcomes were index infusion costs (including ZA costs, professional costs, supplies); OP-related utilization and costs (e.g., office visit, lab, bone mineral density) in the 60 days prior to index ZA infusion; ZA APR-related costs (e.g., visits for side effects such as pain, nausea, fever, atrial fibrillation) in the 14 days from the index ZA infusion; and number with second ZA infusions. Data were analyzed descriptively.

RESULTS: The study identified 603 CO and 286 MA members receiving ZA. The mean age in the CO cohort was 64.3; 51% had pre-index OP medication use (including oral BPs, teriparatide, hormone replacement therapy); and 87% had a pre-index claim with an OP diagnosis. In the MA cohort, mean age was 74.3; 41% had pre-index OP medications; and 90% had pre-index OP diagnosis. Forty-six percent of CO members and 70% of MA members received their index ZA infusions from rheumatologists or in facilities. Mean index infusion costs were $967 for CO

and $1,122 for MA members. In the 60 days prior to index ZA infusions, members had mean OP-associated costs of $92 (CO) and $83 (MA) with creatinine monitoring occurring in 15% of each cohort. In the 14 days following infusion, 30% of CO members had evidence of ZA-related APRs with APR-related mean costs of $146; 42% of MA members had APRs with mean associated cost of $198. Sixty-two percent of CO members and 55% of MA members had second infusions; second infusions occurred within 13 (±2) months of the index infusions, on average.

CONCLUSIONS: The aggregate costs associated with ZA infusions among women with OP may exceed the costs incurred on the day of infusion. Pre-infusion monitoring, utilization with nonprimary care providers, laboratory tests, and potential APRs contribute to the overall cost of ZA therapy. A limitation of this study is the pre-index OP-related costs might not have been exclusively relevant to the index ZA infusions. These findings suggest ZA infusion costs should be further examined by payers.

High-Cost Type 2 Diabetes Mellitus Patients: Findings from a U.S. Managed Care Population

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BACKGROUND: Type 2 diabetes mellitus (T2DM) affects 23.6 million people in the United States.

OBJECTIVE: To compare high-cost (HC) T2DM patients with T2DM patients who were not high cost (NHC) and to assess predictors of being a HC patient.

METHODS: Patients with at least 2 T2DM diagnoses (ICD-9-CM diagnosis codes 250.x0 or 250.x2) between January 1, 2005, and December 31, 2010, were selected from the LifeLink managed care claims database. Patients were followed for 1 year after their first observed T2DM diagnosis; patients not continuously enrolled were excluded. Study measures included annual health care expenditures by component (i.e., inpatient, outpatient, pharmacy) and overall. Patients accruing costs in the top 10% of the overall cost distribution (i.e., patients with costs >$19,921) were defined as "HC," whereas all others were "NHC." A logistic regression model was estimated to assess predictors of being HC, accounting for demographics, underlying comorbidity burden (i.e., the Charlson Comorbidity Index [CCI] score, a weighted measure of 17 comorbidities); diagnoses of renal impairment, obesity, or hypertension; and receipt of insulin, oral antidiabetics only, or no antidiabetics.

RESULTS: A total of 1,720,041 patients met the inclusion criteria, and 172,004 were HC. No differences in demographics and antidiabetic agents received were observed between HC and NHC patients. The mean (SD) CCI score for HC patients was 4.3 (3.0) versus 2.1 (1.7) for NHC patients. Mean (SD, upper 95% CI, lower 95% CI) annual per patient costs were $54,802 ($63,669, $55,103, $54,501) among HC patients and $4,536 ($4,371, $4,557, $4,515) among NHC patients. The largest proportion of the difference in total costs between HC and NHC patients was from inpatient care (47%), and HC patients accrued on average $3,325 more in pharmacy costs versus NHC patients. The strongest predictor of being a HC T2DM patient was having a CCI score ≥2 (odds ratio [OR]=5.178), followed by a diagnosis of obesity (OR=3.191) or renal impairment (OR=2.662) and insulin use (OR=2.142).

CONCLUSIONS: HC T2DM patients accrue $50,000 more in total health care costs annually versus T2DM patients who are NHC. Obesity and

progression to insulin are 2 modifiable factors in HC patients. Further research is needed to explore potential interventions to reduce the likelihood that a patient becomes HC.

■ Hypertension Medication Adherence Association with Hospitalizations and Total Cost of Care

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BACKGROUND: Medication nonadherence has been reported to be associated with worse medical outcomes and increased medical costs. However, minimal data are available quantifying outcome and cost differences between individuals adherent and nonadherent to hypertension medications.

OBJECTIVE: To compare 1-year all-cause hospitalization rates, medical costs, and pharmacy costs among individuals adherent and nonadherent to their hypertension medications.

METHODS: Using retrospective pharmacy and medical claims from a commercially insured population of 3.6 million members with eligibility at any time in 2007 through 2009, members continuously enrolled from 2007 through 2009 with either (a) 2 separate hypertension office visits or (b) a hypertension hospitalization in 2008 were followed for 1 year. Members were required to have hypertension medication supply and/or hypertension with diabetes mellitus (DM), coronary artery disease (CAD), stroke, congestive heart failure (CHF), or chronic kidney disease (CKD). All hypertension drug claims were assessed to identify members as adherent (proportion of days covered [PDC] >80%) or nonadherent (PDC <80%). Due to medical and pharmacy cost skewness, individuals exceeding the 99th percentile were excluded. All medical and pharmacy claim total allowed amounts (plan paid amount plus member cost share) were summed to determine total cost of care. Statistical assessment of the relationship between adherence and all-cause hospitalization was done with chi-square (unadjusted) and logistic regression adjusting for age; sex; Charlson Comorbidity score; existence of baseline DM, CKD, CAD, CHF, or stoke; count of unique drug classes at baseline; high deductible health plan enrollment; and ZIP code income. For costs t-test (unadjusted) and multiple linear regression were performed using the same covariates.

RESULTS: Of the 91,931 members meeting all inclusion criteria, 61,040 (66.4%) were adherent, and 30,891 (33.6%) were nonadherent. The adherent group was associated with a significantly lower all-cause hospitalization rate (odds ratio of 0.80, 95% confidence interval, 0.77 to 0.84), significantly lower medical costs ($317) but higher pharmacy costs ($1,346) and higher total costs of care ($1,029).

CONCLUSIONS: Individuals adherent to hypertension medication had an associated unadjusted 1.0 percentage point lower hospitalization rate which remained significantly lower in multivariate modeling. Although medical costs were lower, higher pharmacy costs contributed to higher total costs of care.

■ Identifying Risk Factors Associated with Nonadherence to Medication in Patients with Ulcerative Colitis

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BACKGROUND: 5-aminosalicylic acid (5-ASA) is a recommended first-line treatment for patients with mild to moderate ulcerative colitis (UC). However, up to 40% to 60% of patients are nonadherent to their treatment regimens. Identifying risk factors associated with nonadherence will help design intervention programs to improve 5-ASA medication adherence.

OBJECTIVE: To investigate risk factors associated with nonadherence to oral 5-ASA medication in patients with UC.

METHODS: IMS LifeLink Health Plan Claims data (January 2007 to June 2009) were analyzed. Adult patients aged 18 years or older were selected if they met the following criteria: (a) initiated at least 1 oral 5-ASA prescription fill (index date) during July 2007 to June 2008; (b) presence of at least 1 diagnosis for UC (ICD-9-CM codes 556.x) 6 months prior to or 12 months post-index date; (c) continuous enrollment in a health plan for at least 6 months prior to and 12 months post-index date; and (d) no prescription fill for 5-ASA, corticosteroids, or immunosuppressive agents 6 months prior to index date. Patients with a diagnosis of Crohn's disease (ICD-9-CM codes 555.x) or irritable bowel syndrome (ICD-9-CM codes 564.1) 6 months prior to and 12 months post-index date were excluded. Medication nonadherence was assessed using medication possession ratio <0.8 for post 12 months index date. Multivariable logistic regression was used to assess risk factors associated with nonadherence with 5-ASA index medication. Independent variables included index drug, demographic, health plan, region at baseline, and variables of used immunosuppressive agents and rectal form of 5-ASA at post-index date.

RESULTS: A total of 2,692 patients were identified. Mean [SD] age was 48.4 [15.0] years; 53.5% were female. Nonadherence to index 5-ASA medication was 83.3%. Patients initiated on multiple daily dosing formulations such as sulfasalazine (17.1%), delayed release mesalamine (17.0%), or balsalazide disodium (8.9%) were less likely to adhere to their medications than those on once-daily formulation of MMX Multi Matrix System mesalamine (22.4%), P<0.001. Patients using the index medication versus balsalazide disodium (MMX mesalamine: odd ratio [OR]=3.11, 95% CI=1.94-4.99, delayed release mesalamine: OR=2.11,

TABLE	Hypertension Medication Adherence Association with Hospitalizations and Total Cost of Care		
1-Year Outcomes Assessment	**Adherent (PDC ≥80%) n = 61,040**	**Nonadherent (PDC <80%) n = 30,891**	**Multivariate Model P Value[a]**
All-cause hospitalization rate, n (%)	6,140 (10.1)	3,422 (11.1)	<0.001
All medical costs,[b] mean [SD] $	7,124 [12,569]	7,441 [12,944]	<0.001
All pharmacy costs, mean [SD] $	3,079 [2,999]	1,733 [2,401]	<0.001
Total cost of care (medical and pharmacy), mean [SD] $	10,203 [13,648]	9,174 [13,564]	<0.001

[a]*Hospitalization rate compared by logistic regression and costs compared by linear regression.*

[b]*All medical costs are allowed amounts (plan paid amount plus member cost share) from all facility and professional claims including office visits, hospitalizations, procedures, laboratory testing, and ancillary.*

PDC = proportion of days covered; SD = standard deviation.

CI = 1.40-3.18, sulfasalazine: OR = 2.02, CI = 1.26-3.24) were more likely to adhere to the index medication. Significant variables associated with nonadherence included without using immunosuppressive agents (OR = 1.65, CI = 1.02-2.67), younger age (<65 years; OR = 2.20, CI = 1.65-2.93), 2007 versus 2008 drug initiation (OR = 1.50, CI = 1.21-1.86), being female (OR = 1.37, CI = 1.12-1.69), health plan payer type of Medicaid or Medicare risk plan versus commercial plan (OR = 2.51, CI = 1.41-4.45), and patients from the South versus Midwest region (OR = 1.65, CI = 1.14-2.39).

CONCLUSIONS: Oral 5-ASA medication adherence in patients with UC was suboptimal. Factors including multiple daily dosing balsalazide disodium index medication, health plan payer type, patient age, and geographic location were significantly associated with medication nonadherence. Intervention/disease management programs designed to improve medication adherence should be tailored according to individual risk factors for nonadherence.

SPONSORSHIP: This research was conducted by Shire, Wayne, PA.

Impact and Results of a High Dose Point-of-Sale Edit Program

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BACKGROUND: The use of excessively high doses of drugs creates patient safety concerns. Specifically, high doses of combination analgesics create concern related to potential abuse of narcotic components, as well as drug toxicity, particularly in the case of acetaminophen combination products.

OBJECTIVE: To identify and reject claims for excessively high doses of certain hydrocodone/acetaminophen combination products but permit pharmacists to override the reject if appropriate and to qualitatively analyze program outcomes including pharmacists' interventions on claims exceeding high dose limits.

METHODS: On November 1, 2010, a High Dose (HD) edit program was implemented at the point of sale for 2 strengths of hydrocodone/acetaminophen combination products (7.5 mg/750 mg and 10 mg/650 mg). High dose limits were based upon a maximum daily dose of acetaminophen of 4 grams. Claims exceeding this threshold were rejected, and online messaging informed the pharmacy of the high dose. Pharmacists were able to override the reject, if clinically appropriate, and indicate the type of intervention made (if any) by using standard National Council for Prescription Drug Program (NCPDP) Professional Service Codes.

RESULTS: From November 2010 to August 2011 (10 months), a total of 23,406 claims were rejected for exceeding the high dose threshold. Of these rejected claims, 11,041 were paid after the pharmacy reduced the total quantity dispensed and/or increased the days supply of the prescription. An additional 8,300 claims were overridden by the pharmacy using standard codes. The remaining rejected claims were never paid by the health plan. Of the claims overridden by the pharmacy, the most common Professional Service code provided was "prescriber consulted" (61%), followed by "pharmacist consulted other source" (30%). Only 5% of rejected claims were overridden without a pharmacist's intervention.

CONCLUSIONS: In most instances, the HD edit results in the pharmacy altering the quantity dispensed or adjusting the days supply of the prescription. These adjustments result in the ability to more accurately monitor the utilization of the product and a reduction in the potential for narcotic abuse while improving patient safety by ensuring the maximum daily dose of acetaminophen is not exceeded. Most claims that are overridden by the pharmacy are overridden after the prescriber has been consulted. As a result of these findings, the HD edit program was expanded in October 2011 to include additional hydrocodone/acetaminophen products.

Impact of a Dalfampridine (Ampyra) Prior Authorization Edit

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BACKGROUND: Dalfampridine has an FDA indication to improve walking in patients with multiple sclerosis (MS). In the 2 FDA approval studies, nonambulatory individuals were excluded, and approximately 40% of MS patients met the primary study endpoint of improved timed 25-foot walk. As stated in the prescribing information (PI), dalfampridine is associated with lowering the seizure threshold and is contraindicated in individuals with a seizure history or those with moderate to severe renal impairment (defined as creatinine clearance less than 50 ml/min). The wholesale acquisition cost (WAC) for a 1-month supply is $1,135 or $13,620 annually. To ensure safe and appropriate dalfampridine use, the health plan developed a 2-phase point–of-sale prior authorization (PA) policy.

OBJECTIVE: To assess the impact of a dalfampridine PA policy on utilization and estimate cost avoidance compared with a concurrent cohort control group not exposed to the policy.

METHODS: Pharmacy claims were queried among commercially insured continuously enrolled members for a dalfampridine paid or rejected claim during the period from August 1, 2010, through October 31, 2010, within the 807,801 PA exposed members (PA policy activated August 1, 2010, with grandfathering of prior dalfampridine utilizers) and the 257,414 non-PA exposed members. Members were required to be continuously enrolled from their first (index) dalfampridine paid or rejected claim for the period from August 1, 2010, through January 31, 2011. PA records were reviewed to assess coverage rejection and approval activity. Phase 1 approval of 2 months was granted if patient met safety criteria (i.e., no seizure history and creatinine clearance >50 ml per min) and a baseline timed 25-foot walk was provided. Phase 2 approval of 1 year was granted when documentation indicating improved timed walking speed was provided. Dalfampridine paid claims utilization was compared between groups using the student's t-test. Dalfampridine reasons for coverage denial are reported using descriptive statistics. A cost avoidance estimate was calculated by the difference in average claims per member from index claim to January 31, 2011, follow-up, multiplied by WAC and number of dalfampridine members.

RESULTS: The 60 PA exposed dalfampridine members average follow-up was 157 days. Phase 1 approval was obtained by 32 (53.3%) members; 4 (6.7%) members received a denial for safety concerns (all with renal impairment); 9 (15.0%) members received a denial due to inability to obtain walking time; and 15 (25.0%) members did not initiate PA process. Phase 2 approval was obtained by 23 (38.3%) of the 60 members. The 60 PA members had a total of 126 claims and an average utilization of 2.1 (SD = 1.75) claims per member. The 20 non-PA dalfampridine members average follow-up was 157 days. These members had a total of 84 claims and an average utilization of 4.2 (SD = 1.96) claims per member. The PA policy resulted in an average of 2.1 (*P* < 0.001) fewer claims per member in the PA group. The total dalfampridine cost avoidance estimate was $143,010 (2.1 claims × 60 members × $1,135) or $0.03 per member per month (PMPM).

CONCLUSIONS: The dalfampridine PA program appears to be improving safety and cost-effectiveness. The 38% of dalfampridine utilizers meeting PA safety and effectiveness criteria is consistent with efficacy results seen in the FDA approval trials.

TABLE	Ampyra Utilization During >5-Month Follow-Up[a]	
Weighted (30-Day Supply) Ampyra Claims During Follow-Up Including Initial Attempt to Fill Ampyra	Control n = 20 (No PA) 157 Days Average Follow-Up (%)	Intervention n = 60 (2-Phase PA) 157 days Average Follow-Up (%)
0 (indicates initial claim denied with no subsequent paid claims)	0	15 (25.0) (4 denials due to safety concerns)
1	3 (15.0)	9 (15.0)
2	2 (10.0)	16 (26.7)
3	3 (15.0)	3 (5.0)
4, 5, or 6	12 (60.0)	17 (28.4)

[a]Members identified by their initial Ampyra claims from August 1, 2010, through October 31, 2010, and followed until January 31, 2011.
PA = prior authorization.

■ Impact of a Suboxone-Opioid Program on Opioid Utilization

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BACKGROUND: According to the World Health Organization (WHO), by 2020 mental and substance use disorders will surpass all physical diseases as a major cause of disability worldwide. The Office of National Drug Control Policy reports a "Monitoring the Future" study, the nation's largest survey of drug abuse among young people, identified prescription drugs are the second-most abused category of drugs after marijuana.

OBJECTIVE: To reduce prescription drug misuse and abuse while ensuring safe and appropriate Suboxone use.

METHODS: Retrospective programming daily identifies overlapping Suboxone and opioid and/or tramadol pharmacy claims. After overlapping claims are identified, a letter including a medication profile is mailed the following day to the Suboxone prescriber. The letter alerts the Suboxone prescriber of the medication overlap as well as informs the physician of the potential medication safety risk. Two weeks following letter mailing, a pharmacist calls the Suboxone prescriber to ensure the letter was received, answers questions, provides additional information and/or education as needed, and upon request, may refer member to Behavioral Health Case Management. On July 1, 2011, Suboxone Pre-Cert was implemented. Pre-Cert criteria includes drug dependence diagnosis and enrollment in a drug addiction treatment program.

RESULTS: Before the Suboxone-opioid program, the number of opioid pharmacy claims per 1,000 members was increasing. When the mailing of letters to Suboxone prescribers was implemented, the number of opioid pharmacy claims resulted in a plateau. When pharmacist outreach started, the number of opioid pharmacy claims began to decrease and further decreased when Pre-Cert started.

CONCLUSIONS: Informing Suboxone prescribers of Suboxone-opioid(s) overlap and pharmacist outreach to Suboxone prescriber prevented an increase in opioid use and over time resulted in decreased opioid use. It may be concluded that the Suboxone Pre-Cert process had an additional impact on decreased opioid use.

■ Impact of a Text Messaging Pilot Program on Patient Medication Adherence

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BACKGROUND: Medication nonadherence is a well-recognized challenge associated with poor health outcomes and increased utilization of health care resources. While many different behavioral and educational strategies are available to improve patient medication adherence,

FIGURE	Opioid Utilization in Rxs Per 1,000 HMO and PPO Members Per Month
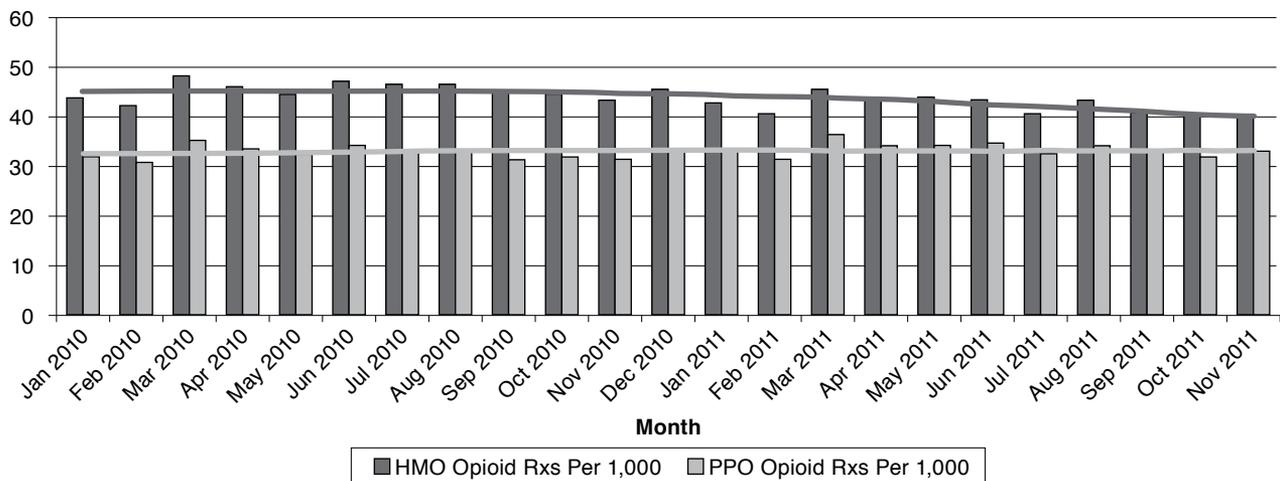
HMO = health maintenance organization; PPO = preferred provider organization; Rx = pharmacy claim.

technological advances, including cell phone text messaging, represent new and innovative modalities to improve adherence and overall health outcomes.

OBJECTIVE: To evaluate medication adherence rates among patients opting to receive text message medication reminders and a well-matched control cohort.

METHODS: This retrospective, observational cohort analysis compared adherence rates of members who opted-in to the text message medication reminder program and a matched control cohort using data from a member portal database and electronic pharmacy claims of a national pharmacy benefit manager (PBM) with commercial and Medicare membership. Continuously enrolled members who opted to receive at least 1 medication-specific dosage reminder for a chronic oral medication of interest and had at least 1 pharmacy claim for the same chronic oral medication of interest were included. Matching was based on medication therapeutic class, then on propensity score (including variables such as age, gender, health plan, Chronic Disease Score, distinct medication count, average rate of baseline medication adherence, and duration of therapy). The primary outcome was chronic oral medication adherence, measured as the proportion of days covered (PDC), between January 1, 2011, and August 31, 2011. Analyses comparing cohorts were conducted using paired t-tests and McNemar's test.

RESULTS: After implementation of the text message program, the mean [SD] PDC was significantly higher for the text message cohort (n = 290) than for the control cohort (n = 290; 0.85 [0.20] vs. 0.77 [0.28], respectively, $P < 0.001$). Of those members identified with a chronic oral antidiabetes medication, the mean [SD] PDC was significantly higher in the text message cohort (n = 48) than the control (n = 48; 0.91 [0.14] vs. 0.80 [0.29], $P = 0.010$). Significant differences in mean [SD] PDC were also seen in members who opted to receive text message reminders for beta-blocker therapy (n = 23) over members in the control cohort (n = 23; 0.88 [0.18] vs. 0.71 [0.29], $P = 0.006$).

CONCLUSIONS: Findings suggest that members opting into a text message reminder program have significantly higher chronic oral medication adherence rates compared with members not opting to receive medication-specific text message reminders.

SPONSORSHIP: This research was conducted by OptumRx, Irvine, CA, without external funding.

■ Impact of a Tier Reduction on Statin Adherence

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BACKGROUND: On January 1, 2011, a Medicare Part D plan sponsor implemented a tier reduction moving atorvastatin and rosuvastatin from the second tier (preferred brand tier) to the first tier (generic tier) for Medicare Part D beneficiaries, including low-income subsidy (LIS) and non-LIS beneficiaries.

OBJECTIVE: To assess if this tier reduction was associated with improved statin adherence.

METHODS: Pharmacy claims and eligibility records between July 1, 2009, and July 31, 2011, were analyzed. New statin initiators (defined as no prescription of statins 6 months prior) in January 2010 (prior to the tier reduction or pre-change period) and in January 2011 (post-change period) continuously enrolled for at least 6 months prior to and after statin initiation were compared. The "tier-reduction" cohort included atorvastatin and rosuvastatin users, and the "no-tier-reduction" cohort, serving as a control group, included fluvastatin, lovastatin, pravastatin,

and simvastatin users. Statin adherence defined by the proportion of days covered (PDC) over a 6-month period was compared between the independent tier-reduction and control cohorts. The association between tier reduction and adherence was evaluated by logistic regression, adjusting for demographic and clinical characteristics. Furthermore, since the impact of the tier reduction on copayments is much smaller for LIS eligible members, we also stratified by LIS status. Separate logistic regressions were estimated for the no-tier-reduction control cohort.

RESULTS: We identified 22,892 members in the tier-reduction cohort with 9,982 from pre-change period (55.2% LIS) and 12,910 from post-change period (38.3% LIS); 38,577 members in control cohort with 22,709 from pre-change period and 15,848 from post-change period. In the tier-reduction non-LIS cohort, mean PDC over 6 months increased from 0.77 to 0.83, and the proportion of members with high adherence (PDC ≥ 0.8) increased from 62.0% to 72.9% (both $P < 0.001$). There was no significant increase in adherence observed in the tier-reduction LIS cohort and the control group of no-tier reduction patients. Members in the tier-reduction non-LIS cohort, who experienced the largest reduction in copayment, were more likely to be adherent (odds ratio = 1.676; 95% CI = 1.544-1.818).

CONCLUSIONS: We observed that this tier reduction was associated with a higher likelihood of statin adherence among non-LIS members. The findings from this quasi-experimental study suggest that financial incentives may improve medication adherence. Future studies should evaluate whether the impact of such financial incentives improves long-term adherence, can be extrapolated across other therapeutic drug categories, and whether improved adherence leads to improved patient outcomes.

SPONSORSHIP: This research was conducted by Pfizer Inc., New York, NY.

■ Impact of Biologics on the Burden of Rheumatoid Arthritis

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BACKGROUND: Rheumatoid arthritis (RA) is a chronic, progressive systemic inflammatory disease that can be associated with severe long-term disability caused by joint destruction. Important sequelae of joint damage include joint replacement (e.g., total knee replacement [TKR] and total hip replacement [THR]). While effective, such surgeries are expensive and can pose risks for patients.

OBJECTIVE: To study the impact of biologics by examining RA patients' need for procedures due to RA-related damage.

METHODS: We performed a retrospective analysis of patient hospital discharges data between 1993 and 2008 in the United States from the Nationwide Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP). We used a coding algorithm to identify all 1,742,935 patients having THR or TKR procedures, 58,036 of which had a diagnosis of RA. The main methodology for this project was the difference-in-differences (DID) technique, to measure the change induced by a particular treatment or event, in this case, the advent of biologics for the treatment of RA. The basic premise of DID was to examine the effect of RA biologics by comparing RA patients before and after the introduction of each biologic (etanercept, infliximab, and adalimumab) to non-RA patients with similar demographics and comorbidity profiles (the "control" group). DID utilized such a "control" group to subtract out other changes (identical to the treatment and control groups) that took place across time. A subsample of patients aged 65 years and over was also conducted.

RESULTS: The number of annual THR procedures more than doubled between 1993 and 2008 (25,987 to 56,478), and the number of annual TKR procedures more than tripled over this period (38,136 to 125,881). However, patients with RA (as a primary or secondary diagnosis) had a statistically significant ($P<0.01$) 32% to 24% reduction in the likelihood of RA being the primary reason for receiving THR or TKR after the time that biologic agents were introduced. For patients aged 65 years and older, the results are consistent with those of the full sample, with approximately a 28% reduction in the likelihood that RA is the primary reason for surgery.

CONCLUSIONS: Since the time of the introduction of biologics for the treatment of RA, there has been a reduction in THR and TKR surgeries among patients with a primary diagnosis of RA. This consistent and significant finding suggests that the availability of biologic agents, as well as other changes in the therapeutic approach to RA, may confer long-term benefits to both RA patients and health care systems.

■ Impact of Community Pharmacist-Led Counseling on Patient Medication Adherence

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BACKGROUND: Patients who are new to therapy on maintenance medications often have poor adherence that can lead to adverse outcomes and higher medical costs. Evidence-based interventions to improve their adherence are needed. In May 2010, two community pharmacies in the Midwest implemented a program of pharmacist-led, face-to-face patient counseling at the site of care for patients who were new to therapy for statin or thyroid medications. The counseling consisted of brief motivational interviewing to assess and improve the patients' confidence and commitment to their prescribed treatment.

OBJECTIVE: To assess the impact of pharmacist-led, face-to-face patient counseling on medication adherence in patients who were new to therapy for statin or thyroid medications.

METHODS: We conducted a retrospective, pre/post cohort study. The pre-period cohort included patients who initiated statin or thyroid medication in May or June 2009. The intervention program began in May 2010. The post-period cohort included patients who initiated statin or thyroid medication in May or June 2010. The community pharmacies implementing the face-to-face counseling were designated as test pharmacies. Two other pharmacies that did not offer the intervention were assigned as control pharmacies; they were selected based on similar pharmacy type, number of years in operation, prescription volume, and corresponding population characteristics. All new-to-therapy patients who started a 30-day supply for statin or thyroid medications at either test or control pharmacies were included in the study. All patients were followed for 12 months to evaluate their medication adherence. Medication adherence was measured by the proportion of days covered (PDC). We calculated patients' average medication adherence for the pre- and post-periods from both test and control pharmacies. To evaluate the impact of the intervention we compared the change in medication adherence from the pre- to post-period in both the test and control pharmacies; significance was determined using t-tests.

RESULTS: For test pharmacies, 76 new-to-therapy patients with usual care were included in the pre-period, and 81 new-to-therapy patients who received pharmacist-led face-to-face counseling were included in the post-period. For control pharmacies that offered usual care, 73 new-to-therapy patients were included in the pre-period, and 81 new-to-therapy patients were included in the post-period. In the test pharmacies, the average 12-month PDC was 0.44 in the pre-period and 0.56 in the post-period; this was a significant improvement of 0.12 ($P=0.033$). In the control pharmacies the average 12-month PDC was 0.48 in the pre-period and 0.50 in the post-period; this difference of 0.02 was not significant.

CONCLUSIONS: Pharmacist-led, face-to-face patient counseling significantly improved adherence in new-to-therapy patients. While not measured in this study, other research has shown that greater medication adherence is associated with improved health outcomes and reduced overall health care costs. Further studies with larger samples and additional medication classes are needed to better understand the full benefit of the program.

■ Impact of Consumer-Driven Health Plans on Member Decisions

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BACKGROUND: Consumer-driven health (CDH) plans differ from a traditional approach to benefit coverage. Typical CDH plans encourage members to actively manage their health care by combining a high deductible with an account which can be allocated to cover a portion of the deductible. Members in a CDH plan may change behavior, including delivery channel, generic options, and utilization patterns. A plan implemented an opt-in CDH plan for its membership. Comparison of the members who chose the CDH option with the remaining utilizers offers insight into member behavior.

OBJECTIVE: To evaluate the effect of the implementation of an opt-in CDH plan on member decisions including delivery channel (mail vs. community), drug type (brand vs. generic), drug choice (need vs. want), and adherence.

METHODS: A retrospective observational study design using claims pre- and post- implementation from an integrated database of administrative pharmacy claims on a 3,100-member employer pharmacy benefit client. The study analyzed the CDH and non-CDH plan's adherence to medications in the cholesterol class, measured by looking at medication possession ratios (MPR) of continuously enrolled employees. The study also measures the shift between delivery channel, drug type, and influence on utilization components (Acute/Life Saving, Chronic Preventative, Lifestyle, Potential Over Utilization).

RESULTS: 45% of utilizing members opted into the CDH plan, increasing to 56% of utilizing members in 2010. The MPR increased in 2009 for plan members who opted-in the CDH plan and decreased for members that did not from 2008. MPR remained higher for members in the CDH plan versus non-CDH members in 2010. The generic dispensing rate (GDR) remained consistent from 2008 to 2009 for members in the CDH plan, and slightly increased for non-CDH members. GDR increased in 2010 for both plans; non-CDH members had a slightly higher GDR. CDH members mirrored utilization trend of the client whole.

CONCLUSIONS: The implementation of CDH plans has little influence on GDR, and members remain adherent to their chronic condition medication.

■ Impact of Generic Step Therapy of Divalproex ER, Levetiracetam, Lamotrigine, and Topiramate on Health Care Utilization in Epilepsy Patients

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BACKGROUND: On January 1, 2011, UnitedHealthcare (UHC) implemented a step-therapy program requiring a trial of generic formulations for 4 multisource brand (MSB) anti-epilepsy drugs (AEDs): divalproex ER, levetiracetam, lamotrigine, and topiramate. Although overrides were available for patients with seizure disorders, some epilepsy patients opted to switch to the generic formulations. There is conflicting literature regarding whether patients on MSB AEDs who switch to AB-rated generic formulations experience epilepsy control disruptions and increased medical utilization.

OBJECTIVE: To identify differences in health care utilization between epilepsy patients who were brand loyal versus generic switchers of MSB AEDs after implementation of a step-therapy program.

METHODS: Using claims data, patients with at least 1 claim in 2010 Q4 for any of the 4 MSB AEDs were identified. If multiple claims were found, the last claim in 2010 Q4 was identified as the index claim. Both continuous enrollment and at least 1 medical claim with a diagnosis of epilepsy (ICD-9-CM codes 345.x) and/or convulsions (ICD-9-CM codes 780.3x) from 180 days prior to the index claim (baseline period) through May 31, 2011, were required. In order to ensure consistent treatment history with the MSB AED, patients had to have at least a 90-day supply of the index drug during the baseline period. Patients were identified as either brand loyal or generic switchers depending on whether the first claim found between January 1, 2011, and March 31, 2011, was for the index MSB AED or its generic equivalent. Regression techniques were used to adjust for baseline differences in patient characteristics between groups. Two-part general linear and regression modeling were performed to evaluate health care utilization factors during the 60-day follow-up after the first index claim in 2011 for brand loyal and generic switcher groups.

RESULTS: A total of 2,806 patients met the inclusion criteria; 421 (15.0%) were generic switchers, and 2,385 (85.0%) were brand loyal. The average age was higher in the generic switchers group (37.2 vs. 34.2 years, $P=0.002$). At baseline, the brand loyal group was more likely to have any outpatient visits (95.2% vs. 92.6%, $P=0.030$) and had higher total AED costs ($3279.41 vs. $2833.25, $P=0.001$). Adjusted results show that in the follow-up period, brand loyal patients averaged $1,537.06 in index MSB AED costs while generic switchers averaged $600.46 ($P<0.001$). No differences were seen in the follow-up period for brand loyal patients versus generic switchers in any hospital or emergency room (ER) visits (9.8% vs. 9.6%, $P=0.922$), hospital plus ER costs ($286.36 vs. $153.18, $P=0.200$), any outpatient visits (73.6% vs. 77.8%, $P=0.056$), the number of outpatient visits per patient (3.26 vs. 3.22, $P=0.864$), outpatient costs ($728.26 vs. $733.73, $P=0.700$), epilepsy- or convulsion-related medical costs ($210.99 vs. $259.51, $P=0.751$), or total medical costs ($1,531.18 vs. $1,500.50, $P=0.638$).

CONCLUSIONS: Although epilepsy patients were provided overrides to a generic AED step-therapy program, some opted to switch to generics. No significant differences in medical utilization or costs were seen between brand loyal and generic switchers. However, statistically and financially significant pharmacy savings were seen from switching to generic MSB AEDs.

■ Impact of HIV-Specialized Pharmacies on Adherence to Antiretroviral Therapy

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BACKGROUND: Human immunodeficiency virus (HIV)-specialized pharmacies are traditional community pharmacies tailored to meet the unique medication needs of HIV patients. By offering special services (such as synchronized refills and refill reminders) and by having HIV-trained pharmacists on hand, these pharmacies may help patients achieve greater adherence to their antiretroviral therapy (ART).

OBJECTIVE: To compare adherence to ART for patients utilizing HIV-specialized pharmacies versus community pharmacies.

METHODS: This was a retrospective analysis that utilized de-identified pharmacy claims from September 1, 2010, through August 31, 2011. Patients aged 18 years or older with a prescription fill for an antiretroviral medication were included in the study. Propensity matching (1:1) was utilized to adjust for baseline differences in age, gender, average number of prescription medications, presence of prescription pain medication, and presence of prescription anxiety and/or depression medication. Adherence was measured via proportion of days covered (PDC). Student's t-test was used to assess for differences in continuous PDC measures and chi-square was used for proportions.

RESULTS: The baseline/unmatched community pharmacy group comprised 15,531 patients, and the baseline HIV-specialized group consisted of 7,064 patients. Propensity matching resulted in 7,064 patients in each group. After propensity matching, patients utilizing HIV-specialized pharmacies had a significantly higher median PDC of 90.3% compared with 87.0% for patients using community pharmacies ($P<0.001$). The HIV-specialized group also had a statistically significantly higher mean PDC (74.1% vs. 70.0%; $P<0.001$). When stratifying by PDC range, the HIV-specialized group had a larger percentage of patients achieving an adherence level of ≥95% (39.3% vs. 35.2%; $P<0.001$).

CONCLUSIONS: Patients using HIV-specialized pharmacies experienced a significant increase in adherence to ART. In an effort to achieve better health outcomes, payers should partner with pharmacies offering enhanced HIV services and encourage their members to use such pharmacies.

■ Impact of Utilization Management Strategies for Febuxostat on the Use of Chronic Gout Therapy

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BACKGROUND: Utilization management strategies can be used to ensure adherence to clinical protocols and are often implemented as a cost containment strategy.

OBJECTIVE: To evaluate the impact of utilization management methods for febuxostat on the use of chronic gout treatment.

METHODS: A retrospective claims database analysis using data from a national pharmacy benefit manager was conducted. Adults with at least 1 rejected febuxostat claim from March 1, 2009, through June 30, 2010, continuous eligibility in the 6-month pre- and 3-month post-index periods, and absence of a febuxostat claim in the pre-index period were included for analysis. Rejection reasons included prior authorization

(PA), drug not covered (NC), step therapy (ST), quantity limits (QL), and other reasons. Patient age, gender, payer type, comorbidities, rejection reason, projected febuxostat copayment, and pre-index prescription costs and claim counts were assessed. Multivariate logistic regression models were used to assess factors associated with filling any chronic gout medication (allopurinol, colchicine/probenecid, febuxostat, probenecid) within 1 month of a rejected febuxostat claim.

RESULTS: 1,034 patients were identified. 36% (n = 369) of the febuxostat claim rejections were attributed to ST, 25% (n = 259) to NC, 18% (n = 183) to QL, 16% (n = 170) to PA, and 5% (n = 53) to other reasons. Most patients were male (73%), aged 65 years or older (41%), and had commercial insurance coverage (63%). In the 30 days following the rejected febuxostat claim, 35% (n = 364) of patients did not fill any chronic gout medication; 46% (n = 474) successfully filled a febuxostat prescription; and the remainder (20%) filled an allopurinol prescription. Positive influencers for filling chronic gout agents were QL compared with NC (odds ratio [OR] = 4.70; $P < 0.001$), at least 40 pre-index drug claims compared with 0-9 claims (OR = 2.71; $P = 0.011$), and a pre-index pharmacy claim for an antihypertensive (OR = 1.56; $P = 0.014$). Negative influencers were febuxostat copayment of $40 to $59 (OR = 0.51; $P = 0.037$) or $100 to $149 (OR = 0.41; $P = 0.003$) compared with a copayment of $0 to $19.

CONCLUSIONS: A gap in chronic gout treatment following a claim rejection of febuxostat was found for this study population. Potential unintended consequences should be considered when utilization management strategies are implemented by managed health care plans.

■ Improving Osteoporosis Outreach Effort: A Randomized, Controlled Study of Program Effectiveness

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BACKGROUND: The Health Net Pharmacy Services/Quality Improvement (HNPS/QI) Osteoporosis Initiative is a member and physician focused intervention for our Medicare members aged 65 to 90 years. The goal is to increase bone mineral density (BMD) testing and/or treatment rate in post-menopausal women who have had an osteoporotic fracture and have not received BMD testing or osteoporosis medications. The osteoporosis initiative was implemented in 2003 as an annual program for Health Net of California (HNCA). Beginning in 2006, the management of osteoporotic fractures became a scored Healthcare Effectiveness Data and Information Set (HEDIS) measure for HNCA, as indicated by the National Committee for Quality Assurance (NCQA). This measure is also driven by the Centers for Medicare and Medicaid Services (CMS) Star Plan Ratings, which measure plan quality and performance. In July 2010, the frequency of the outreach was changed to monthly rather than annually in order to reach high-risk Medicare members in a timely manner.

OBJECTIVE: To establish the impact of the osteoporosis intervention in comparison to the control group, which had no intervention.

METHODS: The osteoporosis initiative is a randomized, controlled trial with equal sized control and intervention groups. Monthly review of medical and pharmacy claims and encounter data identified members in each group by using the HEDIS criteria for Osteoporosis Management in Women with Fractures (OMW) measure. The outreach consisted of mailing educational materials to members and faxing intervention alerts to primary care physicians regarding their identified patients. Interim analysis includes identifying the earliest fracture visit for each random-

ized member from March 1, 2010 (4 months before the start of the intervention) through the extraction date in October 2011. Continuous enrollment of the patient population was also assessed. Time from last fracture visit to interim analysis data extraction must be at least 9 months to allow a minimum of 3 months for data to complete after 6-month post-fracture visit.

RESULTS: There were 932 members in the intervention group and 924 in the control group. In the intervention group, the response rate, defined as percentage of members who had either a BMD test or prescription medication for osteoporosis in the 6 months after the fracture, was 20.7% (193 members) compared with 11.9% (110 members) in the control group (absolute difference between the 2 groups was 8.8% [$P < 0.001$]). Limitations to the program include less time for the data to complete in the interim analysis and exclusion of members identified as already having a BMD test or a prescription medication for osteoporosis post-fracture.

CONCLUSIONS: The outreach program produced a significantly higher response rate in the intervention group with a relative increase of approximately 75.0% in initiating a BMD test or an osteoporosis treatment in the 6 months post-fracture visit when compared with the control group. The study was terminated early for the following reasons: (a) interim analysis showed a significant difference with the intervention group, and (b) all target members should be intervened on in order to ensure all members have the opportunity to receive appropriate treatment.

■ Improving the Participation Rate for Comprehensive Medication Reviews

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BACKGROUND: In 2011, the Pharmacy Quality Alliance (PQA) endorsed "the completion rate for comprehensive medication review (CMR)" as a quality measure for Medication Therapy Management Programs (MTMP). PQA tested the measure with a Medicare Part D sponsor in 2009 and found a CMR completion rate that was slightly over 5%. Although the Centers for Medicare and Medicaid Services (CMS) has not stipulated a minimum rate for CMR participation, it can be expected that CMS will establish a standard to ensure that the MTMP provides its intended benefits to the program's targeted beneficiaries.

OBJECTIVE: To investigate factors that may affect a person's decision to participate in a telephonic CMR.

METHODS: A pilot study was conducted with 56 randomly selected Part D beneficiaries who qualified for MTMP. Recruitment phone calls for CMR were made with these beneficiaries, utilizing a standardized script. During the call, an offer for the CMR service was made after confirming the beneficiary's enrollment in MTMP, and the reactions and responses to the offer were observed and documented by the investigator. Observations from the pilot were analyzed and categorized according to dimensions of the Health Belief Model (HBM), a well-studied theoretical framework that has been used for examining health attitudes and behaviors. A revised recruitment script was then developed under the guidance of the HBM framework and findings from the pilot. The new script was tested through interviews and a focus group to obtain further qualitative information on the relationship between the participants' responses to the CMR recruitment, perception of health status, and the perceived value of CMR.

RESULTS: The pilot study demonstrated 2 significant challenges in

telephonic CMR recruitment: (a) getting a hold of the beneficiaries to complete the call and (b) explaining the value of CMR utilizing a standardized script. The pilot revealed that many beneficiaries had difficulties understanding the MTMP and the purpose of CMR, which could prevent them from viewing CMR as a beneficial service. A revised script was developed to address these issues, and emphasis on the value of CMR was embedded in the script through addressing beneficiaries' perceived benefits and barriers of accepting the service. The revised script was tested with 20 community-dwelling adults aged 55 years or older who were taking multiple chronic medications. All 20 participants were able to comprehend and recall what a CMR entails after listening to the revised script, and 75.0% expressed that they would agree to participate in a CMR when the offer was made to them during the interview. The investigator found that the main motivation behind accepting the CMR offer was the desire to obtain more information on medications, as many perceived that the lack of information can place one at risk of experiencing adverse drug reactions. Although the majority of participants recognized the benefits of a CMR and agreed that they are susceptible to experiencing an adverse drug event, believing that he or she already has a good resource for medication-related information and fears of fraudulent calls may hinder one's willingness in participating in a telephonic CMR.

CONCLUSIONS: Through a better understanding of beneficiaries' perceived benefits and barriers of the CMR service, this pilot study suggests that a more focused recruitment method can be developed to encourage CMR participation. Explaining the value of CMR from the participants' perspective and addressing their concerns in the recruitment script seem to be well received by the study participants. A further study has been planned to test the script with a larger selected Part D population in 2012.

■ **Increasing the Intensity of Interventions Improves Resolution of Drug-Related Problems in a Medication Therapy Management Program**

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BACKGROUND: In 2010, the Centers for Medicare and Medicaid Services (CMS) intensified guidance for Medication Therapy Management Programs (MTMP). Several requirements made a profound impact on patient care: requiring an opt-out method of enrollment, quarterly targeted medication reviews (TMR), and prescriber interventions. In both 2009 and 2010, the Health Net MTMP employed an opt-out method of enrollment. In 2009, pharmacists conducted desktop drug regimen reviews biannually and mailed recommendations to patients. The letters informed patients to follow-up with their providers and to call the MTMP pharmacists with any questions. In 2010, the Health Net MTMP increased the frequency of drug regimen reviews from biannually to quarterly and sent recommendations to both patients and prescribers. Pharmacists sent faxes to prescribers when fax numbers were available and mailed recommendations to prescribers when fax numbers were unavailable.

OBJECTIVE: To determine the impact of quarterly patient and prescriber interventions on both the quantity and resolution rate of drug-related problems.

METHODS: We conducted a retrospective cohort analysis using pharmacy claims data to determine the resolution of identified problems. The problems we evaluated included therapeutic care gaps, noncompliance, opportunities to reduce cost, and therapeutic duplications.

TABLE	Comparative Outcomes for MTMPs 2009-2010				
Problem	Goal	2009 % Achieved	2010 % Achieved	Difference in Means	95% CI
Therapeutic care gap	Add drug therapy	14.40	18.20	3.80	0.7-6.9
Opportunities to reduce cost	Switch to lower-cost alternative	10.10	14.20	4.10	0.2-7.9
Therapeutic duplication	Remove duplicate drug	64.00	66.30	2.30	−1.7-6.4
Noncompliance	Improve compliance	57.50	58.50	1.00	−2.0-4.1

CI = confidence interval; MTMP = Medication Therapy Management Program.

RESULTS: The number of interventions for problems evaluated in this study increased significantly from 2009 to 2010 with very little change in overall membership. Therapeutic care gap interventions increased from 7,315 to 12,589. Opportunities to reduce cost interventions increased from 35,032 to 40,701. Therapeutic duplication interventions increased from 3,708 to 7,367, and noncompliance interventions increased from 24,264 to 52,318. Resolution of therapeutic care gaps and opportunities to reduce cost were significantly improved in 2010 (see table). There was no statistically significant improvement in improving compliance or removing duplicated therapy.

CONCLUSIONS: Our findings provide justification for the increase in MTMP intensity mandated by CMS. Quarterly TMRs designed to identify all drug-related problems significantly increase the number of problems identified throughout the year. Our findings also indicate that contacting the prescriber is effective when trying to resolve therapeutic care gaps and to switch patients to lower-cost medications but may not be relevant when trying to improve medication adherence and discontinue therapeutic duplications.

■ **Integrated Approach to Hepatitis C Virus Triple Therapy Specialty Management Implementation**

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BACKGROUND: A novel triple therapy option for hepatitis C virus (HCV) treatment in those with compensated HCV Genotype 1 infection has been approved for use. This therapy includes pegylated interferon alfa and ribavirin in combination with direct-acting antiviral (DAA) protease inhibitors telaprevir or boceprevir. It has been recommended as the treatment of choice for HCV Genotype 1 by the American Association for the Study of Liver Diseases (ASSLD) as this therapy has demonstrated an improved sustained virological response (SVR) over dual therapy with pegylated interferon alfa and ribavirin. However, the therapeutic regimens are complex, costly, and require more intensive coordination with the prescribing provider and patient.

OBJECTIVE: To assess the impact of a collaborative approach for HCV triple therapy coordination by the pharmacy and care team to implement specialty pharmacy management.

METHODS: Pharmacy provided educational sessions for the care team to review the new therapy treatment regimen and critical points including

the importance of compliance and the relationship to viral resistance patterns, patient dosing instructions with regard to dose schedule and food, the increased frequency of viral titer monitoring, drug-drug interactions, drug-drug contraindications, and side effects. Care nurses educated the prescribing physician and/or office staff on the therapy, documentation requirements for therapy review, and member benefits related to cost share and advantages of specialty network coordination. The specialty pharmacy was engaged in the process to address any barriers identified in the referral process to avoid interruptions in therapy. Pharmacy claims were queried among commercially insured continuously enrolled members for a DAA paid or rejected claim from July 24, 2011, through October 24, 2011, to identify members on therapy and monitor referrals to the specialty network and gaps in therapy.

RESULTS: 101 members were initiated on HCV triple therapy regimen during the implementation time period. At baseline 45% of the members were obtaining HCV triple therapy medications from the specialty pharmacy network. After the implementation, 66% were obtaining HCV triple therapy medications from the specialty pharmacy network. The member cost share of boceprevir therapy decreased from 2.68% to 1.05%. The member cost share of telaprevir therapy decreased from 12.64% to 2.06%. No gaps in therapy were observed as prescription orders were filled on a timely basis.

CONCLUSIONS: The integrated pharmacy and care team approach improved awareness of the parameters involved with HCV triple therapy and applied a successful coordination process. Implementation of HCV triple therapy specialty management resulted in member access to therapy and improvement in cost share without observable gaps in therapy.

■ Integrated Medical and Pharmacy Prevalence of Members Diagnosed and Treated Within a Specialty Condition Drug Class

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BACKGROUND: In 2010, specialty drugs comprised 0.4% of claims but 13.1% of all prescription benefit expenditures across Prime Therapeutics' commercial book of business. Average per-prescription cost was $2,336, and total paid per capita increased 10.9% from 2009 ($10.24 to $11.36 per member per month). Claims for many specialty drugs are also paid through the medical benefit. Given the increasing use of expensive specialty drugs, additional characterization of utilization in each of the pharmacy and medical benefit and additional information about gaps in care are needed.

OBJECTIVE: To identify specialty condition prevalence and examine the percentage of members with treatment for the condition.

METHODS: Integrated pharmacy and medical data from 2.3 million commercial members were queried. Members were continuously enrolled in 2010. Fifteen specialty conditions/drug classes were identified and defined internally. A member was determined to have a diagnosis if 1 of the following was found: (a) 2 separate medical claims with the ICD-9-CM code of interest, (b) 2 separate medical claims with a procedure code for a drug used to treat the condition, or (c) 2 separate pharmacy claims used to treat the condition. For members "diagnosed," medical and pharmacy claims were queried for at least 1 drug procedure code or pharmacy claim associated with the condition/drug class. A member could be represented in more than 1 condition/drug class. The percentage of treated members in each category was reported.

TABLE	Prevalence and Treatment Rates of Selected Specialty Conditions			
Condition/Drug Class	**Prevalence (Per 100,000)**	**Diagnosed (n)**	**Treated (n)**	**Treated (%)**
Cystic fibrosis	39	881	819	93.0
Enzyme deficiencies	14	321	58	18.1
Growth disorder/ growth hormones	80	1,814	656	36.2
Human immunodeficiency virus	118	2,683	2,490	92.8
Hemophilia	13	287	83	28.9
Hepatitis C	80	1,828	348	19.0
Immune deficiency/ immune globulins	30	679	364	53.6
Transplant/immunosuppressants	129	2,934	2,759	94.0
Infertility	294	6,697	4,752	71.0
Cancer	1,607	36,619	5,053	13.8
Lung disorders	131	2,988	510	17.1
Macular degeneration	161	3,668	258	7.0
Multiple sclerosis	157	3,575	2,688	75.2
Pulmonary hypertension	20	445	206	46.3
Rheumatoid arthritis/psoriasis	1,034	23,570	10,370	44.0

RESULTS: The prevalence among the 15 specialty conditions ranged from a low of 13 per 100,000 in hemophilia to 1,607 members per 100,000 in cancer (see table). There was a wide range in treated percentages. The majority of conditions (12 of 15) were found in less than 200 per 100,000 members. A low percentage of members identified with cancer were defined as currently treated (13.8%). The most untreated condition was macular degeneration (7.0%). The conditions/drug classes with the highest percentage of treated members were transplant/immunosuppressants (94%), cystic fibrosis (93%), and human immunodeficiency virus (92.8%).

CONCLUSIONS: Health insurers should utilize integrated medical and pharmacy data to assist them in trending and forecasting specialty medication utilization. For some diseases, it may be easy to identify prevalence and treatment rates via ICD-9-CM codes, procedure codes, and pharmacy claims. For other conditions, more sophisticated algorithms may be needed to properly identify candidates for treatment. Learning where gaps in care exist can also help plans optimize favorable medical outcomes for their members.

■ Managing Specialty Medication Services Through a Specialty Pharmacy Program: The Case of Oral Renal Transplant Immunosuppressant Medications

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BACKGROUND: Immunosuppressive medication therapy after organ transplantation is essential for preventing transplant rejection. Nonadherence to immunosuppressant therapy has been identified as a major risk factor for acute complications and allograft rejection, as well as late graft rejection and return to dialysis post-failed renal transplantation, leading to increase in health care costs and even death.

OBJECTIVE: To evaluate a transplant specialty pharmacy program implemented for a membership of a national commercial health plan for its impact on clinical and economic outcomes for patients post-renal transplantation as compared with membership using traditional community pharmacy services.

METHODS: This program was delivered by a designated specialty pharmacy, which met requirements for contracted rates and provision of clinical programs and services. The study is a 1-year retrospective claims analysis after the implementation of a transplant specialty pharmacy program, which, in addition to medication dispensing, includes clinical management, patient education, and counseling services provided by transplant pharmacology experts. Renal transplant patients using the specialty pharmacy program were matched to those using community pharmacies utilizing a propensity score matching technique based on logistic regression. Primary outcomes were financial, including pharmacy medication costs, medical inpatient, and outpatient costs, and overall health care costs. Patient adherence to transplant medication therapy and health care resource utilization were also evaluated. One-year outcomes and post-specialty pharmacy program implementation were compared between 2 groups with t-tests for continuous variables and chi-square for nominal variables.

RESULTS: After propensity score matching, 495 patients were identified per group for analysis. Baseline parameters were similar between the 2 groups, except for transplant-related outpatient visit costs, which were higher in the community setting. The mean total health care cost per patient per year of follow-up was 16.5% lower in the specialty pharmacy program group ($24,499 vs. 29,325, $P=0.01$). Similarly, the mean medical cost was 27.3% lower in the specialty pharmacy program group ($10,708 vs. $14,735, $P=0.02$). The medication possession ratio was higher (0.88 vs. 0.85, $P=0.02$); the number of patients with a medication gap was lower (29 vs. 49, $P=0.02$); and the number of patients who discontinued was lower (32 vs. 109, $P<0.001$) in the specialty pharmacy program members than in the community pharmacy members. Though the numbers of inpatient hospital visits and transplant-related inpatient visits were only numerically lower in the specialty pharmacy cohort versus the community pharmacy cohort, the inpatient cost ($3,204 vs. $5,368, $P=0.02$) and the transplant-related inpatient cost ($2,837 vs. $5,005, $P=0.01$) were significantly lower for the specialty pharmacy program cohort.

CONCLUSIONS: This specialty pharmacy program is associated with decreased inpatient hospital costs and lower overall health care costs, as well as improved transplant medication adherence within the first year of evaluation. The positive impact of health plan program design and coordinated care and oversight by specialty trained clinicians in a specialty pharmacy program has implications for the current health care reform and requires more research.

SPONSORSHIP: This research was funded by United HealthCare Services, Inc., Minneapolis, MN.

■ Measuring Baseline Proportion of Days Covered: The New Medication Quality Measure for Medicare Part D

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BACKGROUND: Plans are subject to performance measures for Medicare Part D. Proportion of days covered (PDC) is a newly recommended metric for estimation of adherence to chronic medications to be used by Centers for Medicare and Medicaid Services (CMS) to rate the plans. The minimum score necessary to obtain a 5-star rating is a PDC of 70%. Medicare Advantage plans that are awarded a star rating of 3 or higher will qualify for quality-based payments (QBPs).

OBJECTIVE: To demonstrate baseline PDC as a measure of adherence to prescribed therapies in diabetes, hypertension, and high cholesterol populations using prescription (Rx) data in community pharmacies.

METHODS: Participants comprised a total of 220,311 patients aged 65 or older who filled a prescription for angiotensin-converting enzyme inhibitors (ACEIs; n=45,769), angiotensin II receptor blockers (ARBs; n=32,414), statins (n=87,224), biguanides (n=31,416), DPP4s (n=3,836), TZDs (n=5,968), and sulfonylureas (n=13,684) at a community pharmacy in North Carolina. Data were from computerized pharmacy records from January 1, 2010, through December 31, 2010. This retrospective observational study reviewed the prescription activity for patients who received a prescription for any of these classes of drugs during a 12-month period. A frequency of distribution for PDC was created. PDC was calculated as days (total calendar days between index fill and end of follow-up) divided by total prescribed days (prescribed days of supply × number of fills prescribed).

RESULTS: On average, 49.6% (TZDs) to 61.2% (ACEIs) of patients had a PDC of more than 80%; 11.4% (ACEIs) to 14.3% (TZDs) of patients had a PDC of 60%-80%; and 27.4% (biguanides) to 36.3% (DPP4s) had a PDC of less than 60%. Because the study used community Rx data, the plan enrollment dates were not available to us. So there was no adjustment for the member-years of enrollment as accounted for by CMS to calculate PDC.

CONCLUSIONS: Medicare Advantage plans can qualify for QBPs based on their performance ratings. As this analysis showed, only over one-half of the chronic medication users get 80% or higher of their medications filled. Targeted and customized educational interventions to these patients can change their behavior and improve their adherence. Improving adherence (PDC measure) can help improve plans' ratings and result in higher payments to the plans.

SPONSORSHIP: This research was conducted by Adheris, Inc., an inVentiv Health Company, Burlington, MA.

■ Medication Therapy Management: Methods to Increase Comprehensive Medication Review Participation

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BACKGROUND: As part of the Centers for Medicare and Medicaid Services' (CMS) requirements for Medicare Part D, health care plans are required to provide Medication Therapy Management Programs (MTMPs). MTMPs are designed for Part D beneficiaries who meet certain criteria set forth in part by CMS, with a goal to improve the health outcomes of these beneficiaries. Current CMS guidelines require Part D sponsors to offer a comprehensive medication review (CMR) to each beneficiary participating in an MTMP. A CMR is a review of a beneficiary's medications that is intended to aid in assessing medication therapy and optimizing patient outcomes. In 2013, CMS will require Part D plans to report the CMR participation rate for its MTMP. In addition, the Pharmacy Quality Alliance (PQA) has recently proposed new MTMP measures which include the CMR participation rate. By implementing process changes aimed at targeting beneficiaries who may derive a greater benefit from a CMR, this MTMP aims to improve CMR participation rates.

OBJECTIVE: To improve the rate of MTMP beneficiaries participating in a CMR.

METHODS: Clinical algorithms were developed to analyze pharmacy claims and identify opportunities to improve health outcomes by

addressing drug-drug interactions, drug-condition interactions, inappropriate medication dosing, nonadherence, patient safety measures, therapy guidelines, and therapeutic duplication. When opportunities are identified using these clinical algorithms, an outbound phone call is placed to the MTMP participant to address the concern. Once engaged with a pharmacist, the MTMP participant is provided with a secondary offer to participate in a CMR. (The primary offer was included in the member's MTMP introductory letter.) The outcomes measured were the percentage of MTMP participants who engaged in a CMR and the increase in percentage of CMRs performed for MTMP participants. Results were compared with the participation rates for the 2010 MTMP year for the same Part D sponsors.

RESULTS: In calendar year 2010, prior to implementing process changes, a total of 238,970 beneficiaries participated in our MTMPs, with only 451 members participating in a CMR, for a total participation rate of 0.19%. As of October 1, 2011, a total of 186,542 beneficiaries were participating in our MTMPs and had been offered a CMR. Of those members, 10,451 had participated in a CMR, for a total participation rate of 5.6%, which is an increase of more than 2,800% over the participation rate in 2010. By identifying opportunities and suggesting actionable changes to drug therapy to improve the health outcomes of the MTMP participants, the members became engaged and invested in the process and were more willing to participate in a CMR. With an additional 3 months left to complete CMRs in 2011, we expect to continue to see increases in our CMR participation rate.

CONCLUSION: This program was associated with a 2,847% increase in the participation rate of CMRs.

SPONSORSHIP: This research was conducted by The University of Arizona, College of Pharmacy, Medication Management Center, Tucson, AZ, without external funding.

■ **Migraine Prophylaxis Adherence and Persistence: A Systematic Literature Review**

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BACKGROUND: Migraine is a common neurological disease affecting 12% of Americans and millions worldwide. Current guidelines recommend oral prophylactics as first-line treatment of which the 3 most commonly prescribed are propranolol, amitriptyline, and topiramate. Medication adherence has been studied extensively in many chronic conditions, with poor adherence negatively affecting treatment outcome. However, little is known about adherence to oral prophylactics for migraine.

OBJECTIVE: To assess oral prophylactic medication adherence and persistence among migraine patients.

METHODS: A search of PubMed and EMBASE was conducted using terms "migraine prophylaxis adherence/compliance" and "migraine prophylaxis" combined with each of the following medications: propranolol, amitriptyline, and topiramate. Studies were limited to prospective and retrospective observational studies on adherence and persistence of migraine prophylactics and randomized controlled trials (RCTs) of propranolol, amitriptyline, and topiramate. Headache disorders other than migraine, expert opinion, reviews, case studies, animal studies, cost-effectiveness studies, pharmacokinetic studies, and guidelines were excluded. Articles not available in English, and studies conducted in children/adolescents (less than 18 years of age), elderly, and pregnant subpopulations were also omitted. Observational studies were reviewed individually while RCT data were pooled, weighted by sample size, and pooled and stratified by drug and length of study. Average persistence

rates and primary reason for discontinuation were examined for each medication.

RESULTS: A total of 788 unique articles were identified using the search criteria, 33 of which were included in the final review. Observational studies (n = 14) showed adherence ranges of 41% to 95% at 2 months, 21% to 80% at 6 months, and 35% to 56% at 12 months and persistence ranges of 41% to 88% at 2 months, 19% to 79% at 6 months, and 7% to 55% at 12 months. Pooled persistence rates from RCTs (n = 19) showed rates of 77%, 53%, and 56% at 16-26 weeks for propranolol, amitriptyline, and topiramate, respectively. Adverse events were the most common reason for discontinuation cited (24% for topiramate and 17% for amitriptyline).

CONCLUSIONS: Observational studies and pooled data from RCTs show low adherence and persistence to oral migraine prophylactics, with adverse events potentially contributing the most to discontinuation.

SPONSORSHIP: This research was funded by Allergan, Inc., Irvine, CA.

■ **Misuse and Abuse Associated with Buprenorphine Utilization for the Treatment of Opioid Dependency**

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BACKGROUND: The Management of Buprenorphine Medication Assisted Treatment (BMAT), for the treatment of opioid dependency, poses many challenges. The rate of abuse associated with buprenorphine in combination with naloxone is lower compared with methadone; however, misuse and abuse associated with buprenorphine utilization is still a major concern. This analysis investigates medication misuse and poor medication monitoring associated with Suboxone and Subutex utilization.

OBJECTIVE: To assess misuse of Suboxone and Subutex associated with opioid dependence treatment.

METHODS: A claims-based analysis was conducted using data from January 2010 to December 2010 from Massachusetts commercial and Medicaid insurers. Patients were included in this analysis if they filled at least 2 prescriptions for Suboxone or Subutex at consistent doses and if gaps between their 2 prescription-dispensing dates were less than 7 days. Pattern recognition was used to examine concomitant drug therapy and monitoring associated with Suboxone or Subutex utilization.

RESULTS: 1,687 unique patients filled prescriptions for Suboxone or Subutex. Of patients who filled prescriptions for Suboxone or Subutex, 51.7% had been concurrently prescribed benzodiazepines or opiates during the evaluation period. Less than 50.0% of prescribers conducted chemical abuse screens during the evaluation period.

CONCLUSIONS: Pharmacologic intervention for opioid dependence is a challenge for both health care providers and health insurance companies. Concerns surrounding the appropriate use of this therapy include drug diversion and concomitant use of controlled substances. By monitoring for outlier prescribing and utilization patterns, health plans can begin to develop intervention strategies which aim to address misuse and poor medication monitoring associated with BMAT utilization.

SPONSORSHIP: This research was conducted by Beacon Health Strategies LLC, Woburn, MA.

■ **Number Needed to Treat, Cost per Responder, and Budget Impact of Long-Standing Tumor Necrosis Factor-Inhibitors in Psoriatic Arthritis**

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BACKGROUND: Payers have expressed interest in relevant economic assessments of drug classes using methodologically sound indirect treatment comparisons.

OBJECTIVE: Assess the economic impact of tumor necrosis factor (TNF)-inhibitors in psoriatic arthritis (PsA) over 1 year.

METHODS: Published pooled placebo and active treatment Psoriatic Arthritis Response Criteria (PsARC), American College of Rheumatology (ACR) 50, and (Psoriasis Area and Severity Index (PASI) 75 response rates at 12-14 weeks were sourced from a 2010 National Institute for Health and Clinical Excellence (NICE) independent review of adalimumab (ADA), etanercept (ETA), and infliximab (IFX) in PsA when used after failure on standard treatments, including disease-modifying antirheumatic drugs. All final response rates were placebo adjusted by subtracting pooled placebo rates from active treatment rates for each outcome. Relative differences were assumed to be maintained for 1 year. NICE response rates were combined with U.S. annual drug costs of ADA $23,305, ETA $23,527, and IFX $24,145. Drug costs assumed labeled dosing and July 1, 2011, wholesale acquisition costs (WAC). IFX costs (including infusion costs from Centers for Medicare & Medicaid Services Physician Fee Schedule July 22, 2011) assumed a 5 mg per kg dose, an 80 kg patient, and an 8-week dosing interval and infusion rate. The cost per responder and number needed to treat (NNT) were calculated for each treatment response, as well as the budget impact required to achieve 100 responders.

RESULTS: On every outcome studied, NICE concluded IFX demonstrated the highest response rates. These differences lead to the lowest derived cost per responder, NNT, and budget impact over 1 year (see table).

CONCLUSIONS: Derived IFX cost per responder and budget impact over 1 year, based on NICE's independent review, was lower than those of ADA and ETA, whether using PsARC, ACR 50, or PASI 75 outcomes. Sensitivity analyses based on indirect comparison confidence limits are warranted.

SPONSORSHIP: This research was conducted by Janssen Scientific Affairs, LLC, Horsham, PA.

| TABLE | 52-Week Economic Impact of TNF-Inhibitors in PsA Derived from NICE Systematic Review |

	PsARC			ACR50			PASI75		
	ADA	ETA	IFX	ADA	ETA	IFX	ADA	ETA	IFX
Placebo-adjusted response, %	33.8	46.4	54.6	26.2	30.9	38.0	43.3	13.3	72.5
NNT for 100 responders	296	216	183	382	324	263	231	752	138
Cost per responder, ×1,000 ($)	73.7	50.7	44.2	95.1	76.1	63.5	57.5	176.9	33.3
Budget impact for 100 responders, ×1,000 ($)	7,372	5,070	4,422	9,509	7,613	6,354	5,752	17,689	3,330

ACR = American College of Rheumatology; ADA = adalimumab; ETA = etanercept; IFX = infliximab; NICE = National Institute for Health and Clinical Excellence; NNT = number needed to treat; PASI = Psoriasis Area and Severity Index; PsA = psoriatic arthritis; PsARC = Psoriatic Arthritis Response Criteria.

■ Observed Dosing Patterns for Ustekinumab in the Treatment of Moderate-to-Severe Psoriasis: Evaluation of Data from 14 Commercial Health Plans

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BACKGROUND: Ustekinumab (UST) is the newest subcutaneous biologic agent available for the treatment of moderate-to-severe plaque psoriasis (PsO). UST may be dosed at 45 mg (patient weight ≤100 kg) or 90 mg (patient weight >100 kg) and administered at weeks 0, 4, and every 12 weeks thereafter. Payers are increasingly interested in appropriately managing biologic costs, while interpreting comparative cost-effectiveness data in PsO. An understanding of the real-world utilization of 45 mg and 90 mg may offer additional insight and further contribute to a payer's ability to predict UST treatment costs and interpret existing comparative cost-effectiveness data.

OBJECTIVE: To evaluate the observed distribution of 45 mg and 90 mg UST dosing in PsO patients in selected commercial health plans.

METHODS: Data were analyzed from the HealthCore Integrated Research Database (HIRDSM), consisting of integrated enrollment and medical and pharmacy claims from 14 commercial health insurance plans geographically distributed across the United States. Inclusion criteria consisted of at least 1 UST medical or pharmacy claim between September 1, 2009, and November 10, 2010 (date of first UST claim set as index date); patients aged 18 years or older at index; at least 1 PsO diagnosis code (696.1) at or post-index; and at least 12 months pre-index continuous enrollment. Exclusion criterion was medical or pharmacy claim for another biologic on the index date. UST dose was evaluated based on a combined assessment of time between fills (index to third dose) and cost, to account for multiple vials/syringes dispensed in a single claim. Interval patterns were assessed as the time between UST fills based on a window around recommended intervals (i.e., 28±7 days for dose 1 to dose 2 and 84±14 days for dose 2 to dose 3). Intervals were categorized as "expected," "later than expected," or "earlier than expected."

RESULTS: A total of 372 PsO patients receiving UST were identified. Mean (SD) age was 48 (12) years; 56.5% were male. The predominant insurance type was preferred provider organization (75.0%), followed by health maintenance organization (19.9%). Most patients resided in the Midwest (38.4%) and Southeast/Mid-Atlantic (29.6%). Prior to UST initiation, 22.3% of patients had been diagnosed with comorbid psoriatic arthritis. The majority of patients (74.9%) had their index UST dose prescribed by a dermatologist. The proportion of index 45 mg and 90 mg use of UST was 79.0% and 21.0%, respectively. The majority of patients filled the second (95.8%) and third (91.3%) UST doses "as expected" or "later than expected." Median (mean [SD]) interval times were 28 (41 [36]) and 85 (88 [23]) days for first to second and second to third doses, respectively.

CONCLUSIONS: This study's initial distribution of UST dose strength suggests that most PsO patients are initiated with a 45 mg dose. Additionally, the majority of patients had observed UST median interval patterns consistent with the recommended administration schedule. At the reported dose mix and median interval patterns, estimated annual maintenance acquisition costs would approximate $28,739. These are the first health plan data providing real-world evidence of UST dosing and may offer payers a path to treatment cost predictability, as well as a reference for evaluating comparative cost-effectiveness results.

SPONSORSHIP: This research was conducted by Janssen Scientific Affairs, LLC, Horsham, PA.

■ Outcomes After Initiation of Fluticasone Propionate-Salmeterol Combination Versus Anticholinergics in Patients with Moderate Exacerbations of COPD

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BACKGROUND: There are limited data describing patients with moderate chronic obstructive pulmonary disease (COPD)-exacerbations and evaluating the comparative effectiveness of maintenance treatments in this patient population.

OBJECTIVE: To compare COPD-related exacerbations and costs between patients initiating fluticasone propionate-salmeterol 250/50 mcg (FSC) versus anticholinergics (ACs) after a moderate COPD-exacerbation.

METHODS: Administrative claims data from January 1, 2003, through March 31, 2009, were used to identify maintenance therapy-naïve patients (aged 40 years or older) having at least 1 moderate COPD exacerbation defined as a physician visit with a primary diagnosis of COPD (ICD-9-CM codes 491.xx, 492.xx, 496.xx) and having an oral corticosteroid or antibiotic pharmacy claim within 5 days of the visit. A subset of these patients initiating therapy with either FSC or AC within 30 days of the first moderate COPD exacerbation (index event) were then studied (retrospective cohort design). Outcomes during a variable follow-up period included COPD-exacerbation rates (rate per 100 person-years) and COPD-related costs (per patient per month standardized to USD 2009). Outcome comparisons between cohorts were adjusted for differences in baseline characteristics captured during the 1-year pre-index period. Differences in the risk of COPD exacerbations were evaluated using Cox proportional hazards model, and generalized linear models with log-link and gamma distribution were used to analyze differences in COPD-related costs.

RESULTS: A total of 21,524 patients with an initial moderate COPD-exacerbation were identified. During the year following their initial moderate COPD exacerbation, 25% initiated COPD maintenance therapy, and 13% had any subsequent COPD exacerbation. A total of 2,849 patients (FSC=925; AC=1,924) were eligible for the cohort analysis. The FSC cohort had a significantly lower rate of any COPD exacerbation compared with the AC cohort (20.8 vs. 32.8 per 100 person-years, $P=0.04$). After adjusting for differences in baseline covariates, FSC patients were 42% less likely than AC patients to have any COPD-exacerbation in the follow-up period (hazard ratio=0.58, 95% CI=0.38-0.91; see table). FSC significantly reduced adjusted monthly medical costs compared with AC ($82 vs. $112, $P<0.05$). However, the FSC cohort incurred significantly higher adjusted monthly pharmacy costs ($143 vs. $106, $P<0.05$) compared with the AC cohort. Monthly total costs were not significantly different between the cohorts.

CONCLUSIONS: Initiation of FSC compared with AC after a moderate COPD exacerbation was cost-effective and associated with better clinical outcomes.

■ Outcomes Associated with Use of Mealtime Insulin Pens Versus Vials in Patients with Type 2 Diabetes

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BACKGROUND: For patients with type 2 diabetes (T2DM), adherence to their antidiabetic therapy and health outcomes may be affected by the method of delivery.

TABLE	Adjusted Hazard of COPD Exacerbations		
	Reference is AC		
Exacerbation Type	**Adjusted Hazard Ratio[a]**	**95% CI**	**P Value**
Phy + Rx	0.69	0.43-1.10	0.118
Hospitalization/ER	0.24	0.07-0.84	0.026[b]
Any exacerbation	0.58	0.38-0.91	0.017[b]

[a]*Adjusted for pre-index characteristics: gender; age at index; U.S. geographic region (categorized as Midwest, South, West, and reference category East); Charlson comorbidity index score; number of SABA canisters; number of OCS Rx; comorbid conditions including asthma, upper respiratory tract infection, lower respiratory tract infection; use of home oxygen therapy; and physician specialty on the index date (categorized as pulmonary/allergy specialist versus any other specialty).*
[b]*P < 0.05.*
AC = anticholinergic; CI = confidence interval; COPD = chronic obstructive pulmonary disease; ER = emergency room; OCS = oral corticosteroid; Phy + Rx = COPD-related physician visit with oral corticosteroid or antibiotic pharmacy claim within 5 days of physician visit; Rx = pharmacy claim; SABA = short-acting beta-agonist.

OBJECTIVE: To compare medication adherence, hypoglycemic events, and changes in hemoglobin A1c levels among adults with T2DM who initiate therapy with mealtime insulin disposable pens or vials.

METHODS: Data for this study were obtained from the i3 inVision database over the time period from January 1, 2006, through June 30, 2010. Patients with T2DM who initiated mealtime analog insulin via vial or disposable pen were included in the study, with first such use identified as the index date. Patients were excluded from the analyses if they switched method of delivery or used cartridge mealtime insulin, 3 ml vials of mealtime insulin, inhaled insulin, or an insulin pump. Additionally, patients were required to not be diagnosed with type 1, secondary, or gestational diabetes. Finally, patients were required to have continuous insurance coverage from 6 months prior to the index date through 12 months post-index date and to be at least aged 18 years. Multivariate analyses were conducted to examine the impact of pens versus vials on patient adherence (as proxied by the medication possession ratio [MPR] and days persistence on intent-to-treat [ITT] medication regimen) and changes in A1c values, while controlling for a wide range of other factors that may be associated with patient outcomes, including patient demographic and clinical characteristics. Results are reported for the 12-month period following mealtime insulin initiation.

RESULTS: There were 8,374 individuals who fit the study criteria (4,429 initiated on pens and 3,945 on vials). After controlling for patient characteristics, general health, and amount of copayment associated with medication of interest, results indicated that initiation on pens was associated with a 19% increase in the likelihood of having an MPR of at least 0.80 (odds ratio [OR]=1.186; 95% CI=1.065-1.320) as well as 7% increase in MPR ($P<0.001$) and 31-day longer period of persistence ($P<0.001$). There was no difference between the 2 cohorts on the likelihood of having a hypoglycemic event in the post-period (OR=0.904; 95% CI=0.755-1.082). For patients who had at least 1 valid A1c test in both the pre-period and post-period (N=760), initiation on pen therapy, compared with those who initiated on mealtime vial insulin, was associated with a 0.38 point reduction in A1c scores ($P=0.018$).

CONCLUSIONS: Results from this retrospective study indicate that the use of mealtime insulin via disposable pens, compared with vials, was associated with statistically significant improvements in adherence to therapy, a statistically significant reduction in A1c values, and no change

in the likelihood of hypoglycemic events. Future work will examine the cost implications of these results.

■ Patterns of Response to TNF Inhibitors by Mode of Administration from the CORRONA Registry: Implications for Treat-to-Target Strategies

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BACKGROUND: The Consortium of Rheumatology Researchers of North America (CORRONA) is a noninterventional patient registry which does not impose treatment guidelines nor targets. An international task force recently published rheumatoid arthritis (RA) treat-to-target (TTT) objectives, promoting remission and low disease activity (LDA). Published evidence on Clinical Disease Activity Index (CDAI) suggests a threshold of < 10 for LDA, and a change of at least 10 points is clinically meaningful. There is increasing focus on the importance of TTT in rheumatology. Implications of TTT strategies on discontinuation of medication remain unknown.

OBJECTIVE: To examine patterns of response versus published TTT objectives in RA patients initiating an intravenous (IV) or frequently dosed subcutaneous (SQ) tumor necrosis factor inhibitor (TNFi).

METHODS: Biologic naïve RA patients initiating an IV (infliximab) or SQ (adalimumab or etanercept) TNFi in the CORRONA registry were followed for 36 months. Raw data on 2 patient cohorts—Maintainers (defined as no change in TNFi over first 24 months, so that IV vs. SQ TNFi treatment is distinct) and Total patients—are reported here. Response was measured using the CDAI from initiation to 36 months. CORRONA has capacity to collect data at approximately 6-month visit intervals. Overall change over time, proportion of patients achieving low disease activity (LDA), and proportion experiencing clinically significant change in CDAI were calculated.

RESULTS: A total of 820 (288 IV; 532 SQ) patients met inclusion criteria. For Total patients cohort, IV patients had a significantly worse starting CDAI score than SQ patients (CDAI difference = 3.52, $P = 0.001$), although by 6-month visit, there was no difference in mean CDAI between groups. Both IV and SQ patients experienced significant improvement in CDAI scores at each visit versus initiation (baseline). At each visit from 18 months on, change versus baseline was significantly greater for IV versus SQ (modeled, unadjusted maximum difference in CDAI change = 3.2 points). For Maintainers cohort, IV patients were significantly older, had more patients covered under Medicare insurance, and had a significantly higher starting CDAI than SQ patients (CDAI difference = 5.19, $P < 0.001$). In Maintainers with a starting CDAI > 10 and ≤ 22, unadjusted proportion of patients achieving clinically important change from baseline was greater for IV versus SQ patients at 12 months when maintained to 24 months (45% vs. 35%, respectively). In the same subcohort, 61% of SQ patients attained TTT objective of LDA versus 61% of IV patients. Results were consistent in a subset of patients with data at all visits. Differences between cohorts may have resulted from differences in severity and population demographics.

CONCLUSIONS: Patients initiating IV versus SQ in real life are clinically and demographically different. Without compensation, more IV patients may have been discontinued using threshold TTT goals, yet they continued to experience improvement in outcome. TTT objectives for continuation of therapy should consider disease activity at baseline

and improvement in outcome in conjunction with threshold values or consider longer periods before switching treatment, as baseline values may be correlated with achievement of LDA thresholds. Further analysis based on adjusted baseline differences is warranted.

■ Pharmacist-Led Intervention to Improve Clinical Outcomes in Diabetic Patients

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BACKGROUND: A medication management program (MMP) was implemented by Scott & White Health Plan to assist diabetic patients. The MMP was led by pharmacists, who provided counseling on diabetes-related topics and monitored diabetes medications and lab measures during monthly patient visits. Patients signed an agreement stating that they would participate in monthly follow-up visits at the pharmacy; in exchange, they received copayment waivers for all their diabetic medications and supplies.

OBJECTIVE: To determine the effectiveness of the MMP with regards to diabetes control (i.e., hemoglobin A1c measures) and medication adherence (i.e., medication possession ratio [MPR]) to oral diabetic medications.

METHODS: Pharmacy claims data and medical lab values were used to enroll subjects in the MMP and to identify possible candidates to be used as controls. Patients included in the study had to meet the following criteria: (a) at least 1 year of diabetes diagnosis; (b) an A1c level > 7.5% at baseline; (c) at least 6 months of enrollment prior to baseline; (d) continuous enrollment throughout the study interval; (e) aged 18 to 63 years; and (f) at least 1 diabetic medication claim prior to and after enrollment. Enrolled patients and controls were matched 1:1 based on age, gender, baseline A1c, time of enrollment, and Charlson comorbidity index (CCI). The follow-up for matched patients consisted of 2 years, but 1-year outcomes were also looked at to determine short-term effects. Paired t-tests were use to compare changes in A1c and MPR pre- and post-implementation within groups and independent t-tests to assess whether significant differences could be found between groups.

RESULTS: A total of 163 pairs of patients were identified. At baseline, patients in the MMP and controls had a mean A1c value of 9.26% (SD = 1.36) and 9.24% (SD = 1.36), respectively. Assessment of intragroup changes pre- and post-enrollment revealed significant improvements as A1c decreased to a mean of 8.16% (SD = 1.43, $P < 0.001$) in the enrolled group and to 8.57% (SD = 1.75, $P < 0.001$) in the control group. More importantly, when gauging the actual effectiveness of the MMP by comparing the level of improvement in the intervention group to the control group, a significant difference was detected ($P = 0.026$). One year of post-implementation showed significant improvement in MPR within the enrollees (0.748 to 0.786, $P = 0.049$) but not for the controls (0.750 to 0.736, $P = 0.454$). The difference between the groups trended towards significance ($P = 0.052$). At 2-year follow-up, MPR decreased to 0.663 and 0.626 in the intervention and control group, respectively, and no significant difference between the 2 was found.

CONCLUSIONS: The MMP significantly improved A1c measures over 2 years in enrolled patients and between both groups, highlighting the clinical success delivered by this pharmacist-led intervention program. Since no difference in medication adherence was seen, the significant improvement in A1c in the intervention group appears to be attributable

to other aspects of the MMP services (i.e., monthly education visits and improved self-management skills).

Poor Symptom Control with Short-Acting Inhaled Medications in Nursing Home Residents with COPD

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BACKGROUND: Long-acting maintenance medications have been shown to reduce exacerbations and reduce daily symptom severity and frequency in patients with chronic obstructive pulmonary disease (COPD). It is well known that nursing home residents with COPD and cognitive impairment face administration challenges with many short-acting (SA) and long-acting (LA) beta-agonist (BA) medications in handheld inhaler devices (HHD). Patients with moderate-to-severe cognitive impairment may be better suited for nebulized dosage formulations when HHD use is compromised.

OBJECTIVE: To determine the prevalence of shortness of breath in a cohort of cognitively impaired nursing home residents with COPD based on their use of inhaled BA medications.

METHODS: Using a linked data extract of Minimum Data Set (MDS) 2.0 information and pharmacy claims from October 1, 2009, through September 30, 2010, nursing home patients with a diagnosis of COPD were evaluated retrospectively for the presence of medications and shortness of breath. Cognitive function was determined using MDS fields for calculation of the Cognitive Performance Scale (CPS), a 7-point likert scale where 0 is intact and 6 is very severe impairment. HHD and nebulized (neb) SABA and LABA use was evaluated in patients with moderate (CPS = 3), moderately severe (CPS = 4), severe (CPS = 5), and very severe (CPS = 6) cognitive impairment and assessed for the presence of shortness of breath (SOB) on MDS (item J1l).

RESULTS: A total of 126,121 unique patients had at least 1 MDS assessment, and 27,106 (21.5%) of these patients had COPD. SOB was present in 33% of COPD patients receiving COPD medications, and 40% had moderate-to-severe cognitive impairment. Monotherapy with SABA was evident among patients with moderate, moderately severe, and severe/very severe cognitive impairment at rates of 47.9%, 48.1%, and 51.6%, respectively. Neb SABA monotherapy was identified in 36.4% of COPD patients with moderate cognitive impairment; 40.4% exhibited SOB. In patients with moderately severe cognitive impairment, neb SABA monotherapy was the most prevalent COPD treatment, seen in 40.9% of patients, 37.5% of whom exhibited SOB. Neb SABA monotherapy was the most prevalent (46%) COPD treatment in patients with severe/very severe cognitive impairment, and 37.1% of these patients exhibited SOB. HHD SABA monotherapy was identified in 6.3%, 4.3%, and 2.8% of COPD patients with CPS scores of 3, 4, and 5 or 6, respectively. The corresponding presence of SOB was 25.5%, 33.9%, and 29.8% of HHD SABA monotherapy-treated patients with moderate, moderately severe, and severe cognitive/very severe impairment. LABA monotherapy or combined LABA/SABA use represented ≤ 1% of BA use for COPD patients with CPS scores of 3, 4, 5, or 6.

CONCLUSIONS: COPD nursing home patients are a special population at increased risk of SOB. The most common form of treatment is monotherapy with SABAs, which according to the GOLD guidelines is not indicated for maintenance in moderate and more severe stages of the disease. This may be contributing to the high incidence of SOB in this population. Because of the prevalence of cognitive impairment in nursing home residents with COPD, LA nebulized BAs should be a consideration to provide better symptom control.

Prescription Savings Club Membership Drives Medication Adherence

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BACKGROUND: National community pharmacies are providing an opportunity for customers to participate in a Prescription Savings Club (PSC) program that facilitates the purchase of discounted prescriptions, health care products, and services. Although the monetary benefits of participating in such a program are readily apparent, no studies have assessed the impact of membership programs on patient adherence to prescriptions used to treat diabetes.

OBJECTIVE: To compare adherence to chronic prescription medications used to manage diabetes for customers enrolled in a PSC program with those who were not enrolled. It was hypothesized that PSC members would be more adherent to their diabetes medications than nonmembers.

METHODS: A retrospective review of pharmacy claims for diabetes medications from a national community pharmacy chain was conducted. Customers who were enrolled in the PSC program anytime from January to December 2009 were included in the PSC group. This group was propensity matched with nonenrollees on demographics (age and sex) and presence of multiple drug class therapies. Prescriptions were grouped according to generic product identifier group (GPI-2 level classification per MediSpan), and adherence was measured by a medication possession ratio (MPR) metric computed over a 1-year period.

RESULTS: The propensity model based on a 1:1 case matching resulted in 7,533 PSC and 7,533 non-PSC members (see table). Overall, medication adherence (mean MPR) on chronic diabetes medications for PSC program members (77.9%) was found to be 9.8% significantly higher than for those who never enrolled in the PSC program (68.0%; t14,722 = 26.4, $P < 0.001$). Subgroup analysis based on payment types demonstrated higher adherence levels (7.5%) for PSC members who used their PSC cards exclusively during the 1-year follow-up period (75.7%) compared with those nonmembers who solely relied on third-party payments (68.1%; t3,004 = 12.6, $P < 0.001$). Finally, PSC members who alternated PSC and third-party payments had a significantly higher MPR (82.8% vs. 68.1%) than nonmembers with only third-party payments (t8,458 = 34.1, $P < 0.001$).

CONCLUSIONS: Comparison of adherence with medication levels for PSC members and nonmembers revealed significantly higher levels of MPR among members. Differences in adherence held even for nonmembers covered through third-party payments compared with PSC members who solely used their cards for payments or to those PSC members who used either the card or third-party payment option. Results suggest a plausible connection between loyalty program membership and higher medication adherence levels for antidiabetic prescription purchases in the community. Previous research has shown that nonadherence to therapeutic regimens can lead to detrimental health outcomes and increased health care expenditures. This study indicates that prescription membership programs can positively influence adherence with diabetes medications.

TABLE Summary of Mean Adherence (MPR) by Customer Segment

Payment Segmentation by Cohorts	Customer Count n (%)	Mean MPR [SD]
PSC	7,533	77.9 [21.1]
PSC card only	1,788 (23.7)	75.7 [22.0]
PSC card and third party	3,294 (43.7)	82.8 [18.1]
Other[a]	2,451 (32.5)	
Non-PSC	7,533	68.0 [24.6]
Third party only	7,113 (94.4)	68.1 [24.6]
Other[a]	420 (5.5)	

[a]Other includes payment mix with cash, non-PSC cash only, or PSC third party only. MPR = medication possession ratio; PSC = Prescription Savings Card; SD = standard deviation.

■ **Presence of Comorbid Diseases and Use of Concomitant Drugs That Are Contraindicated or Could Potentially Complicate Treatment When Used with Gout Drugs in Patients with Frequent Gouty Arthritis Attacks**

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BACKGROUND: Gouty arthritis attacks typically require drug therapy. However, the presence of certain comorbidities and concomitant drugs can complicate, even limit, gout treatments due to contraindications, drug-drug interactions, safety warnings, or precautions.

OBJECTIVE: To examine the frequency of contraindications and potentially complicating treatment situations in patients with frequent gouty arthritis attacks compared with patients with infrequent attacks.

METHODS: We used the Medstat MarketScan Commercial Claims and Encounter database to identify patients older than 18 years with ICD-9-CM codes for gout (274.xx) or at least 1 pharmacy claim for specific gout-related drugs (allopurinol, febuxostat, probenecid, or colchicine) between July 1, 2005, and June 30, 2010. The date of the first diagnosis or pharmacy claim was the index date. Patients were required to have at least 12 months pre- and post-enrollment data from the index date. Patients were categorized as frequent gouty arthritis (at least 3 attacks within 1-year post-index) using a claims-based algorithm and were compared with patients with infrequent gouty arthritis (less than 3 attacks) who were matched in a 1:2 ratio on age, sex, and geographic region. Frequency of contraindications and complicated treatment situation (comorbid diseases, drug interactions, dose limitation) based on product labeling were assessed (see table).

RESULTS: We identified 5,223 patients with at least 3 (frequent) and 10,446 patients with less than 3 (infrequent) gouty arthritis attacks. The mean age was 58 years, and 77.3% were men. Patients with frequent gouty arthritis had a higher prevalence of contraindications than patients with infrequent attacks: colchicine (0.79% vs. 0.48%, $P = 0.02$); nonsteroidal anti-inflammatory drugs (NSAIDs; 23.4% vs. 17.5%, $P < 0.001$); febuxostat (0.33% vs. 0.37%, $P = 0.56$); probenecid (1.4% vs. 0.7%, $P < 0.001$). Patients with frequent attacks also had a higher prevalence of potential complicating treatment situations than patients with infrequent gout: colchicine (47.1% vs. 46.5%, $P = 0.47$); NSAIDs (91.2% vs. 78.0%, $P < 0.001$); corticosteroids (96.4% vs. 87.3%, $P < 0.001$); allopurinol, (51.% vs. 41.2%, $P < 0.001$); feboxostat (0.61%

TABLE Contraindications and Potentially Complicating Situations with Gout Pharmacotherapy

Gout Therapy	Contraindications	Potential Complicating Situations
NSAIDs	• History of CKD (stages 3, 4, 5); heart failure; or GI ulcer or bleeding • Use of warfarin	• History of cardiovascular disease, CKD (stage 1 or 2, including hypertensive and diabetic), or hypertension • Use of ACE inhibitor, ARB, aspirin, beta-blocker, corticosteroid, or diuretic
Colchicine	• History of CKD AND use of a strong CYP3A4 inhibitor[a] or P-glycoprotein inhibitor;[b] or chronic liver disease AND use of a strong CYP3A4 inhibitor[a] or P-gp inhibitor[b] • Use of a P-gp inhibitor[b] or strong CYP3A4 inhibitor[a]	• History of CKD AND moderate CYP3A4 inhibitor[c]; or chronic liver disease AND moderate CYP3A4 inhibitor[c] • Use of digoxin, fibrate (gemfibrozil, fenofibrate, fenofibric acid), moderate CYP3A4 inhibitor,[c] or statin (atorvastatin, simvastatin, pravastatin, fluvastatin)
Corticosteroids	• None	• History of diabetes; dyslipidemia; heart failure; hypertension; or upper GI ulcer or bleeding • Use of aspirin, digoxin, NSAIDs, or warfarin
Allopurinol	• None	• History of CKD (stage 3, 4, and 5) or chronic liver disease • Use of azathioprine, amoxicillin, ampicillin, chlorpropamide, cyclosporine, mercaptopurine, or thiazide diuretic
Febuxostat	• Use of azathioprine or mercaptopurine	• Use of theophylline
Probenecid	• History of blood dyscrasias (hemolytic anemia) or uric acid kidney stones	• History of CKD, GI ulcer, or gastric esophageal disease

[a]Strong CYP3A4 inhibitors: atazanavir, clarithromycin, darunarvir with ritonavir, indinavir, itraconazole, ketoconazole, lopinavir with ritonavir, nefazodone, nelfinavir, ritonavir, saquinavir with ritonavir, telithromycin, or tipranavir with ritnonavir.
[b]P-glycoprotein inhibitors: cyclosporine or ranolazine.
[c]Moderate CYP3A4 inhibitors: diltiazem, verapamil, amprenavir with ritonavir, or fodamprenavir with ritonavir.
ACE = angiotensin enzyme-converting; ARB = angiotensin receptor blocker; CKD = chronic kidney disease; CYP = cytochrome P450; GI = gastrointestinal; NSAIDs = nonsteroidal anti-inflammatory drugs.

vs. 0.39%, $P = 0.08$); probenecid (8.1% vs. 12.9%, $P < 0.001$). The use of drugs known to cause/worsen gout was more common in patients with frequent attacks than infrequent attacks (46.1% vs. 38.7%, $P < 0.001$).

CONCLUSIONS: Our findings indicated that patients with frequent gouty arthritis attacks presented with an increased prevalence of comorbid diseases and concomitant drug use that are contraindicated or could lead to potential complications when used concurrently with gout therapies.

■ Real-Time Risk Prediction and Outpatient Pharmacy-Based Diabetic Intervention Program Improves Diabetic Care Management

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BACKGROUND: Two outpatient pharmacies located on the University of Toledo's (UT) campuses provide 80% of the medications consumed by UT's population. UT's pharmacy benefits manager (PBM), informedRx, utilizes the Johns Hopkins ACG-PM risk methodology to provide real-time risk scoring to its clients. UT coupled real-time risk prediction with an innovative pharmacy-based intervention program to improve the overall management of diabetes in the UT population.

OBJECTIVE: To demonstrate that an outpatient pharmacy can use risk prediction and pharmacy data to target a cohort of patients and positively influence diabetic care management.

METHODS: Real-time risk prediction, based on pharmaceutical information, was utilized to identify diabetic members of the UT population for pharmacy outreach interventions aimed at improving medication adherence, guideline compliance, and disease management of their diabetes. The program consisted of 3 components, building on each other, that increased the intensity of the intervention. In Phase I, an automated system within informedRx generated a letter to the prescribing physicians of patients missing American Diabetic Association guideline recommended preventive medications. In addition, members were sent automated refill reminder letters when refills for oral antidiabetic medications were late. In Phase II, prescribers for patients persistently lacking the identified medications were contacted by phone by UT pharmacy students. In Phase III, pharmacy prior authorization stops incorporated into the PBM claims processing system alerted the pharmacist to diabetic members with guideline gaps in care. Pharmacists trained in motivational counseling techniques then provided targeted and tailored education materials at the point of sale.

RESULTS: Over the course of 1 year, 80% of the UT diabetic population was identified for inclusion in the program based on total health care risk scores (n=361). At least 1 intervention was provided to 90.6% of the identified members. Targeted medications were initiated in 14.7% of 442 guideline letters. A cohort study of 301 of 991 adherence letters demonstrated a 2.4% increase in medication adherence over time (P=0.018). Information gathered from 110 physicians regarding 187 patients in Phase II indicated that 25% of the physicians would discuss the recommendations with the patient at the next visit. Side effects, sampling, and clinical decisions were cited as reasons for not initiating the medication in 42% of the patients. Initial analysis of Phase III indicates that the majority of patients are open to talking with their pharmacists about their diabetes (108 of 138 encounters). Pharmacists counseled patients on recommended medications in 85% of the encounters and provided information on diabetic management and available services, such as free meters, in 68.5% of the encounters.

CONCLUSIONS: The combination of automated letters, physician outreach, and point-of-sale counseling in an outpatient pharmacy improves the pharmaceutical management of persons with diabetes. Access to real-time risk information, pharmaceutical profiles, and motivational counseling materials demonstrate that improvements in the overall management of complex disease states such as diabetes can be cost-efficient and obtainable.

■ Real-World Outcomes of Switching from Vial/Syringe to Disposable Pen Among Elderly Patients with Type 2 Diabetes Mellitus Who Were Treated with Insulin Glargine

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BACKGROUND: Insulin pens that combine a syringe and insulin cartridge may help patients with type 2 diabetes mellitus (T2DM) and their care givers to overcome physical and psychological barriers associated with the use of traditional syringes and insulin vials. In insulin-naïve patients, initiating insulin via pens instead of vials has been associated with better clinical and economic outcomes and improved adherence to therapy. However, data on elderly patients are currently lacking.

OBJECTIVE: To evaluate outcomes of switching from vial to disposable pen among U.S. elderly patients with T2DM who were treated with insulin glargine.

METHODS: This is a retrospective cohort database study. The MarketScan Medicare database was used to identify T2DM patients aged 65 years or older and treated with insulin glargine vial or disposable pen from January 2007 through June 2009. The study cohort, Pen Switchers, included patients switching to disposable pen after at least 2 prior vial usages, and the first pen usage was assigned as the index event. The control cohort, Vial Continuers, included patients continuing to use vial-only after at least 2 vial usages and a vial claim subsequent to the second vial usage was randomly assigned as the index event. All patients had continuous health plan coverage for 6 months before (baseline) and 1 year after the index date (follow-up). To minimize selection bias, stringent 1:1 propensity score matching was used to balance the 2 cohorts using baseline demographic, clinical characteristics, medication treatment, and health care utilization.

RESULTS: The study included 1,996 matched patients (n=998 each cohort, mean age 73 years, 49% women, Charlson comorbidity index 1.18, number of oral antidiabetic drugs 0.88: 30.6% metformin, 4.5% exenatide). During the 1-year follow-up Pen Switchers were more persistent (65.3% vs. 56.8%, P<0.001) and adherent (adjusted medication possession ratio: 0.82 vs. 0.79, P=0.003) than Vial Continuers on overall usage of insulin glargine. Hypoglycemia rates were similar (14.4% vs. 16.1%, P=0.290). Furthermore, both cohorts incurred similar total health care costs ($24,211 vs. $26,164, P=0.223), but Pen Switchers had significantly lower all-cause hospitalization rate (0.44 vs. 0.52, P=0.042), length of hospital stay (2.69 vs. 3.55 days, P=0.023), and diabetes-related hospitalization costs ($2,252 vs. $3,318, P=0.038), despite higher diabetes medication costs ($3,041 vs. $2,635, P<0.001).

CONCLUSIONS: This real-world study suggested that among elderly T2DM patients treated with insulin glargine, switching from vial to disposable pen may be associated with higher overall insulin glargine treatment adherence and persistence, lower hospitalization rate, and lower diabetes-related hospitalization costs, which offset the higher medication cost with disposable pen. These results may have the potential to assist with treatment decisions and help optimize management of T2DM but need to be confirmed in future pragmatic randomized clinical trials.

■ Reasons for Discontinuation of Subcutaneous Biologic Therapy in the Treatment of Rheumatoid Arthritis: A Patient Perspective

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BACKGROUND: Several factors may lead to discontinuation of biologic therapies by patients with rheumatoid arthritis (RA). The role of these factors in discontinuation of therapy should be examined to determine how best to achieve successful and uninterrupted treatment.

OBJECTIVE: To examine reasons for discontinuation of subcutaneous (SQ) anti-tumor necrosis factor (TNF) treatment in the past 12 months from the RA patient perspective.

METHODS: Data were collected in spring 2011 using self-reported, Internet-based questionnaires. Study inclusion criteria were RA diagnoses; discontinuation of SQ anti-TNF medication (adalimumab, certolizumab, etanercept, or golimumab) within the past 12 months; aged 18 years or older; reside in the United States; consented to participate. Patients reported primary and other reasons for discontinuation. Patients who discontinued more than 1 SQ anti-TNF in the past 12 months reported on the one most recently discontinued.

RESULTS: Completed questionnaires were analyzed for 250 patients. The majority were female (72.8%) and white (80.8%); median age was 51 years. More patients most recently discontinued etanercept (43.6%) or adalimumab (39.2%) than certolizumab (9.6%) or golimumab (7.6%). When prompted about the primary reason for discontinuation, lack of effectiveness (40.8%) was most often cited, followed by injection experience (18.4%; see table). Combining prompted primary and other reasons for discontinuation, 60.8% reported lack of effectiveness, and 40.8% reported injection experience. These injection experience reasons included pain/burning/discomfort after injection (14.4%), pain/burning/discomfort during injection (13.2%), injection reactions such as redness/swelling after injection (12.4%), dislike self-injection (11.6%), dislike frequency of injection (10.4%), fearful of injection/needles (6.8%).

CONCLUSIONS: From the patient perspective, there are remaining unmet needs related to effectiveness and injection experience with SQ anti-TNF medications, which lead to discontinuation. Newer treatment options may address some of these unmet needs. These results demonstrate the importance of including the patient perspective when making access and coverage decisions.

TABLE	Patient-Reported Reasons for Discontinuation of SQ Anti-TNF in Past 12 Months (n = 250)	
Reasons	**Primary Reason[a] (%)**	**Other Reason[b] (%)**	**Combined Primary and Other Reasons[b] (%)**
Lack of effectiveness	40.8	27.6	60.8
Injection experience	18.4	34.0	40.8
Cost or reimbursement issues	12.0	21.2	27.6
Safety	11.6	17.6	26.0
Remission (partial or complete)	7.2	3.2	10.4
Other	10.0	9.2	19.2

[a]Primary reason for discontinuation.
[b]Sums to greater than 100% due to multiple response.
SQ = subcutaneous; TNF = tumor necrosis factor.

■ Recent Trends in the Prevalence of HCV-Infected Medicare Patients and the Associated Cost Burden

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BACKGROUND: Hepatitis C virus (HCV) infection had an estimated prevalence of 3.6 million patients in the United States in 2008. Of the estimated 1.1 million diagnosed chronic HCV patients, approximately 280,000 were covered by Medicare, presenting a significant burden to the public health system.

OBJECTIVE: To determine the number of HCV patients with and without advanced liver disease (ALD) complications (cirrhosis, decompensated cirrhosis, liver cancer, liver transplant) covered by Medicare and the associated costs between 2007 and 2009 (see figure on next page).

METHODS: The Medicare claims database (100% claims from inpatient and outpatient settings and 5% carrier data) was analyzed to determine the prevalence of HCV-infected patients with and without ALD as identified using ICD-9-CM codes and the associated treatment costs in 2007-2009, stratified into 5-year birth cohorts. Carrier data were projected and adjusted to remove any duplicate patient claims.

RESULTS: Between 2007 and 2009, the estimated number of diagnosed Medicare HCV patients grew from 272,304 to 289,806 (annual growth rate of 3.2%); 68.9% of patients were under the age of 65 in 2009, representing a group with severe disability and/or end stage renal disease. This group experienced a rapid progression to liver complications, growing at an annual rate of 9.5% from 35,157 to 42,182 ALD patients in 2007 and 2009, respectively. In this group, progression towards ALD also significantly outpaced the influx of newly diagnosed patients (overall annual growth of 2.6%). In contrast, the overall number of HCV Medicare patients aged 65 and older decreased from 97,106 to 90,188 at an annual rate of -3.6%, as a result of increased mortality rate in this cohort. Correspondingly, the overall estimated cost of patients aged 65 and older remained nearly constant at $0.8 billion, while the cost of HCV patients under the age of 65 to Medicare grew from $1.9 billion to $2.3 billion (annual growth rate of 10.0%).

CONCLUSIONS: The majority of HCV-infected Medicare patients are under the age of 65. As a result of their large number and rapid progression to ALD, the Medicare system experienced an increase of $400 million in overall HCV-related treatment costs from 2007 to 2009. In contrast, HCV-related Medicare treatment costs for patients aged 65 and older remained relatively constant in the same period primarily due to the accelerated mortality of elderly HCV patients.

■ Relative Effectiveness of Chemotherapy in Elderly Versus Nonelderly Stage III Colon Cancer Patients: A Systematic Review

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BACKGROUND: The effectiveness of chemotherapy in clinical practice may differ from the efficacy demonstrated in clinical trials, particularly among populations that are underrepresented in clinical trials, such as elderly patients.

OBJECTIVE: To examine the relative effectiveness of chemotherapy

FIGURE Number of Medicare HCV Patients and the Associated Costs in 2009
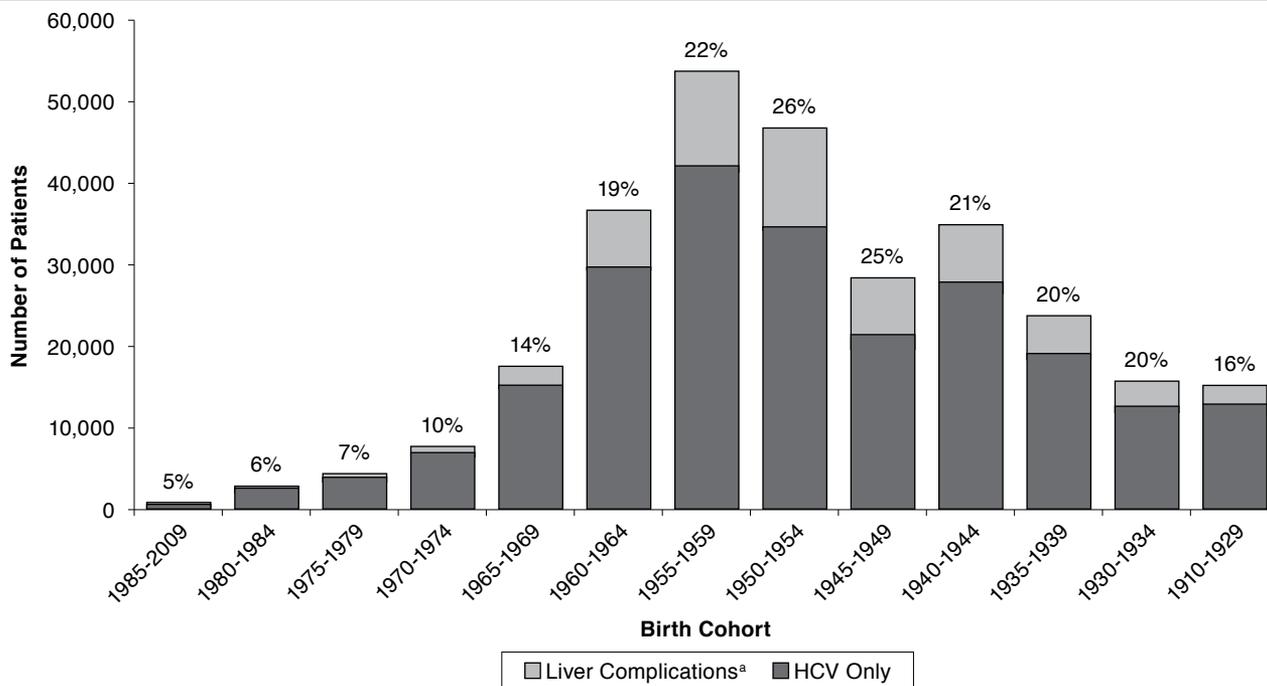
[a]Values indicate overall percentage of patients in each cohort with liver complications (cirrhosis, decompensated cirrhosis, liver cancer, liver transplant).
HCV = hepatitis C virus.

for stage III colon cancer among "real world" elderly versus nonelderly patients.

METHODS: A systematic literature review was conducted using the Agency for Healthcare Research and Quality (AHRQ) approach. Literature searches were performed in Medline and Evidence Based Medicine Reviews databases. All chemotherapy regimens approved for stage III colon cancer were reviewed. Various effectiveness and safety outcomes were extracted.

RESULTS: From 707 identified articles, 29 articles provided 38 reports of relative effectiveness of chemotherapy among elderly versus nonelderly patients. Three of 13 reports showed lower overall survival treatment effects, while 1 of 5 and 1 of 4 reports indicated higher treatment effects for time-to-progression and overall response rate. Chemotherapy treatment effects for grade 3 or 4 adverse events were higher among elderly patients for cardiac disorder (2/5 reports), leukopenia (1/5), neutropenia (4/16), thrombocytopenia (2/13), febrile neutropenia (1/4), infection (2/10), dehydration (2/6), diarrhea (6/20), and fatigue (6/13). Lower treatment effects among elderly patients were reported for neutropenia (2/16), nausea/vomiting (1/16), and neuropathy (1/9).

CONCLUSIONS: The majority of the evidence suggests that chemotherapy has similar effectiveness and safety in elderly versus nonelderly stage III colon cancer patients. When differences are reported, treatment effects are more often worse among the elderly.

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■ **Repository Corticotropin Injection: Cost Analysis and Utilization Management Opportunity Assessment**

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BACKGROUND: Repository corticotropin injection (Highly Purified [H.P.] Acthar Gel) is an adrenocorticotropic hormone (ACTH) analogue which stimulates the adrenal gland to release cortisol, the body's natural glucocorticosteroid. Acthar Gel has a unique indication for infantile spasms (IS) in children under 2 years of age. Glucocorticosteroids have many of the same indications as Acthar Gel, for example, multiple sclerosis (MS), autoimmune disorders, adrenal insufficiency, and inflammatory disorders. The Acthar Gel manufacturer has specifically targeted marketing of its product for the treatment of MS relapse and nephrotic syndrome. Acthar Gel is administered via intramuscular injection, and the average wholesale price (AWP) for one 5 ml vial (80 units per ml) is $25,653. A typical adult dose is 80 units every 24 to 72 hours at an AWP cost of $5,131.

OBJECTIVE: To report Acthar Gel prevalence of use, utilizers diagnoses, prior corticosteroid use, and total expenditures using integrated medical and pharmacy claims data for a utilization management opportunity assessment.

METHODS: Acthar Gel pharmacy and medical claims data were identified among 3.9 million commercially insured continuously enrolled members during January 1, 2010, to December 31, 2010, using Medi-Span Generic Product Identifier (GPI) code beginning with 3030 and procedure code = J0800. Each member's earliest 2010 Acthar Gel claim

was set as the index date. Members were required to be continuously enrolled 365 days prior and 180 days post-index date (total 1.5 years continuous enrollment). Each member's medical and pharmacy claims in the 365 days prior to index date were queried to identify diagnoses and presence of prior corticosteroid use. Each member was assigned a diagnosis using the following hierarchical order: infantile spasm, MS, nephrotic syndrome, or other diagnosis. For each member, Acthar Gel claims and expenditures were summed during the 180 days post-index date.

RESULTS: During 2010, 30 members were identified with 43 combined pharmacy and medical Acthar Gel claims at a total paid amount of $1,214,923, of which 80.6% was pharmacy benefit expenditures and 19.4% was medical benefit expenditures. Infantile spasm diagnosis was found in 1 (3.3%) of 30 members; this member had a total Acthar Gel paid amount of $146,595 (12.6% of all Acthar Gel expenditures). MS diagnosis was found in 19 (63.3%) of 30 members; these members had a total paid amount of $768,620. Nephrotic diagnosis was found in 1 (3.3%) of 30 members; this member had a total Acthar Gel paid amount of $220,479. Nine (30%) of 30 members with a total paid amount of $79,229 (6.5%) had another diagnosis. Thirteen (43.3%) of 29 members did not have a corticosteroid claim in the 365 days prior to their Acthar Gel claim; the member with infantile spasm was excluded as glucocorticosteroids have not been studied in this population.

CONCLUSIONS: Prevalence of Acthar Gel use in 2010 was approximately 1 in 130,000 members. Average cost per member during the 180-day follow-up period was $40,497. Other than infantile spasms, glucocorticosteroids have been used successfully to treat the diseases/disorders for which Acthar Gel is indicated. If utilization of Acthar Gel had been limited to only infantile spasm, $1,068,382 total Acthar Gel expenditures could have potentially been avoided. If Acthar Gel use would have been denied due to no prior corticosteroid use, $694,572 of total Acthar Gel expenditures could have potentially been avoided. Consideration should be given to limiting use of Acthar Gel to members with an infantile spasm diagnosis or requiring a glucocorticosteroid prior to Acthar Gel.

■ Resolving Therapeutic Care Gaps in Community Pharmacies: The Illinois Project

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BACKGROUND: Poor adherence and medication under-utilization are common drug-related problems associated with poor outcomes and increased health care costs. Community pharmacists are in an optimal position to address these therapeutic gaps in care.

OBJECTIVE: To determine if the identification of therapeutic gaps in care from pharmacy claims data, notification of community pharmacists of therapeutic gaps in care, and intervention on those alerts results in increased gap closure, reduced time to gap closure, and reduced proportion of gaps reopening in the case of adherence gaps.

METHODS: This was a prospective, controlled, cluster randomized study. Study pharmacies were independently owned and located in Illinois. Patients were State of Illinois employees and beneficiaries of state health plans, which included spouses, children, and retired workers. For selected conditions and medications, adherence gaps were generated when medication possession ratio dropped to less than 80%, and the medication was not refilled, while omission gaps occurred when

an indicated medication was missing from a patient's profile. Gaps were identified via Medco's advanced clinical platform and sent as alerts to pharmacists in the intervention group only. Intervention group pharmacists were requested to resolve gaps in care through in-person or telephonic communication with the patient and/or communication with the physician as deemed appropriate. Gaps were considered "closed" with a subsequent claim for the medication (or an appropriate substitute for omission gaps). Adherence gaps "re-opened" if a second alert was generated for the same gap after closing. 410 gaps per comparison group were required to detect a difference in absolute gap closure rate of 10%, assuming alpha of 0.05 and power of 0.8. Prescriber, pharmacy, and patient characteristics were analyzed with summary statistics of counts and proportions. Adherence and omission gap closure over the 90-day study period were analyzed with Kaplan-Meier (KM) survival curve approach and Cox proportional hazards models including covariates. The study was approved by the University of Illinois at Chicago Institutional Review Board.

RESULTS: 45 intervention and 47 control pharmacies (1,445 intervention and 1,126 control patients) participated in the study. Pharmacy, patient, and provider characteristics were similar between groups. 1,433 intervention and 1,181 control adherence gaps were generated, while 677 intervention and 534 control omission gaps were generated. Pharmacists intervened on 639 (44.5%) adherence and 505 (74.6%) omission gaps. Gaps were closed more often in the intervention than control at 30 days (55.5% closure rate in intervention vs. 50.6% in control), 45 days (61.1% vs. 58.4%, respectively), 60 days (66.1% vs. 65.2%, respectively), and 90 days (73.0% vs. 72.9%, respectively). This result was statistically significant in the Cox proportional hazards model at 90 days (adjusted hazard ratio (HR)=0.805; P=0.022; 95% CI=0.722-0.897). Adherence gaps reopened less frequently in the intervention group (HR=1.159; P=0.012; 95% CI=1.033-1.301); 89 (13.1%) intervention and 29 (5.4%) control omission gaps closed within 90 days (adjusted HR=0.565; P=0.005; 95% CI=0.377-0.846).

CONCLUSIONS: Independent community pharmacists reduced gaps in care and had fewer reopened adherence gaps. A continuation study of this program will identify if long-term adherence is improved.

■ Results of an Antidepressant Step-Therapy Reject Mitigation Project: Physician Intervention

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BACKGROUND: In April 2009, Health Net restricted branded antidepressants and bupropion XL via prior authorization to promote generic antidepressant medication utilization. An electronic step-therapy edit allowed claims to process for the restricted drugs if a member had a recent history of using 1 of the preferred generic antidepressants. If a member failed to meet the electronic step-therapy requirement, the claim would reject at the point of service, possibly resulting in the member never receiving antidepressant therapy. To ensure members received an antidepressant, Health Net implemented an automated telephonic outreach program to contact members with unresolved rejected claims. The telephonic program resulted in a significant increase in members filling a prescription (absolute difference in fill rate between the 2 groups was 24.8% [P<0.050]) but did not avoid the gap in all patients. In April 2011, Health Net implemented a process to contact the member's physician if a prescription was not filled within 30 days of the rejected claim to inform them of the lack of therapy and continued gap in care.

| FIGURE | Flow Chart for Unresolved Antidepressant Reject Claims April 2011 Through September 2011 |

Antidepressant (AD) Electronic Step-Therapy (EST) Rejects: April 1, 2011, Through August 31, 2011
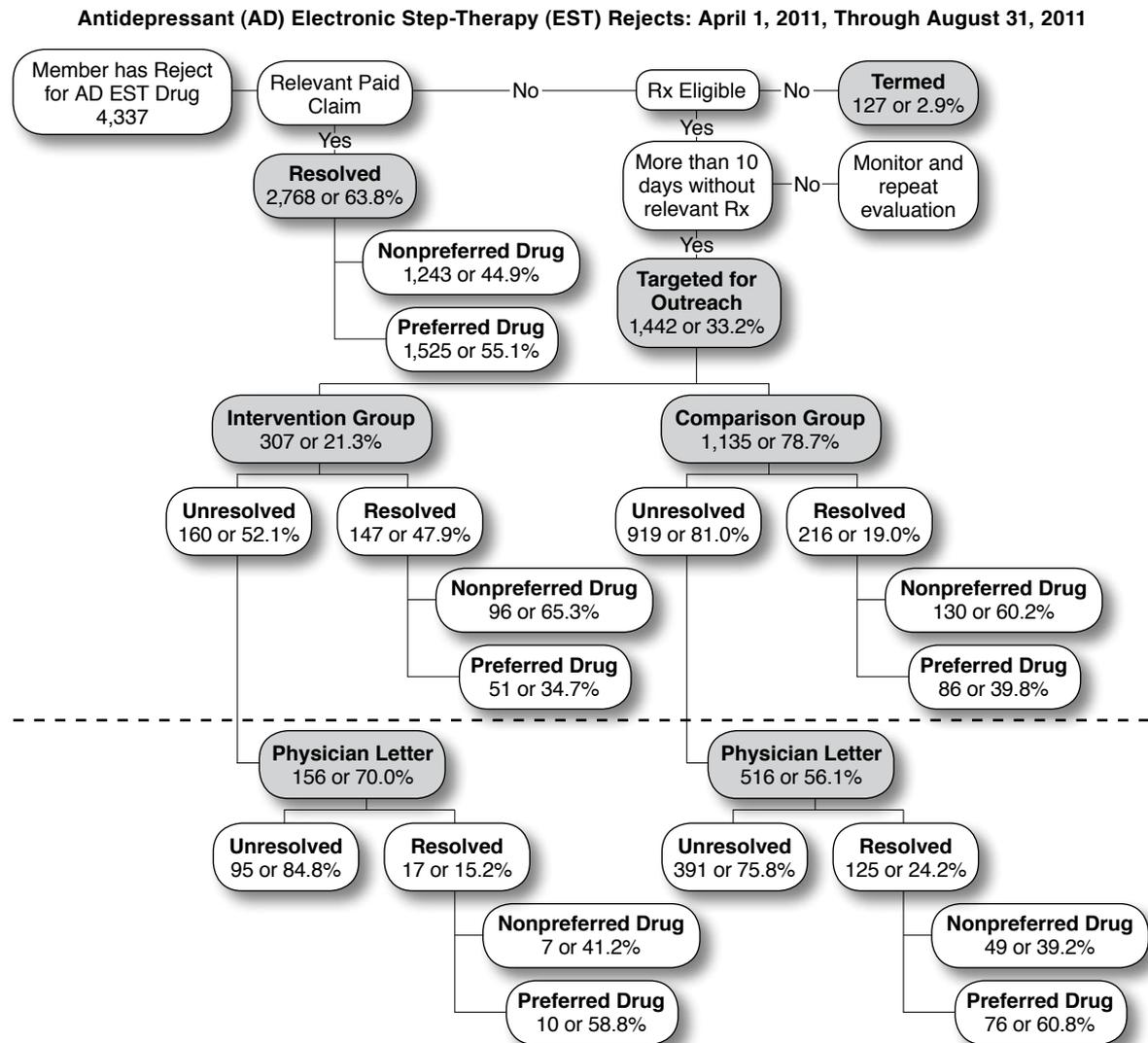
Rx = pharmacy claim.

OBJECTIVE: To determine if the physician follow-up letter for the telephonic outreach program increased the number of members who received an antidepressant beyond the member intervention.

METHODS: Members whose rejected claims remained unresolved after 30 days were identified, and the physicians of these members were contacted by mail or fax to inform them of the continued gap in care. Claims were analyzed again at day 60 to determine the success of the physician intervention.

RESULTS: Between April 1, 2011, and August 31, 2011, 1,442 members were identified for inclusion into the member intervention. A total of 672 members did not resolve their rejected claim after the first 30 days and were eligible for inclusion into the physician intervention population. Thirty days after the physician intervention, 142 (21%) of the physician intervention population had filled a prescription for an antidepressant.

CONCLUSIONS: The use of the physician intervention resulted in an increased number of resolved antidepressant claims and fewer members going without therapy. Limitations for this program include up-to-date phone records for members, up-to-date physician information, and the initial fill of the antidepressant medication for an off-label indication.

SPONSORSHIP: This research was conducted by Health Net, Rancho Cordova, CA, without external funding.

■ **Risk Factors Associated with Nonadherence of Disease-Modifying Drugs Among Patients with Multiple Sclerosis**

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BACKGROUND: Multiple sclerosis (MS) is a chronic condition affecting

approximately 400,000 people in the United States. Although disease-modifying drugs (DMDs) have shown proven efficacy in reducing relapse frequency, many patients struggle to adhere to therapy. It is important to understand the various factors associated with nonadherence, in order to achieve effective management of MS patients.

OBJECTIVE: To identify demographic and claims-based variables associated with medication nonadherence for MS patients prescribed self-injectable DMDs.

METHODS: Medical and pharmacy claims data were obtained from a large, national pharmacy benefits management company in the United States. Patients diagnosed with MS (at least 1 medical claim for MS [ICD-9-CM codes 340.xx]) between 2006 and 2009 were selected. Annual cohorts were created for patients with at least 1 prescription for a self-injectable DMD during the year, were aged 18 years or older, and had at least 12 months continuous enrollment before and after the first DMD prescription. Nonadherence was defined as proportion of days covered (PDC) <0.80 and medication possession ratio (MPR) <0.80. Naïve to DMD was defined as no DMD prescription in the prior year. Patient demographics, resource use, and out-of-pocket copayments were evaluated. Findings from annual cohorts from 2006-2009 were pooled to identify factors associated with DMD nonadherence using a generalized estimation equation (GEE) model, adjusting for the time-varying covariates and clustering effect of repeated measures.

RESULTS: Patient clinical and demographic characteristics were similar across annual cohorts; results from the most recent cohort were reported. 2,769 MS patients using a DMD in 2009 were identified (PDC: 62.3% adherent; MPR: 75.3% adherent, 14.5% were naïve to treatment). Nonadherent patients were significantly younger than adherent patients (47.5 vs. 50.6 years, $P<0.05$). In the year prior to the index date, nonadherers had a significantly higher rate of hospitalization (12.4% vs. 8.6%, $P<0.001$) and emergency room (ER) visits (18.3% vs. 14.3%, $P<0.05$) compared with adherers. The regression model with PDC <0.80 as the outcome suggested that the likelihood of nonadherence decreased with age. Patients with at least 1 hospitalization (odds ratio (OR)=1.14, 95% CI=1.00-1.30, $P<0.05$) or at least 1 emergency room (ER) visit (OR=1.19, 95% CI=1.07-1.33, $P=0.001$) in the year prior to the index date, or a higher copayment (≥$200; OR=1.25, 95% CI=1.05-1.49, $P<0.05$) were more likely to be nonadherent. The regression model with MPR <0.80 as the outcome also suggested that the likelihood of nonadherence decreased with age. Patients with at least 1 outpatient visit in the year prior to the index date (OR=0.87, 95% CI=0.78-0.97, $P=0.014$) were less likely to be nonadherent, while those with at least 1 ER visit (OR=1.22, 95% CI=1.08-1.38, $P=0.001$) or a higher copayment (OR=1.28, 95% CI=1.04-1.58, $P<0.02$) were more likely to be nonadherent.

CONCLUSIONS: MS patients may have challenges adhering to therapy. Demographic and claims-based variables associated with nonadherence are younger age, a history of hospitalization or ER visit, and a copayment of at least $200. Targeted educational programs are needed to emphasize the importance of medication adherence.

SPONSORSHIP: This research was funded by EMD Serono, Inc., Rockland, MA.

■ Role of Patient-Reported Outcomes in the Payer Evidence Evaluation Process

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BACKGROUND: As the pharmaceutical industry prepares to embark on what will be one of the most challenging decades in U.S. health care

FIGURE U.S. Payers Likely to Follow CMS Lead

If CMS publicly leverages the results of these studies, how likely are you to follow CMS's lead in utilizing PRO to guide your coverage decisions?

(on a scale of 1 to 7 where 1=not likely, 7=very likely)

1%
14%
86%

■ Very Likely ■ Likely ■ Not Likely
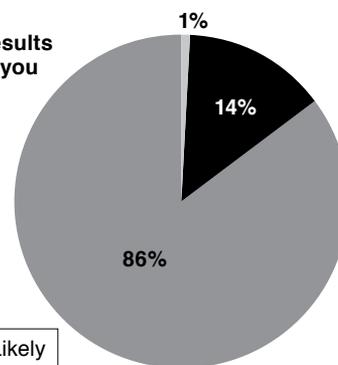
n = 22.
Source: 2011 inVentiv Health Payer Study.
CMS = Centers for Medicare and Medicaid Services; PRO = patient-reported outcomes.

history, one important question still lingers in the minds of those developing evidence for payers: What role will patient-reported outcomes (PRO) play in future coverage decisions made by the payer? Aside from methodological concerns, lack of quality PRO instruments and associated risks with incorporating PRO study data into an Academy of Managed Care Pharmacy (AMCP) dossier submission, are payers likely to weight outcomes from PRO studies in their decisions?

OBJECTIVE: To explore opinions regarding PROs from leading policy makers within the private and government payer communities and make recommendations surrounding evidence development, analysis, and submission.

METHODS: In order to understand payer perspective on the use of PRO results, inVentiv Health conducted a 2-part study with commercial and government payers. The first part of the study consisted of a commercial payer survey with 22 medical and pharmacy directors representing over 50 million lives; the second part of the study consisted of telephonic qualitative research interviews with 6 thought leaders in coverage policy from U.S. government/commercial payer and technology assessment bodies, including the Agency for Healthcare Research and Quality (AHRQ).

RESULTS: Study respondents were asked a variety of questions to assess views on PROs. A sample of study results are presented in this section. When asked about the source(s) for PRO data, the study found that the AMCP dossier was the most prevalent source of PRO study data (86%) versus publicly available information (77%) and submission as part of a Phase III and Phase IV study (50% and 36%, respectively). The study also found that over 20% of respondents had used PRO study data as part of past coverage decisions. One respondent mentioned that therapy class reviews were regularly informed by AHRQ-sponsored PRO study data, while another mentioned AHRQ-sponsored PRO study data as a source for development of prior authorization requirements. Most astoundingly, the study found that 95% of respondents were either likely or very likely to utilize PROs in informing coverage and reimbursement policies in the future and that 99% of respondents would follow the lead of the Centers for Medicare & Medicaid Services (CMS) in future utilization of PRO study data.

CONCLUSIONS: PRO studies are gaining momentum through focused efforts by AHRQ/CMS and pharmaceutical manufacturers. Some

commercial payers are already beginning to leverage the findings of these studies in supporting their policy decisions. The momentum is expected to accelerate in the future as more sophisticated tools become available to effectively measure PROs, and unbiased and respected organizations such as AHRQ, AMCP, Patient-Centered Outcomes Research Institute, and the International Society for Pharmacoeconomics and Outcomes Research become more involved in designing better methodologies. Pharmaceutical manufacturers on the forefront of developing scientific and unbiased approaches to PROs will be rewarded.

■ Safety Monitoring and Reported Tolerability Issues (SMART-I) Index: An Exploratory Evidence-Based Strategy to Summarize Aggregate Drug Safety Data

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BACKGROUND: Formulary decision making is an important responsibility involving the talents of managed care pharmacists. Formulary decision making is supported by evidence derived from many disparate sources and assimilated in a manner that supports thoughtful decision making. Quality data collection and assimilation is imperative given that formulary changes have the potential to impact the quality of care provided to large populations of patients. To date, no aggregate measures of efficacy and/or safety are readily accessible to managed care pharmacists (MCPs) when needed.

OBJECTIVE: To describe an exploratory methodology with potential benefits to MCPs as they seek comparative aggregate safety information to support formulary decisions.

METHODS: Commercially available drug information (DI) systems provide a reliable source of information related to an individual drug's efficacy and safety profile. Some systems also provide a mechanism whereby aggregate safety report data can be generated. Data from the DI systems can be transferred into databases which then allow further analysis to occur. There are 3 types of aggregate safety and tolerability issues that can be computed from currently available DI systems. First, an aggregate measure of drug safety can be derived by taking the number of adverse events assigned to an individual product divided by the total number of adverse events across the class of agents used to treat a particular symptom or disease process. Second, data derived from the DI system can be mapped with ICD-10 codes so that all of the reported adverse events for a given functional body system can be aggregated. Finally, risk adjustments to incorporate severity of events can be computed using measures such as the Charlson indices.

RESULTS: When applied to current or future agents used in the treatment of relapsing forms of multiple sclerosis, over 190 different adverse events are identified from a commercially available DI database. When summarized into an Excel spreadsheet, the aggregate measure of drug safety and tolerability can be derived. Data can also be mapped to a specific body system (e.g., cardiovascular events only) through the Safety Monitoring and Reported Tolerability Issues Index (SMARTI-I) system.

CONCLUSIONS: Currently, the process to obtain aggregate safety and tolerability data to support formulary decision making is tedious and time consuming. When developed as a web-based tool, the SMARTI-I system may provide a potential new strategy to obtain aggregate safety and tolerability data across multiple agents used in the treatment of a specific symptom or disease. Such a tool would provide MCPs with the opportunity to invest in the development of other strategies to improve the health of the population they are entrusted to serve.

■ Student Pharmacists' Teaching Strategies to Lower Medication Costs for Underserved Patients

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BACKGROUND: Underserved patients are vulnerable to the continued rise of health care and out-of-pocket medication costs. The ability to achieve appropriate patient outcomes while containing costs is critical, yet this subject is not taught in most health professional educational programs. As experts in medication selection, use, and cost, pharmacists are in a unique position to help manage a patient's medication for the best therapeutic outcome, while also helping to keep patient's out-of-pocket medication costs low. While promoting interprofessional collaboration, pharmacy student-led lectures may provide a valuable method for helping teach medication cost-containment strategies.

OBJECTIVE: To evaluate the impact of a pharmacy student-led lecture on health care providers' knowledge of cost-containment strategies designed to improve underserved patients' access to needed medications.

METHODS: Four trained pharmacy students delivered a 60- to 90-minute standardized case-based lecture focusing on strategies to help underserved patients with their medication costs. Lectures were given to diverse audiences (nurses, nurse practitioners, medical residents, physician faculty, pharmacy students) in diverse settings (residents' seminars, medical grand rounds, required health policy courses). A pre/post survey was administered to assess whether learners' knowledge improved as a result of the lecture. Survey questions measured learners' knowledge of medication cost-containment strategies (e.g., patient assistance programs, copayment assistance programs, low-income subsidies) and their applicability to uninsured and underinsured patients. The survey was designed to control for pre-test confounding in post-lecture scores. A comparison was made using t-tests between proportions of correct answers before and after the lecture with a stepwise Sidak adjustment (overall significance 0.001, for 5 comparisons). Only questions with complete data were included in the analysis.

RESULTS: From October 2010 to September 2011, the pharmacy student lecturers gave 13 presentations to 411 participants, including 275 affiliated with pharmacy and 110 affiliated with medicine. There was a statistically significant increase in the proportion of correct answers for each knowledge-based question after the lecture compared with before the lecture. The proportion of correct responses increased from 26% to 66% for the low-income subsidy strategy, from 37% to 79% for avoiding the Medicare Part D benefit gap, from 17% to 58% for the number of uninsured patients, from 37% to 79% for correctly using patient assistance programs, and from 32% to 87% for correctly using copay assistance programs. Each individual test had a P value <0.001.

CONCLUSIONS: This study demonstrates that pharmacy student-led lectures given to health care professionals can significantly improve knowledge of medication cost-containment strategies targeted toward vulnerable patient populations.

■ Success with Electronic Chart Flags to Alert Clinicians About Medication Cost-Savings Opportunities at the Time of Patient Visits

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BACKGROUND: Clinicians are encouraged to evaluate patient medication therapy and switch to clinically appropriate lower cost alternatives whenever possible. Identifying these opportunities can be time consuming, and clinicians may not be aware of such opportunities. The "Chart Flag Service" was created by clinical pharmacists to provide clinicians with real-time information about patient cost-saving medication alternatives.

OBJECTIVE: To evaluate the Chart Flag Service for effectiveness, workload implications, and satisfaction from clinical pharmacists and clinicians.

METHODS: A list of patients with upcoming primary care appointments who meet specific exclusion criteria and have been prescribed a non-preferred medication (e.g., brand name angiotensin receptor blocker) is generated monthly. Clinical pharmacists review each patient's chart to determine if an alternative preferred medication is clinically appropriate and, if so, provide a recommendation to the patient's clinician within the electronic medical record (EMR). Communications are sent prior to each patient's scheduled appointment, and the appointment is "flagged" in the clinician's schedule. To evaluate the effectiveness of this service, surveys were sent to 12 clinical pharmacists and 178 clinicians, and chart flags were tracked over a 2-week period in September 2011.

RESULTS: A 25% response rate was achieved for the clinician survey. Eighty-two percent of responders felt they could address chart flags at least 60% of the time, and 80% found that the recommended medication switch could be completed in <5 minutes. Forty-three percent noted that if a chart flag was missed it was due to forgetfulness. Eighty-four percent of clinicians found the service to be useful/very useful, and 16% found it somewhat useful. A response rate of 92% was achieved for the clinical pharmacist survey. One-hundred percent of responders felt they could complete weekly chart flags >50% of the time, with 60% noting they could complete the reviews in 3-4 hours/week and 40% utilizing >4 hours per week. The service was deemed useful/very useful by 83% of respondents. Of 849 patient appointments, 30.6% were considered appropriate for recommending an alternative medication. Clinicians accepted 31.1% of these recommendations. Primary reasons for rejection included recommendation not addressed during appointment (33.1%), appointment cancellation (20.4%), and clinician-determined clinical reasons (15.4%). The average cost savings per medication recommendation included in the Chart Flag Service was $78.33. Estimated annual savings for the cohort of patients included in this 2-week analysis amounted to $51,014. The annualized cost savings for a full year of the Chart Flag Service could be estimated at approximately $850,000.

CONCLUSIONS: The Chart Flag Service results in significant cost savings and is perceived as useful and feasible by the majority of clinicians and clinical pharmacists. Possible improvements for the future include limiting chart flags to high priority medications, more frequent generation of patient lists to avoid cancelled appointments, and inclusion of support staff to improve the rate of recommendation follow-through by clinicians.

■ Synergistic Effects of Personalized Pharmacist Counseling and Pharmacy Benefit Design on Patients with Suboptimal Therapeutic Management of Diabetes

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BACKGROUND: Diabetic patients who are not treated with antihypertensive and antihyperlipidemic medications are at increased risk for cardiovascular disease. A pharmacy plan benefit that improves access to enhanced pharmacist counseling can improve pharmacy care and health outcomes.

OBJECTIVE: To determine whether a pharmacy benefit plan design that incentivizes members to use preferable pharmacy channels, where a concurrent program offers enhanced pharmacist-patient engagement, improves pharmacy care for diabetes patients.

METHODS: We measured initiation rates of antihypertensive therapy (angiotensin-converting enzyme inhibitors [ACEIs] or angiotensin II receptor blockers [ARBs]) and antihyperlipidemic therapy (HMG-CoA reductase inhibitors [statins], bile acid sequestrants, niacin derivatives, and fibric acid derivatives) in continuously eligible plan members with diabetes between January 1, 2011, and July 31, 2011. Three study groups comprised members with 1 or more missing therapies: 71,965 members participating exclusively in a pharmacist counseling program (CVS Caremark Pharmacy Advisor); 73,639 members enrolled concurrently in Pharmacy Advisor and a plan design which allows 90-day supply prescriptions at mail or community CVS pharmacies with no difference in out-of-pocket costs (CVS Caremark Maintenance Choice); and 123,746 control group members not exposed to Pharmacy Advisor or Maintenance Choice. Therapy initiation rates in the 3 classes were compared by study group and missing therapy type (DIA6 and DIA7 for normotensive and hypertensive patients, respectively, without ACEI/ARB therapy; IHD3 without lipid lowering therapy) using descriptive (bi-variate) and multivariate analyses (logistic regression).

RESULTS: A total of 20,454 (14%) eligible members in the case groups initiated 1 or more therapies. In Pharmacy Advisor-only (PA-only), 58% of members chose to fill their prescription medications at CVS community or mail pharmacy channels, similar to controls (61%), whereas 92% of members in the combined Pharmacy Advisor and Maintenance Choice (PA&MC) selected CVS community or mail channels. PA&MC had significantly higher therapy initiation rates than PA-only and control (14.7% vs. 13.4% and 12.4%, respectively, both $P<0.05$). The odds of therapy initiation was 21.3% higher for PA&MA and 10.5% higher for PA-only than the control (both $P<0.001$). When DIA7 and IHD3 therapies were initiated, exposure to both Pharmacy Advisor and Maintenance Choice was associated with greater odds that patients filled the missing medications (DIA7 odds ratio PA&MC=1.264 [95% CI=1.218-1.312], PA-only=1.148 [95% CI=1.104-1.193], referent: control); (IHD3 odds ratio PA&MC=1.151 [95% CI=1.117-1.186], PA-only=1.039 [95% CI=1.007-1.071], referent: control).

CONCLUSIONS: Increasing patient exposure to personalized pharmacist interventions at community pharmacies or mail call centers through a pharmacy benefit design led to improved pharmacy care for diabetic patients.

■ Time to Disease-Modifying Antirheumatic Drug Initiation Among Newly Diagnosed Rheumatoid Arthritis Patients

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BACKGROUND: American College of Rheumatology (ACR) guidelines recommend use of a disease-modifying antirheumatic drug (DMARD) within 3 months of rheumatoid arthritis (RA) diagnosis to slow the progression of the disease.

OBJECTIVE: To evaluate the time to DMARD initiation and whether initiation time varied across different patient characteristics among commercially insured RA patients.

TABLE	Median Time to DMARD Initiation by Clinical Characteristics	
Pre-Index Characteristics	Median Time in Days to DMARD Initiation	95% Confidence Interval
Rheumatoid factor test		
Yes	21	21-22
No	139	126-157
Rheumatologist visit		
Yes	20	17-23
No	66	63-70
NSAID use		
Yes	31	29-34
No	112	101-123
Corticosteroid use		
Yes	37	35-39
No	100	91-109
Charlson Comorbidity Index		
0	51	49-55
1	60	54-67
2	84.5	66-108
3 or greater	141.5	100-216

DMARD = disease-modifying antirheumatic drug; NSAID = nonsteroidal anti-inflammatory drug.

METHODS: Newly diagnosed adult RA patients with 12 months of continuous health plan enrollment before and after the first RA diagnosis (index date) were identified between January 2004 and September 2008 in the MarketScan Commercial and Medicare Research databases. Patients were excluded if they used a DMARD prior to their first diagnosis. Patients were followed for 12 months after index date (up to September 2009) to assess time to DMARD initiation. Characteristics associated with time to DMARD initiation were analyzed using proportional hazards (Cox) regression model. Kaplan-Meier curves were used to estimate median time to DMARD initiation for significant factors from the Cox model. Differences between presence and absence of a characteristic in time to DMARD initiation were tested using chi-square tests.

RESULTS: Among newly diagnosed RA patients (n=26,911), 63.2% initiated DMARD therapy within 12 months. Of those who initiated DMARD therapy, 86.9% started within 90 days of diagnosis; 8.2% started 91-180 days; and 4.9% started 181-365 days after diagnosis. The following factors occurring during the 12 months prior to index date (pre-index period) were associated with a significantly shorter time to DMARD initiation: rheumatoid factor test, rheumatologist visit, nonsteroidal anti-inflammatory drug (NSAID) use, corticosteroid use, and less comorbidity burden ($P < 0.001$ for each factor, see table). In the pre-index period, approximately 65% of patients who saw a rheumatologist compared with 53% of patients with no rheumatologist visit had initiated a DMARD by 3 months after diagnosis. DMARD initiation by 3 months after diagnosis was achieved by 57% of patients with a Deyo Charlson Comorbidity Index score of zero, 54% with score of 1, 51% with score of 2, and 47% with a score of 3 or higher.

CONCLUSIONS: Among a managed care population 63% of RA patients initiated DMARDs within 12 months of diagnosis, with shorter time to therapy initiation for those with fewer comorbid conditions and those seen by a rheumatologist in the pre-index period. Time to DMARD initiation flattened by 90 days, indicating that if patients did not initiate therapy soon after RA diagnosis, they were not likely to do so.

■ **Use of a Claims-Based Relapse Detection Algorithm for the Analysis of Multiple Sclerosis Patients Within an Integrated Health Care System**

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BACKGROUND: Multiple sclerosis (MS) is an autoimmune demyelinating disorder affecting over 400,000 people in the United States. The disease is characterized by periods of exacerbations, often requiring hospitalizations, followed by periods of remission where patients may partially or fully recover. Treatment for MS is multifaceted and may require both pharmacologic and nonpharmacologic interventions to alleviate or prevent remission. Even with treatment, MS patients are highly variable in both relapse rates and disability progression. An integrated health care system in central Texas decided to examine MS patients within the health care system to identify differences that may exist in treatments or resource utilization within the MS population.

OBJECTIVE: To provide a descriptive analysis of MS patients within an integrated health care system and compare resource utilization between relapsing and nonrelapsing patients from a health plan perspective.

METHODS: Using health plan pharmacy and medical claims data, patients with at least 2 ICD-9-CM codes for MS (340.xx) were identified between January 1, 2005, and December 31, 2010. The first diagnosis of MS served as the index date. To be included, patients needed continuous enrollment for a minimum of 12 months post- and 3 months pre-index date. A validated, claims-based relapse detection algorithm was used to identify patient relapses in the post-index date period. Patients with no identifiable relapses post-index date were considered a nonrelapsing patient for the purpose of this study. Baseline characteristics, course of treatment, and resource utilization were analyzed using descriptive statistics, chi-squared tests, parametric, and nonparametric tests as appropriate.

RESULTS: A total of 316 MS patients were identified for the analysis: mean age 52.5 years, 77.2% female, with an average length of follow-up of 46 months. Of the 316 patients, 87 (27.5%) were identified as having relapses post-index date. Relapsing patients were noted to have an average of 1.97 (2.31 SD) relapses per patient with an annualized relapse rate of 0.53. 57.9% of all patients used a disease-modifying treatment (DMT) in the post-index period with significantly more relapsing patients on a DMT (74.7% vs. 51.5%, $P < 0.001$). Pharmacy per member per year (PMPY) costs were significantly higher for relapsing patients ($12,298.32 vs. $9,107.52, $P = 0.004$). Additionally, relapsing patients had significantly higher overall PMPY costs when compared with nonrelapsing patients ($21,760.32 vs. $16,418.40, $P < 0.001$). Relapsing patients also had higher total medical PMPY costs ($8,960.4 vs. $7,183.92, $P = 0.01$). Patients in the relapse cohort were shown to have higher emergency room visits (5.46 vs. 2.47, $P < 0.01$) and more hospital days per year (6.15 vs. 2.89, $P = 0.008$).

CONCLUSIONS: DMTs were used in most MS patients in this population. Not surprisingly, there was a higher utilization rate of DMTs for MS patients in the relapsing cohort having more symptomatic MS-related activity. Furthermore, relapsing patients posed a higher economic burden than the nonrelapsing cohort with significantly higher overall and total medical costs.

■ Use of Health Economic and Outcomes Research in Formulary Decision Making: A Tale of 2 Surveys

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BACKGROUND: Two independent studies of the use of health economic and outcomes research (HEOR) by health plan decision makers were conducted in 2010. Both studies showed that approximately 70% of organizations use HEOR data in formulary decision making. The combined analysis of both studies provides additional insight into the current and future use of this data in managed care decision making.

OBJECTIVE: To compare and contrast findings from 2 studies regarding the use of HEOR by formulary decision makers, including respondent and plan characteristics and current and expected future use of HEOR data by decision makers.

METHODS: Two Internet-based surveys were conducted in 2010 ("A" and "B") among pharmacy decision makers, pharmacy & therapeutic committee (P&T) members, and pharmacists supporting P&T committees. "A" was distributed to the Academy of Managed Care Pharmacy members and "B" was distributed via Qualtrics to a convenience sample known to the investigators. Both surveys contained respondent and organizational demographic questions. "A" contained questions on the current and future use of HEOR data in managed care decisions, and "B" contained questions on use of economic data, outcomes research, other factors, case scenarios, and comparison to published formularies.

RESULTS: A total of 101 completed surveys were received (nA=72, nB=29). Organizations represented in both surveys were similar with medians of 500,000 for both (ranging from 50,000 or 55,000 to 100 or 45 million, respectively). While cost information and outcomes data were deemed important (90% and 86%, respectively) for decision making in "B," only 32% of organizations in "A" reported having procedures for quality control concerning HEOR data. Further, 97% of organizations in "B" felt competent in using cost data, but only 62% felt so with other outcomes research data. A majority of the respondents in "A" expected an increased use of HEOR data for future decision making (81.9%), specifically for contracting (72%).

CONCLUSIONS: Two separate surveys addressing the use of HEOR information in managed care decision making support the continued increased use of this data both in formulary and contracting decisions. Cost data were considered more routinely, but payer decision makers expressed less experience with other outcomes data. A common standard for quality control in evaluating HEOR data is missing. Increased competencies in health economics and outcomes research are needed to enable health plans to make more efficient use of the data.

SPONSORSHIP: This research was conducted by Mercer University, College of Pharmacy and Health Sciences, Atlanta, GA, and University of Utah, College of Pharmacy, Salt Lake City, UT, without external funding.

■ Use of Propensity Scores to Control for Baseline Characteristics in a Comparison of Health Care Utilization

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BACKGROUND: Due in part to the recent emphasis on comparative effectiveness research (CER), methods surrounding claims-based effec-

TABLE	Model Estimates[a] for the Impact of Brand Versus Generic Statin Use on Health Care Utilization		
	Brand ($)	**Generic ($)**	**P Value**
Unadjusted estimate of health care utilization	4,989	4,610	0.005
Model with no propensity score	4,722	4,813	0.45
Model with propensity score	4,727	4,813	0.47
Model with propensity score and directly measured variable	4,741	4,799	0.626
Model with inverse propensity score weighting	4,727	4,823	0.398

[a]*Dollar estimates are inverse log transformations of the model estimates.*

tiveness studies have been evolving over the past few years. Attempts improve the comparability of subjects between treatment groups has increased the use of propensity score methods. The propensity score is the probability of exposure given measured baseline variables and can be used as a matching or stratifying factor, as a covariate in a multivariable model, or to perform inverse probability of exposure weighting. It is unclear if how the propensity score is used influences a study's outcomes.

OBJECTIVE: To compare different approaches to the use of propensity scores in an observational study comparing total health care utilization between brand and generic statin users.

METHODS: This study uses a previously described observational dataset of 2009 and 2010 statin users from a midwestern third-party payer. The dependent variable of interest was total health care spending taken from all medical claims. A natural log transformation was used to adjust for the skewed nature of the data. A propensity score was calculated for each subject using a logit model to predict the probability of receiving a brand statin. Variables included in the prediction model included age, gender, proprietary risk score, if the patient was enrolled in a high deductible health plan, and whether or not the subject was fully or self-insured. Four regression models were run: (a) a linear regression that controlled for all of the previously mentioned variables directly, (b) a linear regression that used the propensity score in place of the other independent variables, (c) a linear regression using both the propensity score and independent variables, and (d) a weighted linear regression using the independent variable and weighted with an inverse propensity score weight. In addition to the previously mentioned independent variables, all models also controlled for patient adherence and the number of medications taken.

RESULTS: The unadjusted health care utilization of brand statin users ($4,989) was higher than generic statin users ($4,610; P=0.005). In the 4 adjusted models (see table), the difference in health care spending was no longer significantly different. All 4 models returned similar parameter estimates ($4,722-$4,741 for brand users and $4,799-$4,823 for generic users) and P values (0.398-0.626).

CONCLUSIONS: While the various methods for using propensity scores to control for exposure to baseline confounding variable are effective, the current study suggests that they may not always be superior to directly controlling of independent variables in a linear regression. Care must be taken to choose the appropriate methods for any given study.

SPONSORSHIP: This research was conducted by University of Nebraska Medical Center, Omaha, NE, without external funding.

■ **Utilization of Anticoagulation Therapy in Medicare 5% Sample Claim Data for Patients with Nonvalvular Atrial Fibrillation: Comparison to Clinical Guideline Recommendations**

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BACKGROUND: The decision to prescribe anticoagulation for patients with atrial fibrillation (AF) requires careful consideration of stroke and bleeding risk. Current guidelines recommend oral anticoagulation (OAC) for AF patients with moderate/high risk of stroke and not at high risk for bleeding.

OBJECTIVE: To compare actual warfarin utilization and stroke incidence with current treatment guideline recommendations in Medicare AF beneficiaries.

METHODS: This was a retrospective analysis of a 5% random sample of Medicare Part A, B, and D claims data from patients who had newly diagnosed AF (ICD-9-CM code 427.31) in 2006 or 2007, had no AF claims for 12 months prior to index diagnosis, and had continuous eligibility for Medicare Part A and B for 12 months prior to and Part A, B, and D for 12 months after diagnosis. CHADS2 stroke risk (Gage 2001) and Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) bleeding risk (Fang 2011) scores were calculated using medical claims 12 months before the index AF diagnosis; warfarin exposure was determined by the presence of 1 or more warfarin pharmacy claims in the 12 months after index AF diagnosis. Rates of ischemic stroke during the 12-month follow-up period were compared by levels of warfarin exposure using chi-square statistics.

RESULTS: Data from 15,086 patients (mean age = 79 years; 58.7% female) were analyzed. Overall, 11,519 patients (76.4%) had moderate (CHADS2 = 2 or 3) or high (CHADS2 ≥ 4) stroke risk, of whom 8,104 patients did not have high bleeding risk (ATRIA ≥ 5) and would meet recommendations for OAC therapy. Of these patients, only 4,268 (52.7%) received 1 or more prescriptions for warfarin within 90 days of AF index date, and only 4,856 (59.9%) received 1 or more warfarin prescription within 12 months of AF index date. Actual warfarin use for all AF patients did not differ by stroke risk ($P > 0.05$) but decreased with higher bleeding risk ($P < 0.001$). The rate of ischemic stroke in moderate to high stroke risk patients was 10.2% among those who did not receive a warfarin prescription during the 12 months after index AF, compared with 9.4% ($P = 0.131$) in those who initiated warfarin therapy any time during the 12 months after index AF diagnosis; 8.5% ($P = 0.003$) in those who initiated warfarin therapy within 90 days of index AF diagnosis; 7.4% ($P < 0.001$) in those who received warfarin therapy for the majority (medication possession ratio ≥ 80%) of the year following index AF diagnosis; and 6.0% ($P < 0.001$) in those who received uninterrupted (medication possession ratio = 100%) warfarin therapy in the year following index AF diagnosis.

CONCLUSIONS: Based on a risk stratification scheme defined by previously published tools such as CHADS2 and ATRIA bleeding risk index, a significant proportion of Medicare beneficiaries with AF are not receiving guideline-recommended anticoagulation and have a higher rate of stroke than those receiving recommended anticoagulation. These preliminary findings highlight quality-of-care issues for AF patients and the need to improve compliance with anticoagulation guidelines in the Medicare population.

■ **Utilization of Mathematical Modeling to Determine Possible Cost Savings and Cost Avoidance for Implementation of MTM Services in a Specialty Population**

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BACKGROUND: While the cost savings and avoidance with medication therapy management (MTM) services have been well documented in general medicine populations, there are little data on these measures in specialty high cost populations. Utilizing published data and results, a mathematical model was used to predict likely cost savings and avoidance from the provision of MTM services to human immunodeficiency virus (HIV) patients.

OBJECTIVE: To determine possible cost savings and avoidance utilizing mathematical modeling of published data on clinical results of MTM services in HIV patients, applicable clinical trial data on adherence to antiretroviral therapy (ARV) and the clinical outcome relationship between the two, and general medical cost data from progressive stages of HIV infection and AIDS.

METHODS: All data used in the mathematical model were abstracted from previously published or presented sources. Data on the cost of care for HIV-infected patients at various stages of HIV infection/acquired immune deficiency syndrome (AIDS) were from presented abstracts. ARV use patterns were pulled from the 2006 U.S. Department of Health and Human Services (DHHS) guidelines for the use of antiretroviral therapy (latest guidelines related to abstracted costs of therapy). Adherence improvement data with MTM therapy for HIV patients were pulled from published reports with the assumptions of an average increase in adherence of 18.2% and decrease in changes to ARV therapy of 22.6%. Data on the relationship between HIV ARV adherence and percent change of having an undetectable viral load, as well the clinical consequences of having an undetectable versus a detectable viral load, were abstracted from published reports. A 1:1 correlation with adherence versus the achieving of an undetectable viral load across the adherence range of 50%-80% was assumed from previously published trials. All patients were assumed to have less than 80% adherence at the beginning of MTM therapy. All cost data were corrected for the rate of health care inflation (averaged to be 3.9% over the past 10 years) to bring values in line with 2011 dollars. Costs of MTM therapy were assumed to be $250 per patient per year. Costs of increased adherence (direct medication costs) were factored in as well. All data were then simulated using mathematical modeling to determine any cost savings or avoidance.

RESULTS: Previously published data had shown significant cost avoidance due to decreased health care utilization, lower medication costs, and decreased incidence of opportunistic infections when failure of an ARV regimen due to nonadherence was avoided. When these factors were modeled with documented increases in adherence and clinical success rates (as measured by percent of viral loads as being undetectable) with increasing adherence, it was possible to estimate total cost avoidance in an HIV-infected MTM population. Cost avoidance was determined to be, on average, $1,177 dollars per patient per year (PPPY) in drug costs and $1,788 PPPY for all health care costs. Cost avoidance for all health care dollars ranged from $881 PPPY for early stage patients, $2,356 in middle stage patients, and $2,531 in late stage patients. When a total cost of MTM care was factored, a return on investment (ROI) of up to 7:1 was determined for the provision of MTM services to HIV-infected patients with low adherence.

CONCLUSIONS: While the model used is limited by using data from various unrelated sources and utilizes data from different time points

and stages in the evolution of ARV therapy, it does allow us to get some sense of the cost avoidance that can be achieved when MTM services are offered to HIV-infected patients. Theoretical cost avoidance of an average of $1,788 PPPY and a maximal ROI of 7:1 on MTM therapy makes further research in this area of interest.

SPONSORSHIP: This research was conducted by Ramsell Pharmacy Solutions, Oakland, CA.

■ Warfarin Pharmacogenomics Testing: Prevalence, Timeliness, and Cost

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BACKGROUND: Potential benefits of warfarin genetic testing include more accurate initial dosing with the possibility of shorter time to reach a therapeutic International Normalized Ratio (INR) and reduced adverse outcomes. Federally funded randomized clinical trials to validate genotype-guided warfarin dosing are underway. Currently, the Center for Medicaid and Medicare Services (CMS) restricts warfarin genetic testing coverage to individuals who (a) have received fewer than 5 days of warfarin therapy, (b) have not been previously tested for the alleles, and (c) are enrolled in a prospective, randomized, controlled clinical study meeting CMS-determined standards.

OBJECTIVE: To identify warfarin pharmacogenomics testing prevalence, appropriateness of genetic testing, and testing cost within a commercially insured population through an integration of medical and pharmacy claims data.

METHODS: Pharmacy and medical claims data from a 1.2 million-member commercially insured population in the Midwest were queried to identify members continuously enrolled for the period from March 1, 2010, through June 30, 2011. The earliest warfarin claim during the period from July 1, 2010, through June 30, 2011, was defined as the index warfarin claim. Warfarin new start was defined as no warfarin claim in the 120 days before the index warfarin claim. Warfarin utilizers' medical claims were queried for the period from March 1, 2010, through June 30, 2011, for the presence of 1 or more of the following molecular diagnostic-related Current Procedural Terminology (CPT) codes: 83890, 83891, 83894, 83896, 83898, 83900, 83901, 83904, 83908, 83909, 83912, 88384, 88385, and 88386, G9143. Allowed amounts from each line of the medical claim with a genetic test CPT code were used to calculate total paid. CMS criteria were used to define appropriateness of genetic testing relative to warfarin therapy. Each member's genetic testing date was compared with the index warfarin claim date for new starts and categorized into those having testing performed within 5 days of the warfarin index claim (i.e., appropriate) or greater than 5 days (i.e., inappropriate). All genetic testing found among non-new start warfarin utilizers was defined as inappropriate.

RESULTS: 948,270 members were continuously enrolled for the period from March 1, 2010, through June 30, 2011, and 8,396 unique members had a warfarin claim from July 1, 2010, through June 30, 2011. A genetic testing claim was found in 334 (4.0%) of 8,396 warfarin utilizers, and the total paid for genetic testing codes was $100,312 with a median of $152 per member (25th percentile $74 and 75th percentile $321). The total number of members with an inappropriate genetic test (greater than 5 days after warfarin initiation) was 224 (67.7%) of 331 warfarin utilizers at a cost of $61,932. Of the 8,396 warfarin utilizers, 4,003 (47.7%) were new starts, and genetic testing codes were found in 212 (5.3%) members. Inappropriate genetic testing was found in 104 (49.1%) of the 212 warfarin new starters at a total paid amount of $24,464. Among the 4,393 non-new starters, 122 (2.8%) were found to have had an inappropriate genetic testing claim, as they were already on warfarin therapy, at a total paid of $37,468.

CONCLUSIONS: Currently, genetic testing associated with warfarin utilization is rare at a rate of 4 per 100 overall and 5 per 100 new warfarin starts. If genetic testing had been performed in all new warfarin starts, $608,456 (4,003 members × $152 median test cost) would have been spent by the plan. If inappropriate testing, defined as greater than 5 days after warfarin is newly initiated, remained at 49.1% then $298,752 or $0.026 per member per month would have been expended without benefit. As pharmacogenomics testing becomes more mainstream, spans more drug classes, and costs increase, health plans should think proactively about how to ensure the right member at the right time is tested.

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