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

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

METHODS: Subjects were 123 members of RAPOLO, a longitudinal, observational study of patients who had participated in etanercept clinical trials, for whom data at entry into the clinical trial were available. CRP, ESR, and HAQ were obtained at clinical-trial baseline. Patient-reported outcomes were from the first RAPOLO interview (mean 51.8 months after clinical-trial baseline). Patient-reported outcomes included an SF-36 Physical Component Summary score; ratings of fatigue and pain impact; number of valued life activities affected and impact; and, for the 2-year interview only, the impact of physical limitations and satisfaction with functioning.

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

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

AGGRESSIVE STEP- THERAPY PROGRAMS REALLY DO SAVE MONEY

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

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

RESULTS: The cost savings resulting from these 3 successful programs has totaled $4.47 PMPM, representing a savings of more than 10% of total retail drug costs for the plan. Costs for the PPIs dropped nearly $2.00 PMPM, and market share for omeprazole and Prilosec OTC is now 65%, compared with 10% nationally. Plan costs for the NSAs and antidepressants...
The effect of etanercept (ETN) treatment on PROs
Based on 1 million lives, the introduction of new drugs were assumed to be dosed and used according to Patient surveys consisting of 10 questions were Extended etanercept treatment in patients with Managed care plans have initiated glaucoma formulary changes (Law et al., 2005). We assessed glaucoma patients’ satisfaction after a recent formulary change to their glaucoma medication.

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

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

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

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

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

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

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

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

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

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were mailed in anonymously by the patients. Five questions asked patients about their satisfaction with their glaucoma medication prior to and following the formulary change on a scale of 1 to 5 (1 = Very satisfied, 2 = Satisfied, 3 = Somewhat satisfied, 4 = Somewhat unsatisfied, 5 = Unsatisfied). Five additional questions inquired about general background information relating to the patients’ medication profile and source of copay change information. Descriptive statistics were generated and the Wilcoxon Signed Rank test was used to determine statistical significance between satisfaction scores.

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

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

BUDGET IMPACT ANALYSIS OF BISPHOSPHONATES FOR FRACTURES IN POSTMENOPAUSAL WOMEN

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

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

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

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

CHARACTERISTICS OF PATIENTS INITIATING TERIPARATIDE (FORTEO) THERAPY

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

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

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

CONCLUSIONS: In this sample of patients enrolled in commercial and Medicare plans, patients selected for teriparatide treatment differed from those initiating bisphosphonates in several important ways. TPTD patients were older, had poorer overall health status, and appeared to have more-severe osteoporosis than patients initiating bisphosphonates.
COMPPLICATION AND CARDIOVASCULAR COMORBIDITY RATES OF NEWLY TREATED TYPE 2 DIABETICS
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INTRODUCTION: The purpose of the study was to evaluate the diabetes-related complication and cardiovascular comorbidity rates in newly treated (NT) patients with type 2 diabetes mellitus (T2DM) in order to identify opportunities for improving medical management of these patients.

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

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

CONCLUSIONS: These data suggest that newly treated T2DM patients have a high incidence of diabetes-related complications and cardiovascular comorbidities. Both glycemic and lipid control contribute to overall cardiovascular risk in patients with type 2 diabetes and require intensive management. Considering the prescription burden of these patients, an unmet need exists for a single agent to address more than one cardiovascular risk factor, such as lowering glycosylated hemoglobin (A1C) and low-density lipoprotein cholesterol. Finally, given the rate of diabetes-related complications and cardiovascular comorbidities in newly treated patients, the cost implications to payers with an initial diagnosis of diabetes-related complication and cardiovascular comorbidity (P<.0001), increasing total monthly expenditure by 38% ($1,069)

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

Payer type also had a significant impact on overall expenditure ($<0.001). Commercially insured patients incurred costs that were 20% higher than for those patients where Medicare was the primary payer ($3,043 vs. $2,529). Increased inpatient cost was the primary driver.

Expenditure PMPM for untreated anemic CKD patients was 17% higher than for patients who received any form of anemia treatment ($4,115 versus $3,504), driven largely by increased inpatient expense. Outpatient and pharmacy expenditures were 9% and 38% lower, respectively, in the treated cohort. Treatment with an erythropoietin-stimulating agent reduced total expenditures by 6% but did not reach statistical significance (P=.159).

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

COST-EFFECTIVENESS OF ALTERNATIVE TREATMENTS FOR OVERACTIVE BLADDER
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INTRODUCTION: An intent-to-treat Markov model was developed to simulate clinical and economic outcomes for primary care management of patients with overactive bladder (OAB)-related incontinence.

METHODS: From a payer’s perspective, we modeled the cost-effectiveness of treatment with solifenacin (SOL), tolterodine (TOL), or no therapy (NT) based on published information, including data from the Solifenacin with Tolterodine as an Active Comparator in a Randomized (STAR) trial. OAB management was simulated in a hypothetical health plan based on 3 phases of care. Diagnosis: assumes 15% of prevalent cases seek treatment and evaluation for OAB; cases not seeking treatment (NST) remain in the model. Titration: assumes three 4-week cycles. Treatment-seeking patients receive SOL 5 mg/10 mg or TOL 4 mg or NT. Treated patients with suboptimal results may discontinue therapy, increase dose (SOL-treated
patients only), or add placebo (TOL-treated patients only). Nonpersistent patients remain symptomatic and off treatment for the duration of the model. Follow-up: assumes both treatment and response remain stable during the 12-month follow-up. OAB treatment costs accrue during titration and follow-up; incident comorbid event treatment and incontinence pad costs accrue during the follow-up phase.

RESULTS: Model results show higher continence rates with SOL (76%) and TOL (67%) than with NT (0%) or patients NST (0%). Annual cost per successfully treated patient (CPST) was lower with SOL ($1,709) than with TOL ($1,742). Annual per patient cost of treating comorbid conditions was higher with TOL ($1,445) than with SOL ($1,421). Average annual savings from reduced pad use were higher in SOL- than TOL-treated patients ($250 vs. $158). In order to achieve the same CPST as SOL, TOL price needed to be reduced by 2.5% or effectiveness increased by 15%.

CONCLUSION: SOL 5 mg/10 mg is cost effective compared with TOL 4 mg in the management of OAB. Additionally, SOL reduces health plan costs associated with management of comorbid conditions and patient costs associated with pad use.

■ COST-EFFECTIVENESS OF DISEASE-MODIFYING AGENTS FOR THE TREATMENT OF RELAPSING MULTIPLE SCLEROSIS

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

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

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

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

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

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

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

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

### COST-EFFECTIVENESS OF VACCINATION STRATEGIES TO PREVENT HUMAN PAPILLOMAVIRUS INFECTION IN THE UNITED STATES

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

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

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

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

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

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

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

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

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


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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

**RESULTS:** Brand medications at 30-day retail cost less than mail order or 90-day retail when 1 copayment per prescription was applied. Mail order and 90-day retail cost less than 30-day retail for brand medications when 3 copayments were applied for 90-day quantities. Supplies produced similar results. Thirty-day retail
Abstracts From Professional Poster Presentations at AMCP’s 2006 Educational Conference

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

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

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

RESULTS: Clients who moved prescription NSAs to nonpreferred status and implemented a step-care program experienced a 46.35% decrease in PMPM cost. Clients who either implemented a NSA step-care program or moved prescription NSAs to non-preferred status experienced a 33.92% and a 24.88% decrease in PMPM costs, respectively. The control clients who maintained the preferred status of prescription NSAs with no step-care program had a decrease of PMPM costs by only 8.84%. By comparison with the control clients, we estimated PMPM cost savings of $0.45 for clients who moved the prescription NSAs to nonpreferred status as well as implemented a step-care program, $0.36 for clients who implemented a step-care program, and $0.14 for clients who moved prescription NSAs to nonpreferred status.

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

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


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

METHODS: Data from the Medstat MarketScan Commercial Claims and Encounters Database for 2000-2004 were analyzed for 3 groups: (1) patients with alcohol-related diagnoses treated with oral naltrexone who had ≥ 1 medical claim with an alcohol-related diagnosis, ≥ 1 pharmacy claim for naltrexone, disulfiram or acamprosate, and ≥ 6 months continuous plan enrollment before and after the earliest naltrexone claim (index date); (2) alcohol controls (patients with alcohol-related diagnoses without naltrexone, disulfiram, or acamprosate pharmacotherapy); and (3) nonalcohol controls (patients with neither alcohol-related diagnoses nor pharmacotherapy). All 3 groups were matched for gender, age, geographic region, relationship to employee, health plan type, and index quarter/year in a 3:1 ratio (3 controls: 1 naltrexone). Alcohol-related, non-alcohol-related, and total health care expenditures were calculated for the 6-month preindex and postindex periods. Univariate and multivariate analyses controlling for potential confounders were used to compare expenditures and provide cost estimates.

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

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

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

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

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

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

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

### IMPACT OF A MANDATORY90 PROGRAM ON PRESCRIPTION DRUG UTILIZATION AND EXPENDITURES

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

**RESULTS:** To date, a total of 684 physicians for 231 unique CD patients with initial response to infliximab main-
total and CD-related costs for patients who lost treatment response in the first year were 35% and 40% higher than those who didn’t lose response. Regression analyses to control for baseline characteristics showed that loss of treatment response was associated with 29% higher annual total treatment costs ($P < 0.0001$), and 29% higher CD-related costs ($P = 0.007$) over 2 years of treatment compared with placebo.

**CONCLUSIONS:** More than 80% of all patients who had initial responses to infliximab and continued on maintenance therapy subsequently lost initial response within 2 years. Loss of response was associated with significant increase in total health care and CD-related costs.

### Natalizumab Improves Health-Related Quality of Life in Patients with Relapsing Multiple Sclerosis


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

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

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

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

### Natalizumab Reduces Corticosteroid Use and Hospitalizations and Increases the Proportion of Disease-Free Multiple Sclerosis Patients


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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

RESULTS: Total of 568 patients, 63.73% females, 68.84% African Americans, median age 52 years, 35.56% on fixed-dose combination therapy, 72.89% started on ACEI/HCTZ, 24.82% complied with therapy. Patients younger than 40 years (odds ratio [OR] = 0.45; P = 0.03, confidence interval [CI], 0.22-0.91), and African Americans (OR = 0.47; P = 0.0066; CI, 0.31-0.73) are less likely to be compliant than patients older than 60 years, and whites, respectively. Those who have a CCI of 1 (OR = 2.03; P = 0.052; CI, 0.99-4.15) and those on fixed-dose combination drugs (OR = 1.55; P = 0.03; CI, 1.03-2.32) are more likely to be compliant than those with higher CCI and those on 2 concurrent pill therapies, respectively.

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

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

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

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

RESULTS: Description of patients with asthma or depression: mean age of 48 years and 79% female. Asthma patients were more likely to have missed a dose of medicine in the past week (47% vs. 37%) and had higher total number of barriers (5.1 ± 3.7 vs. 4.4 ± 3.2) than patients with depression, respectively. Depressed patients were more likely to report worrying about how medicine will affect sexual health (30%) and alcohol getting in the way of taking medicines (8%) than those with asthma or diabetes. Adjusted positive predictors of nonadherence for depression were: forgetfulness (P < 0.0001), alcohol getting in the way of taking medicines (P = 0.0044), hard-to-swallow pills (P = 0.0173), taking meds more/less than prescribed (P = 0.0267), skipped/stopped meds because not working (P = 0.0299), and skipped/stopped meds due to cost (P = 0.0018). For asthma, predictors of nonadherence were: forgetfulness (P < 0.0001), problems getting refills on time (P = 0.0163), inconvenience of taking medicine (P = 0.0168), too many medicines/day (P = 0.010), taking meds more/less than prescribed (P = 0.0069), and skipped/stopped meds due to cost (P = 0.0156).

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

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

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

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

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

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

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

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

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

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

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