Three-Tiered–Copayment Drug Coverage and Use of Nonsteroidal Anti-inflammatory Drugs

Becky Briesacher, PhD; Sachin Kamal-Bahl, PhD; Marc Hochberg, MD, MPH; Denise Orwig, PhD; Kristijan H. Kahler, RPh, MSc

Background: Previous studies of 3-tier formularies are rare, although the evidence suggests that their cost-sharing structure reduces overall drug spending. However, it is unclear how incentive-based formularies affect the selection of medications with safety advantages, or restrict the access that high-risk populations have to recommended therapies in the higher tiers. This study was designed to determine whether 3-tier formularies influence the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in a population of patients with arthritis.

Methods: This retrospective study used the 2000 MarketScan Research Database, which contains person-level claims data for employer-sponsored health plans. The sample for this study consisted of 20868 individuals treated for osteoarthritis or rheumatoid arthritis and using NSAIDs while enrolled in tiered drug plans (n=32). The likelihood of any use of cyclo-oxygenase (COX-2)–selective inhibitors was determined as a function of tiered drug plan coverage, adjusting for other person-level and plan-level covariates.

Results: Use of COX-2–selective inhibitors decreased (63.0% vs 53.6% vs 41.6%, respectively) and use of generic NSAIDs increased (37.7% vs 40.7% vs 55.7%, respectively) as formularies incorporated 1, 2, and 3 tiers. Enrollees in 3-tier plans with arthritis and serious gastrointestinal comorbidities (odds ratio, 0.51; 95% confidence interval, 0.40-0.66) were significantly less likely to use COX-2–selective inhibitors compared with patients in 1-tier plans.

Conclusions: Three-tier formularies appear to reduce the use of COX-2–selective inhibitors among all patients with arthritis, even those at risk of experiencing gastrointestinal complications from using nonselective NSAIDs. These findings are among the first to suggest that tiered-copayment drug plans may be influencing the selection of medications beyond generic and branded products.

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With spending for prescription drugs rising so rapidly, many employers and health insurance providers have experimented with designing their drug benefit packages. The trend has been to incorporate more cost-consciousness into the formulary structure within the context of safety and efficacy issues. Among the most prominent approaches have been 3-tier drug formularies: in these plans, patients receive financial incentives from the employer to use generic medicines over branded products or else select the branded medicine designated as the preferred one. Use of 3-tier drug plans has nearly doubled in the past 2 years, from 29% of covered workers in 2000 to 57% in 2002. The rapid adoption of this benefit design can be explained by 2 features. First, the list of covered medications becomes larger with the additional tiers as many medicines excluded from the single-tier or 2-tier formulary become included medicines in the third tier. This is an important attribute, as limited or tightly controlled drug formularies have been responsible for considerable dissatisfaction among patients and physicians. The second factor is fairly consistent evidence that adding multiple copayment levels to the formulary lowers drug spending, particularly the portion paid by employers. The magnitude of overall cost reduction is debatable; however, employers seem confident that 3-tier drug plans limit their exposure to rising drug expenditures.

The ability of 3-tier drug formularies to contain drug spending raises questions about the incentive structure, because the influence is clearly felt at the level of patients rather than physicians, who are still generally unfamiliar with the costs of
the medications that they prescribe. With 1-tier drug plans, patients have no incentive to use certain formulary medications over others, as the copayment is the same regardless of selection. Under 2-tier arrangements, the plan rewards those who use generic medications over branded products through lower cost-sharing amounts. In most cases, this approach to encouraging the use of less costly medications raises little concern about patient care, because the choice is between equivalent therapies. However, 3-tier drug benefits are another matter. Patients with this kind of coverage are faced with 3 copayment levels—the least for generics, more for preferred brands, and the most for nonpreferred brands. The patient’s financial incentive under these terms includes selecting preferred medications, a status that may denote favorable contractual terms for the plan. Preferred medications are not necessarily tied to such financial arrangements, although negotiated rebates commonly enter into deliberations on formulary status. There are no guidelines about the makeup of the tiers, which may contain medicines offering different safety and therapeutic advantages. Furthermore, there is the question about how much patients can be charged for medications from the third tier and still consider them to be formulary medications: in 2001, patients with 3-tier plans paid an average copayment of $30 for a 30-day prescription from the third tier.

There have been few studies of 3-tier formularies, although the evidence suggests that the cost-sharing structure reduces overall drug spending. Two of these studies were limited to experiences of one or a few health plans while another examined only the elderly population. All of these studies have focused on total prescription use and spending rather than a particular therapeutic drug class. These studies suggest that 3-tier formularies only create more efficiencies as they lower overall drug expenditures by making patients more aware of less costly alternatives. Less is known about how the 3-tier plans work in practice. Clinical practice suggests that most patients generally learn about the nonpreferred status at the time of the prescription purchase, while physicians learn about the designation when the patient, or an agent on behalf of the patient, contacts them requesting a prescription change. No study has examined how this process affects the eventual selection of medications, especially when some agents offer efficacy or safety advantages, nor has research assessed the access that high-risk populations have to recommended therapies in the higher tiers. Examining the medication treatments of a population with arthritis provides an opportunity to assess these types of questions, particularly in the use of typical nonsteroidal anti-inflammatory drugs (NSAIDs) and selective cyclo-oxygenase (COX) 2 inhibitors.

Typical NSAIDs have been the mainstay of treating the symptoms of rheumatoid arthritis and osteoarthritis, but they are limited by gastrointestinal (GI) toxic effects that stem from the inhibition of COX-1 isoenzyme. The NSAIDs have been associated with increased risk of upper-GI adverse effects ranging from dyspeptic symptoms to ulceration in the stomach and duodenum to serious ulcer complications such as hemorhage and perforation. It is estimated that there are more than 100000 hospital admissions per year in the United States and 16500 deaths per year due to NSAID-induced GI complications. Despite these problems, traditional NSAIDs are consumed on a regular basis by more than 13 million people.

Since the introduction of the COX-2 selective inhibitors in 1999, there has been a widespread reevaluation of drug treatments for arthritis. These new agents act by selective inhibition of the inducible COX-2 isoenzyme while preserving the COX-1–dependent gastric prostaglandin synthesis. For this reason, the COX-2–selective inhibitors offer analgesic and anti-inflammatory relief equivalent to those of the nonselective NSAIDs, while conferring lower risk of serious GI toxic effects. Several clinical trials support the efficacy of COX-2–selective inhibitors compared with older NSAIDs when used at therapeutic doses. Numerous studies, including 2 large randomized controlled trials (VIGOR [Vioxx Gastrointestinal Outcomes Research Trial] and CLASS [Celecoxib Long-term Arthritis Safety Study]) have shown a reduction in GI events, such as bleeding, by as much as 50% compared with traditional NSAIDs. Several consensus guidelines recommend that arthritic patients at risk for GI complications from nonselective NSAIDs receive COX-2–selective inhibitors.

In this study, we used data from 2000 on a wide array of employer-sponsored drug plans to assess how 3-tier formularies influence the use of NSAIDs in an arthritis patient population. In particular, we examined how 3-tier plans affect whether arthritic patients at risk for GI complications from nonselective NSAIDs receive COX-2–selective inhibitors.

**METHODS**

We used the 2000 MarketScan Research Database (MEDSTAT, Ann Arbor, Mich), which consists of medical care claims, prescription drug claims, encounter data, and health plan benefit descriptions from approximately 45 large employers, health plans, and government and public organizations. Each year of the data set contains information on approximately 2 million active and retired employees. The encounter files cover data on age, sex, and geography of residence. Prescription drug claims include the national drug codes, date of purchase, metric quantity, days supply for each drug, and expenditure information, including total payments, out-of-pocket payments made by patients, and net payments made by the employer. Health care claims contain the same financial information as well as the date of service, diagnosis, procedure codes, and type of provider. These data can be linked to a health plan data set that contains details on the benefit as abstracted from plan booklets. Plan information includes the dates of enrollment, type of insurance plan (eg, comprehensive plans, preferred provider organizations, health maintenance organizations), mail-order pharmacy options, generic incentives, and descriptions of the prescription copayments, including differential amounts for preferred and nonpreferred branded drugs.

The sample for this study consisted of 20868 individuals treated for osteoarthritis or rheumatoid arthritis and using prescribed NSAIDs while enrolled in tiered drug plans during the year. We examined the outpatient and inpatient claims records to find persons with at least 1 primary or secondary diagnosis of rheumatoid arthritis or osteoarthritis (International Classification of Diseases, Ninth Revision, Clinical Modification codes 714.x and 720.x, respectively).
Table 1. Select Characteristics of Patients With Arthritis by Type of Tiered-Copayment Drug Coverage

<table>
<thead>
<tr>
<th>Personal characteristics</th>
<th>All</th>
<th>1-Tiered Formularies</th>
<th>2-Tiered Formularies</th>
<th>3-Tiered Formularies</th>
</tr>
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<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>3184 (15.3)</td>
<td>1779 (14.6)</td>
<td>346 (8.3)</td>
<td>1059 (23.6)</td>
</tr>
<tr>
<td>45-54</td>
<td>7081 (33.9)</td>
<td>4755 (38.9)</td>
<td>835 (20.1)</td>
<td>1491 (33.2)</td>
</tr>
<tr>
<td>55-64</td>
<td>9477 (45.4)</td>
<td>5463 (44.7)</td>
<td>2454 (59.1)</td>
<td>1560 (34.7)</td>
</tr>
<tr>
<td>≥65</td>
<td>1126 (5.4)</td>
<td>228 (1.9)</td>
<td>517 (12.5)</td>
<td>381 (8.5)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7736 (37.1)</td>
<td>4673 (38.2)</td>
<td>1309 (31.5)</td>
<td>1753 (39.0)</td>
</tr>
<tr>
<td>Female</td>
<td>13133 (62.9)</td>
<td>7552 (61.8)</td>
<td>2843 (68.5)</td>
<td>2738 (61.0)</td>
</tr>
<tr>
<td>Gastrointestinal comorbidity†</td>
<td>2977 (14.3)</td>
<td>1727 (14.1)</td>
<td>654 (15.8)</td>
<td>596 (13.3)</td>
</tr>
<tr>
<td>No</td>
<td>17891 (85.7)</td>
<td>10498 (85.9)</td>
<td>3498 (84.3)</td>
<td>3895 (86.7)</td>
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<tr>
<td>Plan characteristics</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>16</td>
<td>10†</td>
<td>13‡</td>
</tr>
<tr>
<td>Drug copayment range, $</td>
<td>1-31</td>
<td>1-24</td>
<td>4-10 Generic</td>
<td>5-10 Generic</td>
</tr>
<tr>
<td></td>
<td>8-20 Brand</td>
<td>10-16 Preferred brand</td>
<td>20-31 Nonpreferred brand</td>
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<tr>
<td>Plan type</td>
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<tr>
<td>Comprehensive</td>
<td>9</td>
<td>8</td>
<td>1</td>
<td>0</td>
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<tr>
<td>HMO</td>
<td>11</td>
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<td>6</td>
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<td>POS</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>PPO</td>
<td>12</td>
<td>4</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Capitated POS</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviations: HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization.

*The sample consists of 20,868 patients with arthritis enrolled in 32 drug plans. Formulary categories are not mutually exclusive since persons may have switched plans during the year. Data are from the 2000 Market Scan Research Database (MEDSTAT, Ann Arbor, Mich).

†Gastrointestinal comorbidities included gastric ulcer, duodenal ulcer, peptic ulcer, gastrojejunal ulcer, gastritis and duodenitis, stomach function disorder, unspecified disorder of stomach and duodenum, regional enteritis, irritable colon/colitis, other disorders of the intestine, and gastrointestinal hemorrhage.

‡Seven plans switched from 2 tiers to 3 tiers in 2000.

Classification of Diseases, Ninth Revision, codes 714.XX and 713.XX, respectively). From this group, we examined the outpatient pharmaceutical claims to identify users of at least 1 prescription for an NSAID. Finally, we examined the health plan files for evidence of prescription coverage. We excluded persons if they had no drug benefits during the entire year or had insufficient detail in the database to define the copayment structure of their drug formulary.

We extracted the NSAID claims for our sample and calculated a standard copayment for a 30-day supply for each prescription and classified the medications as nonselective generic NSAIDs, nonselective branded NSAIDs, or COX-2-selective inhibitors. The date of drug claim and the date of drug plan enrollment were compared to identify the type of tiered drug coverage held at the time of the purchase. Prescriptions were excluded if they occurred outside a period of drug coverage (ie, if a person picked up drug coverage halfway through the year, we included NSAID use only after initiation of drug benefit). For 1-tier coverage, all medications were assigned to the single copayment level. For 2-tier plans, we assigned generics to the lower level and brands to the higher level. For 3-tier plans, we estimated the modal copayment values for branded nonselective NSAIDs and COX-2 selective inhibitors used by members of the same plan. Modal values were matched to the plan description of the copayment tiers to identify medications with preferred or nonpreferred status.

We estimated the odds of any use of COX-2-selective inhibitors as a function of tiered drug plan coverage, using logistic regression equations adjusting for other person-level and plan-level covariates. Because COX-2-selective inhibitors are recommended for patients at high risk of developing GI problems, we reestimated our regression model with only persons having evidence of GI comorbidities. All logistic regression analyses were conducted with the use of robust cluster estimation commands to control for correlations among enrollees of the same health plan by means of Stata 7.0 (Stata Corp, College Station, Tex).

The main independent variable was the number of copayment tiers in the drug benefit. We also characterized the copayment amounts for COX-2-selective inhibitors and, in the case of 3-tier plans, whether the plan offered preferred copayment levels for any COX-2-selective inhibitors.

Covariates included patient age, sex, and type of health plan (eg, health maintenance organization, preferred provider organization). We also identified concurrent GI conditions on the basis of medical claims with International Classification of Diseases, Ninth Revision, diagnostic codes for any of the following: gastric ulcer, duodenal ulcer, peptic ulcer, gastrojejunal ulcer, gastritis and duodenitis, stomach function disorder, unspecified disorder of stomach and duodenum, regional enteritis, irritable colon or colitis, other disorders of the intestine, or GI hemorrhage.

Table 1 presents select characteristics of our study population and tiered drug plans. More than half (58.6%) of the patients had 1-tier drug coverage, while the other half faced multiple copayment tiers that increasingly incorporated a preferred-product level: 7 plans switched from 2-tier to 3-tier formularies during 2000. Nearly half (45.4%) of the patients were aged 55 to 64 years, 62.9%...
were female, and 14.3% had evidence of GI comorbidities. Patients in 2-tier plans tended to be older and more often female than those in the 1-tier or 3-tier plans. Prevalence of GI comorbidities was similar across the 3 drug coverage groups. Copayment for COX-2–selective inhibitors varied from $1 to $24 in 1-tier plans, $8 to $20 in 2-tier plans, and $10 to $31 in 3-tier plans.

Figure 1 illustrates how multitiered formularies work to create large differences in copayments between the newer- and older-generation NSAIDs. In 1-tier plans, the average copayment differed for generic NSAIDs and COX-2–selective inhibitors by only $1.27 ($6.71 vs $5.44). In contrast, patients in 2-tier plans paid twice as much for COX-2–selective inhibitors as generic NSAIDs ($9.67 vs $5.44), and 3 times as much if in 3-tier plans ($5.46 vs $15.35). Figure 2 shows that selection of generic NSAIDs and COX-2–selective inhibitors tends to follow the copayment incentive structure, but use of branded NSAIDs does not. In 1-tier drug plans, 63.0% of patients received COX-2–selective inhibitors compared with only 37.7% who received generic NSAIDs. Use of COX-2–selective inhibitors decreased with 2-tier drug coverage to 53.6% and use of generics increased to 40.7%. Most markedly with the 3-tier formulary coverage, 41.6% of patients with arthritis selected COX-2–selective inhibitors compared with 55.7% with generic NSAIDs. In contrast, use of branded NSAIDs remained relatively stable across the different tier structures (21.0% for 1 tier, 15.0% for 2 tiers, and 15.1% for 3 tiers).

Table 2 shows that the choice of NSAIDs tracks closely to the type of tiered-copayment drug coverage even after adjustment for sex, age, serious GI comorbidities, and plan type. In the first model with all patients with arthritis included, the odds of using COX-2–selective inhibitors were significantly lower (odds ratio [OR], 0.36; 95% confidence interval [CI], 0.26-0.49) if their drug formulary designated COX-2–selective inhibitors as only nonpreferred products compared with patients with 1-tier drug coverage. Also, copayments for COX-2 prescriptions exceeding $15 lowered the odds of any use (OR, 0.42; 95% CI, 0.25-0.71) relative to copayments of $5 or less. The second model in the table shows that this relationship persisted even for patients with arthritis who had GI comorbidities. These patients were about half as likely (OR, 0.51; 95% CI, 0.40-0.66) to use COX-2–selective inhibitors if their drug formulary covered COX-2–selective inhibitors as only nonpreferred products relative to patients with 1-tier drug coverage. Copayments for COX-2 prescriptions exceeding $15 also lowered the odds of any use (OR, 0.49; 95% CI, 0.25-0.96) compared with those with COX-2 copayments of $5 or less.

The desire to control prescription drug costs has led to the widespread adoption of 3-tier formularies that provide financial incentives to patients who use less costly medications. Our findings suggest that tiered copayment drug plans may also be influencing the selection of medications. We found that the use of COX-2–selective inhibitors was linked to tiered designations, even for patients with arthritis at risk of experiencing GI complications from using nonselective NSAIDs. The difference in access to COX-2–selective inhibitors appears to be related to the way the drug benefit can impose much higher copayments for nonpreferred medications. It is possible, although unknown, that patients may be evaluating formulary drugs as essentially equivalent across the tiers, and so they see no value to the higher copayments. Health plans with 3-tier formularies inform patients only that third-tier medications usually have generic or preferred-brand alternatives, and physicians and pharmacists in the Pharmacy and Therapeutics Committee make the tier assignments. Without the guidance of physicians and pharmacists, patients must be able to rec-
Disorder of stomach and duodenum, regional enteritis, irritable colon/colitis, other disorders of the intestine, and GI hemorrhage.

Hence, we could not assess the possible substitution of over-the-counter acetaminophen use for COX-2-selective inhibitors.

Despite these limitations, we conclude that 3-tier formularies are clearly associated with the selection of NSAIDs. Our findings show a consistent pattern of medication selection based on more than 20000 patients with arthritis and enrolled in 32 different employer-sponsored drug plans.

This finding raises several policy implications. Drug benefits with financial incentives to select less costly medications can encourage important efficiencies when the choices do not compromise therapeutic effectiveness or safety advances. This is the case with 2-tier formularies split by generic and branded products. Another example is reference pricing models. However, for tiered formularies with additional incentives for preferred medications, our results suggest the potential for therapeutic compromises. One possible solution is for health plans to provide patients with information that explicitly describes when nonpreferred products offer important advantages that might make the higher copayment worthwhile. In the example of COX-2–selective inhibitors, established risk factors include age of 65 years or greater, history of peptic ulcer disease or upper GI bleeding, concomitant use of oral corticosteroids or anticoagulants, and possibly smoking and alcohol consumption. Studies have already demonstrated that, despite the higher costs, COX-2–selective inhibitors are cost-effective under these circumstances. Until such information is made readily available, formularies with nonpreferred tiers have the ability to influence the selection of medications beyond only generic and branded products.

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Table 2. Adjusted Odds Ratios of COX-2 Selective Inhibitor Use Among Patients With Arthritis and Risk of Gastrointestinal Complications*

<table>
<thead>
<tr>
<th>Drug benefit features</th>
<th>All Patients With Arthritis (n = 20 868)</th>
<th>Patients With Arthritis and GI Comorbidities† (n = 2077)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted Odds Ratio‡ (95% CI) P Value</td>
<td>Adjusted Odds Ratio‡ (95% CI) P Value</td>
</tr>
<tr>
<td>2 Tiers (reference, 1 tier)</td>
<td>0.58 (0.30-1.12) .10</td>
<td>0.94 (0.52-1.76) .88</td>
</tr>
<tr>
<td>3 Tiers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With preferred COX-2 selective inhibitors</td>
<td>0.67 (0.38-1.21) .18</td>
<td>1.07 (0.64-1.77) .81</td>
</tr>
<tr>
<td>Without preferred COX-2 selective inhibitors</td>
<td>0.36 (0.26-0.49) &lt;.001</td>
<td>0.51 (0.40-0.66) &lt;.001</td>
</tr>
<tr>
<td>Copayment amount for COX-2 selective inhibitors (reference, =5$), $</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-15</td>
<td>0.56 (0.27-1.17) .12</td>
<td>0.47 (0.21-1.02) .06</td>
</tr>
<tr>
<td>16-31</td>
<td>0.42 (0.25-0.71) .001</td>
<td>0.49 (0.25-0.96) .04</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; COX, cyclo-oxygenase; GI, gastrointestinal.

*Data are from the 2000 Market Scan Research Database (MEDSTAT, Ann Arbor, Mich).

†Gastrointestinal comorbidities included gastric ulcer, duodenal ulcer, gastrojejunal ulcer, gastritis and duodenitis, stomach function disorder, unspecified disorder of stomach and duodenum, regional enteritis, irritable colon/colitis, other disorders of the intestine, and GI hemorrhage.

‡Adjusted for sex, age, GI comorbidity, and type of health plan.
REFERENCES