# NSAID utilization patterns following market withdrawal of rofecoxib

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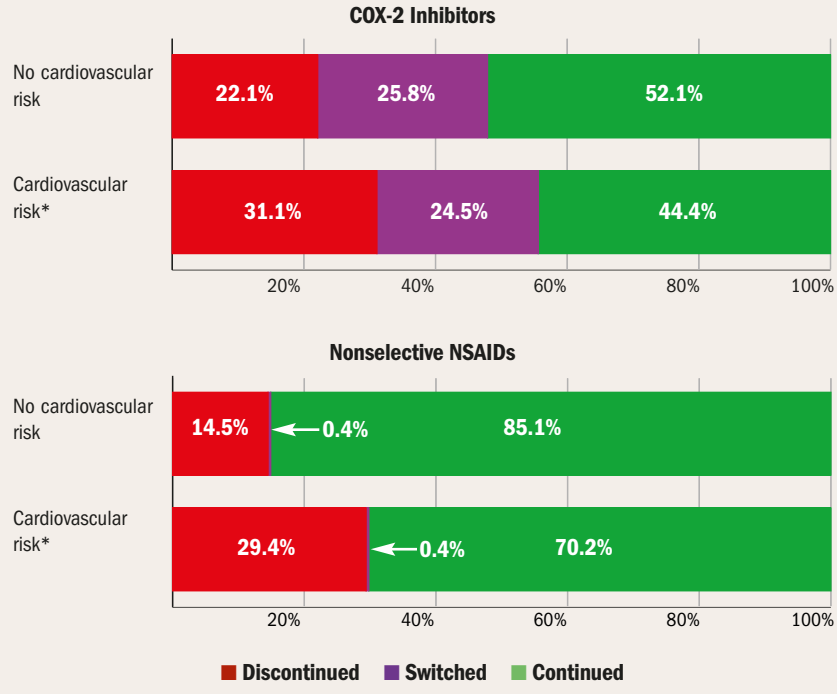
Cyclooxygenase-2 (COX-2)-selective nonsteroidal anti-inflammatory drugs (NSAIDs) have been widely prescribed for patients with arthritis and other conditions because of their lower risk for gastrointestinal adverse events compared with nonselective NSAIDs.[1,2]

On September 30, 2004, the COX-2 inhibitor rofecoxib was withdrawn from the market after a clinical trial demonstrated an increased risk of cardiovascular events in patients receiving chronic therapy with the drug.[3] At the time of withdrawal, little data were available regarding the cardiovascular safety of other COX-2-selective and nonselective NSAIDs.

Figure 1
**Discontinuation, switch, and continuation rates substratified by presence of cardiovascular risk**




*$P<.0001$ for "cardiovascular risk" vs "no cardiovascular risk" subsets.

*Formulary*/Source: Morikawa BH et al

## OBJECTIVES

The objectives of this study included:

- To describe the patient population receiving chronic COX-2 inhibitor or nonselective NSAID therapy prior to market withdrawal of rofecoxib;
- To describe COX-2 inhibitor and nonselective NSAID discontinuation and switch rates among chronic NSAID users following market withdrawal of rofecoxib;
- To compare NSAID utilization patterns in patient populations at higher risk for cardiovascular and cerebrovascular events.

## STUDY METHODS

The study methods included:

**Design:** retrospective analysis of electronic pharmacy claims from a large managed care organization in the United States.

**Time frame:** index date defined as September 30, 2004, with a 4-month pre-index period and a 4-month post-index period.

**Patient identification:** adult patients aged 18 years or older at index who were continuously enrolled during the pre-index and post-index periods and who had pharmacy claim(s) for a COX-2 inhibitor or nonselective NSAID totaling at least a 90-day supply during the pre-index period.

**Cohorts:** patients were stratified by index NSAID (defined by the last NSAID filled during the pre-index period) into 2 cohorts (COX-2 inhibitor or nonselective NSAID), and further substratified based on the presence of cardiovascular risk, which was defined by a prescription fill for a cardiovascu-



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lar or diabetes medication.

**Baseline measures:** demographics; concomitant use of a gastrointestinal-protective agent during the pre-index period; presence of cardiovascular risk.

**Follow-up period outcome measures:** continuation rate; discontinuation rate; switch rate (classified as switched when the first filled NSAID during the post-index period differed from the index NSAID).

**Statistical methods:** continuous variables were compared using t-test; categorical variables were compared using chi-square test.

## RESULTS

The managed care population receiving chronic NSAID therapy tended to be elderly. Those receiving a COX-2 inhibitor were more likely to be female and concomitantly using a GI-protective medication compared to those receiving a nonselective NSAID (Table 1). About one-quarter of patients receiving chronic NSAID therapy (COX-2 inhibitors as well as nonselective NSAIDs) were identified as having cardiovascular risk. Patients with cardiovascular risk were more likely to be discontinued from chronic COX-2 inhibitor as well as nonselective NSAID therapy compared to patients without cardiovascular risk (Figure 1).

Following market withdrawal of rofecoxib, one-third of rofecoxib users discontinued NSAID therapy, with the remaining two-thirds switching to an alternative NSAID (Figure 2). Among rofecoxib users who switched NSAID therapy, 43.6% switched to celecoxib and 35.2% switched to a nonselective NSAID (Figure 3). Approximately one-quarter (25.4%) of valdecoxib users discontinued NSAID therapy, while discontinuation rates were lower among patients receiving celecoxib (18.6%) and those receiving nonselective NSAID therapy (18.3%).

## DISCUSSION

Information from additional studies regarding the safety of celecoxib, valde-

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Table 1

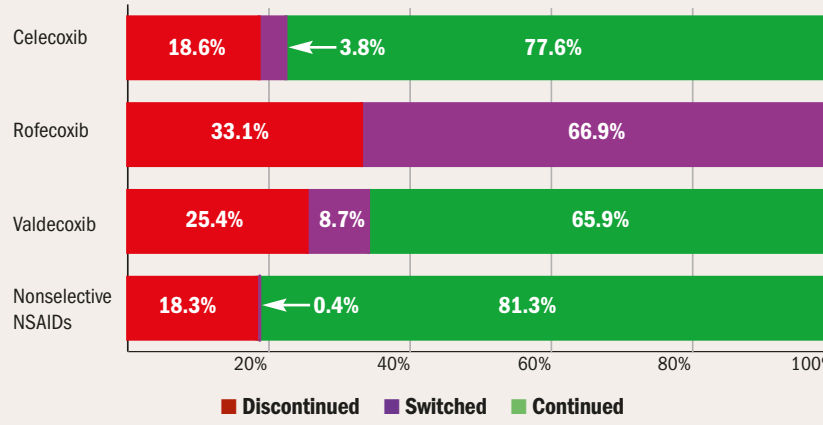
**Baseline measures stratified by cohort (index NSAID class)**

| | COX-2 inhibitor (n=8,098) | | Nonselective (n=19,711) | | *P* value |
|---|---|---|---|---|---|
| Age: Mean (SD) | 69 | (13.2) | 67.9 | (12.9) | <.0001 |
| Female gender: N (%) | 5,857 | (72.4) | 12,773 | (64.8) | <.0001 |
| Use of GI-protective medication: N (%) | 2,356 | (29.1) | 4,122 | (20.9) | <.0001 |
| Presence of CV risk: N (%) | 1,916 | (23.7) | 5,047 | (25.6) | .0007 |

*Formulary*/Source: Morikawa BH et al

Figure 2

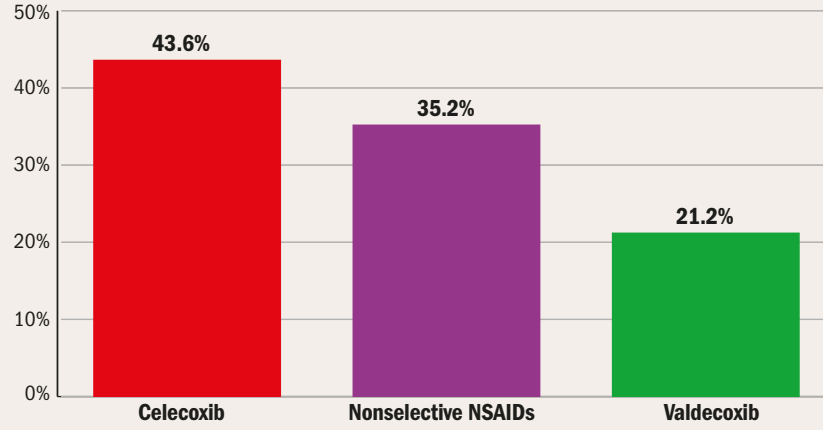
**Discontinuation, switch, and continuation rates stratified by index NSAID**




*Formulary*/Source: Morikawa BH et al

Figure 3

**Subsequent NSAID therapy among patients switching from rofecoxib***




*N=1,812

*Formulary*/Source: Morikawa BH et al

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coxib, and naproxen was made available during the follow-up period, possibly affecting the utilization of these medications and other NSAIDs. In addition, patients with cardiovascular risk were identified using pharmacy claims, which was not validated through a review of medical records.

## CONCLUSIONS

Following rofecoxib's withdrawal from the market, patients with cardiovascular risk who were receiving chronic NSAID therapy were more likely to discontinue treatment with NSAIDs compared to those without cardiovascular risk. Patients and prescribers showed less concern with celecoxib therapy, with the discontinuation rate of celecoxib therapy similar to the discontinuation rate for nonselective NSAIDs, and secondly, the majority of rofecoxib switchers subsequently being treated with celecoxib.

## REFERENCES

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**Editors' Note:**
This study was originally presented as a poster at the Academy of Managed Care Pharmacy (AMCP) 17th Annual Meeting & Showcase, April 20–23, 2005, in Denver, Colo.