Appropriateness of NSAID and Coxib Prescribing for Patients With Osteoarthritis by Primary Care Physicians in Ontario: Results From the CANOAR Study

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Objective: To assess the appropriateness of nonsteroidal anti-inflammatory drug (NSAID) use relative to recent osteoarthritis treatment guidelines from the Second Canadian Consensus Conference.

Study Design: Observational study of self-reported practice in a cohort of physicians from the Canadian Osteoarthritis Rx (CANOAR) study.

Subjects and Methods: Ontario primary care physicians were recruited from the top 10% of NSAID prescribers based on the number of NSAID prescriptions filled per year. Physicians were asked to record office visits on a 1-page data collection form from November 2000 to December 2001.

Results: Of 1400 physicians invited, 185 were enrolled and 119 registered office visits. Data were analyzed for the first visits of 5459 patients for whom a prescribed NSAID was identified, of whom 60% were female and 46% were older than 65 years. Coxibs were prescribed for 56% of study patients and were more commonly used by those with recent gastrointestinal (GI) events (85%), those receiving warfarin sodium therapy (79%), and those with congestive heart failure (68%). Coxib use increased with increasing global assessment of OA severity, but not patient age. Overall, 58% of prescriptions were considered appropriate given patient GI risk factors.

Conclusions: Most coxib and NSAID prescriptions were consistent with the guidelines, but there was considerable underuse of coxibs in at-risk patients and some overuse of coxibs and of gastroprotective agents with NSAIDs in patients with no identified GI risk factors. Increased recognition of relationships between patient age and NSAID-related GI risk would likely promote more appropriate use of traditional NSAIDs, coxibs, and gastroprotective agents in osteoarthritis patients.

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Osteoarthritis (OA) is a joint disease characterized by degenerative changes in the articular cartilage and progressive joint deterioration. It is the most common type of joint disease and is a major cause of disability.[1] In Western countries, radiographic evidence of OA is present in most individuals by 65 years of age and in about 80% of those older than 75 years.[2] In Canada, an estimated 4 million individuals 15 years and older experienced arthritic disorders in 2000, and the direct and indirect costs of these diseases in 1998 were estimated to be at least Can$4.4 billion.[3] Osteoarthritis is expected to account for about half of these costs.[4]

Osteoarthritis typically presents as pain involving 1 or several joints. The primary goal of treatment is to relieve pain, thereby improving function and quality of life. Treatment guidelines in Canada[5] and the United States[6] recommend nonsteroidal anti-inflammatory drugs (NSAIDs) as second-line treatment (after acetaminophen) for mild OA and as first-line treatment for moderate-to-severe OA.

Canadian guidelines further recommend that, in patients at high risk for upper gastrointestinal (GI) adverse events, the use of traditional NSAIDs should be accompanied by prophylaxis with misoprostol or a proton pump inhibitor.[5,7] Risk factors include a history of peptic ulcer disease, GI bleeding, cardiovascular disease, and aged 65 years or older.[8,9]

Alternatively, the use of coxib NSAIDs (cyclooxygenase-2–specific inhibitors) as first-line treatment for high-risk patients is also recommended by Canadian guidelines.[5,7] Large clinical trials have demonstrated that these drugs have efficacy similar to that of traditional (non-coxib) NSAIDs[10-12] and produce fewer GI adverse effects.[13-16] Although coxibs are not medically contraindicated for low-risk patients, economic models suggest that they may not be cost effective in this group.[17,18]

The Canadian Osteoarthritis Rx (CANOAR) study was designed to characterize OA patients in Ontario for whom primary care physicians prescribed NSAIDs. This article examines the use of NSAIDs in this study cohort in relation to recommendations for their appropriate use as published in the Second Canadian Consensus Conference arthritis treatment guidelines.[5]

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METHODS

The CANOAR study was an observational study of a cohort of primary care physicians with high-volume NSAID prescribing practices. The objective was to determine the clinical circumstances under which NSAIDs were prescribed for OA patients in routine clinical practice. The study took place in Ontario, a province of 11 million people under a single healthcare system.

Before conducting the study, a steering committee was formed with 2 primary care physicians, 3 rheumatologists, a biostatistician, a health economist, the chief executive officer of The Arthritis Society, and a patient with OA. The committee met to review and modify an initial draft protocol and data collection form. A review of the modified protocol by 4 rheumatologists, 4 epidemiologists, and 2 health economists further focused the study design.

One-page clinical encounter data forms using anonymous sequential patient identifiers were designed and pilot-tested in collaboration with 7 primary care physicians. The form recorded patient demographics, location of principal OA joint involvement, global physician and patient assessments, concomitant medical problems, history of clinically significant GI events, current drugs, and previous use of and current recommendations for OA therapies and gastroprotective agents (GPAs). The form allowed identification of the following GI risk factors listed in the Second Canadian Consensus Conference guidelines: history of a clinically significant GI event, advanced age (aged 65-74 years was scored as 1 risk factor, while age ≥ 75 years was scored as 2 risk factors), current and continuing use of warfarin sodium, current and continuing use of corticosteroids, hypertension, congestive heart failure, renal insufficiency, and hepatic insufficiency. Renal risk factors recorded were renal insufficiency, hypertension, congestive heart failure, hepatic insufficiency, and concomitant antihypertensive drugs.

The forms were designed to be usable as part of the routines of normal clinical practice. Seven pilot physicians tested the protocol by enrolling 10 patients and provided final assessments and recommendations about office procedures for patient enrollment and consent, data form completion, and data transmission to the data center by toll-free, never-busy facsimile. The pilot physicians also provided estimates of required per patient time, for inclusion in the physician recruitment letter.

After receiving ethics review board approval, the CANOAR study proceeded with physician recruitment. Of the 12 000 primary care physicians in Ontario, 1400 of the top NSAID prescribers, based on the number of NSAID prescriptions filled in 2000, were identified from a physician list sourced from the IMS Health Canada aggregated prescriber-level database. These physicians were invited by letter to participate. Each participating physician was asked to record up to 130 office visits, including follow-up visits, of successive patients for whom they decided to prescribe an NSAID or a coxib (new or renewal) for OA. Participants were not provided with the Second Canadian Consensus Conference guidelines as part of the study protocol and were not told that their results would be compared with guidelines. Physicians were reimbursed Can$20 per completed form.

Although a diagnosis of OA is a determinant of eligibility for coxib coverage by the Ontario Drug Benefits Program, which provides basic drug coverage to all Ontario citizens 65 years and older, the program does not specify OA diagnostic criteria.[19] The phrase "working diagnosis of OA" was therefore used on the data form to avoid telling participating physicians how to diagnose OA. Patients were included in the study if they had a working diagnosis of OA by the treating primary care physician, received a prescription for an NSAID or a coxib as part of routine care on the first study visit, and gave consent for the use of their anonymous data for aggregate analyses.

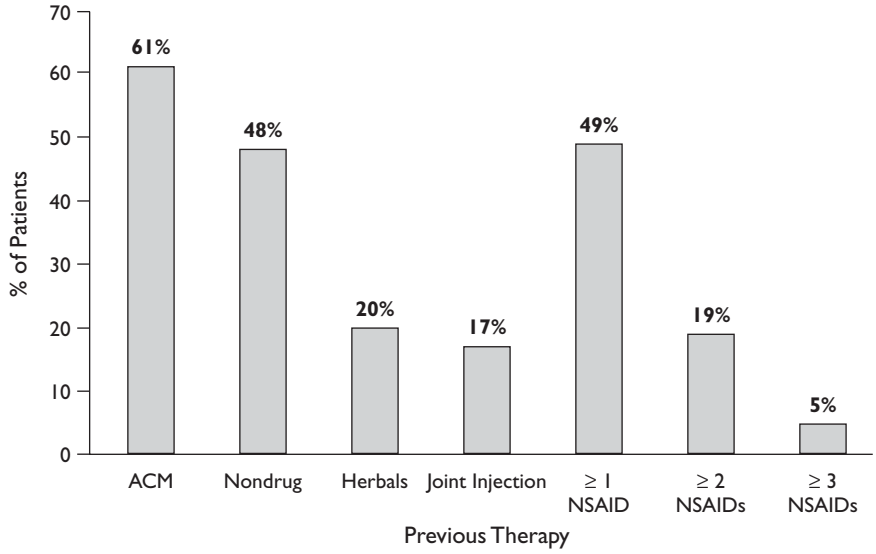
Completed data forms were sent by toll-free facsimile to the data center. Standardized data management protocols for paperless and semiautomated processes adapted to the specific needs of the study were used to aggregate and process the data into a relational database. The Goodman-Kruskal γ statistic was used as a measure of ordinal association. All statistical comparisons were 2-tailed, with $P < .05$ considered statistically significant.

RESULTS

Recruitment

Of the 1400 physicians invited, 185 agreed to participate and were enrolled. It was not possible to examine whether characteristics of participants differed from those of nonparticipants, because the aggregated prescriber list was not ranked and did not preserve prescribing data or other individual characteristics. Data collection continued during 14 months, from November 2000 to December 2001, with 119 (64% of those enrolled) of the physicians registering 8846 office visits of 5947 OA patients in the study (the number of patients with 2, 3, and >3 visits were 1034, 431, and 280, respectively). Data were analyzed for the first visits of the 5459 patients for whom a prescribed NSAID was identified.

Figure 1. Previous Therapies Tried by Osteoarthritis Patients



ACM indicates acetaminophen; NSAIDs, nonsteroidal anti-inflammatory drugs.

Patient Characteristics

Of the 5459 OA patients for whom data were analyzed, 60% were female and 46% were older than 65 years. All residents of Ontario 65 years and older have limited public drug coverage through the Ontario Drug Benefits Program. In this study, 57% of patients younger than 65 years and 19% of patients 65 years or older had private drug coverage.

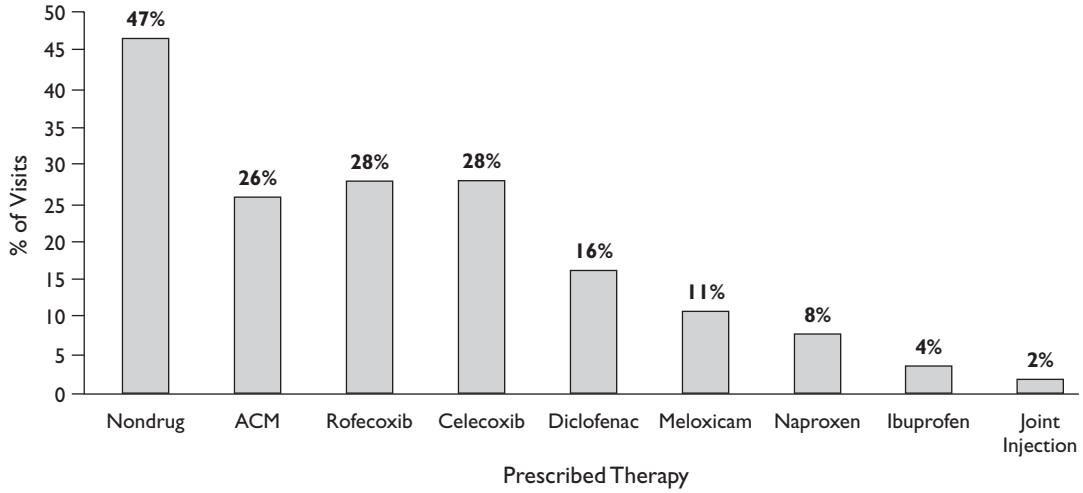
A large number of patients had other concomitant conditions. The most common comorbidities were hypertension (34%) and coronary artery disease (12%). A clinically significant GI event had been experienced by 8% of patients. More than a third (34%) of patients were receiving concomitant antihypertensive therapy, and 17% were receiving low-dose aspirin (the study protocol did not specify a threshold dose because physicians may have differed in their operational definitions of low-dose aspirin for cardiovascular protection).

At the time of the first study visit, 20% of patients were already receiving a GPA. Acetaminophen had previously been tried by 61% of patients for their OA symptoms, and 49% had tried 1 or more NSAIDs (**Figure 1**). Five percent of patients had tried 3 or more NSAIDs. Of the 5459 patients, 1145 (21%) were receiving NSAIDs for the first time at their first CANOAR study visit.

Nonsteroidal Anti-inflammatory Drug Prescribing Patterns

Coxibs were prescribed at 56% of visits in this study cohort, evenly divided between rofecoxib and celecoxib (**Figure 2**). Diclofenac, meloxicam, naproxen, and ibuprofen were less commonly recommended. Forty

Figure 2. Therapies Prescribed or Recommended by Study Physicians



ACM indicates acetaminophen.

patients (0.7%) received aspirin prescriptions at the study visit, and because it was unclear whether they were for OA therapy, these prescriptions are not included in Figure 2.

Coxib use was higher in certain high-risk patient subgroups. Among the 26 patients who had experienced clinically significant GI events in the previous 60 days, 85% were prescribed coxibs (**Table 1**), while 74% of the 214 patients whose GI events had occurred within the last 10 years received coxibs. Most (79%) of the 72 patients receiving warfarin therapy and most (68%) of the 163 patients with congestive heart failure were also prescribed coxibs. However, the percentage (57%) of patients with hypertension who were prescribed coxibs was similar to that (56%) among all patients, and coxib use did not vary with patient age (Goodman-Kruskal $\gamma = 0.07$, SE = 0.02, $P = .60$; data not shown). Although it appeared that coxibs were prescribed more commonly as the number of GI and renal risk factors increased (**Table 2**), these trends were not statistically significant ($P = .93$ and $P = .21$, respectively). However, the results suggested a threshold effect, with higher coxib use for patients with 4 or more risk factors than for those with 3 or fewer. A post hoc analysis in which risk factor categories were pooled confirmed that this difference was significant (GI and renal risk factors, $P < .001$ for both; Fisher exact test). Coxib use increased significantly with increasing global pain assessments (physician and patient assessments, $P < .001$ for both; **Table 3**).

Table 1. Frequency and Percentage of Patients for Whom Coxibs Were Prescribed on Their First Study Visit

Patient Characteristic	No. of Patients	% Prescribed Coxibs
History of clinically significant gastrointestinal event*		
Within 60 days	26	85
Within 10 years	214	74
Concurrent use of warfarin sodium	72	79
Congestive heart failure	163	68
Hepatic insufficiency	14	64
Renal insufficiency	103	58
Coronary artery disease	651	60
Concurrent use of corticosteroids	42	62
Hypertension	1877	57
Overall	5459	56

*Perforation, ulcer, bleeding, or unknown (could not be discriminated between perforation, ulcer, or bleeding) event.

Gastroprotective Agent Prescribing Patterns

Gastroprotective agents were coprescribed with an

Table 2. Prescription of Nonsteroidal Anti-inflammatory Drugs (NSAIDs) According to Gastrointestinal (GI) or Renal Risk Factors and NSAID Type Among 5459 Patients

	GI Risk Factors			Renal Risk Factors		
		% of Patients			% of Patients	
No. of Risk Factors*	No. of Patients	Coxib	Non-coxib	No. of Patients	Coxib	Non-coxib
0	2114	56	44	3353	55	45
1	1457	56	44	382	52	48
2	1137	53	47	1576	57	43
3	573	56	44	126	55	45
4	144	67	33	21	90	10
> 4	34	82	18	1	100	0
≤ 3	5281	55	45	5437	56	44
≥ 4	178	70	30	22	91	9

*Comparison of 0, 1, 2, 3, 4, and > 4 risk factors: GI risk factors, Goodman-Kruskal $\gamma = -0.002$, SE = 0.021; $P = .93$; and renal risk factors, Goodman-Kruskal $\gamma = -0.03$, SE = 0.03; $P = .21$. Comparison of ≤ 3 and ≥ 4 risk factors: GI risk factors and renal risk factors, $P < .001$ for both.

Table 3. Prescribing of Nonsteroidal Anti-inflammatory Drugs According to Physician and Patient Global Pain Assessments

Global Pain Assessment*	No.	% of Patients for Patient Assessments	
		Coxib	Non-coxib
Physician (n = 5390)			
Nil	17	41	59
Mild	1740	50	50
Moderate	3080	57	43
Severe	553	67	33
Patient (n = 5428)			
Nil	4	25	75
Mild	1114	47	53
Moderate	3193	56	44
Severe	1117	65	35

*Physician: Goodman-Kruskal $\gamma = -0.18$, SE = 0.02; $P < .001$. Patient: Goodman-Kruskal $\gamma = -0.21$, SE = 0.02; $P < .001$.

NSAID at 31% of visits. The most common reason given for prescribing a GPA was NSAID GI prophylaxis (39%). Other reasons included dyspepsia (19%), gastroesophageal reflux disease (25%), and a history of ulcer (8%). Misoprostol was the most commonly prescribed GPA, usually in the form of a combination pill of diclofenac and misoprostol, while H_2 antagonists (eg, ranitidine) and proton pump inhibitors (eg, omeprazole) were also used, although less often (**Table 4**). Patients receiving non-coxib NSAIDs were more likely to receive GPAs than were coxib patients (45% vs 21%).

Gastroprotective agent coprescriptions were more commonly given to patients with a higher number of GI risk factors (Goodman-Kruskal $\gamma = -0.20$, SE = 0.04; $P < .001$; **Table 5**). The percentage of patients who were coprescribed a GPA with their NSAID was 25% for patients younger than 65 years, 34% for those aged 65 to 69 years, 39% for those aged 70 to 74 years, 39% for those aged 75 to 79 years, and 45% for those older than 79 years.

Table 4. Gastroprotective Agents (GPAs) Coprescribed with Nonsteroidal Anti-inflammatory Drugs (NSAIDs)*

GPA	Non-coxib (n = 2414)	Coxib (n = 3045)	Any NSAID (n = 5459)
Misoprostol	29	< 1	13
Ranitidine	6	5	5
Omeprazole	2	4	4
Any GPA	45	21	31

*Data are given as percentages of patients.

Acetaminophen Use

Acetaminophen had been tried previously by 61% of study patients. The prevalence of its previous use increased with increasing patient age and the number of GI and renal risk factors ($P < .001$ for all). In addition, previous acetaminophen use was more common among patients with higher patient and physician global assessments of OA severity ($P < .001$).

Appropriateness of Prescribing

Most coxib prescriptions were for patients with 1 or more GI risk factors, but a large percentage (39%) were for patients with no identified risk factors and could be considered to be less cost effective (**Table 6**). Most (56%) prescriptions for a traditional NSAID alone were for patients with at least 1 GI risk factor, for whom a GPA coprescription or a coxib would be recommended. Of 1081 prescriptions for traditional NSAIDs plus GPAs, 31% went to patients with no identified risk factors. Physicians did not indicate a reason for prescribing a GPA in 40% of prescriptions for traditional NSAIDs plus GPAs, so these cases were excluded from the analysis of appropriate prescribing. In 98% of these excluded cases, the prescription was for the NSAID and GPA combination pill Arthrotec (diclofenac sodium and misoprostol). Some physicians who prescribed Arthrotec may not have considered that they were actively prescribing a GPA, which may explain the high rate of nonresponse to this question. This problem was addressed by also excluding from the analysis of appropriate prescribing all 236 Arthrotec prescriptions for which a reason for prescribing a GPA was given. Of the remaining 413 prescriptions for traditional NSAIDs

plus GPAs, 73% went to patients with 1 or more identified risk factors and were counted as appropriate. The other 27% went to patients with no identified risk factors. Of these prescriptions, 63% were prescribed for NSAID GI prophylaxis only and were counted as inappropriate, while the remainder were prescribed for other reasons (30%) or for NSAID GI prophylaxis and other reasons (6%) and were counted as appropriate. Therefore, 83% of prescriptions for traditional NSAIDs plus GPAs were considered appropriate.

Table 5. Coprescription of Gastroprotective Agents According to Gastrointestinal Risk Factors and Nonsteroidal Anti-inflammatory Drug (NSAID) Type Among 5459 Patients

No. of Risk Factors	Coxib		Non-coxib		Any NSAID	
	%	No.	%	No.	%	No.
0	12	1188	37	926	23	**2114**
1	19	812	44	645	30	**1457**
2	26	601	51	536	38	**1137**
3	36	320	59	253	46	**573**
4	48	96	64	48	53	**144**
>4	61	28	83	6	65	**34**

Goodman-Kruskal $\gamma = -0.20$, SE = 0.04; $P < .001$.

For patients with no identified GI risk factors, 33% of nonexcluded prescriptions were considered appropriate, whereas for those with 1 or more risk factors, 74% were considered appropriate. Overall, 58% of nonexcluded prescriptions were considered to be appropriate given patient GI risk factors. If the analysis was restricted further to exclude prescriptions for traditional NSAIDs plus GPAs in which the GPA was prescribed for reasons other than GI prophylaxis alone, 32% of prescriptions for patients with no identified GI risk factors, 73% of those for patients with 1 or more risk factors, and 56% overall were considered appropriate.

DISCUSSION

Treatment guidelines in the United States,[6] Europe,[20] and Canada[5] stress the importance of tailoring OA treatment to individual patient needs. Patient age and the presence of comorbidities should be important factors in treatment selection. The 2000 Second Canadian Consensus Conference guidelines[5] that were available when this study was conducted are a relevant benchmark for prescribing practice at the time. Although subsequently published guidelines[7,21] have refined the criteria for appropriate coxib, NSAID, and GPA pre-

Table 6. Appropriateness of Nonsteroidal Anti-inflammatory Drug (NSAID) and Coxib Prescribing Based on Patient Gastrointestinal (GI) Risk Level*

No. of GI Risk Factors	Coxib	Traditional NSAID	Traditional NSAID and Gastroprotective Agent (GPA)† (Categorized by Reason for GPA Prescription)		
			NSAID GI Prophylaxis	Other‡	NSAID GI Prophylaxis and Other‡
0	1188 (39) (inappropriate)	588 (44) (Appropriate)	71 (32) (inappropriate)	34 (26) (Appropriate)	7 (11) (Appropriate)
>1	1857 (61) (Appropriate)	745 (56) (Inappropriate)	148 (68) (Appropriate)	96 (74) (Appropriate)	57 (89) (Appropriate)
Total	**3045 (100)**	**1333 (100)**	**219 (100)**	**130 (100)**	**64 (100)**

*Data are given as number (percentages) of patients.
†Excludes prescriptions for Arthrotec and those for which no reason was given for prescribing a GPA (see the "Appropriateness of Prescribing" subsection of the "Results" section).
‡Gastroesophageal reflux disease, dyspepsia, ulcer history, or other specified reason.

scription, they identify the same risk factors as did the Second Canadian Consensus Conference and agree on selection of a coxib or an NSAID plus GPA for at-risk patients. On the basis of the Second Canadian Consensus Conference guidelines, 42% of prescriptions in the CANOAR study were inappropriate given patient GI risk factors. There was underuse of coxibs and of NSAIDs plus GPAs for patients with 1 or more risk factors and overuse of these options for patients with no identified risk factors. The percentage of prescriptions deemed appropriate was higher for coxibs than for traditional NSAIDs alone (61% vs 44%) but lower than that (83%) for traditional NSAIDs plus GPAs. Greater appropriate use of traditional NSAIDs in combination with GPAs than of coxibs may reflect the fact that coxibs were a new prescribing option when this study was conducted.

All guidelines recommend acetaminophen as a first-line agent, primarily because of its GI safety. In accord with guidelines, most patients in this Ontario cohort had previously tried acetaminophen, particularly older patients, those with multiple risk factors, and those with severe OA.

Bleeding, upper GI ulcers, and perforation occur in approximately 1% of patients treated with non-coxib NSAIDs for 3 to 6 months.[5] Among patients treated for 1 year, 2% to 4% are affected. These events are costly and can lead to reduced compliance and decreased quality of life.[22] Recent clinical trial evidence found that, compared with acetaminophen alone, NSAIDs in combination with a GPA produced significantly greater improvements in pain scores for patients with moderate OA.[23] In our study, GPAs were prescribed at 31% of visits, and 39% of these prescriptions were for NSAID GI prophylaxis. In addition, GPA prescriptions increased with the number of GI risk factors. For patients with the same number of GI risk factors, those receiving coxibs had a somewhat lower rate of GPA coprescription compared with those receiving traditional NSAIDs, often for reasons other than NSAID GI prophylaxis. In general practice, GPAs are commonly and appropriately prescribed to treat conditions such as gastroesophageal reflux disease and dyspepsia.[24,25]

Comparisons of non-coxib NSAIDs and coxibs suggest similar efficacy,[10-12] and a recent clinical trial suggests that coxibs are similar to or better than acetaminophen.[26] Because they produce fewer GI adverse effects than traditional NSAIDs,[13-16] coxibs are now recommended in the United States and Canada as first-line treatment for patients at risk for GI perforation, ulcer, and bleeding;[5,6] recent updates of European guidelines are in agreement.[27] In this study, 85% of patients who had experienced recent (within 60 days) clinically significant GI events were prescribed a coxib NSAID, while 74% of those whose GI event occurred up to 10 years earlier received a coxib NSAID. Also in keeping with Canadian guidelines, a coxib NSAID was prescribed to most (79%) OA patients receiving warfarin therapy, who are at higher risk for GI bleeding.

Osteoarthritis is the most common chronic condition among older persons,[28] and non-coxib NSAIDs are prescribed frequently in this group.[29] A study[30] of non-coxib NSAID prescribing patterns in Canada reported that older OA patients, who have 3 times the risk for serious GI adverse effects relative to patients younger than 50 years, were frequently given unnecessary prescriptions for non-coxib NSAIDs. In addition, GI complications stemming from non-coxib NSAID use are a leading cause of hospitalization for older persons.[29] Although Canadian guidelines recommend the use of coxibs in patients with GI risk factors, including older patients,[5] coxib prescribing in our cohort was not related to age. As a result, some older patients who could have benefited from a coxib received non-coxib NSAID prescriptions instead, whereas some younger patients for whom traditional NSAIDs may have been appropriate[5] were prescribed more costly coxibs. One possible explanation is that age alone may not have been considered a risk factor by the physicians participating in this study. Alternatively, NSAID prescribing practice may have been correlated with barriers against coxib use, such as access. The finding that older patients had higher rates of GPA coprescription with NSAIDs contradicts the suggestion that physicians failed to recognize age as a GI risk factor, suggesting instead the existence of fewer barriers to coxib prescribing among younger patients than among seniors. Future analyses of the CANOAR study data will examine whether prescribing varied by drug coverage.

Although an association has been found between NSAID use and impaired renal function,[31] NSAIDs are not contraindicated for patients with renal risk factors, including older patients. Rather, renal function should be monitored in all high-risk patients taking NSAIDs. There does not appear to be a difference between non-coxib and coxib NSAIDs in this regard, and in our study there was no relationship between coxib prescribing and elevated creatinine levels. This practice pattern is in concert with treatment guidelines.

More than a third of patients in this study were hypertensive. Meta-analyses studying the effect of non-coxib NSAIDs on blood pressure found that they elevate blood pressure and antagonize the blood pressure–lowering effect of antihypertensive medication.[32,33] The Second Canadian Consensus Conference guidelines noted that coxibs can also adversely affect blood pressure control, but did not mention possible

differences in the hypertensive or prothrombotic effects of rofecoxib and celecoxib.[5] Data collection for this study was largely complete before publication of an analysis that suggested differences may exist among coxibs in the risk of cardiovascular events.[34] It is therefore unlikely that participating physicians prescribed coxibs differentially in the presence of cardiovascular risk factors. More recent meta-analyses have not found increased cardiovascular thrombotic event rates relative to placebo for either coxib.[35,36]

This study has limitations. Prescribing patterns were measured via physician questionnaire responses, without external verification. Self-reported physician practice may not accurately reflect actual practice, introducing the potential for biasing self-reports toward higher quality levels.[37] However, the CANOAR study participants were not told in advance that their responses would be evaluated against guidelines. Furthermore, forms were to be completed during routine clinical practice, minimizing the potential for self-recall bias.

Participation in the study was voluntary, and the 185 physicians who agreed to participate—and the 119 who contributed data—may not represent a random sample of the 1400 high NSAID prescribers who were invited. Although nonresponding physicians were not followed up to determine reasons for their nonparticipation, it is possible that some may have thought that study participation would be onerous, given the need to fill in detailed data forms, obtain patient consent, and perform medical chart review. Some nonparticipants may also have found the financial incentive to be inadequate. This could bias results if, for instance, physicians who are more likely to enroll in such a study and who actually do participate are also more likely to follow prescribing guidelines.

High NSAID prescribers were targeted to capture the highest number of prescriptions with the fewest physicians. Although the prescribing choices of these physicians may not reflect those of all primary care physicians, their disproportionately large share of NSAID prescriptions is expected to be representative of prescriptions for OA in Ontario. These results are not necessarily generalizable to other jurisdictions, however, because prescribing may differ between Canada and the United States or other regions. For example, whereas 39% of coxib prescriptions in the CANOAR study went to patients with no GI risk factors, a recent analysis of claims data from a large preferred provider organization in the US Midwest found that as many as 73% of patients given new coxib prescriptions had no evidence of GI risk factors.[38]

To avoid influencing prescribing decisions, this observational study did not provide physicians with guidelines for OA diagnosis or therapy. This may have increased variability in physician ratings of OA severity, but questions on the data form about other risk factors required yes or no responses that would not be predicted to vary with exposure to guidelines.

Previous use of acetaminophen as reported in this study may be somewhat underestimated, as this commonly used drug is available by prescription and over the counter. Its previous use in either form, perhaps many years earlier, may have been forgotten by physicians or their patients at the time of completing the study data forms.

In conclusion, large, simple observational studies such as the CANOAR study can contribute important practical assessments of the appropriateness of real-world prescribing and guide the development of future interventions designed to enhance the application of evidence-based care in actual clinical practice. Most prescriptions observed in this cohort of OA patients treated by primary care physicians in Ontario were consistent with guidelines from the Second Canadian Consensus Conference,[5] but some could be considered inappropriate. Areas in which improved recognition of risk factors might lead to further increases in the appropriate use of NSAIDs, coxibs, and GPAs in OA patients include the relationship between patient age and GI risk, as well as the benefit of GPAs or coxibs for patients with multiple GI risk factors.

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