

USE OF CELECOXIB IMMEDIATELY POST MARKETING IN CANADA: ACUTE OR CHRONIC PAIN?

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ABSTRACT

Objectives

The diffusion of innovations theory suggests that early users of innovations influence others. This study was undertaken to apply the diffusion of innovations theory to the prescribing of celecoxib and to determine if prescriber and patient characteristics differed amongst early use of celecoxib for acute pain versus chronic musculoskeletal conditions.

Methods

Using Manitoba's population-based prescription and health care databases, diffusion time from market availability to first prescription for celecoxib was determined for each prescriber. The diffusion of prescribing curves for celecoxib in acute pain versus chronic musculoskeletal conditions were compared. Separately for acute and chronic conditions, the likelihood of being an early or late prescriber or user of celecoxib was determined according to physician factors (specialty and place of training) and patient demographics. This multivariate analysis was completed using polytomous logistic regression, with majority prescribers as the reference.

Results

The use of celecoxib for chronic musculoskeletal conditions demonstrated faster diffusion than for acute pain. The majority of early use of celecoxib was for chronic conditions; however 36% of first prescriptions were for acute pain, including the treatment of back pain and injuries. Early prescribers of celecoxib for acute pain were more likely than majority prescribers to be general practitioners (OR = 2.24, 95%CI: 1.53-3.29) and have hospital affiliations (OR=1.54, 95%CI: 1.04-2.27). Early users of celecoxib for chronic conditions were less likely to be low income (OR=0.56, 95%CI: 0.35-0.91).

Conclusions

Immediately after market release in Canada, celecoxib was commonly prescribed for the treatment of acute pain; these prescriptions were associated with general practitioners and hospital affiliation status.

Key Words: *Celecoxib, diffusion of innovations theory, post marketing, acute pain*

Celecoxib is a cyclooxygenase 2 (COX-2) inhibitor type analgesic, approved for use in Canada in April 1999. As compared to conventional non-steroidal anti-inflammatory drugs (NSAIDs), celecoxib demonstrates equivalent analgesic efficacy, with a lower incidence of gastrointestinal mucosal injury than other NSAIDs, but minimal benefit for clinical outcomes such as gastric perforations, ulcers, or

bleeds.¹⁻³ At the time of market release, the approved indications for celecoxib included treatment of the signs and symptoms of osteoarthritis and rheumatoid arthritis in adults.¹⁻⁴ At that time, available data also suggested that celecoxib was better than placebo for the treatment of osteoarthritis and rheumatoid arthritis, but there were no published, randomized controlled trials describing the efficacy of

celecoxib as compared to active treatment.^{5,6} Even less information described the efficacy of celecoxib in acute pain, such as dental pain. Despite this lack of evidence, celecoxib was widely perceived as an innovative drug, and was rapidly adopted into general use.⁷⁻⁹

The diffusion of innovations theory describes a “process by which an innovation is disseminated over time among members of a social system.”¹⁰ Individuals are classified as early, majority, or late adopters of the innovation, and the theory characterizes the early adopters as influential champions of a new idea, who frequently influence the behavior of others.¹⁰ This theory has been applied to studies of newly marketed prescription drugs, but no research has evaluated the diffusion of newly marketed prescription drugs for non-approved indications.¹¹⁻¹³ Early adoption of new drugs appears to be both drug and prescriber dependent.¹¹⁻¹³ Steffensen et al observed that diffusion of prescribing was highly drug dependent, when comparing adoption of sumatriptan, finasteride, tramadol, and clarithromycin in Denmark.¹² Tamblin et al observed an 8-17 fold difference in utilization rates of five classes of new drugs by Quebec physicians.¹³ Dybdahl et al noted that early adoption of one group of drugs (including angiotensin-II antagonists, triptans, COX-2 inhibitors, and esomeprazole) did not predict early adoption of other new drugs in Denmark.¹¹

The objective of this research was to apply the diffusion of innovations theory to the prescribing of celecoxib for approved and non-approved indications. At market release, celecoxib was not approved for the treatment of acute pain. The primary objective was to ascertain the extent of celecoxib use for the treatment of acute pain following its market release and to determine if prescriber or patient characteristics differed amongst early use for acute pain versus chronic musculoskeletal conditions. It was predicted that early and late adopters and users of celecoxib would differ.

METHODS

Study Design

The diffusion of prescribing of celecoxib in approved and non-approved indications was described over a one year period following market

availability (April 21, 1999 - April 20, 2000), using prescription database records in a complete population (the population of a Canadian province with universal health care insurance). The diffusion of innovations framework was applied to identify early, majority, and late prescribers of celecoxib by type of indication. Patient and physician determinants of early and late prescribing of celecoxib, relative to its majority use, were ascertained.

Study Population and Data Sources

Data were obtained from population-based, linked electronic databases maintained by the Manitoba Health Services Insurance Plan (MHSIP), a Canadian provincial health insurance plan that provides health care for all Manitobans. The databases accessed for this study were: patient registration files to characterize patients, physician reimbursement claims and hospital discharge abstracts to determine diagnosis, and claims for prescriptions dispensed in the province of Manitoba. Physician characteristics were determined from the Manitoba Physician Practice database. Household income from the 1996 Census public-use files was also used.

The available information from the MHSIP registration file includes: birth date, sex, and geographic location for every individual eligible to receive insured health services in Manitoba. A fee-for-service system for physician reimbursement for medical care provided ensures that record and patient diagnosis information is available. Diagnosis information at the 3-digit level of the ICD-9-CM classification system and physician specialty was used to determine diagnosis. Discharge abstracts for hospital services were used as an additional source of diagnostic information. These records include information on up to 16 ICD-9-CM diagnostic codes, the first of which is the primary diagnosis responsible for the hospital stay. Records for prescriptions filled at retail pharmacies are submitted for reimbursement by drug insurance plan and for drug utilization review. Information utilized from these records included: date of prescription dispensing, drug name and identification number, dosage form, and quantity dispensed. The MHSIP databases have shown to be highly reliable and valid for describing population drug use and contact with the health care system for specific conditions.¹⁴⁻¹⁶

Anonymized personal identifiers were used to create record linkages among databases and capture longitudinal histories of health care utilization. Ethics approval was obtained from the University of Manitoba research ethics board. The study population included all persons in Manitoba receiving at least one prescription for celecoxib, within a one-year period following its market availability.

Study Measures

All first prescriptions for celecoxib written by physicians were classified according to indication for use: acute pain and chronic musculoskeletal conditions. This classification was chosen to correspond to the approved indications at the time of market release, which were the chronic musculoskeletal conditions of osteoarthritis or rheumatoid arthritis. Presence of a chronic musculoskeletal condition was defined as at least one physician visit for rheumatoid arthritis (ICD9 code=714) or osteoarthritis (ICD9 code=715), at least one prescription for a gold preparation, or intermittent or continuous prescriptions for NSAIDs in the year prior to the first celecoxib prescription. Intermittent use was defined as the ratio of days supply dispensed to total days in dispensing interval of 0.4 to 0.79 or the ratio of days without medication to total number of days supply dispensed medication of 0.21 to 0.61. Continuous use was defined as the ratio of days supply dispensed to total days in dispensing interval of greater than 0.8 or the ratio of days without medication to total number of days dispensed medication of less than or equal to 0.2. This definition has been assessed to have a specificity of 92%.¹⁶

If the definition for a chronic condition was not met, the celecoxib prescription was classified as being prescribed for acute pain. Acute pain was further characterized by health care visits within 7 days of the celecoxib prescription for cancer (ICD9 code=140-239), dental procedures (ICD9 code=520-525 or visit to dental surgeon), post-surgery (hospitalizations with diagnostic related group codes for surgery), back pain (ICD9=code 720-724, 336 or visit to chiropractor), injury (ICD9 codes=800-959, 717-719, 726, 727), and dysmenorrhea (ICD9 code=625, 789 if female). The 'diffusion time' (date of first prescription minus date of market availability) was calculated

for each prescriber. Physicians with prescriptions within the lowest 10% of diffusion times were defined as early prescribers, and those in the highest 10% of diffusion times as late prescribers. Majority prescribers had prescriptions that fell in between these limits. Patients linked to early, majority, or late prescribers were early, majority, or late users. Patients and prescribers were thus categorized according to early, majority, or late prescriber and users of celecoxib. Rather than using Steffensen et al's cutoff of 16%,¹² 10% was selected to classify early and late prescribers because we knew that the uptake of celecoxib was more rapid than many newly marketed drugs, so we were concerned that the 16% cutoff would misclassify the early adopters.

Patient characteristics included: age, gender, neighborhood income quintile (20% of the population residing in the lowest income to 20% of the population residing in the highest income neighborhoods), and prescription reimbursement status (reimbursed by provincial drug program, (Pharmacare) or Income Assistance, or out of pocket expense). Physician measures included: age, gender, location of training (Canada/US versus not), specialty (general practitioner (GP) or specialist), years since licensure (< 20 years versus more), hospital affiliation (treating physician in the hospital database), and type of practice (solo versus group). A solo practitioner was identified with reimbursement claims from one location without claims from other physicians at this location.

Analysis

The diffusion of prescribing curve was compared for prescriptions for celecoxib for acute pain and chronic musculoskeletal conditions. The characteristics of physicians and patients were compared amongst early, majority, and late prescribers and users, and related to indications of prescription use using descriptive and multivariate analysis. Polytomous logistic regression was employed in the multivariate analysis to determine the likelihood (odds ratio) of being an early or late prescriber, relative to a majority prescriber (reference group). The unit of analysis was the physician. Variables were retained in models at the 95% level of confidence.

RESULTS

In the year following its market availability in Canada in April 1999, 240,000 prescriptions for celecoxib were dispensed in Manitoba. This analysis is based on the 1302 first prescriptions for celecoxib written in the year following market release. Most early users of celecoxib (64%) were treated for osteoarthritis or rheumatoid arthritis or had continuously used NSAIDs in the previous year, indicating that they had chronic musculoskeletal conditions (Table 1).

Although celecoxib prescriptions for chronic musculoskeletal conditions dominated early users, this pattern was reversed in late users of celecoxib, in whom more prescriptions (69%) were for acute pain (Table 1).

The use of celecoxib for chronic musculoskeletal conditions demonstrated a faster diffusion onto the market than the use of celecoxib for acute pain (Figure 1).

TABLE 1 Distribution of celecoxib users for acute pain and chronic musculoskeletal conditions by physician adopter category

Celecoxib User	Early Prescribers N (%)	Majority Prescribers N (%)	Late Prescribers N (%)	Total N (%)
Chronic Musculoskeletal Conditions	92 (63.9)	506 (49.4)	41 (30.8)	639 (49.08)
Acute Pain	52 (36.1)	519 (50.6)	92 (69.2)	663 (50.92)
Total	144 (100)	1025 (100)	133 (100)	1302 (100)

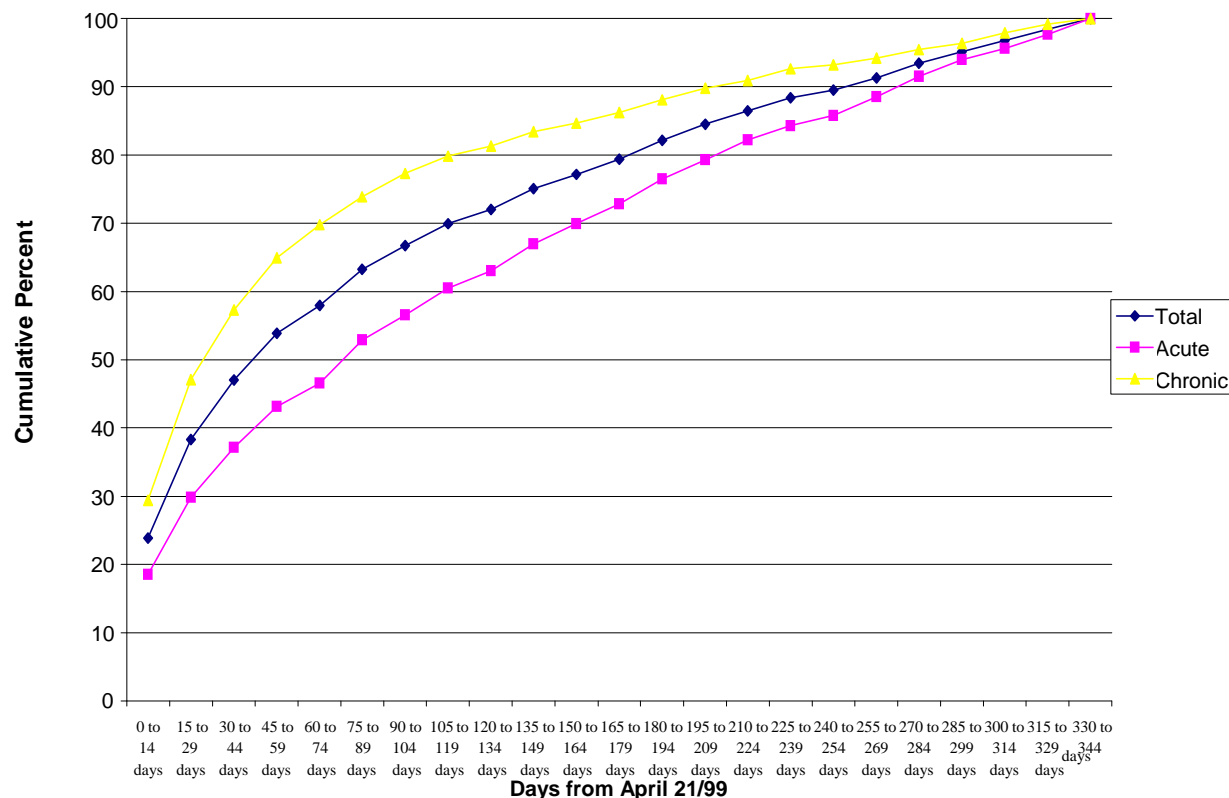
TABLE 2 Distribution of use of celecoxib for acute pain by medical indication and physician adopter category

Celecoxib User	Early Prescribers (%)	Majority Prescribers (%)	Late Prescribers (%)	Total N (%)
Cancer	0.0	2.7	0.0	14 (2.1)
Dental Procedures	0.0	0.6	1.1	4 (0.6)
Post Surgery	3.9	6.0	3.3	36 (5.4)
Back Pain	21.2	10.0	12.0	74 (11.2)
Injury	0.0	13.5	12.0	81 (12.2)
Dysmenorrhea	0.0	0.2	0.0	1 (0.2)
Other*	75.0	67.1	71.7	453 (68.3)
Total	100.0	100.0	100.0	663 (100)

* includes, for example, hypertension

FIG. 1

Figure 1 Cumulative Percent Diffusion of First Prescribing of Celecoxib for Total, Acute and Chronic 1st Prescriptions



For chronic musculoskeletal conditions, the median diffusion time for first prescriptions was 35 days following market release; for acute pain, the median diffusion time was 79 days. Early prescribers for chronic musculoskeletal conditions had written their first prescription within 6 days of market availability; for acute pain this time period was 8 days. Late prescribers for chronic musculoskeletal conditions had written their first prescription 201 days or more after early prescribers; for acute pain this delay was 268 days or more. Celecoxib became a provincial drug plan benefit (unrestricted reimbursement of prescriptions) 238 days after first availability.

Of 1302 prescribers of first celecoxib prescriptions, 72% were general practitioners, 25% were female, 60% were trained in North America, 86% were hospital affiliated, and 16%

were solo practitioners. Most prescribers (62%) were less than 50 years of age, and 74% had been in practice less than 20 years. While early prescribers were more likely to prescribe celecoxib for chronic musculoskeletal conditions, approximately one third (36%) of early prescribers wrote prescriptions for the treatment of acute pain, a non-approved indication at the time. Amongst patients prescribed celecoxib for acute pain, the 'other' category, which frequently contained non pain-related diagnoses such as hypertension, was the most prevalent. From the list of pain and musculoskeletal indications selected for study, injuries and back pain were the most commonly identified (Table 2). Back pain was more prevalent in early than late or majority users. Use of celecoxib for injury pain was more prevalent amongst late users than early users.

TABLE 3 Likelihood (odds ratio, 95% confidence intervals) of an early and late prescriber of celecoxib for acute pain, multivariate model with majority prescriber as reference*

Patient and Physician Characteristics	Early Prescriber	Majority Prescriber	Late Prescriber
Patient Age (< 50 yrs vs. 50+ yrs)	0.65 (0.44-0.96)	Reference	0.76 (0.54-1.06)
Physician Specialty (GP vs. others)	2.24 (1.53-3.29)	Reference	0.65 (0.46-0.92)
Hospital Affiliation (Yes vs. No)	1.54 (1.04-2.27)	Reference	0.73 (0.52-1.01)
Drug Plan Status (Reimbursed vs. Not)	0.62 (0.34-1.13)	Reference	13.15 (6.39-27.07)

GP= General practitioner

* Adjusted for the variables in this model

TABLE 4 Likelihood (odds ratio, 95% confidence intervals) of an early and late prescriber of celecoxib for chronic musculoskeletal conditions, multivariate model with majority prescriber as reference*

Patient and Physician Characteristics	Early Prescriber	Majority Prescriber	Late Prescriber
Income (Low vs. High)	0.56 (0.35-0.91)	Reference	0.74 (0.43-1.27)
Physician Specialty (GP vs. others)	1.35 (0.93-1.97)	Reference	0.34 (0.20-0.59)
Practice (<20 yrs vs. 20+yrs)	0.91 (0.67-1.22)	Reference	2.26 (1.23-4.17)
Hospital Affiliation (Yes vs. No)	1.31 (0.84-2.03)	Reference	0.32 (0.19-0.54)
Training (In NA vs. outside NA)	0.73 (0.56-0.95)	Reference	1.27 (0.75-2.17)
Drug Plan Status (Reimbursed vs. Not)	0.53 (0.19-1.45)	Reference	9.73 (6.10-15.51)

GP = general practitioner, NA = North America (Canada, USA)

* Adjusted for the variables in this model

The characteristics of celecoxib prescribers differed when use was compared for acute pain and chronic musculoskeletal conditions (Tables 3, 4). Independent of the prescription reimbursement status of their patient, early prescribers of celecoxib for acute pain were twice more likely than the majority to be general practitioners (odds

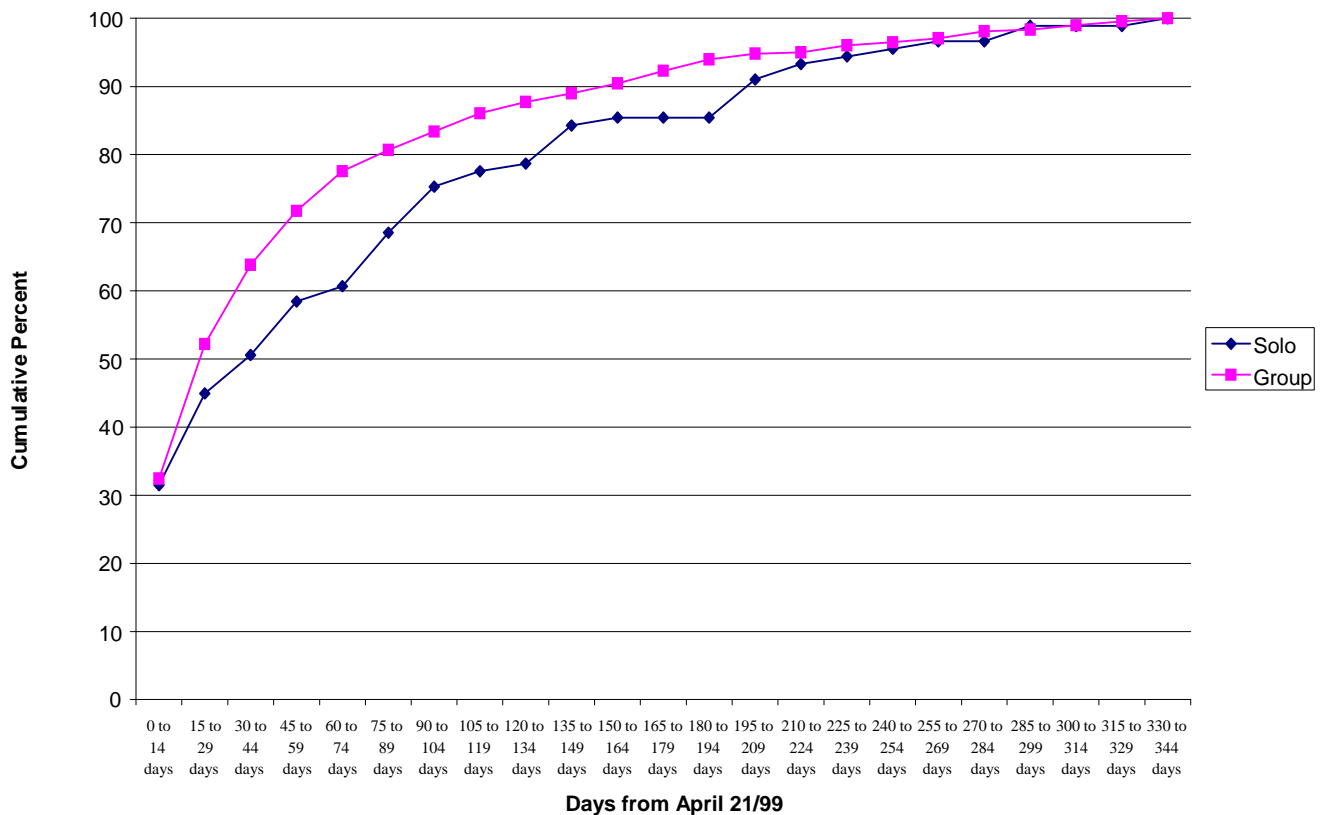
ratio=2.24, 95% CI: 1.53-3.29) and one and a half times more likely to have hospital affiliations (odds ratio=1.54, 95% CI: 1.04-2.27). Conversely, for acute pain, late prescribers were less likely to be general practitioners (odds ratio=0.65, 95% CI: 0.46-0.92). Several other physician characteristics predicted late prescribing of celecoxib for chronic

musculoskeletal conditions. In comparison to the majority, late prescribers of celecoxib for chronic musculoskeletal conditions were less likely to be general practitioners (odds ratio=0.34, 95% CI: 0.20-0.59) and to have hospital affiliations (odds ratio=0.32, 95% CI: 0.19-0.55). These late prescribers for chronic musculoskeletal conditions were also more likely to have practiced for less than 20 years. The only physician determinant of early prescribing of celecoxib for chronic musculoskeletal conditions was location of

training. Physicians trained in Canada or the US were 25% less likely to be early prescribers of celecoxib for chronic musculoskeletal conditions. Finally, although type of practice was not a significant independent predictor of celecoxib use in the multivariate analysis, we observed earlier uptake of celecoxib for chronic musculoskeletal conditions among group than solo practitioners (Figure 2). No differences were found for prescribing in acute pain.

FIG. 2

Figure 2 Cumulative Percent Diffusion of First Prescribing of Celebrex for Chronic Conditions: Solo vs. Group Practitioners



Few patient characteristics predicted early or late use (Tables 3 and 4). Late users of celecoxib for both acute pain and chronic musculoskeletal conditions were much more likely to have celecoxib reimbursed by a drug plan than majority users (celecoxib was listed as a provincial drug plan benefit by this time).

Household income was important in determining early access to celecoxib for the treatment of chronic musculoskeletal conditions, but not acute pain. Early users of celecoxib for chronic musculoskeletal conditions were less likely than majority or later users, to live in low income households (odds ratio=0.56, 95% CI: 0.35-0.91).

DISCUSSION

We observed more rapid diffusion of prescribing of celecoxib for the treatment of chronic musculoskeletal conditions as compared to the treatment for acute pain. However, over one third of first prescriptions for celecoxib written by early prescribers were for the treatment of acute pain. Roger's model of diffusion of innovation was the framework employed to describe celecoxib diffusion in our study, where prescribers were categorized according to early, majority, or late prescribers of celecoxib. The diffusion of innovation theory characterizes early prescribers as innovators who influence the behaviour of others. In our study, early prescribers of celecoxib for acute pain were more likely than the majority to be general practitioners and to have hospital affiliations whereas late prescribers were less likely to be general practitioners. Users of celecoxib prescriptions for acute pain written by early prescribers were more likely to be younger than 50 years, and users of prescriptions written by late prescribers were more likely to have drug coverage. For chronic musculoskeletal conditions, early prescribers of celecoxib were less likely than the majority to have trained in North America whereas late prescribers were less likely to be general practitioners or have hospital affiliations, but more likely to have been in practice for less than 20 years. Users of these celecoxib prescriptions for chronic musculoskeletal conditions written by early prescribers were less likely to have a low income, and users of prescriptions written by late prescribers were more likely to have drug coverage. In the remainder of the discussion we present our findings under the following factors that influence diffusion in Roger's model of diffusion of innovation: perceived attributes of the innovation (efficacy and safety), communication channels (source of information), nature of the social system (solo or group physician practice), and physician characteristics.¹⁰

The diffusion of prescribing theory characterizes early prescribers as innovators,¹⁷ but at the time of market availability of celecoxib in April 1999, little clinical data was available to guide these potential innovators on the efficacy and safety of celecoxib for the treatment of pain related to chronic musculoskeletal conditions or

acute pain, despite a perceived benefit of the innovation.^{5,6} There were several abstracts¹⁸⁻²² and a preliminary report⁵ assessing the use of celecoxib for the treatment of osteoarthritis and rheumatoid arthritis in humans as well as a description of its use in animal models.²³ The preliminary report described results from a two week osteoarthritis and a four week rheumatoid arthritis study, both suggesting superior efficacy of celecoxib compared to placebo.⁵ Although there were abstracts demonstrating the superiority of celecoxib compared to placebo and aspirin, published in 1996 and 1997, respectively,^{24,25} the first trial describing use of celecoxib in the treatment of acute pain described the superiority of rofecoxib as compared to celecoxib for the treatment of dental pain, and was published in October 1999.²⁶

As there was a lack of published material on the efficacy and safety of celecoxib at time of market availability of celecoxib, other communication channels, including the role of peer contact and advertising may have contributed to the dramatic uptake of celecoxib into the prescribing armamentarium for acute non-arthritic pain. Celecoxib was aggressively marketed in Canada. In the year 2000 celecoxib manufacturers produced 613 advertisement pages, and provided 303,000 minutes of detailing to Canadian physicians, an increase of 40% over 1999.²⁷ Advertisements and promotional material are common sources of information on new drugs for physicians.^{28,29}

Information from pharmaceutical industry representatives is often cited as an influential source of information on a new drug and promotional activity has been shown to impact the adoption of new evidence.^{28,30-33} As compared to specialists, general practitioners rely more heavily on commercial sources of information, which often are reported to be their only source of information; this has significant implications for the influence of communication channels on the diffusion of a new technology.^{31,34} We observed that early users of celecoxib for acute pain were more likely to be general practitioners than specialists and late users of celecoxib for acute pain were less likely to be general practitioners; it is possible that general practitioners may have been susceptible to the commercial description of the attributes of the innovation of celecoxib.

Another factor contributing to the use of celecoxib for acute pain by general practitioners includes the nature of patients; perhaps specialists were less likely to see patients with acute pain.

Some aspects of the physician's social system appeared to influence the diffusion of prescribing of celecoxib. The finding that early prescribers of celecoxib for chronic musculoskeletal conditions were more likely than the majority to have hospital affiliations and that late prescribers of celecoxib were less likely to have hospital affiliations may reinforce the role of hospital opinion leaders as an important source of information about a new drug.^{30,35-37} However, early prescribers of celecoxib for chronic musculoskeletal conditions were less likely to have trained in North America, and perhaps less influenced by social systems. Group practice, a social setting where physicians can share prescribing knowledge more easily than in solo practice, has been shown to be a predictor for new drug use in general and specialty practice settings.^{12,28,36} Late prescribers of celecoxib for chronic musculoskeletal conditions were more likely to have been in practice for less than 20 years; perhaps this influenced the social system of these prescribers. Although not an independent predictor of adopter status in our study, physicians in group practices demonstrated more rapid adoption of celecoxib for chronic musculoskeletal conditions.

Despite complex factors, which influence the adoption of a new medication, several pragmatic factors also come into play in Canada, namely patient income and drug coverage. Drug plan status was an important predictor of late celecoxib use for both acute pain and chronic musculoskeletal conditions, and early users of celecoxib were less likely to have low income than majority or late users. Clearly drug cost and out of pocket expenditures influenced the diffusion of innovation and use of this medication.

Several studies have examined patient predictors of new COX-2 use.^{7-9,38,39} In a study of COX-2 use in a health maintenance organization over the two year period following market release, a diagnosis of rheumatoid arthritis, a history of GI problem, female gender, steroid use, and age significantly increased the likelihood of receiving a COX-2 prescription.³⁸ Few studies have examined physician determinants of use. In a

study of Finnish adoption of COX-2 inhibitors, Helin-Salmivaara found that specialists were the fastest adopters of these agents.³⁹ In this analysis, the off-label use of celecoxib for the treatment of acute pain was predicted by two physician characteristics: physician specialty and hospital affiliation and by one patient characteristic, age > 50. Early prescribers of celecoxib for acute pain were more likely than the majority to be general practitioners and to have hospital affiliations.

Amongst new users of COX-2 prescriptions in the Midwest USA, Cox et al found that most prescriptions were for female patients and for a short duration. Similar to our findings of celecoxib use in acute pain, they observed that most COX-2 prescriptions were for back pain (22%) and unspecified joint disorders (20%).⁷ In their assessment of COX-2 prescribing trends in Australia two years after market availability, Kerr et al also noted unspecified pain, back pain, knee pain, and injury as common reasons for COX-2 prescribing.⁸ Similar to our findings, prescription rates in this study increased after COX-2s were covered by the national formulary.⁸ Finally, in an evaluation of COX-2 use in the Pennsylvania Medicare program, patient factors, such as gastrointestinal toxicity were predictive of COX-2 use, but not in a multivariate model, in which physician prescribing preference was an important determinant.⁹

While many characteristics of early prescribers of new drugs have been previously reported, there is little agreement that a clear picture of an early prescriber has been described.^{11-13,36} Several analyses of early prescribers of groups of different new drugs have failed to characterize the 'early prescriber' across different drugs.^{11,12} One Canadian analysis suggested that for general practitioners, greater utilization of new drugs between 1989 and 1994 was associated with male gender, graduating from the most recently established medical school and large practice volume, while lower utilization rates of new drugs were associated with elderly patients and rural practice location.¹³ We did not observe an influence of physician gender, the only common characteristic, on celecoxib adoption. Others have described the early adopter as being board certified, in group practice, involved in academic activities, and caring for a greater number of patients weekly, however this analysis was of pediatricians in 1984, so has limited applicability to the current analysis.³⁶

Limitations of this analysis include an inability to access information regarding the influence of the pharmaceutical industry, advertising, patient requests, or physician samples on the prescribing of celecoxib in the initial period following market availability. We were also unable to capture with administrative claims data the influence of physician and patient perceptions of the efficacy and safety of celecoxib for the treatment of chronic musculoskeletal conditions and acute pain. It is possible that due to the relapsing remitting nature of rheumatoid arthritis and other chronic musculoskeletal conditions that those patients who had these conditions were incorrectly classified as acute users, due to the fact that they may not have had prescriptions for gold, NSAIDs or had physician visits for rheumatoid arthritis or osteoarthritis. However, due to our broad definition of chronic musculoskeletal conditions, it is unlikely that a large proportion of the celecoxib prescriptions were miscategorized as being for treatment of acute pain. Another limitation of this analysis includes the fact that due to the nature of administrative data, for many celecoxib prescriptions for acute pain there was no discernable diagnosis, leading to a majority of these prescriptions as being labeled unclassified. Finally, the nature of using the first prescription to classify early adopters may not have been as sensitive to capturing early adopters, as for example, a measure of the density of prescriptions for new medications after market availability.

In summary, our data support the repeated finding that COX-2s were commonly used for the treatment of acute pain, a non-approved indication in the time period following new market availability. While many characteristics of early prescribers of new drugs have been previously reported,^{11-13,36} early use of celecoxib for acute pain was associated with general practitioner and hospital affiliation status, findings which are consistent with theory on the influence of communication channels and a physician's social system in the prescribing of new drugs.

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