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Research Submission

Public Drug Coverage and Its Impact on Triptan Use Across Canada: A Population-Based Study

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Background.—Public drug coverage for triptan medications varies across jurisdictions in Canada, which may lead to differences in usage patterns and patient risk for medication overuse headache.

Methods.—We conducted a population-based, cross-sectional analysis of publicly funded triptan use in seven provinces across Canada from January 1, 2012 to December 31, 2012. All patients who had filled at least one prescription for a triptan during the study period were included. We defined quantity limits of 6, 12, and 18 triptan units per month to assess the prevalence of high volumes of triptan use, which may place patients at risk for medication overuse headaches, and compared this prevalence between provinces with different funding restrictions.

Results.—We identified 14,085 publicly funded users of triptans in 2012 in the seven provinces studied, 82.5% of whom were aged less than 65 years (N = 11,631). The prevalence of triptan use ranged substantially by province, from 0.04% in Ontario to a maximum of 1.0% in Manitoba ($P < .001$). Furthermore, the percentage of patients in each province using more than 6, 12, or 18 units per month differed significantly between provinces ($P < .001$). In particular, the percentage of patients treated with more than 6 units per month ranged from as low as 2.1% in Saskatchewan to 43.8% in Ontario.

Conclusions.—Differing public drug reimbursement criteria for triptans may be one contributing factor that has led to our observation of considerable variation in both prevalence of triptan prescribing and potential overuse of these medications. We offer that monthly quantity limits may be considered as a tool to decrease risks for medication overuse headache.

Key words: migraine, triptan, medication overuse headache, public drug coverage

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Migraine headaches are a common neurological disorder that can lead to significant pain, disability, and decreased quality of life highlighted by reductions in physical activity, symptoms of photo- and phonophobia as well as nausea and workplace absenteeism.[1] In Canada, migraines affect approximately 15% of the population;[2] however, this differs substantially by gender and age. In particular, the lifetime prevalence of migraines among women is 24% compared with 9% among men,[2] and migraine prevalence is highest among patients between the ages of 35 and 54 years.[3] The overall prevalence of migraine drops substantially in older populations (overall prevalence 8%), although the disparity between male and female sufferers remains.[3,4]

Abortive therapy is the primary therapeutic option for the acute management of migraine headaches. Alternatives include nonspecific analgesics (eg, acetaminophen, nonsteroidal anti-inflammatories [NSAIDs], or opioids) and more targeted therapies such as ergots and triptans. Triptans are generally considered to be both safe and effective for the acute treatment of migraines.[5-7] Systematic reviews have shown that triptans effectively relieve pain at 2 hours and provide sustained relief at 24 hours when compared with placebo,[5,8,9] and various guidelines (eg, Canadian Headache Society and American Headache Society) recommend that triptans can be used to treat moderate to severe migraine headaches.[2,10] Despite this fact, recent studies have shown that fewer than 10% of Canadian migraine sufferers list triptans as their primary medication and at least 200,000 Canadian women are unhappy with their migraine treatments.[2]

One important concern with migraine therapy is that excessive medication intake may potentially lead to medication overuse headaches (MOH),[11-13] and triptan overuse has been shown to lead to MOH more rapidly and with fewer total doses when compared with ergots and nonspecific analgesics.[11] The mean duration of triptan use until onset of MOH has been shown to be as low as 1.7 years (compared with 4.8 years for analgesics) and with as few as 18 single doses per month (compared with 114 doses for analgesics).[11] For this reason, several strategies have been developed by drug policy-makers to curb triptan overuse and reduce risks of triptan-related MOH. These include broadly restricting access to triptan medications and/or establishing quantity limits that restrict the number of triptan doses patients can access monthly. Although triptans are available as insured benefits through all publicly funded drug programs across Canada, the use of these strategies varies substantially across provincial jurisdictions. British Columbia and Quebec have the broadest access, listing these products as general benefits with no quantity limits. In contrast, both Ontario and Alberta require prior authorization for prescriptions, but impose no quantity limits, whereas Manitoba, Saskatchewan, New Brunswick, Nova Scotia, Prince Edward Island (PEI), and Newfoundland and Labrador all impose restrictions on access in combination with quantity limits.[14]

The objectives of this study were to assess how differential accessibility of triptans through public drug programs across Canada impacted the prevalence of both triptan use and high volume use, which might place patients at risk for MOH.

METHODS

Settings and Design.—We conducted a population-based, cross-sectional analysis of drug prescribing databases in seven provinces across Canada (Alberta, Manitoba, New Brunswick, Nova Scotia, Ontario, Saskatchewan, and PEI) from January 1, 2012 to December 31, 2012. Across these seven provinces, a total of 4,937,599 individuals were eligible for drug coverage

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over the study period. The study was approved by the research ethics board of Sunnybrook Health Sciences Centre, Toronto, Ontario.

Sources of Data.—We examined the computerized prescription records for Ontario from the Ontario Drug Benefit Program and used the Canadian Institute for Health Information's National Prescription Drug Utilization Information System (NPDUIS) Database to identify prescription records for all other provinces included in this analysis. These databases contain detailed information on the date prescriptions are filled, the quantity of drug dispensed, the days' supply, and patient demographic information. Of the seven provinces studied, Saskatchewan and Manitoba are the only ones that provide universal public drug coverage. The other five provinces fund medications for specific groups of patients such as those aged 65 years and older, those on social assistance, or those living in long-term care facilities. Only claims where at least part of the claim was accepted by the public drug program, both toward a deductible (if applicable) or for payment, are captured in these databases and included in this analysis. In Ontario, the Registered Persons Database was used to determine the age and gender of included patients. In all other provinces, age and gender was determined from the NPDUIS claims information.

Identification of Patients and Outcomes.—We examined the records of all patients aged 18 years and older across the seven jurisdictions who received at least one publicly funded prescription for a triptan during the study period. The funded triptans available in Canada are: almotriptan (tablets), naratriptan (tablets), rizatriptan (tablets, disintegrating tablets), sumatriptan (tablets, nasal spray, subcutaneous injection), and zolmitriptan (tablets, nasal spray, disintegrating tablets). Eletriptan is funded in the province of Quebec, and frovatriptan is not funded by any public drug plan. Demographic information (including median age at time of first prescription and gender) was defined for each individual, along with the median number of triptan units dispensed per person over the study period. Units are defined as tablets for oral formulations, sprays for intranasal formulations, and milliliters (mL) for injections.

Our primary outcome was the proportion of patients who exceeded predefined quantity limits for triptans over the study period. The Canadian Headache Society defines triptan overuse as use on more than 9 days/month, the International Headache Society defines overuse as triptan use on 10 or more days/month, and a study by Limmroth identified an upper limit of 18 doses per month before manifestation of MOH.[1] Furthermore, across Canada, limits of 6 and 12 units are in place in some provinces. For these reasons (and because triptans are generally packaged in quantities of six), we modeled quantity limits of 6, 12, and 18 units per month. To allow for some flexibility in the timing of prescriptions for triptans over the study period, these quantities were annualized to limits of 72, 144, and 216 units, respectively.

Statistical Analysis.—We used descriptive statistics to report baseline characteristics for all patients included in the study. Binary variables were reported as percentages, and ordinal variables were summarized as medians and interquartile ranges (IQRs). We used chi-square tests to compare the proportion of individuals who exceeded each quantity limit between provinces, and used a type 1 error rate of .05 as a threshold of statistical significance. In these analyses, the *P* values represent whether there is an overall statistically significant difference between the proportions among all provinces. For the analysis of quantity limits, data from New Brunswick and PEI were grouped due to small numbers. When provincial estimates were censored for privacy reasons due to small numbers, these provinces were excluded from the statistical comparisons. All analyses were stratified by age (less than 65 vs 65 years and older). We chose to stratify patients based on age of greater than or less than 65 years and this age is a criteria for public coverage in some provinces (eg, Ontario) and triptan medications are not recommended for use in the elderly population. Although they are not contraindicated in patients over the age of 65 years, these patients may be at higher risk for adverse effects and we wanted to quantify usage in this population. In a subgroup analysis, the proportion of individuals who exceeded each quantity limit was compared between Ontario

and Alberta, the two provinces studied where no quantity limits were in place. All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC, USA) and Microsoft Excel (Microsoft, Redmond, WA, USA).

RESULTS

We identified 14,085 users of triptans in 2012 in the seven provinces studied. The prevalence of triptan use differed substantially between provinces, ranging from 0.04% (N = 1090) in Ontario to 1.0% (N = 6555) (P value < .001) in Manitoba (Table 1). Overall, the ages of triptan users differed slightly between provinces (median ranged from 49 years in PEI to 66 years in Nova Scotia), which is likely driven by differences in public drug plan eligibility across jurisdictions. The median number of publicly funded triptan units dispensed per person over the year was the highest in Ontario (median 60 units per triptan user, IQR 24-126 units) where no quantity limits are in place. Manitoba, the only province with a quantity limit of 12 units per month, had the lowest annual volume of publicly funded triptans per user, with a median of 18 units per user (IQR 6-48).

Among younger beneficiaries, the rate of triptan use was higher in all provinces (range 0.1% in Ontario to 2.3% in Alberta). Interestingly, the median number of triptan units dispensed per person was higher among older beneficiaries (aged 65 years and older) compared with younger beneficiaries in all provinces (Table 1).

Medication Overuse.—We found statistically significant differences in the proportion of triptan users exceeding all three predefined quantity limits across all provinces (P < .001 for all comparisons). Regardless of age or quantity limit, Ontario had the highest proportions of patients exceeding these limits (43.8% of patients exceeding 6 units per month, 19.5% exceeding 12 units per month, and 10.2% exceeding 18 units per month; Table 2). The percentage of patients in each province using more than 6 units per month ranged from as low as 2.1% (Saskatchewan) to almost half of all triptan users (43.8%) in Ontario. Using the highest quantity limit (18 units per month), only Ontario (N = 111; 10.2%), Alberta (N = 218; 5.8%), and Manitoba (N = 53; 0.8%) had more than five patients who exceeded this prescribing volume. Analyses stratified by age were largely consistent with the primary analysis (Table 2).

In the subgroup analysis where we conducted pairwise comparisons between Alberta and Ontario, two provinces where no quantity limits were in place, we found a statistically significant difference in the proportion of patients exceeding the quantity limits of 6, 12, and 18 units/month. Specifically, triptan users in Ontario were more likely to exceed these limits compared with those in Alberta for all comparisons (P < .05) with the exception of individuals aged 65 years and older, where we found no significant difference between the proportion of patients exceeding 18 units per month between the two provinces (8.2% vs 6.8% in Ontario and Alberta, respectively; P = .43).

Interpretation.—In this population-based study of almost 5 million individuals eligible for public drug coverage, we found that triptan prescribing and volume of use varied significantly between provinces, and appeared to reflect the extent to which provincial policies were designed to limit use. In particular, we found that Ontario had the lowest rate of triptan use, yet the highest volume of use per person and the largest proportion of patients exceeding the studied monthly quantity limits. These patterns may in part be due to the combination of the highly restrictive criteria placed on access to triptans in Ontario, combined with the lack of quantity limits once patients obtain access. The strict criteria placed on triptans may lead to only the more severe and complex cases being treated, which is potentially why we see a small number of patients using high quantities. However, this differed significantly from patterns observed in Alberta, the only other province with a policy of restricted access and no quantity limits. In Alberta, the median number of triptan units dispensed over the year was almost half (36 units) of that of Ontario (60 units). This may reflect differences in prescribing patterns such as a higher percentage of patients in Alberta are using preventative medications compared with Ontario, which may be underutilizing prophylactic medications. Furthermore, among the four provinces with a monthly quantity limit of 6 units, the prevalence of patients exceeding these limits differed considerably. In Saskatchewan, only 2.1% of patients

Table 1.—Baseline Characteristics of Public Drug Plan Beneficiaries, by Province, January 1, 2012-December 31, 2012

	Alberta	Manitoba	New Brunswick	Nova Scotia	Ontario	Prince Edward Island	Saskatchewan
All eligible patients							
Patients eligible for coverage	503,192	663,657	108,774	133,756	2,938,205	29,908	560,107
Triptan users (N, %)‡	3731 (0.7%)	6555 (1.0%)	237 (0.2%)	313 (0.2%)	1090 (0.04%)	17 (0.1%)	2142 (0.4%)
Age (median, IQR)	60 (52-66)	49 (40-55)	54 (45-66)	66 (52-70)	52 (44-63)	49 (42-64)	52 (43-60)
Male (N, %)	528 (14.2%)	971 (14.8%)	33 (13.9%)	65 (20.8%)	208 (19.1%)	≤5	317 (14.8%)
Triptan units dispensed per person (median, IQR)	36 (12-16)	18 (6-16)	30 (12-16)	30 (12-16)	60 (24-126)	36 (18-54)	24 (10-16)
Age <65 years							
Patients eligible for coverage	109,887	497,244	37,001	24,243	1,071,382	7980	413,218
Triptan users (N, %)	2522 (2.3%)	6076 (1.2%)	182 (0.5%)	125 (0.5%)	846 (0.1%)	†	1875 (0.5%)
Age (median, IQR)	55 (48-60)	48 (39-54)	49 (42-56)	48 (42-54)	49 (41-55)	43 (42-57)	50 (41-57)
Male (N, %)	314 (12.5%)	887 (14.6%)	22 (12.8%)	18 (14.4%)	164 (19.4%)	≤5	267 (14.2%)
Triptan units dispensed per person (median, IQR)	32 (12-16)	18 (6-16)	30 (12-16)	24 (12-16)	60 (24-126)	36 (18-54)	21 (10-16)
Age ≥65 years							
Patients eligible for coverage	393,305	166,413	71,773	109,523	1,866,823	21,928	146,889
Triptan users (N, %)	1209 (0.3%)	479 (0.3%)	65 (0.1%)	188 (0.2%)	244 (0.01%)	†	267 (0.2%)
Age (median, IQR)	68 (66-72)	68 (66-72)	69 (67-72)	69 (68-70)	70 (67-73)	68 (68-70)	68 (66-72)
Male (N, %)	214 (17.7%)	84 (17.5%)	11 (16.9%)	47 (25%)	44 (18%)	≤5	84 (17.5%)
Triptan units dispensed per person (median, IQR)	39 (18-96)	24 (12-16)	30 (12-16)	30 (12-16)	72 (36-126)	42 (12-16)	24 (12-16)

†In accordance with institutional privacy policies, data suppressed to avoid residual disclosure of small cells.
‡*P* value for comparison of prevalence of triptan use between provinces <.001.
IQR = interquartile range.

Table 2.—Percentage of Publically Covered Triptan Users at Risk for Medication Overuse Headache, by Province, January 1, 2012-December 31, 2012

	Alberta	Manitoba	New Brunswick and Prince Edward Island	Nova Scotia	Ontario	Saskatchewan	*P* Value‡
All eligible patients							
All triptan users	3371	6555	254	313	1090	2142	
Monthly quantity limit modeled							
6 Units/month (%)	1144 (30.7)	1047 (16)	42 (16.5)	42 (13.4)	477 (43.8)	44 (2.1)	<.001
12 Units/month (%)	452 (12.1)	271 (4.1)	≤5	†	213 (19.5)	0	<.001
18 Units/month (%)	218 (5.8)	53 (0.8)	≤5	≤5	111 (10.2)	0	<.001
Age <65 years							
Total users	2522	6076	186	125	846	1875	
Monthly quantity limit modeled							
6 Units/month (%)	729 (28.9)	944 (15.5)	30 (16.1)	14 (11.2)	360 (42.6)	30 (1.6)	<.001
12 Units/month (%)	285 (11.3)	239 (3.9)	≤5	†	166 (19.6)	0	<.001
18 Units/month (%)	136 (5.4)	†	≤5	0	91 (10.8)	0	<.001
Age >65 years							
Total users	1209	479	68	188	244	267	
Monthly quantity limit modeled							
6 Units/month (%)	415 (34.3)	103 (21.5)	12 (17.6)	28 (14.9)	117 (48)	14 (5.2)	<.001
12 Units/month (%)	167 (13.8)	32 (6.7)	≤5	†	47 (19.3)	0	<.001
18 Units/month (%)	82 (6.8)	†	≤5	≤5	20 (8.2)	0	<.001

†In accordance with institutional privacy policies, data suppressed to avoid residual disclosure of small cells.
‡*P* values calculated between provinces where data were available, excluding those where data were censored or where there were fewer than five patients.

exceeded this limit compared with 13.4% (in Nova Scotia) and 16.5% (in New Brunswick and PEI combined).

There are a number of potential reasons for the observed interprovincial differences in triptan use among provinces with similar quantity limits in place. These include differences in provincial prescribing practices, enforcement of criteria for triptan coverage, and characteristics of patients eligible for public drug coverage. While criteria for triptan reimbursement does not vary greatly across the provinces (for example, most provinces do not reimburse for triptans unless patients have failed other therapies such as NSAIDS and ergots), the eligibility criteria for public drug coverage differs across the provinces, which can lead to differences in the characteristics of patient populations able to access these medications. For example, Saskatchewan and Manitoba provide universal drug coverage. Therefore, these populations may be generally healthier than the eligible populations in other provinces studied, which are typically a more select group of patients who are older or have low socioeconomic status. Furthermore, the degree to which quantity limits are enforced in each province is unclear. If some provinces allow prescribers or dispensing pharmacists to override monthly limits, or apply for special access in some patients, this could strongly influence the impact of these policies. This appears to be the case in some provinces where triptan volumes exceed quantity limits imposed by the public drug programs. For example, in New Brunswick, Nova Scotia, and PEI, where quantity limits of 6 units/month are in place, almost 15% of triptan users received quantities that exceed this limit in 2012.

Another finding of note from this study is in the older (≥65 years) age group. Although we know that the prevalence of migraine decreases in this group, the percentage of these patients who were at risk for MOH in our study was higher than that observed in the younger (<65 years) age group. This is an important finding because of concerns about adverse effects when these medications are used in older populations.

Two recently published studies in Italy[15] and Denmark[16] attempted to identify the number of triptan overusers in select populations. Each study found that about 10% of triptan users were in fact overusing their medications. The authors of these studies make no mention of prescribing limits for these medications such as the ones in place across a number of the provinces in this study. The number of users at risk for MOH from their data is similar to the percentage of patients at risk in Ontario and Alberta in our study (no limits). A number of factors may certainly be contributing to discrepancies seen in the number of at risk patients in our study, such as population density, access to headache specialists, and restrictive prescribing. As the data from Ontario and Alberta are similar to what is seen in other countries without limits, we feel these restrictions may be an important factor in differences we have noted across provinces.

Several strengths and limitations of this study merit emphasis. This is a large population-based study that included data on almost 5 million patients across seven provinces in Canada. This cross-sectional analysis allowed us to determine an annualized rate of triptan use at an individual level, providing information on the degree to which Canadians are at risk of triptan-related MOH. Several limitations also warrant discussion. First, because we only have information on prescriptions dispensed, and use this as a surrogate for medication usage, we cannot confirm whether patients are consuming the full amount of medication dispensed. Furthermore, the quantity limits modeled in this study were defined based on the assumption that patients are taking triptan medications according to guidelines, with a maximum of two doses daily. It is unclear if patients who are using more triptans per month are having frequent migraines or are requiring a higher number of repeated doses. We were also unable to assess the usage of other migraine therapies such as analgesics and prophylactics, which may also influence the risk of MOH.

We were not able to identify the headache diagnoses for which the triptans are being prescribed, nor can we diagnose MOH specifically among these patients. We can only highlight patients who are at risk for these headaches based on volume of drug prescribed. There may also other contributory or aggravating factors that can lead to MOH that we are

unable to measure, including underutilization of preventative therapies, and a paucity of education in the general management of migraines. We were also unable to measure the usage of other acute therapies and patients who are using other medications along with triptan therapy may be at an increased risk MOH.

Another limitation of our data is the fact that we report usage entirely from publicly funded databases and thus could be missing patients who have private insurance or who are paying for these medications out of pocket in which case we could be under reporting the total number of triptan users who are at risk for MOH. Furthermore, if patients are switching between triptan agents without using all of their previously dispensed medications, they may appear to be using more triptans than they are actually ingesting and thus we may be slightly overestimating the number of patients at risk for MOH. However, this would apply similarly to all provinces, and therefore should not greatly impact our interprovincial comparisons.

CONCLUSION

We found that the prevalence and volume of triptan use varied significantly across seven provincial drug programs in Canada, which may be a reflection of the differential impact of drug policies designed to promote appropriate and safe use of these medications. These results have important implications for policy-makers who may be considering changes to funding policies and the enforcement of quantity limits. Furthermore, with over 1 in 10 triptan users eligible for the public drug plan in Ontario being prescribed quantities of triptans that potentially put them at risk for development of MOH, headache educational programs are needed across Canada for both clinicians who prescribe these drugs and for patients who take them. This could help to ensure that triptans are being prescribed and used safely, accurately, and effectively and that headaches are being managed according to best practices.

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