ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

The Ontario Drug Policy Research Network Drug Class Review on Triptans for the Treatment of Migraines in Adults

Final Report on Qualitative Study Findings

Prepared by the ODPRN Knowledge Translation Unit , Li Ka Shing Knowledge Institute Knowledge Translation Program, St. Michael's Hospital

Sobia Khan, Alekhya Mascarenhas, Marlon Rhoden, Jennifer D'Souza, Julia E. Moore

April 1st, 2014

Table of Contents

Executive Summary

Background: The Ontario Drug Policy Research Network (ODPRN) conducted a drug class review of triptans for the acute treatment of migraines, which was selected as part of a formulary modernization initiative by the Ontario Public Drug Programs. This report highlights the findings of the qualitative study performed within the drug class review to determine the experiences of managing or treating migraines with triptans.

Methods: We used qualitative methods in a framework approach. One-on-one telephone interviews were conducted with 19 patients, 6 physicians (primary care physicians and neurologists) and 8 pharmacists. Interviews were recorded and analyzed using a framework for pharmaceutical policy analysis (i.e. the "Triple-A" framework: affordability, appropriateness, and accessibility of medications). Emergent findings were integrated to our framework, and the framework was adapted to convey specific experiences and perceptions relevant to triptans funding policies.

Key Findings: Findings in this report are summarized to represent common experiences and perceptions described across patient, physician and pharmacist groups.

Migraines can affect overall quality of life: Patients may experience persistent anxiety associated with migraine management, particularly those patients who have funding limits on drug coverage or do not have drug coverage at all. Migraine sufferers may experience significant productivity losses and may become socially isolated due to repeated migraine episodes.

There are challenges in appropriately treating acute migraines: Treatment options for migraine sufferers are perceived to be limited, and a particular challenge in migraine management is under-diagnosis, which can lead to poorly treated migraines. Self-management or physician-recommended treatment with over-the-counter analgesics is common but not ideal due to limited effectiveness and potential side effects of drugs, and concerns around combining therapies. Triptans were described as the most effective group of drugs available for acute migraine treatment. However, finding the most effective triptan can be difficult; many patients switch between triptans due to side effects or poor results. Positive experiences of triptans users include restored daily functionality and the ability to work. Negative experiences were rare, but included no or diminished effectiveness and over-use headaches.

Accessing triptans can be difficult for many individuals: Patient access to appropriate migraine diagnosis and therapy is perceived to be hindered by several factors: for example, the lack of knowledge and awareness amongst primary care physicians, and the lack of information available for patients on the existence of triptans and on their safe use. However, access is primarily limited by affordability. Although most triptans users have private insurance plans, coverage limitations can impact treatment adherence. Prescribing these drugs to individuals paying out-of-pocket can be extremely challenging due to the high cost of triptans. Accessing triptans through the Exceptional Access Program (EAP) for those eligible for the Ontario Drug

Benefit is described as a particularly significant barrier as many physicians and patients are unaware of the EAP criteria or that triptans can be accessed through the EAP. The application process itself is challenging and can deter physicians from attempting to access triptans for patients who need them.

Conclusion: The findings from the qualitative study of the triptans drug class review informed the methods of other ODPRN research units conducting studies as part of the review, and helped to contextualize the review's results. Overall, our findings shed light on the experiences of prescribing, dispensing and using triptans for migraine treatment, and unveil important information that can impact how patients in need can access these drugs across Ontario.

Part 1: Introduction and Background

The Ontario Drug Policy Research Network (ODPRN) recently received funding to conduct a series of drug class reviews as part of an initiative to update the public drug formulary (i.e. formulary modernization). As such, the ODPRN works closely with the Ontario Public Drug Programs (OPDP), Ministry of Health and Long-Term Care (MOHLTC) to select key priority areas and topics for formulary modernization, then conduct independent drug class reviews and disseminate the results of each of these reviews directly to the OPDP to facilitate informed decision making on public drug funding policies. Triptans were selected as the topic for the first drug class review.

Triptans are a group of drugs used for the acute treatment of episodic migraines. The 2013 Canadian Headache Society Guidelines recommend triptans as an effective therapy within stratified or step-wise approaches to care. This means that migraine treatment often involves various drugs that are appropriate to use at each level of increasing severity of the migraine attack (Worthington et al., 2013). Patients with migraines may start off by using an anti-inflammatory drug like acetylsalicylic acid (ASA, or Aspirin); if their migraine severity increases over time, or if the specific migraine attack escalates in pain severity, triptans are recommended to abort the migraine. This means that for many Canadians who suffer from migraines, triptans are an essential part of their therapy and for some with moderate to severe migraine, may be the first medication they use to abate their pain. Seven types of triptans are available in Canada, including: sumatriptan (Imitrex), almotripan (Axert), rizatriptan (Maxalt), Eletriptan (Relpax), Frovatriptan (Frova), Naratriptan (Amerge), Zolmitriptan (Zomig)

Although there are clinical trial data supporting the effectiveness of triptans for the acute treatment of migraines, there is limited information on how physicians decide to prescribe triptans and patients decide to adhere to their prescribed treatment. In a survey regarding compliance to migraine medication conducted in the United Kingdom, 66% of respondents indicated that they had delayed or avoided taking migraine medication due to fear of side effects (Gallagher and Kunkel, 2003); therefore, the potential side effects of triptans could play a significant role in how triptans are actually used. Given that the time at which a triptan is taken can impact its ability to abort a migraine (Worthington et al., 2013), delaying or avoiding use may also alter perceptions of triptans effectiveness. Physician decision-making on whether or not to incorporate triptans as part of migraine therapy may also be based on perceptions of effectiveness. The Canadian Headache Society Guidelines acknowledge that triptans may fail in about one-third of users, but that switching triptan types to find the most appropriate one may be a solution to this issue (Worthington et al., 2013). It is unknown whether physicians in Ontario are exploring the effectiveness of triptans by trialing different types of therapies.

Moreover, a key issue regarding triptans use in Ontario revolves around access to these drugs, as it is necessary to have drug coverage due to the extremely high cost of this group of medications. Private insurance plans may cover the cost of triptans, but many plans place monthly limitations on access to these drugs and little is known about the affect of such limitations on migraine

treatment. Triptans are available through Exceptional Access Program (EAP) of the Ontario Drug Benefit (ODB) to those who are eligible for this public drug funding program, which requires application to the OPDP from a patient's physician for permission to access the drug. Experiences of obtaining triptans through the EAP and perceptions on the process itself are unknown. These experiences and perceptions of accessing triptans may affect how triptans are prescribed, dispensed and used.

The purpose of the qualitative study that is being conducted as part of the ODPRN drug class review on triptans is to explore the various factors that may be related to triptan prescription, dispensing, and use for acute treatment of migraine. This information is warranted to understand and contextualize prescribing and usage patterns in Ontario, as well as to highlight any health equity issues that may be prevalent but are currently unknown. The findings from the qualitative study were also used to inform the research plans of the other drug class review research units to ensure that stakeholder issues and priorities were being considered in their analysis.

Part 2: Methods

Design

We used a framework approach to qualitative research (Ritchie & Spencer, 1994). This approach helps researchers focus on specific areas of interest when exploring a topic using qualitative methods, which can make the findings more applicable than alternative qualitative procedures. However, the approach also maintains the flexibility of qualitative methodology to incorporate new ideas, emergent issues, or unanticipated results. The framework selected for this study was the "Triple-A" framework (see **Appendix A**) for pharmaceutical policy analysis developed by Morgan et al. (2009). This framework highlights the need to explore affordability, accessibility, and appropriateness of the appropriate drugs when determining policy-relevant issues.

Sampling

Stakeholders identified for the triptans drug class review included physicians (primary care physicians (PCPs) and neurologists) and pharmacists who have prescribed/dispensed triptans, alongside patients with migraines who have current/prior experience using triptans. We aimed to recruit 6 to 8 participants from the physician and pharmacist groups each and 20 to 25 patients, anticipating that this may be sufficient to reach saturation of findings amongst relatively homogenous groups of participants (Kuzel, 1999). Participants were recruited from across Ontario. A purposive sampling approach using a convenience sample was used in order to elicit the specific perceptions and opinions of those who will be involved in or affected by drug policy decisions related to triptans. Recruitment methods included: a) cold calling; b) e-mailing and faxing; c) recruiting at primary care and specialist clinics; d) sending recruitment letters through e-mail distribution lists of professional organizations and advocacy groups; e) posting recruitment notices to the ODPRN website and social media (Twitter, Facebook) accounts; and g) snowball sampling (asking participants to connect with individuals they know who may be able to offer valuable insight to the issue for the purpose of recruitment to the study).

Data Collection and Analysis

Qualitative data were collected through one-on-one, semi-structured telephone interviews that were 30 to 45 minutes in length and conducted between August 2013 and October 2013. All interviews were conducted with a semi-structured interview guide developed using the "Triple-A" framework for pharmaceutical policy analysis (Morgan et. al., 2009) and collaboration from physicians and the drug class review team. Each interview was audio recorded. Interviews were transcribed, and transcripts comprised the primary source of data. The interviewer and/or a note taker took field notes during the interview to serve as a secondary source of data.

The framework approach was used to guide data analysis. Two independent analysts engaged in familiarization of the data by reading all primary and secondary data sources and generating initial codes that could be incorporated to the "Triple-A" framework (Morgan et. al., 2009). This comprised the coding framework, which was reviewed by the qualitative research team and was then applied to the data by two analysts during in-depth analysis. Inter-rater reliability between the two analysts was > 80%. The analysts and the qualitative research team engaged in mapping and interpretation of the coded data to generate the final themes.

Research Ethics

This study was approved by the St. Michael's Hospital Research Ethics Board in Toronto, Ontario, Canada in July 2013.

Part 3: Findings

Participant Demographics

Patients

A total of 19 patients participated in the study. These patients represented a variety of experiences with migraines and triptans use. One patient who revealed during the interview that he suffers from cluster headaches and not migraines was ultimately excluded. Of the 18 patients included in the analysis, 4 (22%) were male and 14(78%) were female. The ages of female participants varied, with 36% (n=5) aged 25 to 44 years; 57% (n=8) aged 45 to 64 years; and 7% (n=1) aged >65 years. In the male group, we interviewed one participant in each of the following age categories: 25 to34 years, 35 to44 years, 55 to 64 years, and 65 to 74 years.

Physicians

There were a total of six physician participants in the study. This included five neurologists practicing primarily in urban settings, three (60%) of whom were headache experts and two (40%) who specialized in general neurology. One PCP participated in the study.

Pharmacists

There were eight pharmacists interviewed for this study. Pharmacist participants were largely from community pharmacies in urban settings. Only one pharmacist was located in a rural

setting. In all, three (38%) of the pharmacists had over 20 years of experience dispensing drugs, four (50%) had 7 to12 years of experience and one (12%) had two years of experience. Over half of the pharmacists interviewed (n=4, 50%) described dispensing triptans at least weekly.

Detailed participant demographics can be found in **Appendix B**.

Key Themes Related to the Migraine Experience and the Treatment of Migraines with Triptans

The following findings are based on the experiences and perceptions of interview participants. The experiences and perceptions of patients, physicians and pharmacists have been summarized into three themes.

1. **The Impact of Migraines on a Patient's Quality of Life**
    a. The Experience of Having a Migraine
    b. Migraine Related Anxiety
    c. Productivity Losses
    d. Social Isolation

2. **The Appropriateness of Acute Migraine Therapies**
    a. Limited Treatment Options for Acute Migraines
    b. Triptans
        i. Perceptions of Effectiveness
        ii. Impact on Quality of Life
    c. Medication Over-Use Headaches

3. **Factors that Determine the Accessibility of Acute Migraine Therapies**
    a. Physician Stigma & Lack of Awareness
    b. Patient Access to Health Information
    c. Pharmacist Advocacy
    d. Affordability of Triptans
        i. The Impact of Cost on Prescription and Adherence to Safe & Suitable Treatment
        ii. Challenges with the Exceptional Access Program

Detailed findings on each of these themes are described below.

The Impact of Migraines on a Patient's Quality of Life

All participants from each participant group perceived that migraines have a significant impact on patient quality of life, although patient interviews revealed that the degree of impact varies greatly. The effect of migraines on quality of life was apparent in discussions on the experience of having a migraine, the persistent anxiety associated with migraines, productivity losses, and impact on migraine sufferers' social networks. This theme is predominantly discussed from the patient group perspective.

A. The Migraine Experience

Onset of Migraines

Physicians described migraine patients in their clinical practice as being primarily young or diagnosed at a young age, and female. This was reflective of the findings from our patient participant group. Half (n= 7) of female patient participants experienced their first migraine during their teenage years and nearly one-third (n=4; 28%) experienced their first migraine between the ages of 20 and 30 years. Some female patient participants described experiencing a reprieve from their migraines during pregnancy. In the male patient group, 3 of 4 participants (75%) experienced their first migraine between the ages of 18 and 30. In general, patient participants described a progression in the severity and frequency of migraines over time. Many patients expressed that they were diagnosed with migraines during their mid to late 20s.

Migraine Triggers

The majority of female patient participants mentioned that their migraines are linked to their menstrual cycle and/or changes in weather. Numerous other triggers were described by patient participants, including sensitivity to light, body temperature, excessive exercise, stress, and lack of sleep. Some participants, including both patients and physicians, described the difficulty in predicting or tracking migraine triggers, which can complicate the management and treatment of migraines.

Frequency of Migraines

When asked about the frequency of their migraines, 39% (n=7) of patients reported having them once a month (Figure 1). Two patient participants (11%) indicated that they have migraines on a weekly basis (i.e., once a week). The remaining patient participants (n=7) were severe migraine sufferers, with four individuals (22%) who experience migraines at least 2 to 4 times a week and three individuals (17%) who experience them every day. One patient participant described having stopped getting migraines after a one-time regimen of five consecutive triptan doses.

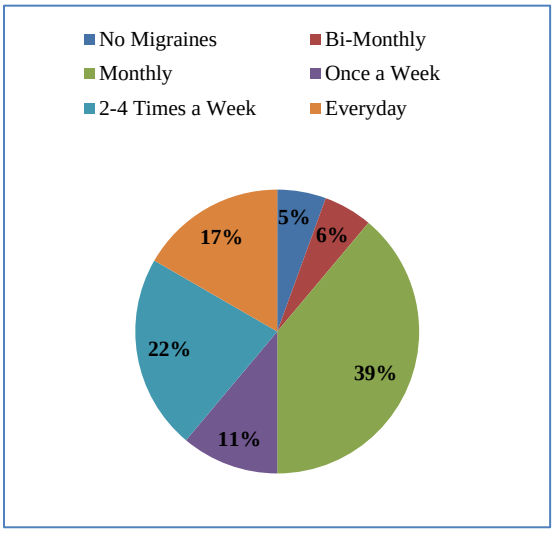


Figure 1.Frequency of migraine among patient participants (n = 18).

Experiences of Associated Migraine Symptoms

Five patient participants described having aura like symptoms with their migraines. These symptoms included flashes of light in the eyes, slurred speech, loss of vision, loss of feeling in the limbs, and vertigo. Seven patient participants described experiencing nausea and vomiting as well as increased sensitivity to light and smell.

> ***"I have thrown up on Yonge Street, I have thrown up on Bloor Street… I threw up one time coming home from a flight, someone was driving me home from the airport and we had to pull over on the 401 so I could throw up"–Patient***

Duration of Migraines without Medication

> ***"when I get a migraine that lasts 36hours, that's basically 36hours of my life that I have lost and I'm never going to get back…I can't do anything during that time"–Patient***

Almost half (47%; n = 9) of participants described that without medication, their migraines last at least 24 hours with an upward limit of 72hours. Of the remaining patient participants, five (28%) indicated that their migraines last at least 14 hours without medication, with an upward limit of 24 hours. Three patient participants (17%) indicated that they last at least 12 to14 hours, and one participant (5%) described having migraines for a duration of 7 to 8 hours.

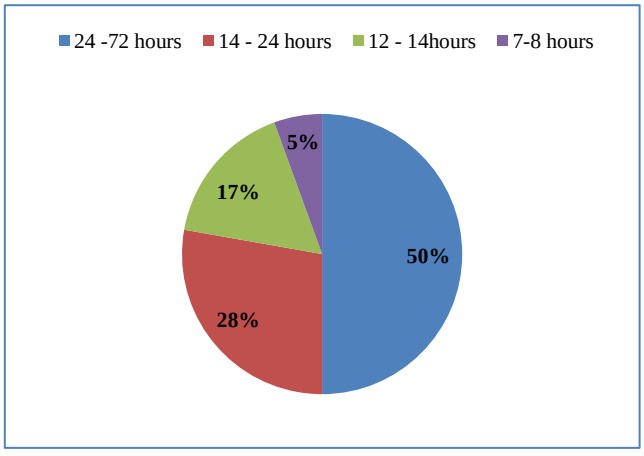


Figure 2. Duration of migraines among patient participants (without medication)

B. The Persistent Anxiety Associated with Migraines

All participant groups described anxiety as a part of the migraine experience that can affect quality of life. Patients in particular discussed that having to constantly discern between a migraine and a regular headache at the initial onset of pain can be an anxiety-producing experience, as waiting to treat a migraine can lead to ineffective treatment while over-treating a headache can lead to the unnecessary use of medication.

> ***"How do I know if this is going to be a full-blown one? How do I know it's going to move toward something? How do I anticipate that? How do I know that… well this is going to be something bigger. Or is it just going to lift and go away by itself? And you know when you wake up at five o'clock in the morning and you have to determine, Okay. What do I do now? Do I take something and… do I take my medication and know that if I take this, in thirty minutes from now, this is going to be gone? Or do I wait? So it's like a game I have to play with myself…I would say every day, maybe every other day." –Patient***

Some patients expressed a desire to conserve triptans due to monthly prescription limits under their drug plans and/or the high cost of triptans, resulting in them "waiting" to take their medication. However, other patients adhered to their prescription to take a triptan or other strong medication such as codeine or Fiorinal at the first sign of pain.

Many participants (patients, physicians and pharmacists) also described that migraine sufferers are constantly anxious that their next migraine will be experienced at an inopportune time (e.g. during a social event, commitment, or at work). Additionally, a migraine sufferer's worst fear was described as getting a migraine with no access to medication. Patients who have limits on their drug plans or those who have had to pay out-of-pocket for their drugs have described a constant anxiety about not having access to their medications.

> ***"it's always at the back of my mind that the drug plan is going to put limits on my meds, and it's a fear to be frank"–Patient***

> ***"…one of the worst parts of being a migrainer is you know headache itself is bad enough, but it's what we call the interictal anxiety. So in-between each attack they are panicking. What if I get an attack on a weekend when I am supposed to be on a date with my husband? Or I am supposed to be the soccer mom and I've only got two pills left. And I can't get them renewed till Tuesday. Oh my God! What's going to happen? You know they worry. And it has a negative impact on quality of life." - Physician***

C. Migraine Sufferers Experience Significant Productivity Losses

Participants from the physician and patient groups described the potential productivity losses that result from being a migraine sufferer. All patient participants described that without medication, migraines are debilitating experiences that interrupt activities of daily living. The interruption of work was most often discussed; however, given that most patient participants experience migraines on a monthly or bimonthly basis, these individuals for the most part are able to work full-time. Some patient participants who suffered from severe migraines described having to take numerous sick days, and one patient participant described having to permanently adjust her work schedule to accommodate potential morning migraines. Two patient participants are on long-term disability as a result of their migraines and one patient described having to retire early because of migraines.

In addition to an impact on work schedules, patient participants reported that the experience of migraines interfered with numerous other activities of daily living, which essentially constituted anything that involved being out of bed. Patient participants described the inability to do regular activities, such as washing dishes or walking the dog.

> ***"So, you know, I'm off work for the... I'm out of commission totally that whole day, and even if it was on a weekend I've essentially lost the day because I'm either, you know, in the bathroom or lying down, and I really, you know, I don't go out. So, I mean, I'm not in a darkened room. Like, you know, sometimes I can maybe watch, you know, twenty minutes of TV and then I'll lie down. I will often get a, you know, cold cloth with ice cubes in it and, you know, either over my forehead or around the back of my neck, that seems to help a little bit, but essentially if one [migraine] runs 36 hours, I mean, I've basically lost 36 hours." –Patient***

This impact on productivity and activities of living was also reiterated by the physician participants, based on their discussion with patients. Furthermore, physicians highlighted the wider impact of such productivity losses and the economic impacts of inadequately treated migraine sufferers on the health care system.

> ***"…you know when you look at costs, this [migraines] is not a particularly big cost in the system in terms of medication cost, but a huge cost to the system in terms of indirect cost in terms of lost revenue, in terms of lost productivity, in terms of accessing healthcare directly." - Physician***

D. Migraines Sufferers may become Socially Isolated

Many patients described having to withdraw from their social networks because of their migraines. For example, a few participants described being unable to sustain romantic relationships, attend important family gatherings, or spend time with friends as a result of their migraines. Others described being unable to take care of their children and other family members when experiencing an attack.

> ***" I have missed out on a lot because of my migraines…I have missed out on the children growing up as far as school activities, vacations, family events, even Christmas, I was supposed to host Christmas and the day before I had a level 10 migraine and so I can't even entertain anymore. If we have family over, I usually lay in bed and the children watch a movie… it has really affected the life of our whole family." -Patient***

Patients also described not being able to engage in recreational activities such as travelling, cultural activities or social gatherings. The term "social recluse" was used to describe the impact that migraines have had on their ability to participate in social activities.

> ***"I've become a loner, you know, because of the…I'm just so preoccupied with managing my pain" –Patient***

Theme Summary: Overall, all participant groups (but patients in particular) described onset of migraines at a young age with varying degrees of migraine severity, frequency and duration across participants. Anxiety can be experienced when attempting to differentiate between migraines and headaches, and about the timing of a migraine and potential disruption this can cause to life events. Migraine sufferers often miss work due to sick days and some are not able to work full-time or at all as a result of their migraines. Activities of daily living are almost always interrupted due to migraine episodes, and the effects of migraines on social networks and activities are apparent. Understanding the impact of migraines on quality of life can shed light on the necessity of effective treatments to alleviate the burden of migraines experienced by sufferers.

The Appropriateness of Acute Migraine Therapies

A. Treatment Options are Limited for Migraine Sufferers

In general, the majority of participants expressed that besides triptans, there is a dearth of effective treatment options for the migraines. In fact, physician and pharmacist participants regard triptans as a first line treatment and the most effective acute treatment currently available for episodic migraines. The types of migraine therapies other than triptans used by patient participants currently or in the past are presented in Table 1 below. Many of these medications

are either not traditionally indicated for migraines, or are general analgesics or therapies used for many other common ailments.

Table 1. Types of current and past migraine therapies used by patient participants

Simple Analgesics (e.g.NSAIDS)
Combination Analgesics (e.g. Fiorinal, Excedrin)
Opioids (e.g. Tylenol #3, Codeine, Percocet)
Anti-seizure/Epileptic Medications (eg. Gabapentin,Topiramate)
Ergot Alkaloids (eg. DHE, Migranal)
Tricyclic Antidepressants (eg. Amitriptyline
Blood Pressure Medications (eg. Beta blockers)
Dietary modifications (e.g. elimination of cheese, chocolate, coffee etc.)
Massage Therapy/Acupuncture
Vitamins, Herbals & Minerals (eg. Magnesium, feverfew)

Patient participants most commonly described using OTC analgesics, prescription analgesics and daily preventative medications. Many patient participants described having used prescription opioids such as Tylenol #3 and combination analgesics such as Fiorinal prior to being switched to triptans. Physicians and pharmacists also described OTC analgesics and opioids as being the first line of treatment typically used by patients coming to neurologists from primary care settings, although the physicians interviewed all agreed that triptans should in fact be the first line of medication for many migraine sufferers.

Most participants (patients, physicians, pharmacists) agreed that migraine therapies other than triptans are generally ineffective for aborting acute migraines. Only one participant described having significant pain relief from a tricyclic antidepressant (amitriptyline). A few other participants described trying this line of drugs and experiencing no relief. Most patients who have used drugs such as Tylenol #3 and OTC analgesics described very limited effectiveness; at most, they have experienced a small and short-lived reduction in pain severity. In addition, these drugs are ineffective at addressing other symptoms such as nausea and sensitivity to light. Physicians reported that select anti-inflammatory drugs are partially effective, while others can actually cause migraines. Physicians and pharmacists in particular were worried about the potential side effects of some drugs that are commonly prescribed, such as over-the-counter codeine combination product (8mg codeine such as in Tylenol #1) and other potentially addictive analgesics such as Fiorinal.

> ***"They were put on narcotics analgesics because they couldn't afford Triptans and their family doctors didn't realize that there is a process for them to access it. Especially if the medication or re-used medication had side effects. Drug dependence and other problems that I would say are completely inappropriate and unfortunate." - Physician***

One patient participant was taking a codeine combination product (acetaminophen, codeine 8mg and caffeine) because of the advice of a PCP to avoid triptans completely.

> ***"I had a bad experience with codeine when I was breast feeding so I was avoiding it, but I have now come back to it. I have to get rid of the migraines but I have to find something besides codeine, I've just kind of settled and I keep taking codeine but I just know that I can't take too much" –Patient***

B. Triptans are Perceived to be Effective for Episodic Migraines

i. Perceived Effectiveness

> ***"It starts to work within an hour and typically 90% of the time I can clear the migraine and be back at work within 3 hours at the most" -Patient***

Participants were asked about the effect of triptans and other medications on the frequency and duration of their migraines. Of the 18 participants included in the analysis, 83% (n=15) were taking triptan medication to treat their migraines. Of the remaining three participants, one was been prescribed amitriptyline, one no longer experienced migraines, and one took an over-the-counter codeine combination preparation (acetaminophen, codeine 8mg and caffeine) after having tried zolmitriptan (e.g., Zomig)and rizatriptan (e.g., Maxalt).

The vast majority of patient participants who were taking triptans described that when taken at the right time, triptans abort their migraines and associated symptoms, and take approximately 30 minutes to 3 hours to cause 90% to 100% pain relief. However, participants also described many factors that may impact the effectiveness of triptans.

> ***"I tried Imitrex – the nasal spray – I tried Amerge, and while there was initially some relief they inevitably came back within a couple of hours. And why I ended up on Relpax, that's the only one I've found that not only removes the symptoms within about a half an hour but it's more lasting." -Patient***

One of the most prominently discussed issues across physician and patient interviews was that patients often have to try more than one triptan to find the appropriate type that effectively treats their acute migraines. Some patients described having to test a series of several triptans that were either generally ineffective or were effective for a period of time until the effect waned, before finding one that actually reduced the severity of their pain. Physicians described going through an exercise of switching triptans due to patients experiencing the drug's side effects or the ineffectiveness of the specific triptan in treating the patient's migraine.

> ***"So the misconception is if one doesn't work, none of the other six will work. But in fact a patient could fail six out of the seven Triptans we have available and when they take that seventh one, they think it's God's gift to their… to their world, because it works. So they are not… the drugs are not so identical that they'll all work or they'll all fail in every person or for every migraine. You know some people need sumatriptan for this headache and they need frovatriptan for that headache." - Physician***

Another significant issue described by participants is the timing of when triptans are taken to treat migraines. Triptans were often perceived to be ineffective when a patient does not take one early enough. The most common reason for holding off on triptan treatment cited by physicians, pharmacists and patients was patient "hoarding" behaviours, where patients prolong taking a triptan after the onset of pain to determine if the pain will escalate to a migraine.

> ***"Sometimes if the Relpax isn't taken soon enough, or if it kind of comes on a little bit more quickly, then the Relpax may not work. It happens rarely. Sometimes I kind of wait and see if, "Well, I'm kind of feeling like one, but maybe it'll go away," because sometimes they do, it doesn't really come on, so I kind of try and wait it out, and so I guess that's what I mean if it gets away from me, I misjudge it, I should have taken something but then it's too late." -Patient***

ii. Impact on Functional Status & Quality of Life

When asked about the impact of triptans on patient functional status and quality of life, physician and patient participants believed that triptans restored functionality and enabled patients to carry on with activities of daily living. Patients who had experienced migraines before triptans were introduced to the market were able to contrast their experiences prior to taking triptans with their experiences using triptans. These patient participants expressed a marked increase in their ability to attend work and participate in normal activities that they otherwise used to miss prior to taking triptans. Most patient participants either described a return to normal functionality or enough of an improvement in functionality to be able to get out of bed and begin to perform some regular activities. For those on disability as a result of their migraines, the effectiveness of triptans served as a source of hope to regain normalcy.

> ***"It was dramatic. I mean… you could actually function while the migraine was in progress. You could do anything… within reason. Didn't mean that you didn't have, you weren't sensitive to light or you weren't sensitive to sound. It's just… you were able to continue on and do your work…I can't over-exaggerate that you know. I think it's impossible to exaggerate it. It was such a change." -Patient***

> ***"The impact that this medication has on quality of life is really significant, I mean, I'm hoping at some point to return to work and contribute in a meaningful way and find something fulfilling for myself, but without this medication that would be completely unreasonable." -Patient***

C. Many Migraine Sufferers are at Risk for Over-Use Headaches

Many participants (patients, physicians, pharmacists) described that patients taking non-triptans medications tend to over use them in order to sustain the short lived pain relief, putting themselves at greater risk for side effects such as medication over-use headaches, commonly known as "rebound headaches".

> ***"So I think most of them don't realize that by over treating and it generally happens with over the counter medications. Most of the patients who are in migraine medication overuse headache are not on a Triptan. There are some of course but you have to use… ten to twelve Triptans every month, month in month out to treat rebound. A lot of people can't afford that. But they can go to the store and buy you know Ibuprofen or Acetaminophen and pop it like its candy. But if the doctor gives them you know Acetaminophen with codeine and they take it on a regular basis. So a lot of them start to treat because they fear headache but also their medication doesn't work very well and we know that as little as… two days a week use of an over the counter analgesic or five days a month of a narcotic type analgesic like Oxys and all those which the government freely allows people to use, creates medication overuse headache." - Physician***

In addition, pharmacist participants noticed that some patients become dependent on certain combination analgesics such as Fiorinal or opioid-based analgesics such as Tylenol #3s.

> ***"Tylenol 3 and to some extent Tylenol 2 mixed with ibuprofen 600. I've quite a few of those prescriptions and when talking to the patient they say it's fine for migraines and you delve deeper into Tylenol 3 and you find actually… well, I've been taking Tylenol 3 for the last couple years.. It's the only thing that works for me. And you tell them about the other side effects, the dependence and you know, constipation and drowsiness, they shouldn't drive, they shouldn't drink alcohol with it .. [Patients say] Oh, what options do I have?" -Pharmacist***

Chronic migraine sufferers who are using triptans on a daily basis are also at risk for medication over-use headaches. Seven patient participants (39%) described having current or past experience with over-use headaches. Many of these participants described not learning about the risk of rebound headaches until many years of medication over- use.

> ***"I was already rebounding from over-the-counter medication when I went to this pain doctor…and I was taking handfuls of over-the-counter pain medication. And so he put me on Imitrex, so it did work initially, but I was already in trouble when I got to him at that point" -Patient***

Some physician participants described medication over-use as the use of combination analgesics, opioids or triptans on greater than 14 days per month, or the use of simple analgesics on 10 days a month or more. In cases where patients are over using their medication, physician participants have strongly recommended prescribing daily preventative medications, such as anti-epileptics or anti-depressants.

Theme Summary: Triptans are perceived to be first line treatment for episodic migraines and are generally regarded as highly effective when used appropriately. However, many migraine sufferers are using OTC medications or prescription analgesics that are perceived by participants to be less appropriate for treating migraines and have potentially harmful side effects. One challenge of using triptans is having to try different types of triptans to find one that is appropriate for the particular patient. Oftentimes, a physician and patient may try one triptan and regard the whole group of drugs as ineffective if the patient did not respond to that particular type. Additionally, over-use headache is often attributed to triptan use. Although triptans users may experience this side effect, the majority of these individuals may be experiencing over-use headache as a result of years of ineffective migraine treatment and use of OTC medications, and not specifically as a result of over-using triptans.

Factors that Determine the Accessibility of Acute Migraine Therapies

Four main factors were described by all participant groups as having an impact on patient access to migraine therapies. These include: a) physicians' stigmatization and lack of awareness of migraine therapies; b)varied access to information on migraine therapy; c)pharmacist advocacy; and d) the affordability of triptans. Overall, there appears to be better access to therapies perceived to be less effective than triptans (e.g. Tylenol #3) than to triptans, which are considered a standard of care for migraine sufferers.

A. Physician Stigma & Lack of Awareness

Many participants from the patient and physicians participant groups perceived physicians to be a significant barrier to accessing triptans. A small number of patient participants referred to their experience of physicians believing that their migraines were common headaches, and felt that this physician belief delayed their triptan treatment. Physician participants described that other physicians often stigmatize the experience of migraine, believing that migraine sufferers are "complainers". This may impede many patients from getting appropriate treatment.

> ***"… I think in the past when you say you suffer from migraines it's, "Oh, you have headaches. Wow, big deal," there's not a lot of, I guess, sympathy for you, so I certainly had that. I think that's why it took 'til university to get finally prescribed triptans, which – as I said – were life-changing for me because it wasn't so debilitating when I got a migraine and I wasn't out for two or three days and feeling terribly. So I do think that back then migraines weren't taken very seriously, and then now I think also because of the complications with my migraines, that people... healthcare providers who know my history do take them quite seriously, and those who don't know me are often quite concerned because I don't present with very normal symptoms." - Patient***

Lack of awareness of migraine diagnosis and what constitutes appropriate migraine therapy was also highly discussed across participant groups as a significant factor related to triptans access. Some patient participants described the experience of having a delayed diagnosis of migraine, which involved years of experiencing pain and using either opioids or OTC medications before they were prescribed triptans or referred to a neurologist. Physicians described there being a general lack of knowledge about migraine diagnosis and therapy particularly in primary care settings.

> ***"One [problem] is the majority of physicians don't know how to diagnose migraine. And I am sure you are familiar with the World Health [Organization] data that shows the average trainee medical student gets about four hours in four years on how to diagnose and manage headache. So we have all these physicians out there who are well-meaning but completely ill-equipped to diagnose it. So patients first of all don't get the right diagnosis and then they obviously don't get prescribed the right drugs." - Physician***

Physician participants also noted that patients and PCPs are misinformed about the proper use of triptans, which can lead to issues such as poorly treated migraines and side effects like over-use headache. Primary care physicians were perceived by neurologists to be hesitant to prescribe triptans because of misconceptions about the side effects, the strength of the drugs and the belief that if one triptan is not effective that the whole line of drugs will not be effective for a patient (as discussed above).

B. Patients have Varied Access to Health Information

All participants groups described the importance of patient education in understanding appropriate migraine treatment and minimizing potential side effects. Patient participants reported having varied access to health information and this has played a role in their access to triptans and other migraine treatment strategies. Some patients felt that they did not receive enough information from their family doctor and subsequently decided to do their own research on the internet or connect with patient advocacy groups. One participant described hearing about triptans on the radio and then approaching her family doctor to receive more information. Other patients have multiple family members who suffer from migraines and used these family members as resources for information and self-management guidance. Overall, patient participants either felt that they were given adequate information to manage their migraines, while others felt that they had very little information to help them use the drugs.

> ***"It would be nice to have someone to talk to about migraines. I find my doctor didn't really know a lot, and the neurologist was very quick to put it off to hormones and I know there's other reasons why. I also sometimes get stress-release. If I have a stressful event I will get a migraine that comes on after that. It's just maybe more information on and resources to talk to, people to talk to and more resources maybe to read about it" - Patient***

Physicians believed that appropriate patient education and counseling is required given the complexity of migraine management and the potential for under or over-treatment when drugs are used inappropriately. Education was seen by these physician participants as a "pay off" down the road that could increase medication adherence and decrease side effects, thus improving overall quality of life.

> ***"…while the patients were waiting [for an appointment] I felt horrible because they show up and say, Oh my God, … If I had known about medication overuse, maybe I could have done something. So now I run an education program six months ahead of when they see me. And they are taught all of this stuff. Appropriate use of a Triptan, appropriate use of other medicines, medication over-use, lifestyle, this and that. And so many patients when they come in that we haven't pulled the data all together yet specifically, but looks like migraine disability drops by anywhere from twenty to fifty percent. So it pays to educate." - Physician***

C. Pharmacist Advocacy

Pharmacists described the successes and challenges of advocating for their patients, and how this advocacy can impact patient access to triptans. A few pharmacists described experiences of having informed customers of the existence of triptans after noting that these individuals were taking opioid medications over the course of several years for their migraines. One pharmacist also described explaining the Trillium Program to low-income customers who required triptans.

Some notable challenges to pharmacist advocacy include: patient unwillingness to try a triptan if another type of drug is marginally effective (i.e. "if it ain't broke, why fix it?"); fluctuating demands for triptans that are seasonal (i.e. because of weather and pressure changes) but do not always keep up with available supply; and an EAP process that does not allow for timely refills.

> ***"I have a client currently waiting for EAP on a renewal on a drug that he should never have stopped taking, that he can't afford and has stopped taking since last January, this is August. The process in place is unwieldy. They have fast track for certain drugs which sounds like a great idea, but if you are going to fast track drugs make them limited use and if you are going to consider things for EAP then you need to make it in a timely fashion."***
> ***- Pharmacist***

Pharmacists were seen by patients to play a key role in the continuity of medication use. Patients cited issues with medication refills when they were obligated to see their physician before prescriptions could be renewed. Two participants cited the common practice of pharmacists lending patients medication between renewals when required; this was seen as a warranted practice for migraine sufferers. The ability for pharmacists to refill prescriptions was seen as a facilitator to triptans access.

D. Affordability of Triptans

> ***"The benefit is significant but it can be quite cost prohibitive for people without coverage and even with coverage because it is still quite expensive…its almost $10 a tablet and you're maybe taking two each time, and that's not, I don't think, a consideration you should need to have when dealing with a significant health issue…you know to sort of have to think, 'should I spend $20 right now to maybe make myself feel better?'" -Patient***

> ***"I think 1 in 8 people have migraines and coupled with the fact that they are young people, they're not retired folks, it does have a big impact on society as well and also their personal life; and even if we can offer something that is clearly a first-line treatment, it targets the specific migraine mechanism and studies have shown that it works fairly well, in terms of migraine treatment, and we cannot offer at least some coverage for the people who need it, I think that's a big problem." - Physician***

i. Those Who Can't Afford Triptans are Less Likely to Adhere to Suitable and Safe Treatments

Almost all patient participants using triptans have private drug coverage, most with monthly coverage limits. This aligned with discussion with physicians and pharmacists, who said that

most individuals on triptans access these through private insurance. However, as described previously, physicians and patients reported patient anxiety regarding exceeding monthly coverage limits and therefore practice prudent dosage management (e.g., delaying the use of triptans until the pain is unbearable, cutting the doses in half). Prudent dosage can lead to taking up to double the dosage of triptans at a later time point to abort a migraine that has already fully progressed. In some cases, patients described not being able to abort the migraine, even with two doses. Physician and pharmacist participants explained that patients who do not have private insurance coverage generally do not fill their prescriptions for triptans, but some patients may pay out-of-pocket for triptans when they feel they have no choice.

> ***"I get the sense that sometimes more people would use triptans if the price wasn't an issue. I have given people the cost of a prescription and have them not fill it because of the cost. Those would be cases where there is no coverage and so they have not had the prescription filled…probably 20-30 age range and some could have been working, but just not able to afford that" -Pharmacist***

> ***"Pharmacist: I have a patient, I know her from 7 to 8 years ago and I know that she is a migraine patient and I have seen her in the attacks. She can't even talk when she has the attack… and she came in to fill the prescription as usual and at that time she had an attack and the insurance did not cover it, they rejected it. So we had to call the insurance, and the insurance said... for triptans, they are putting certain limit per month and this patient exceeded the limit. But I already seen... the patient in front of me, I see the attack, I see the suffering of the patient in front of my own eyes and I told that to the agent, but the agent was not able, really to override it. She said this is the policy so she couldn't do anything. This was one of the experiences with migraine patient I could never forget.***
>
> ***Interviewer: Right, So what was her recourse then? What would she do at that point because her insurer isn't providing it?***
>
> ***Pharmacist: She pulled out her credit card and said 'I cannot not take my medication. I can't afford not to take it so give me one box, I will pay for it'. I said 'okay'. I did."***
>
> ***- Pharmacist***

Moreover, physicians will rarely prescribe a triptan in the absence of insurance coverage. In these cases, patients either self-manage with OTC drugs, or physicians prescribe drugs that are perceived to be less effective but are either less expensive or covered by the Ontario Drug Benefit (if the patient is eligible).

> ***"Other patients, there is no other choice but other than to use prescription analgesics or combination analgesics if the patients are deprived of the opportunity to have optimal treatment. Of course we also, depending on the patient, maybe I will put him on preventative therapy to try and decrease the number of headaches they have so they have less need for acute therapy, but it's never going to eliminate their need for acute therapies." - Physician***

Physicians who have patients that are not able to afford triptans also described giving patients samples as well as attempting to obtain them from pharmaceutical companies through compassionate supply. However, these were seen as temporary strategies and were not perceived to be sustainable methods of facilitating access to triptans

ii. Most physicians and patients are unclear about the Exceptional Access Program

All participant groups reported low rates of patient access to the EAP. Although this was in part due to the fact that most migraine sufferers are not eligible for the ODB, issues with the application process itself were cited by both physician and pharmacist participants as significant barriers to access. One physician highlighted the fact that many very severe migraine sufferers are unable to work and receive assistance through the Ontario Disability Support Program – yet are rarely receiving triptans through the EAP. Physicians described a lack of awareness of the EAP eligibility criteria for triptans, particularly among PCPs who tend not to have a vested interest in migraine, but also among neurologists. These participants generally perceived that information on eligibility criteria were not readily or publically available. Moreover, physician participants with experience obtaining triptans through the EAP reported that application forms frequently bounce back, requiring additional time to be spent providing justifications and detailed technical explanations for the reasons why triptans are being sought for their patients. Most physician participants believed that having to undergo this process is unnecessary, and both physician and pharmacist participants viewed the EAP application process as a deterrent to obtaining triptans through the ODB.

> ***"Usually the doctor does not go through this for patients that he can switch something else with. If we tell the patients to put pressure on the physician, the physician will change it for something covered, like a pain killer or something."***
> ***- Pharmacist***

"… in the vast majority of patients…over-the-counter analgesics and prescription anti-inflammatories are ineffective. It is evidence-based for two decades that [triptans are] the standard-of-care medicine, it's the medicine that's on the guidelines from the American Academy of Neurology, the American Headache Society, the Canadian Headache Society etc. So when we are having to deal with the Section 8 or Exceptional Access Program or what not, it's a frustrating, cumbersome, challenging process. They take time to get responses. Responses come back with only the patient's first name and first initial of their last name, making it extremely difficult for offices to track who the hell they are talking about! They are always requesting additional information. Completely ignore the expertise of the requesting physician. Information [is] ignored and it looks like a stalling tactic just to get more information. So I abandon and don't bother. I would say 99.5 percent of family physicians… have no idea that triptans are available through the Section 8. I have had probably a handful of patients in my career whom family doctors have requested Section 8 funding for triptans…they were put on narcotics analgesics because they couldn't afford triptans and their family doctors didn't realize that there is a process for them to access it." - Physician

Many patient participants had not heard about the EAP, and did not know if they are currently eligible (e.g. through the Trillium Drug Program) or will be eligible to obtain triptans through the ODB upon turning 65 years of age. When patient participants were asked what will happen upon retirement or when they turn 65 years, many were unsure about how they would pay for their triptans. Only one patient participants, who was over 65 years of age, described getting coverage for triptans through ODB through a special access program, which we assume is the EAP.

Theme Summary: Although most migraine sufferers are able to access triptans through private coverage, limitations may hinder effective pain management due to patient anxiety about "running out" of medication. Access is significantly inhibited by the affordability of the drugs for those who do not have private coverage. these patients may resort to using less appropriate but more affordable drugs for migraine treatment. Moreover, physicians may abstain from prescribing triptans to patients without private coverage but may attempt to access triptans for them through samples or compassionate supply. There are important barriers to accessing triptans through the EAP. Most notably, physicians and patients lack awareness of the ability to access triptans through the EAP and the EAP coverage criteria. Furthermore, physicians who have attempted to obtain triptans through the EAP find the process cumbersome and are not likely to continue accessing triptans through this route as a result. Patients who will be eligible for ODB soon are not clear about whether they can access triptans through publically funded means, and are anxious about obtaining triptans in the future.

Discussion

Key Findings

Our study findings demonstrate many key experiences and perceptions related to triptans prescription and use that can facilitate or hinder the appropriate use of, and access to, this group of medications. One key aspect of our findings is the affordability of triptans; although the high cost of triptans primarily inhibits access to these drugs for those who are low-income and/or do not have private coverage, it is also apparent that cost as well as coverage limitations influence the appropriateness of prescribed migraine treatment and can impact overall quality of life. This study also highlights perceptions on appropriate diagnosis and treatment of migraines in general, and on the challenges experienced in understanding what is covered by, and the process of applying to, the EAP. A surprising finding was the extent to which patients, physicians and pharmacists require access to better information on migraine treatment and the EAP, which can be addressed through appropriate education and knowledge translation.

Health Equity Considerations

The findings from this study highlight the disparity in access to appropriate migraine treatment between individuals who do and do not have private drug coverage. This inequity exists in part because of the high cost of clinically effective drugs such as triptans as well as the obstacles to accessing triptans through the EAP. We have found that this disparity is increased when a physician or pharmacist is not able to advocate for or assist in navigating a patient through the necessary applications to receive the appropriate therapy through the EAP. Patients may resort to using less appropriate drugs for migraine treatment that are more affordable, and physicians may abstain from prescribing these drugs to patients without insurance coverage. This may result in significant differences in long-term health outcomes and quality of life between these two populations.

Limitations

Participant recruitment was the primary limitation of our study, although saturation of data was reached across all participant groups. It was difficult to recruit triptans users with coverage through the EAP as the size of the source population is very small. Ultimately only one patient who accesses triptans through the EAP was included.

Primary care physicians were underrepresented as they were non-responsive or reluctant to participate in interviews; only one PCP agreed to participate, and this PCP had more experience with migraines than typical PCPs. Therefore, there may be gaps in understanding PCP perspectives on migraine treatment, triptans use, and submissions to the EAP. Many of our perceptions of migraine treatment in primary care are derived from neurologists' experiences speaking with PCPs or treating patients who are referred to them from primary care.

It should also be noted that qualitative findings are not representative of the general population of individuals from which our study sample was drawn. There may be bias in sampling given that those who responded to interview requests may have been more likely than non-responders to be vocal about discussing the impact of their migraines and may be more highly involved in migraine advocacy initiatives. In an attempt to limit bias, we engaged in negative case sampling, which is to select interview participants who differ from the response trend observed in the recruited sample to date, so as to introduce different viewpoints.

Conclusions

The findings from the qualitative study of the triptans drug class review informed the methods of other ODPRN research units conducting studies as part of the review. Moreover, our qualitative study helped to contextualize the results of the systematic review, pharmacoepidemiological analysis and environmental scan performed within the separate research units of the triptans drug class review. On a broader scale, our study findings fill a gap in knowledge on access to triptans and how this may be impacted by the experience of migraine management, physician and patient perceptions of triptans, and structural barriers to access (e.g. drug coverage and affordability). Overall, our findings shed light on the experiences of prescribing, dispensing and using triptans for migraine treatment, and unveil important information that can impact how patients in need can access these drugs across Ontario.

References

Gallagher, R. M. and Kunkel, R. (2003). *Migraine Medication Attributes Important for Patient Compliance: Concerns About Side Effects May Delay Treatment*. Headache: The Journal of Head and Face Pain, 43: 36–43. doi: 10.1046/j.1526-4610.2003.03006.x

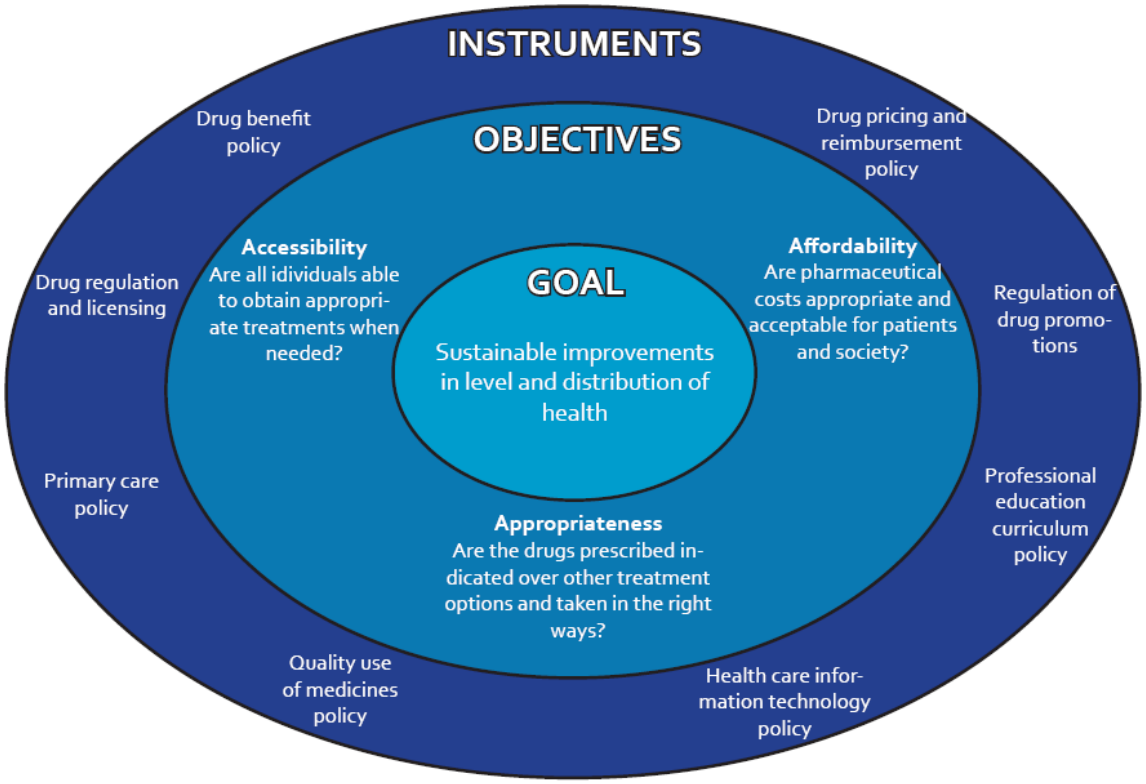
Kuzel, AJ. (1999). "Sampling in qualitative inquiry." In BF Crabtree and WL Miller (Eds.) Doing Qualitative Research (second edition). Thousand Oaks, CA: Sage Publications: 33-45.

Morgan S, Kennedy J, Boothe K, McMahon M, Watson D and Roughead E. (2009) *Toward an Understanding of High Performance Pharmaceutical Policy Systems: A "Triple-A" Framework and Example Analysis.* Open Health Services and Policy Journal: 2;1-9

Ritchie J, Spencer L. (1994). "Qualitative data analysis for applied policy research." In Bryman A, Burgess R, eds. Analysing Qualitative Data. London: Routledge: 173-194.

Worthington, I., Pringsheim, T., Gawel, M.J., Gladstone, J., Cooper, P., Dilli, E., et al. (2013). *Canadian Headache Society Guideline: Acute Drug Therapy for Migraine Headache.* Can J Neurol Sci. 2013; 40: Suppl. 3 - S1-S3

Appendix A: "Triple-A" Framework for Pharmaceutical Policy Analysis



Adapted from: Morgan S, Kennedy J, Boothe K, McMahon M, Watson D and Roughead E. (2009) Toward an Understanding of High Performance Pharmaceutical Policy Systems: A "Triple-A" Framework and Example Analysis. *Open Health Services and Policy Journal:2;* 1-9

Appendix B: Participant Characteristics and Demographics

Patients

Demographic Characteristic (n=18)	n	%
Gender		
Female	14	78%
Male	4	22%
Age		
25 -34	3	17%
35-44	4	22%
45-54	4	22%
55-64	5	28%
65+	2	11%
Employment Status		
Full-time	7	39%
Part-time	1	6%
Unemployed (retired, disability)	10	55%
Years with migraine		
5-15	10	55%
>15	8	44%
Clinician prescribing triptans*		
PCP/Nurse Practitioner	14	82%
Neurologist	3	18%
ODB Eligibility		
ODB eligible	2	12%
ODB eligible receiving triptans through EAP	1	6%

Physicians (Neurologists and Primary Care)

Demographic Characteristic (n=6)	n	%
Years of practice		
5-15	4	67%
>15	2	33%
Type of Practice		
Full-time	5	83%
Part-time	1	17%

Demographic Characteristic (n=6)	n	%
Geographic Location		
Urban	4	67%
Suburban	1	17%
Rural	1	17%
Frequency of Prescribing Triptans		
Never*	1	17%
Weekly	2	33%
Monthly	3	50%
Proportion of Patients on Triptans Covered by ODB		
0%	5	83%
10-19%	1	17%

*note that the participant acts as a consultant and does not directly prescribe migraine therapies.

Pharmacists

Demographic Characteristic (n=8)	n	%
Years of practice		
<5	2	25%
5-15	4	50%
>15	2	25%
Type of Practice		
Full-time	8	100%
Geographic Location		
Urban	7	88%
Rural	1	12%
Frequency of Prescribing Triptans		
Monthly	2	25%
Weekly	5	63%
Daily	1	12%
Proportion of Patients on Triptans Covered by ODB		
0%	3	38%
<10%	4	50%
<20%	1	12%