ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

The Ontario Drug Policy Research Network Drug Class Review on Allergen Immunotherapy Medications

FINAL QUALITATIVE REPORT

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Conflict of Interest Statement

No study members report any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock options, expert testimony, grants or patents received or pending, or royalties) that may present a potential conflict of interest in the Allergen Immunotherapy Drug Class Review.

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Executive Summary

Background: The Ontario Drug Policy Research Network (ODPRN) conducted a drug class review on allergen immunotherapies (AI), which was selected as part of an initiative by the Ontario Public Drug Programs to update the public drug formulary. This report highlights the findings of the qualitative study performed within the drug class review to determine the experiences of managing and treating adult patients using AI.
Methods: We conducted 19 semi-structured telephone interviews with stakeholders, including patients, primary care physicians (PCPs), and allergists. We analyzed the data using the framework approach for policy analysis.
Key Findings: Findings in this report are summarized to represent common experiences and perceptions described across patient and physician groups.

Allergen Immunotherapy prescription: Clinician participants described the various factors they consider before prescribing AI, such as type of allergy, response to traditional pharmacotherapy and non-pharmacological strategies, skin test results, and other patient related factors. Many different health care providers are involved in the process of prescribing, dispensing, and administering AI for the management of severe allergies, such as PCPs, allergists, naturopaths, nurses, manufacturers, and pharmacists. Physician participants considered venom therapy to be first line treatment; they preferred and found the subcutaneous immunotherapy (SCIT) formulation to be more efficacious for environmental allergens, however, if patient compliance was an issue they would prescribe sublingual immunotherapy (SLIT). Primary care physician participants said they screen and refer severe allergy patients to allergists. Allergists will order testing, make the diagnosis, and prescribe AI; preparations may be made either on site or through a manufacturer. Clinician participants expressed some concern that there are individuals in the community who prescribe AI, but are not qualified allergists. Participants speculated that AI prescriptions may rise with the introduction of SLIT and pre-mixed SCIT on the market; however, participants felt that prescription trends are also linked to where and when an allergist has received medical training.

Access to Allergen Immunotherapy: Physician and patient participants described that there were no barriers for patients who need to access AI or barriers to coverage through the Ontario Drug Benefit (ODB) Allergen program. Clinician participants suggested that the limited use criteria for AI should revolve around symptom severity and an adequate trial of traditional pharmacotherapy allergy medication. Participants believed there is a lack of standardization of how AI is dispensed (i.e., on-site, manufacturer, or pharmacy), which has resulted in a variety of prices for the same products across the various dispensing outlets.

Conclusion: Overall, our findings shed light on the experiences of prescribing and using allergen immunotherapies in adult patients, and unveil important information that can impact how patients in need can access these drugs across Ontario.

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) at the Ministry of Health and Long-Term Care (MOHLTC) to select key priority areas and topics for formulary modernization, conduct independent drug class reviews, and disseminate the results of the reviews to the OPDP to facilitate informed decision making on public drug funding policies. Allergen Immunotherapies (AI) (e.g., subcutaneous immunotherapy (SCIT), sublingual immunotherapy (SLIT), and venom therapies) was selected as the topic for the tenth drug class review.

Currently, there is limited information on how physicians prescribe and access AI. Phase 1 of the ODPRN qualitative unit work will involve exploring the various factors that may be related to prescribing, dispensing, and using these therapies. This information is important for understanding and contextualizing prescription and usage patterns in Ontario, as well as to highlight any health equity issues that may be prevalent but are currently unknown. Phase 2 of the ODPRN qualitative work will be to assess the social acceptability and feasibility of the final results and recommendations proposed by the ODPRN research team.

Methods: Phase 1

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 to policy contexts than alternative qualitative procedures. However, the approach also maintains the flexibility of qualitative methodology to incorporate new ideas, emergent issues, or unanticipated results.

Sampling

Stakeholders identified for the AI drug class review include primary care physicians (PCPs), allergists, and patients. Inclusion criteria were: clinicians (PCPs, allergists) who have prescribed, dispensed, or administered AI to adults; and patients over 18 years of age who have experience using SCIT, SLIT or venom immunotherapies.

A purposive sampling approach with 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 AI. Given the rapid nature of study timelines, we aimed to recruit 6-8 participants from both stakeholder groups (i.e., clinicians and patients). We anticipated that this amount of participation may be sufficient to reach saturation amongst relatively homogenous groups of participants (Kuzel, 1999).

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 (e.g., Twitter, Facebook) accounts; and g) snowball sampling (i.e., 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 long and conducted between June and July 2015. 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; 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 qualitative 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). These codes comprised the coding framework. A modified coding consensus approach was used; the framework was reviewed by the qualitative research team and applied to 20% of transcripts by two analysts during in-depth analysis. Inter-rater reliability between the two analysts was > 80%. The remaining transcripts were coded by a single analyst. The analyst and the qualitative research team engaged in mapping and interpretation of the coded data to generate the final themes.

Phase II of the qualitative research study is described below.

Research Ethics

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

Part 3: Findings

A total of 19 participants took part in the study: 9 patients, 8 allergists, and 3 primary care physicians. Detailed participant demographics can be found in **Appendix B**.

Key Themes Related to the Prescription and Use of Allergen Immunotherapies in Adults

PRESCRIPTION OF ALLERGEN IMMUNOTHERAPY

- Perceptions of factors that influence the treatment of severe allergies
- Perceptions of AI and patient adherence

- Perceptions of the role of different healthcare practitioners in the prescribing/dispensing/administering of AI
- Perceptions of AI prescription trends in Ontario

ACCESS TO ALLERGEN IMMUNOTHERAPY

- Affordability and cost structure
- OPDP Allergen Program: Physicians' opinions of potential limited used criteria

Detailed findings on each of these themes are described below.

PRESCRIPTION OF ALLERGEN IMMUNOTHERAPY

PERCEPTIONS OF FACTORS THAT INFLUENCE THE TREATEMENT OF SEVERE ALLERGIES

Clinician participants described various factors that influence their decision to prescribe or refer patients to an allergist for AI. The factors span four categories: types of allergies, trial of traditional allergy medications and non-pharmacological strategies, skin testing, and patient related factors (Refer to table 1).

Table 1: Perceptions of factors that influence physician AI prescription habits

Note: The findings in table 1 were derived from primary care and allergists (i.e., clinician) participants' transcripts.

Theme and Description	Quotes
Type of allergy Clinicians stated that the type of allergy (i.e., venom versus environmental) influenced their decision to prescribe AI. • **Insect Venom.** There was a consensus among participants to prescribe AI as first line because of the curative potential for this life threatening allergy. • **Environmental.** Participants described that AI may not always be first line because it is better suited for certain allergies (i.e., grass, pollen, ragweed) and other treatment options are available (e.g., antihistamines).	*"For venom allergy it's incredibly effective at preventing a potentially life threatening condition… the same risks apply, but you are giving them the immunotherapy in a controlled setting, so it's a completely different risk benefit ratio than it is for the you know respiratory disease where you are treating hay fever, maybe you are treating asthma, but we have other treatments for that… that you know work better, faster, safer and cheaper, but with a venom allergy it's a whole different ball game and that's when I use immunotherapy." - Allergist*

Trial of traditional allergy medicines and non-pharmacological strategies • Majority of participants stated that patients must have exhausted traditional pharmacotherapy (e.g., antihistamines, intranasal corticosteroids) that are safer and non-pharmacological strategies (e.g., allergen avoidance, nasal sprays) before AI is considered.	
Skin tests • Majority of participants require a positive skin test before initiating a trail of AI because participants believed it to be more accurate than a blood test. • Some allergist participants may preform additional testing (e.g., blood, urine, vitro) for patients with a negative skin test, but present clinical symptoms • Participants had differing opinions about the number of skin tests that should be conducted per patient. • Monitoring strategies did not rely on re-testing, but rather on a self-report of patients' symptoms	*"Yeah so my preference is skin testing because it tends to be more sensitive so a negative test would rule it out more effectively, it may also be more specific as well depending on the allergen, and it's generally more cost effective as well." – Allergist* *"I have seen it done [re-testing], you don't really need to, if they are getting you know their ragweed hay fever every year, and they come in and say I need my prescriptions renewed, I go, ok has anything changed, and they go no, and I go, ok fine, why would I retest them? Unless they develop a new pattern of symptoms they don't really need retesting. - Allergist*
Patient related factors • Patient coverage status, age, medication history (i.e., are they on beta blockers or ACE inhibitors), and patient preferences were additional factors considered in prescription decision making.	*"[Ai] can provide more long term benefits to someone who is potentially younger in their teens or 20s who doesn't want to be on medications for decades can do immunotherapy with long term lasting benefits and that's generally why people will choose that over routine medication." - Allergist* *"I will give immunotherapy more quickly to somebody who says you know what I am not interested in failing on two years of three different nasal sprays, this is what I want to*

	do. It's more in keeping with how I want to treat my disease, to me that's acceptable as well, it speaks to patient preference and their expectations of therapy." - Allergist

PERCEPTIONS OF AI AND PATIENT ADHERENCE

Table 2 summarizes clinician and patient participants' thoughts on the effectiveness of AI as a treatment for severe allergies. Participants also commented on factors that may hinder or promote patient adherence to treatment, and described some typical dosing and duration of treatment plans. PCPs in our sample were not familiar with any guidelines or practice parameters for AI and they refer patients to allergists for diagnosis and treatment; PCPs may help in the administration of injections, but will consult allergists if any dosing adjustments are required. Allergist participants mentioned using the following guidelines:

- The Canadian Society of Allergy and Clinical Immunology guideline (1995)
- World Health Organization allergen immunotherapy guideline (2000)
- The American Academy practice parameter (2011)
- The European Academy of Allergy and Clinical Immunology guideline (2012)
- Training manuals/fellow handbooks have been produced by academic or hospital institutions

Participants believed that there is evidence to suggest these therapies are effective and justifies prescription; however, more rigorous research needs to be conducted to further standardize the process for administering AI. Allergist participants speculated that large longitudinal clinical trials for AI may be very expensive, which may be why small manufacturers are unwilling to commission them.

Table 2: Perceptions of AI medications

Note: The findings in table 2 were derived from primary care and allergists (i.e., clinicians) and patient participants' transcripts.

Perceptions of Allergen Immunotherapy	Quotes
Venom Immunotherapy <u>Perceptions of effectiveness:</u> • Clinician participants perceive this therapy to be very effective • They believe it will greatly reduce the chance of anaphylaxis if a patient is stung • Clinician participants considered this to be a	*"I think the one exception for sure is bee keepers. I think bee keepers should stay on it forever if the reaction was long enough, and they're … continuing to work as bee keepers, and then the lumberjacks, and the outdoor people… that's a bit of a tough call. I think the science isn't there so much... that's a bit of a judgment call. It's not the wrong thing to do for the high risk patients, but generally, even for*

first line therapy because it has curative potential Perception of common doses and length of treatment: • Majority of clinician participants agree that treatment duration should be 3-5 years • However, some clinician participants will prescribe life-long for high risk groups (e.g., bee keepers, loggers) Perception of factors that may influence patient adherence: • Some patients see the value and subsequently will come in for shots and others feel it is too inconvenient	*those people, if it's not a life-threatening reaction I'll stop after five years." – Allergist* *"Yeah, we discuss the risks and the benefits and I have people who have elected to continue. I have had people who have elected to quit, you know it's a big commitment. I mean it's hard to get them to come in even the people with this life threatening reaction, they hate coming in for their shot and hanging around, you know it's a big nuisance." – Allergist*
Subcutaneous Immunotherapy (SCIT) Participants perceptions of effectiveness: • Most clinician participants perceived the injections to be effective for those who don't respond to other pharmacological treatments and have moderate to severe symptoms • Clinician participants believe the efficacy varies for different indications (i.e., better for pollens, dust mites, and cats than for mold or dogs) Perception of common doses and length of treatment: • Perennial and seasonal treatment plans (weekly or bi-weekly dosing during build up and monthly during maintenance) • Usually patients take SCIT for 3-5 years • Physicians participants vary in removing patients off medication after 5 years (i.e., out of caution that symptoms will return, some keep patients on SCIT after 5 years) • Participants believed that all injections should be administered under the supervision of a clinician due to the risk of anaphylaxis Perception of factors that may influence SCIT	*"Well you know there is some literature that if you've been on a certain immunotherapy for three years that if you stop that immunotherapy the benefits may be ongoing for the next year meaning that you don't have to continue to take that medication and yet still have benefit for the following year. I don't know how often I have sort of tested that theory in my patients because a lot of them once they finally get relief with immunotherapy may not be that willing to come off just to see if they could take a year off and yet still have the benefits." - Allergist* *"The first major con was that I had to do this on a weekly basis – so I had to make myself available, at the beginning, on a weekly basis; and I had to go to the clinic, and I live kind of a busy life, so it was con but at the same time the pro of it was that I was going to get better, and you just have to do what you have to do in order to, 'cause like I said my symptoms were making me suffer; so after thinking about it for all of about 2-minutes, I thought 'yes, this is something that needs to get done 'cause I need to get better – 'cause my quality of life needs to improve'." – Patient*

prescription: • Can treat multiple allergies at once • More effective than SLIT • Can treat more indications than SLIT • Not daily dosing • Less expensive than SLIT • Types: Mixture of multiple extracts or Pollinex-R© Perception of factors that may influence patient adherence: • Patient adherence varies and may depend on the patient's perception of SCIT effectiveness • Less convenient than SLIT • Minor side effects, but most patient think they are manageable • Some prefer SCIT over SLIT because they feel safer taking the therapy under doctor supervision due to side effects	*"No, I mean… I think I have a positive experience overall, in terms of a reduction of symptoms and the side effects hadn't been that significant.... I wasn't getting the same effect when I was taking over the counter meds or oral meds, they were just having minimal effect. I mean as far as I know this is the best … the best treatment option for me right now." - Patient* *"But I mean I just think it's a more direct form of therapy so I just, I think the shots are just more effective, it goes directly into my blood stream and starts working right away, and does what it has to do, as opposed to the pills, but I, yeah I just like taking the shots, it's just easier, it's faster, I don't have to remember to take anything, I don't know, I just like the injections. I think it's more effective." - Patient*
Sublingual Immunotherapy (SLIT) Perceptions of effectiveness: • Most clinician participants believed SCIT to be more effective than SLIT • Participants mentioned that SLIT is newer and has shown short-term efficacy, but no long-term data exists Perception of common doses and length of treatment: • Only used seasonally, usually start 2-3 months prior to allergy season • Daily therapy Perception of factors that may influence SLIT prescription: • Participants mentioned that SLIT is currently only available for certain indications (e.g., grass, ragweed) • Participants described that it is primarily for	*"None of my patients have wanted to try it yet. They are a little bit anxious about trying that because they have to do it at home. Their first dose has to be taken under observation. So in case they have a reaction. And then they are doing it at home. And then the risk of anaphylaxis is much lower than it is with the subcutaneous, but there have been reports of it. And they can get itchy mouth, itchy throat, they can get vomiting, diarrhea; you know it can be unpleasant." - Allergist* *"The only thing that's kind of annoying and difficult is just the length of time that I, like I explained to you before you have to take this months before the allergy starts whereas with other medications it's just during allergy season so that's kind of annoying and invasive that you're taking it for so long, but on the other hand I have a reduction in symptoms and with severity of allergies so I guess it's a small price to pay for that. If I didn't take it my quality of life – like you asked me before – was pretty bad, like especially during the peak of the allergy*

mono-sensitized patients • Patient participants perceived SLIT to be more convenient than SCIT because they could take the pill at home; however, some participants found the daily dosing to be inconvenient • Clinician participants perceived SLIT to be a better option for children (i.e., less painful) • Participants described SLIT as being more expensive than SLIT • Types: Grastek©, Oralair©, Ragwitek© • Some participants described having difficulty accessing Oralair© because of a shortage at the manufacturer <u>Perception of factors that may influence patient adherence:</u> • Patient adherence varies and may depend on the patient's perception of SLIT effectiveness • Patient participants described minor side effects, but most patients think these effects are manageable • Participants indicated they found SLIT to be more convenient than SCIT because it can be taken from home	*season – it was just constant irritation and I was upset and ineffective, so I don't have a problem paying whatever the small price of dosing for so long." - Patient* *"Yeah, like my eyes were you know really itchy and red, a lot of sneezing, a lot of runny nose. And now since taking Oralair as opposed to like every day problem, I will only have a problem when the pollen count is really, really, really high and it will only be like minor issues, like maybe I will sneeze a couple times or my nose will run just a little bit or my eyes will be itchy and watery just a little bit you know what I mean? So the severity has gone way, way, way down and so has the frequency." -Patient*

PERCEPTIONS OF THE ROLE OF DIFFERENT HEALTHCARE PRACTITIONERS IN THE PRESCRIBING /DISPENSING /ADMINISTERING OF AI

Stakeholder interviews revealed that many different parties (i.e., primary care, allergists, nurses, manufactures, pharmacies, naturopaths) are involved in the prescribing/ dispensing/ administering of AI.

Referral/prescribing

According to clinician interviewees in our study:

- PCPs typically screen and refer patients to allergists for testing
- Allergists will order appropriate tests and develop treatment plans
- Individuals who are not trained as allergists may also be prescribing immunotherapies

"It's a fellowship program. So, you have to take two years of specific allergy immune- allergic medicine. So, you learn how to do all these things. Some people, they don't do that. There can be doctors who… that will call themselves allergists. Like, they have patients, and they treat patients with allergies. Some… I mean with immunotherapy, which without a diagnosis of allergies. I think if you have… if your family doctor's has you on medication for allergies… At this point it's within their range of practice I believe, but if it comes to prescribing things that can cause anaphylaxes… … it becomes… I think sometimes inappropriate." - Allergist

Dispensing medication

According to clinician interviewees in our study:

- Most often, for SCIT, either the allergist or PCP will deal with the manufacturer directly and patients will pay clinics
- Occasionally patients may deal with the manufacturer directly for SCIT or will use pharmacies as a proxy
- Participants mentioned that most pharmacies do not have experience with SCIT and work with the physicians and manufacturer to set up the process
- SLIT patients may contact pharmacies; it is usually a smooth process, sometimes it may take a few days to order AI because they may not have stock on site
- Participants stated that some physicians may prepare these medications on site; some had concerns about the safety and efficacy of these preparations if proper equipment was not used

"Where I worked before, they made all theirs on site, but they had a trained pharmacist who worked in a fume hood with sterile techniques, which would have no difficulties with meeting those criteria, but if you are a community allergist and you don't have that, then I wouldn't be doing it. I think you are just asking for trouble." – Allergist

"A lot of people pretend to do allergy or sublingual, we use the standardized products that are made by a pharma company called Merck. There are other practitioners who will mix up all sorts of lotions and potions and I don't know whether or not any of that is efficacious, but it's out there." – Allergist

Administering shots:

According to clinician interviewees in our study:

- Allergists typically administer majority of venom shots and select environmental shots (i.e., for patients with an increased risk of anaphylaxis)
- Straight forward environmental shots (i.e., normal dosing and low risk of anaphylaxis) can be administered either at a PCP or allergist office based on what patient prefers
- Allergists usually provide PCPs with contingency plans for a missed dose and advise them to

call about dose titration or side effects

- Nurses may also administer shots
- Clinician participants were in consensus that SCIT shots and the first SLIT pill should be administered or taken under the supervision of a physician

"Subcutaneous injections, the non -sublingual, nobody should be doing unless they have the facilities to do so, so everyone who has a crash cart if they have a code blue or whatever that should be on site if you are providing subcutaneous immunotherapy which is why we don't allow people simply to do injections at home". –Allergist

PERCEPTIONS OF AI PRESCRIPTION TRENDS IN ONTARIO

Clinician participants described various perceptions of prescription trends in Ontario.

Some participants perceived that prescription is on the rise, for the following reasons:

- Physicians may be feeling more comfortable prescribing because there is more research evidence behind AI and there is more acceptance of the use of AI for severe allergies
- Physicians may feel more comfortable with the use of newer formulations on the market (i.e., SLIT and pre-mixed SCIT) because they are more straight forward to administer
- Physicians who are not trained as allergists may be prescribing these therapies

Some participants perceived that immunotherapy may be underutilized/over utilized by certain groups for the following reasons:

- Prescription may be linked to perception of roles; pharmacotherapy is perceived to be the family doctor's responsibility and immunotherapy is the allergist's responsibility

"Well, I mean, I don't know, I think that the change that I have seen you know since I have started practicing in the 1990s, is that with our newer graduates I think they are using maybe more of these and I think part of it is because family physicians have become in those years, have become quite familiar with using pharmacotherapy and intranasal corticosteroids so now, before family doctors were not well versed in that when I first started. So now they are and so I think that some of our newer graduates feel they have to you know really offer a lot of immunotherapy to distinguish themselves because if they don't recommend immunotherapy then the family doctor can handle it and they don't get any referrals." – Allergist

- Whether an allergist prescribes AI or not may be linked to whether he or she has completed medical school and received training (i.e., some schools provide more training on AI than others)

"Most training programs don't teach their fellows… their trainees how to prescribe immunotherapy…During residency; even the allergy residents do not learn how to prescribe

immunotherapy properly. Many of them learn it after they go into practice, which is a part of the problem, but that's an issue of concern. "– Allergist

- Prescribing may be linked to when an allergist was trained and his or her comfort level with AI (i.e., therefore older allergists may be more comfortable prescribing)

ACCESS TO ALLERGEN IMMUNOTHERAPY

AFFORDABILITY AND COST STRUCTURE

Affordability:

- Based on patient and clinician accounts it appears most individuals access these medications through third party insurance
- A small minority of our sample had experience accessing AI through the OPDP Allergen Program
    - The participants reported no problems with the application process
    - The participants would send the completed form to the manufacturer who would then liaison with the government for reimbursement
- Physician participants explained that for patients paying out of pocket for these medications it can be quite expensive especially for those using the SLIT

Cost of therapies:

- Clinician participants reported that there is a lack of standardization in the way AI is dispensed (i.e., on-site, manufacturer, or pharmacy), thus resulting in different prices for the same products across the various dispensing outlets

"I think what should be done …the price that people charge patients for serum should be no more than what the companies charge. If Hollister-Stier, or ALK, let's say for yellow jacket. If Hollister-Stier charges a hundred and… let's say 300 bucks a year, or something for yellow jacket, then the government shouldn't cover more than that in my opinion. I don't know what the companies charge in terms of exactly how much, but I think there are probably a few bad apples. I think most people are probably fine, and probably saving the government money to be honest, but I think [if patients were] ordering this through a pharmacy for example would cost the government way more money. The pharmacists are way more aggressive than physicians are, on average. So, if I order venom immunotherapy through a pharmacy, the cost would be way higher. I don't know how much higher, but I know it would be way higher, and I know that because of Pollinex-R that we used to get through… from the company, and now we have to get it through the pharmacies, and it's like quadrupled in price I think. It's some crazy number, right. So, I think the pharmacies make us look like nothing. They're much better at the business side in terms of pushing things." – Allergist

OPDP ALLERGEN PROGRAM: PHYSICIANS' OPINIONS OF POTENTIAL LIMITED USED CRITERIA

Venom allergens:

- Majority of clinicians participants believed:
  1) Patients who are suffering from a life threatening venom allergy should be covered with a positive skin test

Environmental allergens:

- Most participants believed for environmental allergens the following criteria should be fulfilled:
  1) A patient should have moderate to severe allergy symptoms
  2) A patient should have failed an adequate trial of allergen avoidance and traditional pharmacotherapy (e.g., antihistamines, nasal steroids) or must be unable to tolerate side effects associated with these medications

Overall suggestions:

- Some clinician participants provided some overall suggestions:
  1) Patients should not be on beta blockers or ACE inhibitors because these medications make allergic reactions more difficult to treat
  2) Patients should not have any relative contraindications (e.g., rheumatoid arthritis or lupus) because you are administering a foreign protein into their system that could make the condition worse
  3) Patients who would not be able to tolerate anaphylaxis (e.g., unstable angina, cerebrovascular disease, hypotension, severe respiratory symptoms).
  4) As a preventative measure children should be treated with AI as to prevent other allergies from developing
  5) AI should only be prescribed by qualified allergists

Part 4: Discussion

Key Findings

The experiences and perceptions from our interview participants have pointed to some key findings related to the prescription and use of allergen immunotherapy medications for adults. Allergist participants base their decision to prescribe on factors such as the type of allergy, response to traditional pharmacotherapy and non-pharmacological strategies, skin test results, and other patient related factors. In terms of formulary preferences and prescription habits, physician participants considered venom therapy to be first line treatment. They preferred and found SCIT to be more efficacious; however, if patient compliance was an issue, they would prescribe SLIT. Many health care providers are involved in the process of prescribing, dispensing, and monitoring which results in a lack of standardization of practice, which may lead to variability in product prices across the various dispensing outlets. Overall, physicians and patients described that there were no access or

application process barriers for AI through the ODB program. Clinician participants suggested the limited use criteria for AI should depend on symptom severity and an adequate trial of traditional pharmacotherapy.

Healthy Equity Considerations

The findings from this study highlight a few key access issues for adult AI patients. Those who are under 65 and who do not have private insurance will have barriers to access the medication they need; this is common finding across the drug class reviews. In addition, clinicians expressed concerns of self-proclaimed allergists prescribing these therapies in the community, thus advocating for more standardization around AI to ensure the safety of patients.

Limitations

It should be noted that these interview and survey findings are not representative of the general population of individuals from which our study sample was drawn because the sample size is small and because there may be bias in sampling. The potential bias in sampling may exist because those who responded to interview requests may have been more likely than non-responders to be vocal about discussing the impact of AI medications in adults and may be more highly involved in AI advocacy initiatives. Allergists who are involved in on-site preparation of AI and patients who use venom therapy did not respond to our recruitment ads; these individuals may have differing opinions from the allergists and patients that were interviewed.

Conclusions

The findings from the qualitative study of this review on AI medications 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 this review. On a broader scale, our study findings fill a gap in knowledge on access to AI products for adult patients and how this may be impacted by physician and patient perceptions of these drugs. Overall, our findings shed light on the experiences of prescribing, monitoring, and dispensing of AI medications for adults, and unveil important information that can impact how patients in need can access these drugs across Ontario.

Part 5: Phase 2 Methods

Following the completion of this study and the accompanying ODPRN AI research studies, a consolidated report was drafted that includes a set of recommendations for the prescription of AI for adults. Phase 2 of the qualitative work included assessing the social acceptability and feasibility of the recommendations proposed through the two steps outlined below.

Soliciting Participant Feedback

Once the recommendations were developed, the qualitative interview participants from this study were invited to review all ODPRN reports from this drug class review. They were also invited to complete a brief survey about their impressions of the recommendations and the interpretation of the study results. This process invites participants to provide feedback on the authenticity of the study results, which is an important component of qualitative research. The survey also measured aspects of social acceptability including affordability, accessibility and appropriateness of recommendations. The survey was developed online in Fluid Survey. The study coordinator sent the survey link and report through e-mail to participants. The findings from this survey were used by the team to make any necessary revisions to the reports.

Citizens' Panel

We have recruited a diverse set of 15 individuals from the general public to form a Citizen's Panel. The Citizens' Panelprovides feedback on recommendations from all drug class reviews. Feedback from participants was obtained in two surveys and a webinar using a modified RAND Appropriateness Method (Fitch, 2001). First, an online survey was distributed to Citizens' Panelmembers, asking them to read the final report and recommendations, to provide their input. Next, Citizens' Panelmembers attended a webinar meeting, at which we presented key issues, findings and policy implications, and engaged in group discussion on the recommendations. Citizens' Panelmembers completed a second survey after the meeting, enabling them to provide additional feedback and giving them the opportunity to re-rank the policy options. This approach allowed each person to express their idea(s); each person's opinion was taken into account (compared to traditional voting where only the largest group is considered). The findings from the Citizens' Panelsurveys and discussion were used by the team to make any necessary revisions to the reports and draft recommendations.

Part 6: Phase 2 Results

Detailed results are censored in this report so as not to preclude publication. Publications (when available) and/or final unpublished reports will be available on the ODPRN website (www.odprn.ca).

Participant Feedback

Nineteen of the 20 interview participants from this drug class review consented to being contacted to participate in a member checking and acceptability survey exercise. A total of seven participants (one primary care physician, four allergists, and two patients) completed the survey. Participants were asked to rate their level of agreement with the following six recommendations:

1: Limit duration of therapy to 5 years for aeroallergens

2: Require drug identification numbers (DIN) on all prescriptions for subcutaneous allergen immunotherapy

3: Clinical criteria for use of subcutaneous allergen immunotherapy be developed

4: Coverage of sublingual immunotherapy be limited to commercially available SLIT products

5: Develop pricing structure for patient-specific allergen immunotherapy

6: Develop guidelines for safe manufacturing.

Participants were in strong agreement with recommendations 1-4, 6. Allergist participants agreed that SCIT should be prescribed for duration of five years (recommendation 1). They felt three years was too short and in some cases patients may require more than five years; however, overall, they perceived five years to be clinically acceptable. There was some disagreement as to whether venom immunotherapy should be a lifelong therapy. Participants were in agreement with recommendation 3; however, they felt it was vaguely worded and that more detail should be given (e.g., what documentation is involved). There were no additional comments for recommendations 2 and 4.

Participants were in moderate agreement with recommendation 5. Some participants were confused as to whether recommendation 5 is suggesting a limit on the cost of the extract or on the amount physicians are reimbursed for administering the AI. Allergist participants highlighted that the cost is per vial and not per allergen. Overall, participants were in favour of fair pricing limits and thought the price structure should be modeled after a good manufacturing lab (e.g., Omega or ALK).

Citizens' Panel

The ODPRN Citizens' Panelmeeting on allergen immunotherapy took place on Tuesday September 15th, 2015. There were six members in attendance during the meeting. Three members completed the pre-meeting survey and five completed the post-meeting survey. Overall, panel members were in favor of all 6 recommendations, but unanimously in favor of recommendation 3 (Table 1). It was perceived as the most clear and understandable recommendation. One person elaborated:

"Excellent suggestion as it ensures patient safety and the patient's needs and treatment are appropriately aligned. There is also a paper trail of need for escalation of treatment should it be required." –panel member

Table 1. Overall post-survey aspect rankings for recommendations 1-6

	Mean score (Standard Deviation) 1 = Strongly Disagree and 7 = Strongly Agree					
	1	2	3	4	5	6
The policy is a good option to limit the burden of cost on the healthcare system.	6.4 (0.8)	6 (1.3)	7	4.8 (2.1)	6 (0.9)	6 (1.3)
I think this policy will benefit those who require the drugs.	6.4 (0.8)	6.6 (0.8)	7	6.6 (0.5)	6.2 (1.0)	6.6 (0.8)
I think this is an acceptable recommendation.	6.4 (0.8)	6.6 (0.8)	7	6 (1.5)	6.4 (0.8)	6.8 (0.4)

Panel members did not have especially noteworthy comments for recommendations 1, 2, 4, and 6, but they did have some suggestions for recommendation 5. They agreed with any strategy to reduce variation in pricing structure to ensure that the cost is fair and does not become a barrier for patients to access necessary treatment. They thought it may be wise to collect more data first, so that a more accurate and standardized pricing structure can be developed. They perceived that a consumer group should be a key stakeholder when this pricing structure is made, to ensure that the outcome is not just influenced by industry. They also raised concerns that the exposure to environmental allergens can vary by region and that this should be taken into account since patients in certain regions may require more prescriptions.

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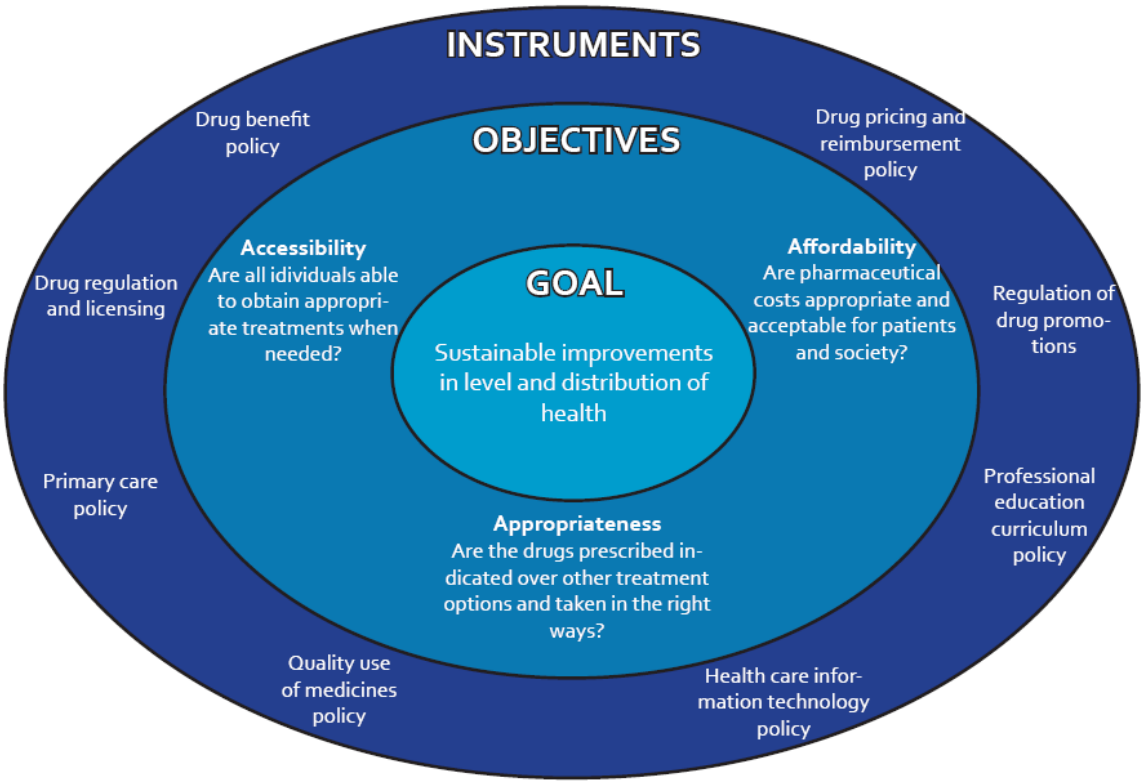
Appendix A: "Triple-A" Framework for Pharmaceutical Policy Analysis



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

Patient Demographics Characteristics (n = 14)	N	%
Gender		
Male	6	67%
Female	3	33%
Years since diagnosis		
< 5 years	7	78%
>15 years	2	22%
Current Medication		
SCIT	5	56%
SLIT	4	44%
Age		
25-34	2	22%
35-44	3	33%
45-54	3	33%
55-64	1	12%

Clinician Demographics Characteristics (n = 11)	N	%
Type of Clinician		
Primary Care Doctor	3	27%
Allergists	8	73%
Years of Practice		
< 5 years	5	46%
5-15 years	3	27%
>15 years	3	27%
Work setting		
Urban	11	64%
Suburban	3	27%
Rural	1	9%