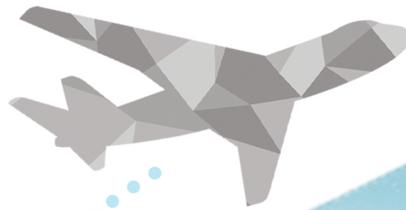




# UBC PHARMACEUTICAL SCIENCES STUDENT JOURNAL

VOLUME 3. ISSUE 1





Volume 3, Issue 1 is warmly dedicated to  
*Elaine Xu & Alysa Pompeo*  
*Garren Cho & Rupen Patel*

Whose continued support, patience, and guidance made  
the publication of the journal possible.

Thank you.

UBC PSSJ

*Designed by: Jasmine Mourh, B.Sc. (Pharm) Candidate 2017*



Thank you to our peer reviewers from Volume 2 Issue 1,  
entitled “No Longer the End but the Beginning”

Dr. George Pachev

Dr. Mike Legal

*Designed by: Sarah Cheng, B.Sc. (Pharm) Candidate 2016*

# If We Don't, Somebody Else Will

James P. McCormack, B.Sc., B.Sc.(Pharm), ACPR, PharmD<sup>1</sup>

<sup>1</sup>*Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

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*"If you don't know where you are going, you might wind up someplace else."*

- Yogi Berra

Regardless of one's country of residence, a pharmacist's job should be centered on working with other health care professionals to ensure our patients get the right Drug, in the right Dose, at the right Date/time, for the right Duration – the 4Ds of medication use if you will. This is the ultimate "personalized medicine".

Unfortunately, a lot of research and experience clearly demonstrates that globally there is substantial ongoing overuse and in some cases underuse of medications.

So why is this?

Internationally, there are a number of unique issues that impact pharmacists and other health care providers from ensuring everyone gets the right "4D" medication. Estimates suggest that one in ten prescriptions worldwide (1) are filled with counterfeit medications. As much as one-third (2) of the world's population lack physical access to essential medicines, the roughly 300-400 medications that the World Health Organization has determined to be those that satisfy the priority care needs of the population. While these two issues are sadly more substantial in third world countries they are not exclusive to these areas.

Another potential issue is 60% (3) of the world doesn't have internet access which severely limits the transfer of knowledge and the ability to provide patients and health care providers with access to up-to-date information and the best available evidence.

Even if we could somehow instantly solve these important problems there is still an awful lot of room for improvement when it comes to the global use of medications.

Is one of the reasons for the inappropriate medication use the lack of pharmacists to help ensure appropriate medication use? At the turn of the century, a number of first world countries lamented we were heading towards a time when there would be a shortage of pharmacists. Interestingly, either because the foreshadowing was wrong (probably), because we have done a poor job of substantially establishing new roles for pharmacists (definitely), or we actually have done (to some degree) a good job of increasing the number of graduating pharmacists, many of these countries are now suggesting that joblessness for new graduates is very much a real potential. On top of this, in many countries, pretty much the sole responsibility of a pharmacist is still to just correctly dispense a prescription. While this is clearly important, whether or not the patient actually needs or wants the medication is often an afterthought if it is even a thought at all.

So at present, we clearly have substandard medication use, possibly too many pharmacists, and some in our profession not doing as much as they should or could do based on their training and experience. With all of this it seems our profession has a golden global opportunity, maybe a necessity for survival, to do something about this issue. We need to focus worldwide more on establishing new pharmacist roles and activities that divorce ourselves from the product and marry us into the role of arbiters of rational evidence-based medication use which incorporates the principles of shared-decision making.

The issue of inappropriate medication defies any international borders – it is a global issue that affects all of us.

So as a profession, let's do something about it before another group does. This will not be easy and the road forward is littered with numerous financial and professional turf issues. But always remember, struggle will always make attaining the outcome far more rewarding.



James P. McCormack, B.Sc., B.Sc.(Pharm), ACPR, PharmD

Professor, Faculty of Pharmaceutical Sciences, The University of British Columbia

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## Our Thoughts on the Change in Pharmacy Practice

Jennifer Jun, B.Sc., B.Sc. (Pharm) Candidate 2016<sup>1,2</sup>

Sarah Cheng, B.Sc. (Pharm) Candidate 2016<sup>1</sup>

<sup>1</sup>Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

<sup>2</sup>Faculty of Sciences, University of British Columbia, Vancouver, BC, Canada



All too familiar to pharmacy students are concerns about the job prospects in the saturated and competitive job market. Complaints about the increased class size, lack of positions in major cities, or a large number of international pharmacy graduates (IPGs) being licensed to practice in Canada are commonly heard. However, we believe what seems like a troubling or stressful time for current and future pharmacists could indeed be an opportunity for growth for individuals and advancement for the profession at large. In this issue, PSSJ presents to the readers the stories of some IPGs, perspectives from the educators, and thoughts of graduating students at UBC. Further, international collaboration in research and interesting work experience abroad are featured. It is our hope that you will feel encouraged and excited about the future with more broadened perspectives, with adventurous and ambitious minds. Good luck on your journey!

Best Wishes,

Jennifer Jun  
Editor-in-Chief 2015-16



The brainstorming process for this issue started early last summer. My co-chief-editor, Jennifer and I wanted to create an issue that would retain our vision of promoting scholarship and dialogue in pharmacy but also to be relevant to the day-to-day life of pharmacy students. After collecting inputs from the team, we decided on the theme of international pharmacy. We believe that it is a topic that is relevant to the student body because globalization has a profound impact on the pharmacy profession. As massive amounts of information are exchanged and people are transported in and out of our country daily, many people see globalization as a threat to their current way of living. For example, international pharmacists are seen as competition for already-limited job openings. However, if we look beyond these competitions, we will also see many opportunities being opened up as a result. These opportunities include global collaboration on pharmaceutical research projects, and utilization of our resources to help those in need across the globe. Still, many more

are awaiting our discovery. I hope this issue can help inspire you to explore and seize these opportunities. Go out and explore!

Wishing you a bright future,

Sarah Cheng

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## OPINION-EDITORIAL

### Working Alongside International Pharmacy Graduates

Martin Cheung

9

### Comparing Pharmacy Practice between India and Canada

Anand Kapoor

11

### Canadian Pharmacy Practice – a Perspective from an International Pharmacist

Buhwan Lee

13

### International Research in Pharmaceutical Sciences: Partnerships between Brazilian Research Institutions and the University of British Columbia

Rachel Magarinos-Torres, Francisca Adilfa de Oliveira Garcia, Paulo Eduardo Potyguara Coutinho Marques, Violet G. Yuen, Glauce Socorro de Barros Viana, Claudia Garcia Serpa Osorio-de-Castro, Larry D. Lynd, John H. McNeill

15

## PRACTICE ISSUES

### Patient-Centered Care: A Two-Way Street in Inter-Professional Practice

Jacky Tang

18

## WORKPLACE SPOTLIGHT

### The Canadian Pharmacy Programme: A Bridge Between Worlds

Sandi Hutty

21

### Pharming in Rural Ghana

Maria Paiva

23

## ORIGINAL RESEARCH

### Why Does a High Extraction Ratio Drug Given Orally Behave Like a Low Extraction Ratio Drug? – An Intuitive Explanation

Elaine Lo, Lawrence Law, Mary Ensom

27

## CASE REPORT

### Preparation of Lower Dosages of SNRI Antidepressants to Ameliorate Discontinuation Symptom: Two Case Studies

Benton Attfield, Lori Bonertz, Cory Hermans, Valerie Kantz

31

# Working Alongside International Pharmacy Graduates

Martin Cheung, B.Sc.(Pharm.) Candidate 2016<sup>1</sup>

<sup>1</sup> Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

International Pharmacy Graduates (IPGs) make up a significant portion of pharmacists working in Canada, and each year the proportion of IPGs in the Canadian workforce increases (1). To new Canadian Pharmacy graduates, this continual influx of competent job-seeking pharmacists may lead to increased competition in the job market, which may translate to a reduction in weekly hours and employment, and heighten anxiety and stress on top of the already competitive job market today. That being said, the arrival of more IPGs may also have its benefits. By increasing the competitiveness of the job market, the rising IPG population may help drive innovation in relation to the discovery of novel approaches for delivering pharmacy-related clinical services and optimizing patient health outcomes. In this regard, the increased competition may help facilitate the advancement of the pharmacy profession. In addition, IPGs may benefit the workforce by offering their diverse cultural backgrounds and unique skills and experiences.

Based on the 2014 Canadian Institute of Health Information (CIHI) report (1), the number of IPGs within the Canadian workforce grew from 22% to 28% during the short span of four years (2010 to 2014). Since the majority of IPGs have experience working as a pharmacist in their country of origin, employers generally see them as being more experienced than new Canadian graduates (2). As well, IPGs licensed to practice in Canada have successfully completed the Pharmacy Examining Board of Canada (PEBC) examinations, which is a requirement of all Canadian-trained pharmacists. Thus, IPGs serve as strong, rising competitors for new Canadian graduates, as their qualifications are very comparable. Despite the increase in supply (~4700) of new licensed pharmacists in Canada from 2010 to 2014, the CIHI report reveals that the employment rate increased from 92.7% to 95.5%. However, estimated weekly practice hours declined significantly (i.e. the proportion of pharmacists working 40+ hours weekly decreased from 44.9% to 30.9% while the proportion working 30-39 hours weekly increased from 33% to 42.7%) (1). It is evident that although an increase in employment has occurred to accommodate for the increase in supply of pharmacists, obtaining a position with higher

guaranteed weekly hours (i.e. 40 and over) has become more difficult. IPGs make up a large portion of new pharmacists entering the workforce each year; therefore, they may be significant contributors to the above issues.

In spite of potential drawbacks, the increase in competition caused by the influx of IPGs may be favourable for growth and enrichment of the pharmacy profession. In times of hardship due to a competitive job market, pharmacists may be forced to think “outside the box”; thus, competition can drive innovation and formation of new ideas by pressuring new pharmacy graduates. Especially today, when the Canadian pharmacy profession is advancing, as evidenced by its expanding scope of practice, it is an ideal time for the development of novel methods for the delivery of pharmacy-related clinical services. A great example of pharmacy innovation is the establishment of the UBC Pharmacists Clinic, a non-dispensing pharmacy that focuses on optimizing patient care strictly through medication-related consultation and collaboration with other healthcare professionals directly involved in the care of the patient. Furthermore, being from extremely diverse backgrounds, IPGs can offer valuable and unique pharmacy-related skills and experiences both in the workplace and to the Canadian pharmacy profession as a whole, in addition to reinforcing Canada’s great multicultural society.

The increasing number of IPGs in Canada may cause panic and anxiety, especially among new Canadian pharmacy graduates and current students, due to increased competition in the job market. As evidenced by the 2014 CIHI report, this has translated to a decline in average guaranteed weekly hours, despite marginal increases in employment. Nevertheless, an increasing IPG population may also serve the pharmacy profession by increasing the development of new, innovative methods for delivering pharmacy-related clinical services and enhancing current pharmacy practice. Furthermore, with various places of origin throughout the globe, IPGs can provide unique skills, experiences and cultural backgrounds that are highly beneficial to the workplace. Since the perpetual nature of job market competition is not something one can perturb, it

would be favourable for new Canadian pharmacy graduates and current students who are worried about employment to take this opportunity in stride and consider exploring and developing new, innovative approaches for advancing the pharmacy profession.

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# Comparing Pharmacy Practice between India and Canada

Anand Kapoor, B.Sc, (Pharm), RPh<sup>1</sup>

<sup>1</sup> *Department of the Pharmacy, Punjabi University, Patala, India*

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My name is Anand and I graduated from Punjabi University in Patala, India, in 1999. My work experience in pharmacy includes: manufacturing medicine, and working as a quality analyst and medical sales representative for a pharmaceutical company around Chandigarh. I moved to Canada because I was intrigued by pharmacy practice in this nation—more specifically, in patient-centered care.

## Overview of Pharmacy Practice in India

India is the seventh largest country in the world with almost 17% of the world population (3). Community pharmacy practice is traced back to British India when allopathic medications were introduced and were made available in the drug stores. During the pre-independence time, community pharmacy practice was unregulated and most of the prescribing and dispensing was performed by doctors. Doctors trained the clinic assistants, called compounders, to dispense medicine and assist in the compounding. The practice changed post-independence when community pharmacies, often called retail pharmacy or retail drug outlets, began to dispense, supply, and sell medicines. Pharmacists in the community practice setting are pharmacists who have obtained a diploma or graduated with a Bachelor of Pharmacy degree. A pharmacist registration certificate issued under the Pharmacy Act is required by the state in which the pharmacist wishes to practice. Most of the community pharmacies are, however, managed by the diploma pharmacists.

The Bachelor of Pharmacy degree is designed mainly for the pharmaceutical industry, drug control laboratories, and drug regulatory bodies, while the diploma program is designed for hospitals and community settings. Diploma pharmacists have a lack of pharmaceutical knowledge — that is, pharmacology and therapeutics — and typically interact with the patients while managing the community store. Bachelor of Pharmacy graduates are more prominent in the pharmaceutical industry, as compared to the community pharmacies, due to the lower salary earned in community practice. There are very few Bachelor of Pharmacy graduates who work in community pharmacies, as diploma pharmacists are typically hired in the community setting. The sale and supply of medicines in community pharmacies is undertaken by the owner of the pharmacy. The owners of the pharmacy are usually businessmen or businesswomen who have no formal pharmaceutical training and may choose to hire neither diploma pharmacists nor graduates of the Bachelor of Pharmacy program. As such, there is minimal regulation of medicines in the community, leading to the improper prescribing and sale of medication. For instance, minor ailments are commonly treated at the pharmacy level, without a doctor's intervention, with antibiotics — a practice that can contribute to antibiotic resistance. Additionally, community pharmacists in India hardly offer any patient-oriented services, such as medication reviews.

Indian people often consider a retail pharmacist to be a person who has acquired a license to supply medications to the public, and they believe that anyone can open a medical store. Medicines are manufactured by pharmaceutical companies and procured by the community pharmacies through distributors or wholesalers. The community retail pharmacy is the primary source of medications for both community and hospital patients — it is essentially an outlet for dispensing drugs to patients.

## Comparing Pharmacy Practice between India and Canada

Compared to India, pharmacy practice in Canada is more focused on providing patient-centered care through patient-oriented services. The role of the community pharmacist in Canada includes supplying and advising patients on the use of prescription and over-the-counter medicines. The role of the pharmacist has expanded in recent years with a wide range of professional services provided by the pharmacist now funded by the government (4). Some of the services performed by pharmacists include smoking cessation, prescription adaptations, medication reviews, injection administration, anticoagulant clinics, and prescribing for minor ailments (5). In contrast, retail pharmacy stores in India focus solely on the dispensing and selling of medications.

Pharmacists in Canada are registered with the provincial government after the Pharmacy Examining Board of Canada (PEBC) examination (6). Once registered, the pharmacist is licensed to work in their province of registration. This differs from India where a graduate of the Bachelor of Pharmacy program only has to submit a copy of their degree to the Pharmacy Council of India, which subsequently provides them with a license to practice.

With regards to drug coverage, each Canadian province has its own drug formulary, which contains the names of the medications to be covered by the province and territory depending on the drug benefit plan offered (7). In British Columbia, for instance, a universal income-based program is offered where eligible prescription drug cost is covered by the provincial government after the patient reaches a set deductible (8). Additionally, some employers in Canada provide private health insurance, which covers drug cost as part of their employee benefits package. There is no government program for patient drug coverage in India — only third party insurances.

### **My Personal Experiences in Pharmacy and Thoughts of the Profession**

The three years that it took for me to get my license in Canada were a time of hardships and struggle. Preparation for the PEBC was challenging because India approaches pharmaceutical education in a more theoretical manner compared to Canada, where pharmacy education focuses on application of knowledge in order to provide patient-oriented care. The Continuing Pharmacy Practice Programme at the University of British Columbia changed my perspective of the profession and allowed my practice to become more patient-focused. I believe that the program should be made mandatory for all international pharmacy graduates practicing in Canada, so that they can raise their level of knowledge and practice as required by the province and gain further professional satisfaction.

In my opinion, the respect of the profession in Canada is increasing with the public's growing understanding of the importance and role of pharmacists in medication management — the pharmacist's easy accessibility for queries about medications has proven its professional worth as a medication expert. There is no doubt that pharmacy practice in India is less developed when compared to Canada. Though I recognize that the pharmaceutical industry requires the expertise of those with a Bachelor of Science in Pharmacy, I believe that a shift towards more patient-centered care in the community setting is crucial to not only minimize medication errors, but also to promote the profession. To achieve this end, change is required within India's pharmacy education system where a stronger foundation in therapeutics and pharmacology is required. As mentioned previously, the majority of community pharmacists are those with a diploma, and liability insurance is not a requirement as the public in India are less aware of the pharmacists' responsibility. Changing how pharmacists are trained will allow pharmacists to practice patient care more confidently and can encourage the evolution of the profession. However, the current structure of pharmacy is so deep rooted in India that the road towards change will be slow and hard to achieve.

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## Canadian Pharmacy Practice – a Perspective from an International Pharmacist

Buhwan Lee, B.Sc.(Pharm.)<sup>1</sup>

<sup>1</sup> Chonnam National University, Gwangju, South Korea

I am Buhwan Lee from South Korea; I graduated with a pharmacy degree from Chonnam National University in 2006. Upon graduation, I served in the Korean Army for three years as a pharmacy officer, taking on roles such as working for the Armed Forces hospital, which helped troops from overseas; serving as the Chief Pharmacist at an Armed Forces hospital in Iraq; and teaching basic pharmacy protocols at the School of Military Medicine. I met friends in Iraq who recommended practicing in Canada because of its promising lifestyle and work environment. Through these interactions and the desire for a better life for my child, I decided to come to Canada to practice as a pharmacist.

I have worked as a pharmacist for a little over two years in Canada after obtaining my Canadian license in 2013. In order to adapt to a new society as an International Pharmacy Graduate (IPG), there were many challenges I had to overcome. One challenge, possibly the toughest one, was language. Not only was it difficult to learn a new language, but being able to convey the correct message to patients presented another barrier for me. Other than lingual skills, there are other outstanding cultural differences between the Canadian pharmacy environment and that of my home country.

The first cultural difference I have identified in pharmacy practice is the way pharmacists communicate with other healthcare professionals and patients. Canadian healthcare professionals are willing to have a discussion with patients regarding their health outcomes and cater to the patients' need(s). More specifically, pharmacists can contribute to the patients' wellbeing by expressing their drug related concerns on patients' outcomes if any drug therapy problems are identified. In contrast, there is a hierarchy in the Korean healthcare system, which interrupts appropriate communication among healthcare professionals. Pharmacist-physician interactions are often limited in the community setting as the nature of pharmacies is more product-based, with a particular focus on over-the-counter and natural health products. Since I did not expect frequent verbal and written communication with healthcare teams, it took a while for me to adapt to this new and unfamiliar practice. However, liaising

with other healthcare providers is now one of the greatest pleasures in my daily work.

Secondly, there are differences between South Korea and Canada, with regards to their regulations and overall healthcare systems. South Korea does not have a College of Pharmacists that would protect public health by regulating pharmacists, or communicate with the government to promote best practices. The Korean government is the main regulatory body for pharmacies and pharmacists in South Korea; as such, I have noticed less flexibility in pharmacy practice regulations and drug pricing compared to Canada. The National Health Insurance Corporation is a governing branch responsible for supervising South Korea's universal health insurance system by regulating drug benefit lists and coverage. One flaw with this system is the South Korean version of Special Authority, as it takes much longer to accept exceptional patient circumstances in order to receive full benefit status. When I first encountered Special Authority requests and the Special Access Program in British Columbia, I was not confident in the system because I expected a similar time frame as my home country in receiving approval. This is one of the many benefits of practicing in British Columbia.

Lastly, knowledge is very important to patient care, but I find that the method of delivering therapeutic information is more of a fundamental skill for pharmacists in Canada compared to South Korea. During my training in South Korea, I did not have any practicums incorporated into my degree. As such, professors focused heavily on the pharmacology and biochemistry of drugs. When practicing in Canada, there was a large difference between real-life practice and what I learned in school. Interactions with patients and other healthcare providers are vital and an aspect that I truly enjoy – a fact that is evident in my pursuit to become a Certified Geriatric Pharmacist. Since a significant proportion of my patients are elderly, I decided to pursue further education to better my delivery of patient care. From this, I have learned, for instance, that two-thirds of Americans over 65 years old have inadequate literacy and may not be able to read pharmacy labels (1,2). A similar statistic may be evident in Canada due to the inherent multiculturalism that exists within society.

This multiculturalism has changed the way I practice as it has allowed me to realize that not only do I experience cultural barriers, but my patients do as well. Being more cognizant of this fact allows me to appreciate diversity and practice in a more culturally-competent manner.

I believe international pharmacists are continually undergoing personal development to overcome the cultural and lingual differences between Canada and their respective home country. Some IPG pharmacists have great therapeutic knowledge; however, such knowledge can be lost in translation as they may find difficulty in transferring their medical knowledge from their native tongue to English in a manner that is appropriate for patients and other healthcare providers. Additionally, some may not be familiar with recognizing empathy cues and expressing empathy or sympathy to patients since it may not be a cultural practice back home. Although these barriers exist, they are by no means factors that IPGs cannot improve on. I believe IPGs share similar values as

Canadian trained pharmacists; for instance, we both continually strive to improve and advance not only our professional practice, but also the Canadian healthcare system. Also, we seek to establish meaningful connections with our patients and colleagues to make our work place environment more enjoyable. In summary, I strongly believe that the contributions and different viewpoints of IPGs provide an enriched multicultural pharmacy practice in Canada.

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# International Research in Pharmaceutical Sciences: Partnerships between Brazilian Research Institutions and the University of British Columbia

Rachel Magarinos-Torres<sup>1,2</sup>

Francisca Adilfa de Oliveira Garcia<sup>3,4</sup>

Paulo Eduardo Potyguara Coutinho Marques<sup>5</sup>

Violet G. Yuen<sup>6</sup>

Glauce Socorro de Barros Viana<sup>7</sup>

Claudia Garcia Serpa Osorio-de-Castro<sup>8</sup>

Larry D. Lynd<sup>9,10</sup>

John H. McNeill<sup>11</sup>

<sup>1</sup> Post-Doctoral fellow, Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, University of British Columbia, Canada.

<sup>2</sup> Professor, Faculty of Pharmacy, Federal University of the State of Rio de Janeiro (Universidade Federal Fluminense - UFF), Brazil.

<sup>3</sup> Post-Doctoral fellow, John McNeill Lab, Faculty of Pharmaceutical Sciences, University of British Columbia, Canada.

<sup>4</sup> Professor, Medical School of Juazeiro do Norte (Estácio FMJ), Brazil.

<sup>5</sup> Researcher, Oswaldo Cruz Foundation, Ministry of Health, Brazil.

<sup>6</sup> Research of John McNeill Lab, Faculty of Pharmaceutical Sciences, University of British Columbia, Canada.

<sup>7</sup> Professor, Medical School of Juazeiro do Norte (Estácio FMJ), Federal University of Ceará (UFC), Brazil.

<sup>8</sup> Senior Researcher and Professor, Sergio Arouca National School of Public Health, Oswaldo Cruz Foundation, Ministry of Health, Brazil.

<sup>9</sup> Professor, Faculty of Pharmaceutical Sciences, University of British Columbia, Canada.

<sup>10</sup> Director, Collaboration for Outcomes Research and Evaluation Scientist, Centre for Health Evaluation and Outcome Sciences.

<sup>11</sup> Professor and Dean Emeritus, Faculty of Pharmaceutical Sciences, the University of British Columbia, Canada.

Brazil has aimed to strengthen its participation in international research through the Science Without Borders program. Science Without Borders is a program funded by the Brazilian government with the goal of promoting “the consolidation and expansion of science, technology, and innovation in Brazil by means of international exchange and mobility. The strategy envisioned aims to (a) increase the presence of students, scientists, and industry personnel from Brazil in international institutions of excellence, (b) encourage young talents and highly qualified researchers from abroad to work with local investigators in joint projects, contributing to the capacitation of human resources and promoting the return of Brazilian scientists working overseas, and (c) induce the internationalization of universities and research centers in Brazil by encouraging the establishment of international partnerships and a meaningful

review of their internal procedures in order to make the interaction with foreign partners feasible” (1).

The partnership between Canada and Brazil has supported 6,797 research projects, of which 1,238 were in Health and Biomedical Sciences areas. This ranks Health and Biomedical Sciences as the second most funded research area in terms of the number of scholarships given by the Science Without Borders program. The University of British Columbia (UBC) has received 311 Brazilian students in the Health and Biomedical Sciences area. Currently, 242 projects are being developed in partnership between Brazil and Canada in the aforementioned area, of which sixteen are at UBC with two in the Faculty of Pharmaceutical Sciences (1).

This text describes the two research projects linked to the Science Without Borders program that are currently being undertaken in UBC’s Faculty of Pharmaceutical Sciences.

## Federal Procurement Profile of Essential Medicines in Brazil

The concept of essential medicines is internationally recognized as a health strategy to rationalize the use of medicines with beneficial clinical and managerial outcomes, while providing a mechanism for the cost-effective use of resources and governance to support health equity (2). Implementation of this concept has led to the preparation and publication of the Essential Medicines List (EML). The selection of medicines to the list is made based on scientific evidence of efficacy, safety, and cost-effectiveness. The concept of essential medicines is also an important focus of Brazil's national drug policy, which guides the provision of medication (3).

The current UBC-Brazil collaborative study is aiming to describe and analyze Brazilian federal procurement of essential medicines in the last ten years, in light of the different editions of the Brazilian Essential Medicines List (4). The study design is a drug utilization study (DUS), which studies medicines consumption by using the volume of drugs procured as a proxy for consumption. This study will utilize publicly available, comparable and reliable Brazilian data on the procurement of medicines, and each drug will be classified with the help of Anatomical Therapeutic Chemical Classification/Defined Daily Dose (ATC/DDD) WHO methodology (5).

The results of this study will answer the following questions: (i) What is the profile of essential medicines use in Brazil? (ii) What is the federal expenditure on these medications and how are the resources distributed among states and municipalities? (iii) Has the publication and revision of the Brazilian list of essential medicines changed the set list of federal procurement? (iv) Has it changed the volume of federal procurement regarding essential drugs? This study will also assist in the creation of a correlation tool between different nomenclatures in medicines, including the International Non-proprietary Names (INN) and Brazilian Non-proprietary Name (DCB) nomenclatures.

### Mechanisms of Action Involved in the Hypoglycemic Activity of an Extract of *Spirulina platensis* in Rats with Streptozotocin (STZ)-Induced Diabetes

The prevalence of diabetes mellitus has increased exponentially over the previous decades and has transformed the disease into an epidemic for public health worldwide (6). Marine algae from the northeastern coast of Brazil have been shown to have a high content of water-soluble macromolecules, including polysaccharides, proteins, glycoproteins, and other low molecular weight components, of which some have demonstrated particular biological

properties *in vitro*. Extracts from algae specific to the country of Brazil have been shown *in vitro* to possess immunohematopoietic, metabolic, and insulin signaling activities (7).

The blue-green algae *Spirulina platensis* (SPI) is a microscopic and filamentous cyanobacterium (8). SPI is used as a food supplement and its nutritional and therapeutic values have been well documented. Current studies performed in Brazil have shown that the oral administration of SPI for 5 or 10 days, in doses of 25, 50 and 100 mg/kg, significantly reduced glucose levels in alloxan-induced diabetic rats. Glucose values observed in the 10-day protocol using the lowest dose (25 mg/kg) were very close to those of normal controls. This same study also observed that SPI (50 and 100 mg/kg, p.o.) significantly decreased triglycerides and total cholesterol levels after a 5-day administration (9). The current proposal is to examine the potential glucose lowering properties of oral administration of SPI in an intact animal model of diabetes mellitus using the streptozotocin-induced diabetic rat (9).

The objectives of this collaborative project are to perform a preliminary study on the oral effectiveness of an extract of SPI on lowering blood glucose levels and improving complications associated with the diabetic disease state using an intact animal model of diabetes, and to provide a training venue for post-doctoral fellows to learn basic techniques in inducing, monitoring, treating, and assessing the effectiveness of drug intervention in diabetic animals (9).

### Final Comments

The research questions that guide both projects are in line with global priorities in health, including drug development and improved access to medicines. The first research project has in its partnership the possibility to broaden knowledge in the field of drug utilization studies. The second collaboration will further study the beneficial effects on diabetes of *Spirulina platensis*, a microorganism with Qualified Presumption of Safety status permitted as a dietary supplement by the FDA and marketed worldwide.

The Science Without Borders Program has proven a triumphant success for Brazil, with many of the program's initial goals already being achieved. The physical presence at UBC of the two Brazilian professors/researchers who are conducting the above research projects has resulted in an exchange of knowledge and the learning of research methods applicable to pharmaceutical sciences. The partnership has helped explore issues related to the access of medicines in a different health system model. As a ramification of the Federal Procurement Profile of Essential Medicines in Brazil study, two new research projects have been designed and applied. Studying the effects of supplementation of the seaweed *Spirulina platensis* in animals with STZ-

induced diabetes will give support to the data already obtained in Brazil using an alloxan-induced diabetes model.

Although the current scope of the program and its partnership with UBC is limited, this initial connection establishes an important link between Brazilian universities and UBC, with different steps of each project being developed in laboratories and research centres of both countries. This technical cooperation between researchers strengthens awareness of the role that national and international networks play in the construction of new knowledge. In spite of the geographic distance between the partner countries, both projects are producing scholarly dialogue and international collaboration that is driving excellence in scientific research.

### Funding

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# Patient-Centered Care: A Two-Way Street in Inter-Professional Practice

Jacky Tang, BSc. (Pharm) Candidate (2017)<sup>1</sup>

<sup>1</sup> Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

**I am a UBC Pharmacy student with three years of study and over four years of work experience in retail pharmacy settings. Through my experiences, I have come to recognize the importance and need for Patient-Centered Care and Inter-Professional Practice in our current health care system.**

## Introduction

Patient-Centered Care is a term that is used repeatedly and has been drilled into the minds of recently graduated clinicians, but what does it mean and why should health care providers care? Interestingly, the term Patient-Centered Care was only recently introduced into the Health Policy Lexicon as recent as 2001 (1). Since then, this term has become a fundamental part of health care practice. In fact, it was featured in a key report from the Institute of Medicine (IOM), *Crossing the Quality Chasm*, as one of the six aims for high-quality health care (1).

Another phrase that is becoming a household term in the current health care system is Inter-Professional Practice. With the explosion of new knowledge and discoveries in the 21<sup>st</sup> century, health care is “often highly specialized and most commonly carried out by teams of health professionals” (2). There is so much to know that it is no longer feasible for one health care provider to manage all aspects of patient care, and the patient must seek various health care providers to suit all their needs through their journey. However, visiting different clinicians may result in a difference in opinions and options, and the patient may have to discuss their condition repetitively to each provider. For instance, a British study in 1999 revealed that patients with cancer interacted with a shocking average of 28 doctors within one year of the diagnosis on top of the other health care professionals required during therapy (2).

Envision the current state of health care – there is a plethora of professionals and specialists to provide care in practically every aspect imaginable: physicians, pharmacists, physiotherapists, nurses, occupational therapists, social workers, and many more. Imagine that you are HN, a 34-year-old dancer newly diagnosed with multiple sclerosis (MS). You arrive at the pharmacy to pick up your injection, only to find out that it is a daily injection, and fear that you may not be able to adhere to the regimen due to your sporadic rehearsal and performance times. Your pharmacist recommends a different injection that uses

a weekly regimen instead; however, your next appointment with your neurologist is three months away and it is impossible to consult with your specialist until then. To top it off, you have not even made an appointment with an occupational therapist and social worker yet, nor do you know what those professionals are supposed to help you with. At this moment, you feel helpless – you have lost control of your own health.

These are all problems that are unnecessary and compound an already debilitating diagnosis. Where did it all go wrong? The problem is found in the disconnect and lack of communication between the patient and the health care professionals, and between the health care professionals themselves. In traditional practice the health care professionals hold all the power in decision-making, and it logically makes sense – the health care providers understand what is best for the patient medically. However, the best medical option may not be the best option for the patient, due to economic, adherence, and lifestyle concerns. By understanding and developing Patient-Centered Care and Inter-Professional Practice as one interconnected concept, issues in health care can be minimized and outcomes are optimized.

## Patient-Centered Care

Patient-Centered Care is the idea of shifting clinicians’ focus to the patient and families and away from the diseases (3). In a time when the health care system is increasingly fragmented with the increase of knowledge and specialties, a Patient-Centered Care approach allows all clinicians to understand and address the patients’ needs; the decision-making process is one that is shared between the clinicians and the patient. Too often are patients and their families left in the dark, not only about the choices they have, but even the details of their conditions. In my personal experience, many patients coming into the pharmacy do not understand what their medications are used to treat or even what their condition is. Without the inclusion of the patient in a shared decision and disease management process, it

can be overwhelming for the patient to navigate the health care system and the options available to them.

In addition to addressing the medical concerns, clinicians must understand and take into account patients' values, beliefs, and personal definition of an acceptable quality of life. This fosters an encouraging environment for patient autonomy where the patient can actively participate in their own care. Patient autonomy is the process in which the clinician works *for* the patient, providing the patient with informed medical options to choose from when applicable. This situation is comparable to that of hiring a lawyer: the lawyer aims to achieve all the needs of the client by providing expertise, with the client having the final say — the lawyer works *for* the client. By placing the power back into patients' hands, patients will be encouraged to speak their mind, provide more information, and ask relevant questions. This two-way street of sharing information is crucial as it not only builds rapport and trust, but also provides the clinician with more information so that they may provide better therapies.

### Inter-Professional Practice

As health care becomes an increasingly complex subject, it is no longer possible for one health care professional to understand and grasp all aspects of a patient's journey through their disease. An inter-professional team can manage all aspects of the patient's health while avoiding unnecessary stress for the patient. It is unlikely that all the health care professionals required (e.g. psychologist, pharmacist, or occupational therapist) are located within a close vicinity of each other, let alone have any form of useful communication between each other. Without proper communication and access to these medical professionals, patients face a tremendous barrier in obtaining the best possible care. As such, this may cause patients to receive contradictory information leading to uncertainty and confusion (2).

An interesting point to note is the difference between an inter-professional team and a multi-professional team. Although both imply varying disciplines working together, the key distinction comes from the prefixes *inter* and *multi* (2). Inter-Professional teams share the same values in helping the patient; these shared values help guide the providers in setting goals, providing treatment, and coming to consensual decisions in a collaborative manner. A collaborative approach ensures that each professional is supported by other areas of expertise, leading to the highest level of care for the patient. On the other hand, a multi-professional team simply refers to a group of professionals working side by side, without the sharing of information/values and the collaborative approach to providing care to the patient (2).

### Integration of Patient-Centered Care into Inter-Professional Practice

Patient-Centered Care is one of the approaches in providing Inter-Professional Practice. In fact, the pinnacle of Inter-Professional Practice features the inclusion of the *patient* in the inter-professional team. One may question, what expertise does the patient bring to the collaboration of an inter-professional team? The patient has an incredible amount of expertise to bring to the table — their own experience and values of their journey through their disease. The experience and values that the patient holds are the very foundation that guide the direction of the therapies given. The patient is the only one living every second of their life with illness, and they are the one who truly knows what works best for them. Since the patient is the one receiving the therapy, they have the final, informed choice; hence it is so important to have the patient included in the inter-professional team.

There is evidence to support the use of Patient-Centered Care to improve care and well-being for the patient (1). A study in obstetrics revealed that a lack of communication is strongly associated with malpractice legal actions and patient dissatisfaction with their physician's care (4). As early as 1989, a study has shown that fostering an environment with more conversation with patients resulted in better health and functional status (i.e. better control of chronic diseases based on surrogate markers) upon follow-up (5). Allowing patients to participate in their own therapy has improved adherence to medication and disease control without increased cost (5).

A concern often arises — how can clinicians integrate Patient-Centered Care into their already limited time? In spite of this common concern, a randomized controlled trial and a Cochrane review showed that interventions that empower patient participation in asking questions had either no significant effect on consultation time or resulted in a *decrease* in consultation time, on top of decreasing anxiety and increasing patient satisfaction (6,7). Moreover, preliminary results from another study have revealed that patient-centered communication actually *decreases* diagnostic testing expenditures, saving money for the health care system (8).

### Implementation into Current Practice

The need for Patient-Centered Care and Inter-Professional Practice was recognized by Health Canada as early as 2003, when there was a federal budget of \$80 million to sponsor the advocacy, training, and implementation of Inter-Professional Education for Collaborative Patient-Centered Practice (IEPCPP) (9). Despite this support, challenges continue to arise, including the lack of understanding or overlap of other health care providers' roles, and certain populations' (e.g. the

socio-economically disadvantaged) limited ability to challenge medical authority due to their access to education and resources (10).

The first step, for students and clinicians alike, is to recognize the importance of Patient-Centered Care and change their current mindset. It is up to the clinician to foster an encouraging environment and to work hard towards building rapport with the patient. It is no longer acceptable to simply learn about textbook therapeutics; it is of paramount importance that a clinician is trained in the ability to recognize and address a patient's needs and preferences. Clinicians can take the initiative to help patients actively participate in their own therapies. For example, decision aids — including videos, information sheets, or online resources — can be given to patients. Providing decision aids not only delivers more information, but can also drive the patient towards increased engagement and understanding about their own health (11). The next step is to recognize and understand other health care professionals' roles, so that a collaborative environment may be fostered.

### Conclusion

With the expansion of knowledge and resources, the health care system is being increasingly fragmented into specialties, becoming a maze in which it will be difficult for a patient to navigate through without support. Without proper integration and interdependence in this fragmented health care system, patients are often presented with conflicting or misinformed information. Moreover, there is a mindset of a paternalistic, single-authority culture that persists in many clinicians — one must not forget that a clinician's ethical and medical responsibility is to respect the patient's autonomy and do everything in the patient's best interest.

To address these issues, current and future clinicians must embrace and understand what Patient-Centered Care and Inter-Professional Practice are, why they are important, and how to implement them into their own practice. There is evidence to support a Patient-Centered Care and inter-professional approach — studies have shown that both approaches consistently provide better patient functional outcome, satisfaction, and self-management of disease states (4,5,6,7,8). It is time to abandon the

traditional health care culture where information is shared in a narrow one-way street from the clinician to the patient and acknowledge that clinicians are experts only within their own scope of practice. With the support of experts from other fields, health care professionals should be working collaboratively, sharing core values with the patient, and facilitating an environment where information sharing between all stakeholders is encouraged — just like a two-way street. I highly recommend that students actively engage in the resources available (e.g. electives and events) that will help develop a foundational appreciation and understanding of inter-professional practice, so that they may become facilitators of change in their future practices.

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# The Canadian Pharmacy Programme: A Bridge Between Worlds

Sandi Huty, B.Sc.(Pharm.), RPh<sup>1</sup>

<sup>1</sup> *Coordinator, Canadian Pharmacy Practice Programme, Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada*

The Canadian Pharmacy Practice Programme (CP3) is a bridging program for International Pharmacy Graduates (IPGs) offered by the Faculty of Pharmaceutical Sciences. CP3 is a relatively small program not well known within the Faculty which began 11 years ago and is now in its 22<sup>nd</sup> session. Its students are from all parts of the world and a typical class can resemble the United Nations.

Faculty members have questioned why we offer a program which helps IPGs prepare for the Pharmacy profession in British Columbia while it is difficult for graduates of the undergraduate program to find employment. My response is that Canada is a nation of immigrants and IPGs are always going to be moving to Canada. It is our responsibility to ensure that they gain the skills and competencies needed to practice Pharmacy in Canada in a way that ensures the safety of the public. This is particularly important because in a majority of countries pharmacists do not have access to patient medical history. As a result, they do not have a record of a patient's current medications to assess for drug therapy problems. In many countries a pharmacist receiving a prescription will dispense a sealed box of medication, return the prescription to the patient and not engage in any conversation except that of drug cost. The patient-centered style of practice in Canada is a difficult cultural shift for many.

CP3 was originally a voluntary program with two sessions per year with a maximum of 20 students per session. Since September 2014, the only way an IPG can complete the required 500-hour Structured Practical Training (SPT) for licensure is through the CP3 program. Sessions have increased to three per year with a maximum of 24 students per session. In 2014, the ratio of IPGs to undergraduate pharmacists becoming licensed to practice in BC was 3:1 (1). The 2015 numbers are forecast to be 1:1.

To be eligible for CP3, an applicant must have had their initial Pharmacy degree evaluated by the Pharmacy Examining Board of Canada (PEBC), passed the Evaluating Examination, met the College of Pharmacists of BC (CPBC) English Language

Proficiency requirements, and be pre-registered with CPBC.

## Program Structure

The CP3 program is based on the Association of Faculties of Canada (AFPC) Educational Outcomes for First Professional Degree Programs in Canada, which is the same as the foundation of the Entry-to-Practice degree. The goal is to educate Medication Therapy Experts: Care Provider, Communicator, Collaborator, Manager, Advocate, Scholar and Professional (2). CP3 activities are similar to those in the undergraduate program, with the addition of a strong cultural component.

A CP3 session runs for 24 weeks: twelve weeks of classroom instruction and 12.5 weeks (500 hours) of SPT placement in a community pharmacy. The classroom component is divided into five modules: Therapeutics, Healthcare Systems Overview, Communications, Patient Dialogue Skills and Practice Skills Lab. Communication, in the general sense, is threaded throughout the curriculum because of the variations in English language skills among the students.

*Therapeutics* begins with an introduction to the concepts of the Therapeutic Thought Process and Drug Therapy Problems, with an emphasis on preparing a care plan. Other topics include Drug Safety, Drug Interactions, Drug Hypersensitivity, Drugs in Pregnancy and Lactation, Geriatrics and Pediatrics, as well as medical conditions such as Asthma/COPD, Diabetes, Hypertension and Infectious Diseases. As a case study module, students have pre-readings to complete before each class and cases to evaluate and review for discussion purposes.

*Healthcare Systems Overview* focuses on legislation and practice issues. There are five lectures on all legislation relevant to the practice of Pharmacy in BC, including PharmaNet and methadone dispensing. Other topics include Ethics, Third Party Insurance, Pharmacy Administration, SOAP Notes and Medication Reviews.

*Communications* has a strong cultural component in addition to its general focus on written and verbal communication. One area this module deals with is expectations in the Canadian workplace, including impacts of cultural diversity, mannerisms, communication styles and values. Extensive focus is placed on language so that IPGs can be effective communicators with a patient or a fellow health professional, such as a pharmacist or physician.

*Patient Dialogue Skills* is a mix of tutorial and role-play sessions, with the latter being in an OSCE format. Teaching strategies in this course include videotaping of role-plays, Standardized Patients, feedback sessions and demonstrations. Students are required to prepare a care plan each week based on their individual patient encounters.

*Practice Skills Lab* has a practical base, focusing on providing the skills and knowledge needed in community pharmacy, and is a mix of tutorial and lab activities. Students learn to read and interpret prescriptions, research and respond to drug information questions, deal with prescription errors, and receive telephoned prescriptions or drug information requests. Telephone activities are of particular importance due to the difficulties inherent in telephone conversations in a second (or third) language.

These last two modules are comparable to the Integration Activities (previously CAPS and the Lab)

in the undergraduate program, utilizing practicing pharmacists to provide relevant reinforcement of the practice issues brought out during the activities.

CP3 is an intensive program and, during the classroom portion of the session, students are in class 24 hours per week from Tuesday to Friday.

### Assessment

Assessment occurs in the *Patient Dialogue Skills* and *Practice Skills Lab* modules but students are expected to integrate knowledge from other modules to complete their activities. Students must achieve an overall passing grade of 60% to participate in their SPT rotations. Students must prepare a care plan every week, worth 35% of their total mark. Other assessed activities include Drug Information, problem prescriptions, calculations, prescription processing/counseling, telephone activities and OSCE-type role-plays.

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## WORKPLACE SPOTLIGHT

# Pharming in Rural Ghana

Maria Paiva, BSP, PharmD, BCPS<sup>1,2</sup>

<sup>1</sup>Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

<sup>2</sup>Clinical Pharmacist, Building for the Future Generation, Mampong, Ashanti, Ghana

**There are a variety of settings and roles available for Canadian pharmacists interested in practicing abroad. I had the opportunity to volunteer as a clinical pharmacist based in rural Ghana. In this workplace spotlight I would like to provide a brief overview of some healthcare and pharmacy-related issues Ghanaians encounter and to share some of my experiences.**

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## Introduction

Opportunities to study and practice abroad are available via multiple channels. Undergraduate and post-graduate pharmacy programs offer international clerkships, countries looking to optimize pharmacy practice recruit clinicians, and non-profit agencies are in need of volunteers. I had an interest in practicing abroad, especially in a developing country. I completed my PharmD in May 2013 and was eager to utilize the array of skills I honed in a unique practice setting and thought this was an opportune time to volunteer abroad for an extended period. I chose my site in Ghana based on a recommendation from a colleague who knew a hospital pharmacy manager that was interested in partnering with a clinical pharmacist. Additionally, the country is politically stable and known for safe volunteer experiences. This workplace spotlight provides a brief overview of healthcare and pharmacy practice, as well as, highlights some of my experiences in Ghana.

## Ghanaian Healthcare

The healthcare system is evolving despite facing a number of challenges. Overall infant and maternal mortality rates are decreasing and a national HIV/AIDS program has been implemented. Challenges include access to quality facilities, healthcare practitioners, and health insurance, mortality secondary to curable diseases, and poor sanitation (1).

Healthcare facilities are unevenly distributed throughout Ghana, leaving rural communities in a deficient state (1, 2). These communities have higher infant and maternal mortality rates compared to urban centers. It is estimated that Ghanaians have to travel on average 16 km to access a healthcare facility with a physician (1). This is a significant distance as the main modes of transportation are foot, bicycle, and taxi. Additionally, alternative healing practices, poverty, and illiteracy further impede the delivery of quality healthcare (1).

There is a mix of public and private healthcare and medical insurance. The Ministry of Health introduced the National Health Insurance Scheme (NHIS) in 2004; it is funded by external donors and a National Health Insurance tax. The NHIS pays for hospitalizations, outpatient doctor visits, basic laboratory testing, and specific medications. It does not pay for HIV medications, thoracic, neuro-, or plastic surgery unless the indication is trauma related, elective procedures, infertility investigations, transplant medications or surgery, hemodialysis, and only covers cervical and breast cancer therapy (2). Private insurance plans offer a range of options, but are rarely affordable for rural Ghanaians (2). Maintaining health insurance is not mandatory for citizens. Uninsured hospitalized patients are charged for all services and medication rendered. Accounts must be settled prior to discharge. For insured patients, invoices are sent to insurance agencies for reimbursement at discharge, but payment can be delayed up to nine months (1).

Infectious diseases remain the leading cause of death; malaria, followed by HIV/AIDS, diarrhoeal disease, and lower respiratory tract infections. National health insurance authorities estimate 80% of the cases burdened on the NHIS are sanitation-related (1).

## Pharmacy Practice

There is one private and two public pharmacy schools and multiple technical institutions that train pharmacy technicians. There are also individuals with non-pharmacy or medical training that work in hospital and community dispensaries. Though there are standards of practice that define pharmacist roles from that of pharmacy technicians, and support staff, they are not enforced; all dispense medication and are involved in patient care (1).

Patients can also purchase prescription and non-prescription medications from Licensed Chemical Sellers (LCS). These shops are geographically more accessible than healthcare facilities, which help provide access to essential medication; however, practices are unregulated and sellers seldom have any medical training (1).

The World Health Organization (WHO) reports that in many developing countries, the ratios of pharmacists and pharmacies to people are low enough to impede the provision of pharmaceutical care (1). The profession has recognized this impediment and is trying to improve. The country's first entry to practice PharmD program was launched in 2012, a Masters degree in clinical pharmacy is available, and continuing education opportunities are promoted.

### My Practice Site

I was based in the rural municipality of Mampong in the Ashanti region in central Ghana from August to December 2013. The municipality has one district hospital, maternity hospital, and seven health centers, which serves a population of at least 88,000 residents, covering a total land area of 449km<sup>2</sup> (3). The healthcare facilities have running water, but surrounding communities do not. The electricity is subject to frequent planned and unplanned outages and Internet is available for purchase via pay-as-you go modems.

I primarily worked in the district hospital. It is a 135-bed facility that provides basic healthcare, including minor surgeries, an ophthalmologist, ears-nose-throat specialist, dentist, psychiatrist, physiotherapist, and pharmacist-run anti-retroviral therapy (ART) clinic, basic laboratory investigations, and X-ray. Cases that cannot be managed are transferred by ambulance or taxi to the closest tertiary hospital, about 55km away. The commute is approximately two hours due to poor road conditions and heavy traffic.

There are three pharmacists and numerous pharmacy support staff with variable training backgrounds. The dispensary provides services to both inpatients and outpatients. Orders are written in the chart, which arrive in the dispensary via the patient (outpatient) or nurse (inpatient) and they wait there for the orders to be processed. Preparation of parenteral formulations takes place on the wards and pharmacy staff is not involved.

### Activities and Projects

I split my time between the dispensary, patient wards, ART clinic, public health programming, and teaching activities. In the dispensary, I helped answer drug information questions and participated in dispensing activities to help understand the distribution process. We reorganized the dispensary to implement a safer workflow where a second independent check of prescriptions and selected medications could take place. There was no training or policy and procedure manual, which in combination with the range of staff experience, led to inconsistencies in the services provided. To help address these issues, we created a training checklist and policy and procedure manual, which included how to review a prescription for appropriateness, provide basic patient counselling and checking for patient understanding, and proper labelling of medications. We were also able to train staff to more effectively manage their medication inventory and track it electronically.

The pharmacists were interested in expanding their services to participate in interdisciplinary rounds. We created patient monitoring forms and started having weekly therapeutic discussions on common diseases that resulted in admission. With the permission of the hospital administrator, we started rounding with a team of physicians and nurses on the adult general medicine wards. Despite our best efforts to start slow and grow into a sustainable service, we were unable to do so due to resource limitations, namely three pharmacists for the entire district and changes in their availability.

One of the disease states we focused on was diabetes as this was one of the leading causes of admission and death at the hospital. I led multiple sessions on management of these conditions with the pharmacy team and nurses, created teaching pamphlets for insulin injection and storage, and we submitted a report to hospital administration addressing the gaps in care for these patients in both the hospital and community.

The ART clinic is a government-funded program that has greatly improved access to quality care and made drug-therapy affordable for most Ghanaians. The cost for one month of ART is approximately \$2.50 USD. The clinic was opened three days a week and staffed with two pharmacists with specialized training in HIV/AIDS management, one pharmacy technician, a community counsellor, and biostatistician. We saw newly diagnosed and

chronic patients and provide ongoing counselling, education, and medication refills. I was also able to utilize my physical assessment skills. With the help of my colleagues translating, we conducted patient interviews and assessed for signs and symptoms and assigned a World Health Organization (WHO) clinical stage (Stages 1 to 4, with 1=asymptomatic, 4=advanced disease). Based on these findings and patient readiness, we assessed if ART and/or opportunistic infection prophylaxis should be initiated as there was a reagent shortage and laboratories are not able to measure CD4 counts. We also developed an ART medication identification manual with descriptions and samples of the all the ARTs we stocked and created a medication timetable with directions in both English and Twi (local language) for patients and their caregivers.

I participated in two public health initiatives. In September, there was an immunization campaign rolled out at multiple primary schools. The pharmacists involved with the ART clinic were on-call for any consults regarding needle sticks. If an incident occurred, we drove to the school, tested the child for HIV with a point of care device, provided counselling to the healthcare practitioner, and initiated a Post-exposure Prophylaxis (PEP) protocol if indicated. I was also asked to lead a hand hygiene session at a primary school. There were no prior presentations to adapt and my online search did not produce any culturally appropriate resources. I created my own posters and games using crayons and watercolours that were culturally relevant and at an appropriate comprehension level for the students.

The pharmacy staff I had the privilege of working alongside was eager to learn. I did several presentations and in-services ranging from pharmacy practice in Canada to the basics of strategic planning and implementing practice change. Together with the pharmacists we created a strategic plan for the department.

I was also involved in research projects on learning styles and pharmacy staff perception of pharmacy practice. We are also in the process of completing systematic reviews on antimicrobial stewardship activities in the region.

### **Successes, Ongoing Activities, and Future Plans**

One of the major successes we achieved was helping improve the care of diabetics. The report we submitted helped to highlight the unmet needs of diabetics in the community. Shortly thereafter, Mampong Government Hospital established an outpatient diabetes clinic. Refining the dispensary workflows to incorporate an independent double check of prescriptions helped improve patient safety. We have also published a paper addressing learning styles of pharmacy team members in the district, which, has been utilized by volunteers and students to help in preparation of educational sessions.

This municipality has hosted multiple pharmacy Structured Practice Experience Program (SPEP) and PharmD students from Canada. With the enthusiasm and support of the local pharmacists, we have been able to create unique rotation site. It is a non-clinical elective rotation that focuses on pharmacy practice from a public health perspective. A fellow Canadian pharmacist and I are off-site primary preceptors and we organize the logistics, rotation activities, and research projects, facilitate telephone therapeutic discussions, and complete evaluations. We rely on local preceptors to provide input for activities and evaluations and help organize cultural activities so students get a rounded experience. Fortunately, I will be returning to Ghana in September 2015 to follow-up with the pharmacy team and co-precept a University of British Columbia PharmD student. This will be the first time I will be on site during a rotation. I anticipate a mutually rich learning experience. We also look forward to precepting six fourth-year pharmacy students from the University of Saskatchewan in February 2016. Through this partnership, we hope to continue public health promotion, clinical development of local pharmacy staff, and research activities. Future plans include developing methods to measure 360-degree impact for the stakeholders in the municipality and student learning. The main challenges in moving forward with these plans include distance and lack of full-time preceptors on site in Ghana.

### **Conclusion**

There are deficits in Ghana's healthcare and pharmacy practice, especially in rural communities. However, strides are being made to help improve the level and quality of care. Change takes time! It takes vision and perseverance. The practitioners and communities that have and continue to advocate for change and provide patient care in the current landscape should be commended. I am grateful for the rights and resources I have as a Canadian citizen and healthcare provider. Though there were obstacles to overcome during my time in Ghana, the experience was extremely rewarding and life-changing. I hope that this workplace spotlight encourages you to explore international opportunities.

## Acknowledgements

I would like to thank all the kind people in Ghana, especially those in Accra, Nsuta, and Mampong that welcomed me into their country, healthcare facilities, and homes and continue to support us with our projects and rotations.

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# Why Does a High Extraction Ratio Drug Given Orally Behave Like a Low Extraction Ratio Drug? – An Intuitive Explanation

Elaine A.G. Lo, PharmD, BCPS<sup>1,2</sup>

Lawrence S.C. Law, MD<sup>3,4</sup>

Mary H.H. Ensom, PharmD, FASHP, FCCP, FCSHP, FCAHS<sup>1,5</sup>

<sup>1</sup> Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

<sup>2</sup> Senior Clinical Pharmacist, Department of Pharmacy, National University Hospital, Singapore

<sup>3</sup> Duke-NUS Graduate Medical School, Singapore

<sup>4</sup> Doctor, Singapore General Hospital, Singapore

<sup>5</sup> Professor, Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

<sup>6</sup> Distinguished University Scholar, University of British Columbia, Vancouver, BC, Canada

<sup>7</sup> Clinical Pharmacy Specialist, Children's and Women's Health Centre of British Columbia, Vancouver, BC, Canada

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A frequently asked question regarding the well-stirred model of hepatic drug clearance (1-3) from undergraduate and graduate students alike is: “Why does a high extraction ratio (E) drug behave like a low E drug when given orally?”\*

Students usually do not have a problem understanding or explaining the concept mathematically (Box 1) (1-3). However, they typically have trouble grasping the concept intuitively. Numerous articles and textbooks define and describe extraction ratio and clearance of high and low E drugs (4-14). While most differentiate between high and low E drugs when given intravenously (IV), we have not been able to identify references that offer an intuitive explanation of why a high E drug administered orally behaves like a low E drug. For instance, although Wilkinson *et al.* (3) show the specific changes in concentration-time profile when parameters such as liver blood flow, extraction ratio and intrinsic clearance vary, these graphs do not satisfy students' requests for an intuitive description. That is, why does the clearance of orally-administered high E drugs become dependent on unbound fraction of drug (f) and intrinsic clearance ( $Cl_i$ ) instead of hepatic blood flow (Q)? Therefore, we have devised simple diagrams (Figure 1) and explanatory text (below), which have received overwhelmingly positive comments from students.

When a high E drug such as propranolol, morphine, or verapamil is given IV, its intrinsic clearance is greater than Q that it can be cleared only as fast as Q. In Figure 1, Q goes through the hepatic artery into the liver and out through the hepatic vein. Thus, the drug depends on Q to be cleared.

In contrast, whenever a drug (regardless of whether it is a high or low E drug) is given orally, it has to first pass through the intestine and the hepatic portal vein to enter the liver. There, the hepatocytes metabolize the drug before it exits through the hepatic vein. In this first round, which is also known as “first-pass metabolism”, clearance depends on  $f \cdot Cl_i$ ; and it is not influenced by Q. From the hepatic vein, the drug reaches the systemic circulation. In this second round, clearance depends on Q and the drug behaves like a high E drug given IV. The higher the E, the lower the bioavailability (F), and the less significant the second round is (Figure 1).

Like the IV route, high E drugs given via other non-oral routes such as subcutaneous, sublingual, buccal, and inhaled also bypass first-pass metabolism and behave like high E drugs with clearance dependent on Q.

\*Address reprint requests and any article inquiries to Elaine A.G. Lo at Faculty of Pharmaceutical Sciences, University of British Columbia, Volume 3 | Issue 1 | March 21, 2016

2405 Wesbrook Mall, Vancouver, BC, Canada V6T 1Z3. Telephone number: 852 6636 5048  
Email address: [elainelo@alumni.ubc.ca](mailto:elainelo@alumni.ubc.ca)

Putting this into a clinical context, if a patient who is given a high E drug IV, such as propranolol, goes into acute heart failure, a drop in cardiac output could lead to a decrease in liver blood flow. This would result in reduced drug clearance and potentially more pronounced therapeutic effects, such as lower heart

a low E drug and its clearance is dependent on  $f \cdot Cl_i$ . An increase in  $Cl_i$  as a result of enzyme induction by drugs like phenytoin, phenobarbital or carbamazepine may lead to increased drug clearance and hence reduced therapeutic effects. Alternatively, alterations in  $f$  from changes in concentration of acute-phase

**Box 1.** Why does a High Extraction Ratio Drug behave like a Low Extraction Ratio Drug when Given Orally? – A Mathematical Explanation

According to the well-stirred model,

$$Cl_h = \frac{Q \cdot f \cdot Cl_i}{Q + (f \cdot Cl_i)}$$

$$E = \frac{f \cdot Cl_i}{Q + (f \cdot Cl_i)}$$

When drugs of high extraction ratio (E) are given IV:  $Cl_i \gg Q$

$$Cl_h \sim \frac{Q \cdot f \cdot Cl_i}{f \cdot Cl_i}$$

$$Cl_h \sim Q$$

When drugs of low E are given IV:  $Q \gg Cl_i$

$$Cl_h \sim \frac{Q \cdot f \cdot Cl_i}{Q}$$

$$Cl_h \sim f \cdot Cl_i$$

When drugs are given orally, regardless of E:

$$\begin{aligned} Cl_o &= \frac{Cl_h}{F} = \frac{Cl_h}{1-E} = Cl_h \div \left(1 - \frac{f \cdot Cl_i}{Q + f \cdot Cl_i}\right) = Cl_h \div \frac{Q}{Q + f \cdot Cl_i} \\ &= \frac{Q \cdot f \cdot Cl_i}{Q + f \cdot Cl_i} \div \frac{Q}{Q + f \cdot Cl_i} = f \cdot Cl_i \end{aligned}$$

$Cl_h$  = Hepatic clearance,  $Cl_i$  = Intrinsic clearance,  $Cl_o$  = oral clearance, E = extraction ratio, f = unbound fraction, F = bioavailability, Q = liver blood flow

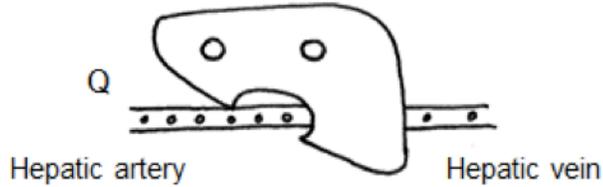
rate and lower blood pressure. On the other hand, if propranolol is given orally, a drop in liver blood flow alone is not anticipated to produce lower heart rate or blood pressure. Propranolol given orally behaves like

reactants such as  $\alpha_1$  acid glycoprotein or from

protein binding displacement by drugs such as valproate may also alter clearance of orally-administered propranolol because the drug is highly bound to plasma proteins.

To complete the story, clearance of low E drugs, such as warfarin or phenytoin, depend on  $f$  and  $Cl_i$ , regardless of route of administration. When given via non-oral routes, liver blood flow is not the rate-determining factor and thus, clearance depends on

1. High E drug given IV



The liver has a big "appetite".

$Cl$  is dependent on the rate drug is brought to it through the systemic circulation, i.e.  $Q$ -dependent.

Low E drug given IV



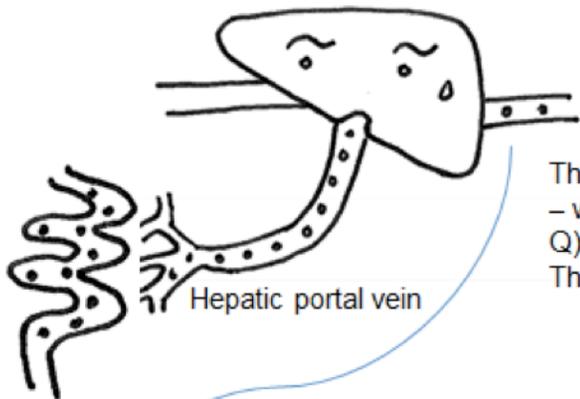
The liver has a small "appetite".

$Cl$  is dependent on  $f \cdot Cl_i$ .

Unbound fraction of drug

Intrinsic clearance

2. High E drug given orally



The drug goes through pre-systemic metabolism – which does not involve hepatic blood flow (i.e.  $Q$ ) but is dependent on  $f \cdot Cl_i$ . The high E drug behaves like a low E drug.



When the remaining drug goes into the systemic circulation and revisits the liver, it is handled like a high E drug given IV again!

$Cl$  = clearance,  $Cl_i$  = intrinsic clearance,  $E$  = extraction ratio,  $f$  = fraction unbound, IV = intravenously;  $Q$  = liver blood flow

**Figure 1.** Why does a high extraction ratio drug given orally behave like a low extraction ratio drug? - An intuitive explanation.

$f \cdot Cl_i$ . When given orally, liver blood flow is not involved during first pass metabolism; during the second round, clearance depends on  $f \cdot Cl_i$  as usual. See Box 1 for the mathematic explanation.

The intuitive explanation provided here aims to explain the change in determinants of clearance of high E drugs when given via different routes. It should be noted that first-pass metabolism *per se* does not explain the concepts illustrated above. Through sharing the illustrations and explanatory text, we hope to facilitate the teaching and learning of the behaviour of high E drugs given orally. While mathematical deduction serves as a logical proof, explaining pharmacokinetic principles from the conceptual and intuitive perspective helps students understand and appreciate the physiology-based associations. This will eventually lead to better retention of knowledge and, hopefully, the ability to apply pharmacokinetic principles to patient care.

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# Preparation of Lower Dosages of SNRI Antidepressants to Ameliorate Discontinuation Symptoms: Two Case Studies

Benton Attfield, B.Sc. (Biology), B.Sc. (Pharm)<sup>1</sup>

Lori Bonertz, B.Sc. (Pharm)<sup>2</sup>

Cory Hermans, B.Sc. (Pharm)<sup>2</sup>

Valerie Kantz, Senior Pharmacy Technician<sup>2</sup>

<sup>1</sup>Hamilton Health Sciences, Hamilton, Ontario, Canada

<sup>2</sup>Fort St. John Pharmacy and Wellness Centre, Fort St. John, BC, Canada

**There is a large body of evidence showing that adverse effects experienced with antidepressant treatment ameliorate over time and that disease-state symptoms improve for many patients (1). However, there is a paucity of information relating to how to stop these medications when a patient's depression has remitted. Presented here are two cases that demonstrate the role pharmacists play in helping patients discontinue SNRI medications through the preparation of lower strength dosage forms.**

## Introduction

Duloxetine (Cymbalta®, Lilly) and desvenlafaxine (Pristiq®, Wyeth/Pfizer) are selective serotonin and norepinephrine reuptake inhibitors (SNRIs) approved for use in Canada for the treatment of major depressive disorder. Duloxetine is also indicated for the treatment of neuropathic pain associated with diabetic peripheral neuropathy, fibromyalgia, generalized anxiety disorder, osteoarthritis of the knee, and chronic low back pain. Duloxetine is available in 30 and 60 mg capsules containing enteric-coated pellets; a 20 mg capsule is available in other countries (2). Desvenlafaxine is available as a 50 mg or 100 mg extended release tablet, with a 25 mg tablet available in other markets (3).

There is scant information in the published literature regarding the process of weaning off either SNRI. While discontinuation reactions from selective serotonin reuptake inhibitors (SSRIs) are well recognized in both the adult and pediatric populations (4), there are no clear guidelines for tapering schedules. SNRIs have also been shown to cause discontinuation symptoms including dizziness, insomnia, irritability, nausea, abnormal dreams, and hyperhidrosis (5). These symptoms can mimic major depression and result in re-treatment due to a misdiagnosis of a relapse (6). Discontinuation symptoms typically manifest within one to seven days of stopping these medications (4). For SSRIs, the availability of fluoxetine, an agent with a longer half-life, can facilitate the weaning process. However, for SNRIs, the medications all have similarly short elimination half-lives, meaning a switch to an alternative SNRI is unlikely to lessen discontinuation symptoms.

## Case 1

A 49-year-old male with a diagnosis of multiple sclerosis was initiated on duloxetine for neuropathic pain. The physician was targeting a dose of 60 mg for treatment, however, the patient was instructed to adjust his dose as needed and was provided with 30 mg capsules. While duloxetine is not approved in Canada for this indication, there is some evidence for its use (7). According to the patient, the physician told him that discontinuation would not be an issue with this medication. Concomitant medications included dalfampridine 10 mg twice daily and a tapering dose of prednisone.

The patient initiated treatment with duloxetine 30 mg daily, and, over a period of 4 months, made attempts to maintain the target dose of 60 mg. He decided to stop the medication, as it did not seem to impact his pain even when taking the 60 mg dose. Prior to discontinuing, the patient had been taking the 30 mg daily dose for two weeks (the lowest dose commercially available). Despite being stable at this low dose, he experienced dizziness, nausea, and 'brain zaps' upon stopping, which affected his ability to work. These symptoms would begin within three days of stopping the duloxetine and necessitated him to reinstate the medication.

We offered to compound a lower dosage of duloxetine to provide a more gradual taper. An experienced pharmacy assistant opened a duloxetine 30 mg capsule and weighed the pellets inside on a digital scale; the contents of one capsule, including excipients, weighed 180 mg. She then weighed out half the amount (90 mg), placed it in a size 3 empty gel capsule and prepared a two-week supply. The patient felt well on the 15 mg dose and the decision was made to prepare two weeks of 7.5 mg capsules. The patient was able to successfully wean off duloxetine with a decrease in the withdrawal symptoms he found most intolerable; however, after completely stopping the medication, he continued to experience ‘brain zaps’ several times a day for a few more days. Despite this, the taper did seem to prevent the development of dizziness and nausea.

## Case 2

In another case, a 36-year-old female presented a prescription from a psychiatrist for a tapering course of desvenlafaxine, with dose decreases of 5 mg weekly starting at 45 mg. The patient had been taking desvenlafaxine for nine months for the treatment of major depressive disorder. Her medical history was insignificant otherwise. Notably, desvenlafaxine is formulated as a hypromellose polymer matrix extended-release tablet that cannot be split, chewed, or crushed. Because of the design of the tablet and how the release of drug is controlled, it is not possible to compound it into a capsule while retaining an extended release profile (8). This was confirmed in discussion with the manufacturer [personal communication, 21/04/15].

Following discussion with the physician, a new prescription for venlafaxine was provided, with an initial dose of 100 mg daily for one week, decreasing by 10 mg weekly. There is little guidance available for switching patients from desvenlafaxine to venlafaxine. Fifty-five percent of a dose of venlafaxine is metabolized to desvenlafaxine (3) and thus many clinicians use a doubling of the desvenlafaxine dose to provide the equivalent venlafaxine dose.

We followed a similar procedure to compound the venlafaxine capsules as we had for the duloxetine. We weighed the contents of five 150 mg PMS-venlafaxine XR capsules, of which the average weight was 401 mg. We then used this to calculate the amount needed for each week of the taper. At follow-up with the pharmacy, three weeks after beginning the taper, the patient had experienced no adverse effects and was happy with the therapy.

## Discussion

Interestingly, when we contacted the medical information department at Eli Lilly, we were provided with a summary of discontinuation-emergent adverse events that included more detailed information than the product monograph.

The product monographs for both duloxetine (Cymbalta®) and desvenlafaxine (Pristiq®) provide information about discontinuation symptoms. Following abrupt or tapered discontinuation in placebo-controlled clinical trials, the following symptoms occurred at a rate greater than or equal to 1% and at a significantly higher rate in Cymbalta®-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, nightmares, insomnia, diarrhea, anxiety, hyperhidrosis, vertigo, somnolence, and myalgia. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, dose titration should be managed on the basis of the patient’s clinical response.

We performed a search of Index Medicus and Medline (OvidSP) using the search terms duloxetine, desvenlafaxine, Cymbalta, or Pristiq, and withdrawal or discontinuation. In a letter, Hou reported long-term withdrawal syndrome in a patient of Asian ancestry treated for depression (9). Indeed, the patient experienced intermittent duloxetine withdrawal syndrome for 10 months. There is a report of withdrawal syndrome in a newborn whose mother was taking 90 mg of duloxetine before and during her pregnancy (10). Another case report described shock-like sensations associated with duloxetine discontinuation (11).

There has been a phase IV, manufacturer-sponsored trial investigating the discontinuation of desvenlafaxine (12). This trial included 357 patients taking a 24-week course of desvenlafaxine who were randomly assigned to three groups: abrupt discontinuation of 50 mg dosages, continuation, or a one-week taper to 25 mg prior to discontinuation. No statistically significant difference in discontinuation events was found in DESS (Discontinuation-Emergent Signs and Symptoms) scores assessed by the trial investigators. However, there was a trend to greater adverse events with abrupt discontinuation, and the fact that both discontinuation groups had higher rates of adverse events suggest there is still a need for strategies to ameliorate withdrawal. Further, this study did not address relapse, was only conducted in patients taking a relatively short course of medication, and did not address previous treatment for depression. Curiously, Pfizer’s USA market monograph still mentions the availability of the 25 mg dosage form to assist with discontinuation, despite the results of this trial.

## Conclusion

Although not recommended by the manufacturer [personal communication, 02/02/15], preparing lower dosages of duloxetine is effective for blunting withdrawal reactions. In the case of desvenlafaxine, the monograph states that tapering is an option; however, there is no practical way of achieving this with commercially available dosage forms. Switching to venlafaxine XR compounded capsules provides the ability to slowly taper a patient's dose and reduce discontinuation symptoms.

A recent article published in the *Journal of Pharmacy Practice* acknowledges the difficulty in selecting a medication regimen for discontinuing antidepressants (13). The authors noted that many trials are not designed to effectively track outcomes after discontinuation. This reiterates the need for including discontinuation outcomes in clinical trials of new antidepressant medications. For those medications already on the market, this represents an area where further research needs to be conducted. It would be helpful to have established guidelines for tapering, such as alternate day scheduling or decreasing by a certain percentage of the dose over time, to try to lessen the likelihood of withdrawal symptoms. Pharmaceutical companies manufacturing SSRIs and SNRIs should be encouraged to produce tapering dosage suggestions in conjunction with initiation schedules.

We encourage pharmacists to highlight to patients and prescribers considering cessation of treatment with duloxetine or desvenlafaxine the possibility of withdrawal symptoms on discontinuation. There is potential for patients and their health care professionals to mistake withdrawal symptoms for a recurrence of depression (6). Pharmacists should follow-up with patients in the weeks following discontinuation to monitor for changes in depressive and withdrawal symptoms.

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