PIAAF-PPS: AN ANALYSIS OF SERVICE RECIPIENTS

PROGRAM FOR THE IDENTIFICATION OF ACTIONABLE ATRIAL FIBRILLATION – ANALYSIS OF PROFESSIONAL PHARMACY SERVICES (PIAAF-PPS): AN ANALYSIS OF SERVICE RECIPIENTS FOLLOWING COMMUNITY PHARMACY SCREENING

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TITLE: Program for the Identification of Actionable Atrial Fibrillation – Analysis of Professional Pharmacy Services (PIAAF-PPS): An Analysis of Service Recipients Following Community Pharmacy Screening

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LAY ABSTRACT

Community pharmacies may be ideal locations for screening of chronic diseases such as diabetes, high blood pressure, and abnormal heart rhythms. It is not well understood how pharmacy services are used in people after screening for these risk factors. This project aims to see if people screening at higher risk levels were more likely to receive pharmacy services than those at lower risk. We used patients' pharmacy data to see what services they had received after screening, and then created statistical models to determine which patient-, pharmacy-, community-, and screening-related factors were associated with a greater chance of receiving pharmacy services. Being at risk of diabetes, high blood pressure, and irregular heart rhythms were not associated with a greater likelihood of receiving pharmacy services, except in those at high risk for diabetes—these patients were found be associated with a higher chance of receiving flu shots.

ABSTRACT

Background and Objectives: Community pharmacy screening for chronic disease risk factors can promote early detection. Little is known about how pharmacy services are used post-screening. The PIAAF Pharmacy study screened elderly participants for hypertension, diabetes, and atrial fibrillation (AF) in 26 pharmacies in Ontario and Alberta. The primary objective was to determine whether patients screening at risk for AF, hypertension and diabetes had increased odds and rates of pharmacy service receipt than those at lower risk.

Methods: Participants' pharmacy data were extracted. A conceptual framework of potentially influential factors was constructed. Measurable factors were used as variables in regression analyses. Generalized estimating equations (GEE) were created to model 1) receipt of all pharmacy services, 2) receipt of medication review, and 3) receipt of influenza vaccination.

Results: 165 of 535 patients received 229 pharmacy services. 64% were medication reviews and 25% were influenza vaccinations. Screening at high risk for diabetes, hypertension, and AF was not associated with increased receipt of pharmacy services, except for influenza vaccine, which was associated with screening as high risk for diabetes (OR = 1.69 [95% CI 1.09, 2.64]). Screening in October (IRR = 2.85 [95% CI 1.67, 4.84]), eligibility for annual-only medication reviews (IRR = 2.15 [95% CI 1.53, 3.01]), number of medications (IRR = 1.92 [95% CI 1.07, 3.46]), new medications (IRR = 2.00 [95% CI 1.37, 2.93]), and living in Alberta (IRR = 1.46 [95% CI 1.07, 2.01]) were associated with increased rates of receiving pharmacy services.

Discussion and Conclusions: Screening results were not associated with increased receipt of pharmacy services, with the exception of influenza vaccine and high risk of diabetes. A gap exists between screening and pharmacy service receipt. Pharmacists can use screening interventions and individual screening results as an opportunity to provide pharmacy services to those with chronic disease risk factors.

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Many thanks to my wonderful supervisor, Dr. Lisa Dolovich—without your support and mentorship, I truly would not be where I am today! Many thanks also to my thesis committee for sharing their expert knowledge and providing me with kind words of encouragement. Thanks to the original PIAAF team for allowing me to undertake this project, as well as to all of those who helped me along the way.

Special thanks to my wonderful family, both old and new, for their unwavering belief in my abilities, and for always reminding me of how lucky I am to have each and every one of you in my life. Thanks to my parents and grandparents for instilling me with a love of learning and always encouraging me to follow my dreams, and to Ashley for convincing me to do this in the first place. Thanks especially to my amazing husband, James, who always had faith that I could do this, even when I didn't believe it myself. You have been my rock throughout this process, and I can't believe how lucky I am to have you as my partner.

This thesis marks the culmination of a long and difficult journey—one that I am so grateful that I did not have to make alone. I dedicate this thesis project to Kent Lancaster, the best father that I could have ever asked for, who sadly did not make it to the end of this journey with me. Know that you will forever be in my heart, and I hope that I have made you proud.

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LIST OF ABBREVIATIONS

Abbreviation:	Definition:
ABC	Alberta Blue Cross
ACE	Angiotensin-converting enzyme
AF	Atrial Fibrillation
AGS	American geriatric society
AIC	Akaike's information criterion
AICC	Finite sample corrected Akaike's information criterion
ANOVA	Analysis of variance
AHS	Alberta Health Services
APA	Additional prescribing authority
ARB	Angiotensin II receptor blocker
ASA	Acetylsalicylic acid
BIC	Bayesian information criterion
CAD	Canadian dollar(s)
CAIC	Consistent AIC
CANRISK	Canadian Diabetes Risk Assessment Questionnaire
CCO	Cancer Care Ontario
CDC	Centre for Disease Control and Prevention
CET	Cerebral Embolism Task Force
CHAD	Community Health Awareness of Diabetes
CHAP	Cardiovascular Health Awareness Program
CHEP	Canadian Hypertension Education Program
CHF	Congestive heart failure
CIHI	Canadian Institute for Health Information
CACP	Comprehensive Annual Care Plan
CPhA	Canadian Pharmacists' Association
CRF	Case report form
C-SPIN	Canadian Stroke Prevention Intervention Network
CV	Cardiovascular
CVD	Cardiovascular disease
DF	Degrees of freedom
DIN	Drug identification number
ECG	Electrocardiogram
GACD	Global Alliance for Public Disease
GEE	Generalized estimating equation
GLM	Generalized linear model
GP	General practitioner
HBA1C	Hemoglobin A1C
HDL	High-density lipoprotein
HIREB	Hamilton Integrated Research Ethics Board

ICC	Intra-cluster coefficient
IRR	Incidence rate ratio
JPHO	Joint Public Health Ontario
LDL	Low-density lipoprotein
MI	Myocardial infarction
ME-ZIP	Mixed-effects zero-inflated Poisson model
MOHLTC	Ministry of Health and Long-Term Care (Ontario)
MSP	Manitoba Society of Pharmacists
NCD	Noncommunicable disease
NHANES	National Health and Nutrition Examination Survey
OAC	Oral anticoagulation
ODB	Ontario Drug Benefits
OPA	Ontario Pharmacists' Association
OPSCP	Ontario Pharmacy Smoking Cessation Program
OR	Odds ratio
OTC	Over-the-counter
PIAAF	Program for the Identification of "Actionable" Atrial Fibrillation
PIAAF-PPS	Program for the Identification of "Actionable" Atrial Fibrillation—Analysis of Professional Pharmacy Services
PIN	Product identification number
PHAC	Public Health Agency of Canada
PHRI	Population Health Research Institute
POP	Pharmaceutical Opinions Program
QIC	Quasi-likelihood under independence model criterion
QICC	Corrected quasi-likelihood under independence model criterion
RCT	Randomized controlled trial
SES	Socioeconomic status
SD	Standard deviation
SL-ECG	Single-lead ECG
SMMA	Standard Medication Management Assessment
TIA	Transient ischemic attack
USPSTF	United States Preventative Screening Task Force
VIF	Variable inflation factor
WCS	Working correlational structure
WHO	World Health Organization
ZIP	Zero-inflated Poisson

DECLARATION OF ACADEMIC ACHIEVEMENT

The PIAAF-PPS project was a secondary analysis of data from the original PIAAF Pharmacy study, which was co-authored by principal investigators, Drs. Lisa Dolovich, Rupinder Sandhu, Jeff Healey, and Gina Agarwal. This study consisted of a community pharmacy screening intervention, wherein elderly community members (65 years and older) in Edmonton, Alberta, and Hamilton, Ontario, were invited to one of 30 participating Rexall pharmacies to receive screening for 3 chronic disease risk factors: atrial fibrillation, diabetes, and hypertension.

The PIAAF-PPS project was conceived by Dr. Lisa Dolovich, with the objectives of investigating how pharmacy services were used in customers following their participation in the three-stage PIAAF Pharmacy screening intervention. The PIAAF Pharmacy study data was held at the Population Health Research Institute, which was extracted for use in the PIAAF-PPS analysis with the help of Alex Grinvalds, Maral Mofrad, and Nazneen Solkar, and subsequently sent back to McMaster University. Patient data from PHRI was then used to link PIAAF Pharmacy participants to their own pharmacy profiles. Data from pharmacy profiles, including claims and medical history data, was extracted by staff members at Rexall head office, with help from Vanessa Prescott and Jennifer Lamch, under the supervision of Vu Nguyen. This extracted data was also sent back to McMaster University for analysis.

Once all data had been extracted, I began the task of cleaning, coding, and analyzing the data. Once the data had been coded, it was double-checked by April Chan, a pharmacist by training, to ensure that the pharmacy data had been interpreted and coded correctly. I performed a literature search to identify evidence, which was subsequently used to construct the theoretical framework. I then performed the data analysis, both descriptive and inferential, based upon the advice and suggestions of my thesis committee, which included Drs. Lisa Dolovich, Lehana Thabane, and Jean-Eric Tarride. After data analysis was completed and interpreted, I then wrote the manuscript, once again upon advisement from my various committee members. For my thesis defense, my thesis committee was joined by Dr. Sherilyn Houle as the external member.

While results of this project have yet to be published, when they are, Drs. Dolovich, Thabane, Tarride and Houle will all be listed as co-authors, as will the original PIAAF Pharmacy study team.

1.0 CHAPTER 1: INTRODUCTION AND BACKGROUND

1.1 Chronic Disease and it's Burden on the Canadian Health Care System

1.1.1 Introduction to Chronic Disease

Chronic diseases are the leading cause of death worldwide. In 2012, as many as 38 million people around the globe died of chronic disease or complications related to chronic (WHO, 2014). In Canada, chronic diseases were responsible for as many as 79% of deaths in Ontario in 2007 (JPHO/CCO, 2012). The World Health Organization (WHO) defines chronic diseases, also referred to as noncommunicable diseases (NCDs), as those that "are not passed from person to person" and that are "of long duration and slow progression" (WHO, 2014). Cardiovascular disease (CVD) and diabetes are two of the most important categories of chronic disease (WHO, 2014), with CVD causing more deaths annually than any other cause of mortality. It is estimated that across the globe, over 17 million deaths per year can be attributed to CVD (WHO, 2016; Adler, 2015). CVD comes in many forms, and may lead to stroke, transient ischemic attacks (TIAs), myocardial infarction (MI), heart failure, peripheral arterial disease, and renal disease. In addition to humanistic costs, CVD also exerts a major burden on healthcare systems. It is estimated that stroke alone costs the Canadian health system over 3.6 billion dollars per year (C-SPIN, 2014). The associated costs of CVD are not only limited to direct costs such as healthcare utilization—morbidity and disability caused by CVD also lead to decreased productivity of those affected, as well as other indirect costs (Adler, 2015).

1.1.1.1 Atrial Fibrillation

Atrial fibrillation (AF) is a heart arrhythmia caused by rapid and chaotic electrical activity in the atria of the heart. AF is the most common cardiac arrhythmia, with a population prevalence of approximately 1-2%. The risk of AF increases drastically with age, so the prevalence in elderly populations may be as high as 9-10% (Go, 2001; Naccarelli, 2009). Large-scale longitudinal studies have found the risk of AF is almost doubled with every decade lived (Moran, 2013; Go, 2001; Stewart, 2001). Amongst patients with AF, the incidence of AF-related stroke also increases dramatically with age, rising from 1-2% in those aged 50-59 to 24% in those aged 80-89. AF may also lead to recurrent strokes (Marini, 2005). AF-related strokes also have a higher mortality rate than

those not attributed to AF, require longer hospital stays, and may lead to worse neurological outcomes (Marini, 2005; CET, 1989).

Other risk factors associated with new diagnosis of AF and diagnosis of AF following hospitalization include male sex, presence of cardiomegaly (enlargement of the heart), and systolic hypertension (Stewart, 2011; Carrol, 2001). Once AF has been detected, it is often recommended that the patient is monitored and started on anticoagulation therapy in order to minimize the risk of embolization and stroke. In fact, Wyse et al. (2002) have found that continuous anticoagulation therapy is appropriate in all patients with AF, even after a normal sinus rhythm is restored. Where AF is detected, preventative treatment with oral anticoagulation therapy (OAC) may reduce the incidence of stroke by up to 64% (Camm, 2010; Hart, 2007; Hylek, 2003).

While some patients may experience symptoms of AF, including heart palpitations, fatigue, weakness and dizziness, AF is frequently asymptomatic—patients may not be aware that they are in AF (Kumar, 2016; Moran, 2013). The asymptomatic nature of this condition, combined with the high risk for stroke and TIA it creates, makes early detection of AF a critical step for prevention of serious cardiovascular or cerebral events. Organized and opportunistic screening interventions are considered highly favourable methods of AF detection, and are recommended by various health organizations including the WHO, the Canadian Medical Association, and the European Society of Cardiology (Camm, 2010; WHO, 2014; Wilson, 2001).

1.1.1.2 Hypertension

Hypertension is the most common NCD for which prescription medications are used in the United States (Egan, 2010). From 2005-2008, the prevalence of hypertension in the US ranged from 29-31% (Egan, 2010). Data from 1998-2008 suggests that approximately 60% of Canadians between the ages of 65-69 have hypertension (Robitaille, 2012). Hypertension is also a major contributor to CVD-associated morbidity and mortality (Adler, 2015). Of yearly CVD-related deaths, approximately 9.4 million may be caused directly or indirectly by raised blood pressure (Adler, 2015). In 2010, 7% of disease burden worldwide was attributed to high blood pressure (WHO, 2014). High blood pressure is defined as $\geq$140/90 mmHg in non-diabetic patients, and $\geq$130/80 mmHg in diabetic patients (WHO, 2014). Hypertension is known to be associated with many serious and potentially fatal health outcomes, including heart failure, ischemic stroke, intracerebral hemorrhage, heart disease, MI, and kidney disease (Adler, 2015). In fact, hypertension has been found to be the most common modifiable risk factor for

cardiovascular disease, beating out such other important factors as smoking, diabetes, and dyslipidemia (Adler, 2015; Basile, 2016; Wilson, 1994).

Hypertension can be treated successfully, although it often requires one or more pharmacotherapeutic agents (Adler, 2015). Poor control of hypertension is a major issue. As few as 50.1% of patients with diagnosed hypertension are able to keep their blood pressure below recommended levels, as reported by the United States National Health and Nutrition Examination Survey (NHANES) (CDC, 2011). If blood pressure control is not adequate, hypertension remains a major risk factor for cardiovascular events, even if a patient is undergoing antihypertensive therapy (Basile, 2016).

With so many negative health outcomes associated with hypertension, it is no surprise that this condition places considerable burden on health care systems across the globe. In 2008, essential hypertension and hypertensive disease cost the Canadian health care system approximately $3.4 billion dollars in direct and indirect costs (PHAC, 2008). Furthermore, hypertension frequently remains undiagnosed. The NHANES survey (1999-2002) estimates that as many as 8% of the US population may have undiagnosed hypertension (CDC, 2011). In order to reduce costs, prompt detection and treatment of hypertension is key. Many guidelines, including those put forth by the 2015 United States Preventative Screening Task Force (USPSTF) and the Canadian Hypertension Education Program (CHEP), recommend hypertension screening for all adults over 18 years old (Adler, 2015). Where possible, blood pressure measurements taken in a clinical setting should be compared to measurements taken elsewhere (e.g. at home) for a more comprehensive picture of blood pressure readings (Basile, 2016; Daskalopoulou, 2015; Siu, 2015).

1.1.1.3 Type II Diabetes

Diabetes mellitus is another leading cause of mortality and morbidity across the globe. It is associated with CVD, blindness, kidney disease, neuropathy, lower-extremity amputation, and premature death (Kaczorowski, 2009). The WHO estimates the global prevalence of diabetes as approximately 8.5% amongst adults (WHO, 2014). Data collected by NHANES from 2011-2014 estimates that approximately 3% of the US population suffer from undiagnosed diabetes (CDC, 2014); approximately 1.13% of Canadians over the age of 20 may have undiagnosed diabetes (Rosella, 2015). Undiagnosed diabetes may remain undetected for 4 to 7 years (Robinson, 2011), by which time, the patient may already be suffering from vascular complications (Robinson, 2011). It is estimated that by 2025, up to 11.4% of Canadians will be diagnosed with diabetes, which would represent a 43% increase from 2015 rates (PHAC, 2014). Rising

diabetes rates in Canada and worldwide may be exacerbated by increasing obesity rates, aging populations, low socioeconomic status (SES), and changing immigration patterns, among other complex factors (Kaczorowski, 2009; CDC, 2016).

Diabetes imposes a considerable burden on the Canadian health care system. In 2008, the total of direct and indirect costs incurred by the Canadian health care system was approximately $2.2 billion (PHAC, 2008). Diabetes and CVD often go hand in hand. Type II diabetes and hypertension frequently co-exist; as of 2008, an estimated one million Canadians have been diagnosed with both conditions (Campbell, 2011). Patients with comorbid diabetes and hypertension have a mortality rate of 2.5 times patients without either of these conditions, and as many as 80% of people with diabetes may die due to cardiovascular complications. Furthermore, patients with diabetes are less likely than non-diabetic patients to reach recommended target blood pressure—as many as two thirds of diabetic hypertensive patients do not reach blood pressure readings of <130/80 mmHg (Campbell, 2011; Leenan, 2008). These facts highlight the importance of early detection in order to prevent or delay the development of full-blown type II diabetes, especially considering that early stages of this disease may be reversible with lifestyle modification (Dhippayom, 2014; Kaczorowski, 2009; Tuomilehto, 2001; Gillies, 2007; Robinson, 2011).

1.1.2 Benefits of Chronic Disease Prevention

In light of the negative consequences associated with CVD, cardiometabolic disease and their burden on both patients and health care systems, prevention is becoming increasingly critical. In 2008, the WHO set forth a global action plan to prevent and manage the burden of chronic diseases such as CVD and diabetes. They outlined six steps:

(1) To raise the priority accorded to NCD in development work at global and national levels, and to integrate prevention and control of such diseases into policies across all government departments
(2) To establish and strengthen national policies and plans for the prevention and control of NCDs
(3) To promote interventions to reduce the main shared modifiable risk factors for NCDs: tobacco use, unhealthy diets, physical inactivity and harmful use of alcohol
(4) To promote research for the prevention and control of NCDs
(5) To promote partnerships for the prevention and control of NCDs

(6) To monitor NCDs and other determinants and evaluate progress at the national, regional, and global levels (WHO, 2013)

One method to prevent chronic disease is the use of opportunistic screening. Opportunistic screening is defined as screening that is "carried out at a time when people are seen, by health care professionals, for a reason other than the disorder in question" (WHO, 2003). The 2013 Cochrane review by Moran et al. found that both systematic and opportunistic screening for AF significantly increased the number of people diagnosed with AF, when compared to routine care. A large-scale randomized controlled trial (RCT) and cost-effectiveness analysis of elderly patients by Hobbs et al. (2005) reported that not only did patients undergoing annual opportunistic screening for AF have the fewest ischemic strokes, but also that opportunistic screening had the lowest incremental cost per additional case detected, when compared to systematic screening and control groups.

There is also evidence that preventative screening for type II diabetes is cost effective. Kahn et al. (2010) created computerized simulation models of various screening strategies leading to early diabetes detection, and found that all screening methods had the potential to reduce macrovascular complications and incidence of MI, while increasing quality-adjusted life years. Screening was found to be most effective if it was started between the ages of 30 and 45 years, with retesting every three to five years. However, these models assume perfect patient compliance with treatment and monitoring, and thus are unlikely to be generalizable in a real-world setting (Kahn, 2010). Diabetes screening may be more cost-effective in patients with known hypertension, or in patients aged 55-75 when compared to universal screening (Hoerger, 2004; Gillies, 2008).

Screening for prevention of hypertension is recommended by many health organizations worldwide in order to help combat CVD. Patients screening positive for hypertension can be started on antihypertensive therapy, which has been shown to reduce relative risk of heart failure by approximately 50%, stroke by 30-40%, and MI and heart failure by 20-25% (Adler, 2015; Turnbull, 2008). In older populations, these risk reductions may be even greater (Basile, 2016). In their 1995 cost-effectiveness analysis, Kupersmith et al. state that "treatment of hypertension…is cost-effective in virtually all patient populations and circumstances and for a wide variety of drugs". Lifestyle modification may also play a role in achieving control of blood pressure, and it is recommended that all hypertensive patients receive education and counselling on this subject (Adler, 2015; Basile, 2016; Eckel, 2014). With all screening, it is imperative that follow-up care for diagnosed patients is appropriate and of high quality (McCulloch, 2016), especially when considering cost-effectiveness and long-term patient outcomes.

1.2 Role of Community Pharmacists in Primary Care

1.2.1 Expanding Scope of Pharmacists in Canada and Cognitive Pharmaceutical Services

The scope of pharmacists has been expanding within Canada, as well as internationally (Fish, 2002). The tide of pharmacist scope has been shifting away from day-to-day dispensing activities and is moving towards a more patient-centred model of care (CPhA, 2016). As such, community pharmacists are now increasingly focused on the provision of cognitive services focusing on medication management and pharmaceutical care (Dolovich, 2016; Fish, 2002; Kelly, 2014; Touchette, 2014). These professional pharmacy services leverage the knowledge of pharmacists while providing easily accessible, front-line primary care to patients. The expanding scope of Canadian pharmacists has been propelled by regulatory and legislative changes, as well as augmented education and training for pharmacists in order to build new competencies (CPhA, 2016). In many Canadian jurisdictions, pharmacists are now able to provide more medication management services than ever before, including medication review services, administration of injections and immunizations, prescribing for emergency medications and minor ailments, adapting and extending existing prescriptions, therapeutic substitution, provision of smoking cessation counselling, and even independent prescribing (Kelly, 2014). Many of these services are remunerated by provincial drug plans.

Unlike many other countries, Canada does not have nationwide pharmacy service programs (Houle, 2014). Each Canadian province or jurisdiction is governed by its own regulatory body or college; as such, the scope of practice of community pharmacists and the services they offer vary from jurisdiction to jurisdiction. Each jurisdiction is therefore responsible for the development, implementation and remuneration of their own programs, as well as the training, education and certification of pharmacists in order to be able to perform these services (CPhA, 2016). Pharmacy services thus tend to vary across jurisdictions in terms of their scope, operational components, documentation requirements, program goals and objectives. Uptake of programs also varies both between and within jurisdictions (CPhA, 2016). As the study population for this analysis was made up of participants from Ontario and Alberta, this summary will focus on the expanded scope of pharmacists within these two jurisdictions.

1.2.1.1 Ontario

Ontario Drug Benefits (ODB) currently reimburses community pharmacies for four professional pharmacy services: medication review (MedsCheck); administration of influenza and other vaccinations, including travel vaccinations; smoking cessation consultations; and the Pharmaceutical Opinion Program (POP), which reimburses pharmacists in cases where a pharmacist identifies a real or potential drug-related problem, consults with a prescriber and makes therapeutic recommendations, which may or may not result in changes being made to prescriptions. The POP, which was introduced as a remunerated pharmacy service in September of 2011, also has a built-in refusal to fill component, where pharmacists can be reimbursed for refusing to fill a prescription based on their professional judgement, or in cases where prescriptions are fraudulent or otherwise suspect (CPhA, 2016; MOHLTC, 2013; OPA, 2016).

Additionally, pharmacists in Ontario have the authority to extend and adapt existing prescriptions, as well as authority to prescribe certain smoking cessation medications, although these services are not funded by the provincial drug plan (MOHLTC, 2013). Smoking cessation consultations, wherein smoking cessation medications may be prescribed to patients, are however remunerated as part of the Ontario Pharmacy Smoking Cessation program (OPSCP). The OPSCP was first implemented in September 2011. This program allows ODB recipients who are attempting to quit smoking to receive two remunerated smoking cessation consultations with a pharmacist, as well as up to seven remunerated follow-up visits per year (MOHLTC, 2012; Wong, 2015). The implementation of OPSCP was followed in 2012 by the initiation of influenza vaccine by Ontario pharmacists (Houle, 2013). As of December 1, 2016, the scope of Ontario pharmacists expanded even further when the Minister of Health announced that pharmacists would now be allowed in provide a wider range of vaccines to the public, including various travel vaccines, the human papillomavirus (HPV) vaccine, and the herpes zoster (shingles) vaccine (OPA, 2016). However, unlike the annual influenza vaccine, provision of these vaccines is not yet publicly funded; patients therefore will need to pay for both the vaccine product and the injection service out-of-pocket (OPA, 2016).

The MedsCheck program, launched in 2007, was the first cognitive pharmacist service to be reimbursed by ODB. This service is available to all Ontario residents taking 3 or more medications for chronic conditions. There are several different types of medication reviews included under the MedsCheck umbrella, including MedsCheck Annual, MedsCheck Diabetes, as well as follow-up MedsChecks, and MedsChecks performed at

home and in long-term care facilities. A MedsCheck generally consists of a one-on-one consultation between an eligible patient and a community pharmacist, and are usually expected to take between 20-30 minutes, although they may take longer for more complex patients (MOHLTC, 2008; Dolovich, 2016). During these consultations, pharmacists will go over a patient's current medication list (including over-the-counter (OTC) medications), updating the list as necessary and helping patients gain an understanding of the medications they are taking, and why they are taking them. A MedsCheck can also be used as an opportunity to identify any challenges to medication adherence, as well as any real or potential drug-related problems. At the end of the MedsCheck, an updated medication list is generated for the patient, which they are encouraged to share with caregivers and other health care providers (MOHLTC, 2008; Dolovich, 2016).

In 2012-2013, a population-based cohort study by Ignacy et al. (2015) found that approximately 27.1% of Ontarians receiving public drug benefits coverage received a pharmacy service, of which 64% received a MedsCheck Annual (Ignacy, 2015). Another cohort study looking at MedsCheck service recipients found that approximately 1.5 million Ontarians had received at least one MedsCheck Annual between 2007 and 2013, with 36% receiving more than one MedsCheck Annual during the same time period (Dolovich, 2016). Patients over the age of 66 were found to receive more annual medication reviews than did younger patients, and nearly all (87.8%) of MedsCheck recipients had at least one morbidity (with hypertension being the most common at 67.9%) (Dolovich, 2016).

Table 1 lists all of the remunerated pharmacy services available in the province of Ontario (as of 2014-2015) with their corresponding Product Identification Numbers (PINs), or Drug Identification Numbers (DINs), where applicable, as well as the dollar amount reimbursed for these services.

Table 1: Remunerated pharmacy services in Ontario (2014-2015)

Pharmacy Service Name	PIN/DIN	Amount Reimbursed by Ontario Drug Benefits (CAD)
RPh Administered Influenza Vaccine	DIN or PIN of vaccine used[a]: • AGRIFLU®: 02346850 • VAXIGRIP®: 02223929 • FLUVIRAL®: 02015986 • FLUZONE®: 09857501 • FLUAD®: 02362384	$7.50
Pharmaceutical Opinion Program (POP)		
Prescription not Filled	93899991	$15.00
No Change to Prescription	93899992	$15.00
Change to Prescription	93899993	$15.00
Medication Review		
MedsCheck Annual	93899979	$60.00
MedsCheck Diabetes	93899988	$75.00
MedsCheck Diabetes Follow-up	93899989	$25.00
MedsCheck LTC Initial	93899985	$90.00
MedsCheck LTC Quarterly	93899986	$50.00
MedsCheck at Home	93899987	$150.00
MedsCheck Follow-Up (hospital discharge)	93899981	$25.00
MedsCheck Follow-up (pharmacist's documented decision)	93899982	$25.00
MedsCheck Follow-Up (physician/NP referral)	93899983	$25.00
MedsCheck Follow-Up (planned hospital admission)	93899984	$25.00
Pharmacy Smoking Cessation Program (PSCP)		
Initial consultation	93899941	$40.00
Primary Follow-up consultations	93899942	$15.00

Pharmacy Service Name	PIN/DIN	Amount Reimbursed by Ontario Drug Benefits (CAD)
Secondary follow-up consultations	93899943	$10.00
(a) DINS/PINS listed for vaccine products covered by ODB for 2014/2015 flu season**.**		

1.2.1.2 Alberta

Alberta as a jurisdiction has a total of eight professional pharmacy service programs funded by the provincial drug plan. These remunerated services are: extending an existing prescription, administration of injections, medication review and care plan assessment, prescription assessment and adaptation (including therapeutic substitution), assessment for refusal to fill a prescription, assessment for a trial prescription, and prescriptive authority (CPhA, 2016).

Alberta pharmacists have had the ability to prescribe independently since 2007. This prescriptive authority is divided into three categories of prescribing: (1) prescribing to adapt a prescription, (2) prescribing in an emergency, and (3) additional prescribing (Yuskel, 2008). Pharmacists may adapt an existing prescription according to their professional judgement (for example to modify dosage or substitute drugs within the same class), or extend existing prescriptions once the original prescription has run out. Prescribing in an emergency can be undertaken when patients are unable to access their other health care providers in order to receive a new prescription. Finally, additional prescribing authority allows pharmacists to prescribe schedule I drugs and blood products (Yuskel, 2008). Alberta pharmacists who have obtained their Additional Prescribing Authorization (APA) are also able to claim higher program fees for remunerated pharmacy services (Houle, 2014) (see Table 2). Prescriptive authority for pharmacists may be beneficial at improving patient outcomes; Rotta et al. found in their 2015 overview of systematic reviews that the effectiveness of pharmacy services in the management of hypertension and diabetes was greater where pharmacists were able to prescribe independently.

Unlike Ontario, pharmacists have to ability to administer injections other than vaccinations. In fact, pharmacists have the authority to administer *all* injectable products

and can claim a fee for the administration of any product covered by Alberta Drug Benefits (Houle, 2013). Seasonal influenza vaccination is also remunerated by the Province (Houle, 2013). As well, medication reviews in Alberta include a pharmacotherapeutic review, in addition to the adherence review and medication reconciliation review that characterize the Ontario MedsCheck program (Dolovich, 2016). Patients with either two chronic conditions, or one chronic condition plus another risk factor such as smoking or obesity, qualify to receive an annual Comprehensive Annual Care Plan (CACPs), as well as follow-up CACP consultations throughout the year. CACPs are intended to provide patients with information regarding their health and chronic conditions, information about their prescribed medications and medication management, as well as outlining health-related goals (AHS, 2016). Patients who do not qualify for CACPs may instead qualify to receive a Standard Medication Management Assessment (SMMA) if they have diabetes, are taking insulin, or if they have another chronic condition and are taking at least three medications. SMMAs can also be used for health-related goal setting, patient education, and medication management (AHS, 2016).

Table 2 lists all of the remunerated pharmacy services available in the province of Alberta, along with their corresponding PINs and DINs, and the dollar amount reimbursed for these services. While claims are processed by Alberta Blue Cross (ABC) on behalf of the Government of Alberta, these services can be billed for all eligible residents of the province with a valid health card.

Table 2: Remunerated pharmacy services in Alberta

Pharmacy Service Name	PIN/DIN	Amount Billed to ABC (CAD)
Comprehensive Annual Care Plan (CACP)	00000071114[a]	$100.00[a]
	00000081114[b]	$125.00[b]
Follow-up CACP	00000071115[a]	$20.00[a]
	00000081115[b]	$25.00[b]
Assessment for the administration of a publically funded vaccine[c]		
Healthcare Worker	05666603	$20.00
Pregnant Woman	05666646	$20.00
FluMist Administered	05666647	$20.00
Routine Recommended Immunization	05666650	$20.00
Standard Medication Management Assessment (SMMA)		
Chronic Disease	00000071112[a]	$60.00[a]
	00000081112[b]	$75.00[b]

Pharmacy Service Name	PIN/DIN	Amount Billed to ABC (CAD)
Diabetes Mellitus	00000071117[a]	$60.00[a]
	00000081117[b]	$75.00[b]
Tobacco Cessation	00000071118[a]	$60.00[a]
	00000081118[b]	$75.00[b]
Follow-up SMMA		
Chronic Disease	00000071113[a]	$20.00[a]
	00000081113[b]	$25.00[b]
Diabetes Mellitus	00000071117[a]	$20.00[a]
	00000081117[b]	$25.00[b]
Tobacco Cessation	00000071118[a]	$20.00[a]
	00000081118[b]	$25.00[b]
Prescription Adaptation and Prescriptive Authority		
Assessment for prescription renewal	00000071111[a]	$20.00
	00000081111[b]	
Assessment for adaptation of a prescription	00000071111[a]	$20.00
	00000081111[b]	
Assessment for Prescribing at Initial Access or to manage ongoing therapy	00000081116	$25.00[d]
Assessment for prescribing in an emergency	00000071111[a]	$20.00
	00000081111[b]	
Assessment for refusal to fill a prescription	00000071111[a]	$20.00
	00000081111[b]	
Assessment for a trial prescription	00000071111[a]	$20.00
	00000081111[b]	
Assessment for the administration of a product by injection	00000071111[a]	$20.00
	00000081111[b]	

(a) if service performed by Clinical Pharmacist; (b) if service performed by Clinical Pharmacist with APA; (c) PINS listed for administration of publically funded vaccine are for the 2014/2015 flu season; (d) service may only be performed by Clinical Pharmacist with APA; (e) DINS/PINS listed for vaccine products covered by ABC for 2014/2015 flu season.

1.2.2 Community Pharmacists' Role in Prevention and Management of Chronic Disease

Over the last 20 years, the role of the pharmacist has undergone a paradigm shift, becoming increasingly focused on patient-centred care rather than drug distribution (CPhA, 2016; Houle, 2014). This mirrors the gradual transition of pharmacist scope from dispensing of medications to a more cognitive-based role in medication and health management, and the provision of enhanced pharmacist services. Cognitive pharmacy services have also been found to lead to high levels of patient satisfaction (Houle, 2014). Despite this, many pharmaceutical services suffer from low uptake and utilization rates (Houle, 2014). Some barriers to the uptake and use of pharmaceutical services in the community include low rates of reimbursement, pharmacist time constraints, perceived or actual lack of private consultation space within the pharmacy, and lack of public awareness about pharmaceutical services (Houle, 2014; Kelly, 2014). The 2014 survey by Kelly et al. found that the more patients utilized pharmacy services and have more frequent interactions with pharmacists, the more likely they are to seek out clinical pharmacy services in the future. This is corroborated by other studies that report that receipt of pharmacy services can be predicted by previous use of pharmacy services (Pechlivanoglou, 2016; Doucette, 2013)

Many systematic reviews have found that pharmacist-delivered services in community pharmacy settings may help improve clinical and patient health outcomes through medication management services and patient counselling, as well as through the provision of education and drug information to other healthcare providers (Altavela, 2008; Fish, 2002; Houle, 2014; Rotta, 2015; Tan, 2014). Tan et al. reported in their 2014 systematic review that pharmacist-led interventions were more effective at improving patient health outcomes when the services provided were multifaceted and included patient follow-up (as opposed to a pharmacy service such as a single medication review performed in isolation). The effectiveness of pharmacist-led interventions was also found to be improved when pharmacists communicated the results of intervention verbally to physicians (telephone or face-to-face communication, with face-to-face communication preferred).

The 2002 systematic review by Fish et al. reported that all included trials focusing on pharmacist-led hypertension management were found to reduce blood pressure significantly. Rotta et al. found in their 2015 overview of systematic reviews that pharmacy services focusing on hypertension management were able to lead to reductions in systolic blood pressure ranging from 8-11 mmHg. The meta-analysis by Tan et al. (2014) also showed significant reductions in both systolic and diastolic blood pressure

following interventions by pharmacists working in GP offices. A mean difference in systolic blood pressure reduction of 5.72 mmHg was also found, which translates into a 20% decrease in the risk of cardiovascular complications over 5 years. Finally, this review also reported that pharmacist intervention (as part of GP practice) led to a significant reduction in 10-year Framingham risk score. Patient education, counselling, and lifestyle modification recommendations were provided by pharmacists in all interventions showing a significant effect of pharmacist intervention for the prevention of CVD (Tan, 2014). Similarly, the 2015 overview of systematic reviews by Rotta *et al*. found that pharmacist interventions targeting management of hyperlipidemia significantly lowered total cholesterol, and that patients receiving pharmacist interventions were able to reach their cholesterol goals, lower their LDL and triglyceride levels, and improve their HDL more frequently than control patients.

Research has shown that intensive monitoring and follow-up of diabetic patients (including blood pressure and blood glucose monitoring) can significantly reduce morbidity associated with type II diabetes (Choe, 2005). Pharmacy services focusing on diabetes management were shown to lead to a reduction in HbA1C ranging from 0.9-2.1% (Rotta, 2015). Dhippayom et al. (2014) found that when diabetic risk assessment tools were administered by health care professionals, this yielded a higher uptake in risk assessment utilization compared to patient self-assessment. As well, those being screened by health care professionals were able to benefit from well-established diabetes management procedures, including follow-up diagnostic testing or referrals (Dhippayom, 2014).

Although cost-effectiveness outcomes are not frequently reported in pharmacy services literature, the 2014 systematic review by Touchette et al. (2014) focusing on economic outcomes of clinical pharmacy services from 2006-2010 found that clinical pharmacy services are frequently cost effective, and generally have favorable benefit-to-cost ratios (Touchette, 2014). This was also confirmed by the 2014 review by Houle et al. who reported that remunerated pharmacy services were found to have a net cost benefit (Houle, 2014). Sadly, there is a paucity of uptake and outcome data for many remunerated services (Houle, 2014). More high-quality research is required in order to draw conclusions as to the utilization, effectiveness, and cost-effectiveness of many programs implemented across Canada, as well as their impact on hard outcomes (i.e. major cardiovascular events, mortality, health services utilization) and patient quality of life (Houle, 2014).

1.2.3 Community Pharmacies as Locations for Preventative Screening

Medication-related problems also impose a considerable burden on health care systems around the world, and are known to be a significant cause of morbidity and mortality (Dolovich, 2016). People with chronic conditions are frequently older, and may take many medications to manage their condition and co-morbidities. Elderly patients with one or more chronic conditions frequently experience diminished quality of life, poor health, and complications related to medication use. As a population, elderly people with chronic disease are known to utilize the vast majority of healthcare resources, and have more health care visits than other populations (JPHO/CCO, 2012; CIHI, 2011). Polypharmacy, defined here as the concurrent use of 4 or more medications, is a major concern in elderly populations, as well as in those with chronic illness. It is well established in the literature that polypharmacy drastically increases the risk of drug interactions, adverse events, and medication errors (Calderon-Larranaga, 2013). Another issue central to the burden of chronic disease on patients, as well as on the health care system as a whole, is the challenge of multimorbidity. Multimorbidity is defined as the presence of two or more chronic illnesses in a single patient, and it is a major health concern in Canada and around the globe (Calderon-Larranaga, 2013). Multimorbidity is associated with decreased functional capacity, decreased quality of life, increased health service utilization, and polypharmacy (Calderon-Larranaga, 2013). At the health care system level, it may promote saturation and misuse of health care services (Calderon-Larranaga, 2013). Furthermore, it is often challenging for health care providers to manage multiple disease states in patients (Calderon-Larranaga, 2013). Clinical practice guidelines may not take multiple morbidities into consideration, and prescribers must be careful to weigh the risks and benefits of pharmacotherapy where co-morbidities and polypharmacy are present (Calderon-Larranaga, 2013). The negative effects of medication-related problems, polypharmacy and multimorbidity may be mitigated by pharmaceutical care, medication management, and regular monitoring by skilled pharmacists. Thus, community pharmacists have an emerging and important role in promoting CVD and stroke prevention, due largely to their role as experts in the safe and effective use of medications, and medication management (Touchette, 2014).

Pharmacists are amongst the most accessible primary care providers (Gasdek Manolakis, 2010). Moreover, pharmacists are highly trusted by patients, and most patients report high levels of satisfaction with the services provided within community pharmacies (Kelly, 2014). A 2010 study by Cavaco et al. found concluded that the less formal atmosphere of the community pharmacy, combined with less structured

questioning behaviour on the part of the pharmacist, contributed to study participants feeling less restricted within the conversation. The 2014 survey by Kelly et al. found that overall, patients felt comfortable discussing their health with pharmacists, and that they trusted pharmacists to maintain the confidentiality of their health information. Patients indicated that they were comfortable with pharmacists having access to their medical information, and even noted that pharmacists with increased access to medical information often provide better patient care. Patients were also in favour of collaboration between their pharmacist and physicians in order to provide better patient care. Over half of surveyed patients responded that they would use community pharmacy screening services if they were made available (Kelly, 2014).

By taking part in both organized and opportunistic patient screening, pharmacists can help identify patients yet to be formally diagnosed with a condition, but who may benefit from medical or therapeutic intervention to prevent progression of disease nonetheless. The highly accessible environment of a community pharmacy can provide easy access for patients who might not otherwise receive regular preventative screening opportunities. In-pharmacy screening may also help reduce the burden on other primary care providers, such as family physicians. Routine and opportunistic screening for cardiovascular and cardiometabolic conditions have been found to have low adoption rates by primary care physicians in routine practice, despite the fact that their use is frequently recommended by many different practice guidelines (Dhippayom, 2014; Kaczorowski, 2009). Some of the barriers preventing more frequent utilization of risk assessment tools by primary care physicians include a lack of knowledge or training, time constraints, and perceived interference with the patient-physician relationship (Dhippayom, 2014). Since uptake rates are low in these primary care settings, community pharmacies may be ideally situated to step in and fill this void by providing screening services to the general public (Dhippayom, 2014). For these reasons, community pharmacies may be ideal locations for preventative screening of chronic disease.

1.3 CHAP Model

1.3.1 Introduction to the CHAP Model

The Cardiovascular Health Awareness Program (CHAP) is a volunteer-led program, utilizing trained lay-persons in the community to administer free screening and monitoring interventions (such as CVD risk assessment and blood pressure monitoring) to community-dwelling elderly individuals (Kaczorowski, 2011). A variety of programs based on the overarching CHAP model have been successfully implemented in several

primary care and residential locations (including community pharmacies) across Canada (Karwalajtys, 2013; Agarwal, 2013). As such, the CHAP model can be used as a robust and evidence-based framework for which to model and operationalize community pharmacy screening programs.

In 2006, the CHAP model was compared to usual care in a large-scale, cluster-randomized trial taking place in 39 mid-size communities across Ontario. 20 of these communities were randomized to receive the CHAP intervention, with the remaining 19 continuing to provide usual care to residents without receiving the intervention (Kaczorowski, 2011). The CHAP intervention consisted of 3 hour risk factor assessment and educational sessions held in local community pharmacies, provided for 10 weeks. A total of 1265 sessions were held across all intervention communities. During these sessions, volunteers took blood pressure readings, provided participants with educational and self-management resources, and informed participants of local community resources (Kaczorowski, 2011). A community health nurse provided additional counselling and follow-up to those patients with raised systolic blood pressure. Additionally, pharmacists were available at each study location to provide medication management counselling where required. Blood pressure readings for consenting participants were subsequently sent to their primary care physician and community pharmacist (Kaczorowski, 2011).

Key elements of the CHAP intervention include the following: (1) community-wide orientation of program to reach all members of the target population, and provision of the intervention at no cost to participants; (2) linkage to appropriate healthcare providers; (3) accessible location/setting and enhanced continuity of care; (4) Blood pressure measurement device and accurate measurement of blood pressure; (5) referral for follow-up; (6) global cardiovascular risk factor assessment and education to raise awareness and provide resources to community members; (7) Feedback of participant results to primary healthcare providers; and (8) Process evaluation of the program. These elements encompass the CHAP model, and are in line with the recommendations set out by the WHO to encourage prevention and monitoring in those at risk of CVD (Kaczorowski, 2011).

The CHAP intervention was successful in its implementation in all 20 intervention communities, and results from the trial found that the intervention was able to significantly reduce the rate of CVD-related hospitalizations in elderly patients aged 65 years or older by 9% at the population level (Kaczorowski, 2011). CVD-related hospitalizations were defined as a composite outcome of hospital admissions with a primary discharge diagnosis of acute MI, congestive heart failure (CHF), or stroke. Separating out the individual hospitalizations from the composite reveals that the CHAP

intervention led to significant reductions in hospitalizations for MI and CHF, although there were no significant reductions for hospitalizations dues to stroke (Kaczorowski, 2011).

While the original CHAP trial focused on hypertension, the CHAP model has subsequently been adapted to target facets of CVD, as well as other health issues in elderly community-dwelling patients, such as type II diabetes (Community Health Awareness of Diabetes, CHAD),(Agarwal, 2013; Karwalajtys, 2013). The CHAP model is also currently being piloted in The Philippines, to determine whether the CHAP model can be used successfully in developing countries (GACD, 2017). The PIAAF Pharmacy study (described below) is an example of a community pharmacy-based screening pilot program that follows the CHAP model.

1.3.2 How the CHAP model can be used in the Community Pharmacy Setting

As stated above, the CHAP model has already demonstrated success in implementing hypertension screening sessions within community pharmacies, and has shown that use of this model can significantly improve health outcomes for community members (Kaczorowski, 2011). The PIAAF Pharmacy study built upon the original CHAP study by piloting screening for atrial fibrillation and type II diabetes risk in addition to blood pressure screening.

The CHAP model has many benefits that would make it an ideal framework for future community pharmacy screening initiatives (Kaczorowski, 2011). Five major benefits are listed here: 1) since the CHAP model is volunteer-based, this takes the onus of running the screening program off of pharmacy staff. Pharmacy staff are able to complete their day-to-day dispensing and cognitive services without the screening initiative impeding heavily on their workflow. 2) Patients who screen at high risk of cardiovascular or cardiometabolic conditions have the opportunity to speak with the pharmacist about their screening results in a timely manner. 3) Pharmacists are able to provide patient counselling and education, and may also be able to provide advice in terms of lifestyle modification and medication management. 4) Pharmacists can also serve as gatekeepers for at-risk patients to initiate or modify therapy, and can act as a liaison between patients and other health care providers to initiate or modify therapies as needed. In the special case of Alberta, many pharmacists are able to initiate medication therapy themselves. 5) Screening in community pharmacies gives pharmacists the opportunity to identify those who would benefit from pharmacy services (e.g. medication review, smoking cessation

counselling), and allows for pharmacists to monitor patients on a regular basis (Kaczorowski, 2011).

1.4 PIAAF Pharmacy Study Objectives and Target Population

The Program for the Identification of "actionable" atrial fibrillation was an organized, community pharmacy intervention to screen elderly, community-dwelling individuals for AF, hypertension, and type II diabetes. Screening clinics were held in 30 community pharmacies in the Hamilton, Ontario and Edmonton, Alberta regions from October 2014 to April 2015. Participants were invited to screening sessions, which were promoted through the Rexall website, by the participating pharmacies, and through the Heart and Stroke Foundation. The screening sessions were run by volunteers from the Heart and Stroke Foundation, and followed the CHAP model of community-based, volunteer-run educational and screening interventions.

1.4.1 Objectives and Target Population

The primary objective of the PIAAF Pharmacy study is to determine the prevalence of "actionable" AF in the study population. "Actionable" AF is defined as AF being detected in a patient who is not currently taking medication for AF, is not contraindicated for OAC therapy, and in whom treatment for AF is possible and appropriate (Sandhu, 2014; Dolovich, 2014). 1175 seniors, aged 65 years old or older from Hamilton, Ontario, and Edmonton, Alberta attended PIAAF Pharmacy screening sessions. Inclusion criteria for the study were: Patients aged 65 years or older; and patients capable of providing written consent (Sandhu, 2014; Dolovich, 2014). Exclusion criteria for the study were: inability for the patient or their caregiver to read or understand English; patients with previously confirmed or diagnosed AF already receiving anticoagulation therapy; and patients considered potentially unreliable by the investigators or pharmacy team in terms of ability to complete follow-up (Sandhu, 2014; Dolovich, 2014).

1.4.2 Description of Intervention

The PIAAF Pharmacy intervention involved the screening of patients 65 years or older for type II diabetes, high blood pressure, and AF. AF was detected using a single-lead, handheld ECG. Patients who screened positive for AF were sent for additional screening and confirmation of AF using a 12-lead ECG. Patients were also scheduled for 6 week and 3 month follow-up appointments with their general practitioner or at an AF clinic. Patients with known AF, who were not on OAC therapy at the time of screening, were

similarly scheduled for follow-up appointments at 6 weeks and 3 months at an AF clinic (Sandhu, 2014; Dolovich, 2014).

Blood pressure was measured using the PharmaSmart blood pressure kiosks located within each participating pharmacy. Additionally, patients aged 65-74 were screened for type II diabetes using the CANRISK questionnaire. The CANRISK criteria screening tool was developed in Canada, and is based on a similar tool used in Finland. However, CANRISK has been augmented to better reflect Canada's multi-ethnic population, and to include additional risk factors for diabetes including smoking status, family history of diabetes, and history of gestational diabetes (Kaczorowski, 2009).

Patients who were found to have high blood pressure received follow-up visits with a physician within a maximum of 3 days depending on the severity of hypertension. Patients normal blood pressure were not scheduled for follow-up, and simply resumed their regular schedule of blood pressure testing (Sandhu, 2014; Dolovich, 2014). Patients screened as being at high risk of type II diabetes were recommended to undergo blood testing for HbA1C level in order to confirm risk. Those at high and intermediate risk of type II diabetes received patient education from the pharmacist, and a letter outlining risk factors and recommendations was sent to the patient and their physician (Sandhu, 2014; Dolovich, 2014).

1.4.3 How can the PIAAF Pharmacy Study be used to Investigate the Role of Pharmacists in Community Screening Interventions?

Patients screening positive for AF, those found to have hypertension, and those found to be at intermediate or at high risk for diabetes would likely be ideal candidates for pharmacy services such as medication reviews, prescription adaptation services, and smoking cessation services. It was hypothesized that pharmacists would be able to use the results from the screening sessions as an opportunity to identify patient risk factors and reach out to participants who would be likely to benefit from such services.

There is a paucity of literature investigating how pharmacy services are used in conjunction with community pharmacy screening initiatives. Moreover, some data suggests that in real-world settings, the people who are actually receiving services such as medication reviews are often patients with more simple medication regimes, and not complex patients for whom such services would likely be more beneficial (Dolovich, 2016). Therefore, the PIAAF-PPS is a secondary analysis of data synthesized from the PIAAF Pharmacy study, pharmacy claims data, as well as data taken from patient pharmacy profiles. The aims of this study are to determine how pharmacy services are

being utilized post-screening, and to analyze the variables associated with receipt of pharmacy services. The implications from these findings can thus be applied to other community pharmacy screening programs, as well as to programs and screening interventions held in other community-based locations where patients are likely to be referred to pharmacists.

2.0 CHAPTER 2: RESEARCH QUESTIONS AND HYPOTHESES

2.1 Program for the Identification of Actionable Atrial Fibrillation—Analysis of Professional Pharmacy Services

This thesis project will build on the results of the PIAAF Pharmacy study by analyzing and describing the use of professional pharmacy services in study participants. Pharmacy services have been shown to improve various patient health outcomes (Leyden, 2013; Tsuyuki, 2002; Houle, 2012; Lee, 2013). It is difficult, however, to determine whether or not these pharmacy services are being provided to those who would stand to benefit the most, especially following screening interventions. Elderly patients and patients with chronic disease generally have more medication management issues than other populations; therefore, these patients may benefit more from pharmaceutical services than others (Dolovich, 2016; Isaksen, 1999; Lee, 2013). This project will investigate whether in-pharmacy screening initiatives such as PIAAF are being used as opportunities for pharmacists to reach out to patients at risk, by examining whether or not people at higher risk levels for chronic disease receive more pharmacy services than those at lower risk. It will describe the use of pharmacy services following a community screening intervention, and it will also explore the patient-, pharmacy-, and community-related factors that may be associated with whether or not a patient receives a pharmacy service. Finally, this project will investigate whether or not community pharmacy screening interventions such as the PIAAF Pharmacy study promote the use of pharmacy services.

2.2 Research Questions

The primary research question addressed by this study is:

Are PIAAF Pharmacy participants who screened as being positive for AF and hypertension, or those screened as being at high or intermediate risk for type II more likely to receive a pharmacy service than those screening negative or at lower risk?

Secondary research questions are:

What are the utilization statistics of pharmacy services in PIAAF Pharmacy study participants within 3 months of screening?

What are the patient-level, pharmacy-level, and community-level factors that influence use of pharmacy services within 3 months of PIAAF screening?

Do participating pharmacies perform more pharmacy services during or within 3 months following the PIAAF Pharmacy study intervention?

2.3 Hypotheses

The hypothesis for the primary objective of the PIAAF-PPS study is:

1. Patients with chronic disease, those screening positive for AF, and patients at risk for type II diabetes and hypertension will be more likely to receive enhanced professional pharmacist services than those without chronic disease or who are screened as being negative for AF, or at low risk for chronic disease.

3.0 CHAPTER 3: METHODOLOGY

3.1. Data Collection

3.1.1 Analysis of Service Recipients—Descriptive Analysis and GEE Models

Data was collected from two sources: case report forms (CRFs) for each PIAAF Pharmacy participant, collected at the time of screening and housed at the Population Health Research Institute (PHRI); and participant pharmacy profile data, including billing data and current medication lists. The first step in data collection was extraction of patient data and information from CRF forms, which was subsequently used to locate and extract data from patient pharmacy profiles. PIAAF participants signed an informed consent package authorizing the study team to access their pharmacy profile and collect data. Ethics approval for the study was obtained from the Hamilton Integrated Research Ethics Board (HiREB).

3.1.1.1 Data extraction from the Population Health Research Institute

Data from the PIAAF Pharmacy study was collected at the time of screening by the study team, and at follow-up appointments where applicable. This data was collected in CRFs, which are housed at PHRI. Data was extracted and validated by the PHRI PIAAF Pharmacy study team.

Data extracted from case report forms used for the PIAAF-PPS analysis in conjunction with pharmacy data included: (1) patient name and date of birth, (2) pharmacy at which screening was performed, (3) date of screening, (4) self-reported medication use, (5) self-reported chronic conditions and limited clinical history, (6) blood pressure readings at time of screening, (7) whether AF was suspected based on results of SL-ECG screening, (8) CANRISK screening results, and (9) smoking status. Extracted CRF data for 1149 PIAAF Pharmacy participants were sent.

3.1.1.2 Data extraction from Rexall Pharmacies

Patient name and date of birth, extracted from the CRFs, were used to locate patient pharmacy profiles held at participating pharmacies. Information from pharmacy profiles, where possible, was extracted by Nexxsys software specialists at Rexall head office

(Mississauga, Ontario). Once pharmacy profile data was extracted and delivered to the PIAAF-PPS study team, patient information was immediately anonymized using pre-existing participant identification numbers created at the time of screening.

For PIAAF participants with an existing Rexall pharmacy profile, the following data was collected, where possible: (1) audit histories for all PINS/DINS billed from October 1, 2014 to October 31, 2015 including fill date, quantity dispensed, quantity authorized, drug or product identification number (DIN or PIN), and prescription status (e.g. completed, cancelled); (2) a list of any chronic conditions/diagnoses listed in a patient's pharmacy profile.

For each participating Rexall pharmacy, the following data was collected: (1) claim reports and audit histories for 19 PINS/DINS billed to Alberta Blue Cross for pharmacy services, from Jan 1, 2014 to Dec 31, 2015 for the participating Alberta pharmacies (including date billed and DIN/PIN billed); and (2) claim reports and audit histories for 21 PINS/DINS billed to ODB for pharmacy services (see list below), per store, from Jan 1, 2014 to Dec 31, 2015 for the participating Ontario pharmacies (including date and DIN/PIN billed). Each participating pharmacy held multiple screening sessions, and each began the screening intervention period at different times (the earliest sessions began in October, 2014 and the last ended in April, 2015). Therefore, for each participating pharmacy, the period of time beginning on Jan 1, 2014 and ending on the date of its first screening session, was considered the baseline period for that pharmacy.

All participants who reported that the pharmacy at which they were screened was also their primary pharmacy were included in the PIAAF-analysis. This information was recorded in CRFs. Patients whose regular pharmacy was reported as being different from the pharmacy at which they were screened were also included in the PIAAF-PPS analysis *if* a partial pharmacy profile was identified, or if they were found to have received a pharmacy service at the pharmacy at which they were screened. Where possible, all current medications and billing data were extracted from profiles.

In some instances, pharmacy data could not be retrieved for patients who reported the pharmacy at which they were screened as being their primary pharmacy. This may have occurred for several reasons, including death of a participant or admission into long-term care (both of which will result in pharmacy profiles being inactivated at the pharmacy level). It is also possible that patients may not have had any prescriptions filled at the pharmacy at which they were screened during the timeframe under investigation. In cases where a pharmacy record could not be retrieved for participants, or where profiles were incomplete, self-reported data from the CRFs was used to impute number of medications.

3.2 Data Analyses

3.2.1 Descriptive Analyses

Descriptive analyses were performed to report on the utilization of pharmacy services by PIAAF Pharmacy study participants. Descriptive statistics presented include the mean number of pharmacy services provided within 3 months of screening, per participant, per region, and per pharmacy; mean dollar amount of pharmacy services billed to provincial drug plans within 3 months of screening per participant, per region, and per pharmacy; counts of each type of pharmacy service provided within 3 months of screening per region, and per pharmacy; and pre- and post-intervention differences in number of pharmacy services provided per pharmacy. All descriptive analyses were performed using SPSS statistical software, version 23.

3.2.2 Conceptual Framework

A conceptual framework was created to describe factors that may be associated with pharmacy service receipt in PIAAF Pharmacy participants. This framework was developed by reviewing pharmacy services literature and similar theoretical models exploring medication review delivery (Pechlivanoglou, 2016; Chan, 2003). Potential factors of pharmacy service delivery that are supported by evidence have been included in the framework, which consists of four major components: 1) patient-related factors, 2) pharmacy-related factors, 3) community-related factors, and 4) participation in PIAAF Pharmacy screening. All factors included in the conceptual framework are summarized in Table 3. Due to the limitations of the available data, not all factors identified in the conceptual framework were able to be included in the inferential analysis. A visualization of the conceptual framework is presented in Appendix 1.

Table 3: Four major components of the PIAAF-PPS conceptual framework and their factors

Component	Factor	Potential to influence patient receipt of pharmacy services	Included in the PIAAF-PPS analysis	Reference
Patient-related	Age	-Only those >65 eligible for some services -Older people tend to receive more medication reviews	Yes	-Brooks, 2008 -Thompson, 2004 -Ignacy, 2015 -Dolovich, 2016 -MSP, 2014 -Pechlivanoglou, 2016
	Sex	-Some studies report that women are more likely to be offered and to receive medication reviews, as well as asking pharmacists more health-related questions	Yes	-Schommer, 2002 -DeSimone, 1977 -Brooks, 2008 -Pechlivanoglou, 2016
	Smoking status	-Smokers may seek pharmacy services for smoking cessation -Smokers may have other health problems leading to an increased need for pharmacy services	Yes	-MOHLTC, 2013 -CPhA, 2016

Component	Factor	Potential to influence patient receipt of pharmacy services	Included in the PIAAF-PPS analysis	Reference
Patient-related	Co-morbidities	-Patients with multiple co-morbidities are linked to polypharmacy and may have an increased likelihood of receiving pharmacy services -Recipients of MedsCheck Annual have been found to have high levels of co-morbidity	Initially, then removed (see p.32)	-El Hajji, 2014 -Ignacy, 2015 -Gandhi, 2003 -Government of BC, 2016 -Dolovich, 2016 -Pechlivanoglou, 2016
	Poly-pharmacy	-Polypharmacy is known to increase with age and may cause real or potential drug related problems -Number of medications is positively correlated with likelihood of receiving a pharmacy service -Average number of medications used in MedsCheck Annual recipients was found to be higher than elderly patients in the general public	Yes	-Brooks, 2008 -El Hajji, 2014 -Kovacevic, 2014 -Gandhi, 2003 -Government of BC, 2016 -Dolovich, 2014 -Pechlivanoglou, 2016

Component	Factor	Potential to influence patient receipt of pharmacy services	Included in the PIAAF-PPS analysis	Reference
Patient-related	New prescriptions	-Patients who receive a new medication are more likely to have a consultation with a pharmacist -New prescriptions represent opportunities for pharmacists to initiate pharmacy services	Yes	-Schommer, 2002 -MOHLTC, 2008 -Pechlivanoglou, 2016
	Medication adherence challenges	-Patients with adherence challenges may stand to benefit from pharmacy services -Can be used as an opportunity for pharmacists to initiate pharmacy services	No	-MOHLTC, 2008 -MSP, 2014 -Samoy, 2006 -Pechlivanoglou, 2016
	New diagnoses	-It is recommended that patients receiving new diagnoses should undergo medication review	No	-MSP, 2014

Component	Factor	Potential to influence patient receipt of pharmacy services	Included in the PIAAF-PPS analysis	Reference
Patient-related	Past use of pharmacy services	-Prior medication review was found to be a predictor of subsequent medication reviews -Certain pharmacy services are annual-only, which may influence what services they may receive within a given timeframe	Yes	-Pechlivanoglou, 2016 -Kelly, 2014
	Prior hospital-ization or recent hospital discharge	-Patients who have had a recent hospital discharge, or who have been in hospital are recommended to receive medication reviews in order to reconcile medications -Many MedsCheck Annual participants were found to have been hospitalized both before and after receiving the service	No	-El Hajji, 2014 -MOHLTC, 2008 -MSP, 2014 -Government of BC, 2008 -Dolovich, 2016

Component	Factor	Potential to influence patient receipt of pharmacy services	Included in the PIAAF-PPS analysis	Reference
Patient-related	Real/ potential drug problems	-Patients who are experiencing any real or potential drug problems have a clinical need for medication review and other pharmacy services -Pharmacy services can be used to identify and resolve drug-related problems	No	-Government of BC, 2016 -Samoy, 2006
	Use of potentially inappropriate medications	-It is recommended that all patients taking potentially inappropriate medications receive medication reviews	Yes	-El Hajji, 2014 -Gandhi, 2003 -MOHLTC, 2008 -MSP, 2014 -Government of BC, 2016 -Dolovich, 2016 -Pechlivanoglou, 2016
Pharmacy-related	Pharmacy volume	-Higher pharmacy volume is correlated with increased provision of medication reviews	No	-Bradley, 2008 -Pechlivanoglou, 2016
	Ownership type	-Chain pharmacies are correlated with increased provision of medication reviews -Chain pharmacies may set pharmacy service quotas	No—all partici-pating pharmacies are owned by the same chain	-Bradley, 2008

Component	Factor	Potential to influence patient receipt of pharmacy services	Included in the PIAAF-PPS analysis	Reference
Pharmacy-related	Pharmacist training and confidence in abilities	-Pharmacist training and confidence in their abilities has been positively linked with implementation of medication review programs	No	-Bradley, 2008
	Pharmacist motivation	-Pharmacist motivation has been identified as a facilitator of medication review implementation	No	-Bradley, 2008
	Support from physicians	-Lack of GP support identified as a major barrier to medication review implementation	No	-Bradley, 2008
	Time management and workflow	-Pharmacists are more likely to provide pharmacy services if they can be effectively incorporated into pharmacy work flow	No	-Bradley, 2008
	Number of pharmacists	-Interview data suggests that stores with more pharmacists may be able to provide more pharmacy services than those with less	No	-Bradley, 2008

Component	Factor	Potential to influence patient receipt of pharmacy services	Included in the PIAAF-PPS analysis	Reference
Community-related	Jurisdiction	-There are differences between the number and types of pharmacy services available in individual jurisdictions	Yes	-CPhA, 2016
	Urbanity/ rurality	-Patients may be less likely to receive medication reviews the further away they live from a pharmacy -Those living in urban centres may receive more medication reviews	No. All partici-pating pharmacies are urban	-Brooks, 2008 -Dolovich, 2016 -Pechlivanoglou, 2016
	SES	-Lower SES is associated with a lower likelihood of receiving medication reviews services	Yes	-Bradley, 2008 -Pechlivanoglou, 2016
PIAAF Screening-related	AF detected on SL-ECG	-As with new diagnoses, patients with suspected AF may benefit from speaking with their pharmacist and receiving pharmacy services	Yes	-MSP, 2014

Component	Factor	Potential to influence patient receipt of pharmacy services	Included in the PIAAF-PPS analysis	Reference
PIAAF Screening-related	CANRISK score	-Patients who are at risk of diabetes may benefit from speaking with their pharmacist and receiving pharmacy services -Specific medication reviews are targeted towards those with diabetes	Yes	-CPhA, 2016
	Hypertension present at time of screening	-Patients with high blood pressure may benefit from speaking with their pharmacist and receiving pharmacy services -The majority of MedsCheck Annual recipients were found to have hypertension, and most were found to be using antihypertensives	Yes	-Dolovich, 2016 -Pechlivanoglou, 2016

3.2.3 Regression Analyses

Regression analyses were performed to investigate whether or not receipt of pharmacy services is higher in at-risk patients than low-risk patients, and to estimate the association of the predictor variables identified by the conceptual framework with the receipt of pharmacy services in PIAAF Pharmacy participants. This was done in two parts: 1) the total number of all pharmacy services received was modeled as a count, and 2) individual groups of pharmacy services, namely medication review and provision of flu shots, were

modeled separately as binary outcomes (did patient receive medication review service/flu shot, yes or no?).

Before being included in regression models, all potential factor variables were tested for multicollinearity by running a simple linear regression and examining the tolerance and variance inflation factor (VIF) for each. In this case, VIF represents the amount of variation within a variable that is attributable to the other independent variables included in a regression model (O'Brian, 2007). As a rule of thumb, many researchers consider a VIF of $\geq$10 and a tolerance of $\leq$ 0.10 to indicate excessive multicollinearity; however, in weaker models, even variables with lower VIFs may cause problems (O'Brian, 2007). All 14 measureable factor variables were found to have VIFs of <2.6 and tolerances of > 0.38. Number of medications had the highest VIF, at 2.52, with a tolerance of: 0.40. Co-morbidity score was calculated using CRF and pharmacy profile information (age, gender, presence of chronic conditions) following the steps outlined by Clark and Von Korff (1995). It was found to have a relatively large amount of multicollinearity with other variables, showing a VIF of 1.74 and a tolerance of 0.58. Since the comorbidity score was calculated using patient factors such as age and gender that were already included in the models as variables, it was removed. This caused the VIF of number of medications to drop to 2.11 with a tolerance of 0.47. Therefore, the following 14 factors identified in the conceptual framework were used as independent variables within the regression models:

- **Age**: used as a continuous variable, calculated as age at time of screening using patient's date of birth and date of screening.
- **Gender**: used as a dichotomous variable (male/female) based on patient self-report on CRFs.
- **Month of screening**: Although this variable was not included in the conceptual framework, it became apparent during descriptive analysis that the month in which screening took place played a large role in the provision of pharmacy services. This was used as a categorical variable based on the month that participants were screened in (October, November, December, January, February, March, and April), based on screening date recorded on CRFs.
- **Number of medications**: used as a continuous variable, based on pharmacy and CRF data. This was estimated based on either available pharmacy data, or where no data could be extracted, on medication self-reports recorded in CRFs. Number of unique prescription (and OTC, where possible) medications was counted using pharmacy claims or CRF data. While most OTC products were unable to be detected, except in a few rare cases. However, low-dose ASA was included in the medication self-report

portion of the CRFs and was noted at time of screening, due to its role in the treatment of CVD and prevention of cardiac events.

- **New medications received either a month prior to screening or within three months post-screening**: used as a dichotomous variable (yes/no). As with number of medications, this was extrapolated based on pharmacy data where available. Pharmacy claims data was examined for repeating patterns of medications being billed before, during, and after the 3-month post-screening period—any novel medications either billed one month prior to screening, or within 3 months post-screening, were considered new medications.
- **Number of potentially inappropriate medications**: used as a continuous variable. High risk medications were defined based on inclusion in the American Geriatrics Society's 2015 updated Beers Criteria list of potentially inappropriate medications in elderly patients. Pharmacy data was used to determine whether or not a patient was considered to be on a high risk medication. If a Beers criteria medication was found in a patients' pharmacy profile (and was likely to be in use by the patient at the time of screening), this was counted as a potentially inappropriate medication.
- **Number of cigarettes smoked per day**: used as continuous variable based on CRF self-reports, with participants identifying as non-smokers coded as smoking 0 cigarettes per day.
- **Prior annual-only medication review within a year of screening**: used as a dichotomous variable (yes/no) based on whether the patient received an annual-only medication review within the year prior to screening (i.e. MedsCheck Annual, MedsCheck Diabetes, MedsCheck at Home, CACP, and SMMA). This was measured by linking PIAAF participants to pharmacy services billed by each participating pharmacy in 2014-2015.
- **Eligible for annual-only medication review**: this was used as a dichotomous variable (yes/no) to determine whether or not participants were eligible for annual-only medication reviews (i.e. MedsCheck Annual, MedsCheck Diabetes, MedsCheck at Home, CACP, and SMMA) based on timing of previous annual-only medication review, number of chronic medications used (e.g. $\geq$3 for MedsCheck), and co-morbidities (e.g. diabetes).
- **Jurisdiction**: used as dichotomous variable based on which province participants were screened in (Ontario/Alberta).
- **Socioeconomic deprivation score**: used as a continuous variable, based on the deprivation score of the Canadian Marginalization Index for the census zone in which each participating pharmacy is located (or adjacent to) (Matheson, 2012).

- **AF Suspected on SL-ECG**: used as a dichotomous variable based on data taken from SL-ECG at time of screening (yes/no). Screening results were recorded on CRFs.
- **CANRISK score**: used a categorical variable to differentiate between patients without known diabetes who were not screened, patients with known diabetes who were not screened, patients who were screened at being of low risk of diabetes, patients screened as being at intermediate risk of diabetes, and patients screened as being at high risk of diabetes (not screened, low risk, intermediate risk, high risk, known diabetes). CANRISK scores were recorded on CRFs.
- **Average Diastolic Blood Pressure**: as a continuous variable. This variable was selected over both average systolic blood pressure (continuous variable) and whether or not patient had high blood pressure at time of screening (dichotomous variable), as it performed better in analyses than the other two variables as a predictor of number of pharmacy services (improved model goodness-of-fit). At time of screening, patients had their blood pressure measured at least twice. The average systolic and diastolic scores were recorded on CRF forms.

3.2.3.1 Total Number of All Pharmacy Services Received

The dependent variable for this analysis was the number of pharmacy services received per participant in the 3 months immediately following screening in the PIAAF Pharmacy study; a count variable. Poisson distributions are frequently used to model count data. However, the Poisson distribution requires that the conditional mean and variance of the dependent variable are equal (Lawless, 1987). The Poisson distribution has only one parameter, meaning the variance cannot be adjusted independently of the mean. In situations where the variance is greater than the mean, the data is said to be overdispersed, and the model may not fit the data appropriately. Overdispersion of count data is very common, and therefore a different approach is sometimes required (Lawless, 1987; Bruce, 2007). A negative binomial distribution is also a discrete distribution, but it has two parameters and thus allows for the variance to be adjusted independent of the mean (Lawless, 1987). In situations where overdispersion is present in the data, negative binomial distributions will provide a better fit for models (Lawless, 1987). In order to determine whether a Poisson or negative binomial distribution was more appropriate for this model, the first step was to determine whether the data was overdispersed.

To measure dispersion, a generalized linear model (GLM) using the variables given above was run using a Poisson distribution and a log link. Dispersion can be measured by dividing the deviance by the degrees of freedom (df), and also by dividing the Pearson

Chi-Square statistic by df. Overdispersion is present where these ratios are > 1. Where these ratios are ≅ 1, the variance and the mean are equal; the data is equidispersed, and the Poisson distribution will be a better fit. The results of this analysis showed $deviance/df = 0.83$ and $Pearson\ Chi\ Square/df = 0.95$, showing slight underdispersion. Underdispersion occurs when there is less variance then would be expected (Kokonendji, 2014). While underdispersion is relatively rare (especially compared to overdispersion, which is far more common), it has been known to occur from time to time in data sets (Bruce, 2007). Goodness of fit statistics from this model are presented in Table 4.

Table 4: Goodness of fit statistics from the initial generalized linear Poisson model

Measure	Value	Degrees of Freedom (df)	Value/df
Deviance	378.73	457	0.83
Scaled Deviance	378.73	457	--
Pearson Chi-Square	431.66	457	0.95
Scaled Pearson Chi-Square	431.66	457	--
Log Likelihood	-357.41	--	--
Akaike's Information Criterion (AIC)	760.83	--	--
Finite Sample Corrected AIC (AICC)	763.25	--	--
Bayesian Information Criterion (BIC)	856.82	--	--
Consistent AIC (CAIC)	879.82	--	--

One common reason for unexpected underdispersion of count data is the presence of clustering effects due to cluster sampling. In this data set, each participating pharmacy where screenings were held is considered a cluster. There may be factors present at the pharmacy level that influence whether or not a patient received a pharmacy service, and therefore patients screened at a particular pharmacy may have more in common with each other than those screened at different pharmacies. It is possible that this clustering effect is at least partially responsible for the underdispersion present in this data set. Other causes of underdispersion of data include small sample sizes, correlation of response items, and heterogeneity of the study population (Kokonendji, 2014).

In order to determine how clustering may have influenced these results, an intra-cluster correlation (ICC) was estimated. ICC was calculated by performing a one-way ANOVA and using the following formula:

$$ICC = \frac{BMS - WMS}{BMS + (m' - 1)WMS}$$

Where BMS is the between-cluster mean square, WMS is the within-cluster mean square, and m' is the adjusted mean cluster size, using the formula:

$$m' = \frac{1}{k-1}\left(n - \frac{\sum_k m_k^2}{n}\right)$$

with k as number of clusters, n as total number of participants, and m as cluster size (Wears, 2002). The ICC was found to be 0.07. The variance inflation factor (VIF) here can be defined as a constant which helps to determine the variance of the overall mean of cluster data, and can help determine whether clustering effects are large enough to be taken into account during analysis:

$$VIF = 1 + (m' - 1)ICC$$

Generally speaking, where $VIF \geq 2$, clustering effects are considered to be important and should be taken into account when performing statistical analysis (Wears, 2002). The VIF here was determined to be 2.32, and it was determined that clustering would have to be taken into consideration when performing regression analysis on this this data set.

In order to model the total number of pharmacy services received as a count, a generalized estimating equation (GEE) was modelled. A mixed-effect zero-inflated Poisson (ZIP) regression was also performed as a sensitivity analysis.

3.2.4 Generalized Estimating Equation Models

GEE modelling was selected as the effect of clustering at the pharmacy level on pharmacy services data must be taken into account. GEE is an extension of the GLM. These models are often used to analyze longitudinal data and other instances where response variables are highly correlated due to clustering, as they are able to estimate regression parameters more efficiently and produce more accurate standard errors where observations are correlated (Hanley, 2003; Cui, 2007). GEEs are generally not used for prediction of events, but rather, to estimate an effect over a population. They are flexible, as they allow for specification of models, distributions, and correlation structures to be used (Hanley, 2003; Wang, 2003). Furthermore, GEE models can be used in situations

where data is either over or underdispersed, as the scale parameter will correct for this (Bruce, 2007).

The primary GEE model will be used to estimate the effect of the factors identified by the conceptual framework on the number of pharmacy services received by the PIAAF-PPS cohort. The dependent variable for this model will be the number of pharmacy services received within 3 months of PIAAF Pharmacy study screening. As the dependent variable for this model analysis is a count, the GEE will require selection of a discrete distribution. Since the count data was found to be slightly underdispersed, a Poisson distribution was used in conjunction with a logit link function. The working correlational structure (WCS) selected was exchangeable. In order to test the robustness of the GEE, sensitivity analyses were also performed using a Poisson distribution with an unstructured WCS, a negative binomial distribution with an exchangeable WCS (Wang, 2003). These count models are presented using incidence rate ratio (IRR), which can be interpreted as the rate of receipt of pharmacy services.

A final sensitivity analysis was performed where the dependent count variable was transformed into a dichotomous variable (did the participant receive a pharmacy service, yes or no) and modeled using a binomial distribution with a probit link function (which was found to fit the model slightly better than when a logit link function was used) and an exchangeable WCS. These models are presented separately from the count models, and are interpreted using odds ratios (OR) instead of IRR. For all GEE models, goodness of fit was measured using the quasi-likelihood under the independence model criterion (QIC) statistic, as well as the corrected quasi-likelihood under the independence model criterion (QICC) statistic. These statistics are analogous to the Akaike's Information Criterion (AIC) used to measure goodness of fit in GLM models (Cui, 2007). For both of these statistics, a lower number indicates a better fitting model. GEE analyses were performed in SPSS 23.0.

3.2.5 Mixed-Effect Zero-Inflated Poisson Model

Another potential problem with this data is the excessive number of zero responses present in the dependent count variable. The majority of patients did not receive a pharmacy service, and thus have a 0 count. Although GEE models are capable of tolerating over and underdispersion, a sensitivity analysis using a zero-inflated model was performed in order examine the effects of the excess zeros. Zero-inflated count models can be used in order to account for these excess zeros (Lambert, 1992). These models

assume that the study population is divided into two groups of individuals: those who have a zero probability of achieving a count greater than 0, and those who do have a probability of achieving a count greater than 0. It also assumes that there are two separate processes that may lead to an outcome of zero (Lambert, 1992; Hall, 2000). Thus, a zero-inflated model is actually two models in one. The first model (generally a binomial regression model) is used to determine which group an individual will fall into. The second is a standard count model (such as Poisson or negative binomial models) for those that have a chance of achieving a count greater than 0 (although it is still possible for them to receive 0 pharmacy services) (Lambert, 1992; Hall, 2000). For this analysis, it can be explained as such: there are two groups of people—those who have zero probability of receiving a pharmacy service within 3 months of screening, and those who do. The zero-inflated model would be used to predict which group a patient would fall into. For patients who have a probability of receiving a pharmacy service, this model will also estimate the number of pharmacy services received using a count distribution.

However, as noted above, the effect of clustering at the pharmacy level must still be taken into account. It is possible to account for clustering using ZIP by adding random effects into the count model (Wang, 2002; Hur, 2002). Here, random effects were added to the variable of pharmacy number in order to account for the clustering effect of each participating pharmacy. Thus, the final model is a mixed-effect ZIP (ME-ZIP). ME-ZIP was performed using SAS 9.4 (code presented in Appendix 2).

3.2.5.1 Individual Pharmacy Service Types: Medication Review and Influenza Vaccination

Secondary GEE models were be also built for the pharmacy service categories of medication review and influenza vaccination in order to estimate the odds of pharmacy service receipt, again using factors identified in the conceptual framework as independent variables. Unlike the previous analysis, these models were built using a binary dependent variable (did the patient receive a medication review/influenza vaccination, yes or no). Therefore, these models utilized a binomial distribution. A probit link was used for the primary analyses, as it was found to fit the model better than a logit link. The WCS selected was exchangeable. As with the count variable GEE models, sensitivity analyses were performed in order to evaluate robustness of the primary model. Sensitivity analyses performed included a binomial distribution with exchangeable CWS and a logit link function, as well as a binomial distribution using a probit link function but with an unstructured CWS. Goodness of model fit was evaluated using QIC and QICC.

4.0 CHAPTER 4: RESULTS

Not all PIAAF Pharmacy study participants in the PIAAF were regular customers of the Rexall pharmacy at which they were screened, and thus pharmacy profile information could not be collected for all participants. Pharmacy profile information and pharmacy services data were obtained for 535 of the PIAAF Pharmacy study participants (46.6%) from 26 of the 30 participating pharmacies. 380 of these participants were from Ontario, and only 111 were from Alberta. 23 (4.3%) participants reported not taking any prescription medications. Number of current medications, new medications, and potentially inappropriate medications could not be obtained for a total of 39 participants (7.3% of the PIAAF-PPS cohort). Figure 1 demonstrates the flow of participants from the PIAAF Pharmacy study through the PIAAF-PPS analysis.

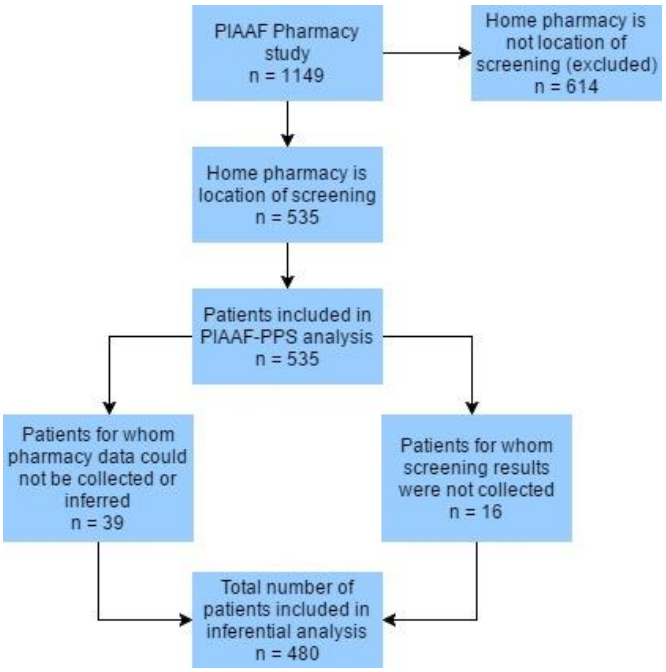

Figure 1: Flow chart of PIAAF Pharmacy participants through the PIAAF-PPS analysis

4.1 PIAAF Pharmacy Study

Results for the PIAAF Pharmacy study will be reported and presented elsewhere; however, Table 5 describes the baseline characteristics of the 1149 participants screened during the PIAAF Pharmacy study for whom CRF data was extracted by PHRI. Table 6 describes the self-reported use of medication in these PIAAF Pharmacy study participants. Significant differences in medication use between jurisdictions were found for ASA (Pearson Chi-Square = 13.3, p = 0.01), beta blockers (Pearson Chi-Square = 10.9, p =0.004), insulin (Pearson Chi-Square = 7.7, p = 0.021), statins (Pearson Chi-Square = 23.7, p < 0.001), and calcium channel blockers (Pearson Chi-Square = 10.0, p = 0.007).

Table 5: Baseline results of all patients screened for PIAAF Pharmacy study

Participant Characteristics (n=1149)	n, % (Unless otherwise stated)
Age: Mean (SD)	74.7 (6.9)
Female participants	680 (59.2)
Known atrial fibrillation	24 (2.1)
History of hypertension	592 (51.5)
Known diabetes mellitus	220 (19.1)
History of heart failure	23 (2.0)
History of vascular artery disease	104 (9.1)
History of stroke	101(8.8)

Table 6: Baseline medication use in all PIAAF participants, self-reported, by region

Medication Class	All participants (%) n =1149	Edmonton Region (%) n =585	Hamilton Region (%) n =564
Low-dose ASA	481 (41.9)	215 (36.8)	266 (47.2)
Diuretics	214 (18.6)	97 (16.6)	117 (20.7)
Beta blocker	190 (16.5)	76 (13.0)	114 (20.2)
Calcium channel blocker	179 (15.6)	72 (12.3)	107 (19.0)

Medication Class	All participants (%) n =1149	Edmonton Region (%) n =585	Hamilton Region (%) n =564
Angiotensin II receptor blocker (ARB)	205 (17.8)	101 (17.3)	104 (18.4)
Insulin	43 (3.7)	13 (2.2)	30 (5.3)
Oral hypoglycemic	159 (13.8)	80 (13.7)	79 (14.0)
Statin	479 (41.7)	204 (34.9)	275 (48.8)
Alpha blocker	17 (1.5)	4 (0.68)	13 (2.3)
ACE inhibitor	223 (19.4)	98 (16.8)	125 (22.2)
Anti-arrhythmic	4 (0.35)	1 (0.17)	3 (0.53)

4.2 PIAAF-PPS: Descriptive Analysis

4.2.1 Baseline Characteristics

Of the 535 patients included in the PIAAF-PPS analysis, 56.3% were female. The mean age (SD) of participants was 75.4 (6.8). On average, PIAAF-PPS participants were taking 4.4 medications, with a standard deviation of 3.3. The number of medications taken ranged from 0 to 19. Just under half of the included participants (48.3%) are considered to have polypharmacy, defined here as four or more concurrent medications. 55.9% of participants reported having a history of hypertension, however, only 29.9% of participants were found to have raised blood pressure at the time of screening. 22.4% of patients had known diabetes, and 8 patients (1.5%) reported having known AF. Well over half of participants (66.6%) were identified as having had a pharmacy service within a year prior to screening, and only 194 (36.3%) were determined to be eligible for an annual-only medication review either on the day of screening, or within 3 months post-screening (this was calculated based on timing of prior annual-only medication reviews and number of medications). Baseline characteristics in participants included in the PIAAF-PPS analysis are described in Table 7. There was a significant difference between the PIAAF-PPS cohort and the overall group of PIAAF Pharmacy participants for the baseline characteristics of known diabetes and history of vascular artery disease, with the PIAAF-PPS cohort having relatively higher proportions of these characteristics (Pearson Chi-Square = 9.71, p = 0.002 for known diabetes; Pearson Chi-Square = 6.64, p = 0.01 for vascular artery disease).

Table 7: Baseline characteristics of participants included in PIAAF-PPS analysis, compared to overall PIAAF Pharmacy participants

Participant Characteristics	n (%) PIAAF-PPS (n=535)	n (%) Overall PIAAF Pharmacy (n=1149)
Age: Mean (SD)	75.4 (6.8)	74.7 (6.9)
Female participants	301 (56.3)	680 (59.2)
Known atrial fibrillation	8 (1.5)	24 (2.1)
History of hypertension	299 (55.9)	592 (51.5)
High blood pressure at time of screening	160 (29.9)	330 (28.7)
Known diabetes mellitus	120 (22.4)*	220 (19.1)*
History of heart failure	19 (3.6)	23 (2.0)
History of vascular artery disease	64 (12.0)*	104 (9.1)*
History of stroke or TIA	48 (9.0)	101 (8.8%)
Participants with polypharmacy (≥4 medications)[1]	237 (48.3)	--
Mean (SD) number of medications	4.4 (3.3)	--
Mean (SD) 3 month co-morbidity score	1258.4 (775.4)	--
Participants who received any pharmacy service within 1 year prior to screening	351 (66.6)	--
Participants eligible for annual-only medication review on day of screening or within 3 months post-screening	194 (36.3)	--
Participants with ≥1 high risk medication[1]	192 (39.1)	--
1) N = 491 patients with available medication data		
*Significant difference between groups at α = 0.05		

4.2.2 Screening Results

The CANRISK screening questionnaire can only be used in adults up to the age of 74. It was also not used in those with previously diagnosed diabetes; therefore, only 203 participants in the PIAAF-PPS cohort were screened using this tool. Almost half (48.8%)

of the participants screened using the CANRISK questionnaire were found to be at high risk for diabetes, with an additional 43.3% at intermediate risk. 15 (2.8%) of PIAAF-PPS participants were found to have screened positive for AF, and only 1.1% of participants were found to have a CHA2DS2 score greater than one. Of patients with known diabetes (22.4%), 10.2% were found to have raised blood pressure at the time of screening. 19.9% of patients without diabetes were also found to have raised blood pressure. The average (SD) blood pressure of was 139.7/75.6 mmHg (21.2/12.1 mmHg), and mean (SD) heart rate was found to be 71.3 (12.4). Screening results for the PIAAF-PPS cohort are presented in Table 8.

Table 8: Screening results from patients included in PIAAF-PPS analysis

Screening Results	n (%)
Completed CANRISK Screening for Diabetes Mellitus (n= 203)	
Low risk for diabetes	16 (7.9)
Intermediate risk for diabetes	88 (43.3)
High risk for diabetes	99 (48.8)
Screened for Atrial Fibrillation with Single-Lead ECG (n=535)	
AF Screened Positive	15 (2.8)
CHA2DS2 – Vasc score =1	529 (98.9)
CHA2DS2 – Vasc score >1	6 (1.1)
Screened for Hypertension (n=518)[1]	
Hypertension, no diabetes	103 (19.9)
Hypertension, diabetes	54 (10.2)
No hypertension, no diabetes	294 (55.8)
No hypertension, diabetes	65 (12.5)
Mean systolic blood pressure (SD)	139.7 (21.2)
Mean diastolic blood pressure (SD)	75.6 (12.1)
Mean heart rate (SD)	71.3 (12.4)
1. 518 had BP measured. 2 people were unsure as to their diabetic status, and they both did not have high blood pressure at the time of screening	

4.2.3 Medication Use

Use of medications is reported here both in terms of self-reported medication use, as taken from CRF forms (Table 9), and pharmacy profile data (Table 10). The most common self-reported medications were statins, with 49.3% of patients reporting use, and low-dose ASA, with 46.7% of patients reporting use. Significantly more participants in the Hamilton region used beta blockers and statins than in Edmonton region (Pearson Chi-Square = 7.16, p = 0.03, and 9.95, p = 0.007, respectively). Analysis of pharmacy claims data confirms that low-dose ASA and statins were indeed the most commonly used medications, with 49.9% and 54% of patients taking them, respectively. When pharmacy claims were analyzed, the difference between use of beta blockers across the two jurisdictions was no longer significant, although the difference in statins use remained significant between provinces (Pearson Chi-Square = 6.64, p < 0.01). Significant differences were also found between Alberta and Ontario for the use of ACE inhibitors, with more patients in Ontario utilizing these drugs (Pearson chi square = 2.29, p = 0.02). Proportions of all investigated medication classes were found to be higher when pharmacy data was analyzed compared to self-reported data. When pharmacy data was compared to self-reports, a significantly higher proportion of participants was dispensed alpha blockers than reported use of alpha blockers (Pearson Chi-Square = 7.36, p =0.006).

Table 9: Medication use in PIAAF-PPS cohort, self-reported and by region

Medication Class	All participants (%) n =535	Edmonton Region (%) n =131	Hamilton Region (%) n =404
Low-dose ASA	250 (46.7)	51 (38.9)	199 (49.3)
Diuretics	116 (21.7)	22 (16.8)	94 (23.3)
Beta blocker	109 (20.4)	16 (12.2)	93 (23.1)
Calcium channel blocker	106 (19.8)	22 (16.8)	84 (20.8)
Angiotensin II receptor blocker	109 (20.4)	32 (24.4)	77 (19.1)
Insulin	27 (5.0)	3 (2.3)	24 (5.9)
Oral hypoglycemic	86 (16.1)	24 (18.3)	62 (15.3)
Statin	264 (49.3)	49 (37.4)	215 (53.2)
Alpha blocker	15 (2.8)	2 (1.5)	13 (3.2)
ACE inhibitor	124 (23.2)	22 (16.8)	102 (25.2)
Anti-arrhythmic	1 (0.19)	0 (0)	1 (0.25)

Table 10: Medication use in PIAAF-PPS cohort, from pharmacy claims and by region

Medication Class	All participants (%) n = 491	Edmonton Region (%) n = 111	Hamilton Region (%) n = 380
Low-dose ASA	245 (49.9)	52 (46.8)	193 (50.8)
Diuretics	135 (27.5)	30 (27.0)	105 (27.6)
Beta blocker	106 (21.6)	17 (15.3)	89 (23.4)
Calcium channel blocker	103 (21.0)	20 (18.0)	83 (21.8)
Angiotensin II receptor blocker	113 (23.0)	33 (29.7)	80 (21.1)
Insulin	28 (5.7)	4 (3.6)	24 (6.3)
Oral hypoglycemic	86 (17.5)	23 (20.7)	63 (16.6)
Statin	265 (54.0)	48 (43.2)	217 (57.1)
Alpha blocker	31 (6.3)	5 (4.5)	26 (6.8)
ACE inhibitor	135 (27.5)	21 (18.9)	114 (30.0)
Anti-arrhythmic	2 (0.41)	0 (0)	2 (0.53)

4.2.4 Participating Pharmacies

Of the 30 pharmacies that participated in the PIAAF Pharmacy study, pharmacy service claims data was able to be retrieved for 28, and patient-level pharmacy claims were able to be retrieved for 26. Site #7 was closed following the screening intervention, which made it impossible to retrieve pharmacy services data. Site #11 does not utilize Rexall's proprietary software system, Nexxsys, and instead uses another pharmacy software, Kroll. For this reason, data extractors at Rexall were unable to retrieve pharmacy claims or patient data for this store. The remaining two stores (for which no patient data was able to be retrieved) did not enroll any regular customers, and no pharmacy services were able to be linked to participants screened at those stores. They were thus removed from the descriptive analysis and inferential analysis. Table 11 shows the breakdown of participants screened at each pharmacy, the number of participants from each pharmacy who were included in the PIAAF-PPS analysis, and the socioeconomic deprivation score for each participating pharmacy.

Table 11: Baseline characteristics of PIAAF participating pharmacies

Site	Number of Participants screened	Number of participants included in PIAAF-PSS analysis	Socio-economic Deprivation Score[1]
Hamilton Region			
Site 1	39	25	0.146
Site 2	53	43	0.791
Site 3	28	22	0.697
Site 4	9	7	2.338
Site 5	31	20	0.260
Site 6	22	16	0.807
Site 7	10	0	0.334
Site 8	46	23	0.308
Site 9	58	45	-0.922
Site 10	31	11	1.820
Site 35	51	32	-0.246
Site 36	24	16	0.225
Site 37	41	37	-1.252
Site 38	127	102	-1.015
Site 39	7	5	-1.089
Edmonton Region			
Site 11	214	0	-0.546
Site 12	22	11	-0.835
Site 13	7	3	-0.610
Site 14	6	4	0.552
Site 15	53	16	0.887
Site 16	79	16	-0.038
Site 17	8	4	-1.45[2]
Site 18	11	8	-0.416
Site 19	11	6	-0.176[2]
Site 20	36	15	0.127
Site 22	60	31	-0.192
Site 23	30	14	-0.735
Site 24	30	3	0.142
Site 25	19	0	-0.768[2]
Site 26	6	0	-0.833[2]

1) Lower numbers equal less deprivation
2) This store did not fall within a census tract; adjacent census tract used as proxy

The average number of pharmacy services billed per month in each jurisdiction, from Jan 2014 through to July 2015 (3 months after the final screening sessions held in April 2015), are given in Table 12, and the total number of pharmacy services billed in this timeframe are presented graphically in Figures 2 and 3. For both jurisdictions, October and November were the busiest months for pharmacy services. In December and January, pharmacy service rates began to decrease again. The average number of pharmacy services billed per month increased during the PIAAF Pharmacy study for 20 stores (11 in Alberta, and 9 in Ontario), but decreased during the study period for 8 stores (3 in Alberta, and 5 in Ontario). Stores whose screening periods occurred from October to December saw an increase in the number of pharmacy services provided, while those stores whose screening periods began in Jan through to April saw a decrease during the screening period. The spike in pharmacy services provided in both provinces is apparent in the figures presented below.

Table 12: Average number of pharmacy services per region from Jan 2014 to Jul 2015

Month, Year	Hamilton Region	Edmonton Region
Jan, 2014	194	147
Feb, 2014	128	132
Mar, 2014	139	166
Apr, 2014	159	166
May, 2014	151	172
Jun, 2014	146	177
Jul, 2014	174	204
Aug, 2014	137	202
Sep, 2014	151	215
Oct, 2014	334	713
Nov, 2014	477	598
Dec, 2014	177	255
Jan, 2015	142	217
Feb, 2015	139	161
Mar, 2015	137	191
Apr, 2015	160	176
May, 2015	144	170
Jun, 2015	159	187
Jul, 2015	166	181

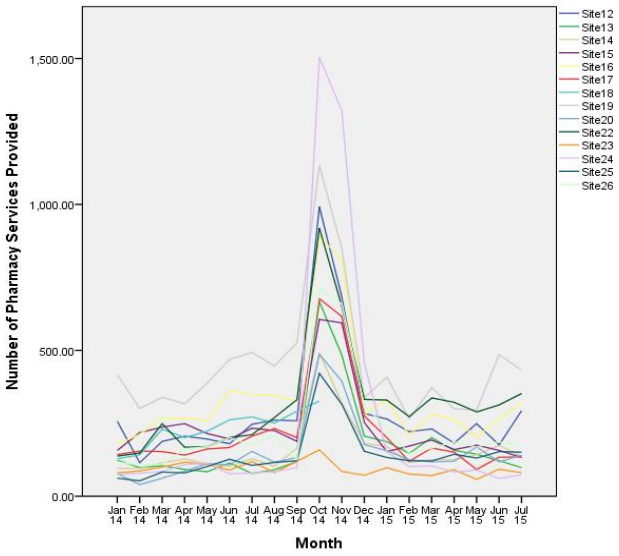

Figure 2: Number of pharmacy services provided per month for participating Alberta stores

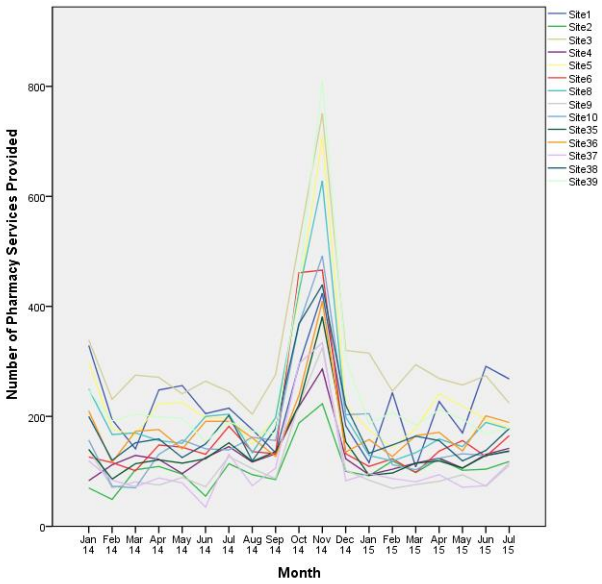

Figure 3: Number of pharmacy services provided per month for participating Ontario stores

4.2.5 Use of Pharmacy Services Post-Screening

In total, 165 participants in the PIAAF-PPS cohort received 229 pharmacy services. The average number (SD) of pharmacy services received by all patients in the PIAAF-PPS cohort was 0.43 (0.76). Of those who received at least one pharmacy service, the average number (SD) of pharmacy services received was 1.43 (0.73). Table 13 and 14 show the breakdown of pharmacy services billed per jurisdiction in total, on the day of screening, within one week of screening, and within 3 months of screening.

4.2.5.1 Ontario

127 of 404 (31.4%) Ontario patients received a total of 167 pharmacy services, of which 99 (59.3%) were medication reviews. The majority of the remaining pharmacy services (28.1%) were influenza vaccinations. 21 pharmaceutical opinions (12.5%), and one smoking cessation consultation (0.6%) were also recorded. When broken down per pharmacy, the number of pharmacy services provided ranged from 1 to 45, with an average (SD) of 11.9 (13.1). The total dollar value reimbursed to pharmacies for remunerated pharmacy services ranges from CAD 60.00 to CAD 1780.00, with an average (SD) per pharmacy of CAD 389.50 (CAD 394.20). The breakdowns of number of pharmacy services provided per pharmacy, and the dollar amounts of monies reimbursed for remunerated pharmacy services are presented in Tables 15 and 16, respectively.

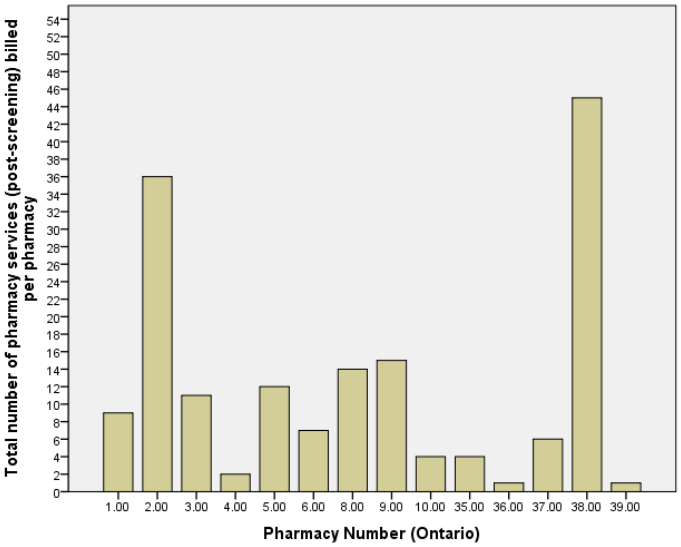

Figure 4: Total number of pharmacy services provided per Ontario store by store number

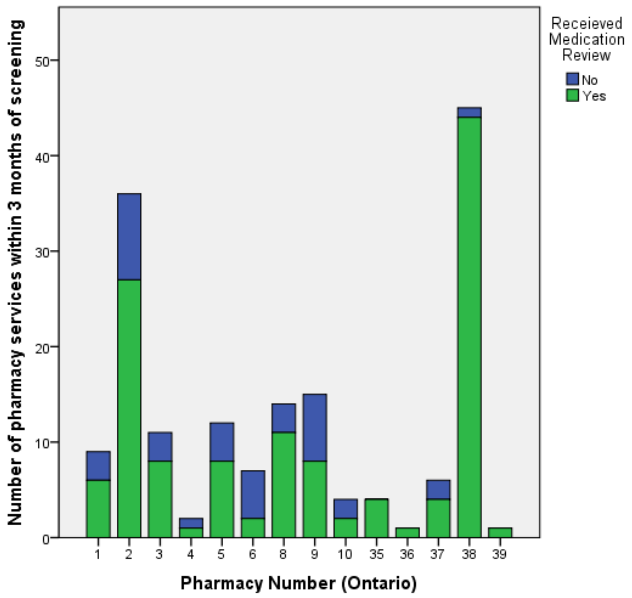

Figure 5: Total number of medication reviews provided per Ontario pharmacy by store number

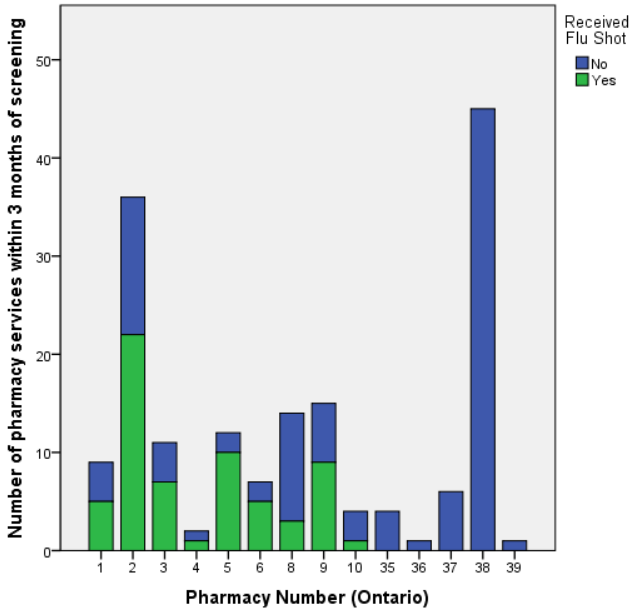

Figure 6: Total number of influenza vaccinations provided per Ontario pharmacy by store number

Table 13: Pharmacy Services billed for PIAAF Pharmacy Participants in Ontario

Pharmacy Service	PIN Billed	Services Billed Day of Screening	Services Billed within 1 Week of Screening	Services Billed within 3 months of Screening	Total
MedsChecks					
MedsCheck Annual	**93899979**	13	2	27	42
MedsCheck Follow-Up: Pharmacist Documented Decision	**93899982**	6	2	16	24
MedsCheck Diabetes: Follow-Up	**93899989**	8	1	7	16
MedsCheck Diabetes	**93899988**	3	0	11	14
MedsCheck Follow Up: Hospital Discharge	**93899981**	0	0	1	1
MedsCheck: Home	**93899987**	0	0	1	1
Influenza Vaccination					
Influenza vaccine: FLUVIRAL	**02015986**	16	2	10	28
Influenza vaccine: AGRIFLU	**02346850**	7	5	7	19
Pharmaceutical Opinions					
POP: Change to Prescription	**93899993**	1	2	11	14
POP: No Change to Prescription	**93899992**	0	0	6	6
POP: Prescription not Filled	**93899991**	0	0	1	1

Pharmacy Service	PIN Billed	Services Billed Day of Screening	Services Billed within 1 Week of Screening	Services Billed within 3 months of Screening	Total
Other Services					
PSCP: Initial	**93899941**	0	0	1	1
Total		**54**	**14**	**99**	**167**
No claims were found for the following pharmacy services in the PIAAF-PPS cohort					
PSCP: Primary Follow-Up	**93899942**	0	0	0	0
PSCP: Secondary Follow-Up	**93899943**	0	0	0	0
Influenza vaccine: VAXIGRIP	**02223929**	0	0	0	0
Influenza vaccine: FLUZONE	**09857501**	0	0	0	0
Influenza vaccine: FLUAD	**02362384**	0	0	0	0

4.2.5.2 Alberta

38 of 131 (29.0%) Alberta patients received 62 pharmacy services. Of these pharmacy services, 47 (75.8%) were medication reviews. 10 (16.1%) were influenza vaccinations, 4 (6.5%) were assessments for prescription renewal, and 1 (1.6%) was an assessment for prescription adaptation. The number of pharmacy services provided per pharmacy ranged from 0 to 20, with an average (SD) of 2.5 (2.4) per pharmacy. The dollar amount reimbursed to pharmacies for remunerated services ranged from CAD 0.00 to CAD 970.00, with an average (SD) of CAD 202.10 (CAD 270.20) reimbursed per pharmacy. The breakdowns of number of pharmacy services provided per pharmacy, and the dollar amounts of monies reimbursed for remunerated pharmacy services are presented in Tables 15 and 16, respectively.

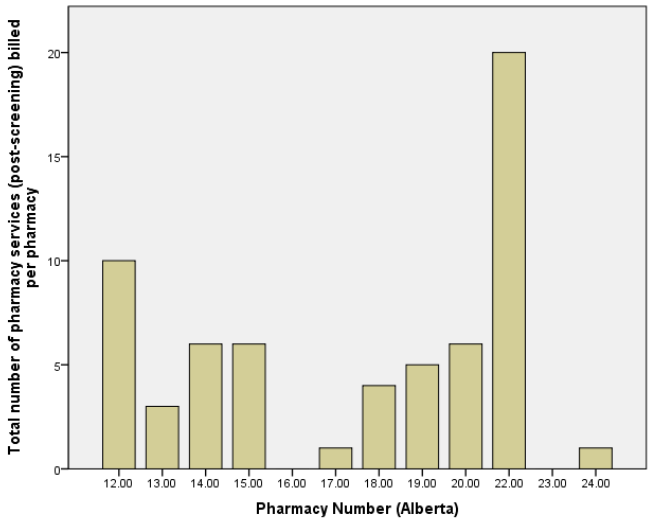

Figure 7: Total number of pharmacy services provided per Alberta store by store number

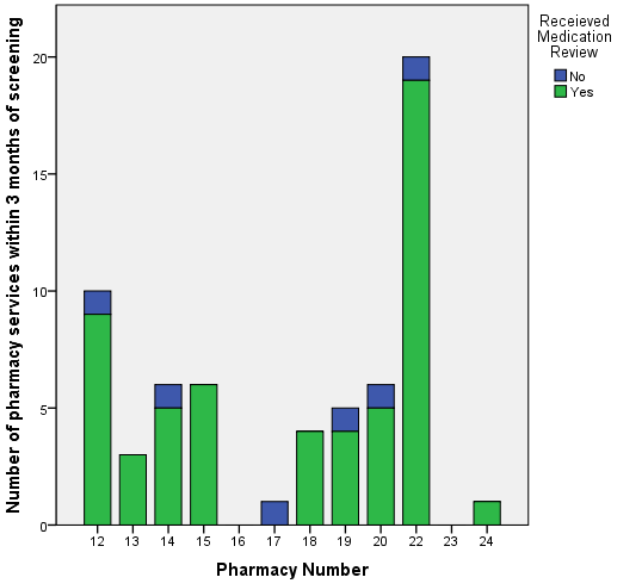

Figure 8: Total number of medication reviews provided per Alberta pharmacy by store number

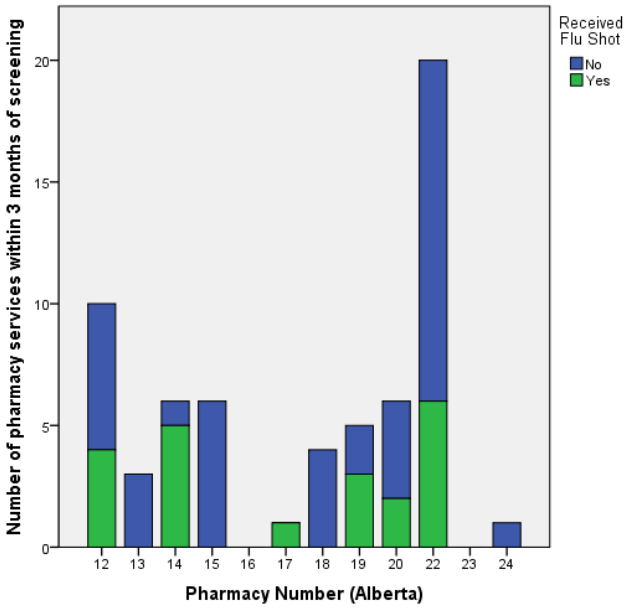

Figure 9: Total number of influenza vaccinations provided per Alberta pharmacy by store number

Table 14. Breakdown of Pharmacy Services billed for PIAAF Pharmacy Participants in Alberta

Pharmacy Service	PIN Billed	Services Billed Day of Screening	Services Billed within 1 Week of Screening	Services Billed within 3 months of Screening	Total
CACPs					
Follow-up CACP	**00000071115**	2	1	17	20
	00000081115	0	0	8	8
Comprehensive Annual Care Plan (CACP)	**00000071114**	0	2	6	8
	00000081114	1	0	3	4
SMMAs					
SMMA Follow-Up: Chronic Disease	**00000071113**	2	0	2	4
	00000081113	0	0	1	1
SMMA: Chronic Disease	**00000071112**	0	1	1	2
	00000081112	0	0	0	0

Pharmacy Service	PIN Billed	Services Billed Day of Screening	Services Billed within 1 Week of Screening	Services Billed within 3 months of Screening	Total
Influenza Vaccination					
Immunization: Routine Recommended Immunization	**05666650**	7	0	3	10
Prescription Adaptation and Prescriptive Authority					
Assessment for prescription renewal	**00000071111**	0	0	4	4
	00000081111	0	0	0	0
Assessment for adaptation of a prescription	**00000071111**	0	0	1	1
	00000081111	0	0	0	0
Total		**12**	**4**	**46**	**62**
No claims were found for the following pharmacy services in the PIAAF-PPS cohort					
Immunization: Healthcare Worker	**05666603**	0	0	0	0
Immunization: Pregnant Woman	**05666646**	0	0	0	0
Immunization: FluMist Administered	**05666647**	0	0	0	0
SMMA & Follow Up: Diabetes Mellitus	**00000071117**	0	0	0	0
	00000081117	0	0	0	0
SMMA & Follow Up: Tobacco Cessation	**00000071118**	0	0	0	0
	00000081118	0	0	0	0
Assessment for the administration of a product by injection	**00000071111**	0	0	0	0
	00000081111	0	0	0	0
Assessment for prescribing in an emergency	**00000071111**	0	0	0	0
	00000081111	0	0	0	0

Pharmacy Service	PIN Billed	Services Billed Day of Screening	Services Billed within 1 Week of Screening	Services Billed within 3 months of Screening	Total
Assessment for refusal to fill a prescription	**00000071111**	0	0	0	0
	00000081111	0	0	0	0
Assessment for a trial prescription	**00000071111**	0	0	0	0
	00000081111	0	0	0	0
Assessment for Prescribing at Initial Access or to manage ongoing therapy	**00000081116**	0	0	0	0
	00000071111	0	0	0	0

Table 15. Breakdown of numbers of remunerated pharmacy services billed for PIAAF-PPS cohort participants, per pharmacy

	Services Billed Day of Screening	Services Billed within 1 Week of Screening	Services Billed within 3 months of Screening	Total
Mean number of services billed per pharmacy (SD) Total, Hamilton region	**3.9 (4.2)**	**1.0 (1.5)**	**7.1 (8.3)**	**11.9 (13.1)**
Site 1	4	0	5	9
Site 2	7	5	24	36
Site 3	2	2	7	11
Site 4	0	0	2	2
Site 5	7	1	4	12
Site 6	3	1	3	7
Site 8	8	0	6	14
Site 9	7	1	7	15
Site 10	0	0	4	4
Site 35	0	0	4	4
Site 36	1	0	0	1
Site 37	0	1	5	6
Site 38	14	3	28	45

	Services Billed Day of Screening	Services Billed within 1 Week of Screening	Services Billed within 3 months of Screening	Total
Site 39	1	0	0	1
Mean number of services billed per pharmacy (SD) Total, Edmonton region	**1.0 (1.1)**	**0.33 (0.65)**	**2.8 (2.5)**	**2.5 (2.4)**
Site 12	1	2	7	10
Site 13	0	1	2	3
Site 14	2	0	4	6
Site 15	0	1	5	6
Site 16	0	0	0	0
Site 17	1	0	0	1
Site 18	1	0	3	4
Site 19	1	0	4	5
Site 20	3	0	3	6
Site 22	3	0	17	20
Site 23	0	0	0	0
Site 24	0	0	1	1
Mean number of services billed per pharmacy (SD) Total, all regions	**2.5 (3.4)**	**0.69 (1.2)**	**5.6 (7.0)**	**8.8 (10.7)**

Table 16. Breakdown of dollar amounts reimbursed for remunerated pharmacy services billed for PIAAF-PPS cohort participants, per pharmacy

	Services Billed Day of Screening	**Services Billed within 1 Week of Screening**	**Services Billed within 3 months of Screening**	**Total**
Mean dollar amount (CAD) reimbursed for pharmacy services per pharmacy (SD) Total, Hamilton region	**110.20 (156.2)**	**19.80 (27.2)**	**259.50 (325.5)**	**389.50 (468.6)**
Site 1	82.50	0.00	212.50	295.00
Site 2	137.50	45.00	817.50	1000.00
Site 3	15.00	67.50	260.00	342.50
Site 4	0.00	0.00	67.50	67.50
Site 5	105.00	25.00	117.50	247.50
Site 6	22.50	7.50	90.00	120.00
Site 8	270.00	0.00	77.50	347.50
Site 9	225.00	7.50	277.50	510.00
Site 10	0.00	0.00	167.50	167.50
Site 35	0.00	0.00	175.00	175.00
Site 36	60.00	0.00	0.00	60.00
Site 37	0.00	60.00	220.00	280.00
Site 38	565.00	65.00	1150.00	1780.00
Site 39	60.00	0.00	0.00	60.00
Mean dollar amount (CAD) reimbursed for pharmacy services per pharmacy (SD) Total, Edmonton region	**28.75 (46.8)**	**23.33 (51.8)**	**150.00 (223.8)**	**202.10 (270.2)**
Site 12	20.00	160.00	220.00	400.00
Site 13	0.00	100.00	40.00	140.00
Site 14	40.00	0.00	85.00	125.00
Site 15	0.00	20.00	185.00	205.00
Site 16	0.00	0.00	0.00	0.00
Site 17	20.00	0.00	0.00	20.00
Site 18	20.00	0.00	60.00	80.00
Site 19	20.00	0.00	240.00	260.00
Site 20	60.00	0.00	140.00	200.00
Site 22	165.00	0.00	805.00	970.00

Mean dollar amount (CAD) reimbursed for pharmacy services per pharmacy (SD) Total, Edmonton region	**28.75 (46.8)**	**23.33 (51.8)**	**150.00 (223.8)**	**202.10 (270.2)**
Site 23	0.00	0.00	0.00	0.00
Site 24	0.00	0.00	25.00	25.00
Mean dollar amount (CAD) reimbursed for pharmacy services per pharmacy (SD) Total, all regions	**72.60 (124.0)**	**21.40 (39.6)**	**208.90 (283.3)**	**303.00 (394.2)**

4.3 PIAAF-PPS: Inferential Analysis

Figure 10 shows the frequency of the number of pharmacy services received by PIAAF participants within 3 months post-screening, as a count. Approximately two-thirds of participants did not receive a pharmacy service within 3 months post screening—thus, it is apparent that the data is skewed towards zero.

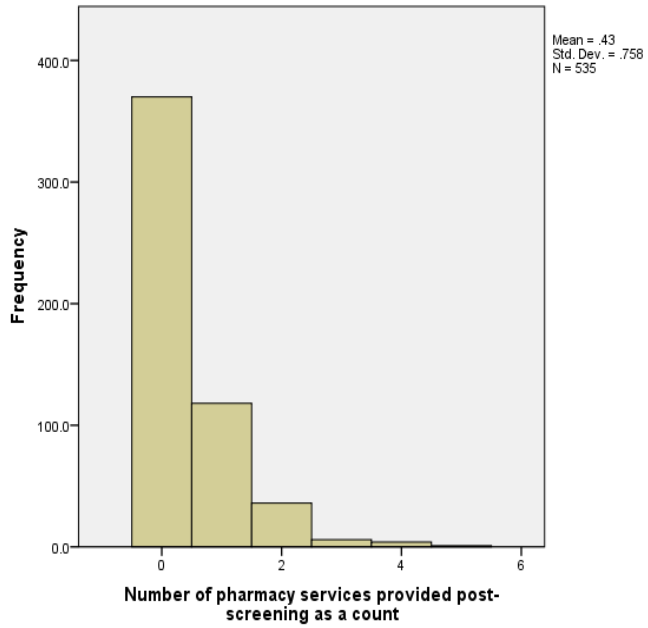

Figure 10: Histogram of the total number of pharmacy services provided post-screening

4.3.1 All Pharmacy Services as a Count

The primary analysis for this GEE model used a Poisson distribution with a log link and an exchangeable WCS. First, the model was run with all 14 previously identified variables included. None of the screening variables (AF detected on SL-ECG, average diastolic blood pressure, and CANRISK score) were found to have a significant association with receipt of pharmacy services—therefore, patients who screened positive for AF, and those found to be at high risk for diabetes and hypertension did not receive pharmacy services at a significantly different rate than those at lower risk levels. The only variables found to be significantly associated with increased rate of pharmacy services within 3 months of screening were: screening in the month of October, screening in the month of November, eligibility for an annual-only medication review, number of medications, new medications (within either 1 month prior to screening or within 3 months post-screening), and being screened in the province of Alberta.

In the final model, these variables remained statistically significant, and the screening result variables remained non-significant. The IRR for screening in October was 2.85 (95% CI 1.67, 4.84), indicating that attending screening sessions in October was associated with an almost tripled rate of receiving pharmacy services, compared to those who attended screening session in April, the reference month. Similarly, being screened in November was associated with an almost doubled rate of pharmacy service receipt, with an IRR of 1.92 (95% CI 1.07, 3.46). Results for the variable of new medications was similar, with IRR = 2.00 (95% CI 1.37, 2.93). Being eligible for an annual-only pharmacy service (either on the day of screening or within the 3 months following screening) was associated with a rate of pharmacy service receipt that was more than doubled compared to those who were not eligible (IRR = 2.15 [95% CI 1.53, 3.01]). Every additional medication taken by a patient was associated with an 8% increase in the rate of pharmacy service receipt; IRR for number of medications = 1.08 (95% CI 1.04, 1.13). Finally, living in, and attended screening sessions in Alberta was associated with an almost 50% increase in the rate of receiving pharmacy services, when compared to patients living in Ontario, with IRR = 1.46 (95% CI 1.07, 2.01).

Sensitivity analyses were consistent with the primary analysis—in fact, changing from an exchangeable to an unstructured WCS made no changes at all to the model. Screening in the month of October, screening in the month of November, number of medications, new medications and jurisdiction all remained significant, even using a negative binomial distribution. Tables 17 and 18 show results of the initial and final GEE models, respectively.

Table 17: Initial GEE model for total number of pharmacy services with all variables included

Variables	**Primary Analysis**	**Sensitivity Analysis**	
	Poisson Distribution Log link Exchangeable correlational structure	Poisson Distribution Log link Unstructured correlational structure	Negative binomial distribution Log link Exchangeable correlational structure
	IRR (95% CI), p	IRR (95% CI), p	IRR (95% CI), p
Intercept	0.06 (0.003, 1.11), 0.06	0.06 (0.003, 1.11), 0.06	0.031 (0.001, 0.70), 0.029*
Age	1.00 (0.97, 1.03), 0.98	1.00 (0.97, 1.03), 0.98	1.01 (0.97, 1.04), 0.78
Sex	1.07 (0.79, 1.45), 0.68	1.07 (0.79, 1.45), 0.68	0.99 (0.73, 1.35), 0.95
Month of screening: October	2.84 (1.62, 4.97), <0.0001*	2.84 (1.62, 4.97), <0.0001*	3.93 (2.26, 6.84), <0.0001*
November	1.92 (1.04, 3.57), 0.038*	1.92 (1.04, 3.57), 0.038*	2.52 (1.37, 4.62), 0.003*
December	1.05 (0.52, 2.11), 0.89	1.05 (0.52, 2.11), 0.89	1.47 (0.73, 2.94), 0.28
January	1.11 (0.46, 2.66), 0.82	1.11 (0.46, 2.66), 0.82	1.37 (0.56, 3.37), 0.50
February	0.80 (0.42, 1.54), 0.51	0.80 (0.42, 1.54), 0.51	0.87 (0.43, 1.76), 0.70
March	0.92 (0.51, 1.66), 0.77	0.92 (0.51, 1.66), 0.77	0.99 (0.54, 1.82), 0.98
April (Reference)	1	1	1
Annual-only pharmacy service w/in 1 year prior to screening?	1.35 (0.93, 1.95), 0.11	1.35 (0.93, 1.95), 0.11	1.34 (0.92, 1.95), 0.13
Eligible for annual-only pharmacy service	2.11 (1.49, 2.99), <0.0001*	2.11 (1.49, 2.99), <0.0001*	2.28 (1.59, 3.27), <0.0001*
Number of medications	1.10 (1.04, 1.16), 0.001*	1.10 (1.04, 1.16), 0.001*	1.12 (1.05, 1.19), <0.0001*

Variables	Primary Analysis	Sensitivity Analysis	
	Poisson Distribution Log link Exchangeable correlational structure	Poisson Distribution Log link Unstructured correlational structure	Negative binomial distribution Log link Exchangeable correlational structure
	IRR (95% CI), p	IRR (95% CI), p	IRR (95% CI), p
New medication	1.99 (1.30, 3.04), 0.002*	1.99 (1.30, 3.04), 0.002*	2.19 (1.40, 3.43), 0.001*
Number of potentially inappropriate medications	0.93 (0.79, 1.10), 0.39	0.93 (0.79, 1.10), 0.39	0.90 (0.75, 1.09), 0.29
Jurisdiction	1.51 (1.09, 2.10), 0.014*	1.51 (1.09, 2.10), 0.014*	1.46 (1.02, 2.08), 0.037*
SES score	1.00 (0.83, 1.20), 0.97	1.00 (0.83, 1.20), 0.97	0.95 (0.79, 1.15), 0.62
AF suspected?	0.77 (0.33, 1.80), 0.54	0.77 (0.33, 1.80), 0.54	0.76 (0.33, 1.77), 0.53
CANRISK screening results			
Not screened	1.26 (0.78, 2.04), 0.35	1.26 (0.78, 2.04), 0.35	1.20 (0.73, 1.96), 0.48
Low risk	1.11 (0.44, 2.82), 0.83	1.11 (0.44, 2.82), 0.83	1.30 (0.53, 3.20), 0.57
Intermediate risk	1.03 (0.61, 1.72), 0.93	1.03 (0.61, 1.72), 0.93	1.01 (0.59, 1.75), 0.96
High risk	1.35 (0.92, 2.00), 0.13	1.35 (0.92, 2.00), 0.13	1.29 (0.86, 1.95), 0.22
Known diabetes (Reference)	1	1	1
Average diastolic blood pressure	1.00 (0.99, 1.01), 0.96	1.00 (0.99, 1.01), 0.96	1.00 (0.99, 1.02), 0.86
Number of cigarettes per day	1.01 (0.99, 1.04), 0.27	1.01 (0.99, 1.04), 0.27	1.01 (0.98, 1.04), 0.44

Variables	**Primary Analysis**	**Sensitivity Analysis**	
	Poisson Distribution Log link Exchangeable correlational structure	Poisson Distribution Log link Unstructured correlational structure	Poisson Distribution Log link Exchangeable correlational structure
	IRR (95% CI), p	IRR (95% CI), p	IRR (95% CI), p
Goodness of Fit			
QIC	423.25	423.25	297.29
QICC	424.73	424.73	312.94
*statistically significant at $\alpha = 0.05$			

Table 18: Final GEE model for total number of pharmacy services as a count

Variables	**Primary Analysis**	**Sensitivity Analysis**	
	Poisson distribution Log link Exchangeable correlational structure	Poisson distribution Log link Unstructured correlational structure	Negative Binomial distribution Log link Exchangeable correlational structure
	IRR (95% CI), p	IRR (95% CI), p	IRR (95% CI), p
Intercept	0.061 (0.03, 0.12), <0.0001	0.061 (0.03, 0.12), <0.0001	0.046 (0.022, 0.093), <0.0001*
Month of screening: October	2.85 (1.67, 4.84), <0.0001*	2.85 (1.67, 4.84), <0.0001*	3.73 (2.20, 6.31), <0.0001*
November	1.92 (1.07, 3.46), 0.030*	1.92 (1.07, 3.46), 0.030*	2.32 (1.28, 4.19), 0.005*
December	1.05 (0.53, 2.07), 0.89	1.05 (0.53, 2.07), 0.89	1.40 (0.71, 2.77), 0.33
January	1.07 (0.46, 2.51), 0.87	1.07 (0.46, 2.51), 0.87	1.26 (0.53, 3.01), 0.60
February	0.80 (0.41, 1.56), 0.51	0.80 (0.41, 1.56), 0.51	0.83 (0.41, 1.68), 0.60
March	0.94 (0.52, 1.68), 0.82	0.94 (0.52, 1.68), 0.82	0.99 (0.54, 1.81), 0.97
April (Reference)	1	1	1

Variables	Primary Analysis	Sensitivity Analysis	
	Poisson distribution Log link Exchangeable correlational structure	Poisson distribution Log link Unstructured correlational structure	Negative Binomial distribution Log link Exchangeable correlational structure
	IRR (95% CI), p	IRR (95% CI), p	IRR (95% CI), p
Annual-only pharmacy service w/in 1 year prior to screening?	1.30 (0.91, 1.87), 0.15	1.30 (0.91, 1.87), 0.15	1.29 (0.89, 1.87), 0.18
Eligible for annual-only pharmacy service	2.15 (1.53, 3.01), <0.0001*	2.15 (1.53, 3.01), <0.0001*	2.32 (1.64, 3.31), <0.0001*
Number of medications	1.08 (1.04, 1.13), <0.0001*	1.08 (1.04, 1.13), <0.0001*	1.10 (1.05, 1.15), <0.0001*
New medication	2.00 (1.37, 2.93), <0.0001*	2.00 (1.37, 2.93), <0.0001*	2.12 (1.42, 3.15), <0.0001*
Jurisdiction	1.46 (1.07, 2.01), 0.02*	1.46 (1.07, 2.01), 0.02*	1.43 (1.03, 2.00), 0.034*
Goodness of Fit			
QIC	408.71	408.71	285.87
QICC	407.78	407.78	293.57
*statistically significant at $\alpha = 0.05$			

4.3.2 All Pharmacy Services as a Binary Outcome

Sensitivity analysis using a dichotomous dependent variable (did patient receive pharmacy service, yes or no) also showed no significant differences between patients screening positive/high risk and those screening negative/low risk. Here, the primary analysis used an exchangeable WCS and a probit link function, as this produced the most precise confidence intervals. Models were also created using an unstructured WCS with a probit link function, and an exchangeable WCS with a logit link function.

Interestingly, in the both initial and final models, the variable of prior annual-only pharmacy service within one year prior to screening was not found to be significant.

However, eligibility for annual-only medication reviews *was* found to be a significant variable in the pharmacy service receipt model. Screening in the month of October, screening in the month of November, number of medications, and new medications were the other variables found to be significant. In the final model, screening in October was associated with an almost quadrupled odds of receiving a pharmacy service, with OR = 3.77 (95% CI 2.46, 5.79. Screening in November was associated with a slightly less drastic, but still significantly increased odds of receiving a pharmacy service, with OR = 2.43 (95% CI 1.54, 3.83). Eligibility for annual-only medication reviews was associated with a 50% increase in the odds of receiving a pharmacy service, with OR = 1.48 (95% CI 1.10, 1.99). New medications were also associated with a 72% increase in the odds of receiving a pharmacy service, with OR = 1.72 (95% CI 1.17, 2.52). Finally, each additional medication taken by a participant was associated with a 17% increase in the odds of receiving a pharmacy service, with OR = 1.17 (95% CI 1.09, 1.25). In this model, no significant differences were found between jurisdictions, meaning there was no associated difference in the likelihood of patients receiving a pharmacy service based on jurisdiction.

Once again, using an unstructured WCS showed no difference from using an exchangeable model. Using a logit link function also did not drastically change the results of the analysis, although estimates for ORs and CIs were much larger.

Table 19: Initial GEE model for total number of pharmacy services as binary response variable

Variables	**Primary Analysis**	**Sensitivity Analysis**	
	Binomial Distribution Probit link Exchangeable correlational structure	Binary Distribution Probit link Unstructured correlational structure	Binary distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Intercept	0.30 (0.019, 5.01), 0.41	0.30 (0.019, 5.01), 0.41	0.10 (0.001, 12.74), 0.35
Age	0.99 (0.96, 1.02), 0.52	0.99 (0.96, 1.02), 0.52	0.99 (0.94, 1.04), 0.64
Sex	0.93 (0.71, 1.21), 0.57	0.93 (0.71, 1.21), 0.57	0.85 (0.53, 1.36), 0.50

Variables	**Primary Analysis**	**Sensitivity Analysis**	
	Binomial Distribution Probit link Exchangeable correlational structure	Binary Distribution Probit link Unstructured correlational structure	Binary distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Month of screening: October	4.20 (2.54, 6.96), <0.0001*	4.20 (2.54, 6.96), <0.0001*	11.13 (4.64, 26.68), <0.0001*
November	2.61 (1.58, 4.33), <0.0001*	2.61 (1.58, 4.33), <0.0001*	5.11 (2.11, 12.39), <0.0001*
December	1.85 (1.03, 3.31), 0.040*	1.85 (1.03, 3.31), 0.040*	2.70 (0.98, 7.40), 0.054
January	1.44 (0.78, 2.67), 0.24	1.44 (0.78, 2.67), 0.24	1.89 (0.64, 5.59), 0.25
February	1.10 (0.65, 1.83), 0.74	1.10 (0.65, 1.83), 0.74	1.09 (0.42, 2.82), 0.86
March	1.23 (0.81, 1.86), 0.34	1.23 (0.81, 1.86), 0.34	1.36 (0.64, 2.88), 0.43
April (Reference)	1	1	1
Annual-only pharmacy service w/in 1 year prior to screening?	0.89 (0.63, 1.24), 0.48	0.89 (0.63, 1.24), 0.48	0.78 (0.43, 1.41), 0.42
Eligible for annual-only pharmacy service	1.49 (1.10, 2.03), 0.011*	1.49 (1.10, 2.03), 0.011*	1.96 (1.14, 3.37), 0.015*
Number of medications	1.18 (1.10, 1.26), <0.0001*	1.18 (1.10, 1.26), <0.0001*	1.33 (1.18, 1.50), <0.0001*
New medication	1.71 (1.14, 2.57), 0.010*	1.71 (1.14, 2.57), 0.010*	2.50 (1.26, 4.97), 0.009*
Number of potentially inappropriate medications	0.85 (0.71, 1.02), 0.079	0.85 (0.71, 1.02), 0.079	0.74 (0.55, 1.00), 0.053

Variables	**Primary Analysis**	**Sensitivity Analysis**	
	Binomial Distribution Probit link Exchangeable correlational structure	Binary Distribution Probit link Unstructured correlational structure	Binary distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Jurisdiction	1.16 (0.83, 1.63), 0.39	1.16 (0.83, 1.63), 0.39	1.29 (0.72, 2.30), 0.39
Socioeconomic deprivation score	0.94 (0.77, 1.14), 0.53	0.94 (0.77, 1.14), 0.53	0.88 (0.63, 1.24), 0.47
AF suspected?	0.94 (0.45, 1.94), 0.86	0.94 (0.45, 1.94), 0.86	0.91 (0.26, 3.28), 0.89
CANRISK screening results			
Not screened	1.32 (0.85, 2.06), 0.22	1.32 (0.85, 2.06), 0.22	1.58 (0.74, 3.35), 0.24
Low risk	1.26 (0.52, 3.06), 0.62	1.26 (0.52, 3.06), 0.62	1.47 (0.32, 6.73), 0.62
Intermediate risk	0.97 (0.62, 1.51), 0.88	0.97 (0.62, 1.51), 0.88	1.01 (0.47, 2.20), 0.97
High risk	1.20 (0.77, 1.83), 0.43	1.20 (0.77, 1.83), 0.43	1.39 (0.67, 2.87), 0.38
Known diabetes (Reference)	1	1	1
Average diastolic blood pressure	1.00 (0.99, 1.01), 0.69	1.00 (0.99, 1.01), 0.69	1.00 (0.98, 1.02), 0.68
Number of cigarettes per day	1.00 (0.97, 1.03), 0.84	1.00 (0.97, 1.03), 0.84	1.00 (0.95, 1.06), 0.91
Goodness of Fit			
QIC	510.02	510.02	510.04
QICC	510.40	510.40	510.55
*statistically significant at $\alpha = 0.05$			

Table 20: Final GEE model for total number of pharmacy services as binary response variable

Variables	Primary Analysis	Sensitivity Analysis	
	Binomial Distribution Probit link Exchangeable correlational structure	Binomial Distribution Probit link Unstructured correlational structure	Binomial distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Intercept	0.15 (0.10, 0.23), <0.0001*	0.15 (0.10, 0.23), <0.0001*	0.044 (0.02, 0.094), <0.0001*
Month of screening: October	3.77 (2.46, 5.79), <0.0001*	3.77 (2.46, 5.79), <0.0001*	9.16 (4.32, 19.43), <0.0001*
November	2.43 (1.54, 3.83), <0.0001*	2.43 (1.54, 3.83), <0.0001*	4.43 (1.99, 9.86), <0.0001*
December	1.71 (1.00, 2.94), 0.052	1.71 (1.00, 2.94), 0.052	2.34 (0.92, 5.92), 0.074
January	1.43 (0.80, 2.54), 0.22	1.43 (0.80, 2.54), 0.22	1.85 (0.67, 5.12), 0.24
February	1.13 (0.68, 1.88), 0.64	1.13 (0.68, 1.88), 0.64	1.16 (0.46, 2.91), 0.75
March	1.21 (0.80, 1.83), 0.36	1.21 (0.80, 1.83), 0.36	1.35 (0.64, 2.83), 0.43
April (Reference)	1	1	1
Annual-only pharmacy service w/in 1 year prior to screening?	0.87 (0.63, 1.19), 0.38	0.87 (0.63, 1.19), 0.38	0.75 (0.43, 1.31), 0.30
Eligible for annual-only pharmacy service	1.48 (1.10, 1.99), 0.010*	1.48 (1.10, 1.99), 0.010*	1.92 (1.14, 3.23), 0.014*
Number of medications	1.17 (1.09, 1.25), <0.0001*	1.17 (1.09, 1.25), <0.0001*	1.32 (1.18, 1.48), <0.0001*
New medication (one month	1.72 (1.17, 2.52), 0.006*	1.72 (1.17, 2.52), 0.006*	2.48 (1.29, 4.75), 0.006*

Variables	Primary Analysis	Sensitivity Analysis	
	Binomial Distribution Probit link Exchangeable correlational structure	Binomial Distribution Probit link Unstructured correlational structure	Binomial distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Number of potentially inappropriate medications	0.86 (0.72, 1.02), 0.073	0.86 (0.72, 1.02), 0.073	0.75 (0.56, 1.00), 0.052
Goodness of Fit			
QIC	492.19	492.19	492.00
QICC	492.27	492.27	492.39
*statistically significant at $\alpha = 0.05$			

4.3.3 Mixed-Effects Zero-Inflated Poisson Model

A ME-ZIP model was performed to investigate whether this approach would be suitable for handling the excess zeros in the pharmacy service data, while simultaneously accounting for clustering at the pharmacy level. The results from the final model are presented in Table 21. Once again, screening results from the PIAAF Pharmacy intervention were not found to have had any significant impact on the receipt of pharmacy services for either model included in the ME-ZIP (zero and count models). That is to say, those at high risk for diabetes and hypertension, and those screening positive for AF were not associated with a higher likelihood of receiving pharmacy services than those at lower risk levels. As well, those screening as positive for AF or as high risk for diabetes and hypertension were not associated with a higher likelihood of receiving additional pharmacy services than those at lower risk levels.

The values for ORs and confidence intervals in the count model appear to be reasonable, and some agreement with the GEE models is present. Jurisdiction, screening in October, and number of medications were all found to be statistically significant variables. Number of cigarettes per day was also found to be a highly significant variable in this model, which is unique when compared to the GEE models. Also unlike the GEE models, receipt of new medication was not found to be significant. Moving on to the zero model, however, it becomes clear that this model is not the best fit for the data at hand.

Although the ORs seem plausible, the 95% confidence intervals are extremely wide, indicating that there is very little to no precision in the estimate.

Table 21: Results from mixed-effects zero-inflated Poisson model after model fitting

Variables	OR	95% Confidence Interval	P
Zero Model (Logit link)			
Intercept	0.013	7.27E-7, 228.74	0.37
Age	1.04	0.93, 1.17	0.48
Number of medications	2.08	1.09, 4.00	0.03*
Socioeconomic deprivation score	0.27	0.061, 1.21	0.085
CANRISK score: Intermediate risk	0.88	0.052, 15.05	0.93
Jurisdiction	3.23	0.33, 31.25	0.30
Prior annual-only pharmacy service	0.45	0.084, 24.39	0.35
Count model			
Intercept	0.19	0.057, 0.66	0.011*
Jurisdiction	1.67	1.02, 2.76	0.044*
Month of Screening: October	1.08	1.04, 1.14	0.0014*
Number of medications	1.88	1.31, 2.70	0.0013*
New medication	0.86	0.72, 1.01	0.69
Number of potentially inappropriate medications	1.02	0.99, 1.05	0.20
Number of cigarettes per day	2.01	1.38, 2.94	0.0008*
Average diastolic blood pressure	0.99	0.98, 1.01	0.36
Goodness of Fit			
-2 log likelihood	718.60		
AIC	750.60		
AICC	751.80		
*statistically significant at $\alpha = 0.05$			

4.3.4 Medication Review

There were 146 post-screening medication reviews identified in the pharmacy data, including all MedsChecks, CACPs and SMMAs (i.e. both annual-only and follow-up). After eliminating participants with missing data, 106 medication reviews remained. This meant that approximately 10 predictor variables could be included in the initial GEE model. The three predictors eliminated were number of cigarettes per day, age, and gender, as these variables performed poorly during model building. Eligibility for receiving an annual-only medication review was not included in this model, as it was thought to predict receipt of medication review too closely. Instead, receipt of annual-only medication review within one year prior to screening was used.

Once again, none of the screening result variables were found to be significantly associated with medication review receipt. Those screened as being at high risk for diabetes and hypertension, and those screening positive for AF were therefore not associated with a higher likelihood of receiving a medication review than those screening negative for AF or at low risk for diabetes. Once again, the only positive significant variables in this model were found to be screening in the month of October, jurisdiction, new medications and number of medications. Additionally, prior annual-only pharmacy service was found to have a significant negative association with medication review receipt, as was number of potentially inappropriate medications. In the initial model, prior annual-only pharmacy review was also found to be significant, however, in the final model, this variable became non-significant with OR = 0.73 (95% CI 0.53, 1.01).

The final GEE model showed that the OR for screening in the month of October was 1.86 (95% CI 1.20, 2.91) indicating that being screened in October was associated with almost twice the odds of receiving a medication review as those screened during the reference month of April. Patients from Alberta were once again associated with a higher likelihood of receiving a pharmacy service, with OR = 1.45 (95% CI 1.01, 2.08). Receiving a new medication (either one month prior to screening or within three months post-screening) was associated with a 66% increase in the odds of receiving a medication review, with an OR of 1.66 (95% CI 1.12, 2.46). Every additional medication taken by a patient was associated with a 23% increase in the odds of receiving a medication review (OR = 1.23 [95% CI 1.15, 1.32]). Surprisingly, each additional potentially inappropriate medication was associated with a decrease of 16% in the odds of receiving a medication review, with OR = 0.84 (95% CI 0.71, 1.00). As with the Poisson GEE, the unstructured WCS gave exactly the same results as the exchangeable WCS. The sensitivity analysis

using the logit link function gave relatively similar results, although the odds ratios for significant variables were less conservative. In terms of goodness of fit, both logit and probit link functions performed well; the probit link function gave a lower QIC than the logit, and the logit gave a lower QICC than the probit link. Tables 22 and 23 show results from the initial and final GEE models, respectively.

Table 22: Initial GEE model with all variables for medication review

Variables	**Primary Analysis**	**Sensitivity Analysis**	
	Binomial distribution Probit link Exchangeable correlational structure	Binomial distribution Probit link Unstructured correlational structure	Binomial distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Intercept	0.20 (0.048, 0.83), 0.027*	0.20 (0.048, 0.83), 0.027*	0.065 (0.005, 0.87), 0.039*
Month of screening			
October	1.84 (1.13, 3.01), 0.015*	1.84 (1.13, 3.01), 0.015*	2.91 (1.20, 7.08), 0.019*
November	1.36 (0.82, 2.27), 0.23	1.36 (0.82, 2.27), 0.23	1.75 (0.70, 4.41), 0.24
December	0.95 (0.49, 1.86), 0.89	0.95 (0.49, 1.86), 0.89	0.84 (0.25, 2.81), 0.78
January	1.25 (0.66, 2.37), 0.50	1.25 (0.66, 2.37), 0.50	1.49 (0.47, 4.74), 0.50
February	0.85 (0.49, 1.48), 0.57	0.85 (0.49, 1.48), 0.57	0.72 (0.26, 2.01), 0.53
March	0.99 (0.61, 1.58), 0.95	0.99 (0.61, 1.58), 0.95	0.97 (0.40, 2.33), 0.94
April (Reference)	1	1	1
Prior annual-only pharmacy service	0.71 (0.51, 0.98), 0.035*	0.71 (0.51, 0.98), 0.035*	0.53 (0.30, 0.93), 0.027*
Number of medications	1.23 (1.14, 1.32), <0.0001*	1.23 (1.14, 1.32), <0.0001*	1.43 (1.26, 1.62), <0.0001*
New medication	1.73 (1.15, 2.58), 0.008*	1.73 (1.15, 2.58), 0.008*	2.53 (1.27, 5.04), 0.009*

Variables	Primary Analysis	Sensitivity Analysis	
	Binomial distribution Probit link Exchangeable correlational structure	Binomial distribution Probit link Unstructured correlational structure	Binomial distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Number of potentially inappropriate medications	0.84 (0.70, 1.00), 0.045*	0.84 (0.70, 1.00), 0.045*	0.73 (0.54, 0.99), 0.044*
Jurisdiction	1.44 (1.00, 2.06), 0.050*	1.44 (1.00, 2.06), 0.050*	1.89 (1.00, 3.58), 0.050*
SES	1.02 (0.84, 1.22), 0.88	1.02 (0.84, 1.22), 0.88	1.02 (0.73, 1.44), 0.90
AF suspected?	0.67 (0.27, 1.65), 0.38	0.67 (0.27, 1.65), 0.38	0.50 (0.089, 2.77), 0.43
CANRISK screening results			
Not screened	0.99 (0.66, 1.49), 0.98	0.99 (0.66, 1.49), 0.98	1.02 (0.50, 2.06), 0.97
Low risk	1.41(0.56, 3.55), 0.47	1.41(0.56, 3.55), 0.47	1.68 (0.34, 8.36), 0.53
Intermediate risk	0.78 (0.48, 1.27), 0.32	0.78 (0.48, 1.27), 0.32	0.67 (0.28, 1.60), 0.37
High risk	0.88 (0.57, 1.37), 0.57	0.88 (0.57, 1.37), 0.57	0.82 (0.38, 1.78), 0.62
Known diabetes (Reference)	1	1	1
Average diastolic blood pressure	1.00 (0.99, 1.01), 0.81	1.00 (0.99, 1.01), 0.81	1.00 (0.98, 1.02), 0.80
Goodness of Fit			
QIC	440.35	440.35	441.01
QICC	439.73	439.73	440.34
*statistically significant at $\alpha = 0.05$			

Table 23: Final GEE model of variables for medication review

Variables	Primary Analysis	Sensitivity Analysis	
	Binomial distribution Probit link Exchangeable correlational structure	Binomial distribution Probit link Unstructured correlational structure	Binomial distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Intercept	0.11 (0.06, 0.20), <0.0001*	0.11 (0.06, 0.20), <0.0001*	0.022 (0.007, 0.065), <0.0001*
Month of screening			
October	1.86 (1.20, 2.91), 0.006*	1.86 (1.20, 2.91), 0.006*	2.95 (1.33, 6.55), 0.008*
November	1.39 (0.86, 2.26), 0.18	1.39 (0.86, 2.26), 0.18	1.78 (0.74, 4.28), 0.20
December	0.98 (0.51, 1.91), 0.96	0.98 (0.51, 1.91), 0.96	0.85 (0.26, 2.79), 0.79
January	1.27 (0.68, 2.36), 0.46	1.27 (0.68, 2.36), 0.46	1.51 (0.49, 4.64), 0.47
February	0.83 (0.48, 1.45), 0.52	0.83 (0.48, 1.45), 0.52	0.70 (0.25, 1.94), 0.49
March	1.00 (0.63, 1.59), 0.99	1.00 (0.63, 1.59), 0.99	0.98 (0.41, 2.30), 0.95
April (Reference)	1	1	1
Prior annual-only pharmacy service	0.73 (0.53, 1.01), 0.055	0.73 (0.53, 1.01), 0.055	0.56 (0.32, 0.98), 0.041*
Number of medications	1.23 (1.15, 1.32), <0.0001*	1.23 (1.15, 1.32), <0.0001*	1.44 (1.28, 1.62), <0.0001*
New medication	1.66 (1.12, 2.46), 0.011*	1.66 (1.12, 2.46), 0.011*	2.38 (1.21, 4.65), 0.012*
Number of potentially inappropriate medications	0.84 (0.71, 1.00), 0.047*	0.84 (0.71, 1.00), 0.047*	0.73 (0.54, 0.99), 0.040*
Jurisdiction	1.45 (1.01, 2.08), 0.042*	1.45 (1.01, 2.08), 0.042*	1.93 (1.03, 3.62), 0.040*

Variables	Primary Analysis	Sensitivity Analysis	
	Binomial distribution Probit link Exchangeable correlational structure	Binomial distribution Probit link Unstructured correlational structure	Binomial distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Goodness of Fit			
QIC	429.77	429.77	429.38
QICC	429.10	429.10	429.13
*statistically significant at $\alpha = 0.05$			

4.3.5 Influenza Vaccination

A general rule of thumb in regression analysis is that there should be approximately 10 events per independent variable. In cases where there are few observations, it may be necessary to reduce the number of variables tested within the model (Concato, 1995). Since only 57 influenza vaccinations were identified, a maximum of 5 factor variables can be included in the model. The predictor variables included are: age, jurisdiction, CANRISK score, AF suspected by SL-ECG, and average diastolic blood pressure.

Only one variable was found to be significant in this GEE model: the CANRISK high risk of diabetes score. The OR for this predictor was 1.84, with a 95% CI of 1.15 to 2.94, which would indicate that patients screening as being at high risk for diabetes were associated with an almost doubled odds of receiving a flu shot (either on the day of screening, or within 3 months post-screening) compared to the reference category, patients with known diabetes. After fitting the final model, this remained as the only significant variable, with a slightly decreased OR = 1.69 (95% CI 1.09, 2.64). This was the only instance in the inferential analysis where screening results from the PIAAF Pharmacy study were associated with increased likelihood of pharmacy service receipt. High risk patients were associated with an almost doubled odds of receiving a flu shot within 3 months of screening than those who did not. Conversely, screening results for AF and blood pressure were not significantly associated with influenza vaccine receipt, nor were mean diastolic blood pressure, age or jurisdiction. Sensitivity analyses for both the overall model and the final model were similar to the primary analysis. Again, the unstructured WCS produced the same results as the exchangeable WCS. Using the logit model instead of the probit model produced larger ORs for most variables, especially with

the CANRISK high risk of diabetes screening variable. However, the probit link model had a slightly lower QIC and QICC and thus was a slightly better fit. Table 24 and 25 present results from the initial and final GEE models, respectively.

Table 24: GEE model with all predictors of influenza vaccination

Variables	**Primary Analysis**	**Sensitivity Analysis**	
	Binomial distribution Probit link Exchangeable correlational structure	Binomial distribution Probit link Unstructured correlational structure	Binomial distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	ORR (95% CI), p	OR (95% CI), p
Intercept	0.14 (0.008, 2.55), 0.18	0.14 (0.0080, 2.55), 0.18	0.027 (9.86E-5, 7.48), 0.21
Age	1.02 (0.98, 1.05), 0.36	1.02 (0.98, 1.05), 0.36	1.03 (0.97, 1.09), 0.36
CANRISK score			
Not screened	0.90 (0.56, 1.44), 0.66	0.90 (0.56, 1.44), 0.66	0.83 (0.33, 2.12), 0.70
Low risk	1.33 (0.56, 3.15), 0.52	1.33 (0.56, 3.15), 0.52	1.78 (0.34, 9.24), 0.49
Intermediate risk	1.31 (0.78, 2.20), 0.32	1.31 (0.76, 2.20), 0.32	1.68 (0.60, 4.68), 0.32
High risk	1.84 (1.15, 2.94), 0.011*	1.84 (1.15, 2.94), 0.011*	3.16 (1.28, 7.79), 0.012*
Known diabetes (reference)	1	1	1
AF detected	1.17 (0.51, 2.66), 0.71	1.17 (0.51, 2.66), 0.71	1.38 (0.29, 6.50), 0.68
Average diastolic blood pressure	1.00 (0.98, 1.01), 0.42	1.00 (0.98, 1.01), 0.42	0.99 (0.97, 1.01), 0.45
Jurisdiction	0.76 (0.53, 1.08), 0.13	0.76 (0.53, 1.08), 0.13	0.59 (0.29, 1.22), 0.16
Goodness of Fit			
QIC	359.64	359.64	359.97
QICC	360.12	360.12	360.28

Table 25: Final GEE model of predictors for influenza vaccination

Variable	Primary Analysis	Sensitivity Analysis	
	Binomial distribution Probit link Exchangeable correlational structure	Binomial distribution Probit link Unstructured correlational structure	Binomial distribution Logit link Exchangeable correlational structure
	OR (95% CI), p	OR (95% CI), p	OR (95% CI), p
Intercept	0.34 (0.20, 0.57), <0.0001*	0.34 (0.20, 0.57), <0.0001*	0.16 (0.054, 0.45), 0.001*
CANRISK score			
Not screened	1.01 (0.67, 1.54), 0.96	1.01 (0.67, 1.54), 0.96	1.04 (0.45, 2.42), 0.93
Low risk	1.33 (0.57, 3.14), 0.51	1.33 (0.57, 3.14), 0.51	1.80 (0.35, 9.22), 0.48
Intermediate risk	1.20 (0.73, 1.97), 0.47	1.20 (0.73, 1.97), 0.47	1.42 (0.54, 3.78), 0.48
High risk	1.69 (1.09, 2.64), 0.020*	1.69 (1.09, 2.64), 0.020*	2.69 (1.15, 6.30), 0.022*
Known diabetes (reference)	1	1	1
Jurisdiction	0.77 (0.54, 1.11), 0.17	0.77 (0.54, 1.11), 0.17	0.62 (0.30, 1.28), 0.19
Goodness of Fit			
QIC	356.08	356.08	356.27
QICC	356.18	356.18	356.32

5.0 CHAPTER 5: DISCUSSION

With the exception of receipt of influenza vaccination, the results from this study indicate that the PIAAF Pharmacy screening results were not associated with receipt of pharmacy services following the screening initiative. Non-significant results for these variables were seen for both the total number of pharmacy services as a count, as well as for medication review, specifically. The exception to this is for the provision of influenza vaccinations, where it was found that screening as being at high risk for diabetes was significantly associated with the receipt of flu shots, when compared to those with known diabetes. This could be due to pharmacists encouraging high-risk screening participants to get a flu shot, or it could be that these individuals came into the pharmacy with the intent of receiving a flu shot, participated in the screening program while they were there, and thus learned that they were at high risk for developing diabetes. The screening sessions provided an opportunity for pharmacists to engage patients in discussion, provide education, and perhaps even initiate (or continue) patient monitoring. This is especially true for patients with known diabetes and hypertension, as patients with these chronic diseases would generally stand to benefit from regular follow-up with a pharmacist to monitor the progression of their condition (Rotta, 2015). The lack of significant association between screening results and pharmacy service receipt may stem from challenges with implementation of the PIAAF screening intervention. For instance, the PIAAF Pharmacy screening sessions may not have been incorporated into day-to-day pharmacy workflow in such a way that pharmacists were easily able review screening results and provide pharmacy services. Other potential issues with the implementation process could include lack of pharmacy staff buy-in to the screening intervention, and lack of time to provide pharmacy services, especially during annual flu shot season (Damschroder, 2013). Nonetheless, considering that almost 30% of participants were found to have high blood pressure at the time of screening, it is apparent that there is room for improvement with respect to the provision of pharmacy services following community pharmacy screening. Ensuring that screening sessions are implemented in a way that allows for easier integration into daily workflow would likely be beneficial for future screening interventions (Proctor, 2013; Damschroder, 2013).

Beyond screening results, the only predictors that were positively and significantly associated with receipt of all pharmacy services were month of screening (October and November), eligibility for annual-only medication reviews, the number of medications taken (with each additional medication associated with an increased rate of receiving pharmacy services), and any new medications started a month before (or within the three months following) screening. The jurisdiction where screening occurred was found to be

significantly associated with an increase in the rate of pharmacy service receipt (favouring patients from Alberta); however, there was no association between jurisdiction and an increased odds of receiving a pharmacy service. These results are not surprising, as prior evidence reports that increased numbers of medications are linked to increases in the likelihood of receiving medication reviews (Brooks, 2008; Thompson, 2004; Ignacy, 2015; Dolovich, 2016; Pechlivanoglou, 2016), as is receipt of new medications (Schommer, 2002; Pechlivanoglou, 2016). Alberta has a larger number of remunerated pharmacy services available, which may explain why patients may be more likely to receive *additional* services than Ontario patients, while patients from both provinces were equally likely to receive *any* pharmacy service. Furthermore, all participating Alberta pharmacies had their intervention periods coincide with the annual flu shot season, whereas a number of the Ontario pharmacies did not begin their screening sessions until spring 2015. Although the Alberta pharmacies enrolled less patients, and performed less pharmacy services on average, they were found to have provided slightly more pharmacy services per person than their Ontario counterparts (mean for Alberta was 0.47, and mean for Ontario was 0.41).

For factor variables associated with receipt of medication reviews, in addition to screening in October, screening in November, number of medications, new medications, and jurisdiction, prior annual pharmacy service was not found to be significant. This may seems strange upon first glance—however, 50 people with a prior annual-only review were found to have had a total of 74 follow-up reviews. Therefore, it seems that having had an annual-only medication review in the year prior to screening was not associated with a reduced likelihood of receiving other types of medication reviews. More disconcerting is the indication that higher numbers of potentially inappropriate medications are associated with a decrease in the odds of receiving a medication review. The pharmacy data indicates that the most commonly used potentially inappropriate medications in this cohort are low dose ASA in patients >79, proton-pump inhibitors, and short-acting benzodiazepines. All three of these drugs are considered potentially inappropriate in the elderly (AGS, 2015), and all three are recommended to be stopped in this population unless there is a clear indication for their use (Van Wormer, 2014; Pottie K, 2016; Farrell B, 2015). In cases where patients are on potentially inappropriate medications (and especially if they are on more than one), it is prudent for pharmacists to monitor and follow-up with patients on a regular basis (El Hajji, 2014; Gandhi, 2003; MOHLTC, 2008; MSP, 2014; Government of BC, 2016; Dolovich, 2016; Pechlivanoglou, 2016). Pharmacists should therefore be performing more pharmacy services for these patients, not less. However, this result may be a function of the screening intervention—use of potentially inappropriate medications was not considered

at the time of screening (e.g. it was not entered on CRFs, nor were pharmacists specifically told to watch out for them). It may also be difficult to determine whether or not a *potentially* inappropriate medication is *actually* inappropriate without further investigation into a patient's clinical context—so it is likely that pharmacists were simply not taking this variable into consideration when offering pharmacy services to participants in the moments after they were screened.

Of the original PIAAF Pharmacy participants, 46.6% were included in the PIAAF-PPS analysis. Compared to the original sample of 1149 PIAAF Pharmacy participants, those included in the PIAAF-PPS cohort were slightly older, and had a significantly higher proportion of known diabetes and vascular artery disease. Slightly less women were included in the PIAAF-PPS cohort than were in the original PIAAF Pharmacy sample, but this was not a substantial difference. The results from the PIAAF Pharmacy screening intervention show that the majority of people included in the PIAAF-PPS cohort who were screened using the CANRISK criteria were found to be at high risk of diabetes. This is on top of the 22% percent of the cohort with known diabetes. These rates are consistent with the Public Health Agency of Canada's 2011 data reporting prevalence rates of approximately 16-25% in Canadians aged 65 and older (PHAC, 2011). While almost 56% of those in the PIAAF-PPS cohort reported a history of hypertension (prevalence of hypertension in Canada is roughly 60% [Robataille, 2012]), just under 30% were found to have raised blood pressure at the time of screening. This may indicate that about a third of participants may require additional intervention to control blood pressure. 15 patients were suspected to have AF following screening with the SL-ECG, which represents about 2.8% of the PIAAF-PPS cohort, compared to a population prevalence of approximately 3-5% in patients $\geq$65 (US data) (Feinberg, 1995). Of these patients, 9 were able to speak to the pharmacist after screening, and 9 received subsequent prescriptions for oral anticoagulants.

The descriptive analysis found that 165 patients, or approximately 31% of the PIAAF-PPS cohort received a total of 229 pharmacy services within 3 months of participating in the PIAAF Pharmacy screening intervention. The average dollar amount reimbursed to pharmacies for remunerated pharmacy services was approximately CAD 303.00 for an average of 8.8 pharmacy services, which works out to approximately CAD 34.43 per pharmacy service. In terms of the monetary value reimbursed to pharmacies for remunerated pharmacy services, it is clear that the pharmacies that provided more pharmacy services generally made more money. However, some pharmacies were reimbursed more money for providing less, but more intensive and time-consuming pharmacy services (such as MedsCheck Diabetes or CACPs) than pharmacies that

performed more, but quicker and less complex pharmacy services (such as influenza vaccinations or pharmaceutical opinions). Pharmacists likely see time spent performing longer, more involved pharmacy services as a trade-off for a larger reimbursement (Bradley, 2008).

Over 50% of those included in the PIAAF-PPS analysis used statins for hypercholesterolemia. These numbers are consistent with estimates from population-based research. Statistics Canada estimates that approximately 47.9% of men and 35.6% of women aged 65-79 use lipid-modifying agents (Rotermann, 2014). Just under half took low-dose ASA on a regular basis. Generally speaking, patient self-reported drug use did not differ significantly from the pharmacy dispensing records, except in the case of alpha blockers—a significantly higher proportion of patients were found to be taking alpha blockers (as determined using pharmacy data) than patients self-reporting use of alpha blockers, which may indicate that patients have less knowledge about this class of drugs and their indications than other classes of drugs. The mean number of medications per person was found to be 4.4, which is consistent with 2012 data from CIHI stating that approximately 34% of all seniors took medications from 5 drug classes or less (CIHI, 2012). Nevertheless, these numbers are slightly lower than other studies have reported in terms of mean number of medications taken (Dolovich, 2016, Pechlivanoglou, 2016). This may be due to a number of reasons, including the possibility that the participants included in the PIAAF-PPS analysis were a healthier cohort of elderly individuals. A more likely reason may stem from the fact that it was not possible to locate pharmacy records for some participants, and in these cases the number of medications was extrapolated from the CRF forms—this may have reduced the average number of prescription medications and resulted in a lower estimate. Despite the fact that the average number of medications was somewhat low, these results still indicate that polypharmacy was present in almost half of the PIAAF-PPS cohort.

Community pharmacy screening programs such as the PIAAF Pharmacy study may have some potential to boost provision of some pharmacy services, although these results indicate that receipt of pharmacy services was generally not associated with the screening results themselves, but rather with other patient factors (e.g. number of medications, new medications, etc.). Whether or not screening results factored into a pharmacist's rationale for provision of pharmacy services, many participants did end up receiving at least one pharmacy service within 3 months of screening. This was especially noticeable in pharmacies where the intervention period began in October or November, and ran through to December of 2014 or later, as in these cases, the screening sessions lined up with the annual influenza vaccination period. 10.6% of the PIAAF-PPS cohort received

influenza vaccinations at the pharmacy at which they were screened, and of these participants, over half (52.6%) were vaccinated on the same day they participated in the screening intervention. This may indicate that patients who were coming into the pharmacy specifically to receive a flu shot stayed for the screening intervention, or vice versa. Being screening in October was also associated with increased rates of pharmacy service receipt, and increased odds of receiving a medication review. Patients, therefore, seemed to receive pharmacy services other than just influenza vaccines during the annual flu shot period (roughly October through December). Rather surprisingly, however, given the large total numbers of flu shots administered by participating pharmacies in October and November, influenza vaccinations only accounted for 24.9% of the pharmacy services provided to the PIAAF-PPS cohort. Medication reviews made up the vast majority of billed pharmacy services, with a combined total of 146 (63.8%) annual and follow-up medication reviews being identified. Other pharmacy services, for example prescription adaptation, pharmaceutical opinions and smoking cessation consultations were far less frequent. With the exception of influenza vaccination, most pharmacy services were not provided on the same day, or even within the same week as screening visits took place. Since the majority of pharmacy services received were medication reviews, which generally take at least 20 minutes to complete, it is reasonable to assume that patients and pharmacists alike preferred to schedule these consultations for later dates. Due to the small sample size, low number of observed pharmacy service events, and alignment of the intervention period with the annual flu shot vaccination period, it is difficult to draw conclusions as to whether or not more pharmacy services were performed during the and after the screening period. More prescription and pharmacy service claims data would need to be extracted, likely from other pharmacies, in order to provide an answer to this question.

This study had several limitations. For instance, there appeared to be a disparity between jurisdictions in terms of patient recruitment for the PIAAF Pharmacy screening intervention. Pharmacies in Ontario tended to recruit more participants, and more of these recruited participants were regular customers. In contrast, pharmacies in Alberta tended to recruit more patients that were not regular pharmacy patrons, which lowered the sample size of the PIAAF-PPS analysis (as pharmacy data and pharmaceutical service billing claims could not be extracted for these participants). Additionally, some patients' pharmacy profiles were unable to be located due to data that was either missing or incorrectly transcribed on the CRF forms. The fact that data could only be extracted from Rexall pharmacies (due to feasibility issues) was also a limitation. Finally, a number of the variables of interest, identified through the creation of the conceptual framework, were unable to be captured in this project. Further research will be required to understand

how these missing pieces fit together alongside the ones that were included in this analysis.

6.0 CHAPTER 6: CONCLUSIONS

The results of this analysis indicate that being screened as being positive for AF or being at high risk of chronic disease was not associated with higher odds of receiving medication reviews, and was not associated with increased rates of pharmacy service receipt. Instead, patient-related factors such as number of medications and new medications were found to be associated with the increased pharmacy service receipt. The exception to this was the provision of influenza vaccines, where those found to be at high risk for diabetes were associated with increased odds of receiving a flu shot. As well, results indicate that patients with more potentially inappropriate medications were negatively associated with receipt of medication reviews. The descriptive analysis showed that approximately 31% of PIAAF Pharmacy participants received a pharmacy service within 3 months of screening, the majority of which were medication reviews. Each pharmacy performed an average of approximately 9 pharmacy services for PIAAF-PPS cohort participants within 3 months of screening, with an average reimbursement amount of CAD 303.00. There is some evidence to suggest that in-pharmacy screening initiatives may be better at increasing the number of pharmacy services provided (including medication reviews) if they coincide with the annual flu shot season, when a higher volume of people are visiting the pharmacy to receive their influenza vaccination.

Optimally, pharmacists would have used the results from patient screening as an opportunity to provide patients with education and appropriate pharmaceutical care, especially in patients found to have screened positive for AF or at high risk for hypertension and type II diabetes. However, patients screened as being at high risk for chronic conditions were not associated with increased receipt of pharmacy services when compared to those at low or no risk. In light of the non-significance of screening results and their negligible association with pharmacy service receipt, it behooves pharmacists to ensure that patients who are found to be at high risk of CVD receive adequate monitoring and follow-up, of which pharmacy services such as medication reviews play in intrinsic role. More research must be done before any firm conclusions can be drawn as to the effectiveness of community pharmacy screening at increasing numbers of pharmacy services in high-risk patients, including high-quality randomized controlled trials and cohort studies (to investigate use of pharmacy services in high-risk patients), as well as qualitative studies (to elicit the opinions of pharmacists and participants regarding pharmacy service provision and receipt following screening).

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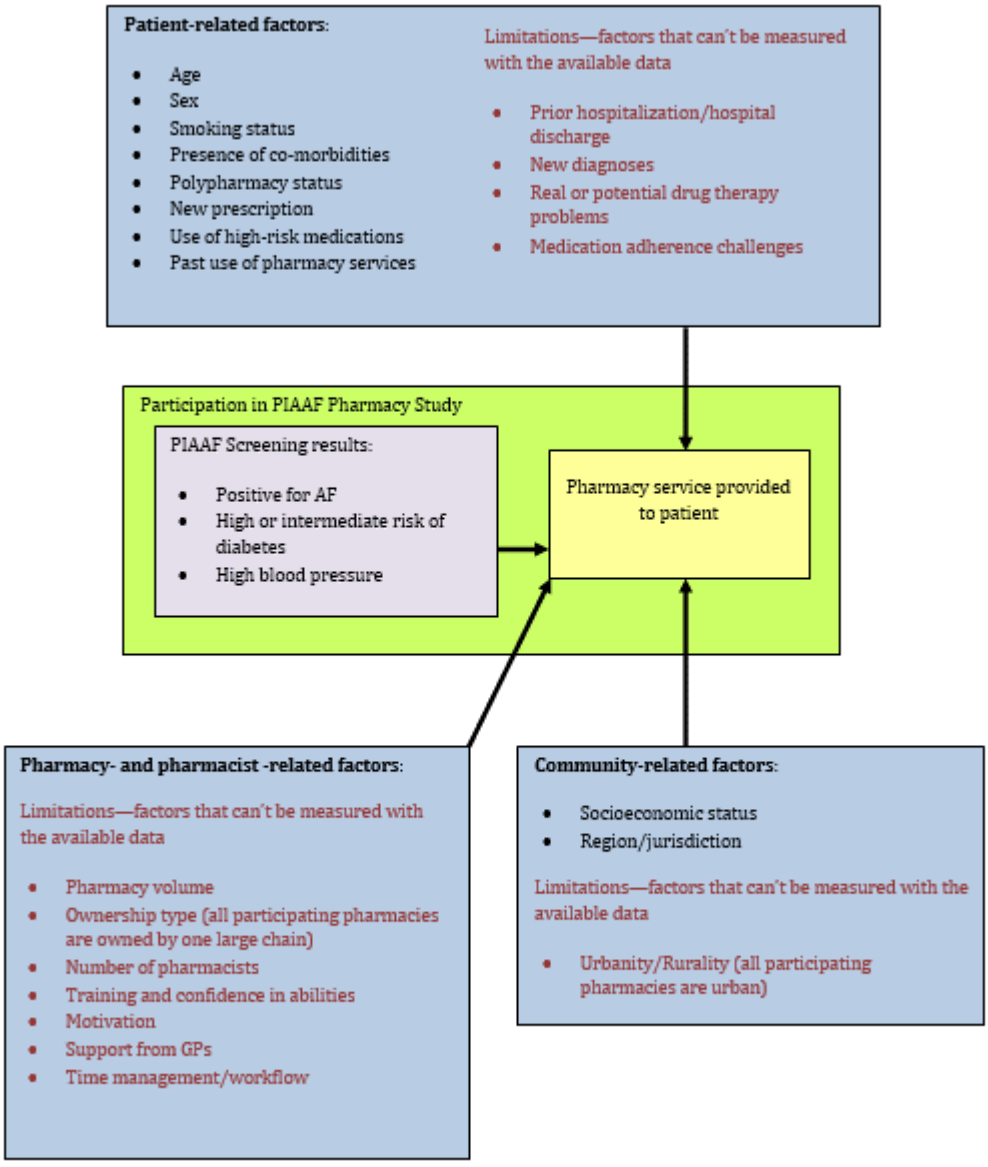
APPENDIX I: VISUALIZATION OF CONCEPTUAL FRAMEWORK



APPENDIX 2: SAS CODE FOR MIXED-EFFECT ZERO-INFLATED POISSON REGRESSION

This code was taken from the following website:

SAS FAQ: How do I run a random effect zero-inflated poisson model using nlmixed? UCLA: Statistical Consulting Group.
http://www.ats.ucla.edu/stat/sas/notes2/

```
data piaaf;
set piaaf;
if catpriorpharmserv = 0 then catpriorpharmserv0 = 1;
else catpriorpharmserv0 = 0;
if catpriorpharmserv = 1 then catpriorpharmserv1 = 1;
else catpriorpharmserv1 = 0;
if catpriorpharmserv = 2 then catpriorpharmserv2 = 1;
else catpriorpharmserv = 0;
if monthofscreening = 1 then monthofscreening1 = 1;
else monthofscreening1 = 0;
if monthofscreening = 2 then monthofscreening2 = 1;
else monthofscreening2 = 0;
if monthofscreening = 3 then monthofscreening3 = 1;
else monthofscreening3 = 0;
if monthofscreening = 4 then monthofscreening4 = 1;
else monthofscreening4 = 0;
if monthofscreening = 5 then monthofscreening5 = 1;
else monthofscreening5 = 0;
if monthofscreening = 6 then monthofscreening6 = 1;
else monthofscreening6 = 0;
if monthofscreening = 7 then monthofscreening7 = 1;
else monthofscreening7 = 0;
if usemecanriskcat = 1 then usemecanriskcat1 = 1;
else usemecanriskcat1 = 0;
if usemecanriskcat = 2 then usemecanriskcat2 =1;
else usemecanriskcat2 = 0;
if usemecanriskcat = 3 then usemecanriskcat3 = 1;
else usemecanriskcat3 = 0;
if usemecanriskcat = 4 then usemecanriskcat4 = 1;
else usemecanriskcat4 = 0;
run;

proc genmod data = piaaf;
```

```
      model numpharmservpostscr = jurisdiction nummeds
monthofscreening1 numhighriskmeds numcigsperday newmeds
avdiasbp  / dist=zip;
      zeromodel age nummeds sesdepscore usemecanriskcat2
jurisdiction catpriorpharmserv1 / link = logit;
run;

proc nlmixed data = piaaf;
      parms b0=-0.7532 b1=0.4995 b2=0.0473 b3=-0.7543 b4=-
0.1832 b5=0.0318 b6=0.7106 b7=-0.0074
            a0=-1.5930 a1=0.0792 a2=-0.8053 a3=-8.2056 a4=-
3.3241 a5=-5.1346 a6=1.0085 a7=1.5520;
      logit0 = a0 + a1*age + a2*nummeds + a3*SESdepscore +
a4*usemecanriskcat2 + a5*jurisdiction + a6*sesdepscore +
a7*catpriorpharmserv1;
      prob0 = 1 / (1 + exp(-logit0));
      mu = exp(b0 + b1*jurisdiction + b2*nummeds +
b3*monthofscreening1 + b4*numhighriskmeds + b5*numcigsperday
+ b6*newmeds + b7*avdiasbp);
      if numpharmservpostscr = 0 then
            ll = log(prob0 + (1 - prob0)*exp(-mu));
      else
            ll = numpharmservpostscr*log(mu) + log(1 -
prob0) - mu - lgamma(numpharmservpostscr + 1);
      model numpharmservpostscr ~ general(ll);
run;

proc sort data = piaaf;
      by pharmacynumber;
run;

proc glimmix data = piaaf noclprint method=laplace;
      class pharmacynumber;
      model numpharmservpostscr = jurisdiction nummeds
monthofscreening1 numhighriskmeds numcigsperday newmeds
avdiasbp / solution dist=poisson;
      random intercept / subject = pharmacynumber;
run;

proc nlmixed data = piaaf;
      parms b0=-1.7021 b1=0.3937 b2=0.1042 b3=-0.4750 b4=-
0.1450 b5=0.02750 b6=0.7643 b7=-0.00525
                  sigma2=0.22;
```

```
      mu = exp(b0 + u + b1*jurisdiction + b2*nummeds +
b3*monthofscreening1 + b4*numhighriskmeds + b5*numcigsperday
+ b6*newmeds + b7*avdiasbp);
      ll = numpharmservpostscr*log(mu) - mu -
lgamma(numpharmservpostscr + 1);
      model numpharmservpostscr ~ general(ll);
      random u ~ normal(0, sigma2) subject=pharmacynumber;
run;

proc nlmixed data = piaaf method=gauss qpoints=25;
      parms b0 -0.7532 b1=0.4995 b2=0.0473 b3=-0.7543 b4=-
0.1832 b5=0.0318 b6=0.7106 b7=-0.0074
                  a0=-1.5930 a1=0.0792 a2=-0.8053 a3=-
8.2056 a4=-3.3241 a5=-5.1346 a6=1.0085 a7=1.5520
                  sigma2=0.1709;
      logit0 = a0 + a1*age + a2*nummeds + a3*SESdepscore +
a4*usemecanriskcat2 + a5*jurisdiction +
a6*catpriorpharmserv1;
      prob0 = 1 / (1 + exp(-logit0));
      mu = exp(b0 + u + b1*jurisdiction + b2*nummeds +
b3*monthofscreening1 + b4*numhighriskmeds + b5*numcigsperday
+ b6*newmeds + b7*avdiasbp);
      if numpharmservpostscr = 0 then
            ll = log(prob0 + (1 - prob0)*exp(-mu));
      else
            ll = numpharmservpostscr*log(mu) + log(1-prob0)
- mu - lgamma(numpharmservpostscr + 1);
      model numpharmservpostscr ~ general(ll);
      random u ~ normal(0, sigma2) subject=pharmacynumber;
run;
```