Antipsychotic Prescribing as a Treatment of Dementia in British Columbia: Physician-Level Characteristics Associated with Receiving Potentially Inappropriate Prescriptions

by

Stephanie Littleford

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Submitted by: **Stephanie Littleford**

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Examining Committee:

Chair of Examining Committee	Dr. Shilpa Dogra
Research Supervisor	Dr. David Rudoler
Examining Committee Member	Dr. Jennifer Watt
Examining Committee Member	Dr. Sara Allin
Thesis Examiner	Dr. Mika Nonoyama, Associate Professor at Ontario Tech University

The above committee determined that the thesis is acceptable in form and content and that a satisfactory knowledge of the field covered by the thesis was demonstrated by the candidate during an oral examination. A signed copy of the Certificate of Approval is available from the School of Graduate and Postdoctoral Studies.

ABSTRACT

Antipsychotic prescribing has increased. One attribute of this is off-label prescribing of antipsychotics to people with dementia to treat behavioural and psychological symptoms, which is not supported by evidence-informed guidelines. This manuscript investigated physician-level factors associated with prescribing antipsychotics to community-dwelling adults with dementia by primary care physicians in British Columbia. Most physician variables were not associated with a patient being dispensed an antipsychotic. A physician's years in practice was significantly associated with a patient's risk of receiving an antipsychotic. Patients who received an antipsychotic were older, had lower incomes, used more prescriptions, contacted a physician more, and had higher comorbidity scores compared to patients who did not receive an antipsychotic. Rarity of outcomes, decreased rate of antipsychotic prescriptions, and little indication of practice-variation indicated physicians appropriately prescribe antipsychotics to patients with dementia. Future studies should investigate career-variation, apply similar methodology in regions of Canada, and investigate qualitative factors associated with antipsychotic prescribing at the physician- and patient/caregiver-level.

Keywords: prescribing; primary care; antipsychotic; dementia

AUTHOR'S DECLARATION

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Stephanie Littleford

STATEMENT OF CONTRIBUTIONS

This research was conducted by Stephanie Littleford while attending OntarioTech University under the supervision of Dr. David Rudoler and guidance of Dr. Sara Allin and Dr. Jennifer Watt. All individuals contributed discussions, editing, and revisions which led to the final manuscript. Stephanie Littleford and Dr. Rudoler developed the theory, conceived the study, and oversaw the overall direction and planning. Stephanie Littleford wrote the manuscript with support from Dr. Rudoler, Dr. Allin, and Dr. Watt. She performed the literature reviews, derived the models, and performed analytic calculations. She also deciphered the statistical findings first. Dr. Rudoler verified the analytic methods used, conceived the original idea, and further examined the study findings. Dr. Allin and Dr. Watt encouraged investigation of specific variables for analyses, guided on policy changes in BC, and supervised the findings of the work.

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LIST OF ABBREVIATIONS AND SYMBOLS

ADR	Adverse Drug Reaction
AP	Antipsychotic
BC	British Columbia
CCI	Charlson Comorbidity Index
CI	Confidence Interval
CPSBC	College of Physicians and Surgeons of BC
DAD	Discharge Access Database
FGA	First Generation Antipsychotic
GEE	Generalized Estimating Equation
LTC	Long Term Care
MD	Medical Doctorate
MIZ	Metropolitan Influenced Zone
MSP	Medical Service Plan
N	Population
PIP	Potentially Inappropriate Prescribing
q	Quintile
RRR	Relative Risk Ratio
Rx	Prescription
SAC	Statistical Area Classification
SD	Standard Deviation
SES	Socioeconomic Status
SGA	Second Generation Antipsychotic
UK	United Kingdom
US	United States
%	Percent
=	Equals
<	Less Than
>	More Than

Chapter 1. Introduction

Antipsychotics (AP) are a class of psychotropic medication used to treat a variety of psychiatric comorbidities. In recent decades, the prescribing rate for APs has increased (1–30). One of the attributes of this increase is off-label prescribing of APs to people with dementia, specifically to treat behavioural and psychological symptoms (5–7,11,12,15,17,23,24,31–37). In Canada, APs are not recommended as a treatment for any dementia symptoms except in severe cases where the patient is a danger to themself or others; the patient's symptoms have not been improved by nonpharmacological interventions; or symptoms are distressing, and antipsychotic use is within a patient’s stated goals and wishes. APs have been used in practice to alleviate symptoms for all forms of dementia (5,6,23,38–42). If an AP was prescribed as a treatment for dementia, it is recommended the prescriber only provide the drug at the lowest effective dose for a duration of three-months or less (5,6,23,38–42). In addition, it is expected the patient receive frequent medication reviews and the medication eventually be discontinued (9,11,34,36,43,44). Even with these guidelines, physicians continue to inappropriately prescribe APs to people with dementia without exhausting nonpharmacological treatments. Many AP prescriptions for people with dementia are for a longer duration than the advised time period and some involve the co-prescribing of two or more AP medications, but monotherapy is the aim of guidelines (11,45–51).

As more older adults plan to age at home and in their community, we need to understand the factors that change the quality of care older adults receive in

the community, including in primary care (52,53). In literature, it is not understood what physician-level characteristics are related to potentially inappropriate prescribing (PIP) of APs to people with dementia. At the patient-level, it has been shown age, biological sex, relationship status (i.e. married, widowed, single), race, residence, socioeconomic (SES) profile, and education are all associated with a patient's risk of receiving an AP (3,4,10,14–16,19,21,23,25,28–31,40,43,44,54,54–62,62–66). At the physician-level, some studies suggest biological sex, prescribing volume, specialty, place of graduation, practice setting, continuity of care, and years since graduation may affect prescribing, but these studies are often un-replicated and are not set in the Canadian context (11,17, 18,21,31,32,43,54,55,57,59,67–79). It has been shown that physicians practice differently at certain stages of their career due to confidence, burnout, work-life balance in relation to things like medication duration, new pharmaceutical uptake, emotional irregularities, and application of knowledge (80–85). Physician-level variation impacts cost, quality, and value of care delivered across patients and may be harming the care individual's receive (81,83,86).

The current paper aims to increase understanding of which physician characteristics are related to patient-level outcomes; specifically what characteristics of primary care physicians—who are the first point of contact between the patient and health care system (87,88)—are associated with a patient's risk of receiving an AP prescription(s) as a treatment for dementia symptoms. This study aimed to answer the following questions:

Amongst primary care physicians who dispense APs to community-dwelling patients with dementia who reside in British Columbia (BC):

1. What patient characteristic differ between those who were dispensed an AP during the study and those who do not?
2. What physician characteristics are related to an increased risk of being dispensed an incident AP prescription; a long-term AP; co-prescription of two or more APs; and/or a long-term co-prescription of two or more APs?

In relation to question 2, the aim was to specifically focus on what is the association between career stage (defined as years in practice) of a primary care physician and the risk of a community-dwelling patient with dementia being dispensed an AP?

At this time, specifically in the province of BC, most policies and guidelines addressing care for people with dementia are based on findings from long-term care (LTC) residents (36,89–92). Research has shown that community-dwellers and residential care patients should be studied separately as the same variables affect each population in different ways (31,69,93). Overall, little is known about the physician-level variables' relationship to risk of dispensing an AP to a community-dwelling patient with dementia. Understanding prescribing patterns for APs for community-dwelling older adults will support policy interventions to curb PIPs in this population.

Chapter 2. Background

This thesis focuses on the prescribing of APs to patients with dementia in the province of BC. It also focuses on the patterns of AP prescribing by primary care physicians. In this section, I provide background information on AP medications, potentially inappropriate AP prescribing, and current recommendations for AP prescribing to people with dementia. I delve into primary care in Canada, specifically on the recent restructuring of health systems in BC striving for full-service, team-based, patient-focused care. This section ends with a description of the prescription drug coverage in BC—PharmaCare—and relevant policy changes in order to understand the current evidence supporting AP prescription guidelines and to better understand the gaps my research could fill. Findings show there is a need for research focused on AP prescribing to older adults with dementia at the primary care level that will coincide with the shift of the health care system underway in BC.

2.1 Antipsychotics

APs are a form of psychotropic medication categorized into two classifications: first-generation antipsychotics (FGA) and second-generation antipsychotics (SGA) (3,19,21,29,34,56,78,94). FGAs, also referred to as typical antipsychotics, were developed in the 1950s as a way to treat schizophrenic disorders (12). FGAs are dopamine receptor antagonists and have a high affinity for the dopamine D2 receptor (31,94). Haloperidol is often the most prevalent FGA prescribed to adults (4,10,26,59,95). SGAs, also known as atypical antipsychotics, were developed in the 1990s to widen the efficiency of APs and

minimize the side-effects of the first-generation version of the medication (3,12,28,58,59,94,96). SGAs are serotonin-dopamine antagonists with a weaker bond to dopamine compared to FGAs (31,94). SGAs were introduced to the market and quickly became the preferable class of APs. Risperidone was the first available SGA in Canada and in the late 1990s and early 2000s, was the most prescribed SGA (19,21,34). Since the late 2000s, preferences concerning the prescribing of SGAs shifted. Currently Quetiapine is the most prevalent SGA, followed by Olanzapine or Risperidone (1,10,14,22,23,31,58,59). Both FGAs and SGAs can be administered in oral or parenteral (often injectable) forms (94).

APs are used to treat mania and psychosis symptoms (1,3,12,8,2,4–7,9–11,13). This includes treatment for diseases such as schizophrenia, bipolar disorder, borderline personality disorder, depression and depressive symptoms without mania or psychosis symptoms (1-13). APs have also been used to alleviate comorbid symptoms of manic and psychotic diseases. Due to the ability to address multiple symptoms in one pill, APs are used to treat multiple mental disorder symptoms to reduce polypharmacy in patients (15–18).

In Canada, prescribing rates for APs have increased over the last two decades, which largely matches global trends (1,13,19–21). The growing size of the Canadian population, advancing age of Canadians, increase in off-label prescribing, and introduction of SGAs are all reasons for this increase (3,10,13,19,21–30,48). Currently, SGAs are in the top five most prescribed therapeutic classes based on dollar sales (97). APs account for 2-5% of all drug spending in Canada and 14% of all AP prescriptions are for Canadians aged 65

years or older (98–101). Overall, approximately 70% of APs are covered by public funding in Canada (102). In 2013 in Canada, over 1.4 billion APs were dispensed with a rate of over 26,000 units dispensed to every 100 persons (2). The province of New Brunswick has consistently had the highest prescribing rates of APs and Newfoundland and Labrador the lowest (2). APs are a psychiatric medication that can be used to treat many comorbidities, but the recent rise of prescribing rates may be cause for concern due to reasons discussed in the next section.

2.1.1 Potentially Inappropriate Antipsychotic Prescribing

APs are often prescribed to treat off-label disorders. Off-label prescribing is when a medication is provided by a health professional to a patient to treat a condition or symptom the drug is not indicated for (15,24,31–33,103). Psychiatric medications have been shown to have high rates of off-label prescribing and older adults—those aged 65 years or older—have an increased risk of receiving a psychotropic medication without a psychiatric diagnosis (29). Although off-label prescriptions do occur frequently, AP on-label prescriptions—drugs prescribed to treat indicated ailments—still make up the majority of total AP prescriptions (1).

A common off-label use of AP is for adults suffering from neuropsychiatric symptoms resulting from dementia (5–7,11,12,34,35,104). These symptoms include aggression, agitation, mood disorders, psychosis, wandering, shouting, sleep disturbances, personality changes, inappropriate behaviour, and paranoia (5–7,11,12,34,35,104). These medications have shown low to moderate effects in alleviating aggression and other symptoms that often develop from dementia.

The use of APs, especially off-label, is scrutinized because of the potentially inappropriate use and relation to adverse drug reactions (ADRs) (69).

Off-label AP usage is related to increased risks of falls, heart disease, pneumonia, diabetes, cognitive decline, sedation, sexual dysfunction, weight gain, hypotension, tardive dyskinesia, and all-cause mortality, especially in the vulnerable population of older adults (12,34,40,105–107). APs, even with an appropriate prescription, are related to impaired quality of life, cognitive decline or impairment, falls, fractures, blurred vision, metabolic risks, confusion, sedation, increased risk of cerebrovascular events, increased likelihood of stroke, morbidity and mortality (3,6,7,17,19,34,40,54,59,69). Long-term AP use, high dosage, increased age, and suffering symptoms of dementia have all been linked to worsened ADR effects (11,17,46). SGAs have been noted as having fewer ADRs than FGAs, but this is inconsistent in the literature and both have been equally associated with universal ADRs such as metabolic effects and death (9,19,40,108).

According to Beers and STOPP/START criteria—two widely-accepted prescribing guidelines—between 20-40% of all older adults taking a prescribed medication will receive a PIP (109–114). PIPs are medications with safer and more effective alternatives or prescriptions that have treatment risks that surpass their benefits (45). People aged 70 years or older are at the highest risk of PIP in Canada. Chronic PIP usage —where patients use a medication for at least one-year consistently—occurs in 25% of Canada’s community-dwelling older adults (30,43,45).

Another prescribing practice that can be considered inappropriate is polypharmacy. Polypharmacy is the prescription of multiple medications to a single patient (15,108). Appropriate polypharmacy is when a patient's quality of life is improved, or life expectancy is extended by multiple medications. Problematic polypharmacy is when the risks of taking multiple medications surpass the benefits (15). Risks of polypharmacy include increased likelihood of ADR; drug interaction, which is the contamination of one medication's effect by another supplement; high-risk prescribing, which is any medication with evidence of significant risk of causing harm to patients; medication errors; hospitalizations; morbidity and mortality (15,108). Other aspects of AP prescribing which can be potentially inappropriate are duration and dosage. These factors of AP prescriptions can affect quality of life or increase mortality.

In most cases, APs are considered off-label prescriptions for dementia treatment in Canada (42,104,115). APs cannot cure dementia and do not treat the disease itself. In Canada, guidelines suggest APs should only be prescribed to reduce or control symptoms of severe agitation, aggression, and psychosis in patients with dementia (42,104,115). APs are recommended to be deprescribed after a short time period and AP polypharmacy is not recommended (39,51). Even so, patients are at risk of ADRs, PIP, polypharmacy, inappropriate dosage and duration when prescribed any medication, but especially psychotropics (30,43,45). A population often prescribed APs inappropriately are individuals with dementia, the reasons for this are discussed in the following section.

2.1.2 Antipsychotic Prescribing to People with Dementia

Older adults are the fastest growing age group in Canada and are the age grouping with the highest prescription drug use (6,30,56). Dementia is a term that encompasses a variety of brain disorders which affect memory, thinking, social abilities, and overall impacts daily life (116,117). Some types of dementia include Alzheimer's disease, which is the most common cause of dementia; Vascular dementia; Lewy body dementia; Frontotemporal dementia; and mixed dementia (117). There are over half a million people living with some form of dementia in Canada with an incidence rate of approximately 14.3 new cases per 1,000 in the older adult population (118,119). The majority of people with dementia in Canada are females and over 75,000 new cases are diagnosed annually (54,56,120). The prevalence rate of dementia is increasing and dementia is prevalent in 25% of Canadians over the age of 85 (119,121).

Increased age has been associated with psychotropic prescription without psychiatric diagnosis and AP use has a relationship with older age (26,29,57,59,65). In Canada, at least one quarter of people with dementia will be prescribed an AP as an off-label treatment to manage their symptoms and 14.5% of all older adults who reside in the community are prescribed an AP (5,23,36,37). From 2007 to 2013, 6.1% of older adult Canadians without a psychosis diagnosis were prescribed a new AP by their family physician within one-year after their dementia diagnosis (6). During 2009/10 in BC, almost one third of people with a dementia diagnoses received an incident AP prescription within the first year of their diagnosis (44).

People with dementia are likely to reside in LTC homes or other residential care units but there are still over 250,000 people with dementia in Canada who reside outside of assisted living (121,122). For older adults in Canada, the desirable living conditions has been reported as "aging in place". Aging in place means these older adults desire to remain in their community, often independently in their own residence, and are cared for by family, acute hospital care, and their primary health care providers (52,53). Studies have found that when looking at AP prescriptions, type of residence of the patient—mainly community-dwelling or within residential care—does influence prescribing at the patient and physician-level (69,123). Therefore, it is recommended that studies isolate each population and investigate them individually.

2.1.3 Antipsychotic Prescribing Recommendations

The global standard for AP treatment before it is considered long-term usage is 12-weeks as determined through a Delphi consensus comprised of 86 scientific, clinical, and consumer experts of dementia disease and AP medication (39). After three-months of AP use, if a patient's symptoms have stabilized or there is no adequate response to the medication, physicians should collaborate with their patient and the patient’s caregivers to begin tapering doses (40). It was found that chronic AP use can be terminated without detrimental effects to the patient's behaviour or cause withdrawal symptoms, but some pilot studies found there may be a change to relapse likelihood and time until relapse (39,124). However, research found no consistent changes to a patient's cognition, mortality, or quality of life after AP treatment was tapered off (39,40).

In 2018, an interdisciplinary team of nurses, psychiatrists, recreational therapists, and managers developed a sequential pathway of AP medications to treat Alzheimer's disease (38). The team compared the commonly administered APs in five main domains. The treatment plan advises any AP prescribed only for neuropsychiatric symptoms of dementia should be discontinued in a three- to 10-day period (38). If these treatments do not show improvement, risperidone should be initiated for a 21-day trial period beginning at 0.5 mg/day. After two-weeks of this initial dosage, it can be increased and re-assessed (38). Again, after two-weeks the dosage can be increased again, but at the four-week mark, a medical review must commence. If risperidone is not showing benefits for patients, aripiprazole or quetiapine should be prescribed for a 21-day trial period and follow similar timelines of re-assessment and increased dosages (38). Slower titration and lower dosage are recommended for frail patients.

The Canadian Deprescribing Network is an organization comprised of health care leaders, clinicians, researchers, and patient advocates focused on encouraging the deprescription of non-beneficial or harmful medication (125). Like above, in August 2019 the Canadian Deprescribing Network released the “Antipsychotic Deprescribing Algorithm”. It documents the appropriate symptoms and timeline for AP usage in patients. The algorithm recommends APs as a treatment of psychosis, aggression, and agitation in people with dementia for no longer than three-months (40,125). The deprescribing algorithm also recommends tapering dosage, discontinuation of APs, and two attempts of AP

medication to be made with a three-month grace period between medications (125).

Although Canadian guidelines recommend a short-term, low-dosage AP prescription to treat distressing neuropsychiatric symptoms of dementia, this does not always occur. A study from Quebec investigated PIP in older adults and found over a quarter of the cohort were still using the PIP after one-year (45). This one-year PIP persistence was highest for incident AP users. A study from the United Kingdom (UK) found by the end of 2012, 87.3 % of AP treatments were continued past the recommended six-weeks, and over 70% of treatments continued past 12-weeks (11). Of adults diagnosed with schizophrenia in France who were treated with monotherapy APs, over 82.9% were kept on long-term monotherapy (over six-months). For patients of the same study who were prescribed AP polypharmacy, 73.8% continued their AP polypharmacy as long-term treatments (6-months or longer) (46). One Canadian study found that amongst individuals who received an incident AP prescription to combat schizophrenia symptoms, approximately 14% received AP polypharmacy; after one-year, AP polypharmacy decreased to 11% of the entire cohort (1). In a study from Australia, care home residents who received APs as a treatment for dementia used the medication for an average duration of 212- to 216-days. This is more than double the recommended length of time (49). The same study found length of duration was affected by biological sex of patient, psychiatric comorbidities, class of AP, as well as patient age.

Long-term use of APs is related to increased expenditures in the health system (76,95), various side-effects (4,9,11,13,65,69,126) and some studies have suggested APs lose their effectiveness with time (127). The side-effect profile in studied long-term AP users indicated prolonged use of these drugs can impact daily life, may cause the drugs to become less effective, creates unnecessary costs, and are unnecessary for a large portion of patients who can cease AP usage and still manage their symptoms.

According to guidelines by the Canadian Medical Association, Canadian Mental Health Association, BC Care Providers, Clinical Pharmacology, and the BC Ministry of Health, best practice would occur when nonpharmacological therapies are exhausted for patients with dementia to find the root cause of their behaviour (9,11,34,36,43,44). If an AP is necessary because nonpharmacological therapies have not improved symptoms, a patient should be prescribed a single AP—specifically risperidone—at the lowest-effective dosage, for three months or less with regular monitoring and the goal of terminating the AP prescription (9,11,34,36,43,44). Yet, high dosage, long duration, and polypharmacy all occur. These attributes could lead to medication burden, decreased quality of life, and mortality (3,5,7,15,23,31,35,40,41,65,107,108).

The preceding sections focused on APs and AP prescribing, particularly to people with dementia. The key messages of this discussion were AP use is increasing due to higher rates of off-label prescribing and the introduction of SGAs (3,10,13,19,21–30,48). Off-label, PIP, and other forms of inappropriate prescribing are common factors of AP prescribing and can lead to serious ADRs,

reduced quality of life, and mortality for patients (11,17,46). Off-label and inappropriate prescribing factors are common among older adults, the population most vulnerable to the side-effects of medication (12,34,40,105–107). APs are often the first defense of neuropsychiatric symptoms of dementia. Since the thesis focuses on AP prescribing in primary care settings, in the following sections turn attention to the primary care context, giving specific attention to the province of BC, highlighting policies that are relevant to prescribing in that province..

2.2 Primary Care

Primary care is typically a patient's point of first contact with the health system and acts as gatekeeper to specialized health care services (87,88). Family physicians—in this thesis are also referred to as primary care physicians—are care providers who are often a patient's first contact with the health system and account for 51% of the Canadian physician workforce (128). The majority of Canadians consider a family physician their main care provider (128). Prescription medication is primarily provided by physicians in Canada and family physicians are responsible for their patient's drug reviews (43,129). Globally, family physicians account for over 50% of prescribers and for almost 70% of prescriptions for community-dwelling older adults (21,31,59,67,130,131). APs are prescribed by family physicians due to a lack of alternative treatments, such as other medications or nonpharmacological interventions (39). Family physicians also find it challenging to stop their patients from taking already

initiated medication due to patient push back and misunderstanding of discontinuation (78).

The majority of older adults are cared for solely by family physicians and this population are at a greater risk of mental disorders and cognitive impairment (15,56,57,93,132,133). Primary care physicians are usually the first or only physicians to address psychiatric symptoms in patients and play a central role in identifying and managing symptoms (15,120). Based on surveys and video records of interactions, it was found physicians are usually the ones to initiate discussion of medication use (41% physician-initiated) in comparison to patients (24% patient-initiated), especially in older adults (120). Family physicians are the most common prescribers of APs globally and it has been shown up to 79.9% of APs dispensed are prescribed by a family physician in a primary care setting (120). The current section of the paper has focused on primary care globally and nationally. The following portion of the thesis discusses primary care in the province of BC.

2.2.1 Primary Care – British Columbia Policy Context

In BC, primary care is funded and strategically overseen by the Ministry of Health Services and the Ministry of Health Living and Sport (134). Primary care providers consist mainly of family physicians within an office or clinic. Primary care services are administered in the community, by private providers, through hospital care and in residential care (134). From 2005/06 to 2011/12 in BC, the number of active family physicians increased by 12.8% (135). Other changes during this time included feminization and aging of the workforce (135). Overall,

there was a decline in service volume among primary care physicians (135). In BC, primary care providers can choose to enroll with Medical Service Plans (MSP) and obtain billing numbers to submit claims as long as they are licensed with the relevant colleges in the province (136). MSP services are not publicly funded without enrollment of the practitioner and patient eligibility for these benefits.

The province of BC has implemented a suite of reforms to restructure primary care. These changes have and will impact the way primary care physician's practice and prescribe. In 2002, the General Practice Service Committee was established through a collaboration between Doctors of BC—a voluntary association of physicians, residents, and medical student in BC (137)—and the Ministry of Health collaborating through the Physician Master Agreement. The partnership aimed to support and sustain full-service family practice (138). Full-service practice is a style of practice which includes most if not all of 14 specified dimensions including health assessments, coordination, continuity, services for acute and chronic conditions, mental health, geriatric health and more (133). In 2017/18, the General Practice Service Committee's produced a report with the purpose of shared learning from diverse care providers on how to support practices and achieve attributes of patient medical homes; support family physicians in the community to design a stronger, more integrated system of care; provide leadership and support for provincial and system enablers; and embed a quality improvement culture across practices and programs (36).

At the end of 2019, the province launched a new primary health care strategy to enable team-based care, which centers around Primary Care Networks (139–141). Primary Care Networks are meant to be comprised of community primary care service providers in a specific district including family physicians, nurse practitioners, registered nurses, physiotherapists, clinical pharmacists, occupational therapists, medical lab technologists, MRI technicians, social workers, registered dietitians, and First Nation resources and Traditional Healers (142,143). The networks provide care in Patient Medical Homes which are health facilities located in BC communities providing access to longitudinal primary care services (144). Primary Care Networks provide continual patient care tailored to the needs of the specific community they are located in. Working in a patient medical home is thought to encourage focus on patient support and enables physicians to access other health care providers, use accurate electronic medical records, get support from a network of colleagues, and access a broader system of services and supports in the community (145).

The primary care sector in BC is changing beyond the increasing numbers, feminization and ageing of the workforce (135). There is a strong emphasis on interdisciplinary collaboration which was initiated by the Physician Master Agreement in 2002. This collaborative care continues with the recent development of Primary Care Networks which emphasize multiple care providers in one patient medical home that serve the needs of the community being cared for and upholding the 14 dimensions of care specified in the reforms (138–141). At the policy level, BC initiatives encourage patient-focused practice, as well as

tailoring care to the needs of the community that a clinic is located in (36,138,145). BC has made major structural changes to shift towards a team-based healthcare sector all of which will contribute to a change in primary care practice and prescribing. Although no related policies or reforms were implemented around the time of the study period for this thesis, we aimed to understand what outcomes may have occurred from the promotion of collaboration between clinicians that predates the 2019 introduction of Primary Care Networks. The following chapter explored policies in BC related to prescribing to further understand the primary care context.

2.2.2 Prescription Drug Coverage in British Columbia

In Canada, prescription drugs are medications authorized by a healthcare professional to a patient as a way to manage health conditions (146). Prescription drugs in Canada play an important role in the health system as a way to save lives, prevent the spread of disease, improve quality of life, and minimize suffering (147). After hospitals, prescription drugs are the second largest component of the Canadian health care expenditure, accounting for 13 to 16% of total health expenditures in 2019 (148–150). Prescription drugs are not covered under the universal health insurance system, Medicare, but all provinces offer a form of public assistance for prescription drugs (151).

In 1996, the Medicare Protection Act was established in BC and under this act, all eligible residents and their dependents must enroll in a MSP (152). The MSP provides coverage for medically necessary services provided by physicians, supplementary health care practitioners, laboratory services, diagnostic

procedures and surgeons as well as other benefits such as podiatry surgical procedures, eye examinations, maternity care, diagnostic services, and dental or oral surgeries when performed in a hospital (136,153). Eligibility for an MSP requires individuals to be a citizen of the province, which is defined as being a citizen of Canada who resides in BC for at least a six-month calendar period or who are dependents of an MSP beneficiary; all First Nations Residents; and all persons on a specified work permit. Dependents include a married, common-law, or cohabiting spouse; a child, as a minor without spouse who is supported by the MSP beneficiary; and a dependent post-secondary student between the ages of 18 and 25 in full-time attendance at a recognized post-secondary institution (136).

In BC, PharmaCare—the provincial drug program—helps residents pay for eligible prescription drugs; fees charged by pharmacy providers; insulin pumps and supplies; prosthetics; ostomy supplies; pharmacy services and various over-the-counter medications (154). The prescription drug coverage selects certain medications to be covered based on effectiveness and costs for an individual. There are a total of seven Pharmacare plans, the largest of which is Fair PharmaCare which is based on the individual's income. BC residents can be covered under more than one plan at a time (154). In BC, a patient would be covered for APs under Plan G of Pharmacare (155). Currently, anyone eligible for a PharmaCare plan would have coverage for 32 APs in BC but Plan G may not cover all formulations and strengths of psychiatric medications in the formulary (8,156).

2.3 Summary

APs are a psychotropic medication used to psychiatric comorbidities (1–30). SGAs are the most prescribed class of this drug with quetiapine, risperidone, and olanzapine often being the most prescribed types overall (1,10,14,19,21–23,31,34,58,59,94). Before the COVID-19 pandemic, amongst community-dwelling patients, AP prescribing rates had increased. This is attributed to the introduction of SGAs, off-label prescribing of APs, and the rapid aging of the global population (1,3,10,13,19,21–30). These medications are related to multiple side effects and ADRs (12,34,40,105). Potentially inappropriate use of APs and AP polypharmacy is scrutinized due to findings relating these variables with ADRs and PIP as well as AP polypharmacy is not recommended in any current guidelines (15,39,69,108). A common off-label treatment of APs is for people with dementia experiencing severe neuropsychiatric symptoms where nonpharmacological treatments have been exhausted. Guidelines recommend APs only be used for a maximum of 12-weeks for people with dementia, beginning at the lowest effective dosage (9,11,34,36,43,44). Tapering dosage and discontinuation of AP treatment is expected.

In primary care, family physicians make up the majority of the physician workforce and older adults consider family physicians to be their sole provider of care (21,31,43,59,67,129,130,154). Primary care physicians also prescribe the most APs to community-dwelling older adults. In BC, the dynamics of primary care have been changing. The physician population has grown, feminized, and

aged over the last decade (135). A suite of policies have been implemented to support a full-service family practice as well as promote interdisciplinary collaboration, with emphasis on team-based care (36,138). In BC, the province provides medical coverage for all eligible residents and their dependents through the MSP. The provincial drug program, PharmaCare, is separate from the MSP and helps patients pay for prescription drug fees (8,155,156). The current portion of this thesis has explored implemented policies in BC and Canada. The following section delves into literature with research focused on patient- and physician-level characteristics that are associated with prescribing patterns, specifically the administration of APs.

Chapter 3. Literature Review

This thesis investigates physician-level variation and the physician characteristics related to an AP prescription to community-dwelling people with dementia in BC. Previous research on patient-level predictors of AP prescriptions will be explored. Patient demographics, medical factors, and SES factors have all been shown to change the risk of AP prescribing (1,3–5,7,10,14,15,19,21,23,30–32,40,44–46,48,54,55,57,59,60,65, 69, 95, 120,123,131,157,158). While there are multiple studies evaluating patient-level characteristics on prescribing, findings are inconsistent. I reviewed the literature describing physician-level factors associated with AP prescriptions to people with dementia. Studies of physician-level characteristics are scarce; most research focuses on patient- or clinic-level factors. Even so, factors such as a physician's biological sex, age,

place of graduation, residential and regional differences have been found as related to AP prescribing at the physician-level.

3.1 Patient Demographics

Of the patient-level factors explored in the literature, demographics are the most researched. Age, biological sex, relationship status, education, and living with others have all been explored (10,14–16,19,21,23,28–31,40,43,44,54–61). When including any adult over the age of 18, the likelihood of receiving an AP was related to younger age, specifically younger than 65 (10,14,57,96). When only individuals over the age of 65 are investigated, patients who are of an advanced age (typically older than 80) are more likely to receive an AP prescription (19,31,61). Yet in other studies, off-label use of APs was associated with older adults in the younger half of the population compared to those over the age of 85 (23,159).

Age has been shown as related to AP prescribing in isolation but other variables such as diagnosis, biological sex, and other demographics interact and change the odds the age factor contributes (49,59). When comparing individuals with an Alzheimer's diagnosis and those without, the likelihood of SGA usage decreased with advanced age for those who were suffering from Alzheimer's specifically. Those who did not have an Alzheimer's diagnosis, but had another form of dementia, were more likely to use SGA as their age increased (59). In a study investigating prevalence of APs in Australian nursing home residents, females in the younger age range (average of 70 years) were less likely to receive an AP compared to females in the older age range (average age of 95)

(49). The same study found young males had the shortest duration of AP usage in comparison to older males and females in either age groupings (49).

Of Canadians with dementia who are prescribed APs, those of female sex make up almost two-thirds of this population (56). Globally and since the introduction of APs, females have been the majority users of these medications (30,58,131,159). This finding may be attributed to females living longer, females making up a larger majority of the older adult and dementia population, and females are more likely to seek care and are more open about mental health concerns (5,30,54). Yet, it has been found that male sex positively associated with the risk of receiving an AP prescription (6,19,31). When results are weighted for population size, men have been shown to be more likely to receive an AP (1,6,31).

Being of female sex has been shown to be correlated with overall use of psychotropics (54,65). In a UK study investigating adults with a mental health diagnosis who received any AP prescription from 2007 to 2011, biological sex was shown to influence the form of AP prescribed (65). Women had a greater chance of receiving haloperidol, trifluoperazine, and quetiapine, but a lower chance than males to receive olanzapine and risperidone. In the United States (US) and UK, a systematic review found that female sex and increased age, in combination, increased a patient's likelihood of experiencing polypharmacy (15). The biological sex of the patient can also affect the duration of treatment. One study about Australian nursing home residents being treated for dementia, found females had a shorter duration of usage when compared to males (49). Although,

the same study found females had longer durations of AP usage when looking at cohorts of only females without psychiatric conditions and females with neuropsychiatric symptoms when compared to their male counterparts (49).

Some variables have shown to be consistent predictors of AP prescribing. Being of lower education levels or having fewer years of education increases a patient's likelihood of receiving an AP (10,14,23,30,37,159). Being in a relationship, married, or living with caregivers or family decreased a patient's likelihood of receiving an AP (23,30,32). Also, a patient residing in a LTC or nursing facility increases likelihood of receiving an AP compared to those who reside in the community (31,103,159,160). A patient’s age, biological sex, education, relationships, and type of residence can affect AP prescribing.

3.1.1 Patient Residence

Living in a rural or urban setting has been shown to change AP prescribing practices. Rates of being AP free are higher in rural areas and rural residents have lower odds of receiving new APs when compared to urban residents (14,57). In a study examining community-dwelling patients diagnosed with schizophrenia in China, living in urban areas and being AP free was related to advanced age, prominent depressive and negative symptoms, fewer hospital admissions, living alone, and lower education levels (57). In the same study, being from a rural setting and being AP free was related to female sex, lower education levels, and more prominent positive and negative symptoms.

3.1.2 Patient Medical Factors

A patient's medical profile is associated with AP prescribing rates. A patient's diagnosis, severity of disease, interaction with the health care system, number of medications, number of ailments, and form of medication have all been researched as factors that can modify prescribing (1,4,6,7,10,15,17,19,20,26,30,31,45,55,65,65,69,93). A diagnosis of dementia, specifically Alzheimer's disease; Parkinsonism (which can be onset after AP initiation); neurocognitive disorders; serious mental illness, such as schizophrenia or bipolar disorder; psychosis or psychotic symptoms; anxiety; delirium; and depression increase one's likelihood of receiving an AP (1,6,19,23,30,31,65,96,103,131,159,160). Having multiple chronic conditions is positively associated with the use of APs (6,30,31,60,131,161,162). Patients who experience vomiting, nausea, vertigo, migraines, and Tourette's syndrome may also be prescribed an AP (163). Suffering from milder symptoms of a disease, specifically mild to moderate dementia and neuropsychiatric symptoms, is related to lower odds of receiving an AP (1,32,60,103,159–161).

3.1.3 Social Determinants of Health

Social determinants of health are associated with AP prescribing. Black patients are more likely to receive FGAs and long-acting or depot injections compared to White patients (4,10,64). Yet, Black patients are also less likely to receive an AP, a SGA, and have shorter AP duration than White patients (4,30,63,64). When non-White patients are prescribed APs, they have a higher chance of receiving FGAs and long-acting injections which are associated with

prolonged use and more severe ADRs. But in a systematic review and meta-analysis investigating ethnic disparities in outpatient use of APs, racial/ethnic variables were not significant in changing the likelihood of receiving an AP prescription (164).

Income, employment, and welfare payments are correlated with AP usage. In a study from England investigating patients with dementia who received an antidementia drug from 2009 to 2019, those living in the least-deprived area are more likely to receive an AP treatment compared to the most-deprived area (165). Low income, at the individual, household and neighbourhood levels, have all been related to an increased likelihood of AP usage (14,30). Patients receiving welfare payments or veteran support payments are also more likely to receive AP prescriptions compared to those not receiving these assistances (25,48,66).

3.1.4 Patient Prescription Factors

Polypharmacy is common in older adults with dementia (6,103,114). Polypharmacy in AP users is more likely in patients with increased utilization of health care services and in individuals prescribed benzodiazepines or antidepressants (1,6,166). When AP polypharmacy occurs, it is often two APs prescribed to one individual and is a combination of one FGA and one SGA (166,167). In individuals who experience AP polypharmacy, the majority were prescribed above the maximum daily dose or were experiencing high daily dosage.

Being prescribed more than one AP was related to male sex, diagnosis of schizophrenia, living in a rural area, receiving welfare payments, lower educational level, never been married, being unemployed, receiving a prescription of a long-acting injection AP, usage of anti-parkinsonism medication, being prescribed a benzodiazepine, and the use of hospital, mental health and other health care services (1,10,48,167,168). AP polypharmacy shares certain predictive factors with characteristics that increase the likelihood of receiving any AP prescription (1,10,15,48,54,56). The overlap of these traits for increased prescription and polypharmacy rate could be associated with PIP and increased ADRs (9,10,15,45,48,54,56,108).

Inappropriate AP usage—including duration and type of medication—can be changed by patient-level characteristics as well (45,69). A retrospective population-based cohort study from Quebec investigated individuals over the age of 66 in 2014 experiencing persistent (one-year continuous) use of PIP. Potentially inappropriate medication use was related to increased age, multimorbidity, male sex, diagnosis of Alzheimer's disease or related dementia, and high numbers of various medications (45). Similarly, it was found older adults in the low-income quintile with dementia have longer durations of APs compared to individuals in higher income brackets (69).

Individual and combined patient characteristics can change AP prescribing patterns. Age, biological sex, relationship status, disease, severity of symptoms, race, SES, and polypharmacy all change the likelihood of AP usage. Age, biological sex, and psychiatric conditions have also been shown to affect duration

of AP usage in nursing home residents (49). Many patient-level factors—such as age, biological sex, medical factors, and residence type—should be investigated to fully understand which combined characteristics have the largest change to one's likelihood to receive an AP (49). Variables can also be controlled to measure isolated variables to see how they associate with the risk of being prescribed an AP.

3.2 Physician Characteristics

Although patient-level characteristics which affect AP prescribing have been explored in literature, prescriber characteristics are relatively understudied. Some studies have found the following factors affect prescribing of psychotropics: a physician's biological sex, prescribing volume, specialty, organizational affiliation, practice setting, and place of graduation but few have been replicated or conducted in a Canadian context (11,18,21,31,32,55,59,67–73,103). In contrast to these findings, one article about primary care physicians who prescribe APs to community-dwelling older adults showed physician characteristics—such as age, biological sex, speciality, type of practice, and hospital affiliation—were not indicative of AP prescriptions (19). As well, another study found physician characteristics did not change high or low polypharmacy rates (169).

Physician age and years of practice have been shown to affect practice overall. Younger prescribers of APs are more likely to order guideline recommended monitoring tests (67). Also, Canadian physicians early in their career (less than 3 years in practice) have reported multiple factors—including

personal, organizational, and system-level factors—restrict the clinical domains they include in part of their family practice (170). Key factors restricting a wider-array of domains in care included competency and confidence, minimal of experience in domains, lack of training and mentorship (170). Related to AP prescription outcomes, findings suggest physicians in the middle of their career (between the ages of 40 and 60) prescribe the widest variety of AP medications and those of the oldest quintile prescribe fewer SGAs compared to other age ranges (71).

A systematic review of studies from 1960 to 2004 investigating the relationship between clinical experience and performance found physicians who have been in practice longer—in terms of years—have less clinical knowledge, are less likely to adhere to standards of care, and may have poorer patient outcomes (171). Overall the systematic review found physicians who have been in practice longer are at risk of providing lower-quality care (171), but other efforts to measure associations between years in practice and patient outcomes have mixed results. One study based in New York focused on physicians years in practice and patients length of stay, readmission, and mortality from 2002 to 2004 (172–177). The study found the more years in practice a physician had, the longer length of stay in hospital for the patients they treated (172). The same study found patient's care for by physicians in practice for 20 years or more had higher in-hospital and 30-day mortality in admissions (172). The systemic review and previously reviewed study are outdated but no replication or more recent studies have focused on physicians' years in practice in association with patient

outcomes. To date, a study focused specifically on AP prescription outcomes to patients with dementia has yet to be studied even though it has been seen that years in practice does influence care, specifically patient outcomes related to quality of care.

Related to years in practice, patient-physician continuity has also impacted prescribing (73,74). One study found the longer a patient and physician relationship was, the less likely a discussion of psychotropic medication was to occur (120). Another study, based in Ontario and focusing on dementia treatment at the primary care level, found that patients who had known the doctor for at least five-years were less likely to be prescribed AP medications (73).

Specifically related to prescribing practice, a study based in Ontario found the volume of daily patients a primary care physician saw affected prescribing to patients with dementia (73). High volume contact physicians—those who saw thirty or more patients in a day—were more likely to prescribe APs, benzodiazepines, and cholinesterase inhibitors to patients with dementia when compared to low-volume physicians (saw fewer than 20 patients in a day) (73). Physicians with more patients, education, and knowledge have greater exposure to a variety of ailments; are more likely to see a diverse patient populations; and have a potentially better understanding of guideline specific recommendations (73).

A physician's knowledge and confidence has also been shown as an indicator of prescribing (18,31,57,78,93,178). Interviews with general physicians

in Cleveland community-based outpatient clinics found all general physicians experience some initial discomfort with new initiatives but those with more years of experience (more than 30) have faster adaption to unlearning old models of care and integrating new ones (179). Board certified physicians (American Board of Medical Specialities or American Osteopathic Association) had higher performance scores overall when compared to physicians without a certification (70).

AP prescribing has also been shown to vary significantly based on the geography and region of the prescriber and is one of the most consistent prescriber level characteristics found to affect prescribing (11,75–78). Physicians in less urban centers have less access to education, various medication exposure, and have fewer peers to discuss treatments with which could result in higher rates of prescribing certain medications repeatedly due to lack of alternative treatment or drug types (75,79).

It was found within primary care practices in Scotland, high risk prescribing is more likely to occur in smaller, non-training practices when compared to larger practices (43). When comparing older adults' psychotropic prescription rates in the US, the least urbanized counties received almost 10% more reports of psychotropic medication compared to highly urbanized counties (54). In the same study, when counties were pooled into two groups, the less urban area were still 5% higher in reports of psychotropic medication use compared to more urban areas. Alternatively, clinics in China in rural settings had higher rates of patients without AP treatment (57). Also studies have shown patients in less urban areas

are more likely to receive an SGA and have lower odds of receiving an AP overall (14,57). At the patient and physician-level, residential characteristics seem to influence AP prescribing but findings have not been consistent.

Many of the studies reviewed are not set in the Canadian context and do not focus on primary care prescribers in isolation. The supported finding that prescribers vary based on region and residential characteristics indicates a study must be tailored to a specific region and cannot be generalized. Due to this, the current paper will focus on the province of BC and further investigate descriptive characteristics at the patient and prescriber level. Many previous studies focus on qualitative factors such as physicians' attitudes and beliefs and are not easily quantifiable. The current study will investigate the defined number of years in practice at the primary care level for physicians who prescribe APs to community-dwelling people with dementia. This will allow for quantifiable understanding of prescriber factors that change treatment trends. Physician-level variability can increase costs of care, reduce quality of care, and causes barriers to accessing or receiving consistent care in the health system (82,83,86).

3.3 Summary

At the patient-level, factors that are associated with AP prescribing are mainly focused on demographics. Age, biological sex, relationship status, and education have all been shown to potentially predict a patient's likelihood of receiving an AP (1,3–5,7,10,14,15,19,21,23,30–32,40,44–46,48,54,55,57,59,60,65,69,95,120,123,131,157, 158). Similarly, a patient's race, residence, and SES also reveal patterns in AP trends. These trends often shown

non-White, low SES, low income, less-educated, unemployed, or those residing in deprived areas are less likely to receive guideline recommended care and are susceptible to prolonged duration, high dosage, and older classes of APs (3,4,10,14,25,30,54,62–66,165). At the patient-level, many previous studies have found common patterns of AP prescribing but these studies often focus on sub-populations such as those living in LTC. BC has also developed fewer policies dealing with AP usage in the community-dwelling population when compared to residential care patients even though BC older adults have reported they prefer to remain in home as they age (53,122).

Research also finds physician-level characteristics may related to AP prescribing though the studies at the prescriber-level are scarce, show mixed results, and have yet to be conducted in the BC context. Of the reviewed studies based in BC, one focused solely on physician demographic changes from the early 90's to 2010; one focused only on patients who were diagnosed with schizophrenia; and the last studied at the patient-level and focused on guideline-consistent medical care for people with dementia from 2009/2010 to 2010/11 (44,69,133).

From the literature, physician's biological sex, prescribing volume, specialty, place of graduation, and practice setting all are potentially influential to prescribing practices (11,18,21,31,32,55,59,67–72,103). Physician in the oldest age quintile have also been show to prescribe a smaller variety of SGAs compared to physicians in younger quintiles (71). But other studies have found physicians who have been in the field for a longer time are more confident and

careful about tailoring their AP treatments to patients (71,100). This may also be attributed to the individual having more practice, education, and confidence in their skills resulting in less preferential patterns occurring in more experienced physicians (18,31,57,73,78,93,120,177).

At the physician and patient-levels, clinic location and neighbourhood characteristics were found to be correlated with AP prescribing (11,14,57,75–78). In rural settings, APs are used more often and prescribed in higher volumes for patients of all ages and when only investigating older adults (14,57). Yet there is conflict at the patient-level as individuals who live in rural areas are more likely to be AP free and have lower odds of receiving an incident AP prescription. Similarly, at the physician-level, the increased prescribing in a rural setting may be biased because physicians have been shown to begin or end their careers in rural settings, but the majority of experienced younger primary care providers are located in urban settings (3,76,79). The contradictions at the residential area occur based on lack of control of potentially confounding variables and few studies being replicated in the same region. The current paper will only focus on one province, patient, and practitioner population to allow for a specific understanding of descriptive factors related to AP prescribing. It will provide clarity into the BC health care system at the primary care level, which has yet to be done in related literature. Focusing on one drug class, one diagnosis, and one level of health care allows for a specific knowledge of a very prominent and vulnerable population.

Chapter 4. Methods

This thesis investigated the relationship between physician-level characteristics and the prescribing patterns of APs to community-dwelling people with dementia in the province of BC. APs are considered off-label treatments for most patients with dementia and have been found to increase ADRs and reduce quality of life (3,6,7,11,12,17,19,34,40,46,54,59,69,105). According to guidelines by the Canadian Medical Association, Canadian Mental Health Association, BC Care Providers, Clinical Pharmacology, and the BC Ministry of Health, APs are only to be used after nonpharmacological interventions have been exhausted and should only be prescribed for a maximum of three-months when treating dementia in Canada (9,11,34,36,43,44). Previous research focused on AP prescribing has explored patient-level characteristics, often in LTC settings. Literature shows a patient's age, biological sex, relationship status, disease, severity of symptoms, race, SES, comorbidities and polypharmacy all change the likelihood of AP usage (1,3–5,7,10,14,15,19,21,23,30–32,40,44, 46,48, 54,55, 57,59,60,65, 69,95,120, 123,131,157,158).

Few studies have explored physician-level variables and were rarely set in Canada. Of the literature focused on physician characteristics, some have shown prescriber's biological sex, prescribing volume, specialty, practice setting, and place of graduation may change psychotropic prescribing (11,18,18,21,31,32,55,59,67–72,103). Some articles also show a physician's confidence/experience can influence their prescribing patterns

(18,31,57,78,93,178). But further studies have found physician variables do not significantly impact psychotropic prescribing (19,169).

From the findings discussed in the background and literature review, it was hypothesized that patients who receive an AP in the study and those that do not will differ significantly based on their age (10,14,23,31,57,61,96,159), biological sex (1,6,15,19,30,31,49,54, 56,58,65,131,159), Charlson Comorbidity Index (CCI) score (1,6,30-32,60,131,159-162), rurality (14,57), and number of unique prescriptions a patient used per year (45,165,166). At the physician-level it is assumed a physician's biological sex (31,59), prescribing volume (73), and career stage (67,71,170-176, 178) will be associated with patient outcomes. Specifically, is it assumed based on literature a physician with more years in practice will increase a patient's risk of receiving any AP because it has been shown they are less likely to follow guidelines, prescribe a wider variety of APs compared to newer physicians, and have worse patient outcomes (71,171,172).

Based on the lack of consistency in findings at the physician-level, the current study answers the following question: do patients with dementia who receive APs differ significantly from those who do not; and are physician-level characteristics associated with a patient's risk of being dispensed a new AP, a long-term AP, a co-prescription of APs, and/or a long-term co-prescription of APs? The following chapter will provide an in-depth description of the study design and analysis process used to answer these questions.

4.1 Study Design and Data Collection

The design was a retrospective cross-sectional study set in the primary care sector in the province of BC. The analysis examined administrative data from datasets provided by Population Data BC. This platform is a multi-university, data and education resource which allows for interdisciplinary studies focused on human wealth, well-being, and development.

The specific datasets used in this thesis included physician registry files collected by the College of Physicians and Surgeons of BC (CPSBC); the services provided by fee-for-service physicians to patients registered to the MSP; Pharmanet; the patient consolidations file; and the Discharge Access Database (DAD). The CPBSC provided data on all physicians registered to the CPSBC. The MSP contained data on the services provided by fee-for-service physicians to patients registered with the MSP. The MSP identifies eligible patients for provincial health insurance and associated physician claims. Pharmanet consisted of every prescription dispensed in a community BC pharmacy. Pharmanet identified dispensed prescription drugs which were eligible for reimbursement under PharmaCare, the provincial drug insurance program. The consolidation file was used for patient-level demographic information. The file included neighbourhood-level information (e.g., postal code information that was linked to neighbourhood income quintiles) via geo-codes to the Statistics Canada Census data. Finally, the DAD contained data on discharges, transfers, and deaths of in-patient and day-surgery patients in hospitals in BC. The DAD identified inclusion/exclusion criteria of the patient cohort based on

hospitalization for dementia and identified discharge diagnoses used to generate a measure of patient comorbidity (see information on the Charlson Comorbidity Index below).

4.2 Study Population

The analysis included two linked cohorts: a cohort of patients with a dementia diagnosis and a cohort of primary care physicians. The study investigated all AP prescriptions to people with dementia from a primary care physician during the 2015/16 and 2016/17 fiscal years. At the patient-level, the cohort was further stratified into patients with dementia who had not received an AP as a treatment from their family physician (control group) and patients with dementia who did receive an AP as a treatment from their family physician (experimental group). There was no expected sample size for the study.

4.2.1 Patient Cohort

This thesis included all patients with a dementia diagnosis by March 31, 2017, who resided in the community in BC. The diagnosis was determined using the algorithm developed by Jaakkimainen et al. (132). In this algorithm, a case of dementia occurred when, during a two-year period, a person had at least three medical service claims with a dementia diagnosis recorded (claims must be at least 30-days apart); or at least one hospitalization or same day surgery with a dementia diagnosis; or at least one prescription drug claim for a dementia medication (cholinesterase inhibitors). The algorithm has a sensitivity of 79.3%

and specificity of 99.1% (positive predictive value of 80.4%, negative predictive value of 99%) (132).

Patients were excluded in the following order: (1) any patient who was not a resident of BC at any point from two-years prior to April 1, 2015; (2) any patients not eligible for provincial health insurance from two-years prior to April 1, 2015; (3) any patient that did not receive a dementia diagnosis by March 31, 2017 (using the algorithm described above); (4) any patient that had LTC billings in 2015/16 or 2016/17; (5) any patient that received a psychosis diagnosis by March 31, 2017; (6) any patient who was registered for fewer than 183-days in 2015/16 and 2016/17; and (7) any patient who received an AP from a physician with speciality other than family practice during the study period.

The fourth patient exclusion—LTC billings—restricted the sample to the target population of community-dwelling older adults. The fifth exclusion criteria—psychosis diagnosis—was used because we were only focused on off-label prescribing of APs to older adults as a treatment for dementia. APs are a common treatment of psychosis (3,12,8,2,4–7,9–11,13,1). Psychosis was determined by the algorithm developed by Kurdyak et al. to generate a population-based sample with chronic psychotic illness from large, administrative databases (180). A patient was flagged for psychosis if they were admitted to a hospital or received three or more claims (on different dates) for schizophrenia, schizoaffective disorder, or psychotic disorders during a rolling 36-month period. The algorithm has a sensitivity of 90% and specificity of 68% (positive predictive value of 71%, negative predictive value of 89%) (180). The sixth exclusion criteria

was used to ensure outcome variables, including grace-periods, could be collected for all patients. This exclusion also ensured that patients were eligible for provincial health insurance and alive for at least 50% of each study year. The seventh exclusion criteria—physician speciality—was used to ensure only prescriptions from family physicians were being studied (18,21,29,31,54,55,59,70,71,100,181). Overall, the patient cohort assumed only BC residents with a dementia diagnosis who resided in the community without psychosis were included.

4.2.2 Physician Cohort

The analysis included primary care physicians registered to the CPSBC who were registered to practice or were in practice from 2015/2016 and/or 2016/2017. Physicians who (1) had a college specialty other than general practice or family medicine; and (2) were missing their year of graduation or had graduated in 2013 or later were excluded from the study. Physician-level exclusions were relatively unrestricted to preserve sample size.

4.3 Variables

4.3.1 Outcomes of Interest

At the patient-level, the outcomes of interest were as follows:

(1) the patient was dispensed an incident AP prescription where incident is defined as the patient had not received a prescription for an AP in the previous 12-months. The one-year without an AP is adapted from Alessi-Severeni et al. and Kjosavik et al. (19, 21).

(2) The patient was dispensed a long-term AP prescription. Long-term is defined as a total day's supply of 84-days or longer. The duration is defined as the first day of the observation period (when the first AP is dispensed) until the days' supply of the last AP prescription elapses. The last AP occurs when there is a gap of 14-days (two-weeks) or larger and does not overlap with a subsequent AP prescription. The 14-day grace period was developed from the methodology from Gardner et al. and Tapp et al. (7,182).

(3) The patient was dispensed co-prescription of any APs (two or more APs differentiated by generic names) with an overlap of 31-days or longer during a 38-day period. The overlap period is used to ensure cross-titration (overlap of medication when switching from initial prescription to another medication for the same purpose) is not occurring and the variable is representative of the co-prescription of APs which is considered inappropriate prescribing (38,166).

(4) The patient dispensed long-term co-prescription of any two APs (differentiated by generic names) with an overlap of 84-days or longer within a 91-day period. See outcome #2 for duration definition.

For the second and fourth outcomes, the 84-days represents the three-month maximum suggested prescription of an AP according to guidelines (9,11,34,36,40,43,44,125) and follows methods used by Malandain et al., Roux et al., and Tapp et al. (45,46,182). All patient-level outcome variables occurred in the 2015/16 and 2016/17 fiscal years.

4.3.2 Other Variables of Interest

The key exposure variable was a physician's years in practice. This variable was defined as the current year (2015, 2016, or 2017) minus the physician's graduation year minus two-years. The two-year subtraction was applied because in BC, it takes approximately two-years after receiving a MD to begin practicing as a physician (183–185). Years in Practice was broken down as follows: "New": less than 10 years in practice; "Mid":10-19 years in practice; "Senior": 20-29 years in practice; "Veteran": 30 or more years in practice based on Lavergne et al. and Reid et al.'s breakdown of similar variables (70,133).

Other variables included in the analysis from the patient cohort were the weighted CCI score for the 2014/15 fiscal year (6,30,31,60,131,161,162); patient residence (metropolitan/urban/rural; defined in Appendix A) (14,57); neighbourhood income quintile (q1 (low) through q5 (high)) (3,14,30,65,69,165); patient's biological sex (male/female) (15,30,49,54,56 ,58,65,131,159), patient age as of April 1, 2015 (10,14,19,23,31,57,61,96,159); number of unique prescriptions in 2014/15 fiscal year (1,10,15,48,54,56); and number of in-person or remote contacts with a family physician during the 2014/15 fiscal year, excluding laboratory or imaging services and no-charge referrals (1,4,6,7,10,15,17,19,20,26,30,31,45,55,65,65,69,93). These variables were included based on literature (as reviewed in chapter 3) and availability in the database. CCI score was included due to its availability from Population Data BC and accounts for 19 pre-defined comorbid conditions which predicts outcomes such as function, hospital length of stay, and mortality rates (186,187). It is used

widely in research and by clinicians (187). Appendix A1 provides a detailed description of all patient variables included in this study.

Other variables included in the analysis from the physician cohort were mean CCI score weighed by contacts; graduation location (Canada/International/Unknown); practice location (metropolitan/urban/rural); practitioner age; practitioner's biological sex (male/female); average and total number of unique prescriptions per patient; number of contacts a physician had categorized by patient age (0-17, 18-44, 45-64, 65-74, 75+); number of contacts a physician had categorized by patient's residence (metropolitan/urban/rural); number of patients with dementia; number of female patients; number of contacts based on patient's SES (q1 (low) through q5 (high)); number of contacts; number of patients; and physician-level continuity at all locations which is defined as the proportion of patients the physician saw within the two-year observation window where the treating physician was that patient's family physician. These physician-level factors were included based on literature (11,18,21,31,32,43,54,55,57,59,67–79,93,100,103,120,178) (as reviewed in chapter 3) and availability of the database. Appendix A2 provides a detailed description of all physician variables included in this study.

4.4 Statistical Analysis

First, the patient cohort was refined using the exclusion criteria, in order, as described above. Missing values were removed, and the patient cohort was divided into the total cohort, patients with dementia who did not receive an AP from a family physician, and patients with dementia who did receive an AP from a

family physician. Finally, the captured patient and physician cohorts were merged based on practitioner numbers using the *left_join* function with the '*dplyr*' package in *R.* Once the cohort captured the desired patients, descriptive statistics were estimated. For continuous variables, mean and standard deviation (*SD*) were reported. For categorical variables, the sum (n) and proportion (%) of each category option was reported. The linked family physicians who meet the above criteria are described using the same techniques as used for the patient cohort. A complete breakdown of the patient and physician cohort size is defined in Figure 1.0.

Next, multiple independent *t*-tests were used to compare patients with dementia who received any AP during the study period to patients with dementia who did not receive an AP based on the following characteristics: patient age, CCI score, number of unique prescriptions, and number of physician contacts during the study period. Normal distribution was assumed because sufficient sample size was met to satisfy the central limit theorem (188) . Bartlett's tests were used to test homogeneity of variance for each variable. Chi-square tests of independence were used to compare the patient cohorts based on patient's biological sex, neighbourhood income quintile, and type of residence. Effect sizes (Cohen's D and Cramer's V [categorical]) were calculated for these comparisons. If significant relationships were found, residuals would be used to analyze what categorical option combinations contained the significant relationships. Appendix C contains the interpretation for effect size measurements used and these

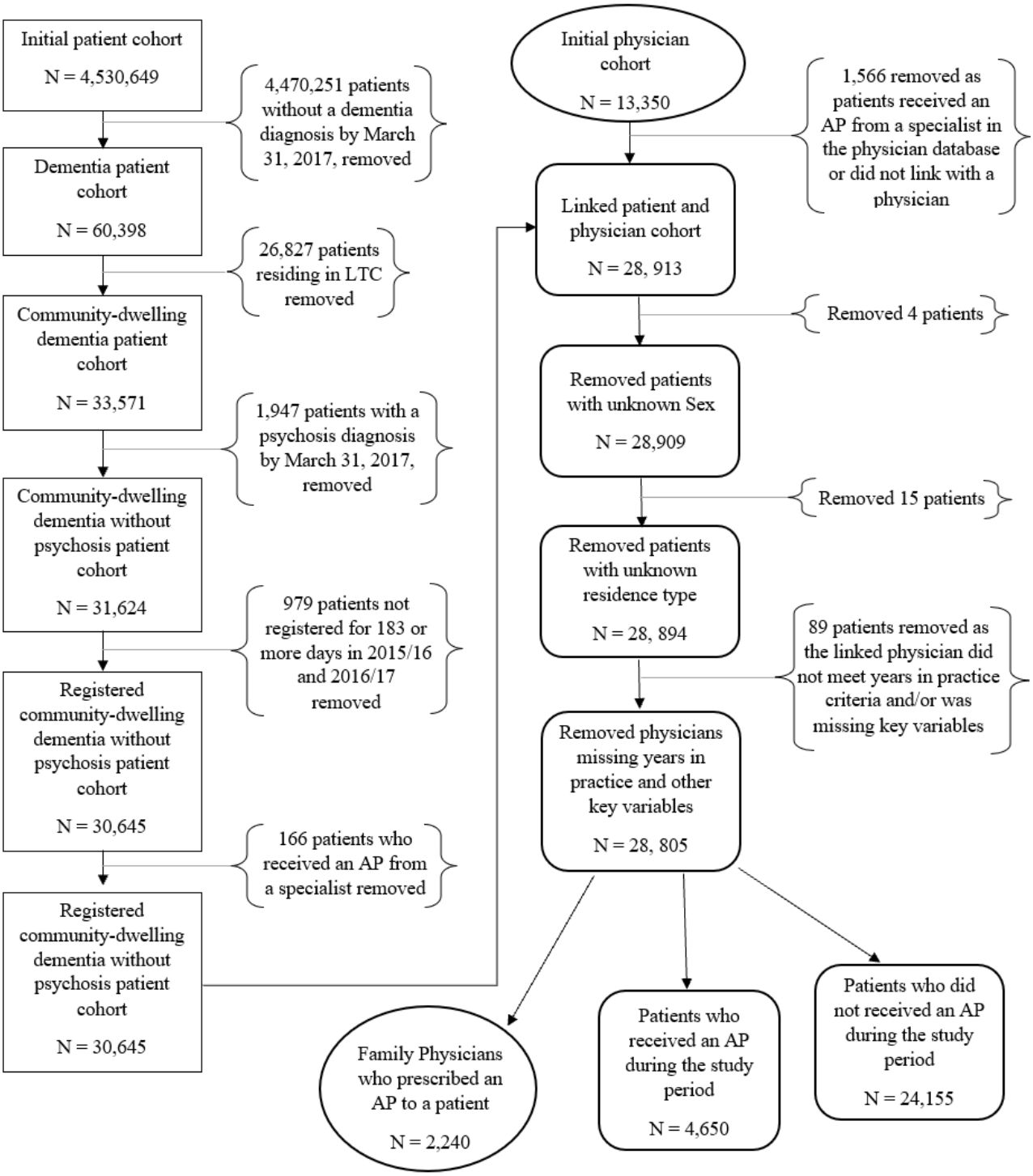
measures are most suitable for these research questions but the thresholds are context-dependent and should be cautious in interpretation (189–191).

To investigate the association between physician-level characteristics and the risk of patients being dispensed a new AP, a long-term AP, co-prescribed APs, and long-term co-prescribed APs from a family physician, multiple regression analyses were carried out. Regressions were estimated using a generalized estimating equation (GEE) using the '*gee*' package in *R.* A modified Poisson estimator—with log link and Poisson distribution outcome—was used to estimate the relationship between exposure variables and outcomes of interest (192). When modelling binary outcomes with the modified Poisson, the exponentiated coefficients can be interpreted as relative risk ratios. All standard error estimates were clustered at the physician-level and assumed an exchangeable correlation structure. A Poisson regression was also selected because relative risk is preferred over odds ratios as we investigated the likelihood of an event occurring—an AP being prescribed (193,194). Relative risk ratios are less likely to overestimate outcomes even if events are rare in comparison to odd ratios (193,194). The summarization of each model and exponentiated estimate coefficients were found using the *tidy* function from the '*broom*' package in *R* (195).

First, unadjusted models were run for each outcome and the following physician-level characteristics in isolation: years in practice, average number of unique prescriptions per patient, place of graduation, practice location, and physician's biological sex. These variables were selected as literature indicates

they may change prescribing practices (11,18,21,31,32,43,54,55,57,59,67–79,93,100,103,120,178) (as reviewed in chapter 3). Next, adjusted models were run conditional on the physician-level. Four adjusted models were run at the physician-level alone. Run for each outcome variable, the adjusted models accounted for years in practice, average number of unique prescriptions per patient, place of graduation, practice location, and physician's biological sex in combination. Subsequent regressions then estimated the relationship of each outcome with the same physician-level variables and the following patient-level variables: biological sex, age, residence, SES, CCI, number of unique prescriptions, and number of contacts with a family physician. These variables were also selected based on literature review findings (3,6,14,30,31,57,60,65,69,131,161,162,165). Four regressions were run conditional to physician and patient-level variables. All analyses were conducted using *R* version 4.0.5 (2021-03-31).

Figure 1.0 Process of Applying Inclusion/Exclusion Criteria to Cohorts



4.4.1 Sensitivity Analysis and Robustness Check

The outcome variables of this study relied on several assumptions that were tested via sensitivity analysis. First, it was assumed the maximum recommended duration for an appropriate AP prescription was three-months (39,40,125). While this assumption was based on guidelines, it could be varied to see how robust the findings are to this assumption. The grace period was increased to 28-days (four-weeks) from the original 14-day (two-week) grace period for a sensitivity analysis. Second, AP co-prescription was defined as a patient was dispensed two or more of any AP prescriptions prescribed at the same time for at least a one-month duration. To test for robustness, the length of AP overlap was adjusted from a duration of 31-days or more during a 38-day time period to a 45-day time period for the same outcome to occur. This adjustment ensured the analysis was only investigating patients who received multiple APs at one time for co-prescription and were not experiencing cross-titration. Lastly, for the long-term co-prescribed AP variable, the 84-day or greater duration must have occurred within a 91-day period for the original analysis. For sensitivity, the period where this occurred was lengthened to 98-days.

The regressions that include the years in practice variable were run again with years since MD instead. This variable is defined as the current year (2015, 2016, or 2017) minus the year since MD was awarded. The years since MD variable did not include the two-year gap that the years in practice variable accounted for.

For the Poisson regression, an independent correlation structure was also employed, rather than the exchangeable correlation structure in the primary analysis. All results of the sensitivity analysis and robustness checks are reported in Appendix D. For the *t*-tests analyses, a Mann-Whitney U was run in place of any tests that were in violation of the normality assumption. Appendix B contains the homogeneity of variance interpretation for the Chi-square tests.

Chapter 5. Results

5.1 Sample Statistic Descriptions

5.1.1 Patient Cohort

Initially, 4,530,649 BC patients were captured during the 2015/16 and 2016/17 fiscal years. After applying the patient-level exclusions, the patient sample size dropped to 30,645. After linking with the physician cohort and removing patients with unknown biological sex and type of residence, the sample reduced to 28,805 community-dwelling patients with dementia. The average age of this cohort was 78.40 years (*SD* = 11.17 years) and there was a slight female majority (n = 15,866.00, 55.08%). Most patients resided in metropolitan areas (n = 18,681.00, 64.85%) and patients were spread almost evenly amongst the five income quintiles (18.24% to 22.01%; range = 3.77). On average, patients had 7.11 unique prescriptions (*SD* = 4.75 units) and contacted a family physician 12.35 times (*SD* = 12.29) per fiscal year. Finally, the average patient's CCI score was 1.73 (*SD* = 1.70) showing the average patient had mild comorbidity (196).

The patient cohort was further divided into two groups: those who received an AP from a family physician captured in the study and patients who did not

receive an AP during the study. Twenty-four-thousand-one-hundred-fifty-five community-dwelling patients with dementia did not receive an AP, which accounted for 83.86% of the total patient sample. This sample had an average age of 78.39 years (*SD* = 11.03 years) and had a slight female majority (n = 13,314.00, 55.12%). These patients mainly resided in metropolitan areas (n = 15,734.00, 65.14%) and were almost equally spread across the five income quintiles (18.34% to 21.60%; range = 3.26%). On average, patients who did not receive an AP had 6.82 unique prescriptions (*SD* = 4.61 units) and contacted a family physician 12.00 times per fiscal year (*SD* = 11.95). Finally, the average patient CCI score was 1.69 (*SD* = 1.69) which was slightly lower than the total cohort average, but the average score is still considered mild.

Table 1 compares the characteristics of patients with dementia who received an AP and those who did not. Four-thousand-six-hundred-fifty community-dwelling patients with dementia received an AP from a family physician, which accounted for 16.14% of the total patient cohort. The average age of this group was 78.48 years (*SD* = 11.88 years), there was a slight female majority (n = 2,552.00, 54.88% vs. n = 2,098.00, 45.12%); and most patients in this grouping resided in metropolitan areas (n = 2,947.00, 63.38%). Those who received an AP had a larger range difference between quintile with the largest proportion of residents (q1, low, 16.80%) and quintile with the smallest proportion of residents (q5, high, 24.11%) (range = 7.31). This sample was more likely to live in lower income neighbourhoods compared to the total patient sample and those who did not receive an AP. Patients who received an AP had a higher

average number of unique prescriptions (*mean* = 8.60, *SD* = 5.16), number of contacts with a family physician during a fiscal year (*mean* = 14.11, *SD* = 13.78), and CCI score (*mean* = 1.90, *SD* = 1.73) than the total sample and the patients who did not receive an AP.

Patients who received an AP (*mean* = 78.48 years, *SD* = 11.88) and those who did not (*mean* = 78.39, *SD* = 11.03) did not significantly differ by age (*p*=0.605, 95CI [-0.47, 0.27], Cohen's d = 0.009), biological sex ([male] 45.12% vs 44.88%; *p* = 0.778; Cramer's V = 0.002), or place of residence ([metropolitan] 63.38% vs 65.14%; *p*=0.065, Cramer's V = 0.014). Patients who received an AP had higher CCI scores (*mean* = 1.90, *SD* = 1.73 vs. *mean* = 1.69, *SD* = 1.69; *p* < 0.001, 95CI [-0.26, -0.15]) and number of contacts with a family physician per year (*mean* = 14.11, *SD* = 13.78 vs. *mean* = 12.00, *SD* = 11.95; *p* <0.001, 95CI [-2.53, -1.69]) compared to patients who did not receive an AP during the study, but effect sizes for these comparisons were small ([CCI] Cohen's d = -0.122; [physician contact] Cohen's d = -0.172). Patients who received an AP (*mean* = 8.60, *SD* = 5.16) had more unique prescriptions than patients who did not receive an AP (*mean* = 6.82, *SD* = 4.61) (*p* <0.001, 95CI [-1.93, -1.62], Cohen's d = -0.377). Living in the lowest income neighbourhood was also significantly related to receiving an AP ([q1] 24.11% vs. 21.60%; *p* < 0.001; Cramer's V = 0.028).

Table 1

Description of Entire Patient Cohort with Missing Values Removed and Inferential Findings

	Patients				
	Total	**Patients with Dementia Prescribed APs**	**Patients with Dementia Not Prescribed APs**		
	N = 28,805	n = 4,650	n = 24,155	***p*- value**	**Effect size**
Age mean (*SD*)	78.40 (11.17)	78.48 (11.88)	78.39 (11.03)	0.605	-0.009
Sex N (%)					
Male	12,939.00 (44.92%)	2,098.00 (45.12%)	10,841.00 (44.88%)	0.778	0.002
Female	15,866.00 (55.08%)	2,552.00 (54.88%)	13,314.00 (55.12%)		
Patient Residence N (%)					
Metropolitan	18,681.00 (64.85%)	2,947.00 (63.38%)	15,734.00 (65.14%)	0.065	0.014
Smaller Urban	6,616.00 (22.97%)	1,120.00 (24.09%)	5,496.00 (22.75%)		
Rural and Remote	3,508.00 (12.18%)	583.00 (12.54%)	2,925.00 (12.11%)		
Neighbourhood Income Quintile N (%)				<0.001	0.028
q1 (low)	6,339.00 (22.01%)	1,121.00 (24.11%)	5,218.00 (21.60%)		

q2 q3 q4 q5 (high) q9 (unknown)	5,882.00 (20.42%) 5,738.00 (19.92%) 5,253.00 (18.24%) 5,320.00 (18.47%) 273.00 (0.95%)	984.00 (21.16%) 900.00 (19.35%) 822.00 (17.68%) 781.00 (16.80%) 42.00 (0.90%)	4,898.00 (20.28%) 4,838.00 (20.03%) 4,431.00 (18.34%) 4,539.00 (18.79%) 231.00 (0.96%)		
CCI mean (*SD*)	1.73 (1.69)	1.90 (1.73)	1.69 (1.69)	<0.001	-0.122
Number of Unique Prescriptions mean (*SD*)	7.11 (4.75)	8.60 (5.16)	6.82 (4.61)	<0.001	-0.377*
Number of Contacts with Primary Care Physician mean (*SD*)	12.35 (12.29)	14.11 (13.78)	12.00 (11.95)	<0.001	-0.172

Abbreviations: AP, Antipsychotic; CCI, Charlson Comorbidity Index; SD, Standard Deviation; q, Quintile

5.1.2 Physician Cohort

Table 2 contains the descriptive statistics of the physician cohort. In the study, 2,240 family physicians prescribed an AP to a community-dwelling patient with dementia without a psychosis diagnosis. The average age of the physician cohort was 51.29 years (*SD* = 11.15 years) and the majority were male (n = 1,1514, 67.59%). Most physicians graduated in Canada (n = 1,362, 60.80%) and practiced in metropolitan areas (n = 1,389, 62.01%). The average years in practice was 22.42 years (*SD* = 11.71 years) and more physicians had been in practice for 20 to 29 years (n = 31.12%) than any other grouping (New = 17.50%, Mid = 22.72%, Veteran = 28.66%).

Table 2

Descriptive Statistics of Family Physician Cohort

Prescribing Physician Cohort N = 2,240	
Age mean (*SD*)	51.29 (11.15)
Sex, n (%) Male Female	 1,514 (67.59%) 726 (32.41%)
Place of Graduation n (%) Canada Outside Canada Unknown	 1,362 (60.80%) 826 (36.87%) 52 (2.32%)
Years in Practice n (%) New (1-9) Mid (10-19) Senior (20-29) Veteran (>=30)	 392 (17.50%) 509 (22.72%) 697 (31.12%) 642 (28.66%)
Years in Practice mean (*SD*)	22.42 (11.71)
Practice Location n (%) Metropolitan Urban Rural and Remote	 1,389 (62.01%) 596 (26.61%) 255 (11.38%)
Contacts mean (*SD*)	10,631 (6,336.14)
Number of Unique Prescriptions mean (*SD*) Total per physician	 4,688 (3,147.25)

Average per physician	1.94 (1.07)
Number of Patients mean (*SD*)	2,762 (2,053.56)
Physician-level continuity mean (*SD*)	0.27 (0.18)
Number of Patient Contacts: Age, years mean (*SD*) 0-17 18-44 45-64 65-74 75+	 911.50 (933.39) 2,474.10 (2,275.25) 3,201.00 (2,165.84) 1,774.80 (1,125.51) 2,270.00 (1,683.94)
Number of Patient Contacts: SES mean (*SD*) q1 (low) q2 q3 q4 q5 (high) q9 (unknown)	 2,272.00 (1,884.31) 2,239.00 (1,792.96) 2,123.00 (1,406.57) 2,018.00 (1,415.18) 1,876.90 (1,562.84) 101.70 (238.53)
Number of Patient Contacts: Sex mean (*SD*) Female	 5,917.00 (3,502.40)
Number of Patient Contacts: Residence mean (*SD*) Metropolitan Urban	 6,812.00 (7,329.68) 2,505.00 (4488.28) 1,302.90 (2,776.79)

Rural and Remote	
Number of Contacts: Patients with Dementia mean (*SD*)	600.20 (998.51)
CCI of Patient Contacts mean (*SD*)	1.40 (1.06)

Abbreviations: AP, Antipsychotic; CCI, Charlson Comorbidity Index; SES, Socio Economic Status based on Neighbourhood Income Quintile; SD, Standard Deviation; q, Quintile; MD, Medical Doctorate

5.2 Description of Outcomes

Table 3 provides the proportional breakdown of each outcome by the prescribing physician's years in practice. Of the entire patient population with dementia, 9.84% were prescribed a new AP, 11.60% were prescribed a long-term AP, 0.80% were co-prescribed APs, and 0.50% were co-prescribed long-term APs during the study period. Four-thousand-six-hundred-fifty patients received an AP to treat their dementia, which represented 16.14% of the total patient sample. The majority of patients who received an AP during the study were prescribed a new AP (60.97%) or long-term AP (71.87%) while co-prescribed and long-term co-prescribed APs were each provided to less than 5% of all patients who received an AP. Senior physicians prescribed the largest proportion of new and long-term APs to patients in the study. Veteran physicians prescribed the largest proportion of co-prescribed and long-term co-prescribed APs. Of all AP outcomes, new physicians prescribed the lowest proportion of each.

Table 3

Antipsychotic Prescribing Proportions by Prescriber's Years in Practice

	Total Prescribed N (%)	**Proportion of Total Patient Cohort** N= 28,805	**Proportion of Patients Who Received an AP** N = 4,650
Any AP	4,650 (100.00%)	16.14%	100.00%
New (1-9)	689 (14.82%)	2.39%	14.82%
Mid (10-19)	1,026 (22.06%)	3.56%	22.06%
Senior (20-29)	1,557 (33.48%)	5.40%	33.48%
Veteran (>=30)	1,378 (29.34%)	4.78%	29.34%
New AP	2,835 (100.00%)	9.84%	60.97%
New (1-9)	493 (17.39%)	1.71%	10.60%
Mid (10-19)	652 (23.00%)	2.26%	14.02%
Senior (20-29)	953 (33.62%)	3.31%	20.50%
Veteran (>=30)	737 (26.00%)	2.56%	15.85%
Long-term AP	3,342 (100.00%)	11.60%	71.87%
New (1-9)	458 (13.70%)	1.59%	9.85%
Mid (10-19)	738 (22.08%)	2.56%	15.87%
Senior (20-29)	1,118 (33.45%)	3.88%	24.04%
Veteran (>=30)	1,028 (30.76%)	3.57%	22.11%
Co-prescribed	229 (100.00%)	0.80%	4.92%
APs	28 (12.23%)	0.10%	0.60%
New (1-9)	44 (19.21%)	0.15%	0.95%

Mid (10-19)	62 (27.07%)	0.22%	1.33%
Senior (20-29)	95 (41.48%)	0.33%	2.04%
Veteran (>=30)			
Long-term Co-prescribed APs	145 (100.00%)	0.50%	3.12%
New (1-9)	15 (10.35%)	0.05%	0.32%
Mid (10-19)	27 (18.61%)	0.09%	0.58%
Senior (20-29)	38 (26.21%)	0.13%	0.82%
Veteran (>=30)	65 (44.83%)	0.26%	1.40%

Abbreviations: AP, Antipsychotic

5.3 Unadjusted and Adjusted Results of Generalized Estimating Equations

5.3.1 New Antipsychotics

Table 4.1 provides the final adjusted regression results for new AP prescriptions. Physician's years in practice was associated with being dispensed a new AP in all regressions. In the unadjusted model, patients were 25% more likely to be prescribed a new AP prescription if they received the AP from a new physician compared to a veteran physician (30 of more years in practice) (95CI [0.70, 0.80]). In the adjusted model accounting for only physician-level variables, patients were 19% more likely to receive a new AP if the prescriber was a new physician compared to a veteran physician (95CI [0.76, 0.97]). In the adjusted model that accounted for patient- and physician-level variables, a patient was 20% more likely to be dispensed a new AP if they received the prescription from a new physician compared to a veteran physician (95CI [0.74, 0.85]).

The average unique prescriptions a physician prescribed per patient was also associated with new AP prescriptions across models. For every unit increase of average prescriptions per patient, the likelihood of a new AP being dispensed decreased by 9% in the unadjusted model, 95CI [0.88, 0.93]; decreased by 8% when adjusting for physician-level variables, 95CI [0.90, 0.94]; and decreased by 6% for every unit increase of average unique prescriptions per patient when accounting for patient-and physician-level factors, 95CI [0.92, 0.96]. In the unadjusted model, it was also found a patient who was prescribed an AP from a physician who graduated internationally were more likely to receive a new AP prescription (RRR = 0.07%, 95CI [1.02, 1.12]) but place of graduation was not

related to likelihood of being dispensed a new AP in either adjusted model. Across all regressions, physician's biological sex and practice rurality were never associated with likelihood of receiving a new AP as a treatment for dementia.

5.3.2 Long-Term Antipsychotics

Table 4.2 provides the final adjusted regression results for receiving a long-term AP. When investigating long-term AP prescriptions, a physician's years in practice was the only variable related to being dispensed a long-term AP across all regressions. If a patient received the prescription from a veteran physician compared to a new physician, they were more likely to receive a long-term AP ([unadjusted] RRR=0.12, 95CI [1.06, 1.19]; [adjusted models] RRR= 0.09, 95CI [1.02, 1.16]). The finding that seeing a new physician decreases likelihood of being dispensed a long-term AP as a treatment for dementia is the inverse of the findings for receiving a new AP prescription. In the unadjusted model, a physician's average unique prescriptions per patient increased a patient's likelihood of receiving a long-term AP prescription (RRR = 0.03%, 95CI [1.02, 1.05]). A physician's place of graduation, practice location, and biological sex did not relate significantly to likelihood of being dispensed a long-term AP in any regression model.

5.3.3 Co-Prescribed Antipsychotics

Table 4.3 provides the final adjusted regression results of receiving co-prescribed APs. Like long-term AP prescriptions, patients were less likelihood to be co-prescribed APs by new physicians compared to physicians later in their

career. If a patient received an AP prescription from a veteran physician compared to a new physician, they were 70% more likely to receive co-prescribed APs in the unadjusted model and 62% more likely when accounting for physician-level variables and patient-level factors ([unadjusted] 95CI [1.12, 2.56]; [physician adjusted], 95CI [1.03, 2.53]; physician and patient adjusted], 95CI [1.04, 2.52]). Although being dispensed co-prescribed APs was affected by physician's years in practice, this outcome only occurred 229 times in the entire cohort. Co-prescribed APs accounted for 4.92% of all APs prescribed during the study and only 0.8% of the total patients were dispensed co-prescribed APs.

Average unique prescriptions per patient by a physician increased likelihood of being co-prescribed APs in the unadjusted (RRR = 0.14%, 95CI [1.05, 1.24]) and first adjusted model (RRR = 0.12%, 95CI [1.02, 1.22]) as seen in the long-term AP unadjusted model. When the adjusted model accounted for patient-level factors, average unique prescriptions did not significantly relate to likelihood of receiving co-prescribed APs. A physician's place of graduation, practice location, and biological sex did not significantly relate to likelihood of being dispensed co-prescribed APs in any regression model.

5.3.4 Long-Term Co-Prescribed Antipsychotics

Table 4.4 provides the final adjusted regression results for receiving long-term co-prescribed APs. A physician's years in practice was the only physician-level variable related to risk of being dispensed long-term co-prescribed APs as a treatment for dementia and findings were similar to the co-prescribed AP outcome. If a patient received an AP prescription from a veteran physician

compared to a new physician, they were 117% more likely to receive long-term co-prescribed APs based on unadjusted results, 95CI [1.25, 3.77]. Patients were 103% more likely to receive long-term co-prescribed APs when physician-level variables were controlled for and 100% more likely when patient- and physician-level factors were accounted for, [physician adjusted] 95CI [1.11, 3.69]; [patient and physician adjusted] 95CI [1.12, 3.57]. Although risk of receiving long-term co-prescribed APs was affected by physician's years in practice, this outcome occurred only 145 times in the entire cohort, which represents 0.5% of total patients in the study.

To review, there was a positive relationship between a patient's risk of being dispensed a new AP and receiving the prescription from a new physician. There was a negative association between a patient's risk of receiving a long-term, co-prescribed, or long term co-prescribed APs and receiving the prescription from a new physician.

In the regression models which accounted for patient- and physician-level variables, the only patient-level variables to affect the likelihood of receiving an AP prescription were biological sex, SES, age, location, and number of unique prescriptions received in a fiscal year. None of these variables were consistent in changing likelihood of receiving any AP across all outcomes. Males were 10.50% more likely to receive a new AP compared to females, 95CI [1.06, 1.15]. Living in a rural area increased patients' likelihood of being dispensed a new AP by 16% when compared to living in a metropolitan area, 95CI [1.04, 1.29]. But rurality of practice was not significant in affecting patient outcomes at the physician-level.

Patient's residing in the highest income quintile (q5) neighbourhoods were 9.40% more likely to receive a new AP compared to those living in the lowest income quintile (q1) neighbourhoods, 95CI[1.02, 1.17]. Alternatively, patients living in the lowest income quintile (q1) neighbourhoods were 8.10% more likely to be dispensed long-term AP compared to those in the second lowest income quintile (q2) neighbourhoods and 7.20% more likely than those in the middle-income quintile (q3) neighbourhoods. A greater number of unique prescriptions a patient received in a fiscal year protected against a new AP prescription (RRR = 0.04%, 95CI [0.95, 0.96]) but increased likelihood of receiving co-prescribed APs (RRR = 0.05%, 95CI[1.02, 1.08]) and long-term co-prescribed APs (RRR = 0.08, 95CI[1.05, 1.11]). Finally, patient's age was protective against receiving co-prescribed APs (RRR = 0.03%, 95CI[0.96, 0.98]) and long-term co-prescribed APs (RRR = 0.04%, 95CI[0.95, 0.97]). Appendix D contains the patient-level findings from the final adjusted models for all outcome variables.

Table 4.1

Adjusted Regression Accounting for Physician- and Patient-Level Variables – New AP Outcome

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	0.89 [0.83, 0.95]	0.91 [0.85, 0.98]	0.90 [0.85, 0.96]
Senior (20-29)	0.86 [0.81, 0.91]	0.91 [0.85, 0.97]	0.90 [0.85, 0.96]
Veteran (>=30)	0.75 [0.70, 0.80]	0.81 [0.76, 0.87]	0.80 [0.74, 0.85]
Average Unique Prescriptions	0.91 [0.88, 0.93]	0.92 [0.90, 0.94]	0.94 [0.92, 0.96]
Place of Graduation			
Canada (ref.)	--	--	--
International	1.07 [1.02, 1.12]	1.03 [0.98, 1.08]	1.05 [1.00, 1.10]
Unknown	1.18 [1.05, 1.34]	1.17 [1.03, 1.32]	1.14 [1.01, 1.28]
Practice Rurality			
Metropolitan (ref.)	--	--	--
Urban	1.06 [1.01, 1.12]	1.03 [0.98, 1.09]	0.99 [0.89, 1.10]
Rural	1.04 [0.96, 1.12]	0.99 [0.91, 1.07]	0.88 [0.78, 1.00]
Physician Sex			
Female (ref.)	--	--	--
Male	0.94 [0.89, 0.99]	1.00 [0.95, 1.05]	0.99 [0.94, 1.04]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index
+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

Table 4.2

Adjusted Regression Accounting for Physician- and Patient-Level Variables – Long-term AP Outcome

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.08 [1.01, 1.16]	1.07 [1.00, 1.15]	1.07[1.00, 1.14]
Senior (20-29)	1.08 [1.02, 1.15]	1.06 [0.99, 1.13]	1.05 [0.99, 1.12]
Veteran (>=30)	1.12 [1.06, 1.19]	1.09 [1.02, 1.16]	1.09 [1.02, 1.16]
Average Unique Prescriptions	1.03 [1.02, 1.05]	1.03 [1.01, 1.04]	1.02 [1.01, 1.04]
Place of Graduation			
Canada (ref.)	--	--	--
International	0.99 [0.95, 1.03]	0.99 [0.95, 1.03]	0.98 [0.95, 1.02]
Unknown	1.03 [0.92, 1.15]	1.03 [0.92, 1.15]	1.03 [0.92, 1.16]
Practice Rurality			
Metropolitan (ref.)	--	--	--
Urban	0.98 [0.94, 1.02]	0.99 [0.95, 1.04]	0.89 [0.80, 0.99]
Rural	0.97 [0.91, 1.04]	0.99 [0.93, 1.06]	0.93 [0.82, 1.05]
Physician Sex			
Female (ref.)	--	--	--
Male	1.02 [0.98, 1.07]	1.00 [0.96, 1.04]	1.00 [0.96, 1.05]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index
+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

Table 4.3

Adjusted Regression Accounting for Physician- and Patient-Level Variables – Co-Prescribed APs Outcome

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.06 [0.66, 1.68]	1.04 [0.65, 1.66]	1.02 [0.64, 1.63]
Senior (20-29)	0.98 [0.63, 1.52]	0.93 [0.59, 1.47]	0.91 [0.58, 1.43]
Veteran (>=30)	1.70 [1.12, 2.56]	1.62 [1.03, 2.53]	1.62 [1.04, 2.52]
Average Unique Prescriptions	1.14 [1.05, 1.24]	1.12 [1.02, 1.22]	1.11 [1.01, 1.22]
Place of Graduation			
Canada (ref.)	--	--	--
International	0.91 [0.70, 1.19]	0.91 [0.70, 1.20]	0.92 [0.70, 1.20]
Unknown	1.43 [0.72, 2.84]	1.54 [0.77, 3.09]	1.62 [0.81, 3.26]
Practice Rurality			
Metropolitan (ref.)	--	--	--
Urban	0.91 [0.68, 1.23]	1.03 [0.76, 1.41]	0.92 [0.49, 1.80]
Rural	0.87 [0.55, 1.37]	0.96 [0.60, 1.52]	1.35 [0.50, 3.70]
Physician Sex			
Female (ref.)	--	--	
Male	0.91 [0.69, 1.20]	0.80 [0.60, 1.08]	0.79 [0.59, 1.06]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index
+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

Table 4.4

Adjusted Regression Accounting for Physician- and Patient-Level Variables – Long-term Co-prescribed APs Outcome

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.21 [0.65, 2.26]	1.18 [0.63, 2.23]	1.17 [0.63, 2.16]
Senior (20-29)	1.12 [0.62, 2.02]	1.08 [0.58, 2.00]	1.01 [0.55, 1.86]
Veteran (>=30)	2.17 [1.25, 3.77]	2.03 [1.11, 3.69]	2.00 [1.12, 3.57]
Average Unique Prescriptions	1.13 [1.01, 1.25]	1.07 [0.96, 1.20]	1.06 [0.93, 1.20]
Place of Graduation			
Canada (ref.)	--	--	--
International	1.10 [0.79, 1.53]	1.13 [0.81, 1.59]	1.13 [0.81, 1.58]
Unknown	0.90 [0.29, 2.80]	0.94 [0.30, 2.95]	1.03 [0.32, 3.31]
Practice Rurality			
Metropolitan	--	--	--
(ref.)	0.71 [0.48, 1.07]	0.77 [0.51, 1.17]	1.25 [0.60, 2.62]
Urban	0.84 [0.48, 1.49]	0.93 [0.53, 1.65]	1.29 [0.35, 4.77]
Rural			
Physician Sex			
Female (ref.)	--	--	--
Male	1.02 [0.71, 1.46]	0.86 [0.59, 1.27]	0.87 [0.59, 1.27]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index
+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

Chapter 6. Discussion

This thesis investigated which physician-level characteristics of primary care providers were associated with a community-dwelling patient with dementia's likelihood of being dispensed an AP in the province of BC. AP interventions have clear, strict guidelines in Canada and are often not recommended to treat dementia symptoms due to risk of ADR(s) and reduced quality of life (9,11,34,36,43,44). Even so, AP prescribing rates have increased in Canada and globally (1,13,19–21). Previous research related to AP prescriptions to people with dementia has focused on patients residing in LTC and few studies have investigated how physician-level characteristics are associated with prescribing rates. This thesis aimed to better understand practice-level variation as it related to AP prescriptions to patients with dementia in a community setting, specifically from family doctors. This thesis also investigated likelihood of being dispensed new, long-term, co-prescribed, and long-term co-prescribed AP(s). APs were assumed to be provided by primary care physicians as a treatment of dementia symptoms for patients who resided in the BC community during the 2015/16 and 2016/17 fiscal years.

Patients were most likely to receive a new AP if the prescribing physician had been in practice for less than 10 years (new physician) compared to seeing a physician later in their career. Alternatively, patients were less likely to be prescribed a long-term, co-prescribed, or long-term co-prescribed AP(s) as a treatment for dementia compared to a veteran physician (practicing for 30 years or more). This result held constant after controlling for patient- and physician-

level characteristics. A physician's average number of unique prescriptions per patient was protective against receiving a new AP but was found to increase the likelihood of being prescribed long-term or co-prescribed APs but only when other physician- and patient-level characteristics were not accounted for. A physician's place of graduation, biological sex, and rurality of their practice were never significantly related to receiving any AP as a treatment for dementia.

The finding a patient is has an increased risk of receiving a new AP from a new physician is not a cause of concern. When a single, low-dosage AP is prescribed for a short duration it is not considered an inappropriate treatment for severe dementia cases (42,104,115). Results show receiving a prescription from a new physician decreased a patient's risk of being dispensed a long-term, co-prescribed, and long-term co-prescribed AP. New physicians also prescribed the lowest proportions of all APs in this study. These results indicate physicians early in their career are following guidelines on duration and co-prescribing, seem to be conducting medical reviews, and are titrating or terminating APs at appropriate times after initiating AP treatment in their patient's care. This aligns with the previous finding younger prescribers (in terms of age) of APs are more likely to order guideline recommended monitoring tests (67). Also, a new physician would be building their practice and would be prescribing new treatments to new patients.

Despite differences in likelihood of receiving an AP prescription by physician career stage, receiving co-prescribed APs or long-term co-prescribed APs each occurred in less than 1% of the entire sample and less than 5% of all

people with dementia who received an AP during the study period. Although a duration of three-months or more and prescribing two or more APs at a time is not recommended in guidelines (11,39,45,46,48,49), physicians are rarely administering these treatments. Donohue et al. found that primary care physicians prescribe lower rates of APs overall when compared to specialty physicians, mainly psychiatrists (100). They also found physician's adjusted duration, dosage, and increased use of SGAs when prescribing based on shifts in guideline recommendations. Taub et al. found physicians later in their career tend to reduce the variety of APs they prescribe and begin tailoring medications based on previous knowledge of how each psychotropic behaved in similar cases (71). Svensson et al. reported family physicians found it easier to some degree to begin prescribing psychotropic medication than to terminate a prescription (78). Often physicians attributed this to patient pushback and misunderstanding of discontinuation. Also, most study physicians found it difficult in some way to change a colleague's prescription of a psychotropic medication (78).

Inappropriate prescription of APs based on duration and co-prescription in this study may have occurred due to patient pushback, attempts at terminating treatment that resulted in reduced quality of life, or physician's unease in terminating another physician's prescriptions (78). The infrequency of inappropriate AP prescription may be attributed to reasons described in previous research. This includes findings that primary care physicians prescribe fewer APs than specialists (100); physicians were found to adjust prescribing behaviour

based on guideline developments and previous successes (100); and/or that physicians later in their career are tailoring treatments (71). The rarity of outcomes and listed researching findings reduces concern of the inappropriate outcomes in this study.

The rate of AP prescriptions by primary care providers to community-dwelling older adults was lower in this study than rates compared to previous findings (5,23,36,37). This thesis found 16.14% of community-dwelling older adults with a diagnosis of dementia, without a diagnosis of psychosis received an AP prescription from a primary care provider during the 2015/16 and 2016/17 fiscal years. Craig et al. found that from 2000 to 2009, 29.5% of community-dwelling older adults with dementia in Quebec received an initial AP prescription based on public drug plan data (5). Wastesson et al. found that 21.0% of patients aged 75 to 89 years old with dementia received an AP during 2005 based on the Swedish Prescribed Drug Register (37). Also, the BC Care Providers Association produced a document in 2018 that compared Canadian and U.S.A. rates of AP by elderly people with dementia, mainly focused on those in LTC setting (36). In acute care, 54% of seniors with dementia were prescribed APs, 26% of home care patients with dementia received an AP prescription, and 48% of LTC residents with dementia are prescribed an AP medication. In Ontario, 22.9% of LTC residents with dementia, without a psychosis diagnosis received an AP medication in 2015/16 (36). In Alberta, 18.1% of LTC residents with dementia, without a psychosis diagnosis received an AP medication in 2015/16 (36). The lower rate of AP prescriptions in this study reiterates the assumption BC primary

care physicians are following guidelines and the initiatives in place are probably reducing the usage of APs as a treatment for dementia.

In this study, senior physicians (practicing for 20 to 29 years) prescribed the largest proportion of new and long-term APs. The BC physician workforce has aged and over 50% of the workforce is between 45 and 65 years of age (135). Also, Taub et al. found physicians between the ages of 42 to 58 (considered to be in the middle of their career) prescribe the widest variety of AP (differentiated by molecular structure). Senior physicians—as defined in this study—represent most of the BC workforce, prescribe the widest variety of APs, and are likely to have patients who have aged with them who have begun showing symptoms of dementia.

Patients were most likely to receive co-prescribed or long-term co-prescribed APs from veteran physicians, but these outcomes were rare. This finding suggests that while there are career-stage differences in the rate of prescribing across generational cohorts of family physicians, most are following guidelines. This is reassuring given family physician provide 70% of prescriptions to community-dwelling older adults (59,131). This thesis also found most physician-level characteristics were not associated with AP prescribing to community-dwelling patients' dementia. Although it was originally hypothesized a physician's biological sex, prescribing volume and years in practice would be associated with patient outcomes in the study based on reviewed literature, only career-stage was significantly related. The insignificant association of many physician-level variables, besides career stage, align with findings from Alessi-

Severini et al. and James et al. who found physician-level characteristics did not relate to the likelihood of receiving or using an AP (19,169). Previous studies have also shown physicians' prescribing patterns change depending on their career stage (100).

6.1 Policy Implications

The findings of this thesis suggest that there may be a statistic difference in prescribing patterns amongst primary care physicians based on years in practice, but outcomes occurred rarely suggesting that most family physicians are following guidelines for AP prescribing no matter their career stage. Based on previous research, physicians later in their career may be prescribing inappropriately only after exhaustion of previous interventions, unsuccessful titration, or continue prescribing APs due to patient pushback (71,78,100). Physicians' prescribing behaviours adapt with experience and patients are receiving tailored care that is assumed as best for them, even if the prescribing goes against guidelines (11,39,45,46,48,49,71,100).

The influence on likelihood of an AP being dispensed cannot be attributed solely to the physician and results of this study indicate that there is clinically, little practice-variation. Policies should focus on continuing to train physicians throughout their careers to ensure quality of care continues. Continuing to educate care providers and work with organizations such as Choose Wisely could reduce overtreatment, resulting in lower costs, less waste, minor diversion of health resources, and benefit both physicians and patients.

Organizations such as Choosing Wisely and the Deprescribing network could use the results of the study as a way to justify focusing education towards physicians who have been in practice for decades as they increased a patient's risk of receiving all outcomes considered inappropriate in this study: long-term, co-prescribed and long-term co prescribed APs. Although these outcomes occurred rarely in the study, physicians should still aim to terminate the use of APs for all their patients with dementia and patients should be made aware of the increased risk of co-prescription and prolonged use of APs.

Policies may also introduce physician collaboration when it comes to continuing a fellow physician's AP prescription, switching to another AP form, or co-prescribing more than one AP at a time. They should also aim to help physicians better educate people with dementia and their caregivers on the need for medical reviews and medication cessation to alleviate patient pushback on medication termination. Overall, primary care physicians seem to be appropriately prescribing APs as a treatment for dementia. Though, there is room for growth on education of prescribing and discontinuation of APs at the physician and patient/caregiver level when it comes to treating symptoms of dementia.

6.2 Strengths and Weaknesses

This thesis demonstrates a clearly defined topic and includes a thorough, well-organized literature review that sets the premise for the rest of the study. It includes clear operational definitions, data collection methods, population of interest, setting, and breakdown of inclusion and exclusion criteria. The

definitions and methodology behind the study are consistently justified via previous research processes and well-developed algorithms. The use of administrative data allowed us to capture all residents eligible for public health insurance and all practicing family physicians in BC. It also allowed for restriction of information, performance, response, acquisition, attrition, and volunteer bias. Finally, the study offers meaningful results that can steer future studies and aid in policy development.

The study does have some weaknesses. Potential sampling bias may have occurred as we were only able to observe patients with access to primary care services—based on registration to the provincial health insurance policy and contact with a primary care physician—which is not the entire provincial population. Also, the study only included APs available in BC. The study was not able to encompass all chemical compounds available world-wide but did include every AP available during the study time, in the province, via a primary care physician. The use of administrative data only allowed observations of AP dispensing, not actual use. Also, the co-prescribed AP and long-term co-prescribed AP outcome occurrence rate was small and makes results related to these outcomes harder to generalize. A reason this may have occurred was the conservative operational definitions used for each prescribing outcome, but this was chosen to not overestimate outcomes. The restricted inclusion/exclusion criteria were put in place based on previous research definitions and input from professionals in the field. The study sample may also be subject to survivor bias as only individuals registered for 183 days or longer in each year were included,

which may have eliminated those who had passed away during the study, potentially over 900 individuals.

Although justified, the use of secondary data meant the following variables could not be included in the study: frailty, race, relationship status, employment status, caregiver distress, patients' understanding and rating of their own health, education level, and type of residence. Although these variables have been shown to impact prescribing in literature, they were not available for analysis in the current study. Clinic-level factors—such as proximity to primary care services, number of physicians on sight, access to secondary and tertiary care providers, and turn-around speed—can affect prescribing patterns as well but were not available for this study. Although these variables do impact prescribing in literature, they are based at the patient and/or clinic-level and the current thesis was focused on physician-level variables. Based on previous literature and inability to include all potentially relevant variables, the use of a qualitative study design to better understand the prescriber/provider, patient, and caregiver's experience could further help with quality of care.

Directly related to this thesis, the finding years in practice was the only physician-level variable to affect risk of being dispensed any AP outcome in all models may have occurred due to the small occurrence rate, residual confounders not measured in the datasets, or the conservative variable definitions or eligibility criteria. Also, the algorithm used to determine psychosis diagnoses from Kurdyak et al. was developed via hospitalization data, a relatively small sample, and set in the province of Ontario not BC. But this variable was not

the main diagnosis of concern and the instrument had high sensitivity, specificity, positive predictive value and negative predictive value.

6.3 Future Research

This thesis highlights opportunities for future studies and policy development. To go beyond the design of this thesis, future studies could quantify the between-physician variability using odds ratios and intra-class correlation. This type of model can show the change in odds of a patient receiving an AP based on changes in physician- or clinical-level variables. It can also show the proportion of the total variability observed that can be explained by each cluster at the patient- and/or physician-level. Research could apply similar study methods to other provinces and/or territories in Canada to allow for a comparison of differences in provincial policy concerning the coverage of AP medications, prescription reviews, roles of pharmacists, and differences in primary care models. A similar methodology and study design could be used to explore what primary care clinic-level characteristics—such as geographic location, accessibility, type of care provided in clinic, other providers in care setting—affect a community-dwelling patient with dementia's likelihood of receiving an AP. Future studies could also use qualitative methods to understand how physician attitudes, experiences, and beliefs relate to variation in AP prescribing to community-dwelling patients with dementia. This could be extended further to patient and/or caregivers as well. Another interesting line of investigation could explore if physicians at different career stages are completing

AP medication cessations, medical reviews, and proper monitoring of other potentially inappropriate medications.

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Appendices

Appendix A.

This appendix contains the details of all variables used in the analysis of this thesis.

A1. Description of Patient-Level Variables Used in Analysis

Variable (variable name in dataset)	**Definition**	**Purpose**	**Ancillary**
Antipsychotic Prescription (antips)	Flag for patient who received an AP prescription in study period	Outcome	Binary (0 = did not receive AP; 1 = did receive AP)
Incident Antipsychotic Prescription (new_antips)	Flag for incident AP prescribed within 12-months	Outcome	Binary (0 = did not receive incident AP; 1 = did receive incident AP)
Long-term Antipsychotic Prescription (lt_antips)	Flag for AP prescription with total-days supply of 84-days or longer (14-day grace period of gaps between prescriptions)	Outcome	Binary (0 = did not receive long-term AP; 1 = did receive long-term AP)
Sensitivity Long-term Antipsychotic Prescription (lt_antips2)	Flag for AP prescription with total-days supply of 84-days or longer (28-day grace period of gaps between prescriptions)	Sensitivity Outcome	Binary (0 = did not receive long-term AP; 1 = did receive long-term AP)

Co-prescription of Antipsychotics (co_antips)	Flag for prescription of two or more APs with an overlap of 31 or more days within a 38-day period	Outcome	Binary (0 = did not receive co-prescribed APs; 1 = did receive co-prescribed AP)
Sensitivity Co-prescription of Antipsychotics (co_antips2)	Flag for prescription of two or more APs with an overlap of 31 or more days within a 45-day period	Sensitivity Outcome	Binary (0 = did not receive co-prescribed APs; 1 = did receive co-prescribed AP)
Long-term Co-prescription of Antipsychotics (ltco_antips)	Flag for prescription of two or more APs (defined by different generic drug names) with an overlap of 84 or more days within a 91-day period	Outcome	Binary (0 = did not receive long-term co-prescribed APs; 1 = did receive long-term co-prescribed AP)
Sensitivity Long-term Co-prescription of Antipsychotics (ltco_antips2)	Flag for prescription of two or more APs (defined by different generic drug names) with an overlap of 84 or more days during a 98-day period	Sensitivity Outcome	Binary (0 = did not receive long-term co-prescribed APs; 1 = did receive long-term co-prescribed AP)
Days Registered in 2015/2016 (DaysReg1516)	Number of days registered in the 2015/2016 fiscal year	Inclusion/Exclusion	

Days Registered in 2016/2017 (DaysReg1617)	Number of days registered in the 2016/2017 fiscal year	Inclusion/Exclusion	
Dementia Diagnosis (Dementia)	Flag for patients who received a dementia diagnosis by March 31, 2017	Inclusion/Exclusion	Binary (0 = did not receive dementia diagnosis; 1 = did receive dementia diagnosis)
Long-term Care Resident (LTC)	Flag for patients who had LTC billings in 2015/16 and/or 2016/17	Inclusion/Exclusion	Binary (0 = did not bill LTC; 1 = did bill LTC)
Psychiatric Diagnosis (PsychDis)	Flag patients who received a Psychotic Disorder diagnosis by March 31, 2017	Inclusion/Exclusion	Binary (0 = did not receive psychosis diagnosis; 1 = did receive psychosis diagnosis)
CCI score (CCI_1415)	Weighted Charlson Comorbidity Index score for patient from the 2014/2015 fiscal year (index)	Control and Exposure	
Patient Residence (MUR)	Based on Statistical Area Classification (SAC) and census Metropolitan Influenced Zone (MIZ)	Control and Exposure	1 = Metro: 100,000 or more residents with at least 50,000 living in the core (SAC Type 1) 2 = Urban: 100,000 residents with at least

			10,000 living in the core (SAC type 2-3) 3 = Rural: 99,999 or fewer residents (SAC type 4-7)
Neighbourhood Income Quintile (QIAPPE)	Identifies if the patient lived in based on neighbourhood income quintile in 2014/15 fiscal year (index)	Control and Exposure	q1 = low-income q2, q3, q4 = middle-income q5 = higher-income q9 = unknown
Patient Sex (SEX)	Identifies patient reported biological sex	Control and Exposure	M = male F = female U = unknown
Patient Age (age)	Patient age as of April 1, 2015	Control and Exposure	Measured in years
Unique Prescriptions (n_ATC_1415)	Number of unique prescriptions at ATC 4th level in 2014/2015 fiscal year (excluding J07 Vaccines, A11 Vitamins, A12 Mineral Supplements, A13 Tonics and V Various)	Control and Exposure	

Physician Contact (n_FPcontacts_1415)	Number of unique patient/physician/date combinations in billings/shadow billings within 2014/15 fiscal year (based on date of service not payment) and was either in-person or remote contacts excluding laboratory/imaging services and no-charge referrals	Control and Exposure	

A2. Description of Physician-level Variables Used in Analysis

Variable (variable name in dataset)	**Definition**	**Purpose**	**Ancillary**
Place of Graduation (IMG)	Place practitioner graduated from	Exposure and Control	0 = Canada 1= International 2= Unknown
Practitioner Age (pracage)	Practitioner age as of December 31, 2015 (2015 – birth year)	Exposure and Control	Measured in years
Charlson Comorbidity Index Score (CCI)	Weighed average of patients CCI scores across all contacts during the	Exposure and Control	
Practice Location (MUR.y)	SACtype/MIZ based on the plurality of contacts in the observation window	Exposure and Control	1 = Metro: 100,000 or more residents with at least 50,000 living in the core (SAC Type 1)

			2 = Urban: 100,000 residents with at least 10,000 living in the core (SAC type 2-3) 3 = Rural: 99,999 or fewer residents (SAC type 4-7)
Practitioner Sex (PracSex)	Biological sex	Exposure and Control	M = male F = female
Years in Practice (YrsinPract)	Years in practice (Years since MD – 2)	Sensitivity Variable	Those with a missing graduation year or fewer than one-year in practice were not included
Years In Practice (CYrsInPract)	Categorical version of above variables	Main Exposure and Control	New = <=9 years Mid = 10 to 19 years Senior = 20 to 29 years Veteran = 30+ years
Average Number of Unique Prescriptions per patient (mean_unique_Rx)	Average number of unique prescriptions at 4th level ATC (excluding J07 Vaccines, A11 Vitamins, A12 Mineral Supplements, A13 Tonics and V Various) per patient where the physician	Exposure and Control	

	is the prescribing physician limited to patient-physician patis observed in the physicians claim data		
Number of contacts: age (n_cont_#)	Number of contacts with patients broken down by age range	Exposure and Control	0-17 18-44 45-64 65-74 75+
Number of contacts: residence (n_cont_MUR)	Number of contacts with patients classified by MIZ/SAC type of residence in 2015/2016 fiscal year	Exposure and Control	1 = Metro: 100,000 or more residents with at least 50,000 living in the core (SAC Type 1) 2 = Urban: 100,000 residents with at least 10,000 living in the core (SAC type 2-3) 3 = Rural: 99,999 or fewer residents (SAC type 4-7)
Number of contacts with dementia (n_cont_dementia)	Number of contacts with patients who have a dementia diagnosis	Exposure and Control	
Number of female contacts (n_cont_female)	Number of contacts with female patients	Exposure and Control	

Number of contacts: Neighbourhood Income Quintile (n_cont_ses)	Number of contacts with a patient from five various income quintiles using 2015/2016 and 2016/2017 observations	Exposure and Control	q1 = low-income q2, q3, q4 = middle-income q5 = higher-income
Number of contacts (n_contacts)	Number of patient/physician/date combinations in billings/shadow billings within the 2015/2016 and 2016/2017 fiscal years at all locations (excluding laboratory/imaging services and no-charge referrals)	Exposure and Control	
Number of patients (n_pts)	Number of patients seen by the physician within the 2015/2016 and 2016/2017 fiscal years at all locations (excluding laboratory/imaging services and no-charge referrals)	Exposure and Control	
Number of Unique Prescriptions (n_unique_Rx)	Number of unique prescriptions at 4th level ATC (excluding J07 Vaccines, A11 Vitamins, A12 Mineral Supplements, A13 Tonics and V Various) per patient where the physician is the prescribing physician limited to patient-physician	Exposure and Control	Numerator used for the Average number of Unique Prescriptions variable.

	patis observed in the physicians claim data		
Physician Continuity (physlvl_cont)	The number of patients the Primary Care provider saw during the 2015/2016 and 2016/2017 fiscal years that were those of said physicians at all locations (excluding laboratory/imaging services and no-charge referrals)	Exposure and Control	

Appendix B.

This appendix contains information from the data analysis not necessary for the questions of interest. It will describe information related to inferential tests and regression models.

B1. Homogeneity of Variance and Chi-Square Residual Results

Homogeneity of variance was met for patient age ($K = 44.41$, $p < 0.001$), patient CCI score ($K = 5.76$, $p = 0.01$), number of unique prescriptions ($K = 104.42$, $p < 0.001$), and number of family physician contacts ($K = 169.49$, $p < 0.001$).

There was a strong, positive correlation between patients who received an AP and residing in the lowest income quintile (q1), which accounted for 40.59% of the chi-square score. There was a negative association between patients who received an AP and resided in the highest income quintiles (q5). This accounted for 7.81% of the chi-square scores. There was a negative association between patients who did not receive an AP and lived in the lowest income quintile, which accounted for 5.91% of the chi-square scores. Alternatively, there was a positive correlation of not receiving an AP and residing in the highest income quintile, which accounted for 30.68% of chi-square scores. The chi-square evidence shows that living in a low SES is associated with receiving an AP while residing in the highest income quintile is protective against receiving this inappropriate treatment of dementia.

B2. Results of Patient-Level Variables from Final Regression of Each Outcome

In the final adjusted model focused on new AP being dispensed, multiple patient-level factors were found to effect risk of a new AP prescription. Males were at a higher risk of receiving a new AP than females (0.10 units, 95CI [0.1.06, 1.15]). This comparison was not significant in any other outcome regressions and patient's biological sex was not found to be related to receiving an AP based on inferential tests. Also, the model found patients that reside in rural areas are at a higher risk of receiving a new AP to treat their dementia compared to patients who reside within a metropolitan area (0.16 units, 95CI [1.04, 1.29]). Like patient's biological sex, this variable was not significant for any other outcome model and was not found as significantly related to receiving an AP as a dementia treatment from inferential results. Patients who live in the highest income quintile (q5) are at a greater risk of receiving a new AP compared to patients in the lowest income quintile (0.09 units, 95CI [1.04, 1.29]). This is the opposite of what was found from inferential results. The chi-square residuals revealed individuals who reside within the lowest income quintile have a strong, positive relation to receiving an AP. Inferential finding also showed patients who live in the highest income quintile are likely to not receive any AP to treat their dementia and have a negative relationship with receiving an AP. Finally, the number of unique prescriptions a patient used in a fiscal year was found to be protective against new AP prescriptions likelihood (0.04 units, 95CI [0.95, 0.96]). This finding matches inferential results, which also found an increased number of unique prescriptions a patient was using was also protective against receiving an AP as a treatment for dementia.

At the patient-level, only SES was significantly impactful on risk of long-term AP use. It was shown that individuals in the lowest income quintile (q1) were at greater risk when compared to patients in the second (q2) and third (q3) lowest income quintiles (0.08, 95CI [0.87, 0.97] and 0.07, 95CI [0.88, 0.98]). This finding is like the chi-square results. Both analyses found patients who reside within the lowest income quintile are the most related or at an increased risk of receiving an AP. This finding is also the opposite of what was shown in regressions focused on new APs being dispensed. A low SES is protective against likelihood of receiving a new AP when compared to the highest income quintile but in terms of long-term AP prescription, low SES increases a patient's risk when compared to only slightly higher SES's.

In the final model accounting for physician- and patient-level characteristics, patient age and number of unique prescriptions were found to affect likelihood of receiving co-prescribed APs. The model found if patient age increased by one year, the likelihood of receiving co-prescribed APs decreased by 0.03 units, 95CI [0.96, 0.98]. This finding is unique to regression analysis, as inferential findings showed no significant relationship between patient age and receiving an AP. For every increase of one unique prescription the patient was taking, the risk of receiving a co-prescribed AP increased by 0.05 units, 95CI [1.02, 1.08]. This is like the findings of inferential analysis that showed a positive relationship between a patient's number of unique prescriptions and receiving an AP. Patient CCI score, number of family physician contacts, biological sex, place

of residence, and SES were not significantly related to co-prescribed APs likelihood of being dispensed.

The only other variables that changed likelihood of receiving long-term co-prescribed APs were the number of unique prescriptions a patient was taking and patient age. These variables were also significant in regression models focused on likelihood of receiving co-prescribed APs. It was found for every one additional prescription a patient was using, the likelihood of receiving long-term co-prescribed APs increased by 0.08 units, 95CI [1.05, 1.11]. When a patient's age increased by one year, the risk of receiving a long-term co-prescribed AP decreased by 0.04 units, 95CI [0.95, 0.97]. As mentioned before, patient age being protective against long-term co-prescribed APs being dispensed is unique to the regression analyses as inferential findings did not show patient age to be significantly related to receiving an AP. Physician's average number of unique prescriptions per patient, practice rurality, physician's biological sex, patient's biological sex, patient rurality, patient SES, patient CCI, and patient's number of unique family physician contacts were not impactful on risk of receiving long-term co-prescribed APs as treatment for dementia.

B3. This appendix contains the Effect Size Interpretation used in the data analysis.

Table C1. Effect Size Interpretation: Cramer's V and Cohen's d[1]

Effect Size Measure	*Small effect size*	*Medium effect size*	*Large effect size*	*Very Large effect size*
Cramer's V				
	0.20 to 0.29	0.30 to 0.49	0.50 to 0.69	0.7 to 1.0
Cohen's d				
	0.2	0.5	0.8	1.30

[1] Table adapted from Table 8.2 in Gravetter F. J. and Wallnau L. B. Statistics for the Behavioural Sciences 10e; Maher J.M., Markey, J.C., Ebert-May D. The other half of the story: effect size analysis in quantitative research; and Table 1 *Strength of effect size* from Mchugh, M. "Cramer's V Coefficient" in The SAGE Educational Research, Measurement, and Evaluation. (189–191)

Appendix C.

This appendix contains the patient-level variable results from the final adjusted model of the regression analyses for each outcome of interest.

C1. Adjusted Regression Accounting for All Physician- and Patient-Level Variables – New AP, Patient-Level Variable Results

Variable	Estimate	Standard Error	95CI
Patient Sex			
Female (ref.)	--	--	--
Male	1.105	0.022	[1.06, 1.15]
Patient Age	1.014	0.001	[1.01, 1.02]
Patient Rurality			
Metropolitan (ref.)	--	--	--
Urban	1.046	0.057	[0.93, 1.17]
Rural	1.160	0.056	[1.04, 1.29]
Neighbourhood Income Quintile			
q1 (low) (ref.)	--	--	--
q2	1.081	0.034	[1.01, 1.16]
q3	1.072	0.035	[1.00, 1.15]
q4	1.076	0.034	[1.00, 1.15]
q5 (high)	1.094	0.035	[1.02, 1.17]
q9 (unknown)	1.034	0.105	[0.84, 1.27]
Patient CCI	1.009	0.008	[0.99, 1.02]
Number of Unique Prescriptions	0.958	0.003	[0.95, 0.96]
Number of Family Physician contacts	1.001	0.001	[1.00, 1.00]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

C2. Adjusted Regression Accounting for All Physician- and Patient-Level Variables – Long-term AP, Patient-Level Variable Results

Variable	Estimate	Standard Error	95CI
Patient Sex			
Female (ref.)	--	--	--
Male	0.962	0.019	[0.93, 1.00]
Patient Age	0.995	0.001	[0.99, 1.00]
Patient Rurality			
Metropolitan (ref.)	--	--	--
Urban	1.127	0.054	[1.01, 1.25]
Rural	1.063	0.058	[0.95, 1.19]
Neighbourhood Income Quintile			
q1 (low) (ref.)	--	--	--
q2	0.919	0.026	[0.87, 0.97]
q3	0.928	0.027	[0.88, 0.98]
q4	0.938	0.028	[0.89, 0.99]
q5 (high)	0.944	0.029	[0.89, 1.00]
q9 (unknown)	1.061	0.008	[0.91, 1.24]
Patient CCI	0.988	0.006	[0.97, 1.00]
Number of Unique Prescriptions	1.013	0.002	[1.01, 1.02]
Number of Family Physician contacts	0.998	0.001	[1.00, 1.00]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

C3. Adjusted Regression Accounting for All Physician- and Patient-Level Variables – Co-prescribed APs, Patient-Level Variable Results

Variable	Estimate	Standard Error	95CI
Patient Sex			
Female (ref.)	--	--	--
Male	1.070	0.131	[0.83, 1.38]
Patient Age	0.969	0.004	[0.96, 0.98]
Patient Rurality			
Metropolitan (ref.)	--	--	--
Urban	1.158	0.337	[0.60, 2.24]
Rural	0.669	0.491	[0.25, 1.75]
Neighbourhood Income Quintile			
q1(low) (ref.)	--	--	--
q2	0.956	0.190	[0.66, 1.39]
q3	1.148	0.184	[0.80, 1.65]
q4	0.843	0.209	[0.56, 1.27]
q5 (high)	1.010	0.207	[0.67, 1.51]
q9 (unknown)	1.149	0.707	[0.29, 4.59]
Patient CCI	0.955	0.045	[0.87, 1.04]
Number of Unique Prescriptions	1.047	0.014	[1.02, 1.08]
Number of Family Physician contacts	1.000	0.006	[0.99, 1.01]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

C4. Adjusted Regression Accounting for All Physician- and Patient-Level Variables – Long-term Co-prescribed APs, Patient-Level Variable Results

Variable	Estimate	Standard Error	95CI
Patient Sex			
Female (ref.)	--	--	--
Male	0.949	0.166	[0.69, 1.31]
Patient Age	0.962	0.004	[0.95, 0.97]
Patient Rurality			
Metropolitan (ref.)	--	--	--
Urban	0.570	0.385	[0.27, 1.21]
Rural	0.760	0.606	[0.23, 2.49]
Neighbourhood Income Quintile			
q1(low) (ref.)	--	--	--
q2	0.939	0.242	[0.58, 1.51]
q3	1.141	0.233	[0.72, 1.80]
q4	0.873	0.260	[0.52, 1.45]
q5 (high)	1.013	0.265	[0.60, 1.70]
q9 (unknown)	1.821	0.255	[0.00, 0.00]
Patient CCI	0.918	0.060	[0.82, 1.03]
Number of Unique Rx	1.082	0.015	[1.05, 1.11]
Number of FP contacts	0.995	0.008	[0.98, 1.01]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

Appendix D.

This appendix contains the sensitivity analysis results.

To note, values reported in Chapter 5, Appendix C, and Appendix D—the current appendix—are a result of running the regression analyses with an "exchangeable" correlation. The same values were produced when regressions were run with an "independence" correlation structure for all outcomes, variables, and models.

D1. Regression results of long-term outcome with grace-period extended to 28-days.

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.08 [1.01, 1.15]	1.07 [1.00, 1.14]	1.07 [1.00, 1.14]
Senior (20-29)	1.08 [1.02, 1.15]	1.05 [0.99, 1.12]	1.05 [0.98, 1.11]
Veteran (>=30)	1.13 [1.06, 1.20]	1.09 [1.03, 1.17]	1.09 [1.03, 1.17]
Average Unique Prescriptions	1.04 [1.02, 1.05]	1.03 [1.02, 1.05]	1.03 [1.01, 1.04]
Place of Graduation	--	--	--
Canada (ref.)	0.98 [0.95, 1.02]	0.98 [0.95, 1.02]	0.98 [0.94, 1.01]
International	1.03 [0.92, 1.15]	1.03 [0.92, 1.15]	1.04 [0.93, 1.16]
Unknown			
Practice Rurality			
Metropolitan (ref.)	--	--	--
Urban	0.98 [0.94, 1.02]	0.99 [0.95, 1.04]	0.89 [0.80, 0.99]

Rural	0.98 [0.92, 1.04]	1.00 [0.94, 1.06]	0.93 [0.82, 1.04]
Physician Sex			
Female (ref.)	--	--	--
Male	1.02 [0.98, 1.07]	1.00 [0.96, 1.04]	1.00 [0.96, 1.04]
Patient Sex			
Female (ref.)			--
Male			0.96 [0.93, 0.99]
Patient Age			0.99 [0.99, 1.00]
Patient Rurality			
Metropolitan (ref.)			--
Urban			1.13 [1.02, 1.26]
Rural			1.07 [0.96, 1.20]
Neighbourhood Income Quintile			
q1(low) (ref.)			--
q2			0.92 [0.88, 0.97]
q3			0.94 [0.89, 0.99]
q4			0.95 [0.90, 1.00]
q5 (high)			0.95 [0.90, 1.00]
q9 (unknown)			1.06 [0.90, 1.24]
Patient CCI			0.99 [0.98, 1.00]
Number of Unique Rx			1.01 [1.01, 10.02]
Number of FP contacts			1.00 [1.00, 1.00]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

D2. Regression results of co-prescribed outcome with grace-period extended to 45-days.

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.02 [0.64, 1.61]	1.00 [0.63, 1.60]	0.99 [0.63, 1.57]
Senior (20-29)	0.96 [0.62, 1.48]	0.91 [0.58, 1.43]	0.89 [0.57, 1.39]
Veteran (>=30)	1.65 [1.10, 2.48]	1.57 [1.01, 2.44]	1.58 [1.02, 2.44]
Average Unique Prescriptions	1.14 [1.05, 1.24]	1.11 [1.02, 1.21]	1.11 [1.01, 1.22]
Place of Graduation	--	--	--
Canada (ref.)	0.89 [0.68, 1.16]	0.89 [0.68, 1.17]	0.90 [0.69, 1.17]
International	1.40 [0.70, 2.78]	1.52 [0.76, 3.04]	1.59 [0.79, 3.20]
Unknown			
Practice Rurality			
Metropolitan (ref.)	--	--	--
Urban	0.92 [0.68, 1.23]	1.04 [0.76, 1.41]	0.94 [0.49, 1.80]
Rural	0.86 [0.54, 1.35]	0.94 [0.60, 1.49]	1.35 [0.50, 3.64]
Physician Sex			
Female (ref.)	--	--	--
Male	0.93 [0.70, 1.23]	0.82 [0.61, 1.10]	0.81 [0.60, 1.08]
Patient Sex			
Female (ref.)			--
Male			1.08 [0.84, 1.39]
Patient Age			0.97 [0.96, 0.98]
Patient Rurality			
Metropolitan (ref.)			--

Urban			1.16 [0.60, 2.23]
Rural			0.66 [0.25, 1.71]
Neighbourhood Income Quintile			
q1(low) (ref.)			--
q2			0.94 [0.65, 1.36]
q3			1.17 [0.82, 1.67]
q4			0.83 [0.55, 1.25]
q5 (high)			0.99 [0.66, 1.49]
q9 (unknown)			1.13 [0.28, 4.53]
Patient CCI			0.96 [0.88, 1.05]
Number of Unique Rx			1.05 [1.02, 1.08]
Number of Family Physician Contacts			1.00 [0.99, 1.01]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

D3. Regression results of long-termed co-prescribed antipsychotic outcome with grace-period extended to 98-days.

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.13 [0.61, 2.09]	1.12 [0.60, 2.09]	1.11 [0.61, 2.03]
Senior (20-29)	1.13 [0.64, 2.01]	1.12 [0.61, 2.04]	1.06 [0.58, 1.91]
Veteran (>=30)	2.09 [1.22, 3.58]	2.03 [1.13, 3.66]	2.02 [1.14, 3.57]
Average Unique Prescriptions	1.12 [1.01, 1.25]	1.07 [0.96, 1.20]	1.06 [0.93, 1.20]
Place of Graduation	--	--	--
Canada (ref.)	1.05 [0.76, 1.46]	1.09 [0.78, 1.52]	1.09 [0.78, 1.51]
International	0.85 [0.27, 2.63]	0.88 [0.28, 2.75]	0.31 [0.74, 3.11]
Unknown			
Practice Rurality			
Metropolitan (ref.)	--	--	--
Urban	0.74 [0.50, 1.09]	0.81 [0.54, 1.22]	1.26 [0.62, 2.56]
Rural	0.88 [0.51, 1.53]	0.98 [0.56, 1.70]	1.35 [0.39, 4.69]
Physician Sex			
Female (ref.)	--	--	--
Male	0.94 [0.66, 1.33]	0.79 [0.55, 1.15]	0.79 [0.54, 1.14]
Patient Sex			
Female (ref.)			--
Male			0.98 [0.71, 1.34]
Patient Age			0.96 [0.95, 0.97]
Patient Rurality			
Metropolitan (ref.)			--

Urban Rural			0.60 [0.29, 1.24] 0.76 [0.25, 2.38]
Neighbourhood Income Quintile q1(low) (ref.) q2 q3 q4 q5 (high) q9 (unknown)			 -- 0.93 [0.59, 1.47] 1.06 [0.68, 1.66] 0.81 [0.49, 1.34] 0.98 [0.59, 1.62] 0.00 [0.00, 0.00]
Patient CCI			0.95 [0.84, 1.06]
Number of Unique Rx			1.08 [1.05, 1.11]
Number of Family Physician Contacts			0.99 [0.98, 1.01]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

D4. Regression results of sensitivity analysis of the new antipsychotic outcome using Years Since MD in place of the Years in Practice Variable

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	0.89 [0.83, 0.96]	0.91 [0.84, 0.97]	0.91 [0.84, 0.97]
Senior (20-29)	0.86 [0.81, 0.92]	0.90 [0.85, 0.96]	0.90 [0.84, 0.96]
Veteran (>=30)	0.74 [0.69, 0.79]	0.80 [0.74, 0.86]	0.79 [0.74, 0.85]
Average Unique Prescriptions		0.92 [0.90, 0.94]	0.94 [0.92, 0.96]
Place of Graduation		--	--
Canada (ref.)		1.03 [0.98, 1.08]	1.05 [1.00, 1.10]
International		1.17 [1.04, 1.33]	1.15 [1.02, 1.29]
Unknown			
Practice Rurality			
Metropolitan (ref.)		--	--
Urban		1.03 [0.98, 1.09]	0.99 [0.89, 1.10]
Rural		0.98 [0.91, 1.06]	0.88 [0.78, 1.00]
Physician Sex			
Female (ref.)		--	--
Male		1.00 [0.95, 1.06]	0.99 [0.94, 1.04]
Patient Sex			
Female (ref.)			--
Male			1.11 [1.06, 1.16]
Patient Age			1.01 [1.01, 1.02]
Patient Rurality			
Metropolitan (ref.)			--

Urban Rural			1.04 [0.93, 1.17] 1.16 [1.04, 1.30]
Neighbourhood Income Quintile q1(low) (ref.) q2 q3 q4 q5 (high) q9 (unknown)			 -- 1.08 [1.01, 1.15] 1.07 [1.00, 1.15] 1.07 [1.00, 1.15] 1.09 [1.02, 1.17] 1.04 [0.85, 1.27]
Patient CCI			1.01 [0.99, 1.02]
Number of Unique Rx			0.96 [0.95, 0.96]
Number of FP Contacts			1.00 [1.00, 1.00]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

D5. Regression results of sensitivity analysis of the long-term antipsychotic outcome using Years Since MD in place of the Years in Practice Variable

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.10 [1.02, 1.19]	1.09 [1.02, 1.18]	1.09 [1.01, 1.17]
Senior (20-29)	1.09 [1.02, 1.17]	1.07 [1.00, 1.15]	1.07 [1.00, 1.15]
Veteran (>=30)	1.15 [1.07, 1.23]	1.12 [1.04, 1.20]	1.11 [1.04, 1.19]
Average Unique Prescriptions		1.03 [1.01, 1.04]	1.02 [1.01, 1.04]
Place of Graduation		--	--
Canada (ref.)		0.99 [0.95, 1.02]	0.98 [0.94, 1.02]
International		1.03 [0.92, 1.15]	1.03 [0.92, 1.15]
Unknown			
Practice Rurality			
Metropolitan (ref.)		--	--
Urban		0.99 [0.95, 1.04]	0.89 [0.80, 0.99]
Rural		1.00 [0.93, 1.06]	0.93 [0.83, 1.06]
Physician Sex			
Female (ref.)		--	--
Male		1.00 [0.95, 1.04]	1.00 [0.96, 1.04]
Patient Sex			
Female (ref.)			--
Male			0.96 [0.93, 1.04]
Patient Age			0.99 [0.99, 1.00]
Patient Rurality			
Metropolitan (ref.)			--

Urban Rural			1.13 [1.01, 1.25] 1.06 [0.95, 1.19]
Neighbourhood Income Quintile q1(low) (ref.) q2 q3 q4 q5 (high) q9 (unknown)			 -- 0.99 [0.87, 0.97] 0.99 [0.88, 0.98] 0.94 [0.89, 0.99] 0.94 [0.89, 1.00] 1.06 [0.91, 1.24]
Patient CCI			0.99 [0.97, 1.00]
Number of Unique Rx			1.01 [1.01, 1,02]
Number of FP Contacts			1.00 [1.00, 1.00]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

D6. Regression results of sensitivity analysis of the co-prescribed antipsychotics outcome using Years Since MD in place of the Years in Practice Variable

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.01 [0.60, 1.70]	1.01 [0.60, 1.70]	0.98 [0.58, 1.64]
Senior (20-29)	1.03 [0.64, 1.66]	0.98 [0.60, 1.61]	0.99 [0.61, 1.61]
Veteran (>=30)	1.58 [1.01, 2.47]	1.52 [0.94, 2.46]	1.46 [0.91, 2.35]
Average Unique Prescriptions		1.12 [1.02, 1.22]	1.12 [1.01, 1.23]
Place of Graduation		--	--
Canada (ref.)		0.91 [0.69, 1.19]	0.93 [0.71, 1.21]
International		1.49 [0.74, 2.96]	1.56 [0.77, 3.13]
Unknown			
Practice Rurality			
Metropolitan (ref.)		--	--
Urban		1.03 [0.76, 1.41]	0.93 [0.48, 1.80]
Rural		0.97 [0.61, 1.53]	1.40 [0.52, 3.81]
Physician Sex			
Female (ref.)		--	--
Male		0.80 [0.60, 1.07]	0.78 [0.59, 1.05]
Patient Sex			
Female (ref.)			--
Male			1.07 [0.83, 1.39]
Patient Age			0.97 [0.96, 0.98]
Patient Rurality			
Metropolitan (ref.)			--

Urban Rural			1.17 [0.60, 1.70] 0.65 [0.25, 1.70]
Neighbourhood Income Quintile q1(low) (ref.) q2 q3 q4 q5 (high) q9 (unknown)			 -- 0.95 [0.66, 1.38] 1.15 [0.80, 1.65] 0.85 [0.57, 1.29] 1.01 [0.67, 1.52] 1.25 [0.28, 4.46]
Patient CCI			0.96 [0.87, 1.04]
Number of Unique Rx			1.05 [1.02, 1.07]
Number of FP Contacts			1.00 [0.99, 1.01]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.

D7. Regression results of sensitivity analysis of the long-term co-prescribed antipsychotics outcome using Years Since MD in place of the Years in Practice Variable

Variable	**Unadjusted** RR [95CI]	**Physician Adjusted** RR [95CI]	**Patient & Physician Adjusted** RR [95CI]
Years in Practice			
New (1-9) (ref.)	--	--	--
Mid (10-19)	1.21 [0.59, 2.47]	1.18 [0.58, 2.43]	1.12 [0.55, 2.27]
Senior (20-29)	1.18 [0.60, 2.31]	1.16 [0.59, 2.29]	1.13 [0.58, 2.20]
Veteran (>=30)	2.23 [1.20, 4.17]	2.13 [1.10, 4.13]	1.95 [1.02, 3.76]
Average Unique Prescriptions		1.06 [0.95, 1.20]	1.05 [0.82, 1.60]
Place of Graduation		--	--
Canada (ref.)		1.12 [0.80, 1.57]	1.14 [0.82, 1.60]
International		0.90 [0.29, 2.82]	0.98 [0.30, 3.14]
Unknown			
Practice Rurality			
Metropolitan (ref.)		--	--
Urban		0.78 [0.51, 1.18]	1.25 [0.59, 2.67]
Rural		0.94 [0.53, 1.66]	1.34 [0.36, 4.99]
Physician Sex			
Female (ref.)		--	--
Male		0.84 [0.57, 1.23]	0.84 [0.57, 1.24]
Patient Sex			
Female (ref.)			--
Male			0.95 [0.69, 1.32]
Patient Age			0.96 [0.95, 0.97]
Patient Rurality			

Metropolitan (ref.)			--
Urban			0.58 [0.27, 1.25]
Rural			0.74 [0.22, 2.43]
Neighbourhood Income Quintile			
q1(low) (ref.)			--
q2			0.93 [0.58, 1.50]
q3			1.15 [0.73, 1.81]
q4			0.89 [0.53, 1.48]
q5 (high)			1.01 [0.60, 1.70]
q9 (unknown)			0.00 [0.00, 0.00]
Patient CCI			0.92 [0.81, 1.03]
Number of Unique Rx			1.08 [1.05, 1.11]
Number of FP Contacts			0.99 [0.98, 1.01]

Abbreviations: ref., Reference Group; q, Quintile; CI, Confidence Interval; CCI, Charlson Comorbidity Index; FP, Family Physician; Rx, Prescription

+ Values were the same if regressions were run with an “exchangeable” or “independence” correlation structure.