Manitoba Centre for Health Policy

Outpatient Oral Anticancer Agents in Manitoba

Summer 2018

Colette Raymond, BScPharm, PharmD, MSc, ACPR, FCSHP
Christine Leong, BSc, BScPharm, PharmD
Randy Fransoo, PhD
Marc Geirnaert, BScPharm
Roxana Dragan, MA
Marina Yogendran, MSc
Tamara Thomson, MSc
Leanne Rajotte, BComm
Ina Koseva, MSc
Jennifer Schultz, MA
Susan Burchill, BMus

University of Manitoba | Rady Faculty of Health Sciences

This report is produced and published by the Manitoba Centre for Health Policy (MCHP). It is also available in PDF format on our website at: **http://mchp-appserv.cpe.umanitoba.ca/deliverablesList.html**

Information concerning this report or any other report produced by MCHP can be obtained by contacting:

Manitoba Centre for Health Policy
Rady Faculty of Health Sciences
Max Rady College of Medicine, University of Manitoba
4th Floor, Room 408
727 McDermot Avenue
Winnipeg, Manitoba, Canada
R3E 3P5

Email: reports@cpe.umanitoba.ca
Phone: (204) 789-3819
Fax: (204) 789-3910

How to cite this report:
Raymond C, Leong C, Fransoo R, Geirnaert M, Dragan R, Yogendran M, Thomson T, Rajotte L, Koseva I, Schultz J, Burchill S. Outpatient Oral Anticancer Agents in Manitoba. Winnipeg, MB. Manitoba Centre for Health Policy, Summer 2018.

Legal Deposit:
Manitoba Legislative Library National Library of Canada

ISBN 978-1-896489-91-9

1st printing (Summer 2018)

This report was prepared at the request of Manitoba Health, Seniors and Active Living (MHSAL), a department within the Government of Manitoba, as part of the contract between the University of Manitoba and MHSAL. It was supported through funding provided by MHSAL to the University of Manitoba (HIPC #2014/2015-38). The results and conclusions are those of the authors and no official endorsement by MHSAL was intended or should be inferred. Data used in this study are from the Manitoba Population Research Data Repository housed at the Manitoba Centre for Health Policy, University of Manitoba and were derived from data provided by MHSAL and Statistics Canada. Strict policies and procedures were followed in producing this report to protect the privacy and security of the Repository data.

About the Manitoba Centre for Health Policy

The Manitoba Centre for Health Policy (MCHP) is located within the Department of Community Health Sciences, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba. The mission of MCHP is to provide accurate and timely information to healthcare decision–makers, analysts and providers, so they can offer services which are effective and efficient in maintaining and improving the health of Manitobans. Our researchers rely upon the unique Manitoba Population Research Data Repository (Repository) to describe and explain patterns of care and profiles of illness and to explore other factors that influence health, including income, education, employment, and social status. This Repository is unique in terms of its comprehensiveness, degree of integration, and orientation around an anonymized population registry.

Members of MCHP consult extensively with government officials, healthcare administrators, and clinicians to develop a research agenda that is topical and relevant. This strength, along with its rigorous academic standards, enables MCHP to contribute to the health policy process. MCHP undertakes several major research projects, such as this one, every year under contract to Manitoba Health, Seniors and Active Living. In addition, our researchers secure external funding by competing for research grants. We are widely published and internationally recognized. Further, our researchers collaborate with a number of highly respected scientists from Canada, the United States, Europe, and Australia.

We thank the Health Research Ethics Board, University of Manitoba, Rady Faculty of Health Sciences, Max Rady College of Medicine, Health Research Ethics Board for their review of this project. MCHP complies with all legislative acts and regulations governing the protection and use of sensitive information. We implement strict policies and procedures to protect the privacy and security of anonymized data used to produce this report and we keep the provincial Health Information Privacy Committee informed of all work undertaken for Manitoba Health, Seniors and Active Living.

The Manitoba Centre for Health Policy

Data | Insight | Informing Solutions

Acknowledgments

The authors wish to acknowledge the contributions of many individuals whose efforts and expertise made it possible to produce this report. We thank the following:

Colleagues at MCHP for their valuable input: Dr. Alan Katz (Senior Reader), Dr. Jennifer Enns (Editor), Ruth-Ann Soodeen (Proofreader) and Selena Randall (Proofreader), Dr. Dan Chateau, Randy Walld, Heather Prior, Jessica Jarmasz, Ken Turner, Charles Burchill, Kara Dyck, Emily Jones, Theresa Daniuk and Jo-Anne Baribeau.

The Advisory Group for their helpful advice and feedback throughout the project:

- Dr. Patricia Caetano (Manitoba Health, Seniors and Active Living)
- Dr. Piotr Czaykowski (University of Manitoba and CancerCare Manitoba)
- Dr. Jeff Onyskiw (Manitoba Health, Seniors and Active Living)
- Dr. Chastity Cleofas (Winnipeg Regional Health Authority)
- Dr. Shawn Bugden (College of Pharmacy)
- Dr. Jill Hardy (College of Pharmacists of Manitoba)

Our external reviewers: Dr. Mario De Lemos at the British Columbia Cancer Agency, and Rohini Naipaul at Cancer Care Ontario.

We acknowledge the Faculty of Health Sciences Research Ethics Board for its review of this project. The Health Information Privacy Committee (HIPC) is kept informed of all MCHP deliverables. The HIPC number for this project is 2014/2015-38. We also acknowledge Manitoba Health, Seniors and Active Living for the use of their data.

Table of Contents

List of Figures

List of Tables

List of Acronyms

DIN	Drug Identification Number
DPIN	Drug Program Information Network
HCDP	Home Cancer Drug Program
ICD	International Classification of Diseases
OAA	Oral Anticancer Agent
PHIN	Personal Health Identification Number
RHA	Regional Health Authority
Q1 – Q 5	Quintile (grouping of the population by average household income)

Executive Summary

This report describes a population-based profile of the use of oral anticancer agents (OAAs) in Manitoba. Since 2012, the Home Cancer Drug Program (HCDP) has made eligible OAA and non-OAA medications available to cancer patients at no individual cost. This report examines the prescribing trends of all classes of OAAs and non-OAA medications (e.g., anti-nauseants) covered by the HCDP.

Specific research objectives included:

- To describe the patient demographics of individuals using OAAs and non-OAA medications covered by the HCDP;
- To examine the prevalence of OAA users from April 1, 2003 to March 31, 2016 and the prevalence of users of non-OAA medications covered by the HCDP from 2012/13 to 2015/16;
- To describe the percentage of Manitobans with specific cancer diagnoses receiving OAAs and non-OAAs over time;
- To describe the impact of the HCDP policy on utilization patterns of OAAs;
- To examine prescription fill patterns for OAAs;
- To describe the rate of contacts with the healthcare system (physician visits and hospitalizations) among OAA users; and
- To describe the annual costs of OAA and non-OAA medications covered by the HCDP.

Study Methods

The study cohort included all Manitoba residents who were insured by Manitoba Health, Seniors and Active Living (shortened to 'Manitoba Health' in this report) and filled prescriptions for OAA and non-OAA medications covered by the HCDP from fiscal years 2003/04 to 2015/16. The following databases were used in the analysis: the Manitoba Health Insurance Registry, prescription medication records, the medical services file, hospital files, and Canada Census files from Statistics Canada. We also used Consumer Price Index data from Statistics Canada. OAA medications were grouped into three categories: i) traditional agents which act on all rapidly dividing cells (e.g,. cyclophosphamide); ii) targeted agents which interfere with specific molecules ("molecular targets") that are involved in the growth, progression, and spread of cancer (e.g., imatinib); and iii) hormonal agents for breast cancer and prostate cancer (e.g., tamoxifen) [1,2].

Measures and Determinants of Use

The prevalence of users of each medication group (traditional, targeted or hormonal) or each individual medication was determined from fiscal years 2003/04 to 2015/16. The fiscal year runs from April to March. Prevalence of use is expressed as OAA users per 100,000 Manitobans per quarter year. We defined the population of OAA users with a cancer diagnosis in the year prior or current fiscal year by the year in which the person filled a prescription for an OAA. Once an OAA user was determined to have a cancer diagnosis, we considered them to have had a cancer diagnosis for the study duration. These patients were included as a subset of the population of total OAA users. We summed pharmacy fees and medication costs as well as compared costs across years. All costs were adjusted for inflation using the Consumer Price Index and are presented in this report in 2015 Canadian dollars.

Policy Impact

The impact of HCDP implementation on OAA use over time was evaluated using generalized linear models. We compared the time period before the introduction of the HCDP to the time period during which the HCDP was active, and evaluated the differences in prescription filling rates in different quarters of the year.

Key Findings

Utilization

Over the study period, there was an increase in the overall use of OAA therapy among outpatient Manitobans with a cancer diagnosis (from 222 to 329 users per 100,000). A total of 21,895 prescriptions for OAAs were filled in 2003/04 for individuals with a cancer diagnosis. This increased to a total of 37,878 prescriptions for OAAs filled in 2015/16. The annual cost of these medications increased from $6.8M to $26.1M. The average annual cost per user increased from $1,650 to $4,162, and the number of users increased from 4,141 (with 21,895 prescriptions) to 6,281 (with 37,878 prescriptions). Users of "targeted agents" were the fastest growing group, increasing from 2.5 to 33.6 per 100,000. The vast majority (80-90%) of prescriptions for OAAs were paid for by Manitoba Pharmacare until the launch of the HCDP in 2012.

Impact of the Home Cancer Drug Program

Prior to the introduction of the HCDP, there was large variation in rates of OAA use and number of prescriptions filled between the first quarter of the year and the third or fourth quarters of the year. This "saw toothed" pattern demonstrates how many people filled prescriptions just before the end of the Pharmacare fiscal year. At the beginning of the next Pharmacare year, patients are required to pay for prescriptions until their income-based deductible is met. Once the HCDP was implemented, this quarterly variation in rates of OAA use and number of prescriptions per 100,000 population was no longer evident. When we modeled these variables using generalized estimating equations, we found the change in pattern to be statistically significant ($p=0.003$ for OAA use; $p=<0.0001$ for number of prescriptions). This suggests that OAA users altered the timing of filling their prescriptions after the HCDP was introduced. We were unable to assess the impact of the program on medication wastage, adherence or patient outcomes.

Patterns of Disease and Medication Use

For prostate cancer, the most commonly used medication was bicalutamide. Manitobans with breast cancer filled prescriptions for many different types of OAAs and non-OAA medications covered by the HCDP. Letrozole and tamoxifen were the most common, although numerous anti-nauseants were also filled. The most commonly prescribed non-OAA medications covered by the HCDP were anti-nauseants such as metoclopramide.

Pharmacy Fill Patterns

Most patients filled their first OAA at their usual pharmacy. This varied by the type of OAA; a greater proportion of first prescriptions for traditional and targeted OAAs than hormonal OAAs were filled at pharmacies that were not the usual pharmacy ($p<0.001$ for both targeted and traditional compared to usual pharmacy). A total of 36.8% of new users of targeted OAAs and 44.5% of new users of traditional OAAs did not fill their first OAA at their usual pharmacy. Individuals who filled a first prescription for a traditional or targeted OAA were more likely to switch pharmacies than those filling hormonal OAA prescriptions.

Health Services Use

Overall, ambulatory physician visit rates and the likelihood of experiencing at least one hospitalization were highest among OAA users in the youngest age category (<40 years) and among those receiving prescriptions for traditional OAAs.

Costs

In 2015/16, the total cost of OAAs for cancer patients exceeded $26M. The total expenditures on this category of medications increased almost four-fold over the study period, from nearly $7M in 2003/04 to over $26M in 2015/16. Maximum annual costs per user exceeded $90,000 in each year of the study. By contrast, the number of users and number of prescriptions of targeted OAAs increased

more than ten-fold over the course of the study, due to increased use and availability of these drugs. Since the mean cost per user per year was approximately $30,000 over all study years, the total cost increased from almost $2M in 2003/04 to almost $19M in 2015/16. The mean cost per day of OAA therapy ranged from less than $6 per day for hormonal OAAs to $30-$50 per day for traditional OAAs (decreased over time) to more than $130 for targeted OAAs (increased over time).

Conclusions and Recommendations

The use of OAAs and the expenses associated with these medications has increased significantly over the years. We observed that the launch of the HCDP altered the prescription filling patterns of OAAs in Manitoba. Starting to fill an OAA prescription was associated with changing pharmacies for some Manitobans. In seeking to balance convenient access to important medications with access to clinical expertise, policymakers could consider making an 'expert' pharmacist or pharmacy available for dispensing certain medications (e.g., targeted oral chemotherapy); this would ensure optimal pharmacist expertise and open prescriber/pharmacist/patient communication to monitor for safety and efficacy. This recommendation would need to be balanced with ensuring that patients in rural and remote areas, where an 'expert' pharmacist might not always be available, continue to have access to important medications.

Chapter 1: Introduction

Cancer is the leading cause of death in Canada [3–5]. Approximately 40% of Canadians are expected to develop cancer during their lifetime, and this means that a significant proportion of Canadians are expected to need anticancer treatments [3]. Cancer treatment is aggressive and has been long regarded as a challenging period for the patients and caregivers.

For most types of cancers, anticancer medications have traditionally been a combination of drugs administered intravenously, usually in a hospital or cancer centre [6,7]. In recent years, there has been a dramatic increase in the number of anticancer agents available in an oral formulation [2,8]. These oral anti-cancer agents (OAAs) are more convenient for cancer patients during therapy and may therefore be more acceptable to patients compared to traditional intravenous chemotherapy [7,9,10].

There are several different types of OAAs. OAAs include traditional chemotherapy agents (e.g., cyclophosphamide), agents prescribed for hormone-based cancers (e.g., tamoxifen for breast cancer), and newer biologic or targeted chemotherapy agents that work by interfering with specific molecules ("molecular targets") involved in the growth, progression, and spread of cancer (e.g., lenalidomide for myeloma) [1,2]. Because many of these agents are new and expensive [2], a subsequent increase in spending on outpatient prescriptions for the treatment of cancer is expected in Canada (as seen previously in the US) [11–15].

There is variability in dispensing practices for OAAs across Canada, with some OAAs being dispensed out of cancer centres and others being dispensed at community pharmacies [16–20]. In Manitoba, prescriptions for OAAs can be filled at any community pharmacy.

Safety issues related to OAAs are important to consider as these agents become a standard treatment option for many types of cancer. The dispensation of OAAs through general community pharmacies raises the issue of optimal communication between pharmacists and prescribers possibly lacking, as well as patient safety. Studies have reported a lack of standardized monitoring and in-depth knowledge about OAAs among pharmacists that dispense these agents in the community [16,19,21–23]. One study found that only 24% of community pharmacists were familiar with the common doses of OAAs and only 9% felt comfortable educating patients on these medications [16,19]. Additionally, while the oral administration of anticancer therapy offers many benefits to cancer patients, they are also then more accountable for ensuring the proper use of such agents [7,9,16,19,21–23]. Currently, there are no standardized protocols for ensuring adherence to OAAs at home, which can adversely impact the effectiveness of cancer treatment [24,25]. Moreover, patients

are responsible for the safe handling of OAAs to avoid inadvertently exposing family members without cancer to the drugs [7].

Newer cancer agents (both intravenous and OAAs) are costly, and expenditures in this therapeutic domain continue to rise [26,27]. Few population-based studies on oral anticancer drug utilization have been conducted [8,28], and we were unable to locate studies examining the prescribing trends of OAAs in a Canadian province from a population perspective.

Study Objective

The objective of this study was to examine changes in OAA utilization over time in the Manitoba cancer patient population. By describing the pattern of OAA use, we provide valuable information for policy makers and for future research studies examining the clinical efficacy, safety, and cost implications of OAA use.

Outpatient Oral Anticancer Agents and Coverage in Manitoba

In Manitoba, patients with a cancer diagnosis are usually treated by specialist physicians (medical or radiation oncologists or hematologists) at CancerCare Manitoba or by specialists and general practitioners at the Community Cancer Programs [29]. Prescriptions for OAAs are usually written by oncologists and hematologists, but may also be given by general practitioners or other specialist physicians for some indications (for example, some medications like cyclophosphamide are indicated for non-cancer reasons). These OAA prescriptions can be filled at any community pharmacy in Manitoba. Manitoba Health, Seniors and Active Living (shortened to 'Manitoba Health' in this report) offers a province-wide medication insurance program to all Manitobans, according to a published list of medication benefits in its Pharmacare Formulary and under conditions of an income-based deductible. Prescription medications are given Part 1, Part 2 or Part 3 status on the Pharmacare Formulary. The Part 1 designation provides open listing, while the second two designations limit access according to pre-determined criteria. Part 2 listings, which are usually second-line therapeutic agents or agents to be used only in specific clinical situations, require an indication on the prescription by physicians or pharmacists that the prescription drug meets Exception Drug Status for the specific criteria for use. Part 3 status is reserved for products that require physicians to contact Pharmacare to obtain prior approval for use. OAAs fall into all Pharmacare categories (Part 1, 2 and 3); however, newer targeted OAAs, which are typically quite costly, fall under Part 3 status. Drugs listed in Part 3 require prior approval and are an eligible benefit for specific clinical criteria only.

Pharmacare provides medication cost assistance to eligible Manitobans who do not have coverage under a federal program (e.g., Non-Insured Health Benefits for First Nations and Inuit) or other provincial program (e.g., Employment and Income Assistance). The Manitoba Pharmacare program normally operates under a published list of medication benefits in the Pharmacare Formulary with a deductible based on taxable income from the previous year. After registering with Manitoba Pharmacare, a family must reach this income-based deductible through the purchase of eligible prescription medications at a pharmacy. Once the yearly deductible is reached, Pharmacare pays 100% of eligible prescription costs for the remainder of the benefit year (April 1 to March 31 of the following year). This program applies to all eligible Manitobans, regardless of age, income or other available private coverage for medications [30]. For costly medications, where a single prescription could cost hundreds or even thousands of dollars, having to pay the entire cost, or even having to pay the entire deductible all at once could place a significant financial burden on individuals or families. Manitoba Pharmacare has introduced the Deductible Installment Payment Program as a way of alleviating the burden of upfront drug costs, allowing eligible patients to distribute their deductible payment across 12 months of the year [31].

Prior to 2012, Manitobans filled prescriptions for all OAAs and non-OAA medications related to their cancer treatment as they would any other medications. The prescriptions filled by cancer patients without private insurance or federal coverage were covered by Pharmacare after the deductible was met. The Home Cancer Drug Program (HCDP) was launched in April, 2012, allowing cancer patients access to eligible outpatient OAA and non-OAA medications at no individual cost, regardless of the person's deductible [32].

Research Questions

This Manitoba Centre for Health Policy (MCHP) report examines the use of OAAs in Manitoba from 2003/04 to 2015/16 and the use of non-OAA medications covered by the HCDP from 2012/13 to 2015/16. It includes an in-depth exploration of the use and prescribing patterns of these medications with a view to understanding the potential factors influencing use from multiple perspectives. Aspects of OAA and non-OAA medication use discussed in this report include patient demographics, diagnoses, pharmacy fill patterns, adherence to medications, health services utilization and medications costs.

Research questions were operationalized in conjunction with Manitoba Pharmacare and stakeholders from

CancerCare Manitoba within the data available in MCHP's prescription and health care databases.

Specific research objectives include:

- To describe the patient demographics of individuals using OAAs and non-OAA medications covered by the HCDP;
- To examine the prevalence of OAA users from April 1, 2003 to March 31, 2016 and the prevalence of users of non-OAA medications covered by the HCDP from 2012/13 to 2015/16;
- To describe the percentage of Manitobans with specific cancer diagnoses receiving OAAs and non-OAAs over time;
- To describe the impact of the HCDP policy on utilization patterns of OAAs;
- To examine prescription fill patterns for OAAs;
- To describe the rate of contacts with the healthcare system (physician visits and hospitalizations) among OAA users; and
- To describe the annual costs of OAA and non-OAA medications covered by the HCDP.

To address these research questions, the project uses data from prescription medication claims in Manitoba and information on patient care from hospital and physician claims.

Chapter 2:
Methods

Scope

The study examines all Manitobans insured by Manitoba Health who filled prescriptions for OAAs in the 13-year period from April 1, 2003 to March 31, 2016 and for non-OAA medications covered by the Manitoba Home Cancer Drug Program (HCDP) in the four-year period from April 1' 2012 to March 31, 2016. Individuals had to be registered with Manitoba Health for at least one day during the study period be to included in the study population.

Data Sources

The data on which we based the analyses were administrative health data from the Manitoba Population Research Data Repository ('the Repository') housed at the Manitoba Centre for Health Policy (MCHP). The Repository contains individual-level information on virtually all Manitobans from a variety of sources and domains, including health. All records in the Repository are de-identified (no names or addresses are attached to the records) and Personal Health Information Numbers (PHINs) and other identifiers are scrambled to protect confidentiality. To further protect individuals' health information, we report all rates and counts as aggregated values; values based on five or fewer individuals, including true zeros, are suppressed.

We used the following databases in this study: the Manitoba Health Insurance Registry; prescription dispensation records from outpatient dispensaries through Manitoba Health's Drug Program Information Network (DPIN); medical services files; hospital discharge abstracts; Canada Census public use files from Statistics Canada; and the Manitoba Home Cancer Drug Program (HCDP) database files. Information on cancer diagnoses was obtained from medical services (physician reimbursement claims) and hospitalization (hospital discharge abstracts) files and identified by International Classification of Diseases Clinical Modification (ICD-9-CM or ICD-10-CA equivalent) codes. Prescription data were linked using specific diagnoses from contacts with the healthcare system. The Manitoba Health Insurance Registry provided the number of residents in Manitoba and basic demographic information on this population (e.g., age, sex). Records from the Registry were linked through the use of a scrambled health identification number. We used data from the fiscal years of 2003/04 to 2015/16. The first quarter (Q1) of each year was April-June, the second quarter (Q2) was July-September, the third quarter (Q3) was October-December, and the fourth quarter (Q4) was January-March.

Detailed descriptions of these databases can be found on MCHP's Repository Data List (webpage: http://umanitoba.ca/faculties/health_sciences/medicine/units/community_health_sciences/departmental_units/mchp/resources/repository/datalist.html)

Categorization of Medications

Medications we examined are listed in Tables 2.1 and 2.2. Medications of interest include OAAs and non-OAA medications covered by the HCDP.

OAAs. OAAs we examined included all oral formulations (e.g., tablet, capsule) for cancer treatment medications prescribed in Manitoba during the study years (Table 2.1). We compiled this list by examining the Anatomical Therapeutic Chemical (ATC) categories L01 (antineoplastic agents), L02 (endocrine therapy), and L04 (immunosuppressants) [33] and Manitoba Health's Drug Identification Number (DIN) master file, as well as consulting with stakeholders and clinical experts. These medications were covered by the HCDP for eligible patients as of April 1, 2012; however, we were interested in how patterns of use changed over time, so we included prescriptions for these medications for all years of the study in our analyses.

OAAs were classified in the following way: [1,2]:

1. **Traditional agents** – alkylating agents (e.g., cyclophosphamide), antimetabolites (e.g., capecitabine), plant alkaloids (e.g., etoposide). These standard or traditional chemotherapy medications act on and often kill all types of rapidly dividing cells, including normal and cancerous cells. Because methotrexate is covered under the HCDP for some leukemias, it was included in the analysis as a medication covered by the HCDP, even though it is often excluded from this category. This class also includes lenolidamide/pomolidamide;
2. T**argeted agents** – e.g., protein kinase inhibitors (e.g., imatanib, dasatanib). Targeted cancer therapies are medications that block the growth and spread of cancer by interfering with specific molecules ("molecular targets") that are involved in the growth, progression, and spread of cancer. These medications are also known as "molecularly targeted" drugs or therapies; and
3. **Hormonal agents** – hormone therapy to treat estrogen receptor-positive breast cancer (e.g., tamoxifen, letrozole) and prostate cancer (e.g., bicalutamide).

We also classified OAAs according to their mechanism of action using the ATC system. This system divides medications into different groups according to the organ or system on which they act and the therapeutic or chemical characteristics of the medication. There are five levels of classification for this system [33]. For example, all alkylating agents (e.g., cyclophosphamide) were grouped together.

Within each group of traditional, targeted, or hormonal agents, there are other ways to categorize medications. For example, abiraterone and enzalutamide are hormonal therapies for prostate cancer that are used after patients progress on hormone therapy. They are newer drugs that are generally more expensive than other hormones and there are no generic alternatives [34]. Other medications in the hormonal drug category have many generic therapies. Lenalidomide (a traditional agent) is generally much more expensive than some other older agents such as cyclophosphamide, but these two drugs are used for different malignancies [35]. Although other systems of drug categorization are possible (e.g., new vs old, expensive vs cheaper), we chose an established categorization system that has been used by others [33].

Table 2.1: Oral Anticancer Agents List*

Drug Group (National Cancer Institute)	Drug Category and Specific Drugs	ATC Code
Traditional	**Alkylating Agents**	
	Busulfan	L01A
	Chlorambucil	L01A
	Cyclophosphamide	L01A
	Lomustine	L01A
	Melphalan	L01A
	Mitotane	L01A
	Procarbazeine	L01A
	Temozolomide	L01A
	Antimetabolites	
	Capecitabine	L01B
	Fludarabine Phosphate	L01B
	Mercatopurine	L01B
	Thioguanine	L01B
	Plant alkaloids	
	Etoposide	L01CB
	Other older anticancer agents	
	Hydroxyurea	L01XX
	Tretinoin	L01XX
	Lenalidomide and Others	
	Lenalidomide	L04AX
	Pomalidomide	L04AX
	Thalidomide	L04AX
Targeted**	**Protein Kinase Inhibitors for Haematological Malignancies**	
	Bosutinib	L01XE
	Dasatinib	L01XE
	Imatinib Mesylate	L01XE
	Nilotinib	L01XE
	Ruxolitinib	L01XE
	Protein Kinase Inhibitors for Solid Tumours	
	Afatanib	L01XE
	Axitinib	L01XE
	Crizotinib	L01XE
	Dabrafenib	L01XE
	Erlotinib	L01XE
	Gefitnib	L01XE
	Ibrutinib	L01XE
	Lapatinib	L01XE
	Pazopanib	L01XE
	Regorafenib	L01XE
	Sorafenib	L01XE
	Sunitinib	L01XE
	Trametinib	L01XE
	Vandetanib	L01XE
	Vemurafenib	L01XE
	Other newer anticancer agents	
	Everolimus	L01XE, L04AA
	Vismodegib	L01XX
Hormonal	**Hormone therapy for breast cancer**	
	Anastrozole	L02BG
	Exemestane	L02BG
	Letrozole	L02BG
	Tamoxifen	L02BA
	Hormone therapy for prostate cancer	
	Abiraterone	L02BX
	Bicalutamide	L02BB
	Enzalutamide	L02BB
	Flutamide	L02BB
	Nilutamide	L01BB

* These drugs were also covered by HCDP at the start of the program

** Targeted anticancer agent definition and reference: https://www.cancer.gov/cancertopics/factsheet/Therapy/targeted

Note: There are no prescriptions for thalidomide or fludarabine as they are not included in DPIN

Non-OAA medications covered by the HCDP. In addition to OAAs, we included in our analyses several non-OAA medications covered by the HCDP [32]. These medications (listed in Table 2.2) are generally used as part of the patient's cancer treatment (for example, to treat nausea) or prescribed through CancerCare Manitoba by an oncologist if for a non-cancer indication. Parenteral (injectable) formulations of chemotherapy and anticancer agents were excluded. The non-OAA medications covered by the HCDP since its inception on April 1, 2012 we included were anti-nauseants, steroids, supportive treatments such as megestrol for cancer or treatment-related appetite suppression, and agents to treat a specific disease (e.g., anagrelide).

Table 2.2: Non-Oral Anticancer Agent Medications Covered by the Home Cancer Drug Program (HCDP)

Drug Group (National Cancer Institute)	Drug Category and Specific Drugs	ATC Code
Medications covered by Home Cancer Drug Program	**Supportive Treatments**	
	Estradiol	G03CA
	Megestrol	G03AC, G03DB, L02AB
	Disease Treatment	
	Acitretin	D05BB
	Anagrelide	L01XX
	Celecoxib	L01XX, M01AH
	Imiquimod	D06BB
	Isotretinoin	D10AD, D10BA
	Ketoconazole	D01AC, G01AF, J02AB
	Methotrexate	L01BA, L04AX
	Anti-nauseants	
	Aprepitant	A04AD
	Domperidone	A03FA
	Granisetron	A04AA
	Metoclopramide	A03FA
	Nabilone	A04AD
	Olanzapine	N05AH
	Ondansetron	A04AA
	Prochlorperazine	N05AB
	Steroids	
	Dexamethasone	H02AB, H02AB
	Hydrocortisone	H02AB, H02AB
	Prednisone	A07EA, H02AB

Note: These drugs were covered by HCDP as of April 1, 2012

Patient Populations

This report includes the following patient populations: 1) all OAA users; 2) OAA users with a cancer diagnosis; 3) users of non-OAA medications covered by the HCDP (not restricted by a cancer diagnosis); 4) users of medications of interest with a specific cancer diagnosis of breast cancer, colorectal cancer or prostate cancer. Each population is further described below.

1. **All OAA users:** All individuals living in Manitoba with at least one day of health coverage during the study period were included in the denominator. Among these, we identified individuals who were prescribed at least one medication of interest within each quarter from April 1, 2003 to March 31, 2016. Prevalence of OAA use for the population of Manitoba was calculated quarterly and presented as prevalence (crude rates) of users per 100,000 Manitoba residents. The number of prescriptions for OAAs (in Manitoba, a prescription can be written for any quantity medication) was calculated quarterly and presented as prescriptions per 100,000 Manitoba residents. The population denominator was calculated annually. No segments of the population were excluded from the denominator. Out-of-province patients who received health services for cancer, including filled prescriptions, were not included in the numerator or denominator. In order to determine prevalence for each quarter, the total count of OAA users was divided by the population of Manitobans registered for coverage for that year. Note that this population filled prescriptions for the entire study period by definition; however, after April 1, 2012, the majority of the OAA prescriptions were covered by the HCDP;
2. **OAA users with a cancer diagnosis:** Prevalence of OAA users who had a cancer diagnosis is presented as a crude rate per 100,000 Manitobans. OAAs are prescribed also for medical conditions other than cancer. For example, a commonly prescribed OAA, cyclophosphamide, is indicated for numerous cancers, but is also used for the treatment of some kidney conditions, such as nephritis [36] or dermatologic conditions [37]. Because some OAAs are used for non-cancer indications, we defined the subset of OAA users with a cancer diagnosis. Cancer diagnosis was defined by a

hospitalization or physician visit code suggestive of a specific cancer diagnosis (ICD-9-CM 140-209 except 173 or ICD-10-CA equivalent C00-C96 except for C44) [2,38]. We searched for a cancer diagnosis during the prior or current fiscal year when the person filled a prescription for an OAA. Once an OAA user was determined to have a cancer diagnosis, we considered them to have had a cancer diagnosis for the study duration. These patients were included as a subset of the population of total OAA. Prescriptions per 100,000 users are presented in Appendix 1. Note that this population filled prescriptions for the entire study period by definition; however after April 1, 2012, the majority of the OAA prescriptions for OAA users with a cancer diagnosis were covered by the HCDP;

3. **Users of non-OAA medications covered by the HCDP (not restricted by a cancer diagnosis)**: Prevalence of users of non-OAA medications covered by the HCDP is presented as a crude rate per 100,000 Manitobans. Examples of such medications include as anti-nauseants (e.g., metoclopramide) and those for disease treatment (e.g., anagrelide). Note that this population filled prescriptions from April 1, 2012 to the end of the study period; and
4. **Users of OAA or non-OAA medications (covered by the HCDP) with a specific type of cancer diagnosis**: For some analyses, we first identified individuals in Manitoba with specific cancer types (breast, colorectal, lung or prostate cancer) [39]. For these patients, we then determined the proportions of Manitobans diagnosed with these specific cancer types who filled prescriptions for OAA or non-OAA medications covered by the HCDP.

Population descriptions are provided in each chapter going forward. For the majority of the analyses presented this report, we used the population of OAA users with a cancer diagnosis.

Sociodemographic Characteristics

The sociodemographic characteristics of the patient populations were defined as follows:

Age groups: <40, 40-64, 65 years and older [39]. Age was determined at the beginning of the year or quarter. Note that the age group <40 includes the pediatric population, which is not reported separately.

Sex: Male or female.

Regional analysis (urban or rural): Medication users were categorized as living in urban (Brandon or Winnipeg) or rural (all other) areas as determined by their postal code registered with Manitoba Health.

Regional analysis (Regional Health Authority): Manitobans were categorized by Regional Health Authority (RHA) based on their postal code as follows: Southern Health-Santé Sud (SH-SS), Interlake-Eastern RHA (IERHA), Winnipeg Regional Health Authority (WRHA), Prairie Mountain Health (PMH), or Northern Health Region (NHR).

Socioeconomic status (SES): Determined using neighbourhood income quintile data from the 2011 Canada Census public use files. Individuals were assigned to one of five neighbourhood income levels (quintiles) using average household income data by enumeration area from the Canada Census. Each income quintile comprises 20% of the population. Each patient's neighbourhood income level was determined based on their postal code in the Manitoba Health Insurance Registry.

Types of cancer: For some analyses, we determined the type(s) of cancer with which the patient was diagnosed using 3-digit ICD 9-CM codes at any physician visit or hospitalization up to one year prior to the prescription of interest. These patients also had to have been insured with Manitoba Health for one year prior to receiving the prescription of interest. We also examined the proportions of Manitobans diagnosed with specific cancer types (breast, colorectal, lung or prostate cancer) who filled prescriptions for OAA and non-OAA medications covered by the HCDP.

Prescription Characteristics

Characteristics of each prescription were defined as follows:

Prescription Medication Payer [30,40]:

- Pharmacare (income-based deductible applies);
- Pharmacare – Personal Care Home (no deductible);
- Pharmacare – Palliative Care Program (no deductible);
- Home Cancer Drug Program (no deductible);
- Employment and Income Assistance (no deductible); and
- Other –includes federal public drug benefit programs with separate formularies and coverage, such as Non-Insured Health Benefits for First Nations and Inuit, Veterans Affairs Canada, and out-of-pocket or cash prescriptions, and prescriptions with private insurance [41].

HCDP Prescriptions: The HCDP covered many OAA prescriptions and many non-OAA medications (e.g. anti-nauseants). This program requires that a special form be completed by an authorized prescriber, outlining the diagnosis, chemotherapy regimen, start date and the patient's primary oncologist. Individuals who are covered by a different provincial/federal medication benefit program are not eligible for the HCDP [32]. We identified HCDP prescriptions through a file that was created by Manitoba Health. The file contained scrambled PHINs, DINs, and dates of coverage. HCDP users were defined as

individuals who filled at least one HCDP prescription for an OAA or non-OAA medications covered by the HCDP.

An individual's first OAA prescription was an OAA prescription filled following at least one year without any prior OAA prescriptions filled.

Pharmacy Characteristics

We determined which pharmacy dispensed OAAs and categorized pharmacies where patients filled prescriptions as follows:

Usual pharmacy: the pharmacy dispensing the majority of prescriptions for a patient with a cancer diagnosis in the year before their first OAA prescription. We excluded individuals with no prescriptions, only one prescription, missing pharmacy identifier/location, or multiple usual pharmacies (same number of prescriptions at each) in the year prior to their first OAA prescription. For all patients filling an OAA prescription (targeted, traditional and hormonal), the usual pharmacy was categorized by pharmacy characteristics as described below.

Pharmacy type [42]:

- Independent – not affiliated with any corporate banner, franchise or chain program;
- Hospital – run by a hospital pharmacy department (note that this does not include chain or franchise pharmacies that operate within a hospital);
- Banner – independent pharmacies affiliated with a central office and using a recognized name (e.g., Pharmasave);
- Franchise – franchisees may not own the physical store but may participate in programs developed by head office (e.g., Shoppers Drug Mart);
- Chain – part of a large national or international chain. Pharmacy managers are salaried employees of head office (e.g., Pharma Plus); and
- Food stores and Mass Merchandisers – departments within a supermarket or mass merchandise outlet. Pharmacy managers are salaried employees of head office (e.g., Safeway, Sobeys).

For the purposes of this report, we grouped pharmacy types as follows:

- Independent/Hospital;
- Banner/Franchise/Chain; and
- Food stores and Mass Merchandisers.

Close to cancer centre: several pharmacies are known to be physically proximate (directly beside or across the street from) the two major cancer treatment centres in Winnipeg. Due to a presumed professional relationship between prescribers and pharmacists as well as a presumed familiarity with OAAs, we classified these select few pharmacies as 'close to a cancer centre'. All other pharmacies were considered not to be close to a cancer centre. Of note, lenalidomide, which is only dispensed by pharmacies that are registered by the RevAid Program [43], is dispensed through a pharmacy close to a cancer centre. In Manitoba, thalidomide prescriptions are not included in the DPIN data, and are therefore not included in this report.

Pharmacy offering rewards program: pharmacies offering some sort of inducement when filling prescriptions include Safeway, Rexall™, Sobeys (Air Miles®), Shoppers Drug Mart (Optimum® Points), Zellers (HBC rewards®), London Drugs (LDExtras™) and Superstore (PC Plus®). Note that several Canadian provinces (Ontario, Newfoundland, PEI and Quebec, but not Manitoba) prohibit incentive programs on prescription medications.

Distance from home to pharmacy: the distance between the patient's postal code and the pharmacy's postal code for the usual pharmacy was calculated. Distance was computed using the Statistics Canada Postal Code Conversion File, which provides correspondence between six-digit postal codes and Statistics Canada's standard geographical areas (e.g., Census divisions, Census subdivisions). As some rural postal codes consist of a very large geographic area, this method may over- or underestimate distance for some rural populations [44,45].

Prescription Filling Characteristics

We examined the pharmacy location where the first OAA prescription was dispensed, as well as the location where subsequent OAA prescriptions and prescriptions for other medications were dispensed in the year after the first OAA prescription. A 'usual pharmacy' was then determined for OAA prescriptions and for all other prescriptions.

Patients were categorized as:

- **Continue at usual pharmacy:** usual pharmacy for OAAs and other medications did not change from one year before to one year after filling the first OAA prescription;
- **Change pharmacy for all medications:** usual pharmacy for OAAs and other medications changed from one year before to one year after filling the first OAA prescription;
- **Change pharmacy for OAA only:** usual pharmacy changed for OAA only; and
- **Other:** any other pattern not otherwise defined.

We describe the following characteristics for all OAAs for users with a cancer diagnosis and users of non-OAA medication covered by the HCDP by medication class:

- **Number of prescriptions per user per year** (prescriptions can be for any duration);

- **Days supplied per prescription** (number of days of therapy that a prescription contains). In Manitoba, this field is entered manually by a pharmacist. For example, if a prescription is for 100 tablets of tamoxifen and the instructions are for one tablet daily, the days supplied would be 100. This number may not always accurately describe the patient's medication-taking behaviour. For example, if a prescription was for 30 tablets of ondansetron, 8 mg three times daily as needed for nausea, the days supplied would be 10. But if the patient takes more or less than prescribed, then there would be a difference in the number of days the prescription was actually taken; and
- **Days supplied for all medications** within a category per user per year.

Use of Health Services

We describe the following for all OAA users with a cancer diagnosis:

- **Number of physician visits** to any ambulatory care physician [46]. This includes all physician visits to primary care providers and specialists;
- **Percentage with at least one inpatient hospitalization** [47]; and
- **The number of visits or hospitalizations an OAA user had for each year they used OAAs.**

Prescription Costs

We describe the cost for each prescription for all OAA users with a cancer diagnosis as follows [48]:

- **Total prescription cost:** sum of ingredient cost plus professional fee;
- **Ingredient cost:** cost of medication without pharmacy professional. Where this was not available, it was imputed [49]; and
- **Professional fee:** the total fee charged on a per-prescription basis by the pharmacy for prescriptions dispensed; there is no minimum or maximum cost. The professional fee in claims from the Personal Care Home data was zero, because personal care homes pay a set fee to the pharmacy per month based on the number of beds in the personal care home [49].

For each year of data, we present the following costs by OAA medication class (traditional, targeted, or hormonal):

- **Total prescription spending for all payers** (regardless of drug plan);
- **Total ingredient cost and professional dispensing fee;**
- **Cost per prescription (total cost, ingredient** cost and professional fee); and
- **Prescription cost per user per days supplied** (sum of total cost divided by sum of total days supplied in a year).

All costs were adjusted for inflation using the Consumer Price Index and presented in 2015 Canadian dollars [50].

Analysis

Demographic Information

Demographics are described for all OAA users, for the subset of OAA users with a cancer diagnosis, and for users of OAA and non-OAA medications covered by the HCDP (not limited to a cancer diagnosis). We report demographics by group of medications (traditional, targeted, hormonal OAAs and non-OAA medications covered by the HCDP). We also present the demographics for type(s) of cancer. For all OAA users, we determined which type of cancer they were diagnosed with (based on ICD-9 codes for physician visit or hospitalizations one year prior to first OAA prescription). For Manitobans diagnosed with breast, colorectal, bladder, lung and prostate cancer, we calculated how many used OAAs or non-OAA medications covered by the HCDP.

Prevalence of OAA prescriptions

Prevalence of users of OAAs and non-OAA medications covered by the HCDP is described quarterly. Use of each medication group (traditional, targeted, or hormonal) and individual types of medications within a group is described for patients with a cancer diagnosis. Quarterly prevalence of drug users is presented per 100,000 Manitobans.

Cancer Diagnoses

We determined which types of cancer OAA users had using 3 digit ICD-9-CM codes from physician visits or ICD-10-CA codes from hospitalizations (note that physician visits for this report excludes nurse practitioners). The diagnosis had to occur within one year before the first OAA prescription was filled. Among Manitobans with common cancer types defined in administrative health claims data (breast, colorectal, lung or prostate cancer), we determined the percentage who filled prescriptions for OAAs and non-OAA medications covered by the HCDP.

Patterns of OAA Prescriptions

For OAA users with a cancer diagnosis, we examined patterns of prescribing in the year before the first OAA prescription and the year after the first OAA prescription. We present the proportion of OAA prescriptions dispensed by pharmacy type (Independent/Hospital vs Banner/Chain/

Franchise vs Food store/Mass merchandise), by whether or not the pharmacy was close to a cancer centre, and by whether the pharmacy had a rewards pharmacy or not. We describe patterns of prescription dispensation for the first OAA prescription and then subsequent OAA prescriptions. First and subsequent OAA prescription dispensations were categorized as being at the patient's usual pharmacy or not. Patterns of prescription filling according to pharmacy type were compared to the usual pharmacy using chi-squared tests (and Fisher's exact text where appropriate). We determined if patients switched pharmacies for their OAA prescription only or for all prescriptions once an OAA was initiated using multinomial logistic regression with 'continue at the usual pharmacy' as the reference category. For all years of data, we described the annual number of prescriptions and days supplied for all OAAs by medication group (traditional, targeted, or hormonal).

Measures of Health Services Use

We counted the number of physician visits and proportion of OAA users with a cancer diagnosis making them in the year after the first OAA prescription. Measures of health services use are presented by age group, sex and medication group (traditional, targeted or hormonal).

Cost Analysis

We determined annual total prescription spending by each OAA group (traditional, targeted, or hormonal), as well as the annual total ingredient cost, professional dispensing fee, cost per prescription (total cost, ingredient cost and professional fee) and total prescription cost per user per days supplied (sum of total cost divided by sum of total days supplied in a year). All costs were adjusted for inflation using the Consumer Price Index and are presented in 2015 Canadian dollars [50]. This analysis was performed for the OAA users with a cancer diagnosis in the year of, or year prior to, their first OAA prescription.

Policy Impact

We used generalized linear models to determine the effect of the introduction of the HCDP on the utilization patterns of all OAAs in the Manitoba population (prevalence of users and prescriptions per user with a cancer diagnosis). Specifically, we explored the quarterly variation in rates of users and prescriptions in the lowest quarter of the year with the highest quarter of the year for OAA users with a cancer diagnosis. Using PROC GENMOD with a Poisson distribution, we included a contrast statement to determine if the difference between the highest and lowest quarterly rates before the HCDP was implemented was significantly different ($p<0.05$) than after the program. Fiscal year was considered a categorical variable.

Analysis Software

The analyses for this report were conducted using SAS® statistical analysis software, version 9.4.

Chapter 3:
Demographics

This section describes the patient demographics of those who received the following types of prescriptions:

a. OAA users with any indication (note that this can include some non-cancer diagnoses). These medications were covered by a variety of drug programs prior to 2012; the majority were covered by the HCDP after implementation;

b. OAA users with a cancer diagnosis; and

c. Users of the HCDP (i.e., users of OAAs and non-OAA medications covered by the HCDP). These medications are not limited to cancer patients; some medications paid for by the HCDP are for non-cancer indications that are treated by hematologists and oncologists.

Over the entire study period from 2003/04 to 2015/16, a total of 28,362 Manitobans filled 488,315 prescriptions for OAAs (Table 3.1). Among these, 114,698 prescriptions were for traditional agents; 26,364 prescriptions were for targeted agents; and 347,253 prescriptions were for hormonal agents. Prior to 2012/13 most OAA prescriptions were paid for through Pharmacare. From 2012/13 onward, HCDP covered all OAA prescriptions.

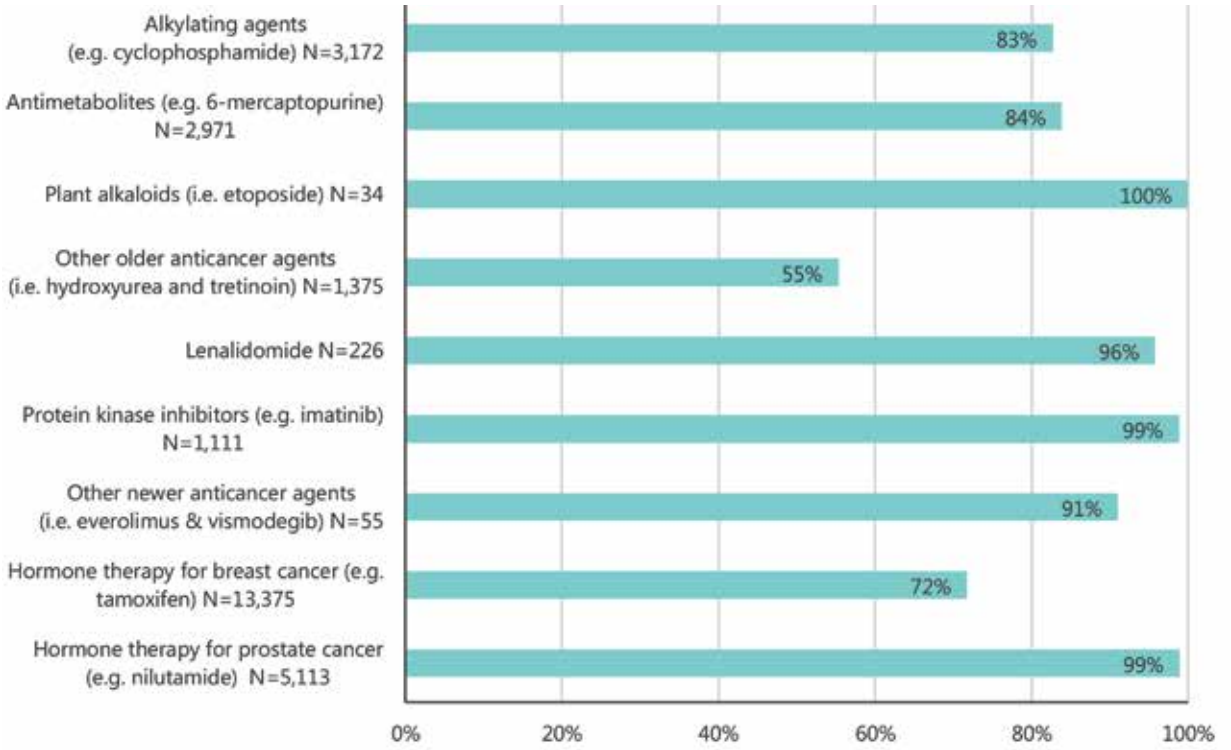
Table 3.1: Demographics for all Manitobans Using Oral Anticancer Agents, 2003/04-2015/16

	All OAA N=28,362 (%)	Traditional N=7,768 (%)	Hormonal N=20,328 (%)	Targeted N=1,620 (%)	Non-OAA (HCDP only)* N=9,669 (%)
Age					
39 and younger	17.71	12.68	19.90	6.11	6.26
40-64	34.36	39.35	32.34	48.58	46.83
65 and older	47.93	47.97	47.75	45.31	46.91
Sex					
Male	35.49	48.16	28.71	56.98	43.17
Female	64.51	51.84	71.29	43.02	56.83
RHA					
Interlake-Eastern RHA	10.44	10.71	10.35	11.30	11.68
Northern Health Region	3.12	3.69	2.85	4.26	1.93
Southern Health-Santé Sud	12.14	11.80	12.19	12.10	12.92
Prairie Mountain Health	14.40	15.44	14.11	12.10	14.06
Winnipeg RHA	59.91	58.35	60.5	60.25	59.42
Socioeconomic Status					
Q1 (Lowest)	17.54	18.58	16.99	18.15	15.04
Q2	21.41	21.32	21.45	20.31	19.48
Q3	21.21	20.67	21.44	20.62	22.91
Q4	18.97	18.55	19.23	19.14	20.27
Q5 (Highest)	19.47	19.81	19.42	20.68	21.74
Percent of Prescriptions by Payer					
Pharmacare	60.34	64.00	61.10	34.49	0.00
HCDP	25.17	21.06	24.59	50.80	100.00
Personal Care Home	6.39	4.80	7.36	0.40	0.00
Employment/Income Assistance	2.78	4.19	2.38	1.84	0.00
Palliative Care	1.13	1.12	1.15	0.99	0.00
Other**	4.19	4.82	3.43	11.47	0.00

* This category includes supportive care agents and specific anticancer medizcations covered by the HCDP program from 2012/13 onwards.
** This category includes federal public drug benefit programs with separate formularies and coverage such as: First Nations and Inuit Non-Insured Health Benefits. Veterans Affairs Canada, and out-of-pocket or cash prescriptions (these prescriptions may have private insurance coverage) and prescriptions with private insurance.

When we limited the analysis to OAA users with a cancer diagnosis, the proportion of OAA users who were removed from the analysis varied by medication group (Figure 3.1). The greatest exclusions for cancer diagnosis ICD occurred in the medication group containing hydroxyurea, antimetabolites (e.g., 6-mercaptopurine) and alkylating agents (e.g., cyclophosphamide), which are used for a variety of non-cancer indications.

Figure 3.1: Percent of Manitobans using Oral Anticancer Agents with a Cancer Diagnosis, 2003/04-2015/16



Among OAA users with a cancer diagnosis, a total of 22,393 people filled 416,382 prescriptions for OAAs over the entire study period (2003/04 to 2015/16). This subset of the total Manitoba population that filled OAAs was on average older than the Manitoba population (57.1% of individuals with a cancer diagnosis were 65 or older vs 47.9% individuals in the Manitoba population) (Tables 3.1 and 3.2). The subset had a smaller proportion of females than the overall Manitoba population (59.3% of the subset vs 64.5% in the Manitoba population). Those with prescription hormonal therapies were mostly women (taking OAAs for breast cancer) (Table 3.2), and those with prescriptions for targeted therapies were mostly men (taking OAAs for a variety of cancer types) and slightly younger on average than other groups (Table 3.2). There were an additional 9,431 people who filled prescriptions for non-OAA medications covered by the HCDP.

Table 3.2: Demographics for all Manitobans with a Cancer ICD Code Using Oral Anticancer Agents, 2003/04-2015/16

	All OAA N=22,393 (%)	Traditional N=6,043 (%)	Hormonal N=16,094 (%)	Targeted N=1,587 (%)	Non-OAA (HCDP only)* N=9,431 (%)
Age					
39 and younger	4.07	9.22	2.22	6.11	6.20
40-64	38.79	39.35	38.52	48.77	47.04
65 and older	57.13	51.43	59.26	45.12	46.76
Sex					
Male	40.65	48.80	35.22	57.47	43.29
Female	59.35	51.20	64.78	42.53	56.71
RHA					
Interlake-Eastern RHA	11.25	11.05	11.36	11.41	11.74
Northern Health Region	3.02	3.52	2.76	4.35	1.92
Southern Health-Santé Sud	11.93	12.25	11.71	11.97	12.99
Prairie Mountain Health	14.99	14.84	15.19	12.16	13.89
Winnipeg RHA	58.80	58.33	58.98	60.11	59.46
Socioeconomic Status					
Q1 (Lowest)	17.70	17.99	17.41	17.96	15.08
Q2	21.90	21.60	22.05	20.16	19.47
Q3	21.58	20.82	21.87	20.86	22.86
Q4	18.23	18.68	18.14	19.28	20.39
Q5 (Highest)	19.15	19.87	18.98	20.73	21.67
Percent of Prescriptions by Payer					
Pharmacare**	57.47	59.23	58.92	34.68	0.00
HCDP	27.95	26.14	26.52	50.62	100.00
Personal Care Home	6.41	3.76	7.46	0.36	0.00
Employment/Income Assistance	2.47	2.91	2.42	1.86	0.00
Palliative Care	1.31	1.78	1.24	1.01	0.00
Other†	4.38	6.17	3.43	11.46	0.00

* This category includes supportive care agents and specific anticancer medications covered by the HCDP program from 2012/13 onwards.
** Pharmacare is associated with patient out-of-pocket costs (deductible).
† This category includes federal public drug benefit programs with separate formularies and coverage such as: First Nations and Inuit Non-Insured Health Benefits, Veterans Affairs Canada, and out-of-pocket or cash prescriptions (these prescriptions may have private insurance coverage) and prescriptions with private insurance.

A total of 21,895 prescriptions for OAAs were filled in 2003/04 for individuals with a cancer diagnosis. This number increased to a total of 37,878 prescriptions for OAAs filled in 2015/16. The vast majority (approximately 80-90%) of prescriptions for OAAs were covered by Pharmacare until the HCDP came into effect. With the launch of the HCDP, the pattern of how prescriptions were covered changed. Approximately 80% of prescription OAAs for OAA users with a cancer diagnosis were covered by the HCDP (Figures 3.2, 3.3); a small proportion was still covered by Pharmacare. Possible explanations for these medications covered by Pharmacare include some individuals having prescriptions for hormonal therapies prescribed outside of the HCDP. Other programs continued to operate in Manitoba for individuals not covered by the HCDP.

Figure 3.2: Frequency of Oral Anticancer Agent Prescriptions by Payer for Manitobans with a Cancer Diagnosis, 2003/04-2015/16

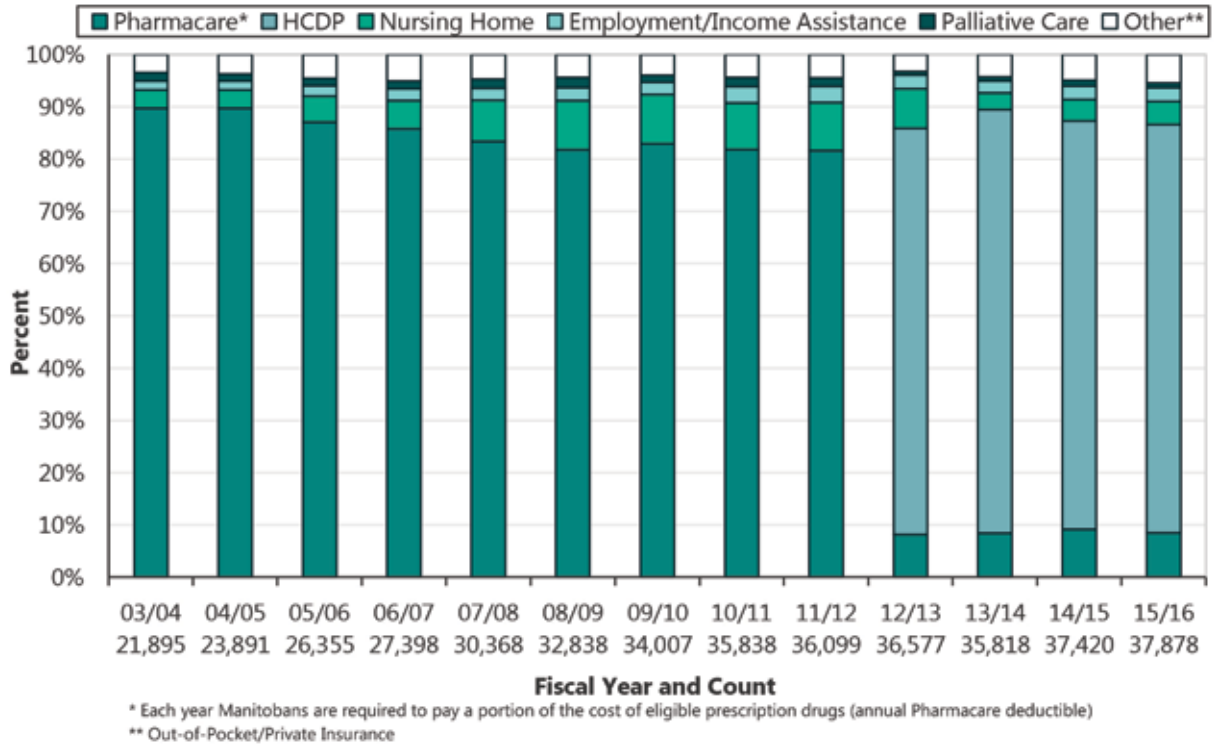
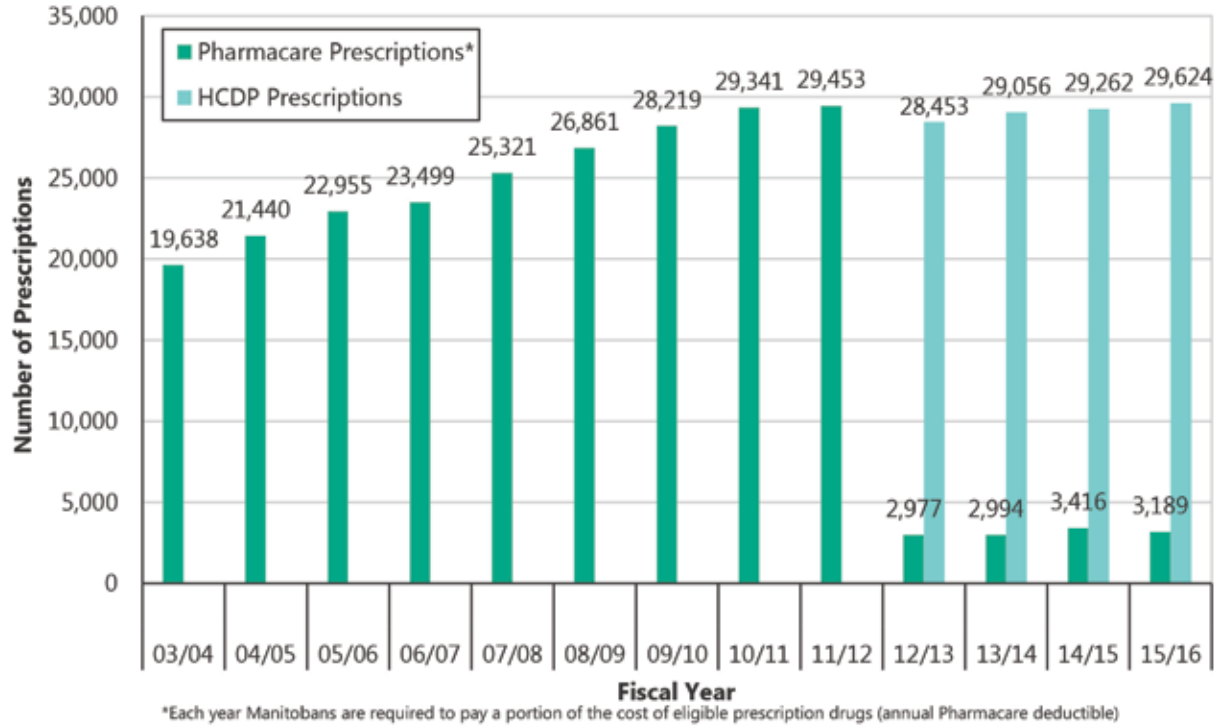


Figure 3.3: Number of Oral Anticancer Agent Prescriptions Covered by Pharmacare and the Home Cancer Drug Program (HCDP) for Manitobans with a Cancer Diagnosis, 2003/04-2015/16



The demographics of the population filling at least one prescription for an OAA or non-OAA medication covered by the HCDP (for any indication – cancer or non-cancer) are described in Table 3.3. The demographics for all users of OAAs with a cancer diagnosis who were included in the analysis of pharmacy dispensation patterns are available in Appendix 2.

Table 3.3: Demographics of Manitobans with at least one Home Cancer Drug Program (HCDP) Prescription, 2012/13-2015/16

	OAA and Non-OAA (HCDP only) N=16,036 (%)	All OAA N=9,956 (%)	Traditional N=2,187 (%)	Hormonal N=7,154 (%)	Targeted N=998 (%)	Non-OAA (HCDP only)* N=9,669 (%)
Age						
39 and Younger	4.46	3.25	7.73	1.79	4.41	6.26
40-64	41.92	39.43	39.6	39.11	44.39	46.83
65 and Older	53.61	57.31	52.67	59.10	51.20	46.91
Sex						
Male	39.53	35.60	47.78	28.85	55.81	43.17
Female	60.47	64.40	52.22	71.15	44.19	56.83
RHA						
Interlake-Eastern RHA	11.55	11.21	10.97	11.18	12.22	11.69
Northern Health Region	1.94	1.96	2.19	1.86	2.71	1.93
Southern Health-Santé Sud	12.76	12.84	14.77	12.26	12.42	12.94
Prairie Mountain Health	14.84	15.20	13.99	15.95	11.72	14.03
Winnipeg RHA	58.92	58.80	58.07	58.75	60.92	59.41
Socioeconomic Status**						
Q1 (Lowest)	15.23	14.85	15.18	14.61	s	15.02
Q2	20.50	21.04	19.80	21.44	20.34	19.47
Q3	22.57	22.17	21.76	22.27	20.94	22.89
Q4	19.77	19.82	20.26	20.03	19.74	20.34
Q5 (Highest)	21.41	21.63	22.41	21.20	23.55	21.73
Percent of Prescriptions by Payer						
Pharmacare	9.09	3.19	3.13	3.55	0.56	8.72
HCDP	87.82	95.25	95.66	95.1	96.48	88.36
Personal Care Home	0.72	0.56	0.18	0.74	0.08	0.32
Employment/Income Assistance	0.19	0.14	0.09	0.13	0.24	0.22
Palliative Care	0.90	0.20	0.24	0.21	0.07	1.35
Other†	1.27	0.66	0.69	0.28	2.56	1.03

s indicates suppression due to small numbers
* This category includes supportive care agents and specific anticancer medications covered by the HCDP program from 2012/13 onwards.
** "Missing income" is not shown (percentages may not add up to 100).
† This category includes federal public drug benefit programs with separate formularies and coverage such as: First Nations and Inuit Non-Insured Health Benefits, Veterans Affairs Canada, and out-of-pocket or cash prescriptions (these prescriptions may have private insurance coverage) and prescriptions with private insurance.

Chapter 4:
Prevalence of OAA Users and OAA Prescription Rates in Manitoba

Overall, the prevalence of OAA users among Manitobans with a cancer diagnosis increased over the study period. Prevalence of Manitobans using OAAs for all indications increased from 271.5 to 399 per 100,000 people over the course of the study (from the first quarter of 2003/04 to the last quarter of 2015/16). The most commonly used group of medications were hormonal agents, specifically those used for breast cancer (e.g., tamoxifen).

We observed the saw-toothed pattern in prescription dispensing that is typical for Manitoba when data are analyzed quarterly [51,52]. The pattern demonstrated how patients tend to fill prescriptions at a higher rate in the first quarter (before the end of the Pharmacare year on March 31), since they must begin paying their income-based deductible again starting in April of each year [30]. However, once the HCDP was launched in 2012, the quarterly saw-tooth pattern for prescription dispensing was no longer observed, suggesting that patients no longer felt the need to fill their OAA prescriptions at any particular time of year.

Quarterly Prevalence of OAA Users Among Manitobans with a Cancer Diagnosis

The overall prevalence of OAA users among Manitobans with a cancer diagnosis increased from 222.3 to 328.9 per 100,000 Manitobans over the study period (Figure 4.1). The increase was primarily due to an increase in the prevalence of people using hormonal agents for the treatment of hormone receptor-positive breast cancer; the prevalence of OAA users of this group of medications increased from 153.8 to 231.1 per 100,000 people over the course of the study (Figure 4.2).

The impact of the HCDP was evaluated using a generalized linear model. When compared to the time period before the HCDP was introduced, the relative difference between the prevalence of OAA users from the highest quarter of the year to the lowest quarter of the year was significantly greater than after the HCDP was introduced (Relative Rate = 1.05 with upper and lower bounds 1.02-1.08, alpha 0.05, standard error 0.01, chi-squared value 13.37, p=0.003). This suggests that the pattern of OAA user prevalence changed after the HCDP was introduced. Under the Pharmacare plan (pre-2012), Manitobans were more likely to be an OAA user early in the first quarter of the year so they could delay having to pay a deductible. Once the HCDP was implemented (April 1, 2012 onwards), patients no longer had to pay a deductible and there was no particular pattern to when they used OAAs. A non-significant interaction (p=0.64) between HCDP and year indicates that the annual increase in prevalence remained stable after the implementation of the HCDP. We were unable to assess the impact of the program on medication wastage, adherence or patient outcomes.

Figure 4.1: Quarterly Prevalence of Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people

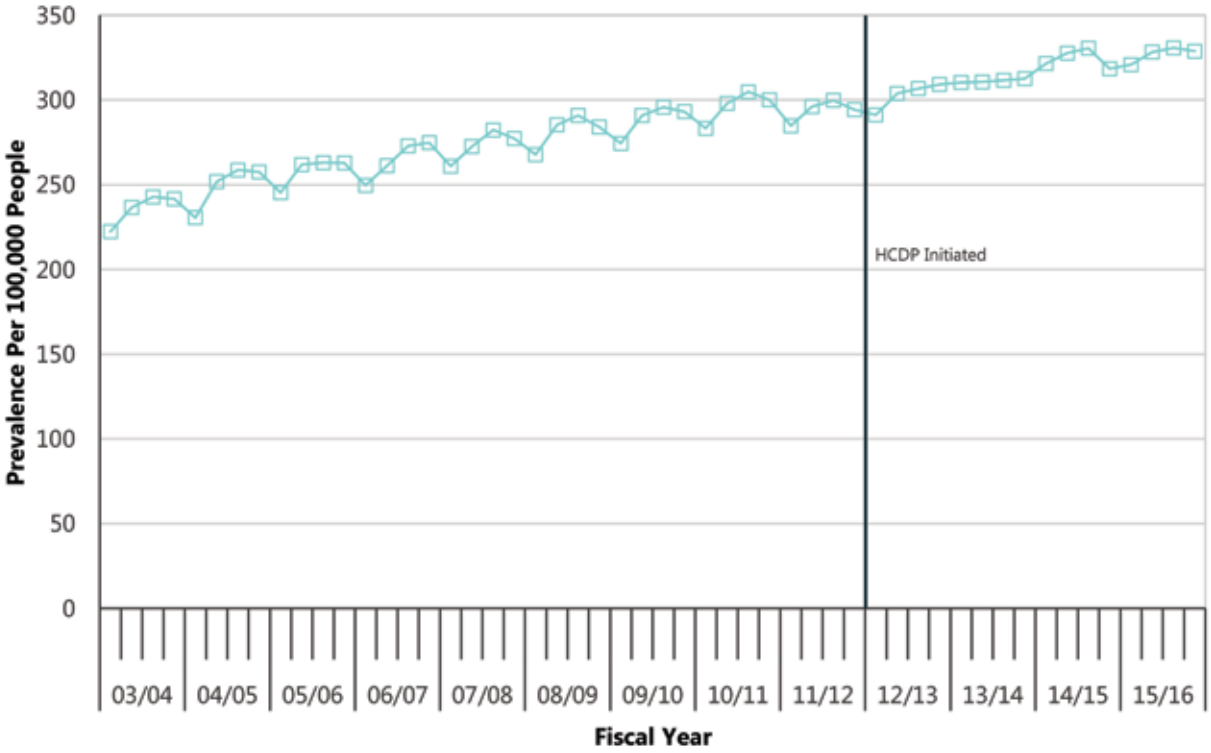
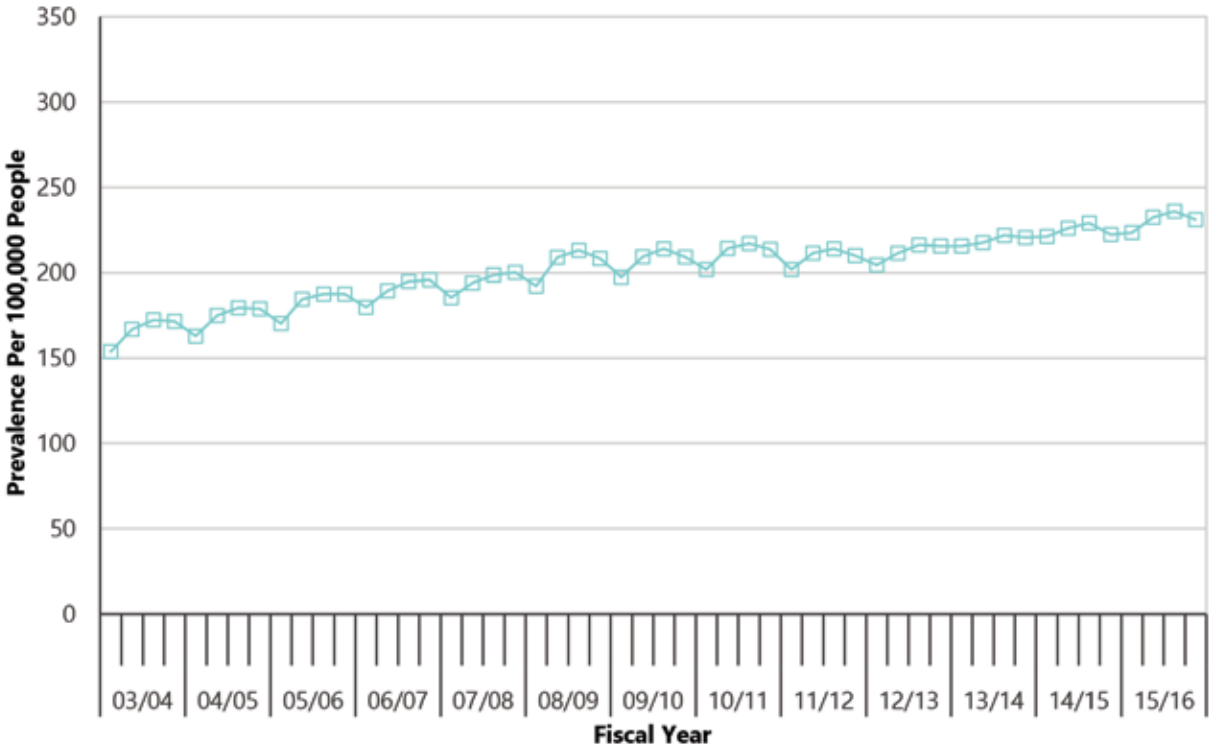
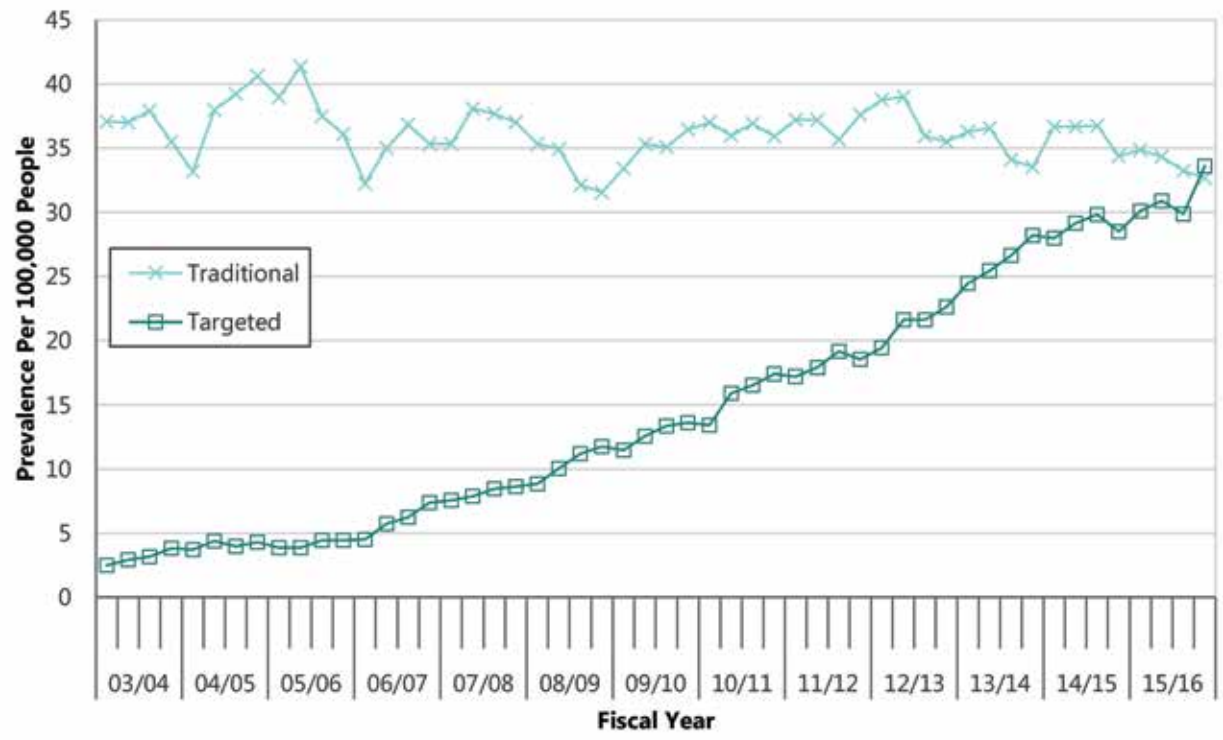


Figure 4.2: Quarterly Prevalence of Hormone Therapy for Breast Cancer Users Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people



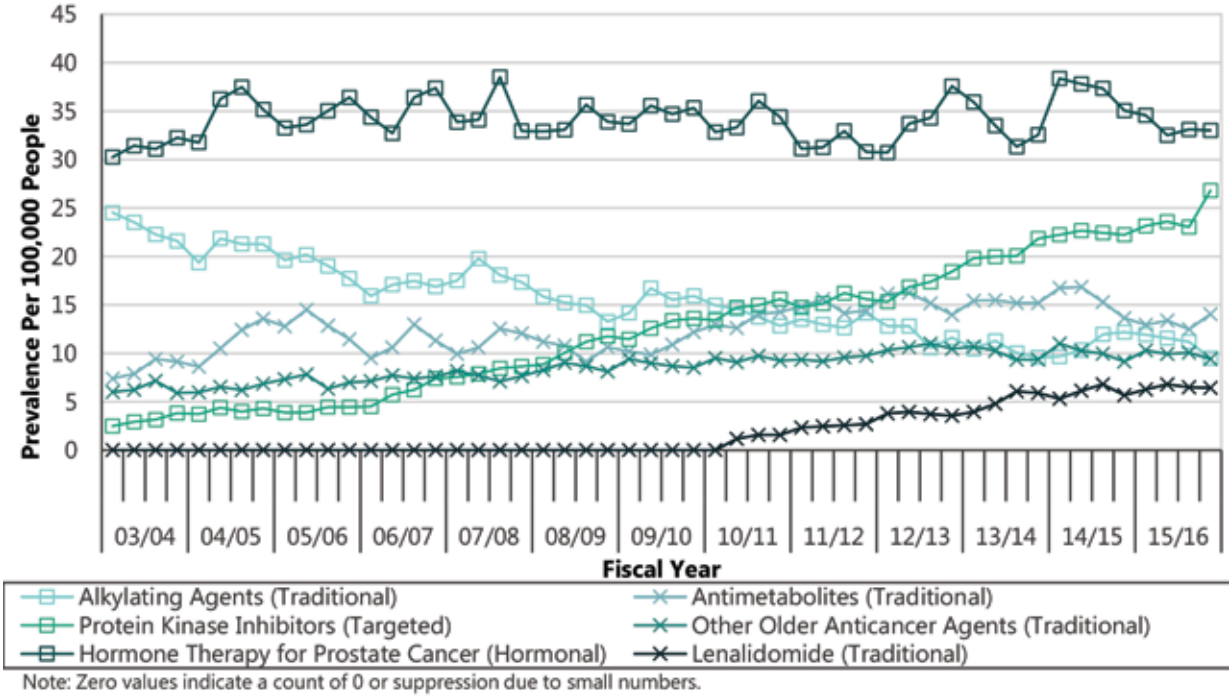
We observed a decrease in the prevalence of people who used traditional OAAs over the course of the study from 37.1 to 32.7 users per 100,000 people (Figure 4.3). Conversely, there was an increase in the prevalence of people who used targeted OAAs. Prevalence of people who used targeted agents (protein kinase inhibitors) increased from 2.5 to 33.6 users per 100,000 people (Figure 4.3). This aligns with an increase in the number of new targeted agents that have become available in the last decade.

Figure 4.3: Quarterly Prevalence of Traditional and Targeted Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people



We took a closer look at specific types of traditional and targeted OAAs. The prevalence of people who used alkylating agents (traditional OAAs) decreased from 24.5 to 9.4 users per 100,000 people over the study period (Figure 4.4). The prevalence of people who used antimetabolites (traditional OAAs) increased from 7.4 to 14.0 users per 100,000 people (Figure 4.4). As nearly 100% of people who used protein kinase inhibitors (targeted OAAs) had a cancer diagnosis linked to that use, prevalence did not change very much among this limited population. Over the course of the study, the prevalence of protein kinase inhibitor users taking these drugs for their cancer increased from 2.5 to 26.8 users per 100,000 people (Figure 4.4).

Figure 4.4: Quarterly Prevalence of Oral Anticancer Agent Users by Drug Category Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people

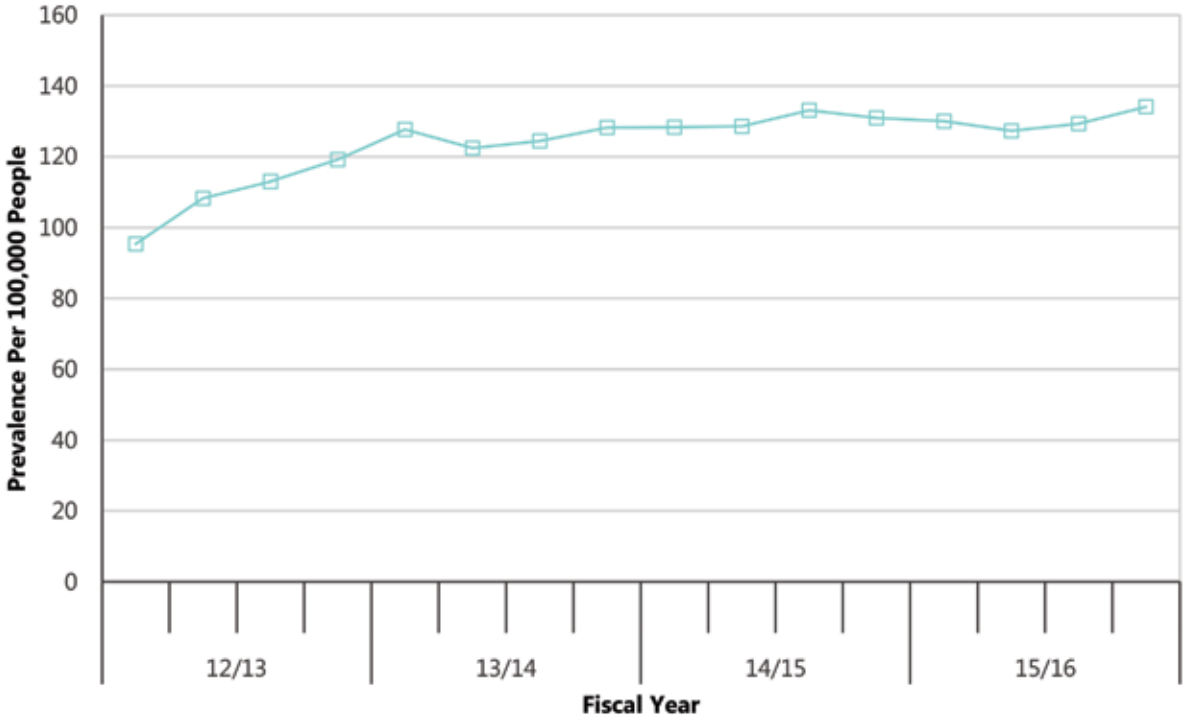


Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Plant Alkaloids (Traditional) and Other Newer Anticancer Agents (Targeted) are not shown in the figure due to low use, but counts are included in the total.

The prevalence of people who used non-OAA medications covered by the HCDP also increased throughout the study period. Overall, the number of non-OAA medications dispensed increased from 21,708 prescriptions in 2012/13 (at the start of the HCDP) to 28,200 prescriptions in 2015/16. The quarterly prevalence of people who used these non-OAA medications increased from 95.4 to 134.1 users per 100,000 people from the first quarter of 2012/13 to the last quarter of 2015/16 (Figure 4.5). This increasing trend in the prevalence of non-OAA medication users was due to growing use of metoclopramide, dexamethasone and ondansetron, which are all anti-nauseants used to treat nausea associated with any type of cancer treatment (including intravenous chemotherapy).

Figure 4.5: Quarterly Prevalence of Users of Non-Oral Anticancer Agent Medications Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16

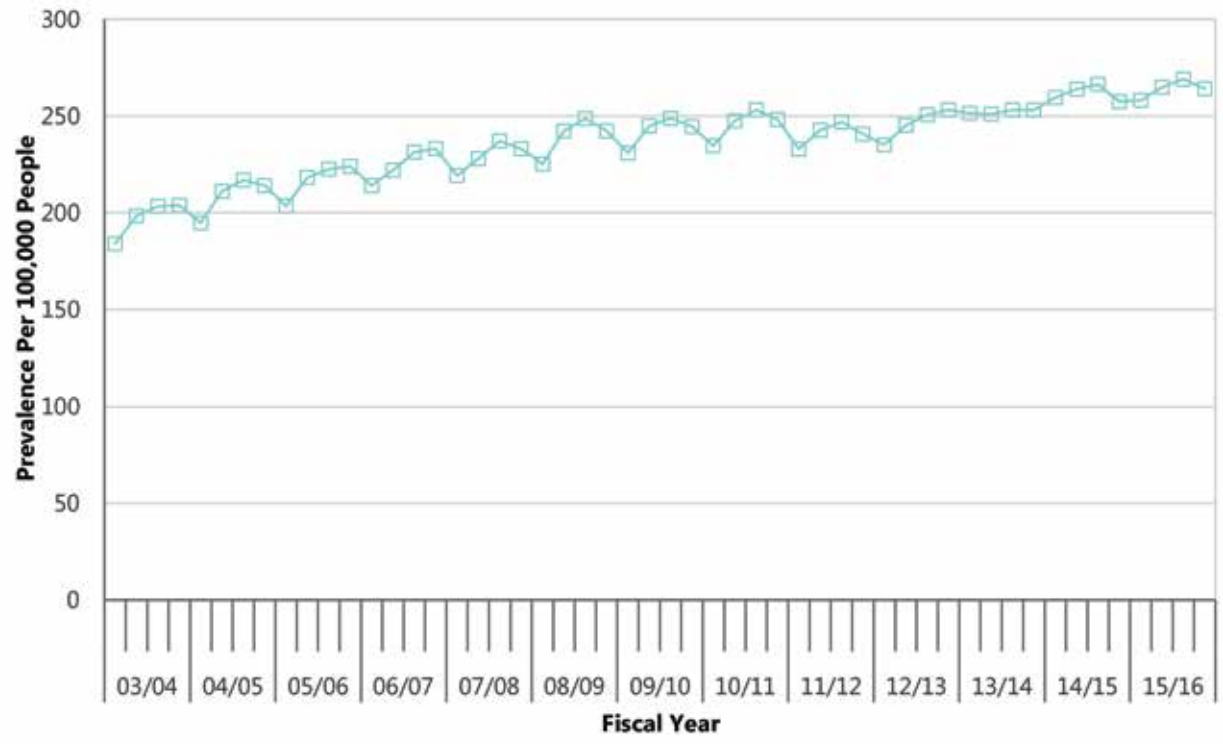
Per 100,000 people



Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

We observed a decrease in the prevalence of people who used traditional OAAs from 37.1 to 32.7 users per 100,000 people (a larger decrease over the study period than the prevalence of people in the general population using OAA for non-cancer indications), and an increase in the prevalence of people who used targeted OAAs from 2.5 to 33.6 users per 100,000 people (Figure 4.3). The prevalence of people who used hormonal agents increased from 184.1 to 264.0 users per 100,000 people (Figure 4.6).

Figure 4.6: Quarterly Prevalence of Hormonal Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people



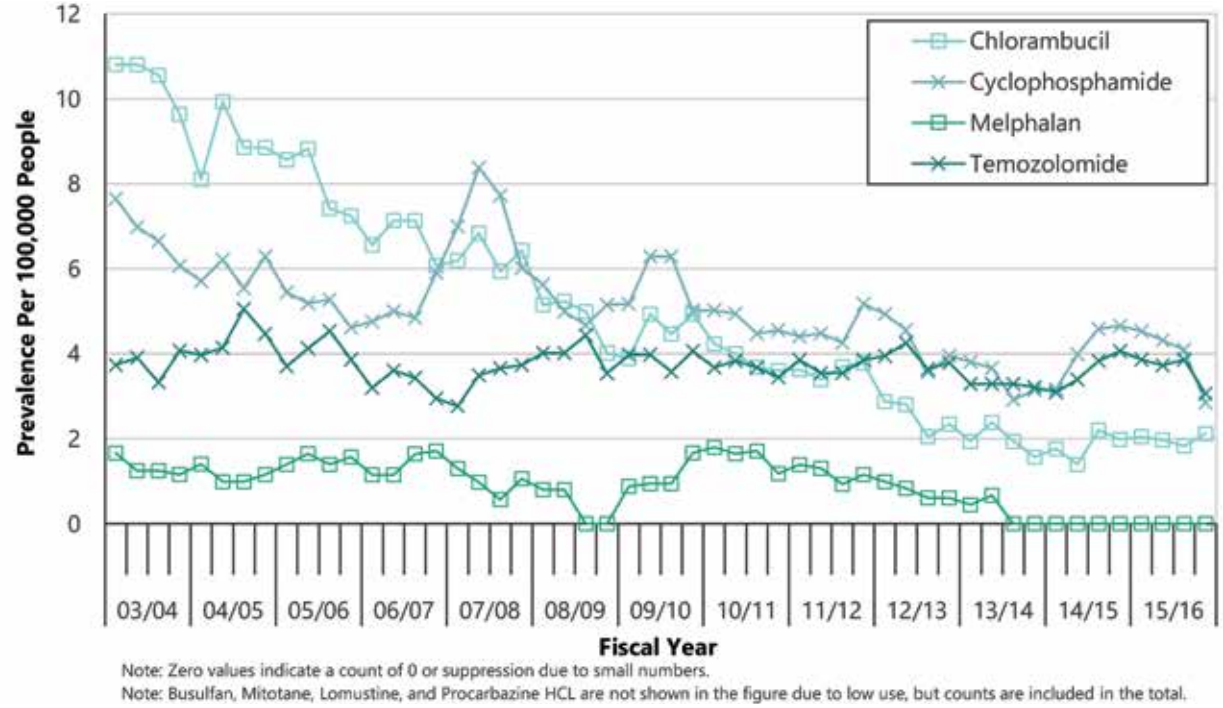
Figures 4.7-4.14 show the quarterly prevalence of people who used specific types of OAAs.

Types of Traditional OAAs

There was a decrease in the prevalence of people who used the alkylating agents chlorambucil (10.8 to 2.1 users per 100,000 people) and cyclophosphamide (7.7 to 2.9 users per 100,000 people) during the study period (Figure 4.7). The prevalence of people who used antimetabolites increased over the study period, with capecitabine use increasing from 3.8 to 10.4 users per 100,000 people and 6-mercaptopurine increasing from 2.8 to 3.7 users per 100,000 people (Figure 4.8).

Figure 4.7: Quarterly Prevalence of Users of Alkylating Agents (Traditional Oral Anticancer Agents) Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

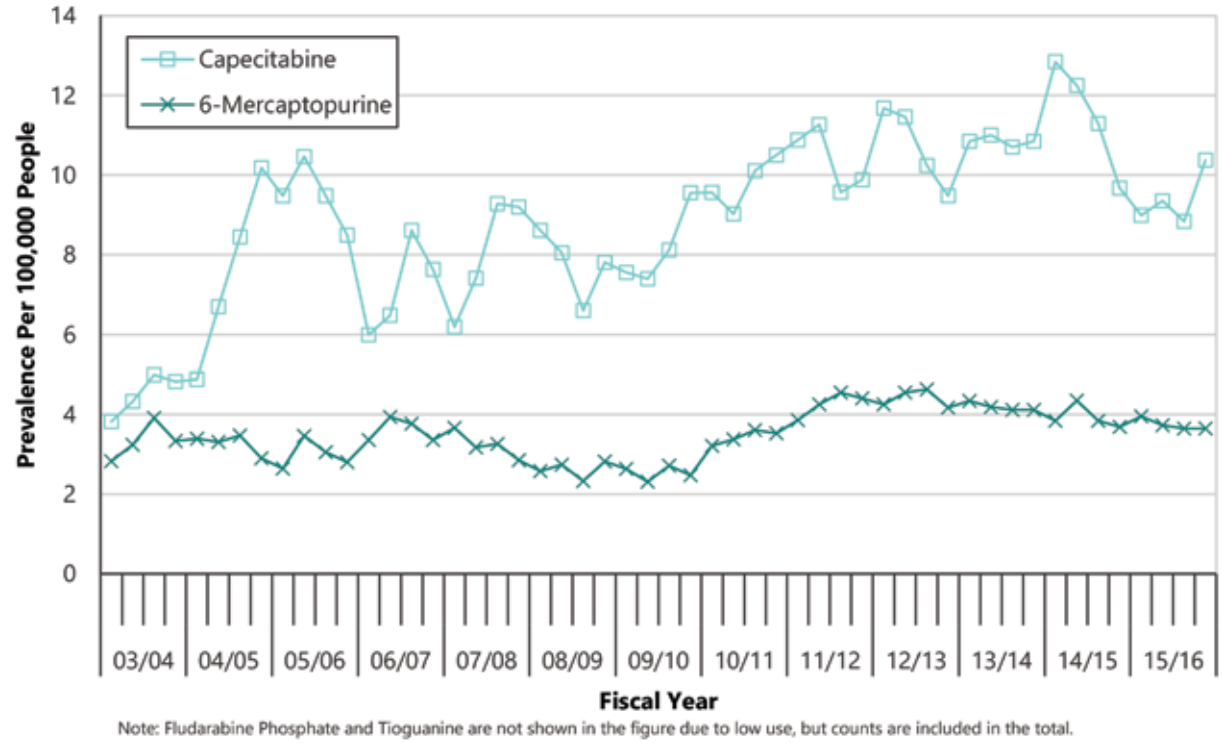
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Busulfan, Mitotane, Lomustine, and Procarbazine HCL are not shown in the figure due to low use, but counts are included in the total.

Figure 4.8: Quarterly Prevalence of Users of Antimetabolites (Traditional Oral Anticancer Agents) Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

Per 100,000 people

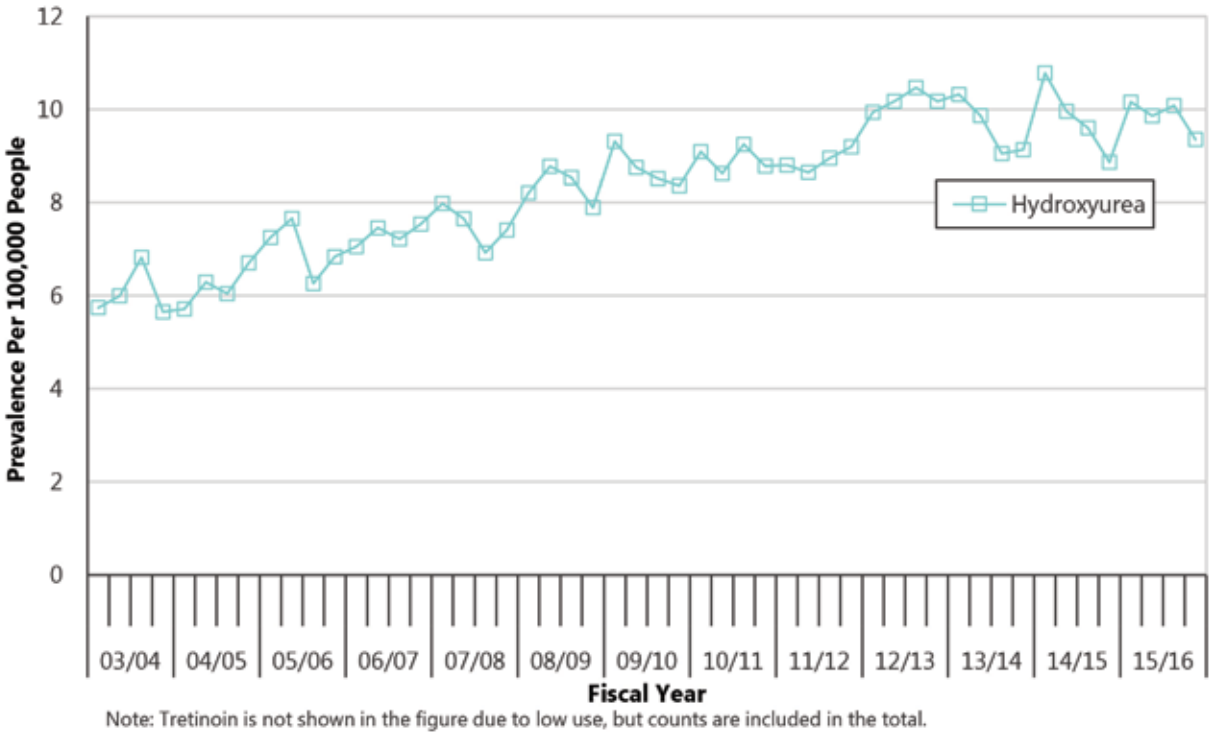


Note: Fludarabine Phosphate and Tioguanine are not shown in the figure due to low use, but counts are included in the total.

The prevalence of people who used hydroxyurea, an older traditional OAA, increased from 5.7 to 9.4 users per 100,000 Manitobans over the course of the study (Figure 4.9). There was quarterly variability in the prevalence of users before and after the introduction of the HCDP in 2012. Although drugs like hydroxyurea are sometimes prescribed for non-cancer indications, such as essential thrombocythemia and sickle cell anemia, here we determined the prevalence of users only within the population of Manitobans with a cancer diagnosis.

Figure 4.9: Quarterly Prevalence of Users of Other Older Anticancer Agents (Traditional Oral Anticancer Agents) Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

Per 100,000 people



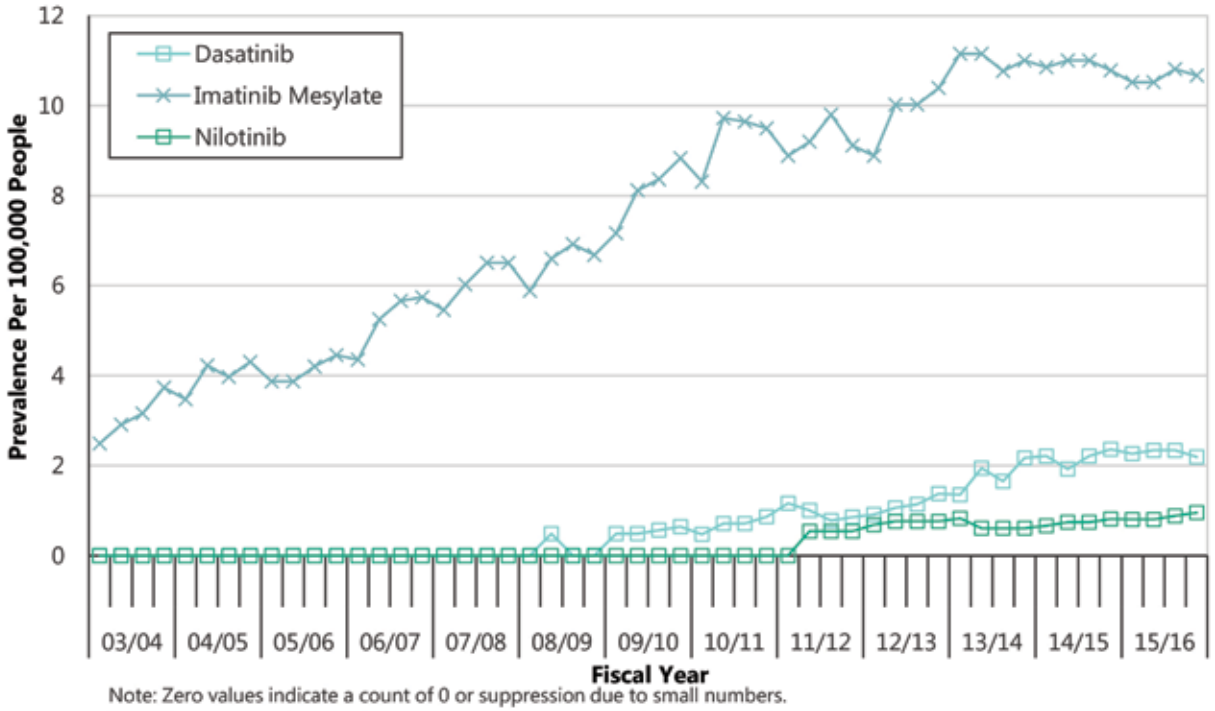
Note: Tretinoin is not shown in the figure due to low use, but counts are included in the total.

Targeted OAAs

Nearly all users of protein kinase inhibitors were diagnosed with cancer. The most commonly used protein kinase inhibitor was imatinib; the prevalence of people using this drug increased from 2.5 to 10.7 users per 100,000 people over the study period (Figure 4.10). The generic form of imatinib was launched in Canada in 2013, at which time the prevalence of imatinib users began to plateau, corresponding with increased use of other protein kinase inhibitors (particularly dasatanib) for treatment of haematological malignancies.

Figure 4.10: Quarterly Prevalence of Users of Protein Kinase Inhibitors for Haematological Malignancies (Targeted Oral Anticancer Agents) Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

Per 100,000 people

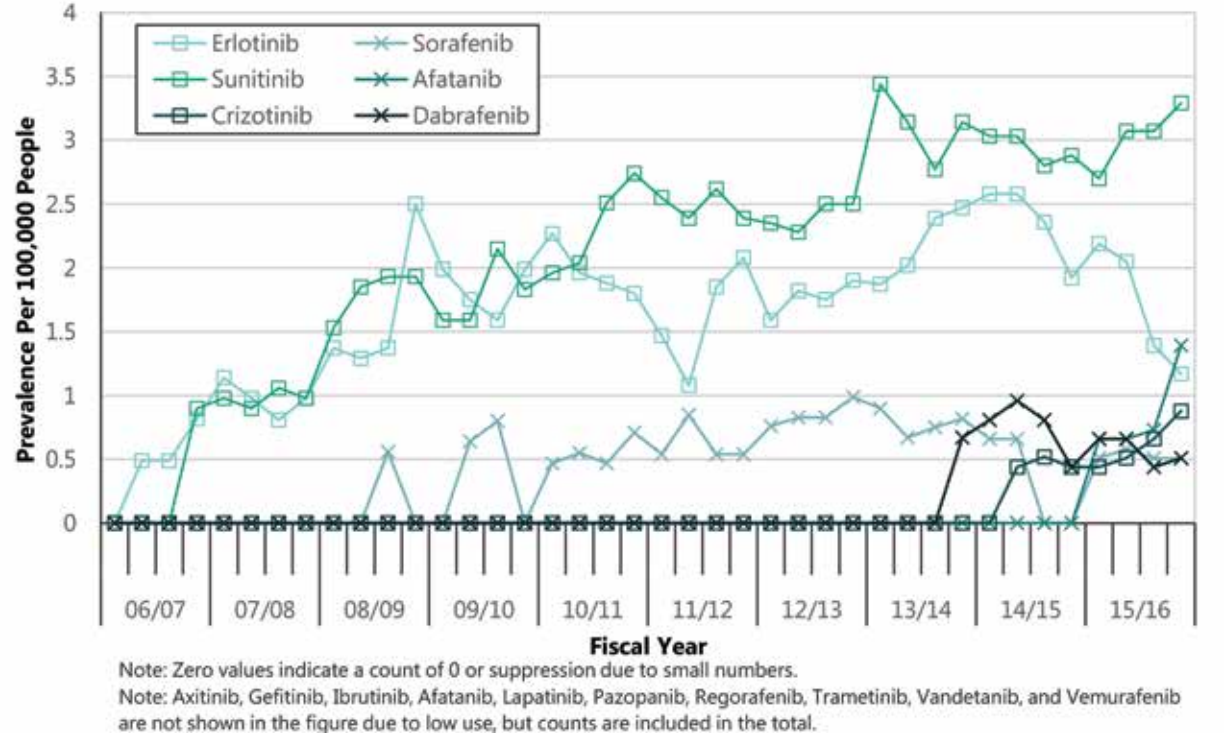


Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Bosutinib and Ruxolitinib are not shown in the figure due to low use, but counts are included in the total.

The most common protein kinase inhibitor used for solid tumours (as opposed to haematological malignancies) was sunitinib; the prevalence of people who used sunitinib increased from 0.90 to 3.3 users per 100,000 people over the study period (Figure 4.11).

Figure 4.11: Quarterly Prevalence of Users of Protein Kinase Inhibitors for Solid Tumours (Targeted Oral Anticancer Agents) Among Manitobans with a Cancer Diagnosis, 2006/07-2015/16

Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Axitinib, Gefitinib, Ibrutinib, Afatanib, Lapatinib, Pazopanib, Regorafenib, Trametinib, Vandetanib, and Vemurafenib are not shown in the figure due to low use, but counts are included in the total.

Hormonal OAAs

Bicalutamide was the most commonly used hormonal OAA for prostate cancer; the prevalence of bicalutamide users increased from 24.0 to 26.4 users per 100,000 people over the course of the study (Figure 4.12). Bicalutamide is shown on its own to be able to clearly observe the changes in the much lower rates of use of other hormonal OAAs (Figure 4.13). The prevalence of abiraterone users increased from 0.5 users per 100,000 people in 2012 (when it first became available) to 5.3 users per 100,000 people by to the fourth quarter of 2015/16 (Figure 4.13). Abiraterone rapidly replaced nilutamide, flutamide and bicalutamide for many Manitoba patients using hormonal OAAs for prostate cancer.

Figure 4.12: Quarterly Prevalence of Users of Bicalutamide (Hormonal Oral Anticancer Agent) Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

Per 100,000 people

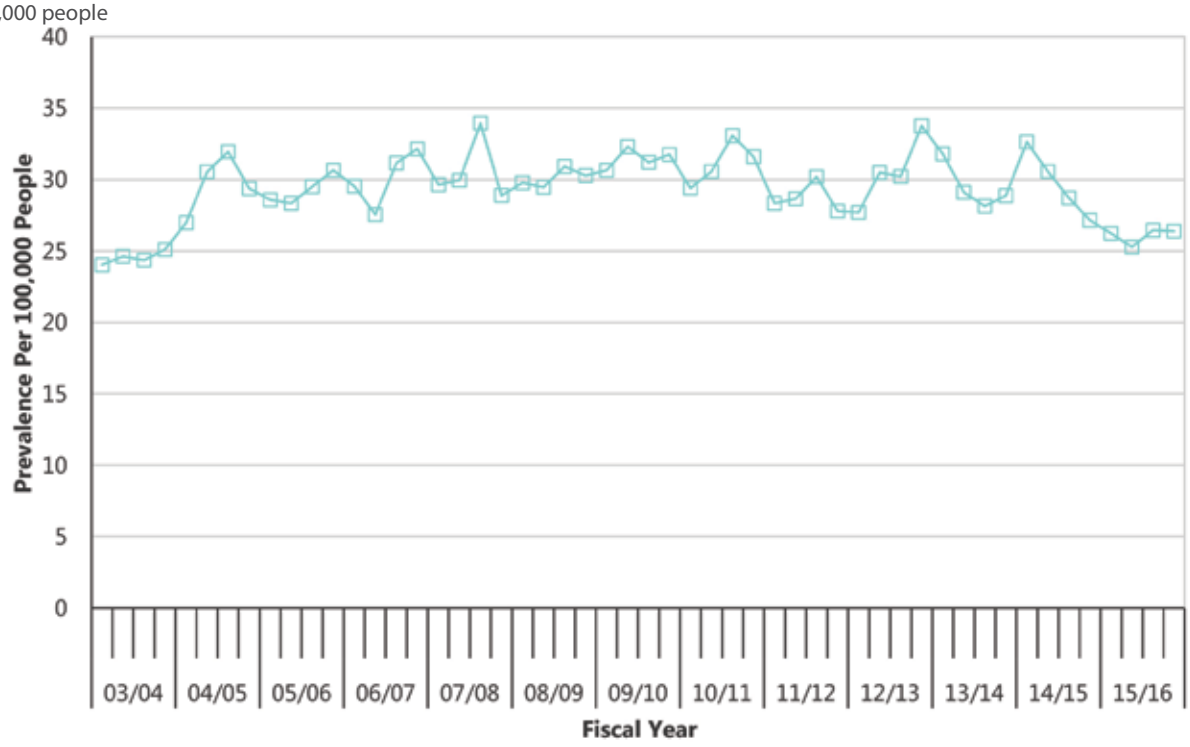
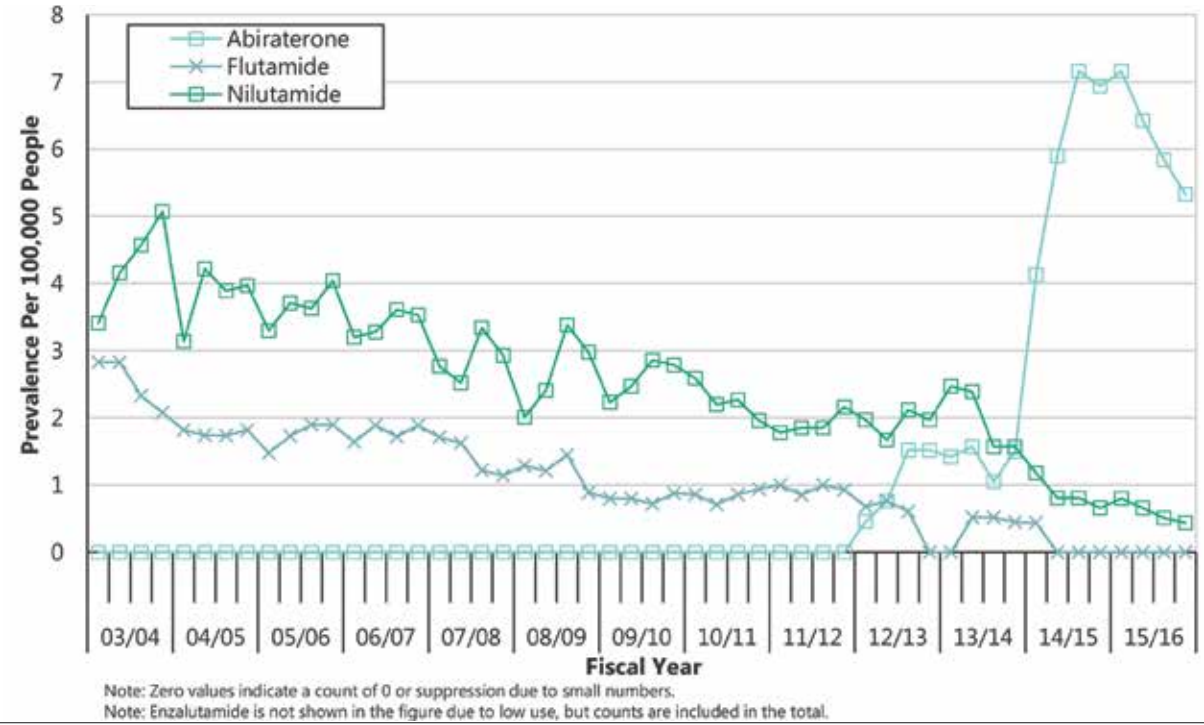


Figure 4.13: Quarterly Prevalence of Users of Hormonal Oral Anticancer Agents for Prostate Cancer Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

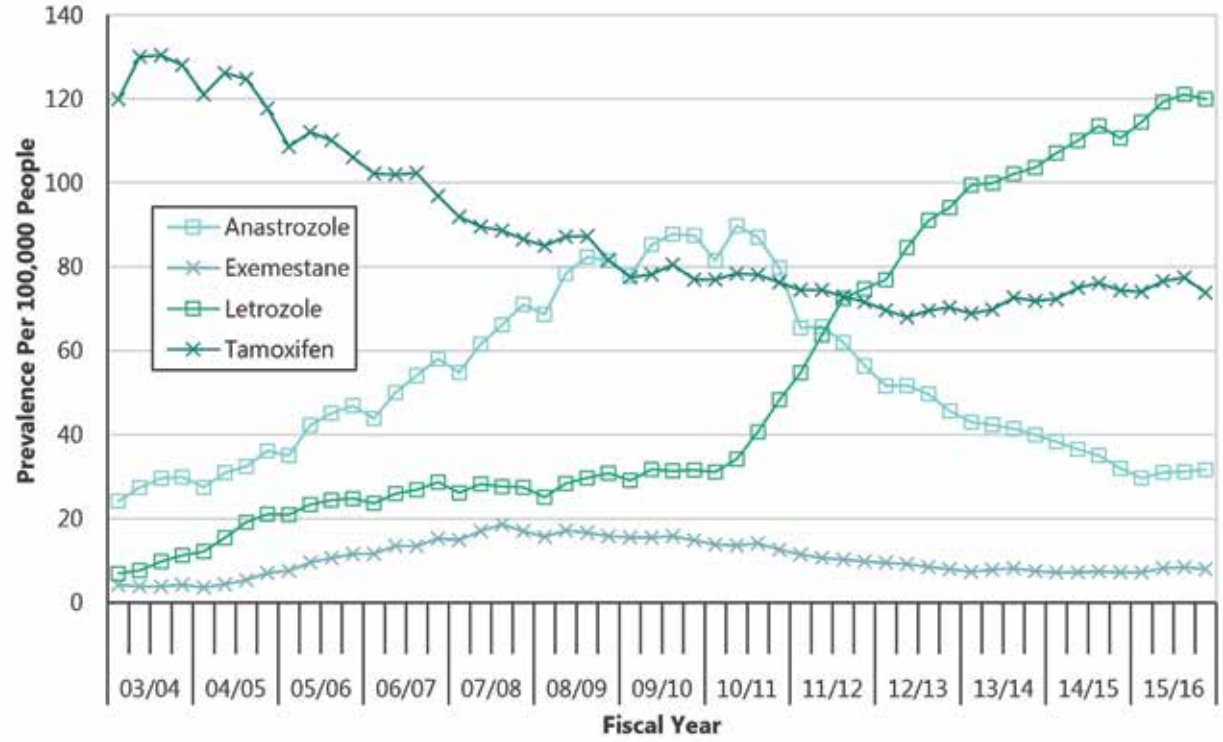
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Enzalutamide is not shown in the figure due to low use, but counts are included in the total.

There was a dramatic shift in the use of breast cancer therapies over the study period. The prevalence of people who used tamoxifen decreased from 119.9 to 73.8 users per 100,000 people, while the prevalence of people who used letrozole increased from 7.0 to 120.0 users per 100,000 people (Figure 4.14).

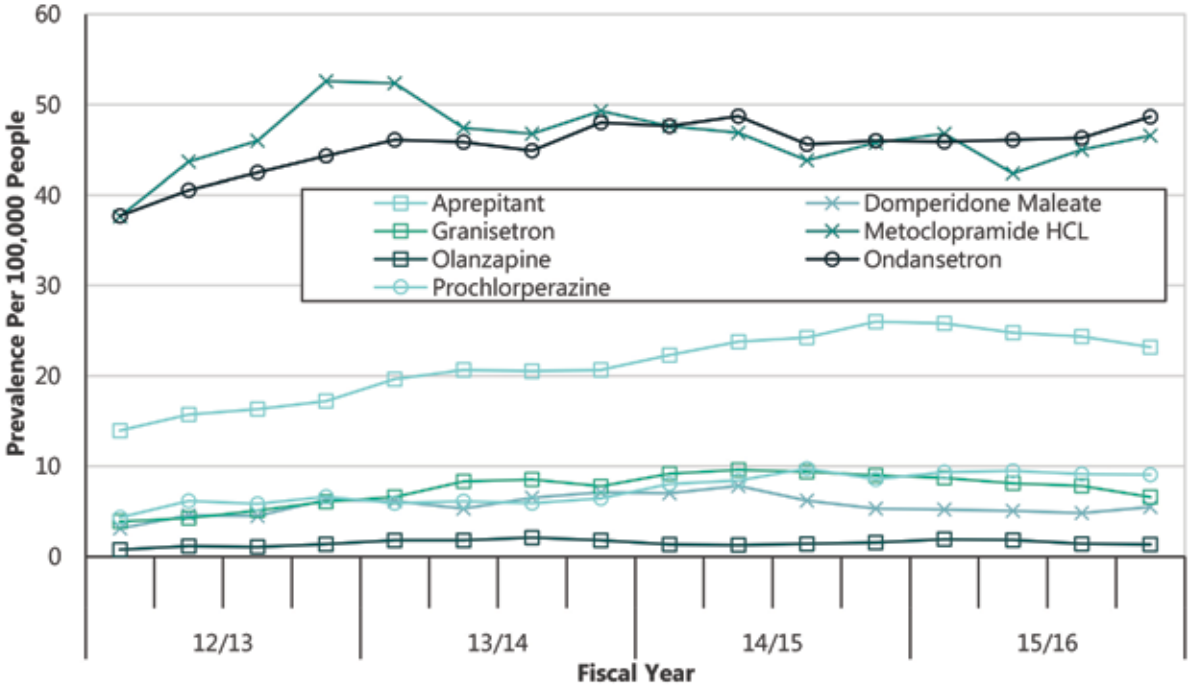
Figure 4.14: Quarterly Prevalence of Users of Hormonal Oral Anticancer Agents for Breast Cancer Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people



Non-OAA Medications Covered by the HCDP

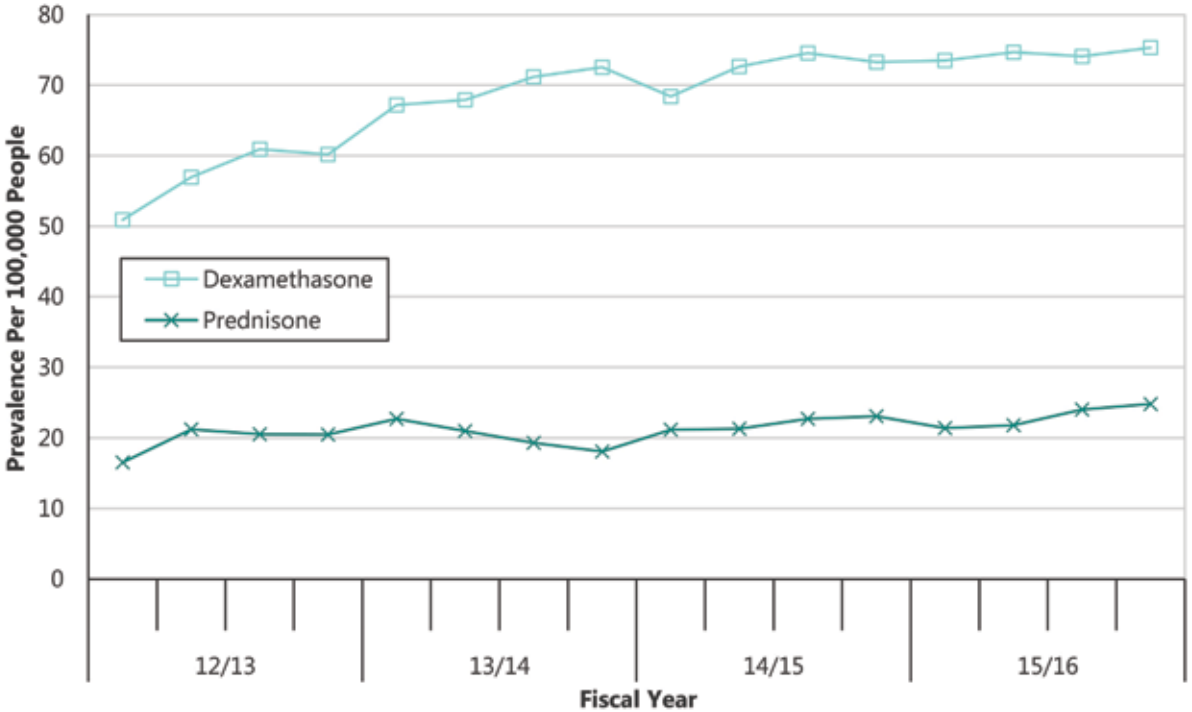
The prevalence of users of non-OAA medications covered by the HCDP are presented in Figures 4.15 - 4.18. The most common anti-nauseants used included metoclopramide and ondansetron (Figure 4.15). The steroid dexamethasone was frequently prescribed as well (Figure 4.16). Steroids are used as active treatment for some central nervous system tumours and myelomas; however, the majority of steroid use shown here was likely for supportive use in cancer patients, for example, for nausea/vomiting, bowel obstruction, pain or palliative care.

Figure 4.15: Quarterly Prevalence of Users of Anti-Nauseant Medications Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16
Per 100,000 people



Note: Nabilone is not shown in this figure due to limited use, but counts are included in the total.
Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

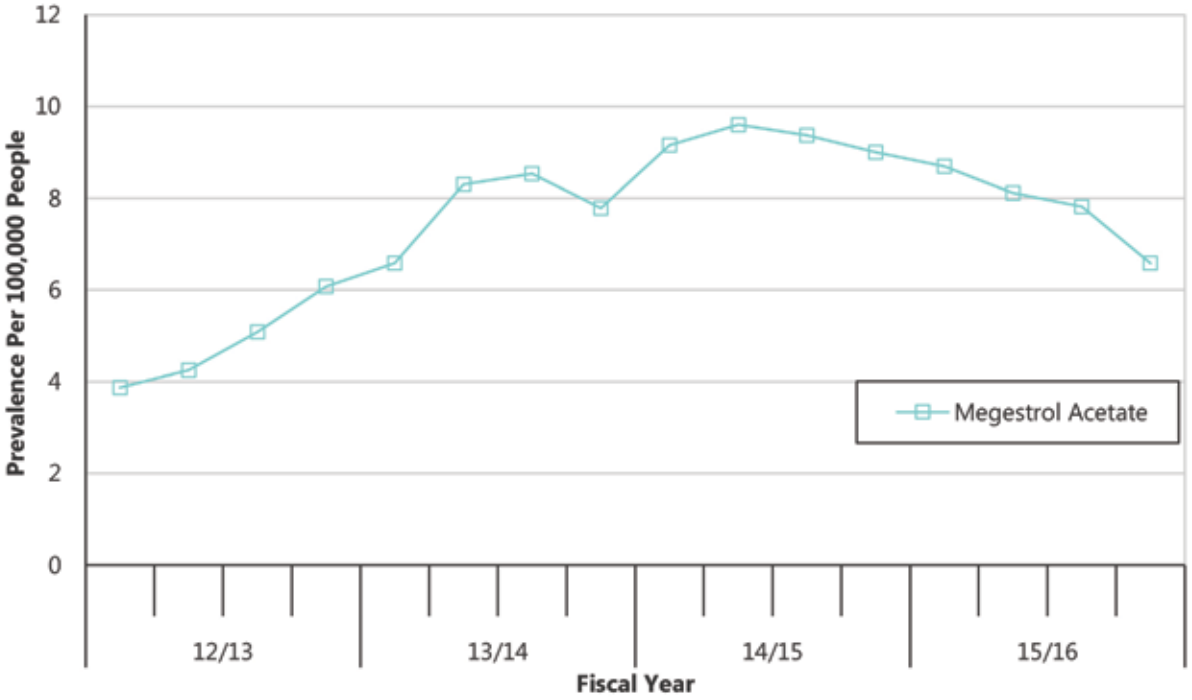
Figure 4.16: Quarterly Prevalence of Users of Steroids Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16
Per 100,000 people



Note: Hydrocortisone is not shown in this figure due to limited use, but counts are included in the total.
Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

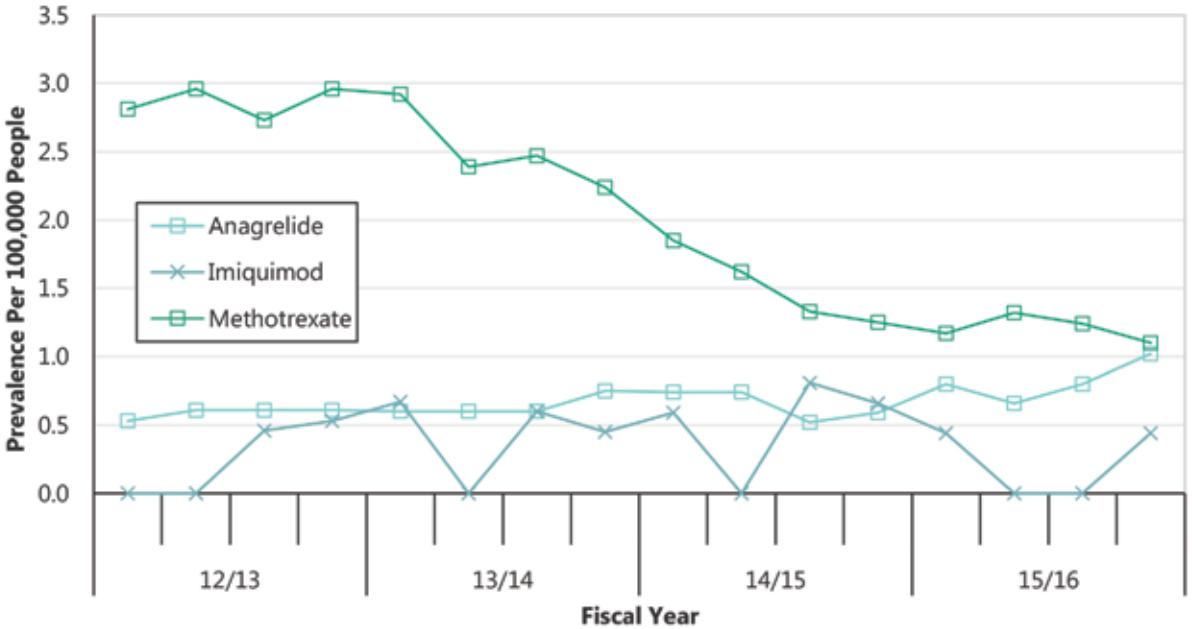
The use of megestrol (Figure 4.17) and methotrexate (Figure 4.18) have declined in recent years.

Figure 4.17: Quarterly Prevalence of Users of Supportive Care Medications Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16
Per 100,000 people



Note: Estradiol is are not shown in this figure due to limited use, but counts are included in the total.
Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

Figure 4.18: Quarterly Prevalence of Users of Medications for Disease Treatment Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Acitretin, Celecoxib, Isotretinoin and Ketoconazole are not shown in this figure due to limited use, but counts are included in the total.
Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

OAA Prescription Rates Among Manitobans with a Cancer Diagnosis

The impact of the HCDP on the number of OAA prescriptions was evaluated using a generalized linear model. When compared to the time period before the introduction of the HCDP, the difference between prescription rates from the highest quarter of the year to the lowest quarter of the year was significantly greater than after the introduction of the HCDP (Relative Rate=1.16 with upper and lower bounds 1.14-1.18, standard error 0.01, chi-squared 251.81, p=<0.0001). This suggests that the timing of OAA prescription among Manitobans with a cancer diagnosis changed after the HCDP was introduced. Under the Pharmacare plan (pre-2012), Manitobans filled prescriptions early in the year to delay having to pay a deductible. Once the HCDP was implemented (April 1, 2012 onwards), patients no longer had to pay a deductible and there was no particular pattern to when they filled their prescriptions. The impact the launch of the HCDP had on the prevalence of OAA users (Figure 4.19) was more pronounced than on the rate of OAA prescriptions (Figure 4.20 and 4.21). This suggests that some prescriptions that were not part of the HCDP (for example, prescriptions for hormonal therapies that were prescribed by family physicians as continuation of therapy) may have affected this analysis. We were unable to assess the impact of the policy on medication wastage, adherence or patient outcomes.

Figure 4.19: Quarterly Prevalence of Oral Anticancer Agent Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people

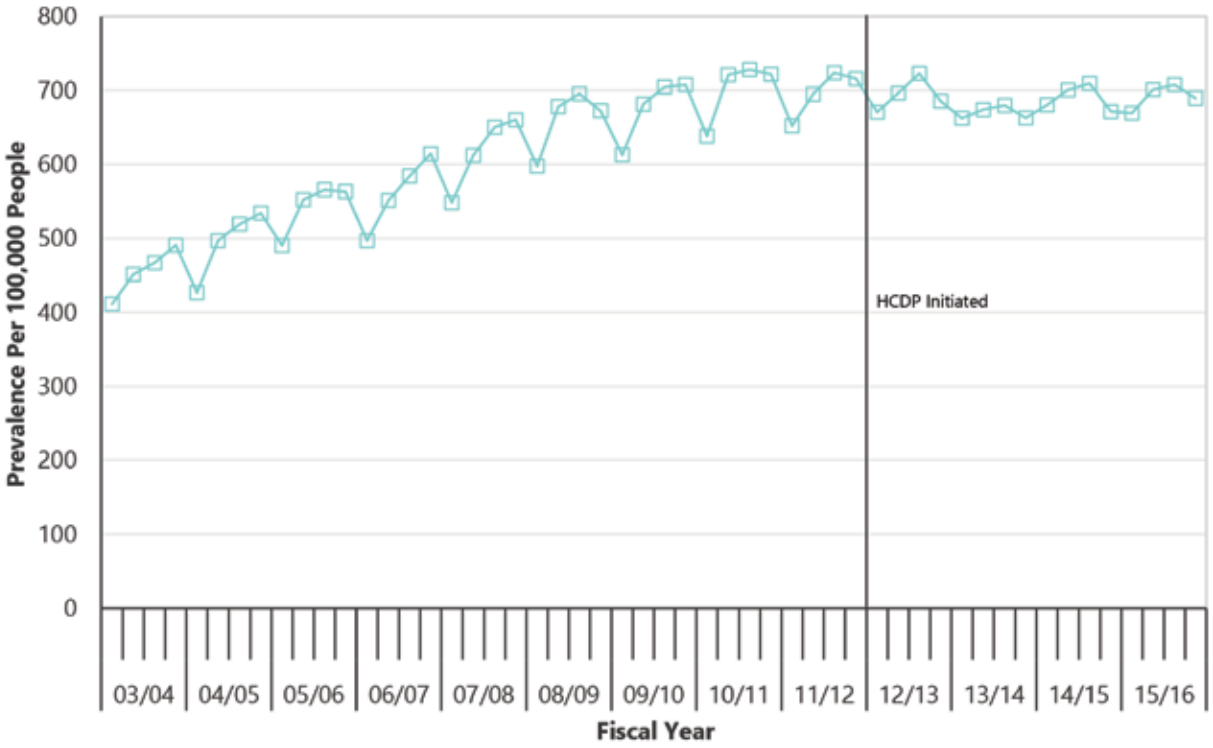


Figure 4.20: Quarterly Rate of Traditional and Targeted Oral Anticancer Agent Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people

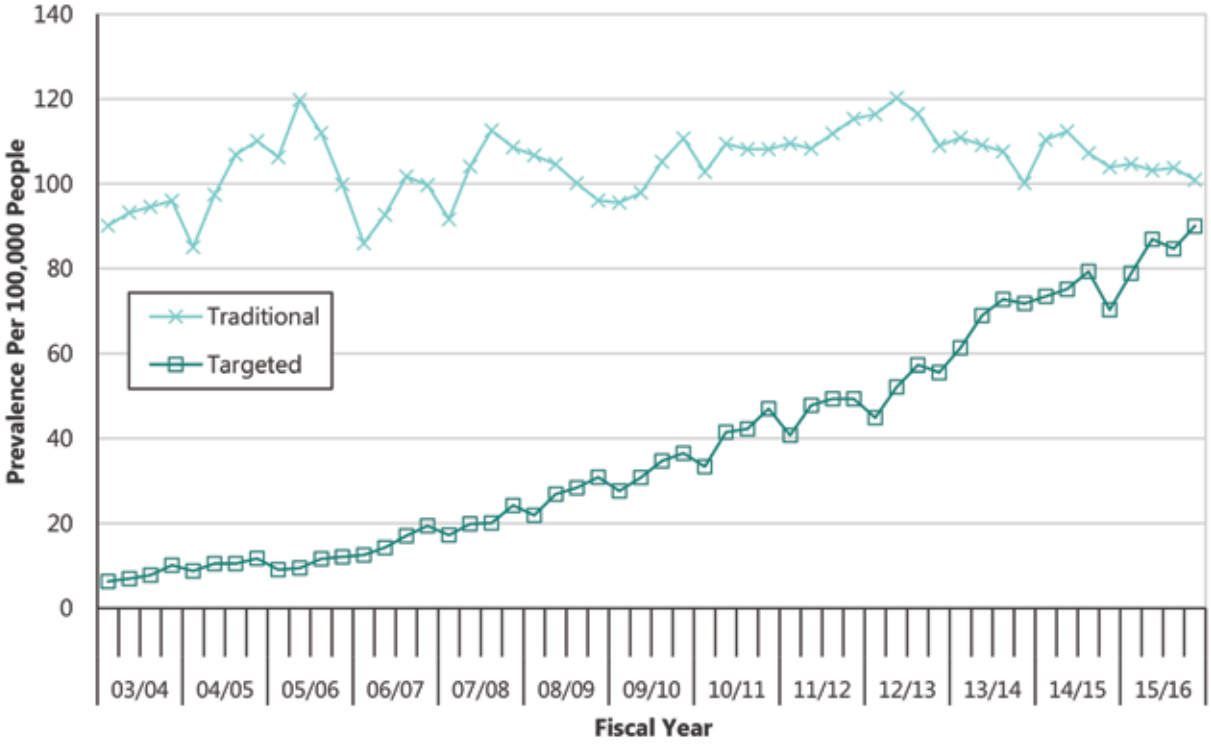
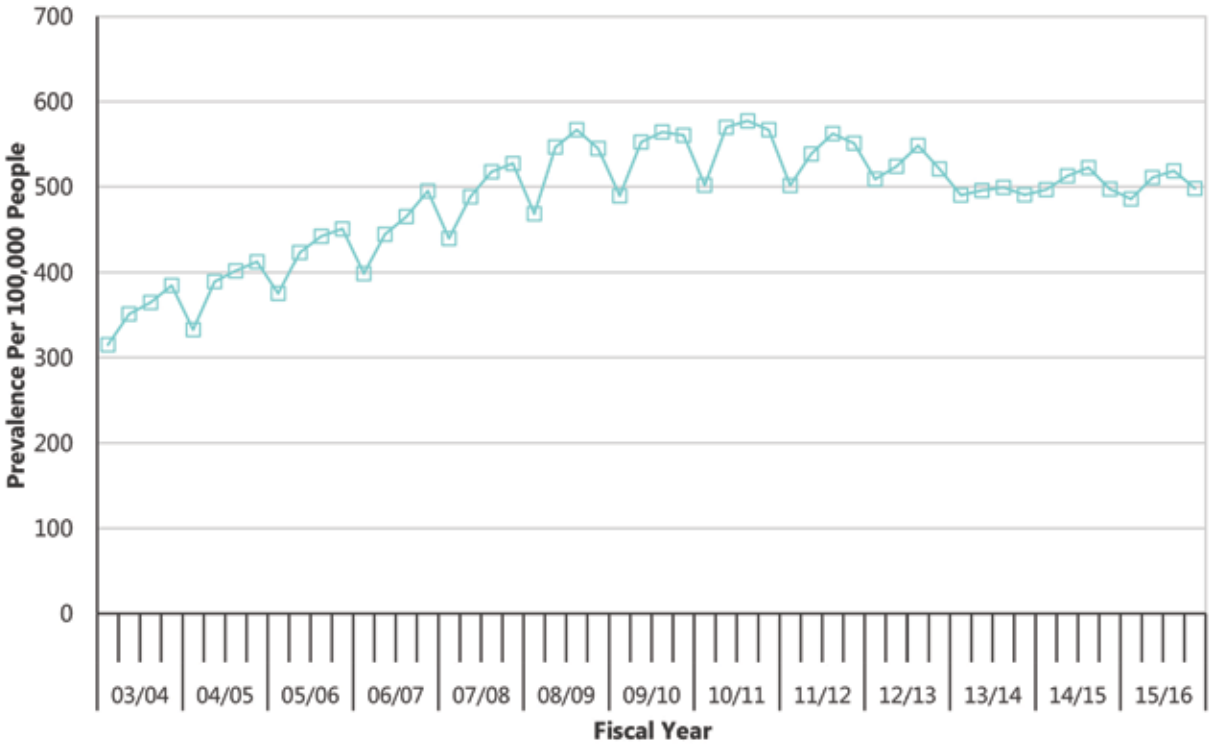


Figure 4.21: Quarterly Rate of Hormonal Oral Anticancer Agent Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people



Chapter 5:
Cancer Diagnosis Patterns Among OAA Users

Percentage of OAA Users with Specific Cancer Diagnoses

For this analysis, the population was OAA users with a cancer diagnosis. We used 3-digit codes from physician visits (ICD-9-CM) or hospitalizations (ICD-10-CA) up to one year prior to the first OAA prescription in the study period to describe the cancer types with which OAA users were diagnosed. We compared 2004/05 (or the first year that data was available) to 2014/15.

The percentage of OAA users with a particular cancer diagnosis ICD code varied by medication. For medications with many indications, such as the alkylating agent cyclophosphamide, 26.1% of cyclophosphamide users in 2004/05 were diagnosed with multiple myeloma, and this increased to 45.7% in 2014/15. Other medications had narrower indications, such as bicalutamide (a hormonal medication for prostate cancer). In 2004/05, 89.5% of bicalutamide users were diagnosed with prostate cancer, and this increased to 94.6% in 2014/15.

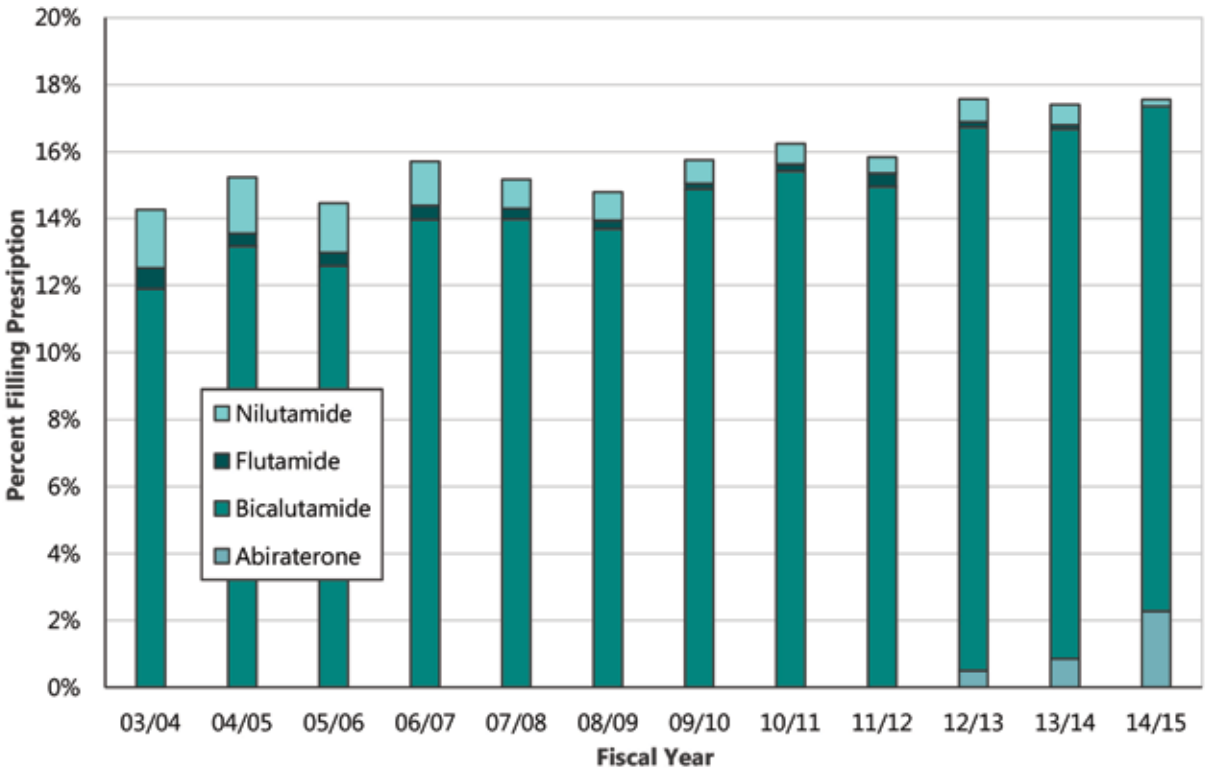
Further results of this analysis are presented in Appendix 3.

Medication Use by Cancer Type

For this analysis, the population was OAA users or users of non-OAA medications covered by the HCDP with a specific cancer diagnosis. We determined the percentage of this population who were diagnosed with several specific and common cancer types (prostate, breast and colorectal cancer) [39] and who filled prescriptions for OAA and non-OAA medications covered by the HCDP within the first year of that cancer diagnosis.

For prostate cancer, the most commonly used medication was bicalutamide (Figure 5.1). The majority of Manitobans diagnosed with prostate cancer did not receive any OAAs, as the primary treatment for this type of cancer is radiation or surgery.

Figure 5.1: Most Commonly Used Oral Anticancer Agents Among Manitobans Diagnosed with Prostate Cancer, 2003/04-2014/15



In contrast, Manitobans diagnosed with breast cancer filled prescriptions for many different types of OAAs and non-OAA medications covered by HCDP. Letrozole and tamoxifen were the most common, although numerous anti-nauseants were used as well (Figure 5.2 and 5.3).

Figure 5.2: Most Commonly Used Oral Anticancer Agents Among Manitobans Diagnosed with Breast Cancer, 2003/04-2014/15

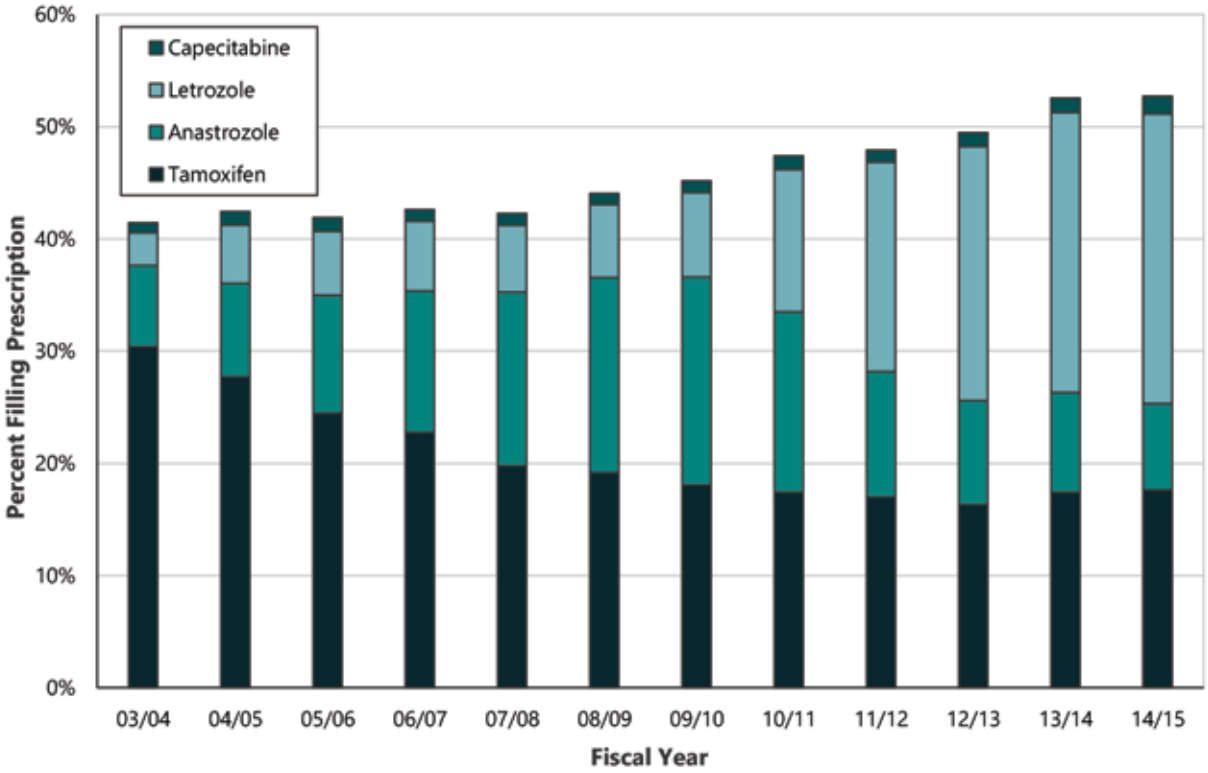
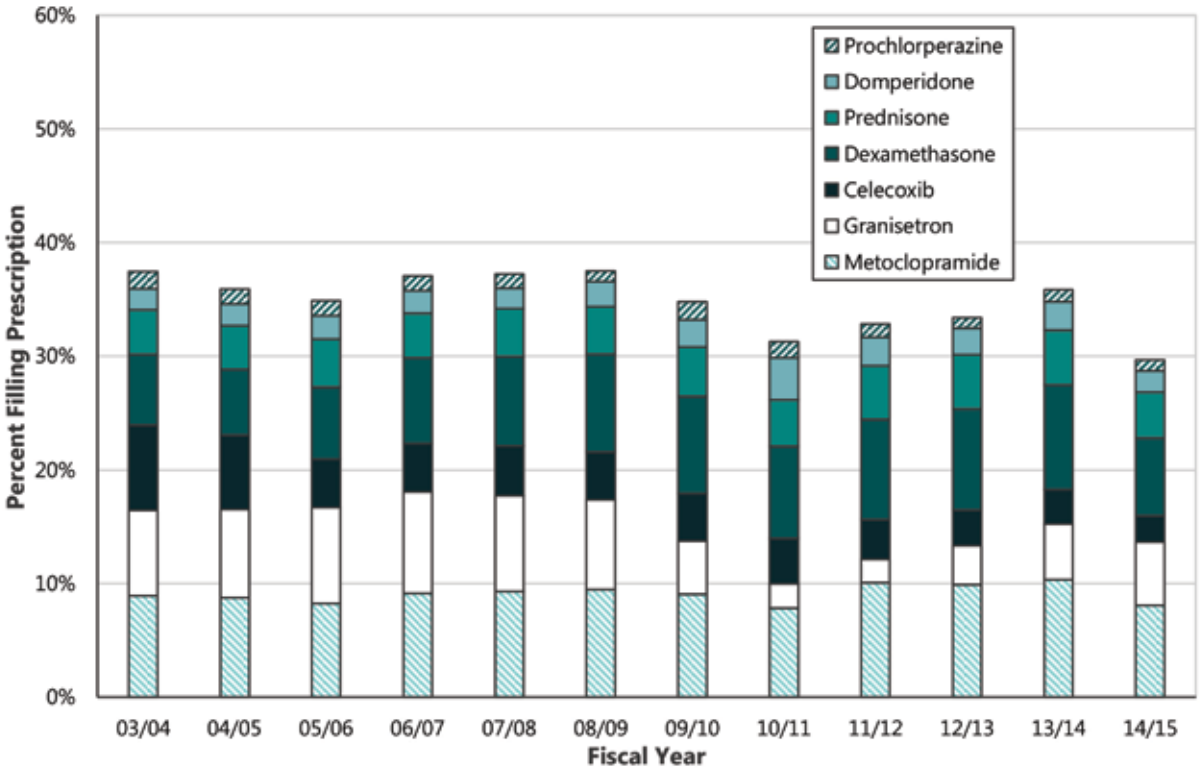
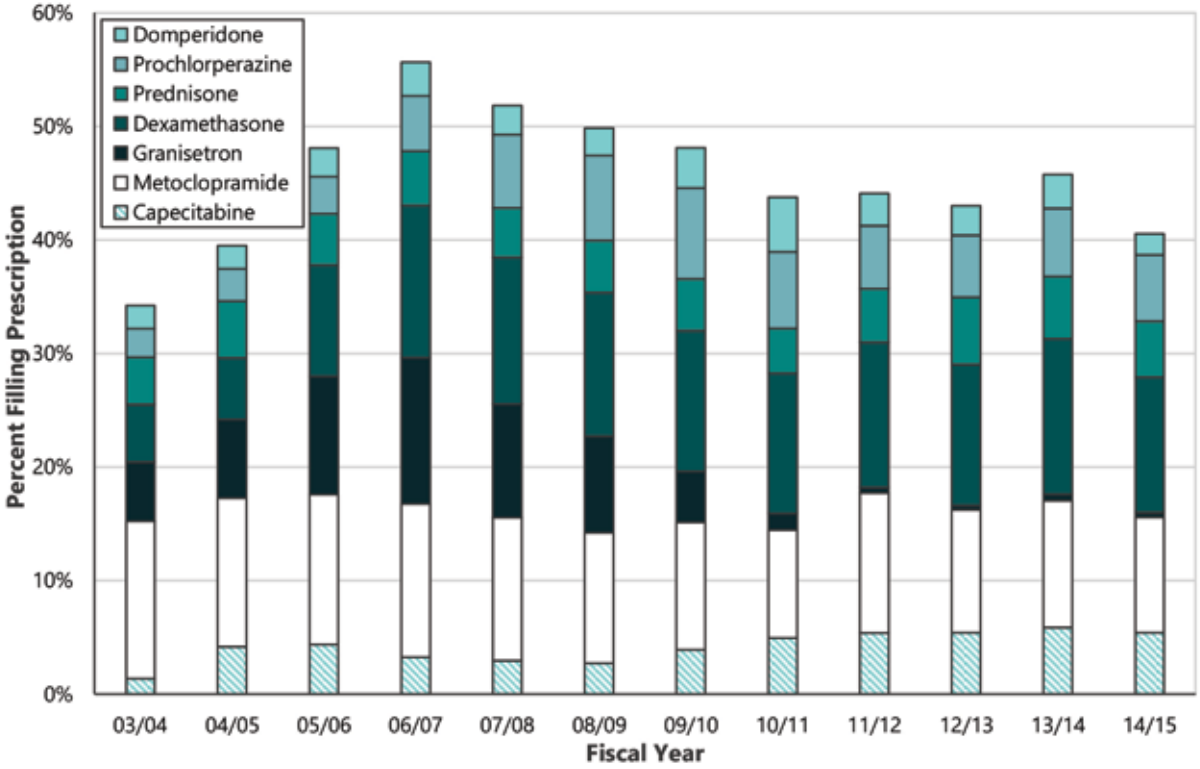


Figure 5.3: Most Commonly Used Non-Oral Anticancer Agent Medications Among Manitobans Diagnosed with Breast Cancer, 2003/04-2014/15



For Manitobans diagnosed with colorectal cancer, the most commonly prescribed non-OAA medications covered by HCDP were anti-nauseants such as metoclopramide and steroids such as dexamethasone or prednisone (Figure 5.4).

Figure 5.4: Most Commonly Used Non-Oral Anticancer Agent Medications Among Manitobans Diagnosed with Colorectal Cancer, 2003/04-2014/15



Chapter 6:
Pharmacy and Prescription Fill Characteristics

For this analysis, the population was OAA users with a cancer diagnosis. To examine fill patterns (at de-identified pharmacies), we first identified cancer patients' usual pharmacy for the year prior to their first OAA prescription. We determined the distance from each patients' residence to their usual pharmacy and compared fill patterns for the three types of OAAs (traditional, targeted and hormonal).

Pharmacy Characteristics

For most patients (38.6%), the usual pharmacy prior to filling an OAA prescription was a Food store/Mass Merchandiser, followed by 33.1% whose usual pharmacy was an Independent pharmacy (Table 6.1). After patients received their first OAA prescription, this pattern shifted slightly, with more OAA prescriptions being filled at Banner/Franchise/Chain pharmacies ($p<0.001$ for both the first and subsequent OAA prescriptions when compared to usual pharmacy). The pattern shifted for both traditional and targeted OAAs; a greater number of first and subsequent targeted OAAs were filled at Banner/Franchise/Chain pharmacies than at the usual pharmacy ($p<0.001$ for all comparisons to usual pharmacy).

A very small minority (1.2%) of cancer patients had a usual pharmacy with close proximity to a cancer centre (Table 6.1). This percentage increased most dramatically for patients using traditional OAAs (approximately 12%; $p<0.001$ for first and subsequent prescriptions when compared to usual pharmacy) and targeted OAAs (nearly 19%; $p<0.001$ for first and subsequent prescriptions when compared to usual pharmacy) (Table 6.2).

Over half of cancer patients (53.4%) had a usual pharmacy that was a pharmacy offering a rewards program (Table 6.1). For first prescriptions for traditional and targeted OAAs, the percentage filled at a rewards pharmacy increased slightly to approximately 60% ($p<0.001$ for first and subsequent prescriptions for traditional and targeted therapies when compared to usual pharmacy) (Table 6.2).

The median distance to a patient's usual pharmacy was 1.82 km. This increased very slightly to 2.08 km for the first OAA and 1.96 km for subsequent OAA prescriptions (Table 6.1). The median distance from home to the pharmacy for the first dispensation of traditional and targeted OAAs was further than for hormonal OAAs, likely due to the nature of prescribing these medications. Traditional and targeted therapies would typically be prescribed by specialists as part of active treatment for cancer, whereas chronic hormonal therapies could generally be prescribed by family practitioners (Table 6.2).

Table 6.1: Overall Oral Anticancer Agent Pharmacy Fill Patterns, 2003/04-2014/15

	Number and Percent of Prescriptions Filled by Dispensation Occurrence		
	Any Drug from Usual Pharmacy*	All OAAs	
	All Filled Prescriptions	First	Subsequent
Pharmacy Type			
Banner/Franchise/Chain**	5,488 (28.29%)	**5,299 (32.50%)**	**3,371 (30.12%)**
Food Stores and Mass Merchandisers†	7,487 (38.59%)	**6,164 (37.80%)**	**4,274 (38.19%)**
Independent/Hospital‡	6,427 (33.13%)	**4,844 (29.71%)**	**3,546 (31.69%)**
Close to a Cancer Centre			
	227 (1.17%)	**913 (5.60%)**	**498 (4.45%)**
Rewards§			
	10,367 (53.43%)	**9,408 (57.69%)**	**6,221 (55.59%)**
Distance from Residence			
Mean (Standard Deviation)	13.73 (54.18)	23.8 (81.72)	15.66 (60.02)
Minimum	0.00	0.00	0.00
10th Percentile	0.00	0.00	0.00
25th Percentile	0.65	0.76	0.71
Median	1.82	2.08	1.96
75th Percentile	5.74	7.51	6.24
90th Percentile	24.95	47.20	27.93
Maximum	1,011.94	1,012.18	1,011.94

Bold indicates a significant difference from the usual pharmacy
* Pharmacy with the greatest number of prescriptions in the year prior to first OAA dispensation
** Pharmacies with a recognized name and a central head office
† Departments within a supermarket or mass merchandise outlet. Pharmacy managers are salaried employees of head office
‡ Independent pharmacies are not affiliated with a banner, franchise, or chain. Does not include some chain pharmacies that operate within a hospital
§ Rewards pharmacies offer some sort of inducement when filling prescriptions

Table 6.2: Oral Anticancer Agent Pharmacy Fill Patterns by Drug Group, 2003/04-2014/15

	Number and Percent of Prescriptions Filled by Drug Group and Dispensation Occurrence					
	Traditional		Targeted		Hormonal	
	First	Subsequent	First	Subsequent	First	Subsequent
Pharmacy type						
Banner/Franchise/ Chain**	**1,363 (36.86%)**	**897 (33.55%)**	**350 (41.37%)**	**219 (39.18%)**	**3,586 (30.49%)**	**2,255 (28.34%)**
Food Stores and Mass Merchandisers†	**1,235 (33.40%)**	**876 (32.76%)**	**244 (28.84%)**	**175 (31.31%)**	**4,685 (39.83%)**	**3,223 (40.50%)**
Independent/Hospital‡	**1,100 (29.75%)**	**901 (33.69%)**	**252 (29.79%)**	**165 (29.52%)**	**3,492 (29.69%)**	**2,480 (31.16%)**
Close to a cancer centre						
	493 (13.33%)	**314 (11.74%)**	**160 (18.91%)**	**103 (18.43%)**	**260 (2.21%)**	**81 (1.02%)**
Rewards§						
	2,267 (61.30%)	**1,530 (57.22%)**	**521 (61.58%)**	**350 (62.61%)**	**6,620 (56.28%)**	**4,341 (54.55%)**
Distance from Residence						
Mean (Standard Deviation)	30.09 (94.38)	22.24 (74.8)	29.57 (97.18)	31.43 (110.16)	21.41 (75.89)	12.34 (47.89)
Minimum	0.00	0.00	0.00	0.00	0.00	0.00
10th Percentile	0.10	0.00	0.32	0.32	0.00	0.00
25th Percentile	0.82	0.74	1.12	1.13	0.72	0.69
Median	2.40	2.14	3.32	2.99	1.97	1.85
75th Percentile	9.31	8.02	11.74	11.50	6.71	5.30
90th Percentile	69.86	46.23	73.59	61.20	40.58	22.69
Maximum	988.31	1,004.89	1,011.94	1,011.94	1,012.18	1,008.85

Bold indicates a significant difference from the usual pharmacy
* Pharmacy with the greatest number of prescriptions in the year prior to first OAA dispensation
** Pharmacies with a recognized name and a central head office
† Departments within a supermarket or mass merchandise outlet. Pharmacy managers are salaried employees of head office
‡ Independent pharmacies are not affiliated with a banner, franchise, or chain. Does not include some chain pharmacies that operate within a hospital
§ Rewards pharmacies offer some sort of inducement when filling prescriptions

Most patients filled their first OAA at their usual pharmacy. Where patients filled their first OAA varied by OAA medication group; a greater proportion of first prescriptions for traditional and targeted OAAs were filled at pharmacies that were not the usual pharmacy than hormonal OAAs (Table 6.3). A total of 36.8% of new users of traditional OAAs and 44.5% of new users of targeted OAAs filled their first OAA at a pharmacy that was not their usual pharmacy.

Table 6.3: Prescription Fill Patterns for Oral Anticancer Agents, 2003/04-2014/15

Drug Group and Prescription Fill	Pharmacy Pattern			
	Continue at Usual Pharmacy*	Change Pharmacy for OAA Only**	Change Pharmacy for All Medications†	Other‡
Traditional				
First	2,002 (63.2%)	468 (14.8%)	331 (10.4%)	368 (11.6%)
Subsequent	1,587 (67.3%)	252 (10.7%)	369 (15.6%)	150 (6.4%)
Targeted				
First	405 (55.5%)	144 (19.7%)	74 (10.1%)	107 (14.7%)
Subsequent	285 (56.9%)	97 (19.4%)	78 (15.6%)	41 (8.2%)
Hormonal				
First	7,438 (74.7%)	921 (9.3%)	727 (7.3%)	873 (8.8%)
Subsequent	5,372 (79.7%)	286 (4.2%)	854 (12.7%)	232 (3.4%)

* Usual pharmacy for OAA and other medications did not change in the first year after receipt of first OAA from the one year prior to first OAA
** Usual pharmacy changed for OAA only
† Usual pharmacy for OAA and other medications changed in the first year after receipt of first OAA from the one year prior to first OAA
‡ Other pattern not otherwise defined

Individuals who filled a first prescription for a traditional or targeted OAA were more likely to change pharmacies for both first and subsequent prescriptions than who filled a first prescription for a hormonal OAA (Table 6.4). Individuals filling prescriptions for traditional and targeted OAAs were more likely than those filling hormonal OAAs to change pharmacies for their OAA only in the first year filling that prescription than they were to change pharmacies for all medications. The demographics for individuals included in this analysis are included in Appendix 2. "Demographics for All Manitobans Included in the Prescription fill pattern analysis"

Table 6.4: Estimated Odds Ratios of Pharmacy Use Patterns, 2003/04-2014/15

Drug Group (Ref=Hormonal Therapy)	Prescription Use Pattern (Ref=Stay at Usual Pharmacy for All Medications)	First OAA Prescription	Subsequent OAA Prescription
Traditional			
	Change pharmacy for OAA only *	1.69 (1.47-1.94)	1.46 (1.28-1.67)
	Change pharmacy for all medications **	1.89 (1.67-2.13)	2.98 (2.50-3.57)
	Other †	1.57 (1.37-1.79)	2.19 (1.77-2.71)
Targeted			
	Change pharmacy for OAA only *	1.87 (1.44-2.42)	1.72 (1.33-2.23)
	Change pharmacy for all medications **	2.87 (2.35-3.52)	6.39 (4.93-8.29)
	Other †	2.25 (1.80-2.82)	3.33 (2.34-4.74)

* Usual pharmacy changed for OAA only
** Usual pharmacy for OAA and other medications changed in the first year after receipt of first OAA from the one year prior to first OAA
† Other pattern not otherwise defined

Prescription Fill Characteristics

The average number of prescriptions filled per year is presented in Table 6.5. The population for this analysis is OAA users with a cancer diagnosis. When examined by medication group, Manitobans filled more prescriptions annually for targeted and non-OAA therapies than for traditional and hormonal. Since a prescription can be for any number of days, we evaluated prescription-filling patterns according to the number of days supplied per prescription per year to more accurately reflect the duration of prescription by category. Prescriptions for hormonal medications were for the longest duration, followed by targeted, then traditional, and then prescriptions for non-OAA medications covered by the HCDP.

The context of the very different indications of these classes of medications should be taken into consideration when interpreting these findings. For example, active treatment for cancer (such as traditional and targeted therapies) is very often closely monitored, and these medications are generally only prescribed for a duration of one month. Hormonal therapies (such as for breast cancer) are generally used for a longer duration to prevent recurrence. Finally, non-OAA medications, such as anti-nauseants, are generally prescribed "as needed," for instance, in the days immediately after an intravenous chemotherapy treatment. This is evident from the relatively fewer days non-OAA medications are supplied per prescription and per user. Additionally, since the number of days supplied is entered by the pharmacist, and since patients take supportive medications, such as anti-nauseants, as needed, the days supplied listed on the prescription may not be reflective of the days supplied that the patient actually consumed the medication.

Table 6.5: Average Annual Number of Prescriptions Filled and Days Supplied for Manitobans with a Cancer Diagnosis, by Drug Group, 2003/04-2015/16

	Number of Prescriptions Filled Per User	Days Supplied Per User	Days Supplied Per Prescription Fill
All Oral Anticancer Agents			
Average (SD)	6.20 (5.94)	239.6 (140.4)	38.6 (27.5)
Median	5	270	30
Traditional			
Average (SD)	6.36 (6.39)	147.6 (126.8)	23.2 (21.0)
Median	4	107	14
Targeted			
Average (SD)	7.13 (5.38)	226.0 (155.6)	31.7 (14.0)
Median	6	220	30
Hormonal			
Average (SD)	5.97 (5.74)	254.0 (134.5)	42.5 (28.3)
Median	4	300	30
Non-Oral Anticancer Agents (HCDP only)			
Average (SD)	8.43 (7.48)	105.3 (123.2)	12.5 (16.2)
Median	7	56	5

When examined by medication type, antimetabolites and lenalidomide (traditional OAAs), as well as protein kinase inhibitors (targeted OAAs) have the highest number of prescriptions per year, while plant alkaloids (traditional OAAs) and medications for prostate cancer (hormonal agents) have the lowest (Table 6.6). When assessed by medication group, the prescriptions given for the longest duration were for hormonal therapies for breast cancer, and the shortest duration were for antimetabolites. There were insufficient prescriptions for plant alkaloids to make an accurate comparison.

Table 6.6: Average Annual Number of Prescriptions Filled and Days Supplied for Manitobans with a Cancer Diagnosis, by Drug Category, 2003/04-2015/16

	Number of Prescriptions Filled Per User	Days Supplied Per User	Days Supplied Per Prescription Fill
Traditional: Alkylating Agents			
Average (SD)	5.65 (6.01)	126.2 (113.7)	22.3 (22.0)
Median	4	90	21
Traditional: Antimetabolites			
Average (SD)	6.93 (5.84)	125.6 (111.1)	18.1 (12.1)
Median	5	84	14
Traditional: Plant Alkaloids			
Average (SD)	2.28 (1.72)	38.5 (42.9)	16.9 (15.8)
Median	2	21	14
Traditional: Other Older Anticancer Agents			
Average (SD)	6.23 (7.15)	227.7 (141.7)	36.5 (27.8)
Median	4	242	30
Traditional: Lenalidomide			
Average (SD)	7.39 (4.93)	208.2 (164.2)	28.2 (10.5)
Median	7	175	28
Targeted: Protein Kinase Inhibitors			
Average (SD)	7.05 (5.44)	228.3 (153.2)	32.4 (14.5)
Median	6	227	30
Targeted: Other Newer Anticancer Agents			
Average (SD)	5.20 (5.44)	148.9 (165.2)	28.6 (6.8)
Median	3	90	30
Hormonal: Hormone Therapy for Breast Cancer			
Average (SD)	6.53 (5.82)	288.0 (116.4)	44.1 (29.2)
Median	5	330	30
Hormonal: Hormone Therapy for Prostate Cancer			
Average (SD)	3.97 (4.98)	131.0 (123.3)	33.0 (20.2)
Median	2	77	30

Chapter 7:
Costs of OAA Prescriptions

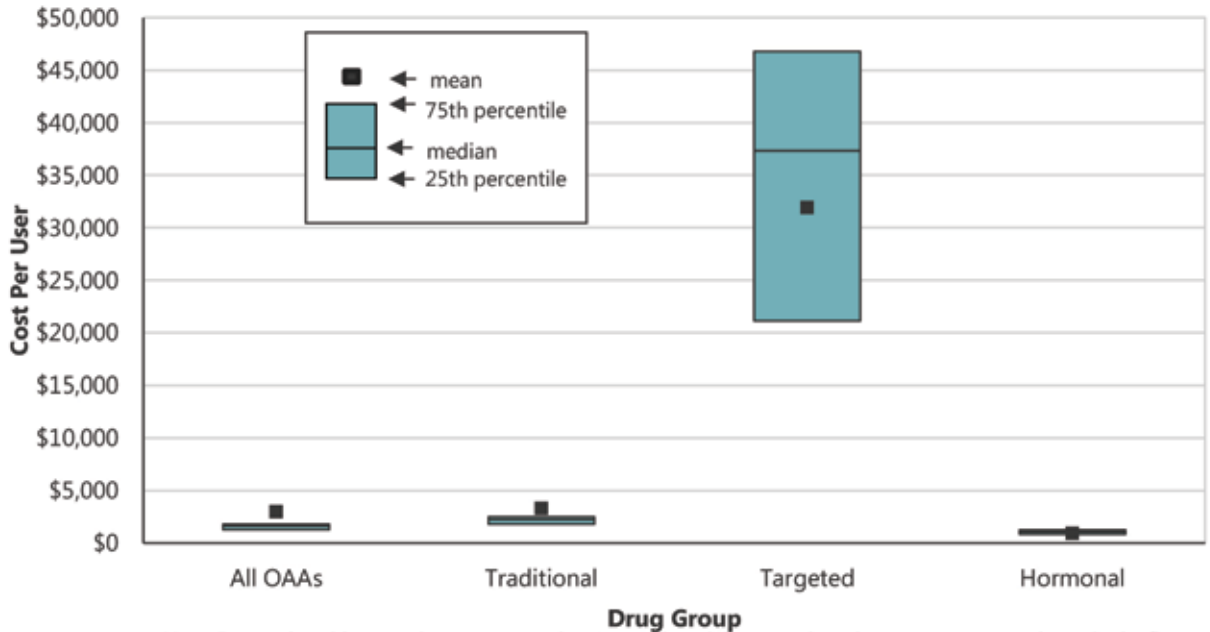
For this analysis the population was OAA users with a cancer diagnosis. We determined annual total prescription spending for all payers by each medication group for OAAs (traditional, targeted, and hormonal). We also describe total ingredient cost, annual professional dispensing fee, annual cost per prescription (total cost, ingredient cost and professional fee), and annual total prescription cost per user per day (sum of total cost divided by sum of total days supplied in a year). All costs were adjusted for inflation using the consumer price index and presented in 2015 Canadian dollars [50]. This analysis was performed only for OAA users with a cancer diagnosis in the year of or the year prior to their first OAA prescription.

In 2015/16, there were 6,281 OAA users with a cancer diagnosis, almost 38,000 prescriptions, and the total cost exceeding $26 million dollars (Table 7.1). The total expenditures on this category of medications increased almost four-fold over the study period from nearly $7 million in 2003 to over $26 million in 2015. The overall cost per user for traditional and hormonal drugs was less than $5,000, while targeted drugs were more than $30,000 per user (Figure 7.1).

Table 7.1: Cost of Oral Anticancer Agents Used by Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal Year	Total Cost	Average Annual Cost	Number of Users	Number of Prescriptions
2003/04	$ 6,837,337.29	$ 1,651.13	4,141	21,895
2004/05	$ 8,498,974.35	$ 1,939.08	4,383	23,891
2005/06	$ 9,222,117.76	$ 2,075.65	4,443	26,355
2006/07	$ 9,588,355.77	$ 2,090.33	4,587	27,398
2007/08	$ 11,010,159.30	$ 2,297.61	4,792	30,368
2008/09	$ 13,066,054.03	$ 2,675.28	4,884	32,838
2009/10	$ 14,842,557.55	$ 2,902.91	5,113	34,007
2010/11	$ 16,811,833.48	$ 3,148.28	5,340	35,838
2011/12	$ 19,151,161.30	$ 3,536.03	5,416	36,099
2012/13	$ 20,996,830.06	$ 3,668.85	5,723	36,577
2013/14	$ 22,354,140.89	$ 3,836.96	5,826	35,818
2014/15	$ 24,109,216.49	$ 3,891.72	6,195	37,420
2015/16	$ 26,146,644.34	$ 4,162.82	6,281	37,878
2003/04 - 2015/16	$ 202,635,382.59	$ 3,018.82	22,393	416,382

Figure 7.1: Cost Per User Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars



Note: Due to the wide range in costs across drug types, the minimum and maximum costs are not shown in the figure.
All OAAs: $5.52 - $226,059.76
Traditional: $5.52 - $76,699.03
Targeted: $6.85 - $226,059.76
Hormonal: $5.65 - $78,200.78

When broken down by medication group, the number of users of traditional OAAs was similar over each of the study years, as were the mean cost per user per year and the number of prescriptions per year (Table 7.2). By contrast, the number of users and number of prescriptions of targeted OAAs increased more than ten-fold from the first year of the study to the last, due to an increase in the number of users and in availability of these medications (Table 7.3). Since the mean cost per user per year for targeted OAAs was approximately $30,000 over all study years, the total cost increased from almost $2 million in 2003/04 to almost $19 million in 2015/16 (Table 7.3).

Table 7.2: Cost of Traditional Oral Anticancer Agents Used by Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal Year	Total Cost	Average Annual Cost	Number of Users	Number of Prescriptions
2003/04	$ 2,582,540.07	$ 2,989.05	864	4,498
2004/05	$ 3,160,629.80	$ 3,727.16	848	4,829
2005/06	$ 3,281,217.59	$ 3,797.71	864	5,315
2006/07	$ 2,474,933.00	$ 3,160.83	783	4,635
2007/08	$ 2,601,345.63	$ 3,156.97	824	5,123
2008/09	$ 2,843,706.44	$ 3,776.50	753	5,064
2009/10	$ 2,980,275.35	$ 3,767.73	791	5,144
2010/11	$ 3,125,643.79	$ 3,721.00	840	5,467
2011/12	$ 3,103,754.69	$ 3,604.83	861	5,765
2012/13	$ 3,142,018.54	$ 3,498.91	898	6,091
2013/14	$ 2,545,909.00	$ 3,108.56	819	5,719
2014/15	$ 2,394,718.05	$ 2,690.69	890	5,880
2015/16	$ 1,723,570.91	$ 2,066.63	834	5,646
2003/04 - 2015/16	$ 35,960,262.86	$ 3,308.52	6,043	69,176

Table 7.3: Cost of Targeted Oral Anticancer Agents Used by Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

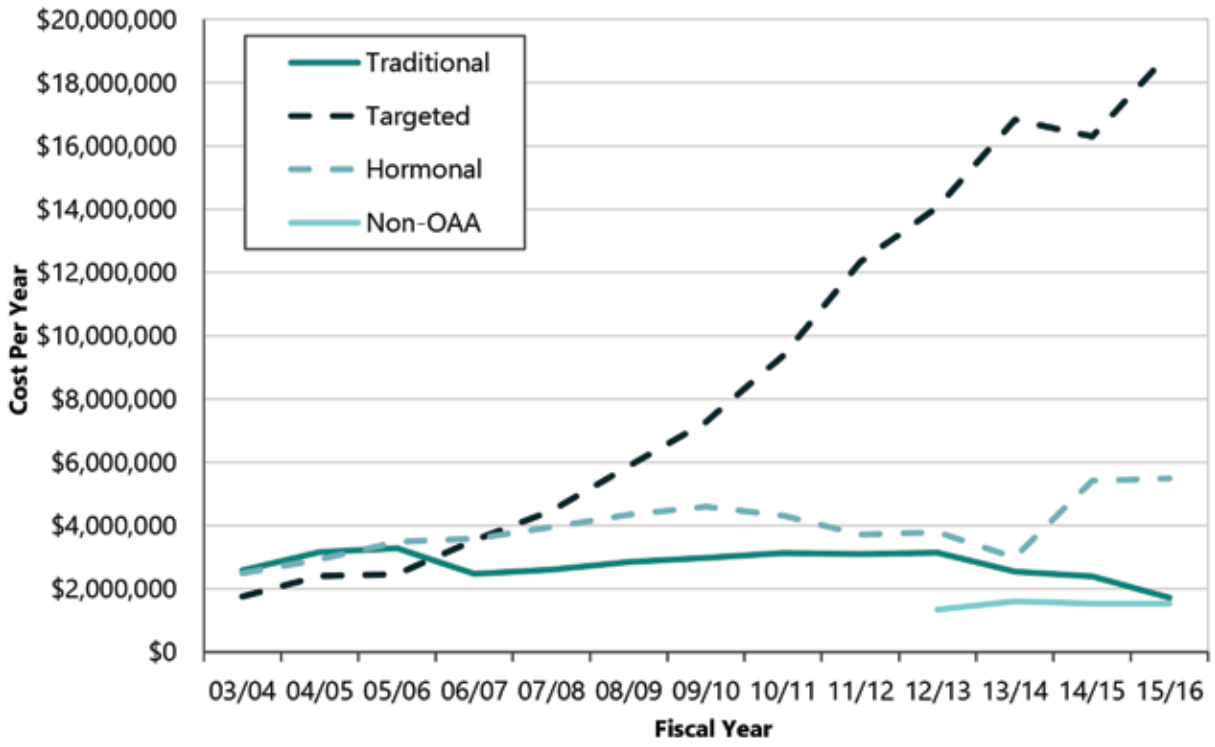
Fiscal Year	Total Cost	Average Annual Cost	Number of Users	Number of Prescriptions
2003/04	$ 1,759,957.02	$ 32,591.80	54	376
2004/05	$ 2,406,002.13	$ 38,806.49	62	502
2005/06	$ 2,462,788.03	$ 35,692.58	69	513
2006/07	$ 3,529,871.58	$ 33,617.82	105	772
2007/08	$ 4,462,021.20	$ 31,871.58	140	1,001
2008/09	$ 5,884,723.64	$ 28,428.62	207	1,343
2009/10	$ 7,272,033.68	$ 30,049.73	242	1,630
2010/11	$ 9,374,657.87	$ 31,671.14	296	2,095
2011/12	$ 12,334,885.67	$ 36,820.55	335	2,428
2012/13	$ 14,070,335.54	$ 33,106.67	425	2,767
2013/14	$ 16,820,947.64	$ 33,441.25	503	3,673
2014/15	$ 16,295,541.71	$ 29,203.48	558	4,041
2015/16	$ 18,929,741.17	$ 30,384.82	623	4,662
2003/04 - 2015/16	$ 115,603,506.87	$ 31,943.49	1,587	25,803

The number of users and prescriptions for hormonal OAAs increased steadily over the study period, and comprised the greatest proportion of users and prescriptions of all OAAs (Table 7.4). The cost per user increased over the study period, as did the total cost. However, as cost per user per year was relatively inexpensive compared to traditional and targeted therapies, the total expenditure on the thousands of prescriptions for hormonal OAAs to treat breast and prostate cancer was far less than for targeted OAAs for most of the study period (Figure 7.2).

Table 7.4: Cost of Hormonal Oral Anticancer Agents Used by Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal Year	Total Cost	Average Annual Cost	Number of Users	Number of Prescriptions
2003/04	$ 2,494,840.19	$ 754.64	3,306	17,021
2004/05	$ 2,932,342.42	$ 828.81	3,538	18,560
2005/06	$ 3,478,112.13	$ 969.37	3,588	20,527
2006/07	$ 3,583,551.19	$ 949.54	3,774	21,991
2007/08	$ 3,946,792.48	$ 1,007.86	3,916	24,244
2008/09	$ 4,337,623.95	$ 1,083.32	4,004	26,431
2009/10	$ 4,590,248.52	$ 1,101.84	4,166	27,233
2010/11	$ 4,311,531.83	$ 1,006.90	4,282	28,276
2011/12	$ 3,712,520.95	$ 859.78	4,318	27,906
2012/13	$ 3,784,475.97	$ 839.50	4,508	27,719
2013/14	$ 2,987,284.24	$ 646.32	4,622	26,426
2014/15	$ 5,418,956.72	$ 1,116.85	4,852	27,499
2015/16	$ 5,493,332.26	$ 1,116.53	4,920	27,570
2003/04 - 2015/16	$ 51,071,612.87	$ 949.39	16,094	321,403

Figure 7.2: Cost of Oral Anticancer Agent and Non-Oral Anticancer Agent Prescription Fills per Year Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars



Total Cost per User per Day of Therapy

As prescriptions can be for any duration of therapy, we calculated cost per user per day of therapy (Tables 7.5-7.8). Mean cost per user per day of therapy ranged from less than $6 per day for hormonal OAAs (Table 7.8), to $30-$50 per day for traditional OAAs with a decrease over time (Table 7.6), to greater than $130 for targeted OAAs with an increase over time (Table 7.7). Notably, the medication group of traditional OAAs includes lenalidomide and pomolidomide, which are immunomodulating agents for myeloma and are very costly (more than $300 per day) [35,53].

Table 7.5: Cost of Oral Anticancer Agents per User per Day of Therapy (All Oral Anticancer Agents), 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal Year	Total Cost	Average Annual Cost	Number of Users	Number of Prescriptions
2003/04	$ 62,485.92	$ 15.09	4,141	21,895
2004/05	$ 57,057.60	$ 13.02	4,383	23,891
2005/06	$ 62,089.74	$ 13.97	4,443	26,355
2006/07	$ 55,392.33	$ 12.08	4,587	27,398
2007/08	$ 63,169.89	$ 13.18	4,792	30,368
2008/09	$ 70,869.43	$ 14.51	4,884	32,837
2009/10	$ 84,054.14	$ 16.44	5,113	34,007
2010/11	$ 94,010.24	$ 17.60	5,340	35,838
2011/12	$ 104,254.09	$ 19.25	5,416	36,097
2012/13	$ 120,554.43	$ 21.06	5,723	36,577
2013/14	$ 119,193.73	$ 20.46	5,826	35,818
2014/15	$ 128,825.59	$ 20.80	6,195	37,420
2015/16	$ 136,723.39	$ 21.77	6,281	37,878
2003/04 - 2015/16	$ 1,158,680.52	$ 17.26	22,393	416,379

Table 7.6: Cost of Oral Anticancer Agents per User per Day of Therapy (Traditional Oral Anticancer Agents), 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal Year	Total Cost	Average Annual Cost	Number of Users	Number of Prescriptions
2003/04	$ 45,843.83	$ 53.06	864	4,498
2004/05	$ 36,893.17	$ 43.51	848	4,829
2005/06	$ 41,247.92	$ 47.74	864	5,315
2006/07	$ 28,328.43	$ 36.18	783	4,635
2007/08	$ 30,070.21	$ 36.49	824	5,123
2008/09	$ 27,159.22	$ 36.07	753	5,064
2009/10	$ 34,830.98	$ 44.03	791	5,144
2010/11	$ 30,881.88	$ 36.76	840	5,467
2011/12	$ 32,051.77	$ 37.23	861	5,765
2012/13	$ 33,267.30	$ 37.05	898	6,091
2013/14	$ 28,926.15	$ 35.32	819	5,719
2014/15	$ 26,237.38	$ 29.48	890	5,880
2015/16	$ 19,593.11	$ 23.49	834	5,646
2003/04 - 2015/16	$ 415,331.33	$ 38.21	6,043	69,176

Table 7.7: Cost of Oral Anticancer Agents per User per Day of Therapy (Targeted Oral Anticancer Agents), 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal Year	Total Cost	Average Annual Cost	Number of Users	Number of Prescriptions
2003/04	$ 7,286.63	$ 134.94	54	376
2004/05	$ 8,459.52	$ 136.44	62	502
2005/06	$ 9,469.34	$ 137.24	69	513
2006/07	$ 15,495.68	$ 147.58	105	772
2007/08	$ 19,433.33	$ 138.81	140	1,001
2008/09	$ 30,865.91	$ 149.11	207	1,343
2009/10	$ 34,427.94	$ 142.26	242	1,630
2010/11	$ 49,601.44	$ 167.57	296	2,095
2011/12	$ 61,897.19	$ 184.77	335	2,428
2012/13	$ 76,224.38	$ 179.35	425	2,767
2013/14	$ 81,352.08	$ 161.73	503	3,673
2014/15	$ 82,027.01	$ 147.00	558	4,041
2015/16	$ 96,067.15	$ 154.20	623	4,662
2003/04 - 2015/16	$ 572,607.60	$ 158.22	1,587	25,803

Table 7.8: Cost of Oral Anticancer Agents per User per Day of Therapy (Hormonal Oral Anticancer Agents), 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal Year	Total Cost	Annual Average Cost	Number of Users	Number of Prescriptions
2003/04	$ 12,011.96	$ 3.63	3,306	17,021
2004/05	$ 14,227.94	$ 4.02	3,538	18,560
2005/06	$ 15,421.83	$ 4.30	3,588	20,527
2006/07	$ 15,324.17	$ 4.06	3,774	21,991
2007/08	$ 16,173.35	$ 4.13	3,916	24,244
2008/09	$ 17,062.52	$ 4.26	4,004	26,430
2009/10	$ 18,322.59	$ 4.40	4,166	27,233
2010/11	$ 17,373.26	$ 4.06	4,282	28,276
2011/12	$ 15,321.41	$ 3.55	4,318	27,904
2012/13	$ 17,347.81	$ 3.85	4,508	27,719
2013/14	$ 14,812.29	$ 3.20	4,622	26,426
2014/15	$ 26,435.68	$ 5.45	4,852	27,499
2015/16	$ 25,506.80	$ 5.18	4,920	27,570
2003/04 - 2015/16	$ 225,341.61	$ 4.19	16,094	321,400

Total Cost per Prescription

Costs per prescription are presented in Tables 7.9-7.17. As prescriptions can be for any duration of therapy (including as little as 1 day), this measure must be interpreted with caution. Prescription costs are further broken down by ingredient cost and professional fee costs. These are presented separately for each medication group.

While the mean professional fee per prescription was slightly higher for the class of targeted OAAs (approximately $140 per prescription) (Table 7.14) compared to traditional OAAs (approximately $30 per prescription) (Table 7.11) and hormonal OAAs (approximately $13 per prescription) (Table 7.17), the maximum professional fees per prescription for targeted OAAs exceeded $1,000. However, this occurred for only a few outliers; the median fee for targeted OAAs was $81.82, and the 75th percentile was $200.62. The 90th percentile was $331.93; the 95th percentile was 395.96 and the 99th percentile was $779.61.

Table 7.9: Overall Cost per Prescription of Traditional Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 2,582,540.07	$ 574.15	864	4,498
2004/05	$ 3,160,629.80	$ 654.51	848	4,829
2005/06	$ 3,281,217.59	$ 617.35	864	5,315
2006/07	$ 2,474,933.00	$ 533.97	783	4,635
2007/08	$ 2,601,345.63	$ 507.78	824	5,123
2008/09	$ 2,843,706.44	$ 561.55	753	5,064
2009/10	$ 2,980,275.35	$ 579.37	791	5,144
2010/11	$ 3,125,643.79	$ 571.73	840	5,467
2011/12	$ 3,103,754.69	$ 538.38	861	5,765
2012/13	$ 3,142,018.54	$ 515.85	898	6,091
2013/14	$ 2,545,909.00	$ 445.17	819	5,719
2014/15	$ 2,394,718.05	$ 407.26	890	5,880
2015/16	$ 1,723,570.91	$ 305.27	834	5,646
2003/04 - 2015/16	$ 35,960,262.86	$ 519.84	6,043	69,176

Table 7.10: Ingredient Cost per Prescription of Traditional Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 2,421,156.61	$ 538.63	864	4,495
2004/05	$ 2,979,757.76	$ 617.18	848	4,828
2005/06	$ 3,095,245.99	$ 582.36	864	5,315
2006/07	$ 2,322,314.21	$ 501.04	783	4,635
2007/08	$ 2,435,429.73	$ 475.39	824	5,123
2008/09	$ 2,668,280.30	$ 527.02	753	5,063
2009/10	$ 2,790,487.45	$ 542.69	791	5,142
2010/11	$ 2,937,852.94	$ 537.48	840	5,466
2011/12	$ 2,922,145.72	$ 507.67	861	5,756
2012/13	$ 2,952,300.94	$ 484.86	898	6,089
2013/14	$ 2,365,906.20	$ 413.69	819	5,719
2014/15	$ 2,230,600.03	$ 379.48	890	5,878
2015/16	$ 1,592,397.05	$ 282.14	834	5,644
2003/04 - 2015/16	$ 33,713,874.93	$ 487.53	6,043	69,153

Table 7.11: Professional Fee Cost per Prescription of Traditional Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 161,383.46	$ 35.88	864	4,498
2004/05	$ 180,872.04	$ 37.46	848	4,829
2005/06	$ 185,971.60	$ 34.99	864	5,315
2006/07	$ 152,618.79	$ 32.93	783	4,635
2007/08	$ 165,915.90	$ 32.39	824	5,123
2008/09	$ 175,426.14	$ 34.64	753	5,064
2009/10	$ 189,787.90	$ 36.90	791	5,144
2010/11	$ 187,790.85	$ 34.35	840	5,467
2011/12	$ 181,608.96	$ 31.50	861	5,765
2012/13	$ 189,717.60	$ 31.15	898	6,091
2013/14	$ 180,002.81	$ 31.47	819	5,719
2014/15	$ 164,118.02	$ 27.91	890	5,880
2015/16	$ 131,173.86	$ 23.23	834	5,646
2003/04 - 2015/16	$ 2,246,387.93	$ 32.47	6,043	69,176

Table 7.12: Overall Cost per Prescription of Targeted Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 1,759,957.02	$ 4,680.74	54	376
2004/05	$ 2,406,002.13	$ 4,792.83	62	502
2005/06	$ 2,462,788.03	$ 4,800.76	69	513
2006/07	$ 3,529,871.58	$ 4,572.37	105	772
2007/08	$ 4,462,021.20	$ 4,457.56	140	1,001
2008/09	$ 5,884,723.64	$ 4,381.77	207	1,343
2009/10	$ 7,272,033.68	$ 4,461.37	242	1,630
2010/11	$ 9,374,657.87	$ 4,474.78	296	2,095
2011/12	$ 12,334,885.67	$ 5,080.27	335	2,428
2012/13	$ 14,070,335.54	$ 5,085.05	425	2,767
2013/14	$ 16,820,947.64	$ 4,579.62	503	3,673
2014/15	$ 16,295,541.71	$ 4,032.55	558	4,041
2015/16	$ 18,929,741.17	$ 4,060.43	623	4,662
2003/04 - 2015/16	$ 115,603,506.87	$ 4,480.24	1,587	25,803

Table 7.13: Ingredient Cost per Prescription of Targeted Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 1,699,763.89	$ 4,532.70	54	375
2004/05	$ 2,320,421.61	$ 4,678.27	62	496
2005/06	$ 2,381,087.06	$ 4,677.97	69	509
2006/07	$ 3,419,203.02	$ 4,429.02	105	772
2007/08	$ 4,331,731.85	$ 4,344.77	140	997
2008/09	$ 5,694,106.35	$ 4,239.84	207	1,343
2009/10	$ 7,033,627.89	$ 4,315.11	242	1,630
2010/11	$ 9,101,582.37	$ 4,361.08	296	2,087
2011/12	$ 11,957,583.48	$ 4,924.87	335	2,428
2012/13	$ 13,647,663.83	$ 4,932.30	425	2,767
2013/14	$ 16,330,931.54	$ 4,476.68	503	3,648
2014/15	$ 15,802,349.96	$ 3,947.63	558	4,003
2015/16	$ 18,283,865.05	$ 3,955.83	623	4,622
2003/04 - 2015/16	$ 112,003,917.91	$ 4,362.03	1,587	25,677

Table 7.14: Professional Fee Cost per Prescription of Targeted Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 60,193.13	$ 160.09	54	376
2004/05	$ 85,580.52	$ 170.48	62	502
2005/06	$ 81,700.97	$ 159.26	69	513
2006/07	$ 110,668.55	$ 143.35	105	772
2007/08	$ 130,289.34	$ 130.16	140	1,001
2008/09	$ 190,617.29	$ 141.93	207	1,343
2009/10	$ 238,405.79	$ 146.26	242	1,630
2010/11	$ 273,075.49	$ 130.35	296	2,095
2011/12	$ 377,302.19	$ 155.40	335	2,428
2012/13	$ 422,671.71	$ 152.75	425	2,767
2013/14	$ 490,016.10	$ 133.41	503	3,673
2014/15	$ 493,191.75	$ 122.05	558	4,041
2015/16	$ 645,876.11	$ 138.54	623	4,662
2003/04 - 2015/16	$ 3,599,588.96	$ 139.50	1,587	25,803

Table 7.15: Overall Cost per Prescription of Hormonal Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 2,494,840.19	$ 146.57	3,306	17,021
2004/05	$ 2,932,342.42	$ 157.99	3,538	18,560
2005/06	$ 3,478,112.13	$ 169.44	3,588	20,527
2006/07	$ 3,583,551.19	$ 162.96	3,774	21,991
2007/08	$ 3,946,792.48	$ 162.79	3,916	24,244
2008/09	$ 4,337,623.95	$ 164.11	4,004	26,431
2009/10	$ 4,590,248.52	$ 168.55	4,166	27,233
2010/11	$ 4,311,531.83	$ 152.48	4,282	28,276
2011/12	$ 3,712,520.95	$ 133.04	4,318	27,906
2012/13	$ 3,784,475.97	$ 136.53	4,508	27,719
2013/14	$ 2,987,284.24	$ 113.04	4,622	26,426
2014/15	$ 5,418,956.72	$ 197.06	4,852	27,499
2015/16	$ 5,493,332.26	$ 199.25	4,920	27,570
2003/04 - 2015/16	$ 51,071,612.87	$ 158.90	16,094	321,403

Table 7.16: Ingredient Cost per Prescription of Hormonal Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 2,272,031.27	$ 133.48	3,306	17,021
2004/05	$ 2,674,140.89	$ 144.14	3,538	18,552
2005/06	$ 3,185,033.86	$ 155.19	3,588	20,523
2006/07	$ 3,277,620.56	$ 149.04	3,774	21,991
2007/08	$ 3,614,035.03	$ 149.07	3,916	24,244
2008/09	$ 3,982,667.99	$ 150.68	4,004	26,431
2009/10	$ 4,215,800.33	$ 154.80	4,166	27,233
2010/11	$ 3,930,946.66	$ 139.02	4,282	28,276
2011/12	$ 3,357,021.31	$ 120.30	4,318	27,906
2012/13	$ 3,417,298.03	$ 123.28	4,508	27,719
2013/14	$ 2,618,980.43	$ 99.14	4,622	26,418
2014/15	$ 4,932,349.46	$ 179.36	4,852	27,499
2015/16	$ 5,018,123.81	$ 182.01	4,920	27,570
2003/04 - 2015/16	$ 46,496,049.64	$ 144.67	16,094	321,383

Table 7.17: Professional Fee Cost per Prescription of Hormonal Oral Anticancer Agents, 2003/04-2015/16
Adjusted for inflation using the Consumer Price Index; all dollar values are in 2015 dollars

Fiscal year	Total Cost	Average Annual Cost per Prescription	Number of Users	Number of Prescriptions
2003/04	$ 222,808.92	$ 13.10	3,306	17,002
2004/05	$ 258,201.53	$ 13.92	3,538	18,554
2005/06	$ 293,078.27	$ 14.28	3,588	20,527
2006/07	$ 305,930.63	$ 13.91	3,774	21,991
2007/08	$ 332,757.44	$ 13.73	3,916	24,244
2008/09	$ 354,955.95	$ 13.44	4,004	26,417
2009/10	$ 374,448.19	$ 13.75	4,166	27,233
2010/11	$ 380,585.16	$ 13.46	4,282	28,273
2011/12	$ 355,499.64	$ 12.74	4,318	27,906
2012/13	$ 367,177.95	$ 13.25	4,508	27,719
2013/14	$ 368,303.82	$ 13.94	4,622	26,426
2014/15	$ 486,607.26	$ 17.70	4,852	27,499
2015/16	$ 475,208.45	$ 17.24	4,920	27,569
2003/04 - 2015/16	$ 4,575,563.23	$ 14.24	16,094	321,360

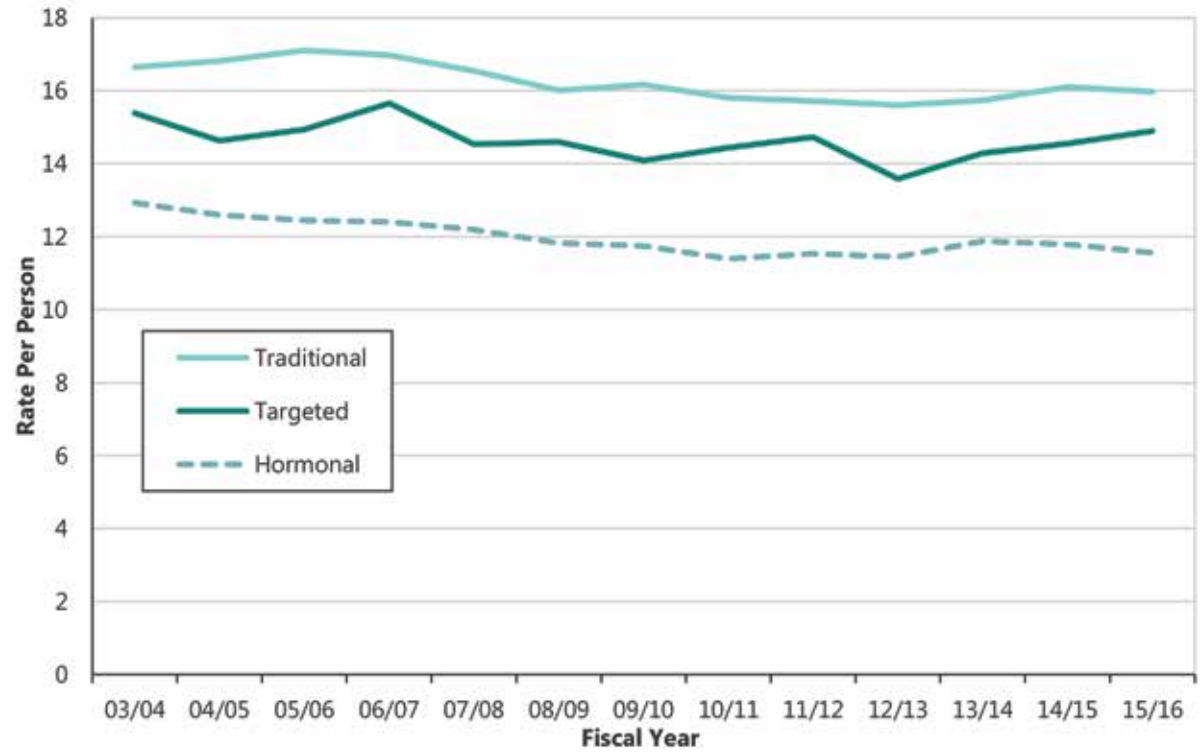
Chapter 8:
Health Services Use

We described the health services use of OAA users diagnosed with cancer by calculating the number of physician visits they made and determining the percentage who experienced at least one inpatient hospitalization while they were OAA users. Each year a person was determined to be an OAA user, they contributed to the number of visits or hospitalizations for the year.

Ambulatory Visits

Those receiving traditional OAAs had the highest rate of ambulatory physician visits, followed by those receiving targeted and hormonal agents (Figure 8.1). Ambulatory physician visit rates by age and sex are presented in Appendix 4. Overall, ambulatory physician visit rates were highest among OAA users in the youngest age category, and among those receiving prescriptions for traditional OAAs. Ambulatory physician visit rates among female patients receiving hormonal OAAs were consistently lower for than among males.

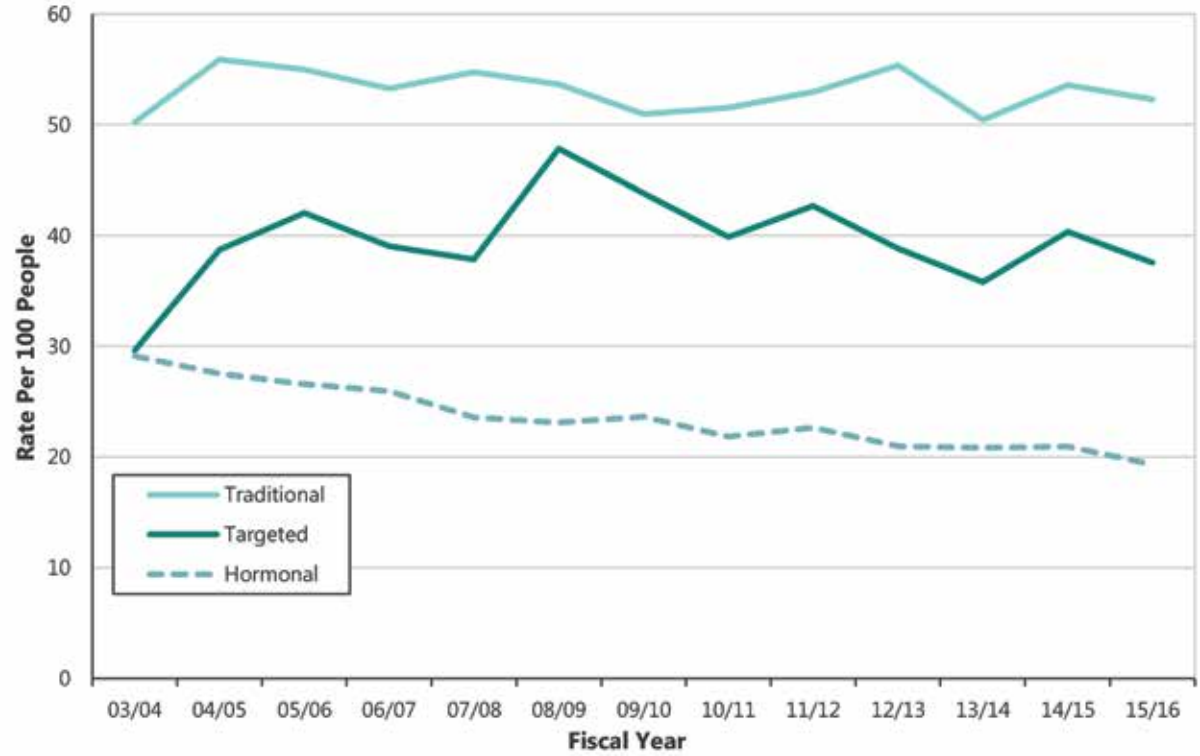
Figure 8.1: Crude Annual Ambulatory Visit Rate for Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis, by Drug Group, 2003/04-2015/16
Rate per user



Inpatient Hospitalizations

Overall, the percentage of OAA users diagnosed with cancer who experienced at least one hospitalization was highest among OAA users receiving prescriptions for traditional OAAs (Figure 8.2). Not surprisingly, these rates are considerably higher than in the general population. Inpatient hospitalization rates by age and sex are presented in Appendix 5. The patterns of rates of hospitalization for different medication groups varied by age, and were consistently lower among females receiving hormonal OAAs than among males.

Figure 8.2: Crude Inpatient Hospitalization Rate for Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis, by Drug Group, 2003/04-2015/16
Per 100 people



Chapter 9:
Discussion, Conclusions and Policy Recommendations

Discussion

Prevalence of OAA Use

Similar to what others have observed [8,54], we found an overall increase in the Manitoban population's use of OAAs over time. OAAs are a diverse group of medicines used for many different indications. This increased use reflects a greater availability of medications to treat a variety of malignancies.

There was a steady increase in the use of targeted OAAs and of hormonal therapies for breast and prostate cancer, while use of traditional OAAs plateaued (except for lenalidomide/pomolidamide use, which increased). Changes in diagnosis patterns, cancer incidence, and availability of OAAs impacted these trends. It is important to note that within each of the medication groups (traditional, targeted and hormonal), there is significant heterogeneity in terms of the types of cancers these OAAs are used for. Additionally, within each type of cancer, the role of OAAs within the therapeutic pathway differs. For example, some OAAs for some cancers replace intravenous chemotherapy, and some OAAs for some cancers are used together with intravenous therapy. Although a different categorization of medications, for example, medication use by cancer, would be informative, such a review is beyond the scope of this project.

Pharmacy Fill Patterns

Our study provides evidence that a small number of patients changed pharmacies upon receipt of a prescription for a new OAA. This was most evident in those receiving targeted OAAs. This practice could be the result of patients switching to pharmacies located closer to a cancer centre, meaning increased convenience for patients, greater pharmacist expertise, and better medication availability (for example, lenalidomide is only available at a single pharmacy in Manitoba due to a controlled distribution program). It could also reflect the reluctance of some pharmacies to obtain such a costly stock item. More new users of targeted and traditional OAAs filled prescriptions at Banner/Franchise/Chain (e.g., Shopper's Drug Mart) than at their usual pharmacy. This change in pharmacy choice could also be due to patients wanting to switch to pharmacies closer to a cancer centre (3 of 4 pharmacies close to a cancer centre are in the Banner/Franchise/Chain category).

Another aspect of pharmacy fill patterns is the pharmacy reward system offered at many community pharmacies. In professional colleges, the use of such reward or inducement programs is controversial [55]. Some stakeholders have expressed concerns that inducement programs may

have deleterious health effects and could potentially be unsafe and unethical [56]. We observed an increase in the use of rewards pharmacies upon receipt of OAAs, particularly with the more costly traditional and targeted classes of OAAs. This could mean that patients are switching to rewards pharmacy to receive benefits related to costly OAAs. Very little scientific literature has described the impact of community pharmacy-based inducement programs and patient outcomes. Simpson et al. found that diabetes or hypertension patients in Alberta who filled new prescriptions for statins (a class of drug that reduces cholesterol levels) at community pharmacies offering inducement programs had better adherence than those who filled prescriptions at other types of pharmacies. Filling a statin prescription at an inducement pharmacy was not directly associated with a higher risk of adverse health outcomes [57]. Future work in Manitoba could examine the impact of rewards pharmacy on adherence to OAAs and associated patient outcomes. We were unable to assess possible reasons for pharmacy switching due to the nature of administrative data research; future work could explore reasons for pharmacy switching from a patient perspective and measure the impact of switching on patient outcomes.

In an effort to balance patient safety and convenience, policy makers must consider a trade-off between patients travelling to (or pharmacies shipping medication to) certain centralized pharmacies where specialized services are offered, and patients receiving those services at a known pharmacy but where the pharmacist may lack specialized clinical expertise. Some evidence suggests that community pharmacists generally lack the expertise to prepare and dispense OAAs; a survey of Canadian community pharmacists found that many lack knowledge of cancer treatment and do not have specific training in oncology medications or diseases [19]. And while pharmacists with oncology expertise working at CancerCare Manitoba and oncology nurses play an important role in the care of patients receiving OAAs in the community, these health professionals may not be able to keep up with the demands of this rapidly growing population of patients. Given the potential for prescribing errors, medication administration errors, and the potential for harm with OAAs (relative to many other medications), there have been calls for specialized pharmacies in order to prevent patient harm related to OAAs [19,28]. In many cancer centres, specialized pharmacists educate and counsel patients on new OAA prescriptions, perform medication reconciliation to evaluate patients for medication interactions, and assess toxicity and adherence between cycles of chemotherapy [58]. A recent systematic review on interventions to improve oral chemotherapy safety and quality suggests that effective programs should include personal contact with patients during the first several weeks of therapy with OAAs [59]. This underscores the importance of a care team to ensure safe and effective use of OAAs.

In Manitoba, community pharmacists can use the Drug Program Information Network (DPIN) to see all prescriptions that patients have filled in the past six months through the prescription drug database. Therefore, a pharmacist dispensing an OAA at a new pharmacy can check for potential drug-drug interactions; this check is outside pharmacy-specific software as would be the case if a patient filled the OAA at the usual pharmacy. This factor, combined with pharmacist lack of familiarity with the patient and possibly the drug may place the patient at risk of medication misadventure. Having multiple prescriptions at multiple pharmacies could also lead to lack of adherence, misaligned fill schedules or lack of understanding of refill schedules and special instructions.

Without a clear and well-established framework for community pharmacy clinical expertise and insight, attention to dispensing, and education and follow-up for OAAs, there is potential for medication misadventure. National practice standards have been developed in order to ensure appropriate handling of these important prescriptions, and pharmacist expertise is key [60]. In the absence of information related to indication and pertinent lab or clinical information (such as prior dose modification), the appropriateness of a specialized OAA prescription is difficult for a community pharmacist to assess. Manitoba previously lacked information on the impact of type or location of community pharmacies on patient outcomes, and this current work is an important first step in order to describe where and how often Manitobans are filling prescriptions for OAAs. Healthcare provider education will continue to be important to balance access to medications with safe and appropriate OAA use, including communication with the healthcare team about medication management and accessible and appropriate drug information [61].

Health Services Use

The patterns of health services use that we observed were generally as we expected. We observed the lowest rates of physician visits for females with breast cancer taking hormonal therapies, which would be expected given the chronic nature of this largely preventative therapy. Health services use depends on both the underlying cancer and the impact of the OAAs on the cancer and side-effect profile. Good patient education and pre-emptive supportive medication prescribing can improve patient quality of life and reduce healthcare system use. Hospitalizations were, as expected, much higher than in the general population. There is no indication of how often the hospitalizations were related to the OAAs or their side-effects. It is encouraging that there are no increases in hospitalization that were temporally associated with the increased use of OAAs.

Costs of OAA Prescriptions

The costs of cancer therapies, including OAAs, have risen dramatically over the past decade, largely due to the availability and uptake of new targeted therapies [13,14,62]. With costs of up to approximately $400 per day of therapy, it is important to consider the impact that targeted OAAs can have on provincial pharmacare programs. In Manitoba, a rigorous approval process is required before a medication is funded by Pharmacare. Formulary decisions are generally informed by the Canadian Association for Drugs and Technology in Health (CADTH) Pan-Canadian Oncology Drug Review (pCODR) review. The HCDP also ensures that each prescription covered is reviewed on a case-by-case basis for appropriate indication and context of prescribing. (As a reminder, Manitoba has universal income-based medication coverage for pharmaceuticals, but the HCDP eliminates the family income-based deductible for OAAs and select non-OAA medications).

In the context of a public payer such as Manitoba Pharmacare or the HCDP, the range of professional fees charged in Manitoba for targeted OAAs was important to note. Although fee maximums can vary with private insurance, the majority of prescriptions in this study were covered through Pharmacare or the HCDP, which is also paid for by Manitoba Health. With no cap on professional fees during the study period, a small proportion of pharmacies charged over $1,000 per prescription to dispense targeted OAAs. Outside of these relatively few cases, the markup was about 6% for traditional, 9% for hormonal, and 3% for targeted OAAs. A dispensing fee cap implemented in Manitoba in August 2017 will limit the maximum professional fee per prescription to $30 [63].

Home Cancer Drug Plan Impact

The HCDP covered the cost of 190,847 deductible-free prescriptions from inception in 2012 to the end of 2015/16. The saw-toothed pattern of seasonal prescription filling for OAAs was eliminated after the implementation of the HCDP. While it makes sense that most patients would be diligent about filling their cancer therapy prescriptions at all times, the change in timing of prescription fill patterns we observed provides evidence that the program impacted how and when patients filled these prescriptions. We were not able to explore the impact of this change on OAA adherence, including primary non-adherence where patients have a prescription written but never filled, due to limitations of the administrative data. This analysis would require reconciliation between prescriptions in the CancerCare Manitoba Electronic Medical Record with the dispensations recorded in DPIN.

Limitations of Administrative Data

All data used in this report are derived from Manitobans' contacts with the healthcare system. The DPIN system contains records of prescriptions dispensed from outpatient dispensaries. Because not everybody who seeks medical attention and receives a prescription for a medication actually fills the prescription, our analyses may underestimate the number of prescriptions written for OAAs and non-OAA medications covered by the HCDP. Medication use not captured in the DPIN system may include physician samples, although the possibility is low for these types of medications. There are some systems of compassionate use or dispensing outside of DPIN system for OAAs; notable examples include thalidomide, which is dispensed through a pharmaceutical company, and oral fludarabine, which is not included in DPIN as it is dispensed through the CancerCare Manitoba pharmacy. The DPIN system does not contain records on Manitobans who are incarcerated or members of the RCMP; however, these individuals make up a very small proportion of the Manitoba population (<1%). It should be noted that approximately 25% of personal care homes in Manitoba do not fill prescriptions at community pharmacies, and are therefore also not included in the DPIN system.

We presented prevalence of OAA use as crude population rates to help standardize by population size, but we did not present age standardized rates to account for changing population demographics over the study period.

For several analyses, we used administrative data to determine medical diagnosis of cancer or other conditions. The use of administrative data may have caused us to underestimate the prevalence of a given condition in the population, because it requires a patient to seek contact with the healthcare system to receive a diagnosis. Some diagnoses may have been missed if a physician visits resulted in a single billing code that masked the diagnosis. There is also a small potential for underestimating or overestimating a given condition due to misclassification.

Conclusions and Policy Recommendations

The use of OAAs and the expenses associated with these medications has increased significantly over the years. We observed that the launch of the HCDP altered the prescription filling patterns of OAAs in Manitoba. Starting to fill an OAA prescription was associated with changing pharmacies for some Manitobans. In seeking to balance

convenient access to important medications with access to clinical expertise, policymakers could consider making an 'expert' pharmacist or pharmacy available for dispensing certain medications (e.g., targeted oral chemotherapy); this would ensure optimal pharmacist expertise and open prescriber/pharmacist/patient communication to monitor for safety and efficacy. This recommendation would need to be balanced with ensuring that patients in rural and remote areas, where an 'expert' pharmacist might not always be available, continue to have access to important medications.

References

1. National Cancer Institute. Targeted Cancer Therapies. https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet. Published 2017. Accessed July 24, 2017.
2. Shih Y-CT, Smieliauskas F, Geynisman DM, Kelly RJ, Smith TJ. Trends in the cost and use of targeted cancer therapies for the privately insured nonelderly: 2001 To 2011. *J Clin Oncol*. 2015;33(19):2190-2196.
3. Canadian Cancer Society. Cancer statistics at a glance. http://www.cancer.ca/en/cancer-information/cancer-101/cancer-statistics-at-a-glance/?region=on. Published 2017. Accessed April 10, 2017.
4. Statistics Canada. Leading causes of death, by sex. http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/hlth36a-eng.htm. Accessed January 25, 2014.
5. Milan A, Statistics Canada. Mortality: Causes of death, 2007. Report on the Demographic Situation in Canada. http://www.statcan.gc.ca/pub/91-209-x/2011001/article/11525-eng.htm. Accessed January 25, 2014.
6. Krzyzanowska MK, Powis M. Extending the quality and safety agenda from parenteral to oral chemotherapy. *J Oncol Pract*. 2015;11(3):198-201.
7. Canadian Association of Pharmacy in Oncology. Standards of Practice for Oncology Pharmacy in Canada. http://www.cancercare.ns.ca/site-cc/media/cancercare/StandardsofPracticeFORWEB.pdf. Published 2009. Accessed April 7, 2014.
8. Timmers L, Beckeringh JJ, van Herk-Sukel MP, Boven E, Hugtenburg JG. Use and costs of oral anticancer agents in the Netherlands in the period 2000-2008. *Pharmacoepidemiol Drug Saf*. 2012;21(10):1036-1044.
9. Aisner J. Overview of the changing paradigm in cancer treatment: Oral chemotherapy. *Am J Heal Syst Pharm*. 2007;64(9 Suppl 5):S4-S7.
10. Eek D, Krohe M, Mazar I, et al. Patient-reported preferences for oral versus intravenous administration for the treatment of cancer: a review of the literature. *Patient Prefer Adherence*. 2016;10:1609-1621.
11. Morgan S, Smolina K, Mooney D, et al. *The Canadian Rx Atlas*. 3rd ed. Vancouver; 2013. http://hdl.handle.net/2429/50349.
12. Naipaul R, Beca J, Gavura S. Shifting trends: An analysis of IV and take-home cancer drug use and public spending in Ontario. *J Popul Ther Clin Pharmacol*. 2016;23(Suppl 1):e11.
13. Dusetzina SB. Share Of Specialty Drugs In Commercial Plans Nearly Quadrupled, 2003-14. *Heal Aff*. 2016;35(1544-5208 (Electronic)):1241-1246.
14. Dusetzina SB. Drug Pricing Trends for Orally Administered Anticancer Medications Reimbursed by Commercial Health Plans, 2000-2014. *JAMA Oncol*. 2016;2(7):960-961.
15. Raborn ML, Pelletier EM, Smith DB, Reyes CM. Patient out-of-pocket payments for oral oncolytics: results from a 2009 US claims data analysis. *Am J Manag Care*. 2012;18(5 Spec No. 2):SP57-SP64.
16. Abbott R, Edwards S, Edwards J, Dranitsaris G, McCarthy J. Oral Anti-Cancer Agents in the Community Setting: A Survey of Pharmacists in Newfoundland and Labrador. *Can Pharm J / Rev des Pharm du Canada*. 2011;144(5):220-226.
17. Broadfield L, Shaheen P, Rogez M, Jamieson K, McCallum M. Guidelines for outpatient cancer care by community pharmacists. *Can Pharm J (Ott)*. 2016;150(1):24-31.
18. Ahmad N, Simanovski V, Hertz S, Klaric G, Kaizer L, Krzyzanowska MK. Oral chemotherapy practices at Ontario cancer centres. *J Oncol Pharm Pract*. 2015;21(4):249-257.
19. Abbott R, Edwards S, Whelan M, Edwards J, Dranitsaris G. Are community pharmacists equipped to ensure the safe use of oral anticancer therapy in the community setting? Results of a cross-country survey of community pharmacists in Canada. *J Oncol Pharm Pract*. 2014;20(1):29-39.

20. Cancer Care Ontario. Think Tank: Enhancing the delivery of take-home cancer therapies in Ontario. https://d3n8a8pro7vhmx.cloudfront.net/cancertainty/pages/34/attachments/original/1419012064/Think_Tank_Proceedings_Report_December_2014.pdf. Published December 31, 2014. Accessed December 31, 2014.

21. Weingart SN, Flug J, Brouillard D, Morwayl L, Connor M . Oral chemotherapy safety practices at US cancer centres: questionnaire survey. *BMJ.* 2007;334(407).

22. Leveque D, Delpeuch A, Gourieux B. New anticancer agents: role of clinical pharmacy services. *Anticancer Res.* 2014;34(1791-7530 (Electronic)):1573-1578.

23. Conde-Estévez D, Gómez-Ulloa D, Bundó AV, et al. Oral anticancer agents: a prospective pilot study of a patient educational surgery run by a pharmacist and a nurse. *Eur J Hosp Pharm.* 2012;19(2):185.2-185.

24. Timmers L, Boons CC, Kropff F, et al. Adherence and patients' experiences with the use of oral anticancer agents. *Acta Oncol.* 2014;53(1651-226X (Electronic)):259-267.

25. Bassan F, Peter F, Houbre B, et al. Adherence to oral antineoplastic agents by cancer patients: Definition and literature review. *Eur J Cancer Care (Engl).* 2014;23(1):22-35.

26. Prasad V, De Jesús K, Mailankody S. The high price of anticancer drugs: origins, implications, barriers, solutions. *Nat Rev Clin Oncol.* 2017;14(6):381-390.

27. Davis C, Naci H, Gurpinar E, Poplavska E, Pinto A, Aggarwal A. Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13. *BMJ.* 2017;359:j4530.

28. Hammond L, Marsden E, O'Hanlon N, King F, Henman MC, Keane C. Identification of risks associated with the prescribing and dispensing of oral anticancer medicines in Ireland. *Int J Clin Pharm.* 2012;34(6):893-901.

29. CancerCare Manitoba. Services for Rural Patients in Manitoba. http://www.cancercare.mb.ca/home/patients_and_family/treatment_services/treating_patients_in_rural_manitoba/. Published 2017. Accessed December 13, 2017.

30. Manitoba Health. About the Manitoba Pharmacare Program. http://www.gov.mb.ca/health/pharmacare/. Published 2017. Accessed July 24, 2017.

31. Government of Manitoba. Deductible Instalment Payment Program for Pharmacare. http://www.gov.mb.ca/health/pharmacare/dippp.html. Published 2018. Accessed February 23, 2018.

32. CancerCare Manitoba. Manitoba Home Cancer Drug Program. https://cancercare.mb.ca/Treatments/pharmacy/home-cancer-drug-program/. Published 2012. Accessed July 24, 2017.

33. World Health Organization. WHO Collaborating Centre for Drug Statistics Methodology. https://www.whocc.no/. Published 2017. Accessed July 24, 2017.

34. Norum J, Nieder C. Treatments for Metastatic Prostate Cancer (mPC): A Review of Costing Evidence. *Pharmacoeconomics.* 2017;35(12):1223-1236.

35. pCODR. pCODR expert review committee (PERC) final recommendation. https://www.cadth.ca/sites/default/files/pcodr/pcodr_lenalidomide_revlimid_nd-mm_fn_rec.pdf. Published 2015. Accessed March 1, 2018.

36. Hebert LA, Rovin BH. Oral cyclophosphamide is on the verge of extinction as therapy for severe autoimmune diseases (especially lupus): should nephrologists care? *Nephron Clin Pract.* 2011;117(1):c8-14.

37. Kim J, Chan JJ. Cyclophosphamide in dermatology. *Australas J Dermatol.* 2017;58(1):5-17.

38. National Cancer Institute. ICD-9-CM to ICD-10-CM Based on FY2014 ICD-9-CM codes: Reportable Neoplasms. https://seer.cancer.gov/tools/conversion/2014/ICD9CM_to_ICD10CM_2014CF.pdf. Published 2014. Accessed July 24, 2017.

39. Lix L, Smith M, Pitz M, et al. *Cancer Data Linkage in Manitoba: Expanding the Infrastructure for Research*. Winnipeg: Manitoba Centre for Health Policy; 2016. http://mchp-appserv.cpe.umanitoba.ca/reference//Candata_web_final.pdf. Accessed March 9, 2016.

40. Manitoba Centre for Health Policy. Administrative Health Data: Drug Data. http://www.umanitoba.ca/faculties/health_sciences/medicine/units/chs/departmental_units/mchp/protocol/media/drug_data_guide.pdf. Published 2009. Accessed January 1, 2017.

41. Government of Canada. Federal Public Drug Benefit Programs. https://www.canada.ca/en/health-canada/services/health-care-system/pharmaceuticals/access-insurance-coverage-prescription-medicines/federal-public-drug-benefit-programs.html. Published 2005. Accessed July 24, 2017.

42. Pharmacy Trends Report: Introduction. http://216.150.136.82/article.asp?catId=1638&pgId=5060&siteID=273. Published 2003. Accessed May 4, 2017.

43. Celgene Corporation. RevAid. https://www.revaid.ca/revaid/?AspxAutoDetectCookieSupport=1. Published 2017. Accessed March 1, 2018.

44. Ng E, Wilkins R, Perras A. How far is it to the nearest hospital? Calculating distances using the Statistics Canada Postal Code Conversion File. *Heal reports.* 1993;5(2):179-188. http://www.ncbi.nlm.nih.gov/pubmed/8292757.

45. Manitoba Centre for Health Policy. Concept: Distance to Hospital - A Method to Calculate. http://mchp-appserv.cpe.umanitoba.ca/viewConcept.php?conceptID=1155. Published 1998. Accessed July 24, 2017.

46. Manitoba Centre for Health Policy. Term: Ambulatory Visits - Physician. http://mchp-appserv.cpe.umanitoba.ca/viewDefinition.php?definitionID=102246. Published 2013. Accessed November 21, 2017.

47. Manitoba Centre for Health Policy. Term: Inpatient Hospitalization. http://mchp-appserv.cpe.umanitoba.ca/viewDefinition.php?definitionID=104244. Published 2013. Accessed November 21, 2017.

48. Manitoba Centre for Health Policy. Concept: Calculating Costs/Expenditures for Pharmaceuticals. http://mchp-appserv.cpe.umanitoba.ca/viewConcept.php?conceptID=1124. Published 2011. Accessed November 21, 2017.

49. Metge C, Black C, Peterson S, Kozyrskyj AL. The population's use of pharmaceuticals. Med Care. 1999;37(6 Suppl):JS42-59. http://www.ncbi.nlm.nih.gov/pubmed/10409017.

50. Statistics Canada. CANSIM 326-0021 Consumer Price Index. http://www5.statcan.gc.ca/cansim/a05?lang=eng&id=3260021. Published 2016. Accessed June 8, 2016.

51. Raymond C, Metge C, Alessi-Severini S, Dahl M, Schultz J, Guenette W. *Pharmaceutical Use in Manitoba: Opportunities to Optimize Use.* Winnipeg: Manitoba Centre for Health Policy; 2010. http://mchp-appserv.cpe.umanitoba.ca/reference/Rx_Optimize_WEB.pdf. Accessed May 29, 2013.

52. Kozyrskyj A, Raymond C, Dahl M, et al. *Effects of Manitoba Pharmacare Formulary Policy on Utilization of Prescription Medications.* Winnipeg: Manitoba Centre for Health Policy; 2009. http://mchp-appserv.cpe.umanitoba.ca/reference/Rx Policy.pdf. Accessed May 31, 2013.

53. Government of Ontario. 2015/16 Report Card for the Ontario Drug Benefit Program. http://www.health.gov.on.ca/en/public/programs/drugs/publications/opdp/docs/odb_report_16.pdf. Published 2016. Accessed March 14, 2018.

54. Benjamin L, Maroun R, Maurel F, Bardoulat I, Ricarte C. Patterns of use of oral anticancer treatments in France: a Retrospective Analysis of Cancer Treatments given ORally from 2004 to 2012 (Re-ACTOR study). *Curr Med Res Opin.* 2015;31(2):323-332.

55. Cotter J. Alberta court ruling says pharmacist regulator can ban reward points for drugs. METRO Winnipeg. http://www.metronews.ca/business/2017/09/22/alberta-court-ruling-says-pharmacist-regulator-can-ban-reward-points-for-drugs.html. Published September 22, 2017.

56. College of Pharmacists of British Columbia. Paying Patients for Prescriptions is Unprofessional, Unethical, and Unsafe. The practice must end. 2013;38(3).

57. Simpson SH, Lin M, Eurich DT. Community Pharmacy-Based Inducement Programs Associated With Better Medication Adherence: A Cohort Study. *Ann Pharmacother.* 2017;51(8):630-639.

58. Abbott R. Comment: Oral anti-cancer agents: A paradigm change. *Oncol Exch.* 2014;13(2):2014.

59. Zerillo JA, Goldenberg BA, Kotecha RR, Tewari AK, Jacobson JO, Krzyzanowska MK. Interventions to Improve Oral Chemotherapy Safety and Quality: A Systematic Review. *JAMA Oncol.* June 2017.

60. Canadian Association of Provincial Cancer Agencies. Oral Cancer Drug Therapy Safe Use and Safe Handling Guidelines. http://www.capca.ca/wp-content/uploads/En-Oral-Chemotherapy-Guideline-Final-11-May-2015.pdf. Published May 11, 2015. Accessed August 10, 2017.

61. van Rooij T, Rix S, Marsh S. AntiC: A practice tool for the safe use of oral chemotherapeutics by community and hospital pharmacists. *Can Pharm J (Ott).* 2015;148(3):118-124.

62. Banna GL, Collova E, Gebbia V, et al. Anticancer oral therapy: Emerging related issues. *Cancer Treat Rev.* 2010;36(8):595-605.

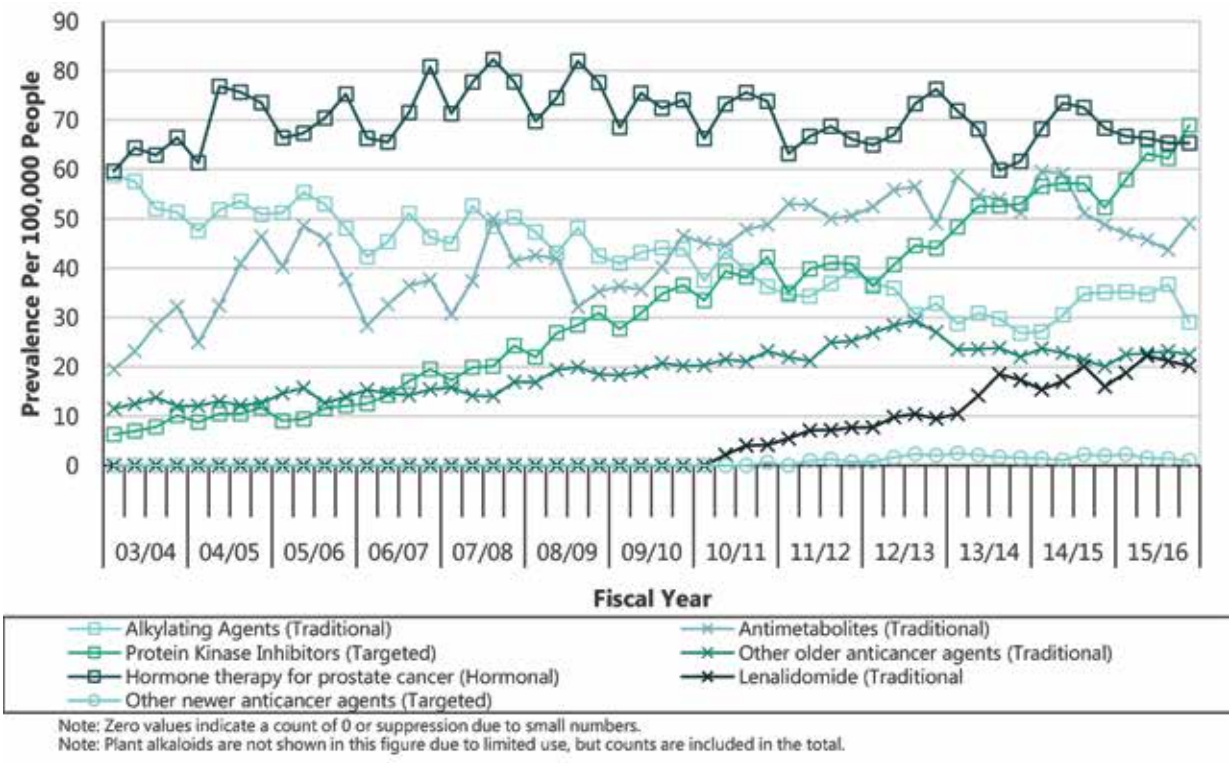
63. Government of Manitoba. Changes to Dispensing Fees. https://www.gov.mb.ca/health/pharmacare/docs/dispensingfeechanges.pdf. Published 2017. Accessed May 8, 2018.

Appendices

Appendix 1: Prescriptions Among Manitobans with a Cancer Diagnosis

Appendix Figure 1.1: Quarterly Prevalence of Oral Anticancer Agent Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

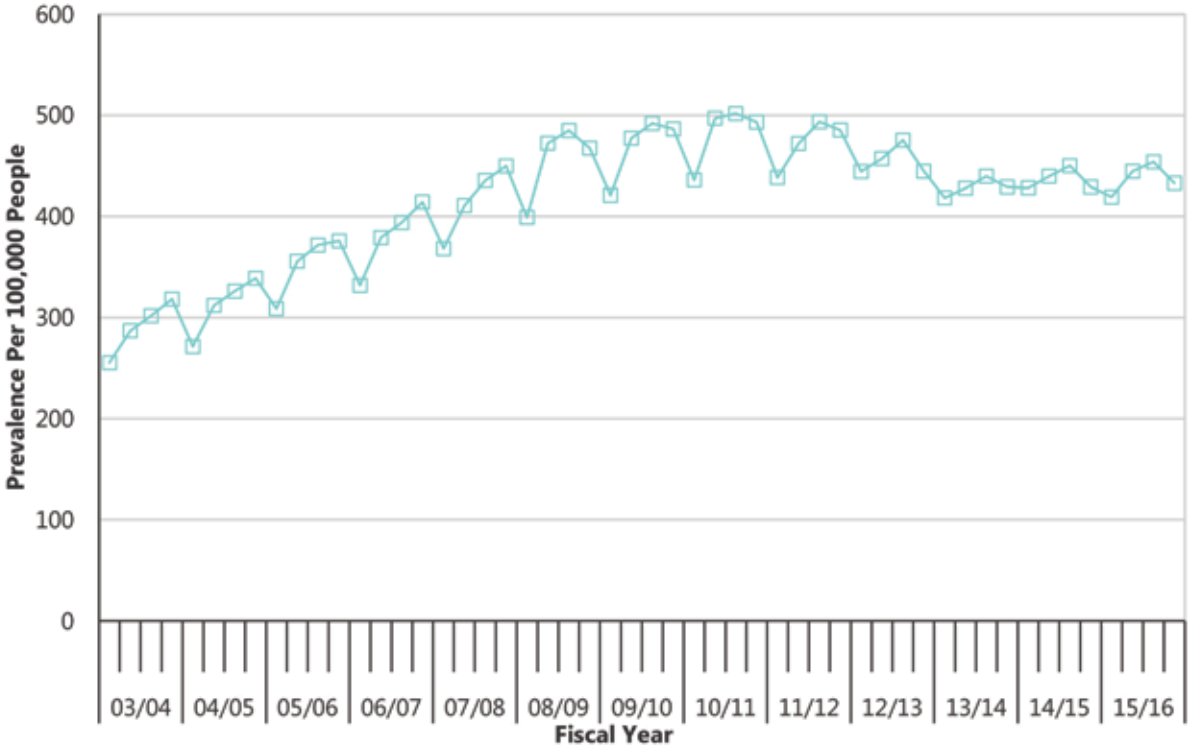
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Plant alkaloids are not shown in this figure due to limited use, but counts are included in the total.

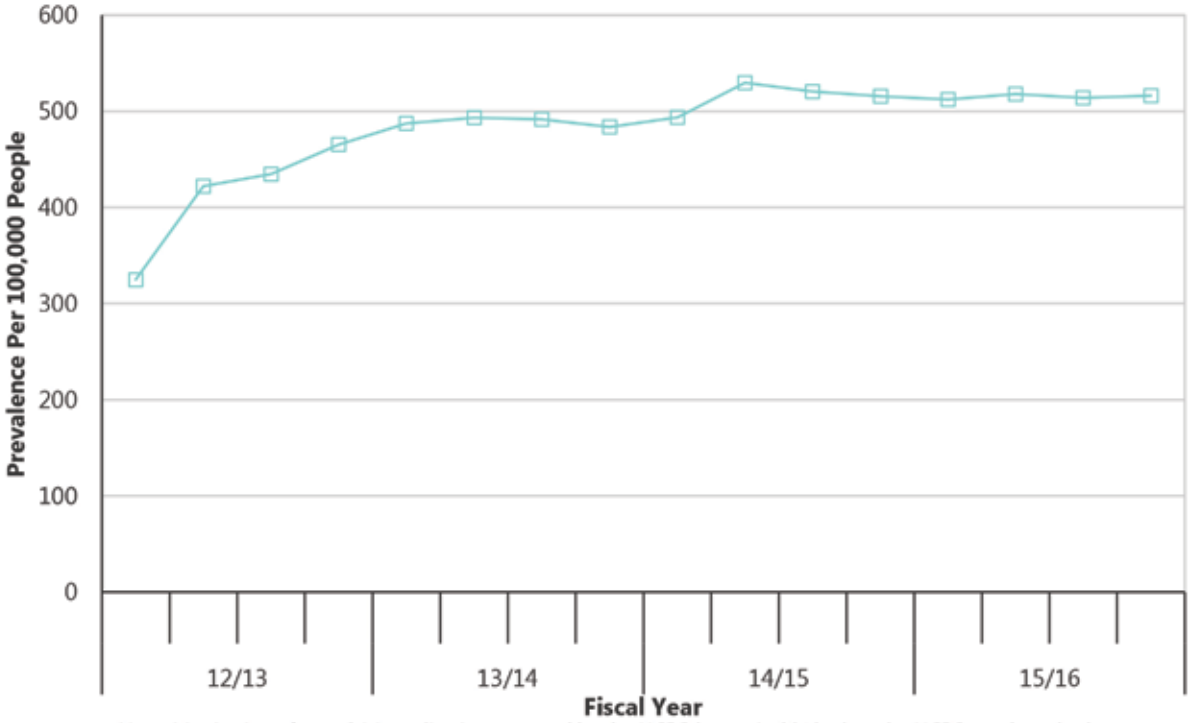
Appendix Figure 1.2: Quarterly Prevalence of People Using Hormone Therapy for Breast Cancer Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

Per 100,000 people



Appendix Figure 1.3: Quarterly Prevalence of Non-Oral Anticancer Agent Prescriptions Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16

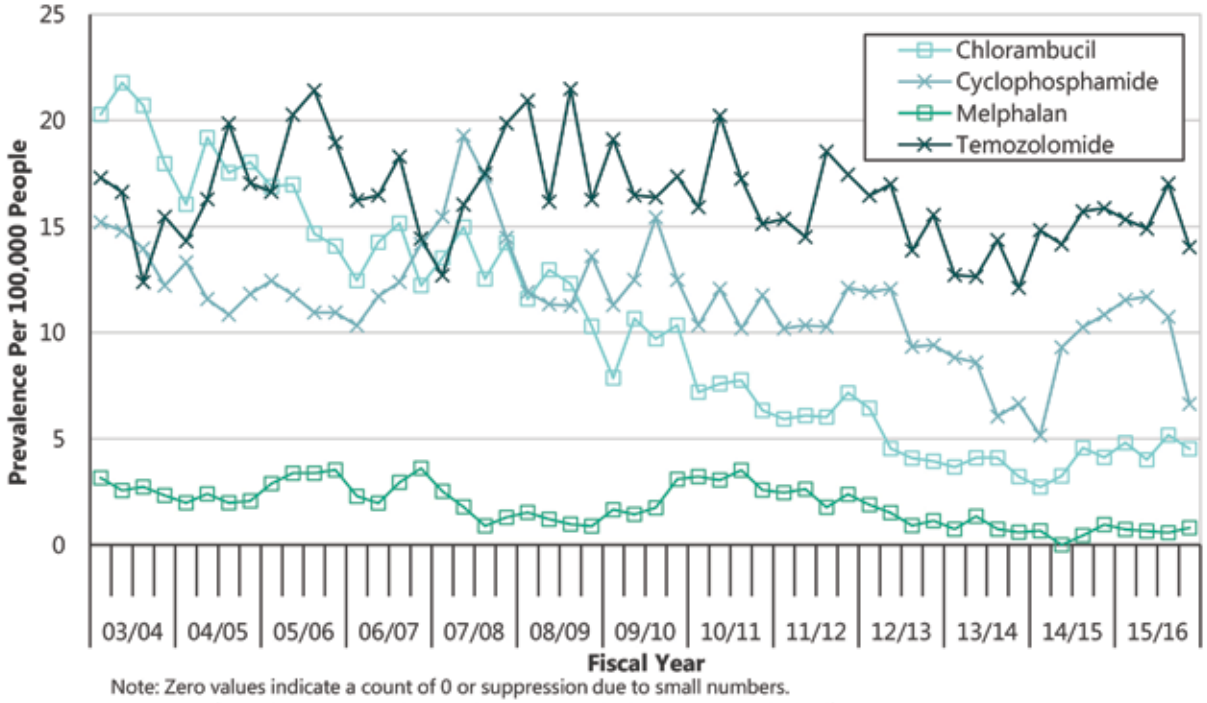
Per 100,000 people



Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

Appendix Figure 1.4: Quarterly Prevalence of Alkylating Agent (Traditional Oral Anticancer Agents) Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

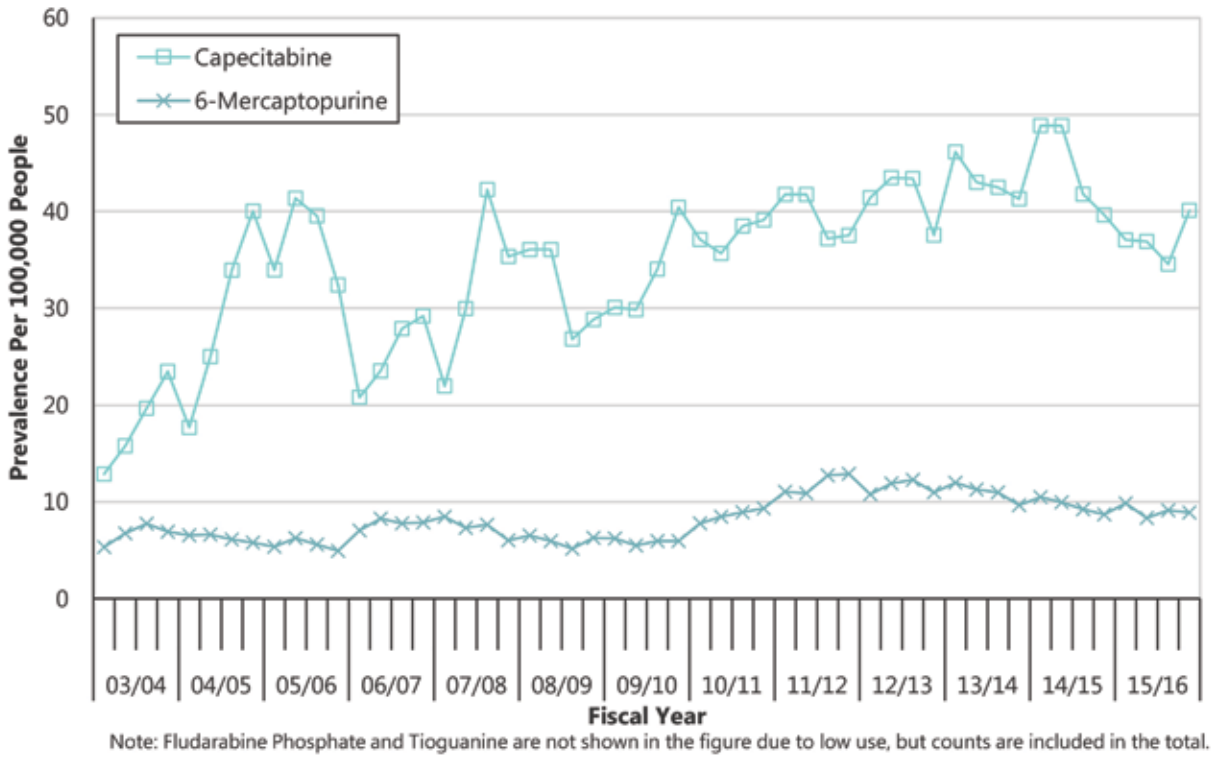
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Busulfan, Mitotane, Lomustine, and Procarbazine HCL are not shown in the figure due to low use, but counts are included in the total.

Appendix Figure 1.5: Quarterly Prevalence of Antimetabolite (Traditional Oral Anticancer Agents) Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

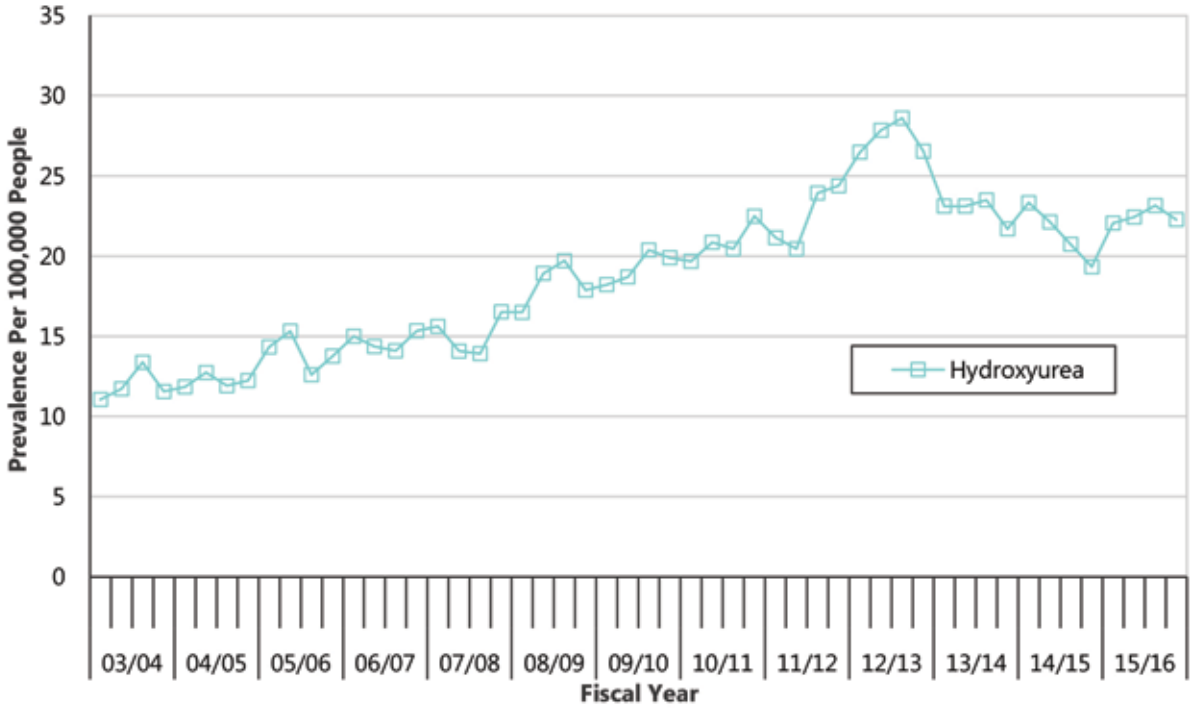
Per 100,000 people



Note: Fludarabine Phosphate and Tioguanine are not shown in the figure due to low use, but counts are included in the total.

Appendix Figure 1.6: Quarterly Prevalence of Other Older Anticancer Agent (Traditional Oral Anticancer Agents) Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

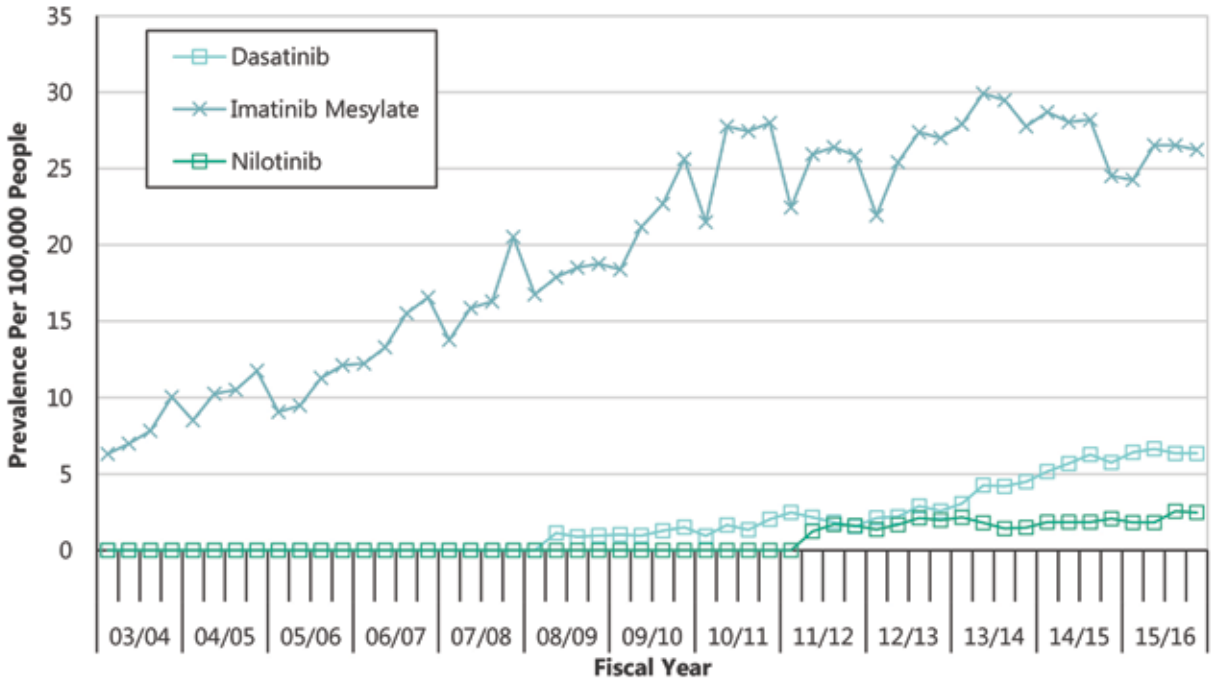
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Tretinoin is not shown in the figure due to low use, but counts are included in the total.

Appendix Figure 1.7: Quarterly Prevalence of Protein Kinase Inhibitors for Haematological Malignancies (Targeted Oral Anticancer Agents) Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

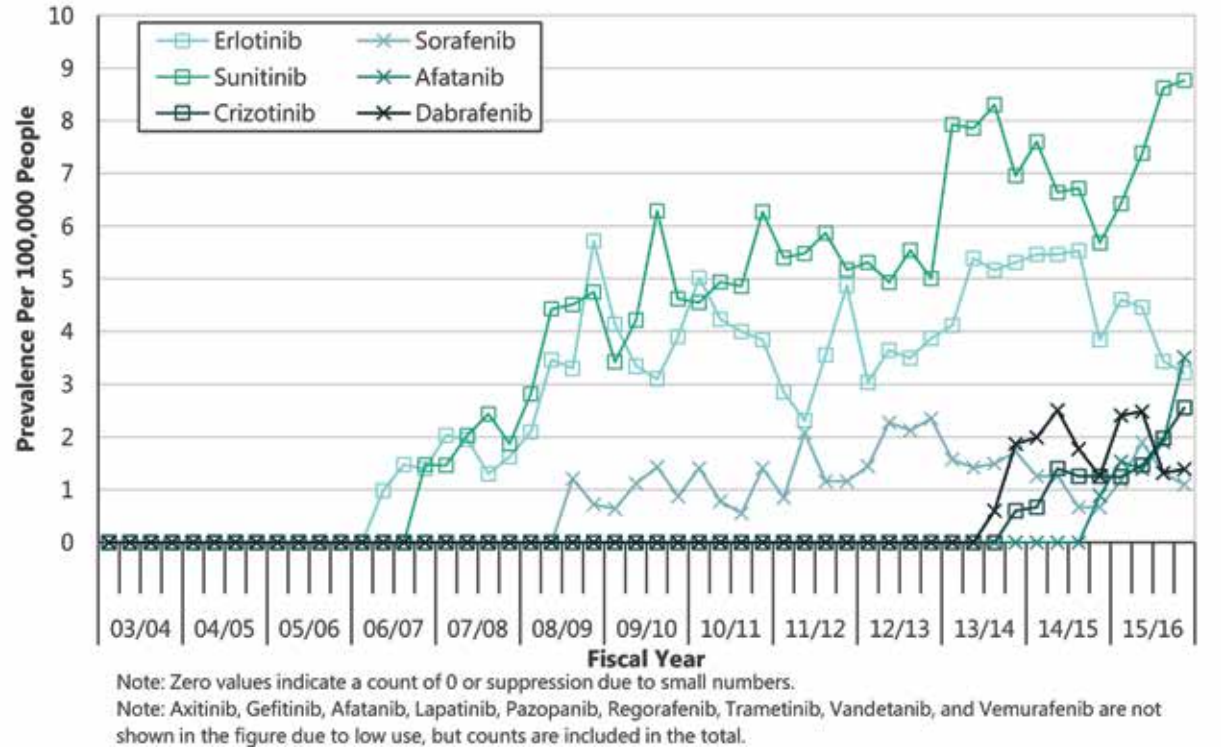
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Bosutinib and Ruxolitinib are not shown in the figure due to low use, but counts are included in the total.

Appendix Figure 1.8: Quarterly Prevalence of Protein Kinase Inhibitors for Solid Tumours (Targeted Oral Anticancer Agents) Prescriptions Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

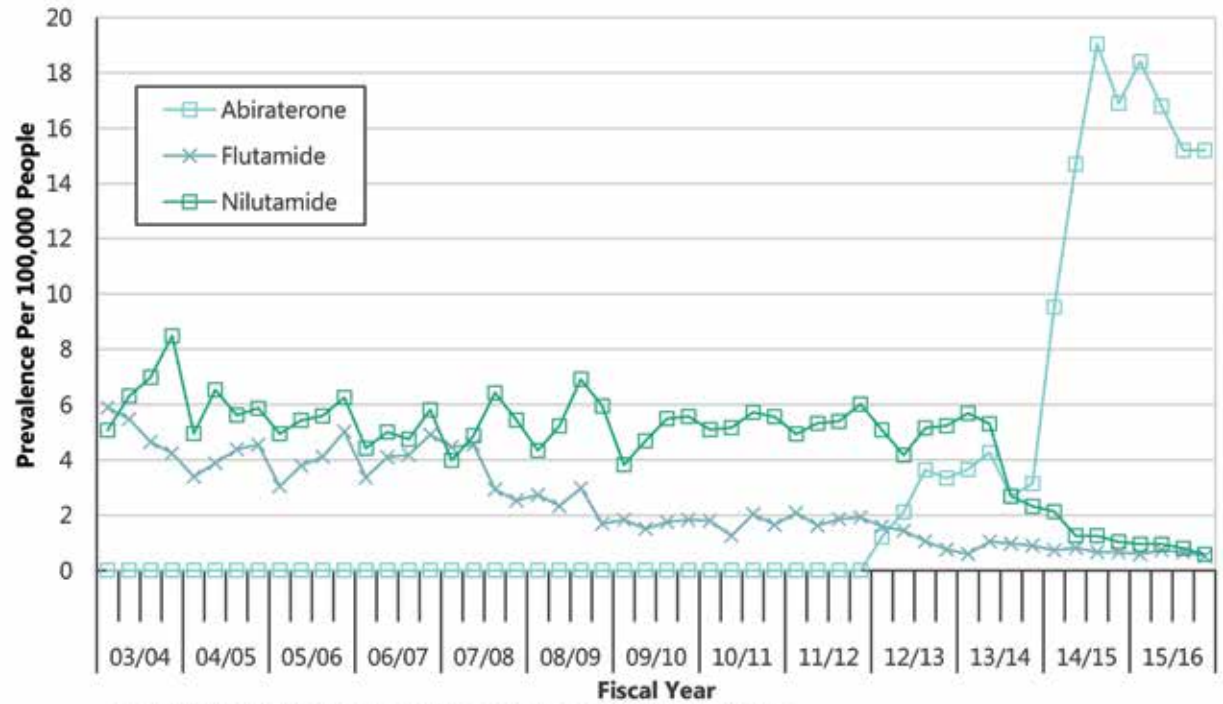
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Axitinib, Gefitinib, Afatanib, Lapatinib, Pazopanib, Regorafenib, Trametinib, Vandetanib, and Vemurafenib are not shown in the figure due to low use, but counts are included in the total.

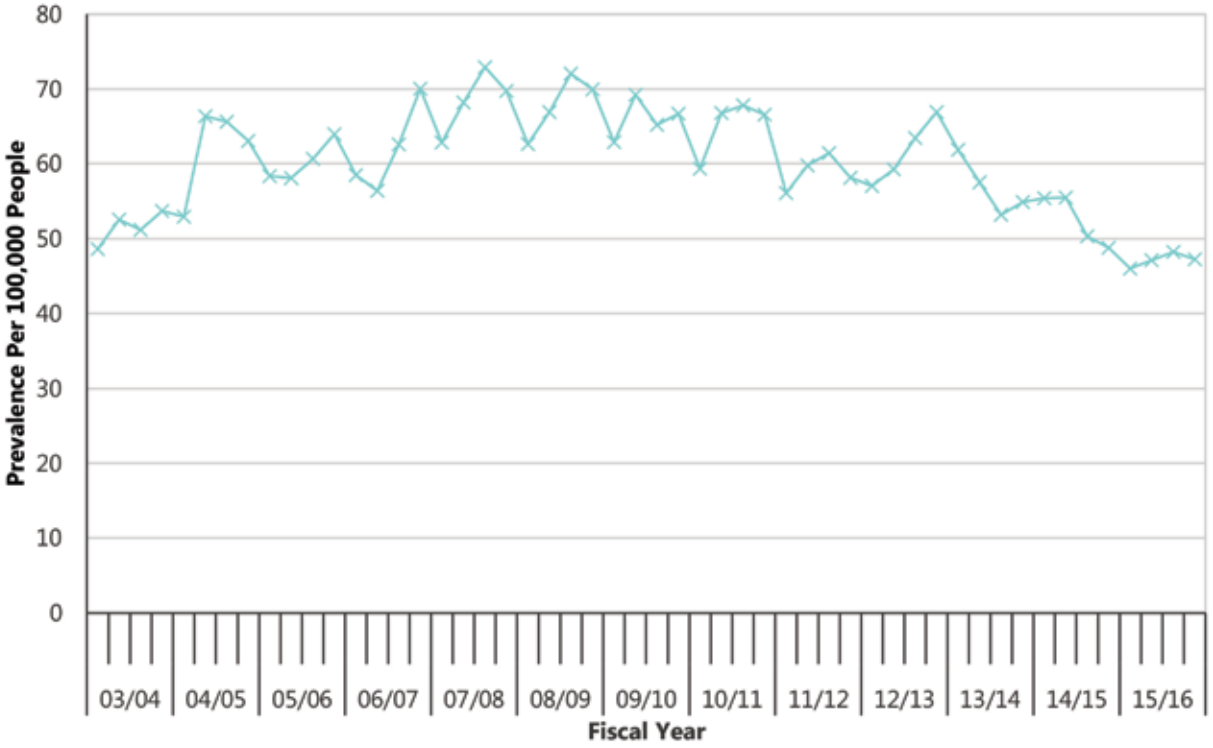
Appendix Figure 1.9: Quarterly Prevalence of Prescriptions for Hormonal Oral Anticancer Agents for Prostate Cancer Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16

Per 100,000 people

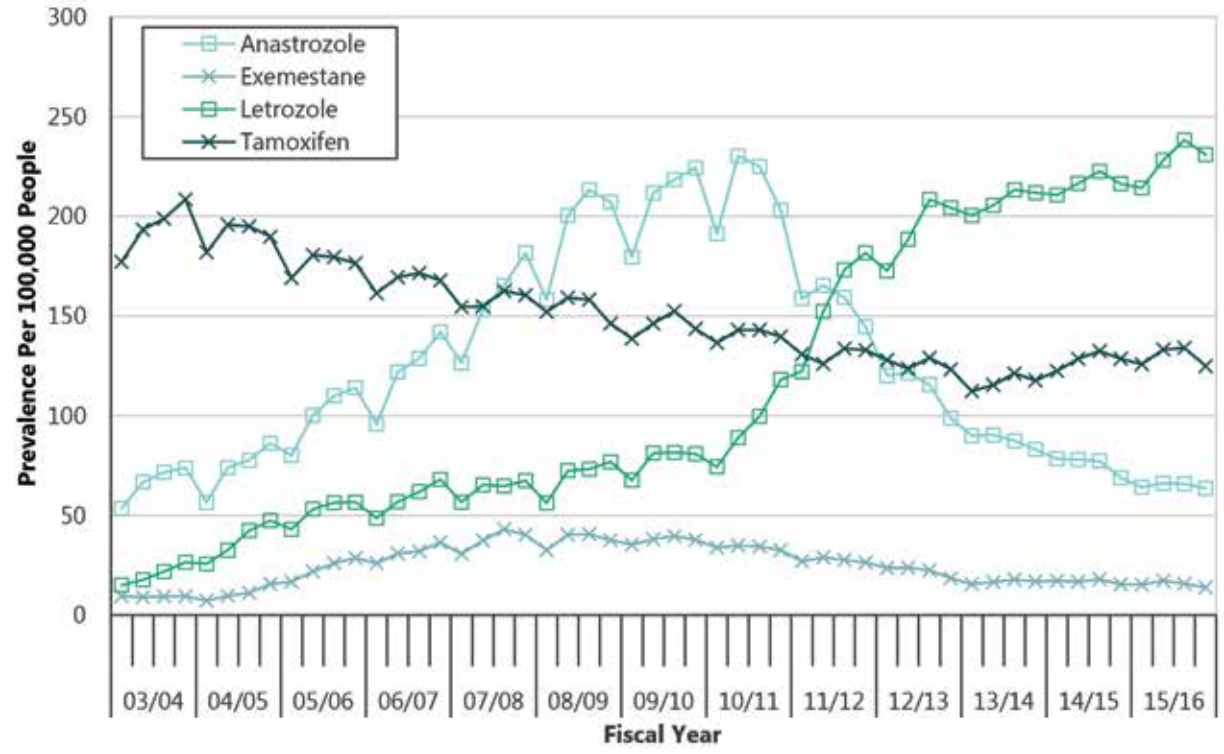


Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Enzalutamide is not shown in the figure due to low use, but counts are included in the total.

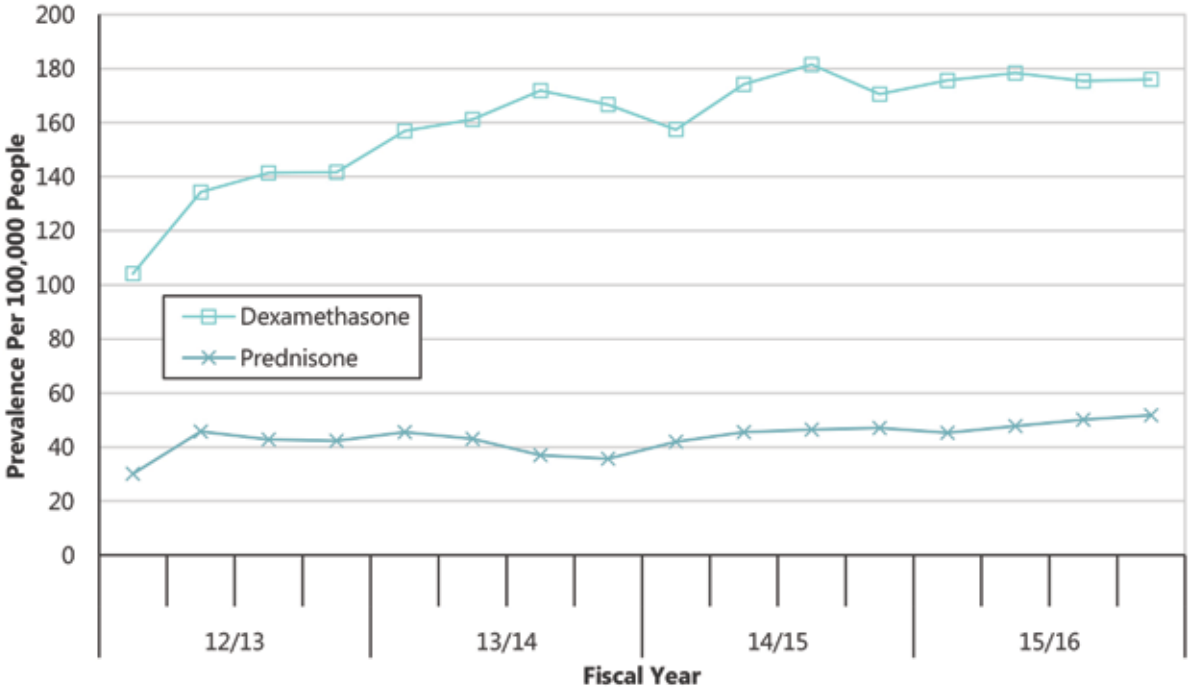
Appendix Figure 1.10: Quarterly Prevalence of Prescriptions for Bicalutamide (Hormonal Oral Anticancer Agent) Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people



Appendix Figure 1.11: Quarterly Prevalence of Prescriptions for Hormonal Oral Anticancer Agents for Breast Cancer Among Manitobans with a Cancer Diagnosis, 2003/04-2015/16
Per 100,000 people

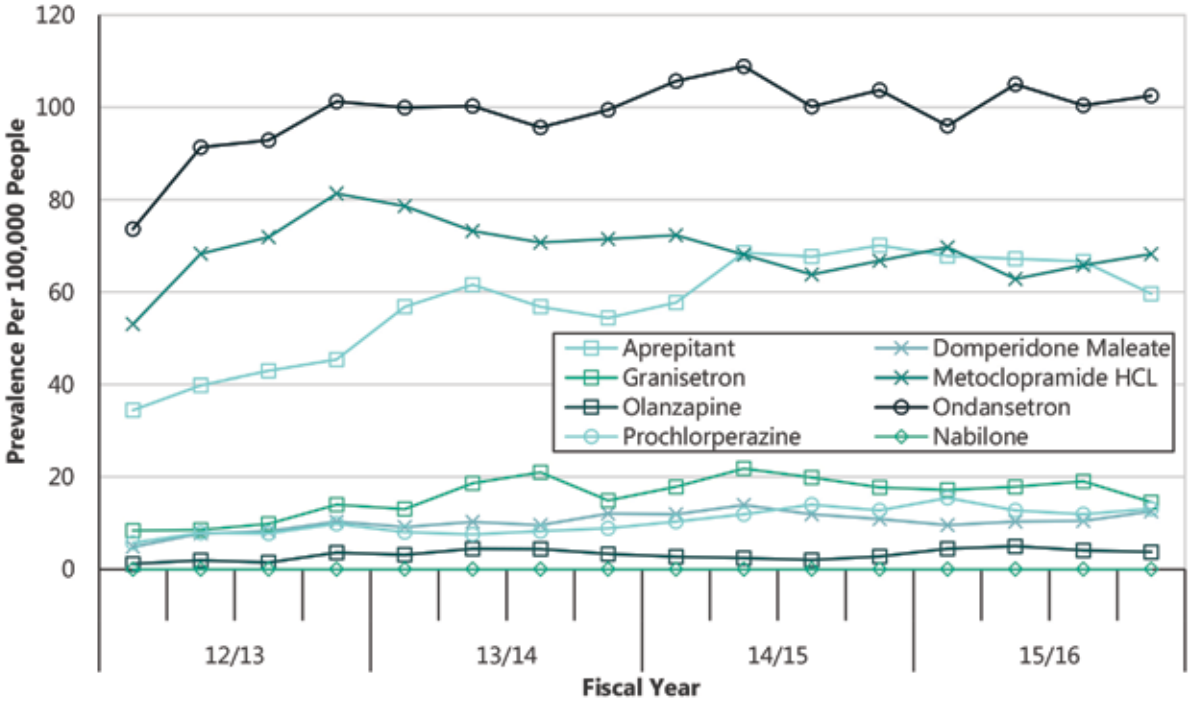


Appendix Figure 1.12: Quarterly Prevalence of Prescriptions for Steroids Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16
Per 100,000 people



Note: Hydrocortisone is not shown in this figure due to limited use, but counts are included in the total.
Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

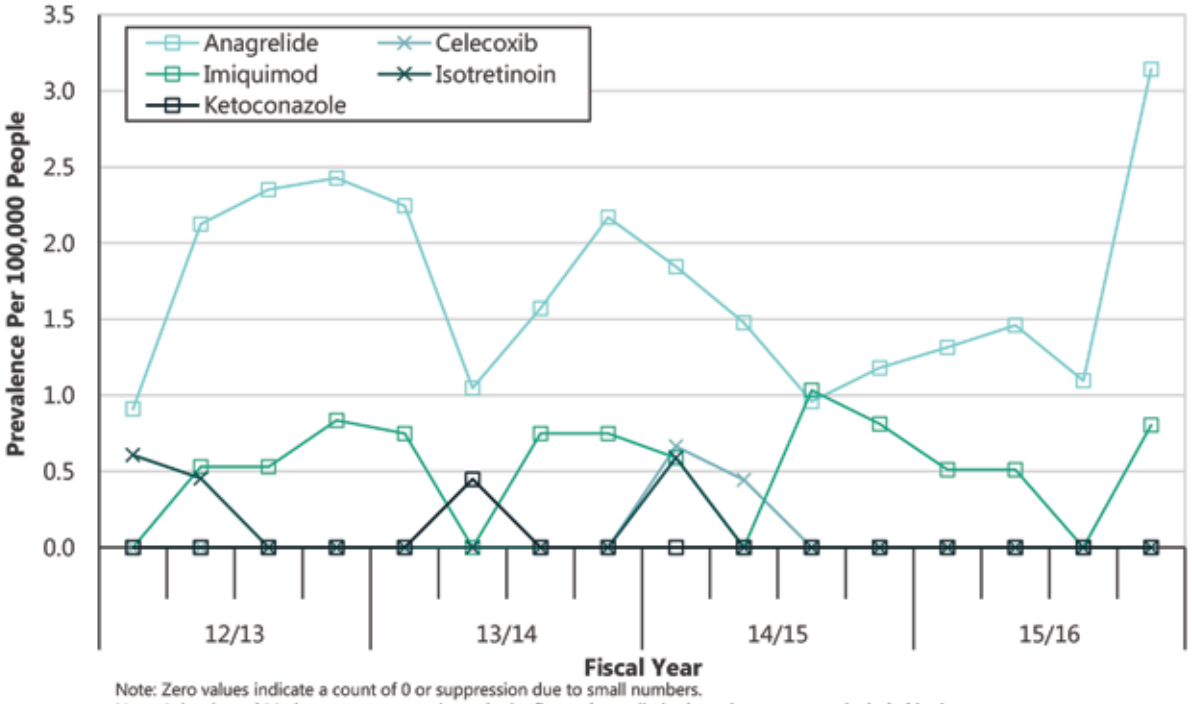
Appendix Figure 1.13: Quarterly Prevalence of Prescriptions for Anti-Nauseant Medications Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

Appendix Figure 1.14: Quarterly Prevalence of Prescriptions for Medications for Disease Treatment Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16

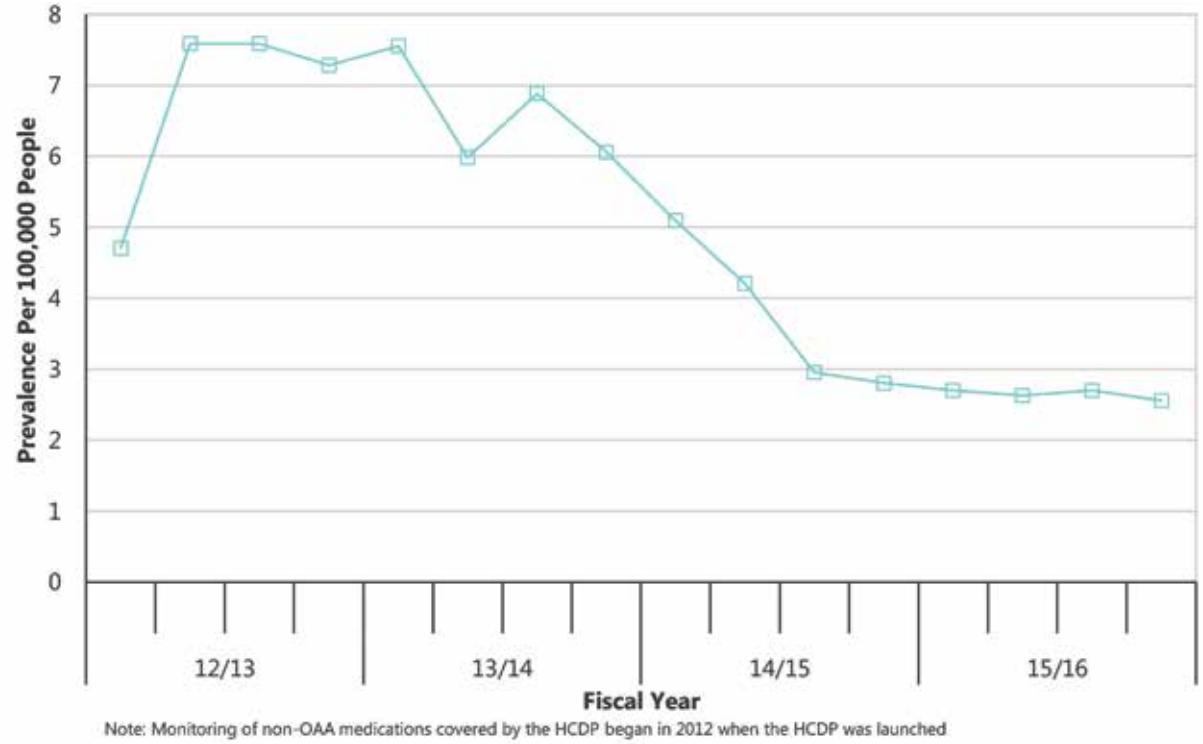
Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Acitretin and Methotrexate are not shown in the figure due to limited use, but counts are included in the total.
Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

Appendix Figure 1.15: Quarterly Prevalence of Prescriptions for Celecoxib (Disease Treatment Home Cancer Drug Program) Prescriptions Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16

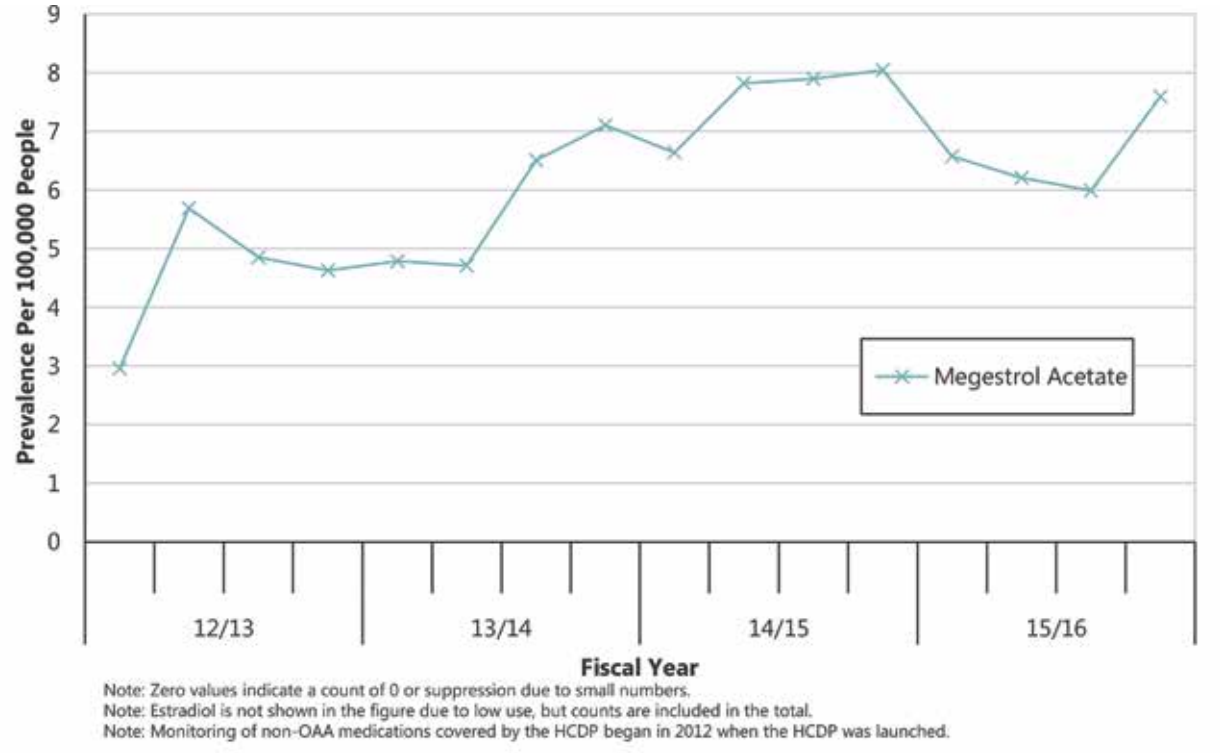
Per 100,000 people



Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched

Appendix Figure 1.16: Quarterly Prevalence of Prescriptions for Supportive Care Medications Among Manitobans with a Cancer Diagnosis, 2012/13-2015/16

Per 100,000 people



Note: Zero values indicate a count of 0 or suppression due to small numbers.
Note: Estradiol is not shown in the figure due to low use, but counts are included in the total.
Note: Monitoring of non-OAA medications covered by the HCDP began in 2012 when the HCDP was launched.

Appendix 2: Demographics for All Manitobans Included in the Prescription Fill Pattern Analysis

Appendix Table 2.1: Patient Demographics of OAA users with a Cancer Diagnosis Included in the Prescription Fill Pattern Analysis, 2004/05-2014/15

	All OAA N=13,858	Traditional N=3,169	Hormonal N=9,959	Targeted N=730
Age at First OAA*				
Mean Age (years)	67.21	63.56	68.77	61.72
Median Age (years)	69	67	70	63
39 Years and Younger	3.34%	8.90%	1.55%	3.70%
40-64	34.93%	35.31%	33.54%	52.33%
65 Years and Older	61.73%	55.79%	64.92%	43.97%
Sex				
Male	43.35%	50.71%	39.92%	58.08%
Female	56.65%	49.29%	60.08%	41.92%
RHA				
Interlake-Eastern RHA	11.47%	10.82%	11.69%	11.23%
Northern Health Region	3.17%	3.98%	2.81%	4.38%
Southern Health-Sante Sud	11.55%	11.23%	11.67%	11.37%
Prairie Mountain Health	15.54%	15.53%	15.92%	10.27%
Winnipeg RHA	58.28%	58.44%	57.92%	62.74%
Socioeconomic Status				
Q1 (Lowest)	18.24%	18.93%	17.98%	18.90%
Q2	22.18%	22.18%	22.37%	19.04%
Q3	21.84%	20.61%	22.34%	20.68%
Q4	17.79%	18.37%	17.55%	19.04%
Q5 (Highest)	18.56%	19%	18.21%	21.10%
Percent of Prescriptions by Payer				
Pharmacare	83.86%	81.67%	83.94%	79%
Nursing Home	6.53%	3.13%	7.87%	0.98%
Employment/Income Assistance	2.84%	2.66%	2.86%	3%
Palliative Care	1.61%	2.53%	1.43%	1.9%
Other**	5.17%	10.01%	3.9%	15.13%

* An individual's first OAA prescription was an OAA prescription filled following at least one year without any prior OAA prescriptions filled.
** This category includes federal public drug benefit programs with separate formularies and coverage such as: First Nations and Inuit Non-Insured Health Benefits, Veterans Affairs Canada, and out-of-pocket or cash prescriptions (these prescriptions may have private insurance coverage) and prescriptions with private insurance.

Appendix 3: Percentage of OAA with Specific Cancer Diagnoses

Appendix Table 3.1: Alkylating Agents (Traditional Oral Anticancer Agents): Diagnosis of Prevalent Users in the Year prior to 1st Prescription by Fiscal Year

Drug Name	Diagnosis	Users of Drug	Percent of Users	Diagnosis	Users of Drug	Percent of Users
	2004/05 (N=219)			2014/15 (N=58)		
Chlorambucil	Oth Malig Neo Of Lymphoid/Hist Tis	119	54.34%	Lymphoid Leukemia	45	77.59%
	Lymphoid Leukemia	92	42.01%	Oth Malig Neo Of Lymphoid/Hist Tis	18	31.03%
	Leukemia Unspecified Cell Type	32	14.61%	Leukemia Unspecified Cell Type	11	18.97%
	Oth Malignant Neoplasm Of Skin	10	4.57%			
	Malig Neo Trachea, Bronchus, Lung	7	3.20%			
	Malignant Neoplasm Of Prostate	6	2.74%			
	2004/05 (N=215)			2014/15 (N=175)		
Cyclophosphamide	Multiple Myeloma,Immunoprolif Neos	56	26.05%	Multiple Myeloma,Immunoprolif Neos	80	45.71%
	Oth Malig Neo Of Lymphoid/Hist Tis	34	15.81%	Oth Malig Neo Of Lymphoid/Hist Tis	29	16.57%
	Malignant Neoplasm - Female Breast	25	11.63%	Lymphosarcoma & Reticulosarcoma	8	4.57%
	Lymphoid Leukemia	13	6.05%	Lymphoid Leukemia	8	4.57%
	Secondary Unsp Malig Neo Lymph Nds	12	5.58%	Malig Neo Trachea, Bronchus, Lung	7	4.00%
	Malig Neo Trachea, Bronchus, Lung	7	3.26%	Oth Malignant Neoplasm Of Skin	7	4.00%
	Malignant Neoplasm Of Prostate	6	2.79%	Malignant Neoplasm - Female Breast	7	4.00%
	Leukemia Unspecified Cell Type	6	2.79%	2Nd Malig Neo Other Specified Site	7	4.00%
	2004/05 (N=99)			2014/15 (N=84)		
Temozolmide	Malignant Neoplasm Of Brain	74	74.75%	Malignant Neoplasm Of Brain	72	85.71%
	Malig Neo Trachea, Bronchus, Lung	15	15.15%			
	2Nd Malig Neo Other Specified Site	12	12.12%			
	Oth Malig Neo Of Lymphoid/Hist Tis	7	7.07%			
	Malig Neo Gallbladder,Extrahep B D	6	6.06%			
	2Nd Malig Neo Respir,Digest System	6	6.06%			

Appendix Table 3.2: Antimetabolites (Traditional Oral Anticancer Agents): Diagnosis of Prevalent Users in the Year prior to 1st Prescription by Fiscal Year

Drug Name	Diagnosis	Users of Drug	Percent of Users	Diagnosis	Users of Drug	Percent of Users
	2004/05 (N=197)			2014/15 (N=344)		
Capecitabine	Malignant Neoplasm Of Colon	101	51.27%	Malignant Neoplasm Of Colon	154	44.77%
	Malignant Neoplasm - Female Breast	91	46.19%	Malig Neo Rectum,Rectosig Jct,Anus	130	37.79%
	Secondary Unsp Malig Neo Lymph Nds	49	24.87%	Malignant Neoplasm - Female Breast	114	33.14%
	2Nd Malig Neo Respir,Digest System	45	22.84%	2Nd Malig Neo Other Specified Site	75	21.80%
	Malig Neo Rectum,Rectosig Jct,Anus	36	18.27%	2Nd Malig Neo Respir,Digest System	67	19.48%
	2Nd Malig Neo Other Specified Site	28	14.21%	Secondary Unsp Malig Neo Lymph Nds	49	14.24%
	Malig Neo Oth Digest Orgns/Periton	13	6.60%	Malignant Neoplasm Of Stomach	20	5.81%
	Malignant Neoplasm W/O Site Specif	13	6.60%	Malignant Neoplasm W/O Site Specif	18	5.23%
	Malig Neo Trachea, Bronchus, Lung	8	4.06%	Malig Neo Liver,Intrahepat Bile Dt	16	4.65%
	Malignant Neoplasm Of Stomach	6	3.05%	Oth Malignant Neoplasm Of Skin	15	4.36%
				Malig Neo Oth Digest Orgns/Periton	12	3.49%
				Malig Neo Trachea, Bronchus, Lung	12	3.49%
				Malig Neo Gallbladder,Extrahep B D	10	2.91%
				Malignant Neoplasm Of Esophagus	8	2.33%
				Malignant Neoplasm Of Pancreas	8	2.33%
	2004/05 (N=299)			2014/15 (N=179)		
Mercaptopurine	Leukemia Unspecified Cell Type	44	14.72%	Lymphoid Leukemia	49	27.37%
	Lymphoid Leukemia	37	12.37%	Leukemia Unspecified Cell Type	28	15.64%
	Oth Malig Neo Of Lymphoid/Hist Tis	8	2.68%	Oth Malig Neo Of Lymphoid/Hist Tis	15	8.38%
	Monocytic Leukemia	8	2.68%			
	Myeloid Leukemia	7	2.34%			

Appendix Table 3.3: Other Older Anticancer Agents (Traditional Oral Anticancer Agents): Diagnosis of Prevalent Users in the Year prior to 1st Prescription by Fiscal Year

Drug Name	Diagnosis	Users of Drug	Percent of Users	Diagnosis	Users of Drug	Percent of Users
Hydroxyurea	2004/05 (N=409)			2014/15 (N=484)		
	Leukemia Unspecified Cell Type	28	6.85%	Myeloid Leukemia	32	6.61%
	Myeloid Leukemia	27	6.60%	Oth Malignant Neoplasm Of Skin	18	3.72%
	Monocytic Leukemia	20	4.89%	Leukemia Unspecified Cell Type	15	3.10%
	Lymphoid Leukemia	17	4.16%	Malignant Neoplasm Of Prostate	9	1.86%
	Malignant Neoplasm - Female Breast	9	2.20%	Lymphoid Leukemia	9	1.86%
	Oth Malig Neo Of Lymphoid/Hist Tis	9	2.20%	Malignant Neoplasm - Female Breast	6	1.24%
	Malignant Neoplasm Of Brain	8	1.96%			
	Malignant Neoplasm Of Prostate	7	1.71%			
	Malig Neo Trachea, Bronchus, Lung	6	1.47%			
	Oth Malignant Neoplasm Of Skin	6	1.47%			
Tretinoin	2010/11 (N=8)			2014/15 (N=6)		
	Myeloid Leukemia	8	100.00%	Myeloid Leukemia	6	100.00%
	Leukemia Unspecified Cell Type	8	100.00%			

Appendix Table 3.4: Protein Kinase Inhibitors for Haematological Malignancies (Targeted Oral Anticancer Agents): Diagnosis of Prevalent Users in the Year prior to 1st Prescription by Fiscal Year

Drug Name	Diagnosis	Users of Drug	Percent of Users	Diagnosis	Users of Drug	Percent of Users
Dasatinib	2008/09 (N=7)			2014/15 (N=39)		
	Myeloid Leukemia	6	85.71%	Myeloid Leukemia	35	89.74%
				Leukemia Unspecified Cell Type	10	25.64%
				Lymphoid Leukemia	8	20.51%
Imatinib	2004/05 (N=58)			2014/15 (N=175)		
	Myeloid Leukemia	29	50.00%	Myeloid Leukemia	118	67.43%
	Monocytic Leukemia	23	39.66%	Leukemia Unspecified Cell Type	24	13.71%
	Leukemia Unspecified Cell Type	20	34.48%	Malignant Neoplasm Of Stomach	17	9.71%
	Lymphoid Leukemia	19	32.76%	Lymphoid Leukemia	13	7.43%
	Malignant Neoplasm Of Stomach	11	18.97%	Malig Neo Oth Digest Orgns/Periton	8	4.57%
				2Nd Malig Neo Respir,Digest System	8	4.57%
Nilotinib	2011/12 (N=8)			2014/15 (N=13)		
	Myeloid Leukemia	8	100.00%	Myeloid Leukemia	12	92.31%

Appendix Table 3.5: Protein Kinase Inhibitors for Solid Tumours (Targeted Oral Anticancer Agents): Diagnosis of Prevalent Users in the Year prior to 1st Prescription by Fiscal Year

Drug Name	Diagnosis	Users of Drug	Percent of Users	Diagnosis	Users of Drug	Percent of Users
Erlotinib	2006/07 (N=17)			2014/15 (N=64)		
	Malig Neo Trachea, Bronchus, Lung	16	94.12%	Malig Neo Trachea, Bronchus, Lung	64	100.00%
				2Nd Malig Neo Respir,Digest System	22	34.38%
				2Nd Malig Neo Other Specified Site	17	26.56%
				Secondary Unsp Malig Neo Lymph Nds	7	10.94%
Sorafenib	2008/09 (N=10)			2014/15 (N=17)		
	Malig Neo Liver,Intrahepat Bile Dt	6	60.00%	Malig Neo Liver,Intrahepat Bile Dt	10	58.82%
	Malig Neo Kidney,Oth Unsp Urin Or	6	60.00%			
Sunitinib	2006/07(N=11)			2014/15 (N=64)		
	Malig Neo Kidney,Oth Unsp Urin Or	10	90.91%	Malig Neo Kidney,Oth Unsp Urin Or	54	84.38%
				2Nd Malig Neo Other Specified Site	21	32.81%
				2Nd Malig Neo Respir,Digest System	16	25.00%
				Malig Neo Trachea, Bronchus, Lung	8	12.50%
				Malignant Neoplasm W/O Site Specif	7	10.94%
				Malignant Neoplasm Of Bladder	6	9.38%
Afatanib	2014/15 (N=7)					
	Malig Neo Trachea, Bronchus, Lung	7	100.00%			
Darafenib	2013/14 (N=8)			2014/15 (N=16)		
	Malignant Melanoma Of Skin	8	100.00%	Malignant Melanoma Of Skin	16	100.00%
Gefitnib	2014/15 (N=7)					
	Malig Neo Trachea, Bronchus, Lung	7	100.00%			
Pazopanib	2013/14 (N=8)			2014/15 (N=6)		
	Malig Neo Connective/Oth Soft Tiss	6	75.00%	Malig Neo Connective/Oth Soft Tiss	6	100.00%
Vemurafenib	2013/14 (N=8)			2014/15 (N=8)		
	Malignant Melanoma Of Skin	8	100.00%	Malignant Melanoma Of Skin	6	75.00%

Appendix Table 3.6: Everolimus (Targeted Oral Anticancer Agents): Diagnosis of Prevalent Users in the Year prior to 1st Prescription by Fiscal Year

Drug Name	Diagnosis	Users of Drug	Percent of Users	Diagnosis	Users of Drug	Percent of Users
Everolimus	2011/12 (N=10)			2013/14 (N=23)		
	Malig Neo Kidney,Oth Unsp Urin Or	8	80.00%	Malig Neo Kidney,Oth Unsp Urin Or	17	73.91%
				2Nd Malig Neo Other Specified Site	9	39.13%
				2Nd Malig Neo Respir,Digest System	7	30.43%

Appendix Table 3.7: Estrogen Receptor Positive Breast Cancer (Hormonal Oral Anticancer Agents): Diagnosis of Prevalent Users in the Year prior to 1st Prescription by Fiscal Year

Drug Name	Diagnosis	Users of Drug	Percent of Users	Diagnosis	Users of Drug	Percent of Users
Anastrozole	2004/05 (N=520)			2014/15 (N=615)		
	Malignant Neoplasm - Female Breast	499	95.96%	Malignant Neoplasm - Female Breast	495	80.49%
	Secondary Unsp Malig Neo Lymph Nds	55	10.58%	Secondary Unsp Malig Neo Lymph Nds	28	4.55%
	2Nd Malig Neo Other Specified Site	30	5.77%	2Nd Malig Neo Other Specified Site	19	3.09%
	Oth Malignant Neoplasm Of Skin	19	3.65%			
	Malig Neo Trachea, Bronchus, Lung	13	2.50%			
	Malignant Neoplasm W/O Site Specif	13	2.50%			
	2Nd Malig Neo Respir,Digest System	12	2.31%			
Exemestane	2004/05 (N=116)			2014/15 (N=114)		
	Malignant Neoplasm - Female Breast	114	98.28%	Malignant Neoplasm - Female Breast	129	89.58%
	2Nd Malig Neo Other Specified Site	25	21.55%	2Nd Malig Neo Other Specified Site	33	22.92%
	2Nd Malig Neo Respir,Digest System	15	12.93%	Secondary Unsp Malig Neo Lymph Nds	11	7.64%
	Malignant Neoplasm W/O Site Specif	11	9.48%	2Nd Malig Neo Respir,Digest System	11	7.64%
	Secondary Unsp Malig Neo Lymph Nds	7	6.03%			
Letrozole	2004/05 (N=458)			2014/15 (N=2,923)		
	Malignant Neoplasm - Female Breast	324	70.74%	Malignant Neoplasm - Female Breast	1,644	56.24%
	2Nd Malig Neo Other Specified Site	35	7.64%	Secondary Unsp Malig Neo Lymph Nds	129	4.41%
	Malig Neo Trachea, Bronchus, Lung	17	3.71%	2Nd Malig Neo Other Specified Site	81	2.77%
	2Nd Malig Neo Respir,Digest System	17	3.71%			
	Secondary Unsp Malig Neo Lymph Nds	15	3.28%			
	Malignant Neoplasm W/O Site Specif	11	2.40%			
Tamoxifen	2004/05 (N=2,059)			2014/15 (N=1,344)		
	Malignant Neoplasm - Female Breast	1,784	86.64%	Malignant Neoplasm - Female Breast	1,091	81.18%
	Secondary Unsp Malig Neo Lymph Nds	148	7.19%	Secondary Unsp Malig Neo Lymph Nds	81	6.03%
				2Nd Malig Neo Other Specified Site	60	4.46%
				Malig Neo Ovary,Oth Uterine Adnexa	28	2.08%
				Malignant Neoplasm Body Of Uterus	27	2.01%

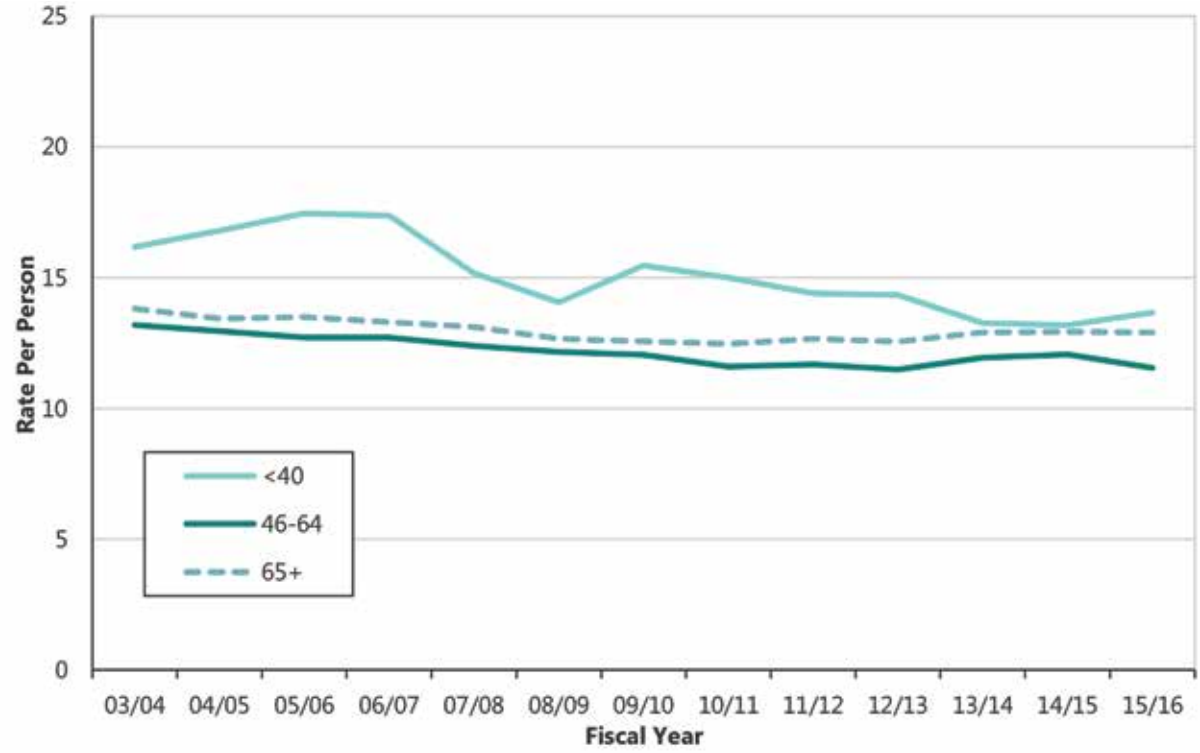
Appendix Table 3.8: Prostate Drugs (Hormonal Oral Anticancer Agents): Diagnosis of Prevalent Users in the Year prior to 1st Prescription by Fiscal Year

Drug Name	Diagnosis	Users of Drug	Percent of Users	Diagnosis	Users of Drug	Percent of Users
Abiraterone	2012/13 (N=27)			2014/15 (N=141)		
	Malignant Neoplasm Of Prostate	27	100.00%	Malignant Neoplasm Of Prostate	141	100.00%
	2Nd Malig Neo Other Specified Site	11	40.74%	2Nd Malig Neo Other Specified Site	53	37.59%
				Malignant Neoplasm Of Bladder	6	4.26%
Bicalutamide	2004/05 (N=742)			2014/15 (N=969)		
	Malignant Neoplasm Of Prostate	664	89.49%	Malignant Neoplasm Of Prostate	917	94.63%
	2Nd Malig Neo Other Specified Site	35	4.72%	2Nd Malig Neo Other Specified Site	63	6.50%
	Oth Malignant Neoplasm Of Skin	30	4.04%	Oth Malignant Neoplasm Of Skin	40	4.13%
				Malignant Neoplasm Of Bladder	25	2.58%
Flutamide	2004/05 (N=33)			2013/14 (N=10)		
	Malignant Neoplasm Of Prostate	22	66.67%	Malignant Neoplasm Of Prostate	7	70.00%
Nilutamide	2004/05 (N=94)			2014/15 (N=969)		
	Malignant Neoplasm Of Prostate	88	93.62%	Malignant Neoplasm Of Prostate	16	84.21%

Appendix 4: Ambulatory Visit Rates Among Manitobans with a Cancer Diagnosis

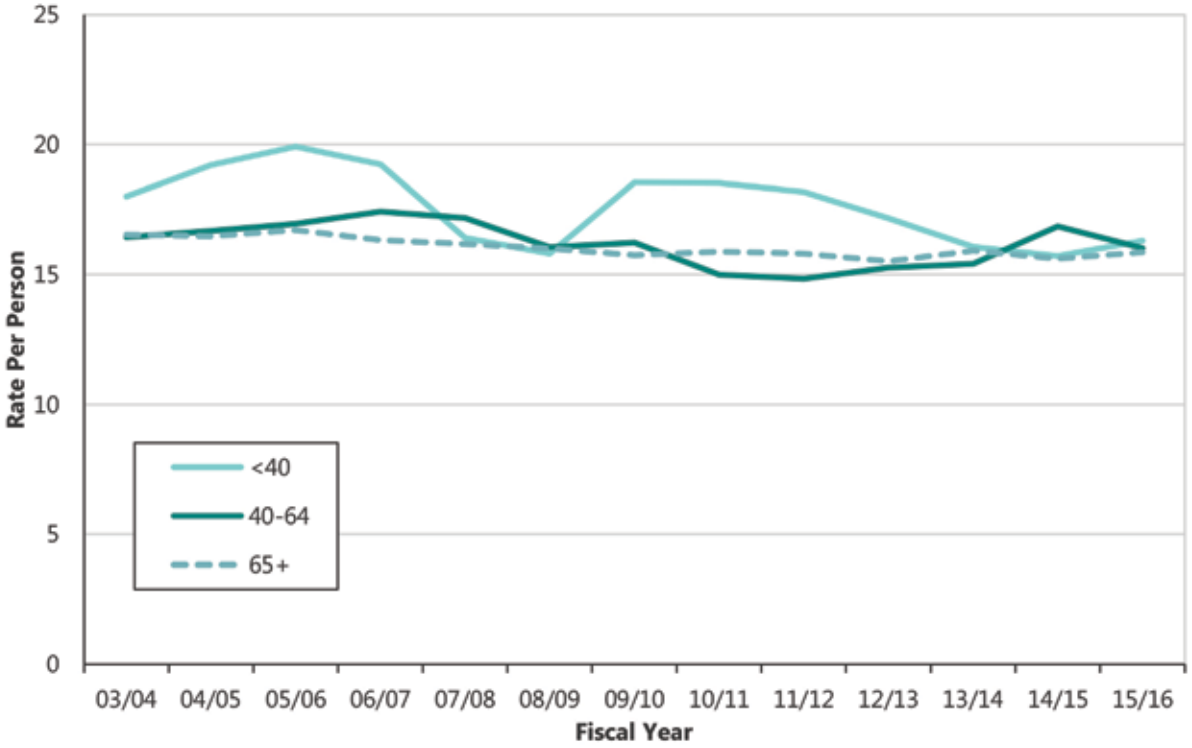
Appendix Figure 4.1: Annual Ambulatory Visit Rate for Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Age Group, 2003/04-2015/16

Rate per user



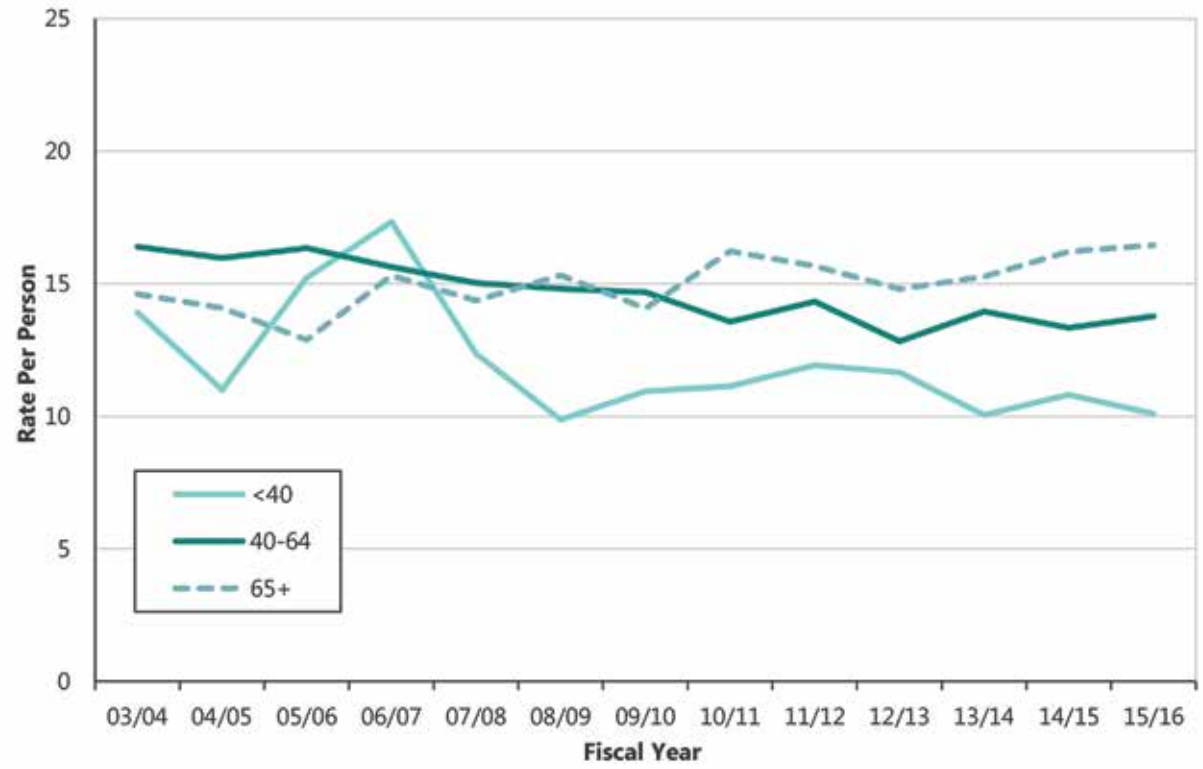
Appendix Figure 4.2: Annual Ambulatory Visit Rate for Traditional Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Age Group, 2003/04-2015/16

Rate per user



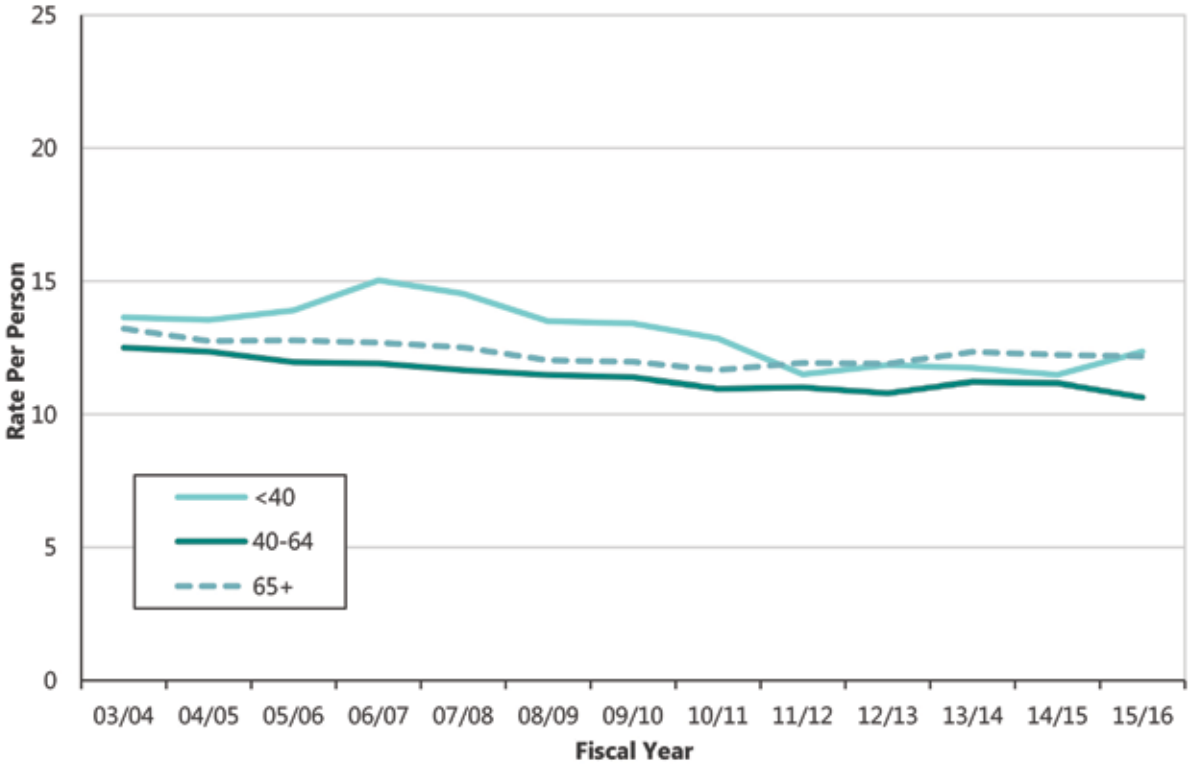
Appendix Figure 4.3: Annual Ambulatory Visit Rate for Targeted Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Age Group, 2003/04-2015/16

Rate per user



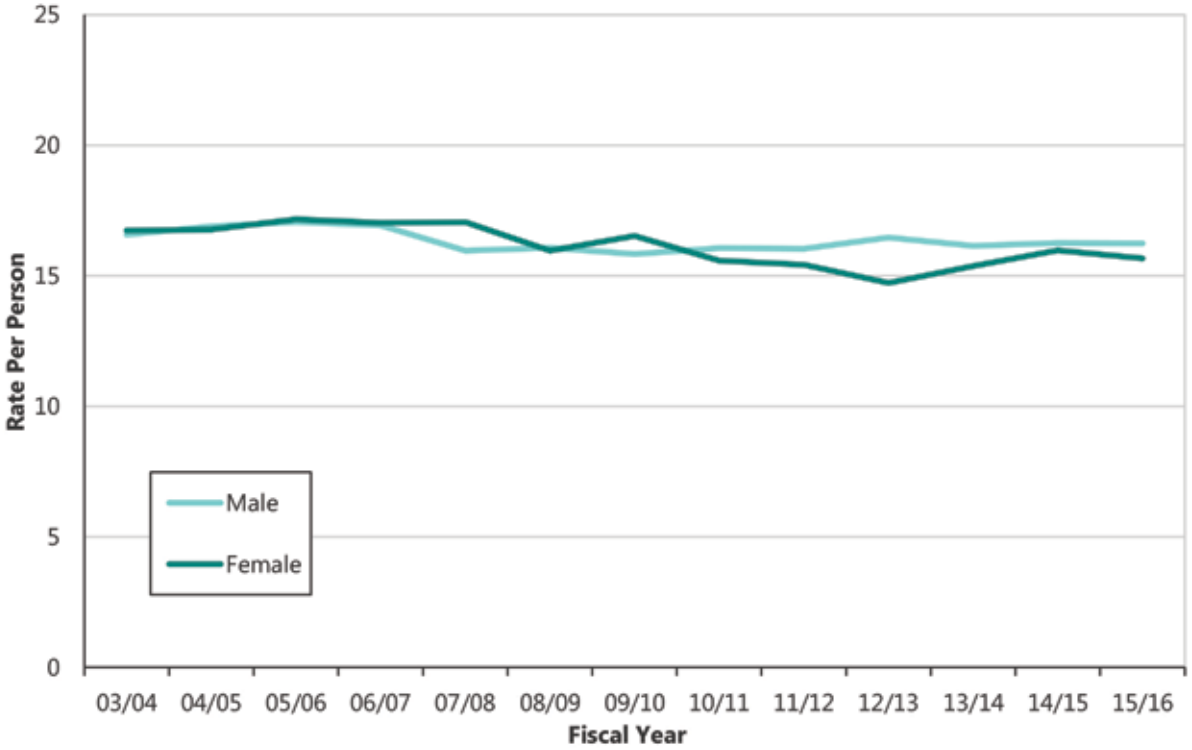
Appendix Figure 4.4: Annual Ambulatory Visit Rate for Hormonal Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Age Group, 2003/04-2015/16

Rate per user



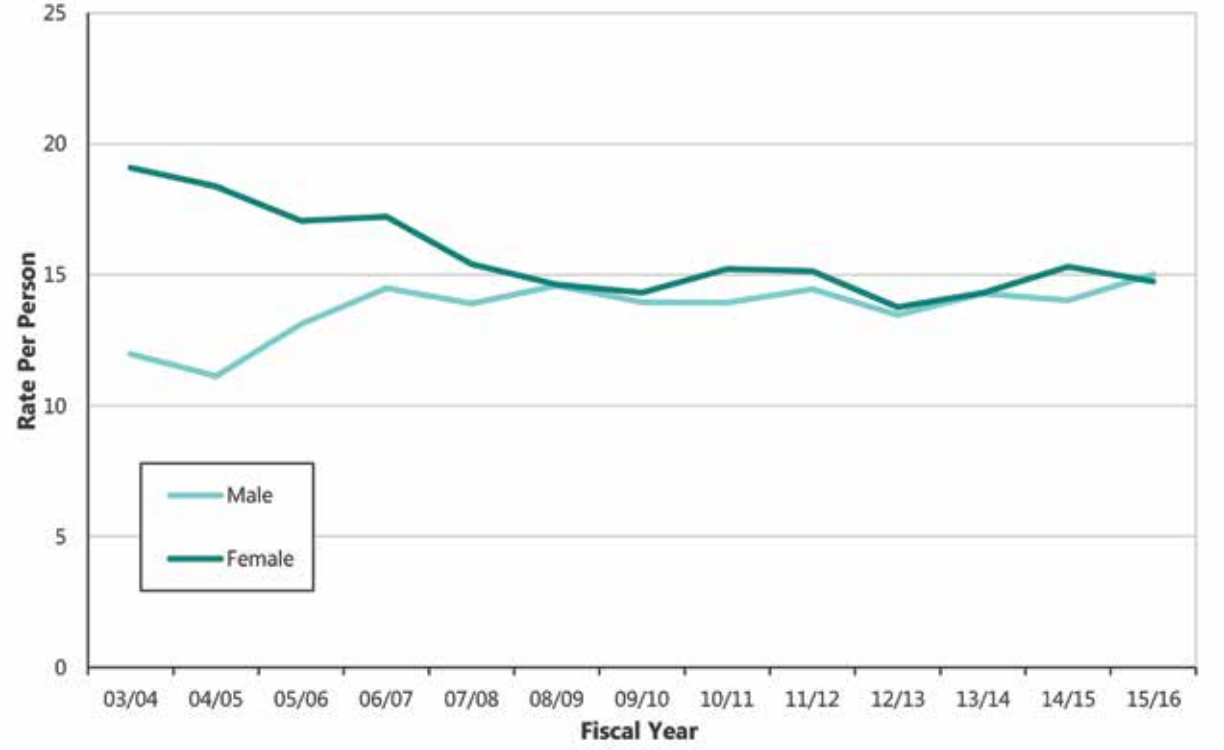
Appendix Figure 4.5: Annual Ambulatory Visit Rate for Traditional Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Sex, 2003/04-2015/16

Rate per user



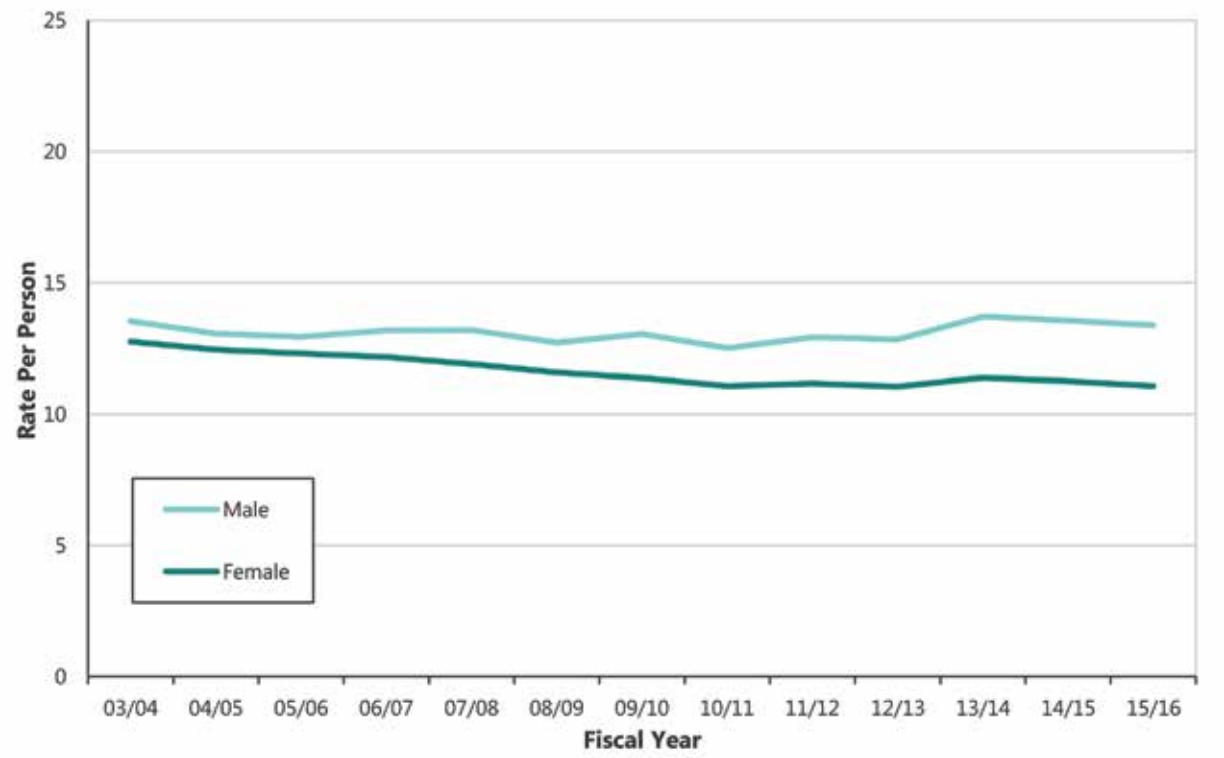
Appendix Figure 4.6: Annual Ambulatory Visit Rate for Targeted Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Sex, 2003/04-2015/16

Rate per user



Appendix Figure 4.7: Annual Ambulatory Visit Rate for Hormonal Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Sex, 2003/04-2015/16

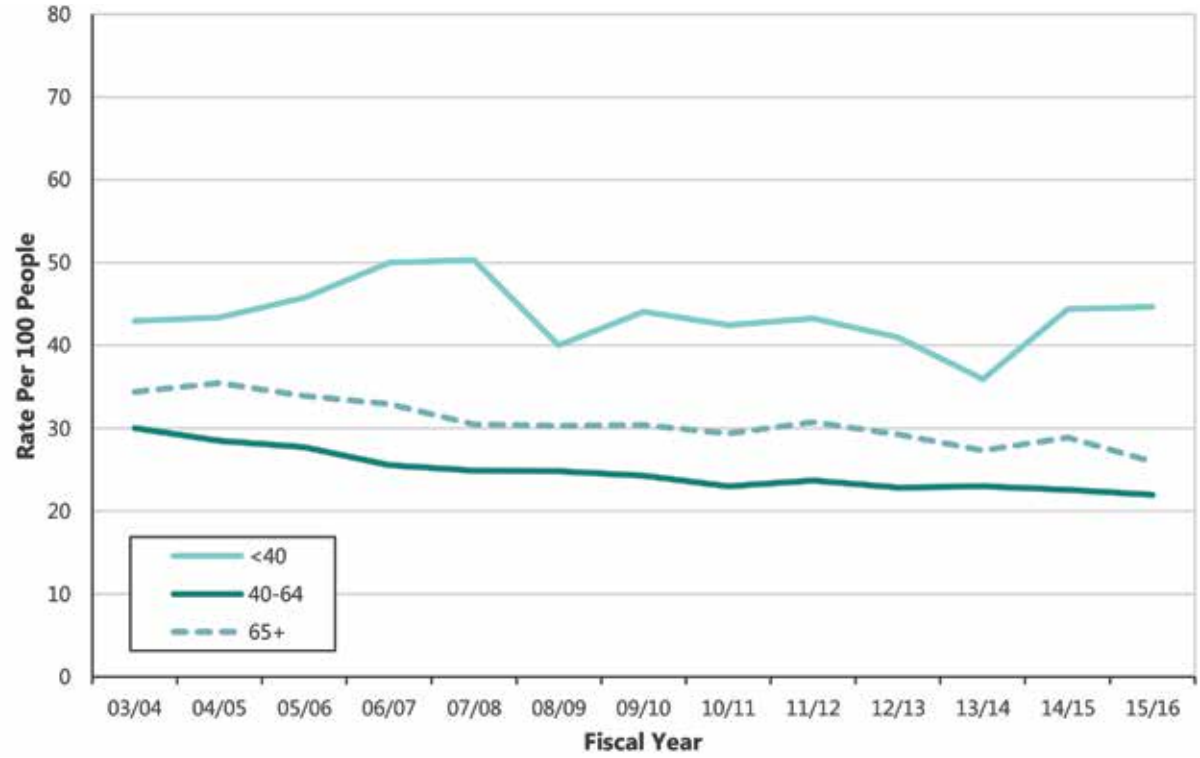
Rate per user



Appendix 5: Inpatient Hospitalization Rate Among Manitobans with a Cancer Diagnosis

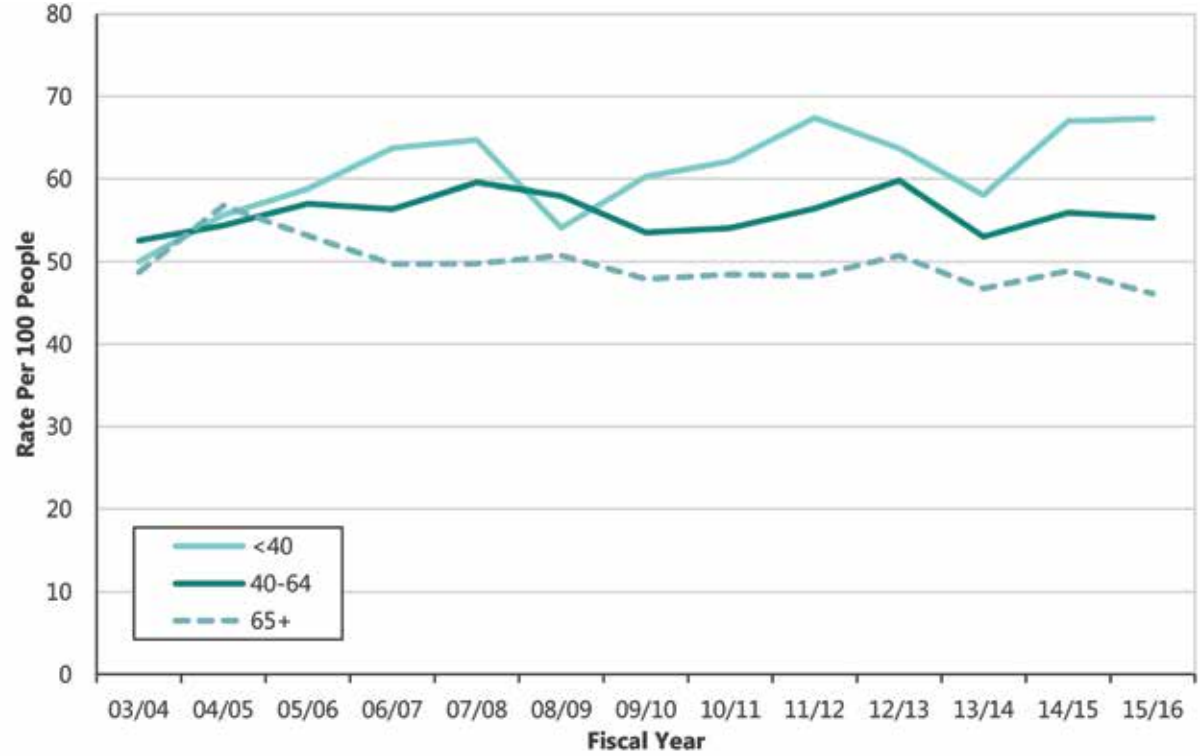
Appendix Figure 5.1: Crude Inpatient Hospitalization Rate for Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Age Group, 2003/04-2015/16

Per 100 people



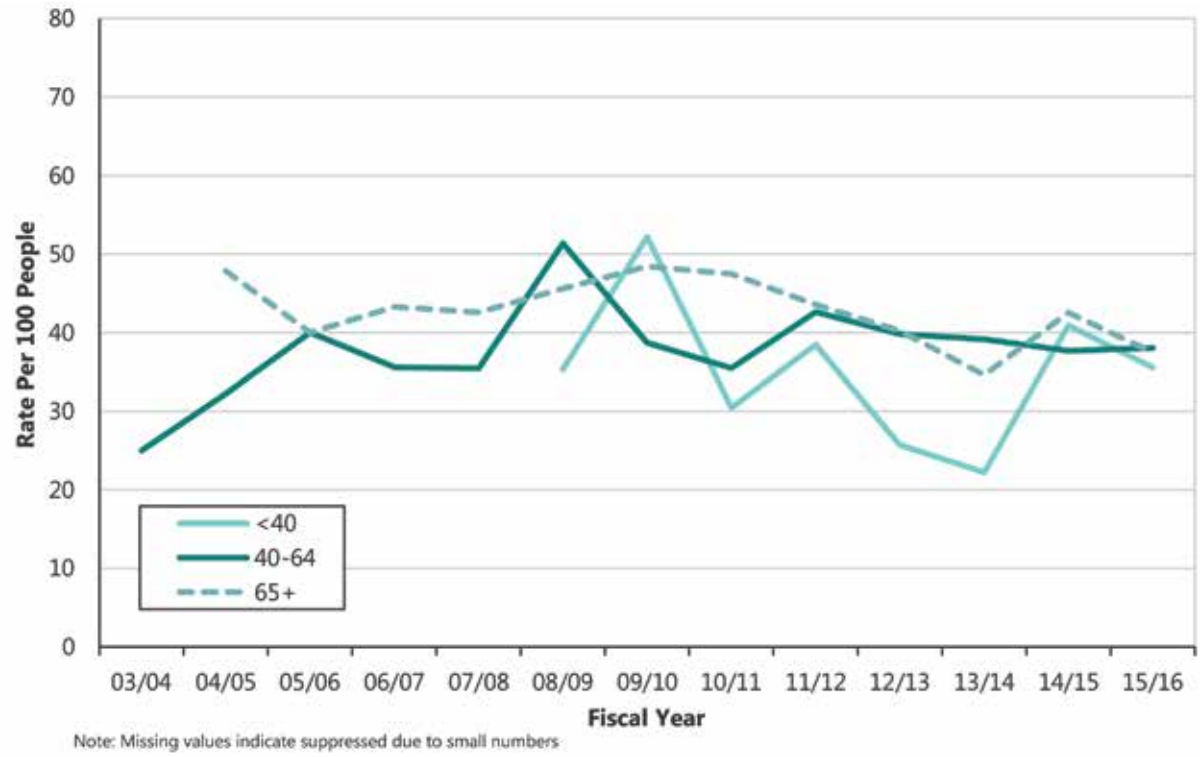
Appendix Figure 5.2: Crude Inpatient Hospitalization Rate for Traditional Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Age Group, 2003/04-2015/16

Per 100 people



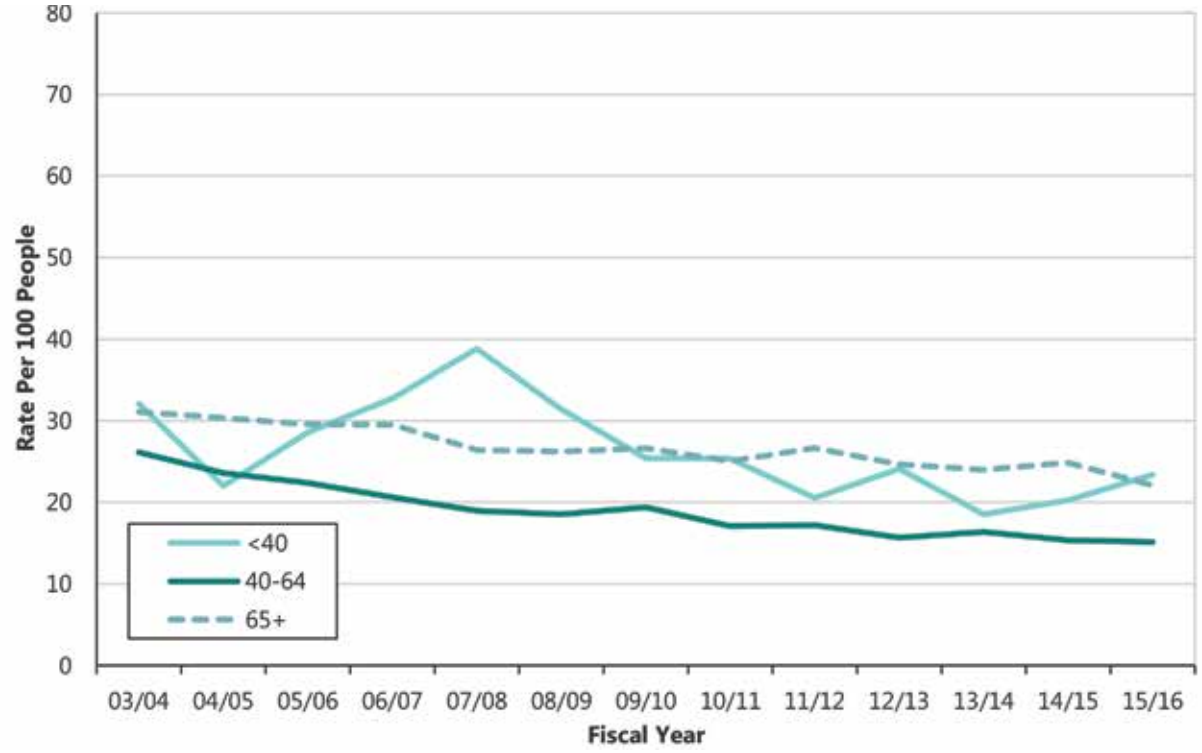
Appendix Figure 5.3: Crude Inpatient Hospitalization Rate for Targeted Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Age Group, 2003/04-2015/16

Per 100 people



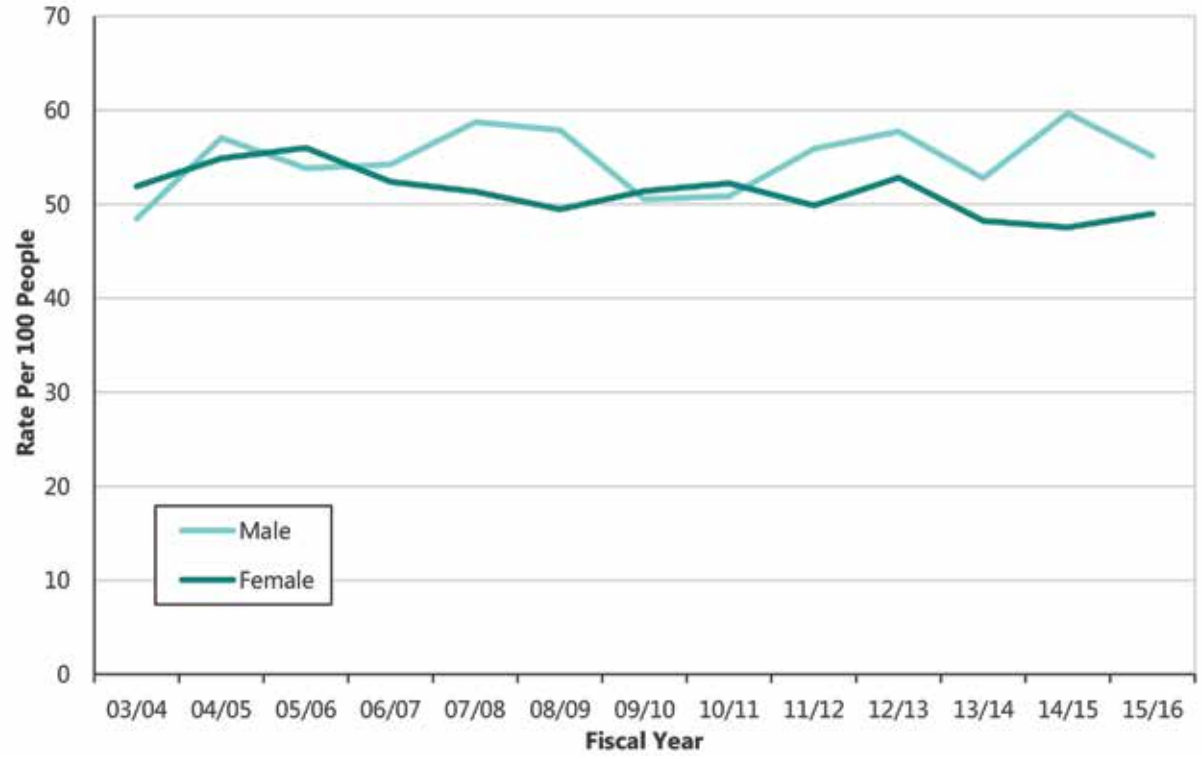
Appendix Figure 5.4: Crude Inpatient Hospitalization Rate for Hormonal Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Age Group, 2003/04-2015/16

Per 100 people

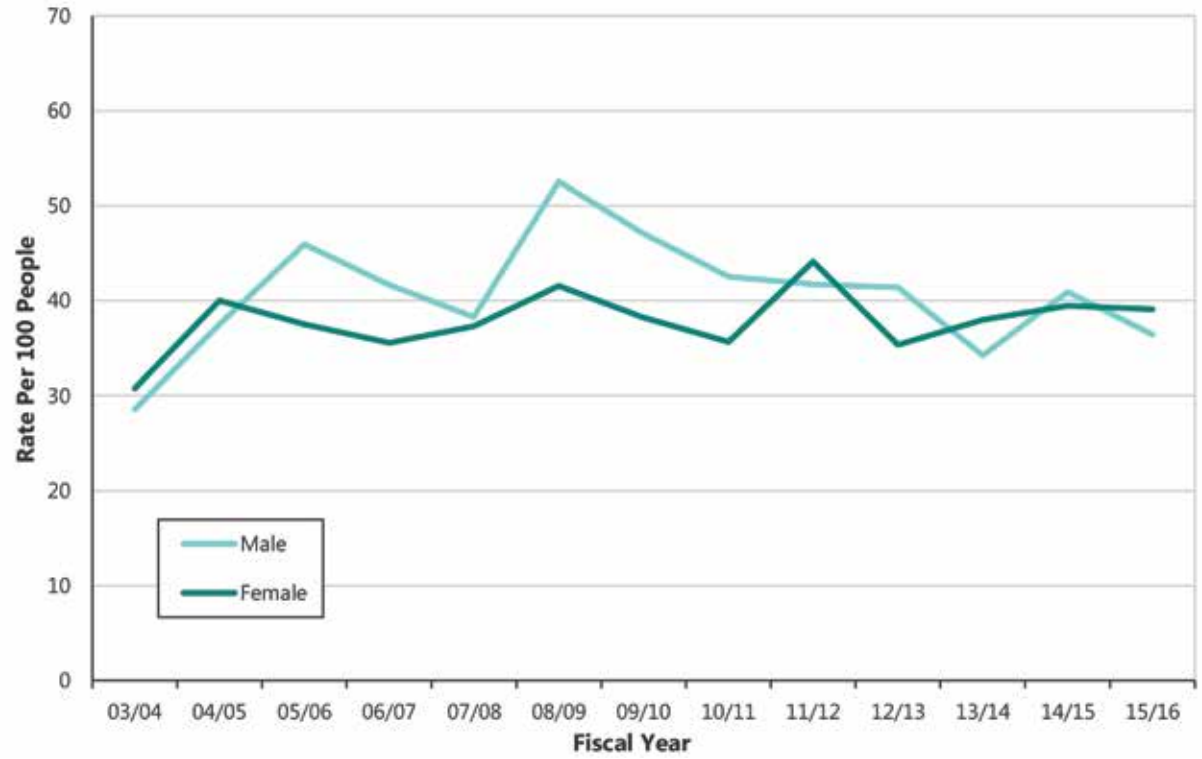


Appendix Figure 5.5: Crude Inpatient Hospitalization Rate for Traditional Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Sex, 2003/04-2015/16

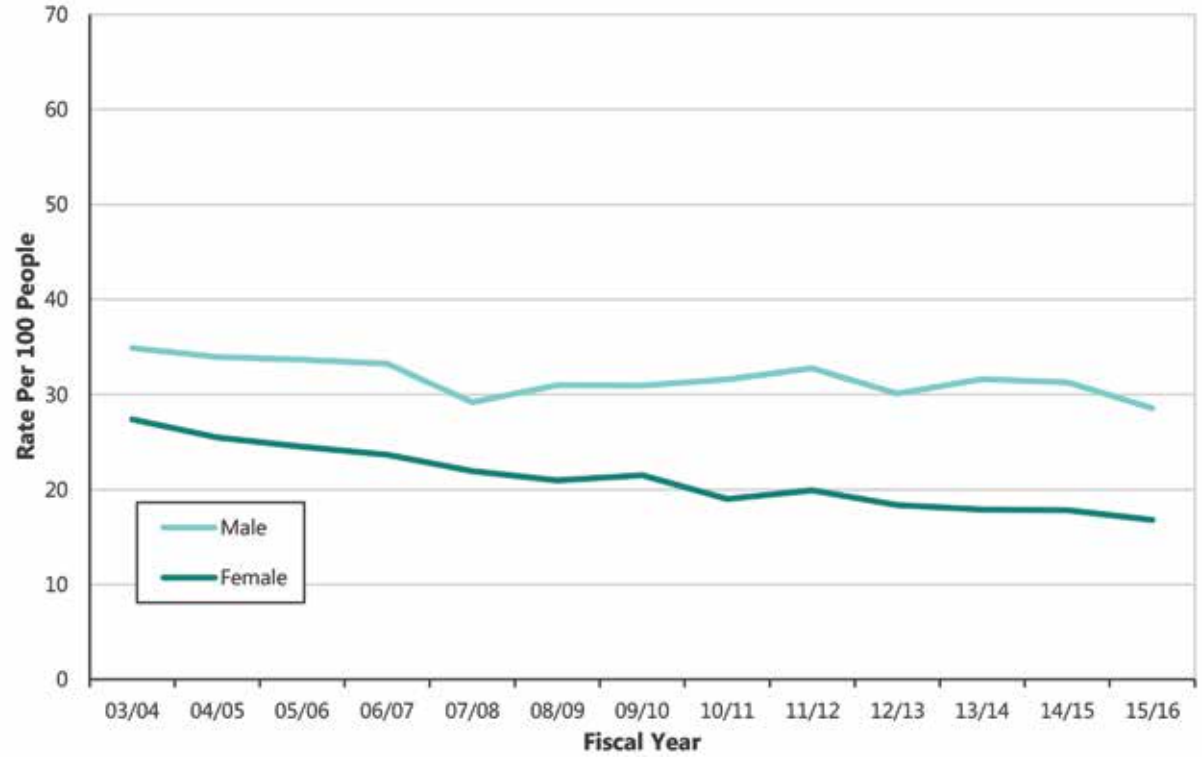
Per 100 people



Appendix Figure 5.6: Crude Inpatient Hospitalization Rate for Targeted Oral Anticancer Agent Users by sex, 2003/04-2015/16
Per 100 people



Appendix Figure 5.7: Crude Inpatient Hospitalization Rate for Hormonal Oral Anticancer Agent Users Among Manitobans with a Cancer Diagnosis by Sex, 2003/04-2015/16
Per 100 people



University of Manitoba | Rady Faculty of Health Sciences

Manitoba Centre for Health Policy

Data | Insight | Informing Solutions

University of Manitoba
Max Rady College of Medicine
Rady Faculty of Health Sciences

408-727 McDermot Avenue
Winnipeg, Manitoba, Canada
R3E 3P5

Tel: (204) 789-3819
Fax: (204) 789-3910
Email: reports@cpe.umanitoba.ca

www.mchp.ca