TWO-DIMENSION OLIGOPOLISTIC PRODUCT DIFFERENTIATION AND A MULTILEVEL MODEL OF CANADIAN PRESCRIPTION DRUG PRICE DYNAMICS

by
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Dedication

This thesis is dedicated to my wife, Rong. I wouldn't have achieved what I have today without her selfless and loving support.

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Abstract

Prescription drugs play an increasingly significant role in the Canadian healthcare system. Drug spending accounts for a considerable share of total healthcare expenditure and continues to be one of the fastest growing expenditure components in Canada. But, drug manufacturers' price setting behaviours are not well understood in the literature.

I develop a framework of oligopoly theory with two-dimension product differentiation based on a synthesis of the literature on the institutional history and development of the Canadian pharmaceutical system. I find that: (1) The differentiation in perceived quality between brand-name and generic drugs can explain the generic competition paradox. The degree of the product differentiation can be pivotal in shaping the brand-name drug manufacturers' price setting behaviours in response to the shift in patients' preference and changes in government policies. (2) Copay and generic drug price-cap policies are commonly adopted by the Canadian public drug plans to contain drug reimbursement cost. Policy-makers should use caution when applying these policies in combination or separately in order to reach the intended outcomes. (3) The generic drug price-cap can elicit competition among brand-name drug manufacturers, but it may need coordinated regulations on patented drug prices. Without full coordination among major stakeholders and across jurisdictions, the benefits of lowered drug prices for some can become additional costs for others.

I innovatively adopt the multilevel model to analyze the pharmaceutical market structure and evaluate the net effect of the generic competition paradox. The empirical research on the drug price dynamics is consistent with the predictions of the previously developed theory. I find that: (1) More generic substitutes in a drug molecule are associated with a net effect of increases in drug prices, after other contextual variables are properly controlled for. (2) More therapeutic substitutes do not have a net effect of lowering drug prices. (3) When a generic substitution policy is in place, the studied brand-name drugs maintain net price premiums over their generic substitutes. But, the net price premiums in the case when there is a generic substitution policy are lower than those where there is no such policy.

List of Abbreviations and Symbols Used

ANOVA

Analysis of Variance

APX

Apotex Inc.

ATC

Anatomical Therapeutic Chemical Classification

AZE

AstraZeneca Canada Inc.

BRI

Bristol-Myers Squibb Canada Co.

CADTH

Canadian Agency for Drugs and Technologies in Health

CDR

Common Drug Review

CGPA

Canadian Generic Pharmaceutical Association

CIHI

Canadian Institute for Health Information

COB

Cobalt Pharmaceuticals Inc.

CRTC

Canadian Radio-television and Telecommunications Commission

DDD

Defined Daily Dose

DIN

Drug Identification Number

DTCA

Direct-To-Consumer Advertising

FRS

Merck Frosst Canada Ltd.

GPM

Genpharm Inc.

GRP

Generic Reference Pricing

GSK

GlaxoSmithKline

HMO

Health Maintenance Organization

IGLS

Iterative Generalized Least Squares

IV

Instrumental Variable

JAN

Janssen-Ortho Inc.

JNJ

Johnson & Johnson Inc.

LCA

Least-cost Alternative

LIN

Linson Pharama Inc.

MAC

Maximum Allowable Cost

MFDV

Most-Favourite Drug Variant

MFN

Most-Favoured Nation

NAFTA

North American Free Trade Agreement

NOC

Notice of Compliance

NOP

Novopharm Ltd.

NPDUIS

National Prescription Drug Utilization Information System

NPS

National Pharmaceutical Strategy

NRP

No Reference Pricing

NVR

Novartis Pharmaceuticals

NXP

Nu-Pharm Inc.

ODBP

Ontario Drug Benefit Program

OTC

Over-the-counter

PFI

Pfizer Canada Inc.

PMPRB

Patented Medicine Prices Review Board

PMS

Pharmascience Inc.

R&D

Research and Development

RAN

Ranbaxy Pharmaceuticals

RCMP

Royal Canadian Mounted Police

REML

Restricted Maximum Likelihood

RPH

Ratiopharm Inc.

SDZ

Sandoz Canada Inc.

TAR

TaroPharma Inc.

TRP

Therapeutic Reference Pricing

WHO

World Health Organization

WTO

World Trade Organization

Glossary

Anatomical Therapeutic Chemical (ATC) Classification system

The Anatomical Therapeutic Chemical (ATC) Classification System is used for the classification of drugs. It is controlled by the WHO Collaborating Centre for Drug Statistics Methodology (WHOCC), and was first published in 1976. The classification system divides drugs into different groups according to the organ or system on which they act and/or their therapeutic and chemical characteristics. Several different drug products share the same code if they have the same medicinal ingredients and indications.

Bioequivalence

Bioequivalence or bioequivalency is a term in pharmacokinetics used to assess the expected in vivo biological equivalence of two proprietary preparations of a drug. In Canada, the Scientific Advisory Committee of the Therapeutic Products Directorate at Health Canada is responsible for issues related to bioavailability and bioequivalence of drugs at the federal level. Each province also has an independent expert committee for the evaluation of drug bioequivalence. Each drug first needs to pass the bioequivalence test by Health Canada for market entry. If the drug passes the provincial bioequivalence test, the drug can be listed on the provincial formulary.

Brand-name drug

Brand-name drug refers to a patented drug (or an off-patent drug) that is sold under a registered and distinguished brand-name.

Compulsory licensing

Under a compulsory license, the government forces the holder of a patent, copyright, or other exclusive right to grant use to others. The patent holder usually

receives some royalties, either set by law or determined through some form of arbitration.

Copay

Copay (or copayment) is a payment paid by a patient each time a prescription is filled. It is technically a form of coinsurance, but is defined differently in health insurance where a coinsurance is a percentage payment after the deductible up to a certain limit. Copay must be paid up-front.

Deductible

Deductible is the amount of expenses that must be paid out-of-pocket before an insurer will cover any expenses.

Defined daily dose

The defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. A DDD will only be assigned for drugs that already have an ATC code. The DDD is a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose. Drug consumption data presented in DDDs only give a rough estimate of consumption and not an exact picture of actual use. The DDD provides a fixed unit of measurement independent of price and dosage form (e.g. tablet strength), which enables researchers to assess trends in drug consumption and to perform comparisons between population groups.

Drug

A pharmaceutical drug refers to any unique combination of medicinal ingredient(s), strength(s), and dosage form. Health Canada assigns a unique Drug Identification Number (DIN) to each drug. A drug product refers to a version of a drug sold by a particular manufacturer.

Excipient

An excipient is the non-medicinal ingredient used as a carrier for the medicinal ingredients of a drug. Excipients are usually inert substances (such as gum arabic, syrup, lanolin, or starch) that form a vehicle for a drug or antigen.

Formulary

A formulary is a list of prescription drugs. A formulary determines the reimbursable drugs accessible to all qualified beneficiaries. The development of formularies is based on evaluations of efficacy, safety, and cost-effectiveness of drugs. Each Canadian province makes its own decision regarding the formulary used by their provincial drug plans

Generic drug

A generic drug (generic drugs, short: generics) is a drug which is produced and distributed without patent protection. The generic drug may still have a patent on the formulation but not on the medicinal ingredient. Health Canada requires that a generic drug must contain the same medicinal ingredients as the original brand-name drug with respect to pharmacokinetic and pharmacodynamic properties. Generic drugs are considered identical in dose, strength, route of administration, safety, efficacy, and intended use. A generic drug is bioequivalent to its brand-name original drug and is allowed to be produced and marketed after the brand-name drug's patent has expired or when the patent has proved invalid.

Maximum-reimbursable cost

Maximum-reimbursable cost mechanisms have been used extensively in Canada and globally to manage the cost of pharmaceuticals. In practice, maximum-reimbursable-cost type of strategies can exist in different forms such as the maximum-allowable cost (MAC), least-cost alternative (LCA), and reference-based pricing policy (or reference drug program). The MAC (LCA) price is

the maximum allowable cost (lowest cost) per unit established by the drug plan for an interchangeable drug category. The MAC/LCA price is determined by examining costs available from each manufacturer and is based on the lowest price available to pharmacies. Under reference-based pricing, the drug plan provides full coverage of only the reference drugs — those considered to be the most medically effective and the most cost-effective in that category.

Patented drug

Patented drugs are drugs that fall under the Patent Act's definition of a patented medicine and are subject to price review from the Patented Medicine Prices Review Board (PMPRB). In contrast, non-patented drugs are drug products that are not subject to the PMPRB's price review at any point in time. Therefore, non-patented drugs encompass both off-patent brand-name drugs, drugs without patents but sold under a particular trade-name, and generic drugs.

Pharmacare

Pharmacare programs (also knowns as provincial drug plans) are drug insurance plans for eligible groups, provided by the provincial/territorial governments of Canada. Some are income-based universal programs. Most have specific programs for population groups that may require more enhanced coverage for high drug costs. These groups include seniors, recipients of social assistance, and individuals with diseases or conditions that are associated with high drug costs.

Prescribed drug

A prescribed drug is a substance considered to be a drug under the Food and Drugs Act, which is sold for human use as the result of a prescription from a health professional. Strictly speaking, prescription drugs are broader than prescribed drugs since the former may include veterinary medicines. The two terms are used interchangeably in this thesis since both of them refer to drugs for human use only.

Prescription drug

A prescription drug is usually prescribed by a physician or other health professional, dispensed by a pharmacist and received either in hospital or in the community. A prescription drug may or may not be patented. An over-the-counter (OTC) drug or non-prescription drug is legally available without a prescription but may be prescribed. A small number of OTC drugs are patented. OTC drugs are usually paid out-of-pocket by patients. But, when OTC drugs are prescribed, they may be covered by public and/or private drug plans.

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Chapter 1

Introduction

The Canadian pharmaceutical industry manufactures approximately 18,000 pharmaceutical products[1] in Canada, and medications play an increasingly significant role in the Canadian healthcare system.

The rising cost of pharmaceuticals is among one of many heated policy debates for researchers in Canada and globally. In 2009, total expenditure on drugs was estimated to be CAD $30 billion in Canada, representing a 16.5% share of the total healthcare expenditure.[2] In addition, since 1997, drugs have accounted for the second-largest share among major categories of health expenditure, after hospitals (CIHI, 2010a). The soaring drug expenditure has profound impacts on the sustainability of both the public and private insurance systems in Canada. Because the outpatient prescribed drug spending is partially covered by the public drug plans, Canadians will have to ultimately shoulder this increasing drug cost burden, either directly through increasing out-of-pocket drug spending, or indirectly through future taxes to support the health system.

Existing research on the Canadian drug expenditure[3] decomposes the drug expenditure into numerous determinative factors. These include: price-related factors, volume-related factors, population-related factors, new-yet-costly technology factors embodied in new drugs, and health system-related factors, and so on. Until recently, the volume of drug utilization has received the most attention from researchers and policy-makers, because the huge magnitude in the volume-related factors can be the major target for drug cost containment. Viewed from a different angle, however,

[1] They include human pharmaceutical and biological drugs, veterinary drugs, and disinfectant products. The information was retrieved at http://www.hc-sc.gc.ca on May 4, 2010.

[2] The total drug expenditure here includes the expenditure on prescribed and non-prescribed drugs.

[3] For example, the annual reports of drug expenditure by the Canadian Institute for Health Information (CIHI) and Morgan (2002), etc.

drug medication is an investment with the intent to improve the health of patients and/or to reduce demands for other healthcare services (Morgan, 2008). It is therefore shortsighted to focus on cost saving from pricing policies alone in the pursuit of a sustainable Canadian healthcare system reflecting multidimensional values. After all, the ultimate goal is to enhance individual and population health through healthcare at reasonable costs.

This thesis focuses on the price-related factors in the setting of the Canadian pharmaceutical market and institutions, which are exposed to relatively little research scrutiny.

Traditional economic theories predict that the entry of competing firms in an industry will drive price to fall in the equilibrium. However, in the Canadian pharmaceutical industry, one may find that "drug prices ... have been relatively stable over the past 10 years" (CIHI, 2010a) despite the fact that there is an increasing number of therapeutic and generic competitors available in the market. It can be misleading to draw a hasty conclusion based on the above observation that the drug price factor is insignificant in shaping the current and future drug expenditure. With the huge volume multiplier, even an infinitesimal decrease in the price of some best-seller drug may be translated into tremendous savings nationwide over time. Moreover, having stable drug prices for years may not be desirable for policy-makers, if the stable prices are maintained by some anti-competitive market forces and if the prices are otherwise expected to fall.

Why do drug prices not fall over time in the presence of an increasing number of drug manufacturers? Traditional economic theories do not have direct answers to this question. This knowledge gap necessitates in-depth research regarding the drug manufacturers' price setting behaviour.

This thesis contributes to the existing literature in the following aspects. First, I provide the stylized facts from the literature on the unique institutional history and development of the Canadian pharmaceutical system. Second, I develop a theoretical framework for analyzing what the impacts of market structures and Canadian legislations are on the drug manufacturers' price setting decisions. Third, I introduce the

multilevel model to fit the "tree-like" data structure and analyze the drug price dynamics.[4] The research improves the understanding of the drug manufacturers' price setting behaviour in the context of the changing market structures and policies.

The rest of the chapter is organized as follows: Section 1.1 introduces the key aspects of the Canadian pharmaceutical market structure in a nutshell. Section 1.2 presents the motivation, key questions, and research methodology for this research. The contributions of this research are then highlighted. Finally, the organization for the rest of the thesis is offered in Section 1.3.

1.1 Key Aspects of the Pharmaceutical Market Structure

The Canadian pharmaceutical industry is composed of two sectors, namely, brand-name drug manufacturers (including biopharmaceutical companies) and generic drug manufacturers. Both sectors produce prescription and non-prescription drugs. For any therapeutic market[5] where a group of drugs have the same therapeutic effect, it is characterized by two-tier competition, where a drug product may face the competition from its therapeutic substitutes ("me-too" drugs)[6] and from its generic substitutes.

When an innovative brand-name drug in some therapeutic class is first launched to the market, the drug product is under patent protection and it is free from price competition by any generic substitutes. But, the patent cannot insulate the drug product from the competition of its therapeutic substitutes. Driven by potential profits, a competing brand-name drug manufacturer may choose to enter this therapeutic market later in time by introducing a differentiated brand-name drug but without infringing on the original patent.[7] The degree of differentiation from a new drug can vary significantly in the pharmaceutical industry, from "providing a breakthrough or substantial improvement" to "providing moderate, little or no therapeutic advantage

[4] In this thesis, I use nested data structure and tree-like data structure interchangeably to describe the hierarchical structure of the data. A graphical presentation of the data structure is formally introduced in Chapter 4.

[5] The therapeutic market is defined by the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) Classification system.

[6] Drugs with similar therapeutic values are also known as "me-too" drugs. But note that some therapeutic substitute drugs may have markedly different pharmacodynamics and pharmacokinetics. "Me-too" therefore is only a metaphorical term describing the status of market competition.

[7] The new brand-name (me-too) drug normally also carries its own patent.

over comparable medicines" (Canadian Generic Pharmaceutical Association, 2008). However little the medical advancement the "me-too" drug might bring to patients, in economics terms, the brand-name original drug is no longer the monopolist in the therapeutic market. Following this logic, we would observe an evolving market structure with an increasing number of therapeutic substitutes over time.

As far as the generic drug manufacturers are concerned, an effective and valid patent is indeed one of the key barriers for market entry.[8] Only after the patent of a brand-name drug expires, can bioequivalent drugs in the generic version be allowed to enter the market.[9] Sometimes, the legitimacy of a patent may be challenged by a generic drug manufacturer. In the case that the patent's validity is overruled, the generic version drugs can also be allowed to enter before the actual date of expiration of the patent.

Standard economic theory predicts that product competition is likely to propel evolution in the underlying market structure from a monopoly to the ultimate perfect competition. In reality, this prediction does not apply to the pharmaceutical industry.

1.2 The Motivation, Key Questions, and Methodology

Both the brand-name and the generic drug manufacturing sectors of the Canadian pharmaceutical industry are heavily concentrated in market shares, due to the high barrier of entry and economies of scale in the industry. In particular, brand-name drugs can enjoy considerable price premiums over their bioequivalent generic substitutes.

Why can brand-name drug manufacturers maintain a downward price rigidity for their off-patent drug products in spite of the generic drug competition? What is so special about the Canadian pharmaceutical industry? Can I use economic theories

[8] Another important barrier of entry is data exclusivity, under which pharmaceutical companies provide regulatory authorities data on safety and efficacy of a new medicine and in return these data will be kept as a trade secret for a limited period from potential competitors including generic drug companies. The provisions on data exclusivity may overlap with and complement patent protection and may extend beyond it (Adamini et al., 2009).

[9] The bioequivalency of generic drugs to the patented drug is approved by both Health Canada at the federal level and an expert committee for each provincial government. To fulfil this responsibility, Health Canada and the provincial expert committees examine drug's safety, effectiveness, and quality.

to explain the stories behind these observations? These questions reflect a knowledge gap between the stylized facts about the Canadian pharmaceutical industry and how much we understand these phenomena.

One may attribute the price premiums between the brand-name original drug and its generic substitutes to the fact that the brand-name drug manufacturer incurs immense research and development (R&D) investment to discover and develop a new drug therapy. But, this explanation is untenable. In fact, anticipating the potential market entry of generic competitors after the patent expiry, a brand-name manufacturer is able to sufficiently recoup its R&D investment when it still enjoys the market exclusivity under the patent protection. In theory, after its patent expiry, the brand-name drug is expected to compete with the bioequivalent yet cheaper generic substitutes to maintain market shares and profitability. In practice, however, the brand-name drug manufacturer may choose to keep price premiums in the face of generic drug competition. Moreover, it may still maintain positive market shares and remain profitable. Scherer (1993) coins this phenomenon as the "generic competition paradox".

This thesis attempts to explain why the brand-name drug manufacturer does not compete with the generic drug manufacturers in price. Looking from the consumers' point of view, I try to explain why some patients maintain strong loyalty to the brand-name drug rather than switch to the cheaper and also equally reliable generic drugs.

In this thesis, I approach the paradox differently from previous research. First, I present the key stylized facts of the Canadian pharmaceutical institutions. Then, I develop the oligopoly theory with two-dimension product differentiation, and analyze the impact of factors related to market structures and policies on the drug manufacturers' price setting behaviour. Finally, I introduce the multilevel model to fit the "tree-like" data structure and evaluate whether the generic competition paradox still exists after the contextual variables are properly controlled for in the empirical model.

Little research in the existing literature offers an appropriate theoretical framework to explore the impact of market structures and legislations on the drug manufacturers' price setting decisions. Brekke et al. (2007) propose a theory close to

that proposed in this thesis. They use product differentiation for the pharmaceutical market and discuss the drug manufacturers' price setting practice in the setting of different reference pricing regimes of European Union countries. But they do not consider the change in patient preference and government reimbursement policies and how drug manufacturers' price setting strategies reflect the change.

The theoretical model developed in this thesis is a step forward. I use the two-dimension product differentiation to model the typical Canadian prescription drug market. I focus on the examination of the impacts of the shift in patient preference and change in government policies on drug manufacturers' price setting behaviour in different settings. The in-depth discussions presented bring new insights to the impact of these parameters on drug manufacturers' price setting behaviour.

The thesis benefits from an interdisciplinary approach involving economics, statistics, pharmacy, and related public policy. It integrates the theoretical models from oligopoly theory and the institutional background of the Canadian pharmaceutical industry.

Following the theoretical discussion, I explore the Canadian drug price dynamics to seek support from the empirical data. I use the multilevel regression approach to evaluate whether the generic competition paradox remains after the contextual information is properly controlled for. The approach has not been adopted in the literature to date. Specifically, I examine three major research hypotheses in the empirical study. (1) More generic substitutes do not have a net effect of lowering drug prices. (2) More therapeutic substitutes do not have a net effect of lowering drug prices. (3) Given that a generic substitution policy is available, brand-name drugs still maintain net price premiums over their generic substitutes.

Because the pharmaceutical market data are always unbalanced and hierarchical in nature, the ordinary least squares models, the time-series models, and the conventional panel data models are often inadequate to model the drug price dynamics. The multilevel model is proposed as a more suitable alternative to model the tree-like data structure.

A multilevel model that explicitly incorporates the tree-like or nested data structure, where drugs are grouped within molecules or manufacturers, has several advantages which the existing literature does not offer. First, it can model contextuality by incorporating the clustering information in the model. Second, it can be used to interpret random heterogeneity at various "between-" and "within-" levels. Third, it can capture unbalanced data structures.

The empirical regression results from the multilevel analysis provide sufficient evidence for the three research hypotheses. That is, this thesis confirms and corroborates that the generic competition paradox is present after the contextual variables are properly controlled for. Given that many blockbuster drugs will come off patent in the years to come, the research results may be informative for drug cost containment endeavours for both the public and private drug plans in Canada.

1.3 The Organization of the Thesis

I start the analysis in Chapter 2 by offering a comprehensive synthesis of the Canadian pharmaceutical system including key stylized facts of the market structures and legislations.

In Chapter 3, I develop a theoretical framework for analyzing the impact of market structures and legislations on drug manufacturers' price setting decisions. I focus on the analysis of three important preference/policy parameters in the theoretical analysis. I show how these parameters may impact drug manufacturers' price setting behaviour in different settings.

Following the theoretical model with two-dimension product differentiation, I conduct the empirical analysis on the drug price dynamics in Chapter 4. I use the multilevel model to control the contextual variables, to analyze the "tree-like" pharmaceutical market structure, and to evaluate the net effect of the geneirc competition paradox.

Finally, I conclude in Chapter 5. I summarize the major research findings and contributions to the literature. I also discuss the limitations of this research and future research plans.

Chapter 2

Review of the Canadian Pharmaceutical System

2.1 Introduction

Prescription drugs play an increasingly significant role in the healthcare system of major developed economies, in the context of the evolving demography, technology, and economic and policy environments. Canada represents one of the major pharmaceutical markets in the world; it is the 9^{th} largest globally, with a 2.5% share of the global market (Industry Canada, 2010). Total expenditure on drugs[1] in Canada, estimated at CAD $30 billion in 2009, was either reimbursed by public or private drug insurance plans or paid out-of-pocket by patients. It remains the second-largest expenditure component in 2009 and continues to be one of the fastest growing expenditure components of the Canadian healthcare system (CIHI, 2010a). The soaring cost of pharmaceuticals is among one of many heated policy debates for researchers in Canada and globally.

The healthcare system in Canada is characterized by strong government intervention. Public provision and funding of healthcare are the major founding principles of the Canada Health Act. Canadians believe that "an inability to pay for treatments and/or drugs may be a barrier to care; thus, additional coverage (e.g. for pharmaceuticals) may increase healthcare utilization by those who need but cannot afford treatment" (Curtis and MacMinn, 2008).

A publicly-funded healthcare system for all Canadians does not stand on equity grounds only. Government intervention may also represent a policy response to inadequate competition in a market, if the market includes products considered to be necessities and if the market has been publicly subsidized to avert under-consumption

[1]Here, total drug expenditure is composed of estimates that represent the final costs to Canadian consumers, including dispensing fees, markups and appropriate taxes. According to CIHI (2010a), total drug expenditure includes expenditure on both prescribed and non-prescribed drugs (over-the-counter drugs and personal health supplies).

(OECD, 2008). As key components of modern healthcare, prescription medications are considered necessities to prevent or combat a serious illness or debilitating health condition. As a result, most consumers may not be sensitive to price signals because of the extensive insurance coverage from public or employer-supported drug plans.

The Canadian pharmaceutical system is complex. For example, there are a large number of drug products, market structures are dynamic, and health policies and legislations across the country are segmented. Moreover, the consumption of pharmaceutical products involves multiple parties, including manufacturers, distribution channels of pharmaceuticals, public (therefore, taxpayers) and private insurers, health professionals, and finally patients — the consumers of pharmaceutical products.

Many reports, such as the OECD health working paper by Paris and Docteur (2007), the two reports on the generic drug sector by the Canadian Competition Bureau (2007, 2008), and the two discussion papers by Bell et al. (2010) and Health Council of Canada (2010), have provided their unique perspectives on the multifaceted Canadian pharmaceutical system. In this chapter, I offer a review of the history and synthesis of the existing literature by discussing government policies related to the pharmaceutical system from both the industry and health perspectives. Industry policies primarily target economic growth and employment on efficiency grounds, while health policies mainly focus on safety and efficacy of drugs to improve population health on an equity basis. A sound pharmaceutical system must balance the objectives of industry and health policies. The discussion on the institutional background of the Canadian pharmaceutical system in this chapter offers support for the theoretical and empirical discussions in the following chapters.

The rest of the chapter is organized as follows. In Section 2.2, I briefly review the history of the legislations and regulatory framework on pharmaceuticals, both at the Canadian federal and the provincial/territorial level. Then in Section 2.3, I examine the major stakeholders, their relationships, and their roles in the pharmaceutical system. After a discussion on other important aspects of the Canadian pharmaceutical system in Section 2.4, I offer concluding remarks in Section 2.5.

2.2 Canadian Legislations on Pharmaceuticals

The pharmaceutical industry in Canada is regulated by both the federal and provincial/territorial governments. In the current system, the federal government is responsible for approving drug products to guarantee safety and efficacy, regulating patented drug prices from being excessive, and enforcing intellectual property laws such as the Patent Act. The federal government also provides prescription drug coverage for about one million Canadians who are members of eligible groups. These groups include First Nations and Inuit, members of the military, veterans, members of the RCMP, and inmates in federal penitentiaries.[2] The provincial/territorial governments are responsible for the delivery of the public drug (insurance) plans. Each province makes its own generic substitution regulations and assesses the cost-effectiveness of drugs by its independent professional committee. As Health Canada states,

> [i]nstead of having a single national plan, we have a national program that is composed of 13 interlocking provincial and territorial health insurance plans, all of which share certain common features and basic standards of coverage.[3]

Characterized by a lack of synergy among different levels of government, this unique Canadian approach leaves room for the pharmaceutical industry to manoeuvre. A National Pharmaceutical Strategy (NPS), which Canadians have called for since 1964,[4] still stumbles in its conceptual stage (Gagnon, 2010).

2.2.1 A Brief History of Canadian Legislations on Pharmaceuticals

Canadian legislations and corresponding regulatory frameworks on pharmaceuticals evolved with the changing environment of science and technology, international

[2]The information was retrieved at http://www.hc-sc.gc.ca on November 25, 2010.

[3]The above information was retrieved at http://www.hc-sc.gc.ca on December 6, 2010. Note that since the federal government also provides prescription drugs for certain eligible groups, there are more than 13 public drug plans in Canada other than the provincial/territorial plans.

[4]The expansion of Medicare to include universal drug coverage was recommended by Justice Emmett Hall's Royal Commission on Health Services in 1964.

obligations, and the demands of various stakeholders, including the pharmaceutical industry and consumers.

The pharmaceutical industry was virtually unregulated in Canada until the first effective drug regulation at the federal level, the Patent Medicine Act, was drafted in 1909. This legislation required the documentation and approval of a small number of "secret formula" drugs issued by doctors.

The modern system of Canadian drug regulation was developed from the Food and Drugs Act of 1920, in the context of the growing complexity of the pharmaceutical industry and increasing public concerns over drug safety. The government began to play a more active role intervening in the domestic pharmaceutical industry, but, it was not until the 1939 Amendment to the Act that the federal government started to limit the terms of sale of any drug. By 1941, the Canadian federal government had established the first list of drugs that would be available by prescription only (Morgan, 2000). The 1951 Amendment made it mandatory for all drug manufacturers to seek approval from the federal government before advertising and distributing all pharmaceutical products.

The Thalidomide tragedy[5] in the early 1960s prompted the approval of federal regulations on proof of drug efficacy under tighter safety standards. From then on, drug manufacturers were required to submit their dossiers and receive notices of compliance (NOC) showing that their products were effective for the conditions recommended.

The Canadian Constitution endows powers and jurisdictions for both the federal and provincial governments. Provincial governments gradually enhanced their roles in the Canadian healthcare system with close interactions with the federal government. The first publicly-funded health insurance plans were introduced in Saskatchewan in 1946 and for other provinces in the late 1940s. These provincial policy initiatives demanded further and deeper involvement of the federal government. The two pioneering federal legislations, the Hospital Insurance and Diagnostic Services Act passed in 1957 and the Medical Care Act passed in 1966, and the succeeding Canada Health Act passed in 1984, made it clear that provincial governments have responsibility and

[5]Thalidomide was commonly prescribed to pregnant women for morning sickness before the 1960s. The drug was later identified to be associated with congenital malformations of the limbs in babies; about 115 babies were born in Canada with these congenital malformations.

jurisdiction over the funding of all healthcare services except for those provided to First Nations and Inuit, the military, and a few others. These federal legislations are the fundamental pillars of the Canadian "Medicare" system. However, none of these legislations would mandate the universal public coverage for out-patient prescription drug spending, except for certain population groups at-risk. For example, British Columbia, Manitoba, Quebec and Saskatchewan have broader coverage. Other provinces provide drugs to senior citizens and those on social assistance (Coombes et al., 2004; Bell et al., 2010; Canadian Institute for Health Information, 2010b).

In the 1960s, the federal government determined to act against high drug prices after three separate commissions of inquiry reached the conclusion that drug prices in Canada were too high. Without having a consensus on how to regulate drug prices, Parliament found a compromise by amending the Patent Act in 1969 to broaden access to compulsory licensing for pharmaceuticals.[6] The Amendments created the burgeoning growth of generic drug competition and demonstrated remarkable effectiveness in lowering drug prices.[7]

The pharmaceutical compulsory licensing provisions ended up being repealed through two federal Bills, C-22 and C-91 in 1987 and 1993, respectively, after the policy received a tremendous backlash from the pharmaceutical industry both within and outside Canada. In the meantime, the Patent Act was amended such that the patent protection was extended from seventeen years to twenty years. Subsequently, regulations were adopted linking the issuance of notices of compliance for generic drugs to the expiry of the patent protection period for the innovator drug. The two Bills supplemented Canadian patent laws and highlighted the government's stance on protecting intellectual property in Canada, encouraging pharmaceutical R&D, and respecting international trading obligations. They also marked the transition of federal policies in regulating drug prices, from relying on market mechanisms for drug cost control under compulsory licensing to a direct price control by the federal

[6]Under the 1969 Amendments, the federal government permitted compulsory licences to import medicines into Canada. This allowed generic drug producers to import a medicine's active ingredients and process them into the final form for sale. The Commissioner of Patents was authorized to issue compulsory licences to import and to fix a royalty for them. Royalty rates were set at 4% of the net selling price of a drug in its final dosage form.

[7]The information was retrieved at http://www.pmprb-cepmb.gc.ca on October 20, 2010.

government.[8]

As a result, Bill C-22 created the Patented Medicine Prices Review Board (PMPRB) and Bill C-91 further strengthened the PMPRB's mandates:

> ... [of] ensuring that the prices charged by manufacturers of patented medicines are not excessive ... and ... reporting to Canadians on the trends in drug prices in Canada and on the R&D spending of patent-holding firms.[9]

As a powerful quasi-judicial tribunal, the PMPRB regulates the prices of patented drug prices at the national level. But the federal government can be insulated from the impact of its policies to some extent, because it is the provincial governments who are primarily responsible for the funding of all healthcare services, including pharmaceuticals (Anis, 2000). The provinces, however, only have limited discretion over the prices of drugs covered by the provincial drug plans. In addition, these controls on drug prices are fragmented across provinces. In recent years, provincial governments have sought to innovate their price control measures, but only by leveraging their purchasing power independently. For example, the Ontario Drug Benefit Program (ODBP), among other provincial drug plans, sets the maximum price for reimbursement by listing any generic drug on the provincial formulary at or below a predefined percentage of the reference brand-name drug price. As a key component of the province's drug reform, the percentage cap on generic drugs has been lowered progressively, from 63% to 50% in March 2007, then to 25% starting July 2010. Moreover, this same pricing policy will also be gradually phased in for drugs covered by private drug insurance plans and those purchased out-of-pocket (Ontario Ministry of Health and Long-Term Care, 2010).

As noted above, collaboration between the federal and provincial governments or among the provincial legislatures is very limited. In 1997, the National Forum on Health, and in 2002, two federal reports, the final report of the Senate Committee on Social Affairs (the Kirby report) and the Romanow Commission report, called for

[8]The information was retrieved at http://www.pmprb-cepmb.gc.ca on October 20, 2010.
[9]The information was retrieved at http://www.pmprb-cepmb.gc.ca/ on October 20, 2010.

a National Pharmaceutical Strategy (NPS) to implement a universal public pharmaceutical insurance plan. Under the proposed NPS, no Canadian should suffer undue financial hardship in accessing needed drug therapies. In addition, it also made clear that affordable access to drugs is fundamental to equitable health outcomes for all Canadian citizens. There has been moderate but incremental collaboration between federal, provincial and territorial governments since the 2000s. Recently, Canada's premiers have been discussing potential opportunities and strategies for pooling their purchasing power for drugs and medical supplies (Howlett, 2010). But in general, the NPS was not backed up by further legislative support from Parliament and has not been fully carried out.

Another noteworthy aspect of Canadian legislations on pharmaceuticals is direct-to-consumer advertising (DTCA). DTCA refers to the marketing of pharmaceutical products directed toward patients, rather than health professionals. It may be in forms of television, print, radio, and other mass and social media. These ads may induce patients' demand for prescription drugs that may not be medically necessary. Out of ethical and regulatory concerns, most countries, including Canada, prohibited DTCA of prescription drugs. There are two exceptions: New Zealand and the United States. This poses a challenge for Canadian law enforcement because some television and cable networks in the US have access to the Canadian market and because the US is Canada's largest trading partner.

Canada's Food and Drugs Act clearly prohibits the DTCA of prescription drugs under two provisions. First, the Act includes a broad prohibition on advertising prescription-only drugs (Schedule F) to the public. Second, Section 3 and Schedule A of the Act set out a list of diseases for which preventatives, treatments or cures may not be advertised to the public. This list includes many conditions treated by drugs that have been advertised to the public in the US, such as impotence, baldness, diabetes, asthma, and heart disease (Mintzes, 2006).

What makes the reinforcement of the DTCA ban difficult is the fact that terrestrial broadcasters and some cable broadcasters in neighbouring States, with access to the Canadian market via Canadian Radio-television and Telecommunications Commission (CRTC) regulation, effectively bypass and override Canada's ban on DTCA

of prescription drugs. The CRTC has not yet ruled on this issue.

To make the matter even more complicated, CanWest MediaWorks Inc., a bankrupted Canadian media company, which owned eleven major daily newspapers including the National Post, a major television channel and other media outlets, launched a legal challenge to the federal ban on DTCA of prescription drugs as an infringement of freedom of expression.[10] The lawsuit created a debate because the Act imposed a restriction on a domestic entity while at the same time a foreign entity was not subject to the restriction in its operational practice.[11] At the heart of the case was the balance between the "commercial interests" of CanWest and the societal interest of protecting Canadians, public health and the healthcare system from the harms associated with DTCA of prescription drugs (Silversides, 2009).

2.2.2 Current Canadian Regulatory Framework on Pharmaceuticals

Having reviewed the Canadian legislations on pharmaceuticals from the historical perspective, I now summarize the current Canadian legislative and regulatory framework on pharmaceuticals as follows:

The Canadian Constitution sets out two autonomous levels of governments: the federal and the provincial/territorial governments, each level with its own power and jurisdiction. As such, the Constitution established the role and power for each level of government in creating and administering key elements of Canada's healthcare system, including the subsystem of pharmaceuticals.

The federal government is responsible for drug product approval and ensuring the safety and efficacy of drug products. Health Canada is the federal department monitoring and executing the compliance and enforcement activities according to the regulatory requirements set out in federal legislations, e.g., Food and Drugs Act, Canada Health Act, and Controlled Drugs and Substances Act, etc. As the federal regulator, Health Canada collaborates with other levels of governments, health professionals, patients and consumer interest groups, research communities and drug manufacturers, to minimize the health risk factors and improve the health of all Canadians.

[10] CanWest's broadcasting assets were sold to Shaw Communications Inc. in October 2010. CanWest's newspaper holdings, including the National Post, were sold separately.

[11] The lawsuit has been granted an indefinite adjournment due to CanWest's bankruptcy.

The quasi-judicial PMPRB develops various regulatory standards regarding the introductory prices of new drug products. For example, the PMPRB regulates the "factory-gate" prices of patented drugs with "breakthrough therapeutic improvement" to ensure that these prices are not excessive, compared to the prices in the selected developed countries, i.e. France, Germany, Italy, Sweden, Switzerland, the UK, and the US. For new drugs with "substantial improvement", "moderate improvement", and/or "slight or no improvement", the PMPRB implements other standardized tests to regulate the introductory prices, including the Therapeutic Class Comparison test, the Reasonable Relationship test, the International Price Comparison test, and the International Therapeutic Class Comparison test, etc.[12] The PMPRB also monitors and reports to Canadians on the trend in drug prices in Canada and on the R&D spending of patent-holding firms. However, the PMPRB does not regulate off-patent drugs, and does not monitor drug prices paid by consumers, which can be marked up by the drug product distribution channel, such as wholesalers and retail pharmacies.

Provincial legislative authorities are responsible for the delivery of almost all areas of health services. These include health insurance regulation, the distribution of prescription drugs, and the training, licensing and terms of employment for health professionals. Provinces are also responsible for funding these services, with assistance from the federal government in the form of fiscal transfers.

Provinces do not have jurisdiction in regulating drug prices directly, but they can develop various mechanisms to contain reimbursement costs of the drugs covered by the provincial drug plans. Provincial formularies are established and maintained to include drugs that are qualified for reimbursement. Generic substitution regulations, in combination with other cost-sharing measures, such as insurance deductibles and copays, are passed to assist in making pharmacare programs efficient and affordable and provide financial incentives to substitute cheaper (generic) drugs for more expensive (brand-name) drugs.

Overall, the Canadian pharmaceutical legislative and regulatory system is composed of several fundamental federal legislations and a patchwork of provincial laws and regulations. It lacks full coordination among the different levels of governments.

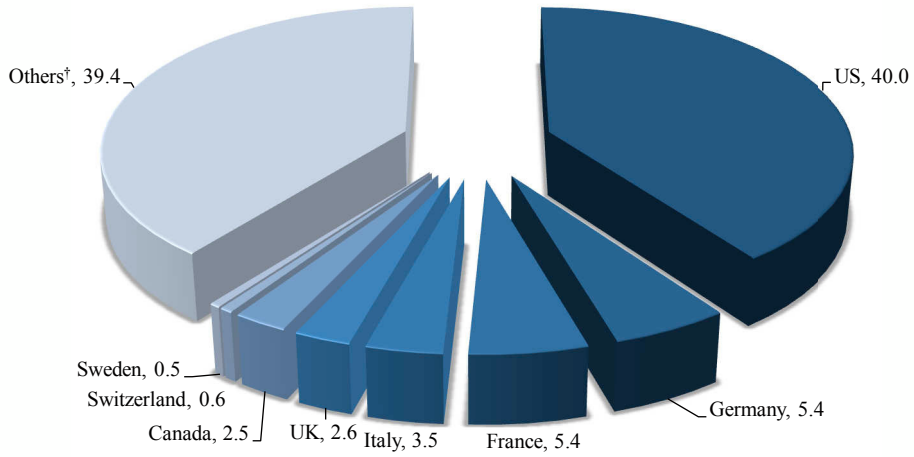
[12]The information on the methodology and technical discussion of patented drug price regulation implemented by the PMPRB is accessed at http://www.pmprb-cepmb.gc.ca on February 12, 2011.

Therefore, the stakeholders of the Canadian healthcare system strive to reach an agenda on developing a national strategy, which involves not only a universal public drug insurance plan but closer collaboration among regulatory authorities at different levels. However, the NPS is still in its conceptual stage due to the lack of political enthusiasm.

2.3 The Canadian Pharmaceutical System

The pharmaceutical industry represents one of the most dynamic and profitable industries in Canada. Pharmaceutical sales in Canada were around 2.5% of the total sales globally in 2009 (Figure 2.1), the 9^{th} largest in the world. During the period of 2004-2008, Canada recorded a 7% average annual growth, which was the 4^{th} fastest growing market globally, after Brazil, China, and Spain (Industry Canada, 2010).

Figure 2.1: Distribution of Global Drug Sales among Major National Markets (%), 2009



Source: PMPRB (2010)

† Some countries with leading drug sales, such as Japan, were categorized under others because the PMPRB focuses on the selected OECD countries as comparators to compile its patented drug price index.

The pharmaceutical industry is composed of two distinct sectors, namely the brand-name and generic drug manufacturers. Brand-name drug manufacturers undertake R&D for discovering and testing new patented drug products. The generic drug manufacturers do not incur the cost of drug discovery, and therefore they are

able to manufacture bioequivalent copies of off-patent brand-name drugs by reverse-engineering existing drug compounds or through special arrangements with brand-name firms.[13]

The global pharmaceutical industry is dominated by a number of multinational brand-name giants based in the United States and European countries (Table 2.1). Most of these foreign-owned multinationals have Canadian subsidiaries, mainly headquartered in two Canadian provinces, Ontario and Quebec (Table 2.2). These firms, together with a few Canadian-based brand-name drug manufacturers, accounted for about 76% of total pharmaceutical sales in Canada in 2009.[14] As one of the major contributors to local economies,[15] they may pose influence over policy-making at various levels of government.[16]

As shown in Figure 2.2, the total revenue of generic companies ($5.2 billion or 24.2%) is dwarfed by that of their brand-name counterparts ($16.3 billion or 75.8%), mainly because brand-name drugs are more expensive. In 2009, generic drugs accounted for over 54% of the total prescriptions in Canada (or 263 million generic prescriptions).[17] This percentage is expected to grow, due to the many cost containment endeavours by the public and private drug insurance plans across the country.

The Canadian pharmaceutical industry produces approximately 18,000 pharmaceutical products, categorized by the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) Classification system. The ATC classification system, established by the WHO in 1976, is the most commonly used drug product classification system worldwide. Drugs are divided into different groups according to the

[13]Reverse engineering a drug is a way of discovering how a drug product is manufactured based on a finished drug product through the analysis of its structure, function, and operation. During the reverse engineering, chemists identify variants of molecules and diverse synthesis processes, and sometimes even propose improvements (Cassier and Correa, 2003).

[14]The information was retrieved from the Canadian Generic Pharmaceutical Association (CGPA) website, at http://www.canadiangenerics.ca on October 20, 2010.

[15]In 2009, the manufacturing sector of the pharmaceutical industry employed over 28,000 Canadians (with two thirds in brand-name companies) and provided 35,000 indirect jobs (Industry Canada, 2010).

[16]For example, to attract more pharmaceutical investment, Quebec reimburses the full cost of brand-name drugs for 15 years after they have been listed on the provincial, despite there may have been generic versions in the market (Bell et al., 2010).

[17]The information was retrieved from the Canadian Generic Pharmaceutical Association website, at http://www.canadiangenerics.ca on October 20, 2010.

Table 2.1: Top 15 Pharmaceutical Companies by Global Sales (USD Million), 2008

Rank	Company	Sales (US$M)	Headquartered in
1	Pfizer†	43,363	US
2	GlaxoSmithKline	36,506	UK
3	Novartis	36,506	Switzerland
4	Sanofi-Aventis	35,642	France
5	AstraZeneca	32,516	UK/Sweden
6	Hoffmann-La Roche	30,336	Switzerland
7	Johnson & Johnson	29,425	US
8	Merck & Co.	26,191	US
9	Abbott	19,466	US
10	Eli Lilly & Co.	19,140	US
11	Amgen	15,794	US
12	Wyeth†	15,682	US
13	Teva	15,274	Israel
14	Bayer	15,660	Germany
15	Takeda	13,819	Japan

Source: IMS Health (2008), Top 15 global corporations.

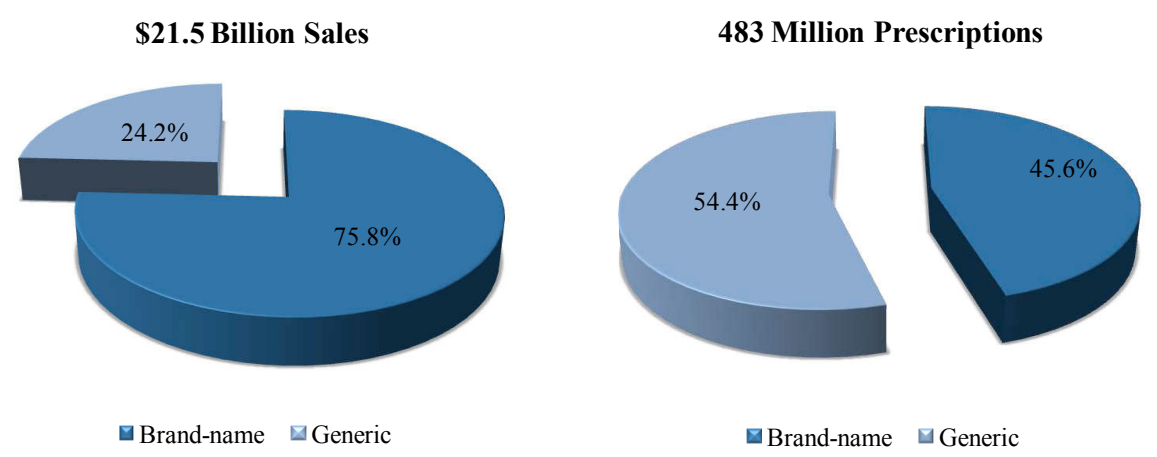
† Pfizer (1^{st}) acquired Wyeth (12^{th}) on October 15, 2009.

Table 2.2: Top Ten Pharmaceutical Companies in Canada by Sales (CAD Billion), 2009

Rank	Company	R&D Location	Sales (CA$B)	Market Share (%)
1	Pfizer	Montreal	2.94	13.4
2	Apotex	Toronto	1.55	7.0
3	AstraZeneca	Montreal	1.44	6.6
4	Schering-Plough	Montreal	1.33	6.0
5	Johnson & Johnson	Toronto	1.16	5.3
6	Novopharm	Toronto	0.92	4.2
7	Novartis	Toronto	0.89	4.0
8	GlaxoSmithKline	Toronto	0.88	4.0
9	Abbott	Montreal	0.85	3.9
10	Roche	Montreal	0.68	3.1

Source: Industry Canada (2010)

Figure 2.2: Distribution of Drug Sales and Number of Prescriptions in Canada (%), 2009



Source: Canadian Generic Pharmaceutical Association (2009)

* The total Canadian prescription drug sales, including retail and hospital sales, were $21.5 billion in 2009. The number of Canadian retail prescriptions was 483 million in 2009.

organ or system on which they act and/or their therapeutic and chemical characteristics. Different drug products share the same ATC code if they have the same medicinal ingredients and indications. Each ATC code has five different levels. The first level of the code indicates the anatomical main group and consists of one letter. There are 14 main groups.[18] The second level of the code indicates the therapeutic main group and consists of two digits. The third level of the code indicates the therapeutic/pharmacological subgroup and consists of one letter. The fourth level of the code indicates the chemical/therapeutic/pharmacological subgroup and consists of one letter. The fifth level of the code indicates the chemical substance and consists of two digits. For example, sumatriptan is a type of drug used to treat migraine headache, with the ATC code N02CC01. Specifically, N refers to the nervous system; N02 refers to analgesics; N02C refers to the group of antimigraine preparations; N02CC refers to the group of selective serotonin (5HT1) agonists; finally N02CC01 refers to sumatriptan.[19]

In Canada, the leading therapeutic class in terms of annual patented drug sales in

[18]The 14 main groups at the 1^{st} level of the ATC Classification system are presented in Table C.1.

[19]The information was retrieved at http://www.whocc.no, on October 14, 2010.

2009 is the cardiovascular system drugs. Three of the top ten pharmaceutical products in Canada in 2009 belong to the cardiovascular system (Table 2.3). The data reflect the fact that cardiovascular disease is the leading cause of death in Canada and other developed economies (Table 2.4), accounting for at least 36% of all deaths, or about 80,000 people each year.[20]

Table 2.3: Leading Pharmaceutical Products in Canada in 2009

Rank	Leading Products	Manufacturer	ATC Code	Therapeutic Subclass	Sales† ($ Millions)
1	Lipitor®	Pfizer Canada	C10AA05	Cholesterol reducer	1249.2
2	Crestor®	AstraZeneca	C10AA07	Cholesterol reducer	521.7
3	Remicade®	Schering	L04AB02	Anti-arthritic	360.5
4	Norvasc®	Pfizer Canada	C08CA01	Blood pressure control	350.2
5	Plavix®	Bristol-Myers Squibb	B01AC04	Blood circulation	271.0
6	Nexium®	AstraZeneca	A02BC05	Stomach and control	264.6
7	Enbrel®	Amgen	L04AB01	Anti-arthritic	257.7
8	Oxycontin®	Purdue	N02AA05	Pain killer	217.1
9	Humira®	Nycomed	L04AB04	Anti-arthritic	188.5
10	Advair®	Abbott	R03AK06	Asthma therapy	188.1

Source: Industry Canada (2010)
† The sales data are all in 2009 Canadian Dollars.

Now I will discuss the two-tier pharmaceutical industry structure, other important stakeholders in the market, and their relationships.

2.3.1 A Two-tier Industry Structure

The pharmaceutical industry is typically characterized by a two-tier structure, namely, the sectors of brand-name manufacturers and of generic manufacturers. The former discovers and develops innovative pharmaceuticals. With patent protection, brand-name drugs are usually sold at high prices to recover the immense R&D investment. The latter manufactures bioequivalent replicas of the innovative brand-name drugs.[21] Since generic firms do not incur the costs of discovering and developing drugs, they tend to be much cheaper.

[20] The information was retrieved at http://www.cihr.ca/e/24939.html on October 20, 2010.

[21] Generic is the term used for a drug that contains the same medicinal ingredients as the original brand-name product. But, generic drugs may differ in peripheral features, such as pill colour or shape, inert binders and fillers, and the specific manufacturing process. Generic drugs may contain different non-medicinal ingredients (excipients), including stabilising, bulking, flavouring, colouring, and sweetening agents. They affect the size and shape of the drug and occasionally influence the acceptability of drugs (Strom, 1987; Bell et al., 2010; Ferner et al., 2010).

Table 2.4: Drug Sales by Major Therapeutic Class for Canada and Comparator Countries (%), 2009

Therapeutic Class	CAN	US	FRA	ITA	GER	SWE	SUI	UK
A: Alimentary Tract and Metabolism	12.6	12.4	10.4	10.7	11.9	9.9	12.6	11.0
B: Blood and Blood-Forming Organs	4.0	6.6	8.3	7.6	5.4	7.2	5.3	5.3
C: Cardiovascular System	21.6	11.9	15.0	16.8	11.6	9.0	14.3	12.5
D: Dermatologicals	2.8	2.1	2.3	2.2	2.5	2.3	3.5	3.1
G: Genito-Urinary System and Sex Hormones	4.6	5.4	3.3	4.1	4.1	4.8	4.4	4.2
H: Systemic Hormonal Preparations	1.0	1.4	1.7	1.7	2.0	2.4	1.4	1.9
J: General Antiinfectives for Systemic Use	6.6	10.2	11.5	13.6	10.2	10.2	11.2	9.8
L: Antineoplastics and Immunomodulating Agents	10.0	11.6	14.6	13.1	14.8	14.5	12.9	10.7
M: Musculo-Skeletal System	6.0	4.5	5.3	5.7	5.9	7.1	6.8	5.3
N: Nervous System	18.1	20.3	13.9	11.6	16.2	18.6	16.1	19.1
P: Antiparasitic Products	0.2	0.1	0.2	0.0	0.1	0.1	0.1	0.3
R: Respiratory System	6.9	8.1	6.4	6.1	7.2	8.4	6.6	9.9
S: Sensory Organs	2.2	2.2	2.1	1.7	1.9	2.2	2.5	2.6
V: Various	3.6	3.1	5.0	5.1	6.2	3.3	2.2	4.2
All Therapeutic Classes	100.0*	100.0*	100.0	100.0	100.0	100.0*	100.0*	100.0*

Source: PMPRB (2010)

* Values in this column are in percentages and may not add up to 100.0 due to rounding.

A generic manufacturers must conform to regulated high-quality manufacturing procedures and acquire a notice of compliance (NOC) from Health Canada to demonstrate that its product is bioequivalent to the corresponding brand-name original. As noted, by law the marketing of generic drugs is permitted only after the patent of the brand-name original drug expires.

In practice, however, a brand-name manufacturer can apply for multiple patents on a single drug over the drug's life cycle. The strategy is known as "patent evergreening": after receiving the initial patent, the brand-name manufacturer can add more patents on packaging or other non-medicinal aspects of the drug product. Without

being challenged, each extra patent can effectively evergreen the drug's market exclusivity.[22] If the remaining patents can be challenged, as either invalid or not-infringed by any new product, a generic manufacturer may start marketing its generic product before all patents associated with the brand-name product expire.[23] Apparently this counter-strategy comes with risks: the brand-name manufacturer may initiate a patent-infringement lawsuit. Such lawsuits can be very costly and have uncertain outcomes for any generic manufacturer. Consequently, patent litigation is perhaps one of the most important considerations for generic manufacturers (Bell et al., 2010). Hollis (2009) compares this uncertainty in the process of generic patent litigation to the process of discovering a new drug.[24]

The early bird catches the worm. Timing is a crucial aspect for generic manufacturers. The earlier the market entry, the greater market share a generic manufacturer gets (Hollis, 2002). However, being the earliest may not be desirable, because the generic firm that challenges the patent would likely be involved in a patent litigation. With the first firm assuming all the uncertainty of the costly patent-infringement lawsuit, its generic competitors may free-ride by entering the market immediately after the challenge clears without any litigation cost. To encourage early generic entry in the US, the first generic entrant can be granted a six-month market exclusivity period; such "compensation" mechanisms are rarely found in the Canadian legislations. An exception is found under the proposed Ontario drug reform. In Ontario, the first listed generic drug that challenges a brand-name drug's patent will be granted a three-month grace period to price the generic drug up to 50% of the brand-name drug price, rather than the 25% stipulated for all generic drugs (Ontario Ministry of Health and Long-Term Care, 2010).

Given the generic substitution policies established in the public and/or private drug insurance plans, once generic entry occurs, a brand-name drug's market share is expected to drop. However, lowering its drug price may not always be the best option

[22]For example, the largest brand-name manufacturer Pfizer holds as many as 17 patents for the global blockbuster Lipitor®. The first patent was filed in 1990 and expired in 2010. While the latest patent was filed in 2002 and will not expire until 2022 (Hollis, 2009).

[23]The most recent case in point is that the Canadian generic manufacturer giant Apotex started marketing Atorvastatin, the generic version of Lipitor®, 12 years before its last patent expires.

[24]Note that it is a different issue to compare the magnitude of the cost in new drug R&D and that in patent-challenging lawsuits.

for a brand-name manufacturer. This is also confirmed in my theoretical models and empirical studies. Brand-loyalty may retain a fair number of consumers who perceive the brand-name drug to have superior quality compared to its generic version. In addition, these brand-name manufacturers may participate in the generic market by making confidential arrangements with their subsidiary company or some generic firm to release "authorized generics". Such authorized generic drugs are also known as "pseudo generics". Their manufacturers are "authorized" or "pseudo" generic manufacturers, in contrast to "independent" generic manufacturers (Grootendorst, 2007).

Independent generic drugs bring genuine product competition against brand-name drugs, while authorized generics can be produced for anti-competition purposes by insulating brand-name drugs from generic competition. First, an early authorized generic entry that does not fear a patent lawsuit may deter or at least disincentivize the independent generic manufacturers to enter the market (Grootendorst, 2007). Second, by cannibalizing the low-end market, brand-name drugs may succeed in insulating the high-end market and retaining high prices.

It is usually not easy to assess empirically the real impact of the authorized generics because it is challenging, and sometimes impossible, for researchers to verify the genuine identities of generic drugs on a case by case basis. However, some Canadian-based studies greatly contribute to the relevant literature; to name a few, Grootendorst (2007), Competition Bureau (2007), and Hollis (2009). Their estimates show that authorized generics are available for 40% of drugs but only account for about 7% of generic sales in Canada. The numerical discrepancy is thought to be caused by late market entries of authorized generic drugs compared to the independent generics (Bell et al., 2010).

The Canadian pharmaceutical industry is heavily concentrated in market shares, due to the high barriers of entry and economies of scale in the industry.[25] In 2009, the top ten companies accounted for almost 60% and the top five accounted for nearly 40% of the total wholesale pharmaceutical sales in Canada. Among them, Pfizer Canada had the largest market share with 13.4% of Canadian drug sales which is

[25]Economists develop numerical indicators, such as the Herfindahl-Hirschman Index (HHI) and Concentration Ratio, to measure market concentration, indicating the competitiveness of an industry.

approximately double the individual market share of the other leading companies, except for Apotex (Table 2.2).

For the generic sector of the Canadian pharmaceutical industry, the concentration of market shares is even higher. The top five out of more than a dozen Canadian generic manufacturers accounted for over 80% of the total generic sales in 2006 (Competition Bureau, 2007).[26] Among them, two firms dominate the Canadian generic market. The Canadian-owned Apotex and Novopharm, owned by Teva Pharmaceuticals of Israel, took almost half of the Canadian generic market shares in 2006 (Table 2.5). When the brand-name sector is also taken into account, the two Canadian generic giants accounted for approximately 7.0% and 4.2% of the total drug sales in Canada in 2009, respectively (Industry Canada, 2010).

Table 2.5: Ranking of Canadian Generic Manufacturers by Sales CAD(000s), 2006

Rank	Manufacturer	Sales ($ 000s)	Generic Market Share (%)	Cumulative Market Share (%)
1	Apotex	1100.8	34.16	34.16
2	Novopharm	483.0	14.99	49.15
3	Genpharm†	365.3	11.34	60.48
4	Ratiopharm	359.5	11.16	71.64
5	Pharmascience	280.5	8.70	80.34
6	Sandoz Canada	190.1	5.90	86.24

Source: Competition Bureau (2007).

† Mylan Laboratories Inc. of the US acquired Genpharm in 2007, as part of its acquisition of Merck KGaA's generic business, Genpharm's parent company.

Since consumer-targeted prescription drug promotion is banned in Canada, brand-name manufacturers normally employ sales forces to market their drug products to prescribers. The sales representatives reach out to physicians and other health professionals with prescribing privileges through the detailing process.[27]

In contrast, generic manufacturers do not hire as many sales representatives to promote their drug products. Instead, they compete by offering rebates to pharmacies for shelf space considering that pharmacies are reluctant to switch generic products

[26] This includes sales to both hospitals and retail pharmacies in Canada.

[27] Sales representatives from the pharmaceutical industry can visit physicians or other prescribers in their offices or stores to promote drug products of their company with the intent of influencing prescribing practice.

once a specific generic product is stocked (Bell et al., 2010).[28]

Pharmaceutical manufacturers typically use product differentiation strategies to soften price competition. In general, one brand-name drug manufacturer strategically differentiates its product from that of another brand-name drug manufacturer in the dimension of therapeutic variants. A brand-name drug manufacturer also strategically differentiates its product from the generic substitutes in the dimension of perceived quality.[29] The successful implementation of those strategies also depends on the influence of other important players in the system.

As mentioned in the introduction of this chapter, the consumption of pharmaceutical products involves multiple parties, including manufacturers (brand-name and generic), distributors of pharmaceutical products (wholesalers and retail pharmacies), the public (therefore, taxpayers) and private insurers, health professionals (physicians, nurses, and pharmacists, etc.), and patients. It is essential to clarify the interactions among the major stakeholders to understand how the system works. In the next section, I discuss the roles the key stakeholders play as well as their interrelationships in the pharmaceutical system.

2.3.2 Other Key Stakeholders in the Pharmaceutical System

Patients

Patients are the consumers of prescription drugs and the ultimate recipients of professional services provided by other stakeholders. However, patients normally lack the knowledge and expertise to make choices on which drugs to buy.[30] Ultimately, they must rely on their physicians, pharmacists, or other health professionals to make the purchase decision. In this sense, patients' demand for prescription drugs is *induced* by these health professionals based on the medical conditions of the patients.

Patients may not need to pay, or only pay partially, when prescriptions are filled because 98% of the Canadian population is covered by some forms of public or private

[28]The reason could be to avoid unnecessary operational costs. However, it may well be the result of an arrangement in exchange of the rebates.

[29]Chapter 3 examines the two-dimension product differentiation in detail.

[30]Patients may develop limited knowledge on prescription drugs through certain channels, such as DTCA, communication with health professionals, or educational campaigns with respect to prescription drugs Shrank et al. (2009a).

drug insurance plans (Bell et al., 2010). Consequently, the majority of Canadian consumers do not respond promptly to changes in prescription drug prices in the same way as they may react to price changes in other consumer products and services. As Kephart et al. (2007) and Grootendosrt (2008) find, most individuals have inelastic demand for prescription drugs due to "small income effects, limited substitution opportunities or high marginal valuation of health". In addition, cost-sharing strategies such as copay, coinsurance, deductibles, etc. do not have significant impacts on patients' demand for prescription drugs, as long as they are applied appropriately, e.g. in combination with annual limits on the total copays.[31] As such, the separation of the payer, the decision-maker of purchase, and the final consumer of prescription drugs renders competing objectives and interests from various stakeholders. This distinguishes pharmaceutical products from other consumer products and services.

Government

Canadian public drug insurance plans paid for almost 40% of the total drug expenditure in 2009 (CIHI, 2010a) making them one of the largest purchasers of pharmaceuticals in the country. As a result, the public sector is highly cost-conscious. At the federal level, the PMPRB implements tight price regulations over patented drugs offering breakthrough or substantial improvement in therapy. The PMPRB uses seven developed counties as comparators and indexes the growth of drug price to the annual CPI. At the provincial level, various strategies to contain drug costs have been developed based on provincial generic substitution regulations in combination with other cost-sharing measures, such as insurance deductibles and/or copays.

Broadly speaking, the provinces use both maximum-reimbursable-cost type of strategies and provincial formularies to control drug costs. But each province can interpret these policy tools in different ways.[32] The implementation of maximum-reimbursable-cost type of policies vary across the provinces. For example, British Columbia's Reference Drug Program currently includes five classes of drugs.[33] The

[31]Note that excessive copays can reduce drug utilization and may be associated with adverse health consequences (Kephart et al., 2007). In particular, certain cohorts, such as the poor and unhealthy, may be very sensitive to changes in drug prices. Most provincial drug plans impose tiered copays and/or deductibles according to household income (see Appendix A).

[32]Detailed information on the provincial/territorial drug plans is offered in Appendix A.

[33]They include: Histamine 2 Receptor Blockers (H2 Blockers), Non-Steroidal Anti-Inflammatory

province may provide full coverage for the reference drugs — those drugs considered to be the most medically effective and the most cost-effective in that category (CIHI, 2010a; CIHI, 2010b). Other provinces, such as Nova Scotia or Alberta, use the Maximal Allowable Cost (MAC) and/or the Least Cost Alternative (LCA) policies, in which provincial drug plans reimburse a specific unit cost within an interchangeable therapeutic class.[34] A provincial formulary is a list of prescription drugs covered by the provincial drug plan. The formulary determines the reimbursable drugs accessible to all qualified beneficiaries. Each province makes its own decision regarding the formulary used by the provincial drug plans.

Despite considerable differences at the operational level across the country, the generic substitution laws and drug reimbursement policies all serve one ultimate goal: to promote and/or require the substitution of cheaper generic drugs over the more expensive brand-name drugs.

Three of the four largest provinces (Alberta, Ontario, and Quebec) also employ a price-cap policy to further control generic drug prices and periodically all three provinces have attempted to achieve more savings for their drug plans by lowering the price-cap (Bell et al., 2010). The price-cap policy may be an effective mechanism to lower drug reimbursement costs for the provincial drug plan. However, it is possible that the benefit of these savings to the drug plans results in increased generic drug prices for patients not covered by the public plans. In response, Ontario's drug reform intends to phase in the same price-cap policy for generic drugs that are covered by private insurance plans and purchased out-of-pocket before 2012 (Ontario Ministry of Health and Long-Term Care, 2010).

Provincial drug plan managers also commit to guaranteeing Canadians timely and convenient access to prescription medications (generic drugs, in particular). This can be a competing priority with the drug cost containment agenda (Bell et al., 2010). The reduction of generic drug prices may have other unintended effects yet to be

Drugs (NSAIDS), Nitrates, Angiotensin Converting Enzyme Inhibitors (ACE inhibitors), and Dihydropyridine Calcium Channel Blockers (Dihydropyridine CCBs).

[34]The MAC price is the maximum allowable cost per unit (e.g., tablet, capsule, milliliter, etc.) established by the provincial drug plan for an interchangeable drug category. A maximum allowable cost is determined by examining costs available from drug manufacturers and is based on the lowest price available to pharmacies. The LCA price is the lowest unit cost established for a drug product within a set of interchangeable drug products (CIHI, 2010b).

identified and studied. For example, there were nationwide shortages of a variety of generic drugs after the ODBP implemented the 25% generic price-cap in July 2010. Many patients were reportedly forced to switch from treatments they had used successfully for years. However, the generic industry did not explicitly associate the drug supply shortage with the policy change. The generic industry claimed that the shortage would be temporary and was caused by worldwide shortages of medicinal ingredients, changes to regulations, shutdowns at major manufacturers and other production changes (Blackwell, 2010).

Prescribers

Although the prescribing privileges are now extended to many health professionals, including pharmacists, nurses, optometrists, midwives and podiatrists, etc., under certain circumstances, Canadian physicians remain the profession to write the majority of prescriptions (Sketris, 2009; Bell et al., 2010).

Prescribing practices can be influenced by the practice of detailing, including both profit-driven detailing from the pharmaceutical industry and non-commercial-based academic detailing.

There has long been a close relationship between sales representatives from the brand-name drug firms and prescribers. It has been estimated that about 6,000 drug representatives visit Canadian physicians regularly (Kondro, 2007; Health Council of Canada, 2010). Through the detailing sessions, drug sales representatives discuss their company's latest drug products, provide free samples, or offer gifts, in the hope that the prescribers can remember and prescribe their products to patients more often and more widely.[35]

Academic detailing can also influence prescribing habits and patterns. In contrast to drug representatives' detailing, academic detailing is an unbiased university or non-commercial-based educational outreach activity, delivered by health educators, typically pharmacists, physicians, or nurses hired by the university. A key component

[35]Note that with the knowledge of the latest drug therapies through the detailing practice, prescribers may opt for prescribing a new patented drug product rather than substituting generic drugs for the old brand-name drug that is off-patent. For example, ezetimibe (WHO-ATC code (5^{th} level): C10AX09) is a relatively new drug product used to lower cholesterol compared to statin drugs (WHO-ATC code (4^{th} level): C10AA) (Lioudaki et al., 2011). Prescribers may prescribe brand-name ezetimibe rather than generic statins.

of the academic detailing practice is that the detailers do not have any financial links to the pharmaceutical industry.[36]

It is noteworthy that prescribers may have the privilege to write "no substitution" on the prescription, an exception in the generic substitution regulations (Competition Bureau, 2007). In this situation, pharmacists cannot substitute the generic version for the brand-name drug either at their discretion or under the legal requirements. Only the brand-name drug specified in the prescription will be dispensed to patients. This may occur when a patient must receive a specific brand of drug for medical reasons, for example, the patient is allergic to certain excipients contained in generic drugs. In addition, a patient may also self-request "no substitution" and he or she pays any additional drug costs out-of-pocket (Bell et al., 2010; Competition Bureau, 2007).[37] This important fact is modelled in Chapter 3.

Pharmacists and Pharmacies

Pharmacists represent the final portal for patients in the drug product delivery process. They dispense prescribed drugs to patients, after the drugs are manufactured by the industry, distributed to pharmacies, and prescribed by physicians.

The functions provided by pharmacists as health professionals go beyond dispensing prescription drugs. The role of pharmacists is expanding under recent regulatory changes across Canada (Bell et al., 2010). Besides compounding, preparing, and dispensing drugs, their functions also involve providing counselling to patients, taking and maintaining patients' medication histories, making recommendations to prescribers for medication adjustments, monitoring patients to prevent or minimize the potential adverse drug reactions, and prescribing certain drugs under some conditions, among many other responsibilities (Canadian Pharmacists Association, 2008).

Pharmacies hire pharmacists and technicians to serve patients. At the same time, pharmacies also are the major customers of the generic drug industry. In particular, Canadian pharmacies' profits strongly rely on dispensing generic drugs, regardless

[36] See Avorn and Soumerai (1983).

[37] Similar findings are also identified in a US-based study. Shrank et al. (2009b), in their study on American patients' perceptions on generic drugs, demonstrate that about one-third of the survey respondents ask their physicians or pharmacists to substitute generic drugs for the brand-name counterparts most or all of the time.

of the various forms of pharmacies in the country (Bell et al., 2010).[38] An effective approach used extensively by generic manufacturers to compete for customers is off-invoice rebates that attract pharmacies to stock and dispense their drug products. The nature of these rebates is not transparent, and therefore, not well-documented.[39] But rebates from generic manufacturers clearly play a significant role in pharmacies' traditional business model, because their services are paid for, in part, by rebates.

Currently, rebates are not allowed in Ontario and Quebec. The Ontario Transparent Drug System for Patients Act of 2006, prohibits rebates to pharmacies for the drugs covered by the provincial drug plan. Meantime, a variant of the rebates, professional allowances, is still allowed in the province. The professional allowance may be as high as 20% of the invoice generic drug price (Competition Bureau, 2007). However, the proposed new provincial legislation in Ontario not only completely bans the professional allowances (rebates) for the public plan, but also rigorously stipulates that the professional allowances cannot be higher than 50% of the generic drug price for the private plan. Moreover, this percentage will be lowered gradually over time and reduced to zero by 2013 (Ontario Ministry of Health and Long-Term Care, 2010). Manufacturers and pharmacies may find other ways to continue the rebate practice, e.g. by providing discounts for bulk purchases from pharmacy chains and franchises (Bell et al., 2010).[40] This block-funding type of practice renders drug manufacturers' price setting behaviour for individual drugs unclear and uncertain.

The path diagram in Figure 2.3 summarizes the relationships of the key stakeholders in the pharmaceutical system under the out-patient setting. Figure 2.3 is adapted from Figure 2 of Bell et al. (2010, pp.26). It should be noted that I exclude from the original figure the distributors and hospitals.[41] In this thesis, I focus on the discussion of drug price and the associated market structure and policies on the

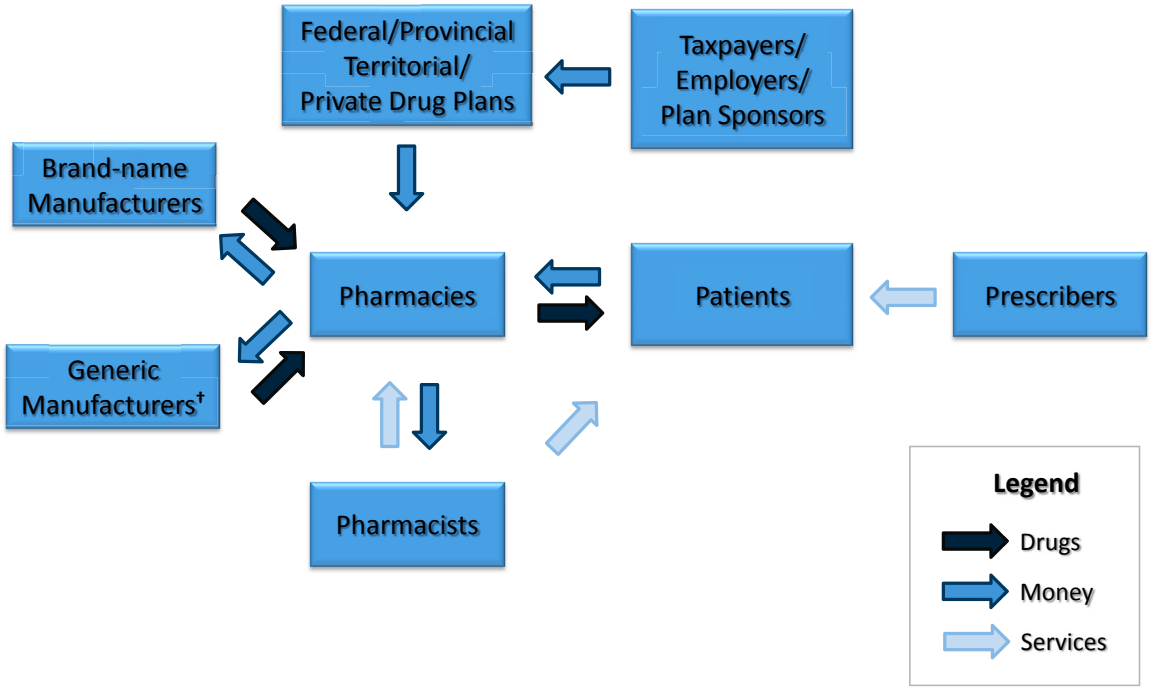
[38] Pharmacies in Canada can be categorized broadly in three types: independent, retail pharmacy groups, and food and mass-merchandiser pharmacies.

[39] It is estimated that the average rebates could be at 40% of the invoice price (Competition Bureau, 2007).

[40] Similar bulk-purchase discount/rebates may also exist between manufacturers and public drug plans.

[41] They are important stakeholders in the system. I exclude them in the discussion because (1) the distributors do not interact directly with other key stakeholders and (2) hospitals play their roles only in the in-patient setting.

Figure 2.3: Overview of Key Stakeholders of the Canadian Pharmaceutical System



Source: Adapted from Bell et al. (2010)

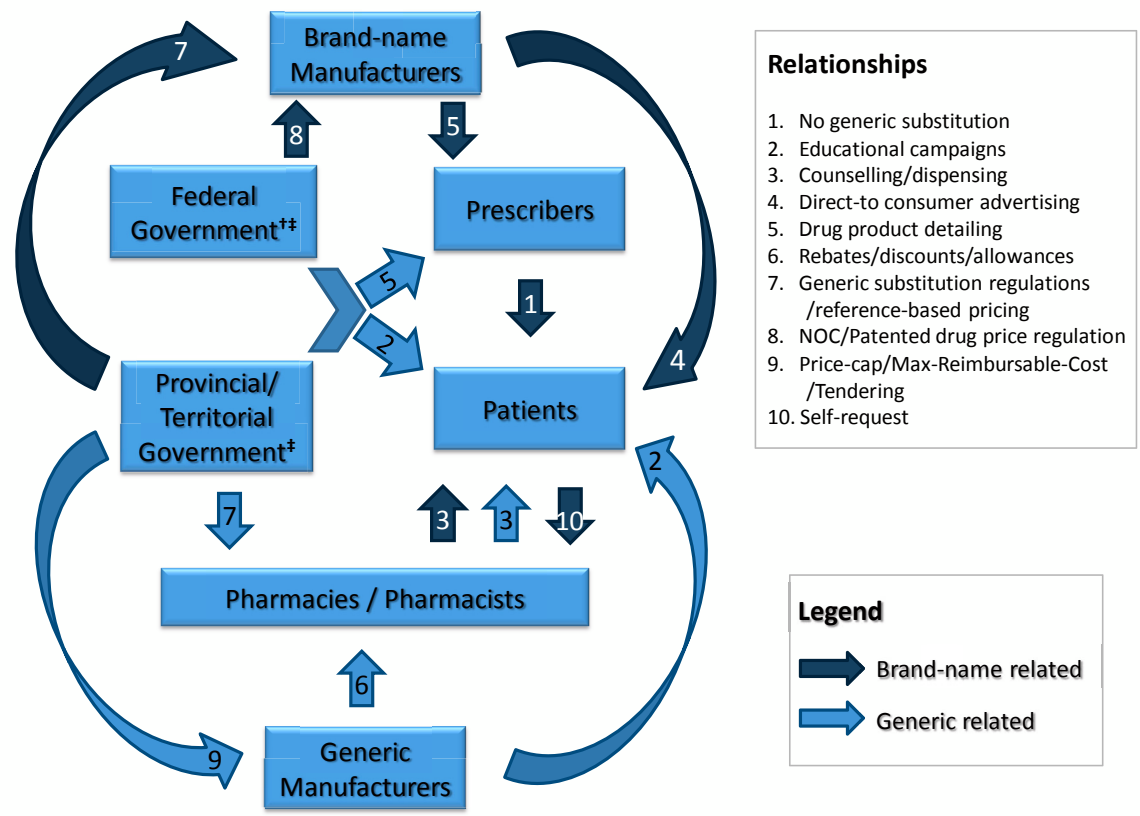
* Only the stakeholders in the out-patient setting are included. Some drug products may be sold through wholesaler, which is not included in the diagram.

† Authorized generic manufacturers produce generic drugs under special arrangements with brand-name drug manufacturers.

out-patient setting.

It should be noted that a consumer who takes prescription medications is rarely the one who pays for the purchase or the one who makes the purchase decision in the first place. Yet no one can dictate a patient's final purchase and consumption decisions. It is the combination of the stakeholders' forces and incentives that shape the market demand for prescription pharmaceuticals. With these characteristics, I can use Figure 2.4 to summarize how some stakeholders in the pharmaceutical system influence others and how these stakeholders jointly determine patients' demand for either brand-name or generic drugs.

Figure 2.4: A Flow Chart toward Drug Products by Key Stakeholders of the Canadian Pharmaceutical System



* This flow chart focuses on the relationships among key stakeholders of the public sector in the Canadian pharmaceutical system. The private sector is excluded in the chart. The chart demonstrates key stakeholders' attitude/incentives toward brand-name or generic drug. It does not compare the magnitude of these attitude/incentives. Some drug products may be sold through wholesaler, which is not included in the diagram.

† Health Canada and the PMPRB are the federal department/agency responsible for issuing the NOC and regulating patented drug price, respectively.

‡ Provincial/territorial governments are primarily responsible for the funding of pharmaceuticals, but the federal government also have public drug plans for eligible groups.

2.4 Other Key Stylized Facts of the Canadian Pharmaceutical System

So far the discussion focuses primarily on the institutional background of the Canadian pharmaceutical system in the domestic setting. However, the Canadian pharmaceutical market operates in the world marketplace through many bilateral or multilateral trade agreements such as the WTO and the NAFTA.

In fact, given the relatively higher US brand-name drug prices, geographic proximity between the US and Canada, and lack of insurance coverage for Americans, there has been a long history of cross-border sales by Canadian pharmacies to US customers (Paris and Docteur, 2007). This trend culminated with the expansion of Internet pharmacies in the early 2000s, with estimated annual drug sales of US$ 1 billion from the Canadian pharmacies to the US customers (Morgan and Hurley, 2004). This accounts for almost half of the total Canadian export of pharmaceuticals. The growth of sales by Internet pharmacies is a key concern to the brand-name industry, which operates in both Canadian and the US markets. Because of the implementation of the US Medicare Part D[42] and the strengthening Canadian dollar, cross-border Internet pharmacy sales between Canada and the US have steadily declined since then (Industry Canada, 2010).

Some American customers without insurance coverage turned to Canadian pharmacies to fill their prescriptions because it could save them thousands of dollars a year. The US brand-name drug manufacturers are concerned, as this practice of cross-border shopping sabotages manufacturers' price discrimination strategies within the US domestic market. To influential customers who have the bargaining power of millions of beneficiaries, such as government drug plans, insurance companies, or Health Maintenance Organizations (HMOs), the brand-name drug manufacturers can offer confidential and discounted prices, while to the uninsured, the brand-name drug manufacturers would charge significantly higher prices at the retail level.

Even though the majority of Canadians are covered by some form of drug insurance, regional disparities do exist (Grootendorst, 1999; Coombes et al., 2004).[43] As I have shown, Canadian policies on prescription drugs are somewhat fragmented at the provincial level. For instance, the insurance coverage for new drugs may be broader and their approval may be faster in some provinces, but narrower and slower in others (Table 2.6). In addition, leveraging their large population sizes, some provinces (e.g. Ontario) may be able to implement tight controls over generic drug prices for public

[42]Medicare Part D is a federal program to subsidize the costs of prescription drugs for Medicare beneficiaries in the United States. It was enacted as part of the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003 and went into effect on January 1, 2006.

[43]Detailed information on the provincial/territorial drug plans can be found in Table A.1.

drug plans and affect private drug plans and patients without any insurance coverage. Small provinces (e.g. the Atlantic provinces) cannot afford to do so, given the much smaller population sizes. As a result, while prescription drug prices may not be much different at the "factory-gate" level across the country, the actual costs at the retail and/or claim level can vary significantly (Table 2.7).

Table 2.6: Formulary Listing of New Products by Provinces

Province	**% of New Drugs Reimbursed*** **2004 Jun - 2006 May**	**Average Time to Listing (in days)**** **2004 Jun - 2006 May**
Alberta	19%	293
British Columbia	15%	371
Manitoba	25%	422
New Brunswick	8%	547
Newfoundland & Labrador	10%	298
Nova Scotia	17%	341
Ontario	13%	417
Prince Edward Island	9%	632
Quebec	31%	361
Saskatchewan	24%	381

Source: Adapted from Paris and Docteur (2007)

* Listings for Single-Source Products Launched June 1, 2004 to May 31, 2006.

** Average Time to Listing for Full and Restricted Listings June 1, 2004 to May 31, 2006.

There are disparities for residents within a province. As the most influential purchasers of pharmaceuticals, government drug plans are capable of controlling prescription drug reimbursement costs by regulation. In contrast, individual private insurance companies normally do not have the leverage to reach the drug cost containment goal to the same degree without government intervention, nor do out-of-pocket patients. It leaves room for price discrimination against different groups within a province. If a province chooses to impose price-caps on the reimbursement prices for public drug plans only, pharmacies may be able to recoup their lost revenue through private payers. They could increase either drug prices or dispensing fees that they charge to private plans and out-of-pocket patients (Bell et al., 2010). For example, of the three provinces that employ the price-cap policy, only Ontario clearly states that the province will phase in the same low percentage applied to the public drug plan

for private drug plans and out-of-pocket patients (Ontario Ministry of Health and Long-Term Care, 2010).

Table 2.7: Prices of Commonly Prescribed Drugs in Ontario, Quebec, Manitoba, and Newfoundland and Labrador

Generic Drug Name†	**ON Price ($)**	**MB Price ($)**	**NL Price ($)**	**MB Price Diff.*** **(%)**	**NL Price Diff.*** **(%)**
Paroxetine 20mg	0.79	1.10	1.09	+39	+38
Ramipril 10mg	0.47	0.66	0.72	+40	+53
Simvastatin 20mg	1.10	1.52	1.51	+38	+37

Source: Adapted from Hollis (2009) - prices drawn from provincial formularies as of 16 June 2008, and rounded to the nearest cent per pill.

† These are examples of commonly prescribed drugs (ranked top 200 in 2006 world sales). Paroxetine is used to treat major depression, obsessive-compulsive, panic, social anxiety, and generalised anxiety disorders in adult outpatients. Ramipril is used to treat hypertension and congestive heart failure. Simvastatin is used to control hypercholesterolemia (elevated cholesterol levels) and to prevent cardiovascular disease.

* Price differences indicate the price premium paid in Manitoba and Newfoundland and Labrador compared with prices in Ontario.

In general, there is a lack of national strategy or an inter-provincial coordination mechanism in controlling drug prices.[44] As major purchasers of pharmaceuticals, provincial drug plans find their own way to control prescription drug spending. For example, Alberta, Ontario, and Quebec adopt the generic price-cap policy, British Columbia uses a reference-based pricing reimbursement system for selected drugs, Saskatchewan applies competitive tendering for selected generic drugs,[45] and all provinces adopt the maximum-reimbursable-cost type of policies in various degrees. However, without an inter-provincial coordination mechanism, a beneficial policy in some provinces may bring unintended negative effects for others (Competition Bureau, 2008).[46] For example, the most-favoured nation (MFN) clause requires

[44]Nevertheless, there is a successful prototype of inter-provincial collaboration in drug policies, namely the Common Drug Review (CDR). The CDR is a national drug assessment process, performed by the Canadian Agency for Drugs and Technologies in Health (CADTH).

[45]Competitive tendering normally involves the restriction of generic products that will be reimbursed by a public plan based upon bids provided by potential suppliers. It is used extensively by Canadian community and hospital pharmacy sectors to obtain competitively priced generic drugs. But currently only Saskatchewan has used competitive tendering at the provincial plan level (Competition Bureau, 2008).

[46]Interested readers may refer to Competition Bureau (2008) for a more detailed discussion.

that a province be granted the same lowest price that is provided to another province or private payers.[47] While this policy may be designed to acquire favourite conditions for the residents in a province, it fuels the disincentives for pharmaceutical manufacturers to sustain high prices in other provinces so that they are not obliged to lower prices in the MFN province.

2.5 Concluding Remarks

This chapter provides an overview of the multifaceted Canadian pharmaceutical system, with a special focus on drug price related factors based on the most recent literature. It also provides a broad institutional background for the theoretical discussion and the empirical research that follow.

The policies and legislations in the Canadian pharmaceutical system are fragmented. The Constitution established the roles and power of both the federal and the provincial/territorial governments in creating and administering key elements of the Canadian healthcare system, including the subsystem of pharmaceuticals. The federal government is responsible for drug approval guaranteeing safety and efficacy and enforcing the intellectual property laws, such as the Patent Act. The federal agency, PMPRB, regulates the prices of the breakthrough patented drugs from being excessive, compared to the prices in the selected seven industrialized countries. The provincial/territorial governments are responsible for the delivery of the public drug (insurance) plans. Each province makes its own generic substitution regulations and assesses the cost-effectiveness of drugs by its independent professional committee.

The pharmaceutical industry has a two-tier structure composed of brand-name drug manufacturers and generic drug manufacturers. These two sectors produce bioequivalent drug products but the brand-name and generic drug manufacturers use distinct strategies to market their products and to compete with their rivals. As a result, the two sectors are subject to different types of government regulations. But they all need to conform to the basic safety and efficacy standards. Both the Canadian brand-name and generic sectors are heavily concentrated in market shares, due to the high barriers of entry and economies of scale.

[47] Currently, MFN clauses are effective in Quebec and Newfoundland and Labrador.

The consumption of drugs involves multiple parties, including manufacturers, public and private insurers, prescribers, pharmacies and pharmacists, and patients. These key stakeholders play different yet significant roles in the delivery and consumption process of drug products. The changing Canadian policies and legislations impact the relationships among these stakeholders in the pharmaceutical system.

There are ongoing issues under debate in the Canadian pharmaceutical system, such as the de-facto cross-border DTCA and the federal ban on domestic DTCA and the National Pharmaceutical Strategy. There are existing and widening disparities in pharmaceutical policies within and between Canadian provinces. This lack of a national strategy or an inter-provincial coordination mechanism remains one of the major obstacles for effective pharmaceutical policies that are designed to improve the health of all Canadians.

Chapter 3

An Oligopolistic Model with Two-dimension Product Differentiation for a Typical Canadian Prescription Drug Market

3.1 Introduction

After a comprehensive overview of the institutional background of the Canadian pharmaceutical market in Chapter 2, this chapter offers an economic theoretical framework to systematically analyze the research questions raised at the beginning of this thesis. The theoretical analysis in this chapter also underpins the empirical study on drug price dynamics of the Canadian pharmaceutical market in Chapter 4.

A typical market of prescription drugs in Canada is usually concentrated with no more than a dozen of manufacturers, including both brand-name and generic drug manufacturers. Many empirical studies have found that brand-name drug manufacturers are able to maintain a downward price rigidity for their drug products in the face of competition from generic substitutes. In addition, brand-name drugs normally enjoy considerable price premiums over their generic substitutes. What is so special about the Canadian pharmaceutical market? Can I use economic theories to explain the above empirical findings?

To answer these questions, I use oligopoly theory with product differentiation to model a typical Canadian prescription drug market. I conduct comparative statics to study the qualitative characteristics of the equilibrium prices. I investigate the impact of preference/policy change on pharmaceutical firms' price setting strategies in equilibrium under different settings.

The chapter is organized as follows. Section 3.2 presents a review of literature on the oligopoly theory with product differentiation. Then in Section 3.3 I introduce the baseline model characterized by two brand-name drugs and one generic drug in

a typical therapeutic market with two-dimension product differentiation. With and without a generic price-cap, the equilibrium prices and the impact of preference/policy change are studied in detail. Sections 3.4 and 3.5 extend the baseline model, with a reimbursement system of therapeutic reference pricing and with four players, respectively. The policy implications are summarized in Section 3.6. Finally, Section 3.7 concludes.

3.2 Literature Review of the Oligopoly Theory with Product Differentiation

The concept of product differentiation is a relatively new branch of economics rooted in the oligopoly theories from over a hundred years ago.

The first formal model on oligopoly can be attributed to Cournot (1838), in which firms compete in quantities, and prices are determined by the interplay of supply and demand. An antithesis by Bertrand (1883) predicts that firms always undercut each other's price in the hope of getting a larger market share. Following this line of reasoning, marginal cost pricing will eventually prevail and firms earn zero profit irrespective of the number of firms in the market. However, lack of empirical evidence from the field makes Bertrand's original theory unrealistic.

Since Bertrand (1883), oligopoly theories have modified and improved Bertrand's paradigm by relaxing one or more counterfactual yet crucial assumptions. For example, in Bertrand's paradigm the following assumptions were made: (1) There is no product differentiation and therefore, products are perfect substitutes to each other. (2) Firms do not have production capacity constraint so firms are able to supply the whole market. (3) Consumers have full information about the market, and consumers' taste is homogeneous such that a marginal price-cut is sufficient to win over all consumers from the opponents. (4) Price competition is a one-shot game hence a firm chooses the best strategy taking into account the best strategies chosen by the opponents (Nash equilibrium) and the market clears once and for all.

The first restrictive assumption of no product differentiation has received most of the critiques throughout the development of oligopoly theory. This is also the focal

point of the discussion in this chapter. Chamberlin and Hotelling are two representative economists who substantially relaxed the first assumption.

Chamberlin (1933) analyzes the model of monopolistic competition. With a monopolistic competitive market structure, each firm only produces and sells a single and unique product, and each firm faces a downward-sloping demand curve. However, it is different from a monopolistic market since market entry and exit is assumed to be free. In addition, products are differentiated in a symmetric fashion such that at the Nash equilibrium price, every firm faces zero reactions by other firms to its own price changes (Lancaster, 1990). Should positive (negative) economic profit exist in the short run, the market will attract (drive) firms to enter (exit) the market. In the long run, "[e]ntry ceases when the demand curves for all products have fallen to the point where it is tangent to the average cost curve, with price equal to average cost and marginal revenue equal to marginal cost" (Lancaster, 1990). The number of firms (also conceived as the degree of product differentiation, since every firm only produces its single product) are thereby determined in the long run. Product differentiation enables the firm to charge more than its marginal cost. This market power thus distinguishes a monopolistic competitive firm from one in a perfect competitive market.

Hotelling's (1929) "address approach" is distinct from Chamberlin's "non-address approach" in the sense that the former introduces "the location of firm", as the strategic variable.[1]

Hotelling (1929) does not directly propose differentiation in a product's inherent attributes. Instead, he assumes that two firms may locate in different positions on the linear "main street" selling identical products.[2] Consumers, on the other hand, are assumed to be homogeneous in taste and uniformly distributed in the linear space. If a consumer's distance to firm 1 is shorter than his or her distance to firm 2, he or she strictly prefers firm 1's product because of the higher transportation cost he or

[1]In the literature of product differentiation, the address approach is more successful because more model variants under this branch can be identified and they are more capable of explaining the reality.

[2]But it is straightforward to interpret or internalize those characteristics, such as product accessibility in Hotelling's model. After all, consumers observe these differences of all aspects in product even though the difference may be small.

she would have to pay to purchase firm 2's product, and vice versa.[3]

Suppose that firm 1 charges price p_1 for the product. At the price of $p_2 = p_1 + i$ (for an arbitrarily small but positive i), firm 2 is still able to sell its product to those consumers close to firm 2. The price differential i is more than offset by the difference in transportation costs. Therefore, Hotelling predicted that the competitive equilibrium suggested by Bertrand (1883), where both p_1 and p_2 are set to the marginal cost, is no longer the solution. Alternatively, he showed that duopolists have the incentive to locate closer to the street center to maximize profits. However, this "principle of minimum differentiation" by Hotelling does not explain the fact that firms do differentiate their products in the real world.

How to interpret Hotelling's result properly remained an open question. The study on product differentiation was not advanced for half a century until economists started to employ the ideas of strategic behaviours from game theory in the late 1970s.

By modifying the functional form of the transportation cost in Hotelling's model to a quadratic one, d'Aspremont et al. (1979) demonstrated that firms will locate at both ends of the one-dimension street to maximize profits. They explain the "maximum differentiation" as follows. On the one hand, if prices are given, both firms have strong incentives to locate in the street center. This is driven by the force of market demand and is consistent with Hotelling (1929). On the other hand, the two firms try to differentiate (in location) from each other to soften price competition. This is driven by the force of strategic moves. Therefore, the maximum differentiation is a result of the tradeoff between the two forces.

For ease of interpretation, the "location" of the product from a firm is internalized in the firm's strategic decision regarding its product such that it can be conceived as specific product attributes, e.g. iphone® vs. blackberry® in the smart phone market, SPSS® vs. SAS® in the market of statistical packages, or front-loaded vs. top-loaded washing machines in the home appliance market, etc. Consumers' preference is not homogeneous. In other words, a consumer chooses the ideal product according to his or her individual preference. The products are considered to be broadly of equivalent quality, and therefore, the heterogeneous consumers do not necessarily agree with one

[3]Hotelling interprets a higher transportation cost as a consumer's disutility from not consuming his or her ideal product.

another on the ranking of the products. The product differentiation in "location" is termed "horizontal" product differentiation.

If all characteristics of one product dominate those of another in some measures, e.g. a Lamborghini® vs. a Smart® in the automobile market, Windows® 7 vs. Windows Vista^{TM} in the computer operating system market, or a suite in a five-star hotel vs. a motel room, then there is "vertical" product differentiation in those measures.[4] All consumers rank the products universally by some measures, such as product quality. Shaked and Sutton (1982), among others,[5] first proposed the vertical product differentiation. They model a simple duopolistic equilibrium characterized by distinct quality levels chosen by the two firms, with both firms enjoying positive profits. The intuition, in line with that of the horizontal product differentiation model, is that the demand effect may drive both firms to choose close qualities, but the strategic effect outweighs the demand effect under the assumption of uniformly distributed income.[6] Quality differentiation diminishes price competition and the profits of both firms are maximized.

Horizontal and vertical differentiation models are in fact the two sides of a coin. Champsaur and Rochet (1989) noticed that "some particular models of vertical differentiation and horizontal differentiation produce results of the same nature". Cremer and Thisse (1991) summarized the idea:

> Every model belonging to a very large class of Hotelling-type models (including all the commonly used specifications) is actually a special case of a vertical product differentiation model.

The simplification of one-dimension horizontal or vertical differentiation models lends us many insights understanding oligopolists' behaviour. But, product is rarely measured in only one dimension in the real world. DePalma et al. (1985), Economides (1989), Neven and Thisse (1990), Vandenbosch and Weinberg (1995), Irmen and

[4]Of course, price of a product is not considered as a characteristic of the product.

[5]These include Gabszewicz and Thisse (1979) and Mussa and Rosen (1978).

[6]Neven (1986) discussed that non-uniform distribution, such as uni-modal or other centered distributions, may result in minimized differentiation, in which both firms have an incentive to locate close to the peak of the distribution to enjoy stronger "market retention". In this situation, the demand effect outweighs the strategic effect which drives both firms to move apart to relax price competition.

Thisse (1998), and Tabuchi (2002), among many others, add a second dimension to the analysis. They found that under certain circumstances, firms maximize product differentiation in only one dimension and minimize the differentiation in the other dimension in equilibrium, rather than maximize differentiation in both dimensions. It is commonly known as a "Max-Min" equilibrium.

Brekke et al. (2007) studied the pharmaceutical market on the policy implication of reference pricing under a setting of European Union countries. The model involves three pharmaceutical firms with differentiated drug products in both the horizontal and vertical dimensions. They analyzed pharmaceutical firms' price setting strategies under different reimbursement regimes by comparing drug price levels quantitatively. Brekke et al. (2007) conclude that among the generic reference pricing (GRP), no reference pricing (NRP), and the therapeutic reference pricing (TRP), the TRP regime has the lowest drug price level.[7] But, it also reduces patent-holding firms' profitability and potential R&D activities.

In the following section, I develop my baseline model following Brekke et al.'s (2007) GRP case. My model is unique in the following aspects. First, I model patients' preference on drug quality differently so that the heterogeneity in patients' perceived quality is embodied in the different attitudes for the brand-name drug with generic substitutes, given the different types of patients. Secondly, I analyze the qualitative characteristics of the drug prices – the comparative statics of the equilibrium price when exogenous shocks, such as shift in preference or policy change, are introduced to the therapeutic market. My theoretical model reflects the Canadian institutional context.

[7]Note that Brekke et al. (2007) assume only *one* generic drug for each class. Therefore, the term GRP is equivalent to the MAC/LCA policy in the Canadian provinces such as Nova Scotia or Alberta, in which the interchangeable therapeutic class is defined with respect to each drug molecule and all drugs are covered (subject to copays and/or out-of-pocket brand-name price premium). Similarly, the term TRP in Brekke et al. (2007) is equivalent to the Special MAC policy in Nova Scotia or the reference-based pricing policy in British Columbia, in which the interchangeable therapeutic class is defined with respect to many drug molecules and only the cost of the generic drug is covered (subject to copays and/or out-of-pocket brand-name price premium). When there are more than one generic drug within the drug class, however, the Special MAC policy is not exactly the same as the reference-based pricing policy, where the former is based on the maximum allowable unit cost in a broad therapeutic class; the latter is based on some predetermined "reference" drug — normally the most medically effective and the most cost-effective drug in the broad therapeutic class.

3.3 The Baseline Model

The baseline model assumes that there are three single-product pharmaceutical firms in one therapeutic market, with two brand-name firms and one generic firm. One brand-name drug, named 0, is not under patent protection and therefore, has a generic substitute, named G. The other brand-name drug in this therapeutic market, named 1, is still on patent.[8] The price of the generic drug G is capped by a predetermined percentage of the price of its brand-name original, drug 0.

All patients are assumed to be covered by some form of drug insurance,[9] under which patients are only responsible for paying pharmacies out-of-pocket insurance deductibles and copays. The public/private drug plan reimburses the rest of the drug cost to the pharmacies.[10] With the knowledge of patients' preference and government's pricing and reimbursement policy options, the three firms compete in price in a one-shot game framework. It may be true that given the insurance coverages, a large majority of Canadians would not see the retail price of their medications as a significant factor when choosing a pharmacy (Bell et al., 2010). Nevertheless, the following analysis can help us understand pharmaceutical firms' price setting behaviour when there are fundamental policy or preference changes.

3.3.1 Drug Products, Firms, and Induced Demand for Drug Products

In my model, drug products take two forms in the market: either a brand-name or a generic drug - the bioequivalent version of its brand-name counterpart.[11] Both

[8] It can also be the case that drug 0's patent is challenged by the generic drug G's manufacturer, while drug 1's patent remains valid and intact.

[9] There is a small proportion of Canadians not covered by either public or private insurance plans for their prescription drug spending. For the rest of the population, drug coverage is not full either. Nevertheless, I assume that in my model the drugs are used to treat chronic conditions that exist more often in the senior cohort. The majority of Canadian seniors are fully covered by public drug plans, but with varying degrees of patient cost-sharing. Detailed information on the provincial/territorial drug plans is available in Appendix A.

[10] When the generic version of a brand-name drug is available but the prescription is filled by the brand-name drug instead, the patient needs to pay his or her copay for the generic drug plus the price differential between the generic drug and its brand-name original.

[11] The term "brand-name" here only refers to a patented drug (or an off-patent drug) with a registered and distinguished brand-name. Strictly speaking, however, a generic drug may have its own brand name. In practice it is normally named after the generic name of the active ingredient with a prefix of the manufacturer. For example, Lipitor® is the brand-name original of atorvastatin,

brand-name and generic drug in a given therapeutic market offer patients the same therapeutic quality, denoted by q, where q can be any positive scalar.[12] But meantime, patients' perceptions on drug quality may differ. The idea is similar to Brekke et al. (2007) but as I show next, I model the heterogeneity of patients' perceptions on drug quality in a different way.

Specifically, I assume that the characteristics of drug products are defined along two dimensions, namely, their therapeutic variant and perceived quality.

First, drugs within a therapeutic market may exist as rather distinct therapeutic variants, in terms of their interactions with certain kinds of food and other medications, their mechanism of action, and/or their pharmacokinetics, and so on. The two brand-name drugs 0 and 1 in the model are differentiated in this sense.

Second, the perceived quality of a drug reflects a patient's perception of a drug's effectiveness. It may have little or nothing to do with the actual therapeutic quality of the drug, q. But rather, the perceived quality is based on the manufacturer's (or brand's) image, patient's (or family/friends') experience with the drug or other products offered by the manufacturer, and what prescribers and/or pharmacists say about the drug.[13] Patients' knowledge and perception pertaining to prescription drugs are shaped by mass educational efforts, financial incentives, and communication among patients and health professionals (Hassali, et al., 2009), in particular, the way health professional perceive the drug products. To some patients, brand-name drugs are perceived to possess superior quality compared to their generic counterparts because the former has longer (and exclusive, while brand-name drugs are on

which is mainly used to treat high-levels of cholesterol. While Apo-atorvastatin is the generic version manufactured by the generic manufacturer Apotex.

[12]By definition, a generic drug must contain the same medicinal ingredient as the original formulation in its corresponding brand-name drug. Health Canada requires that a generic drug must contain the same medicinal ingredients as the original brand-name drug with respect to pharmacokinetic and pharmacodynamic properties. By extension, therefore, generic drugs are considered identical in dose, strength, route of administration, safety, efficacy, and intended use.

[13]As I have discussed in Chapter 2, generic drugs and their brand-name counterparts are bioequivalent in terms of medicinal ingredient but they may differ in peripheral features. In addition, there may also be issues related to drug formulation such as excipients. The literature identifies that specific generic drugs can be associated with potential side-effects because some patients are allergic to certain excipients contained in generic drugs (Guberman and Corman, 2000; Gumbs et al., 2007; Kesselheim et al., 2010). However, this does not impact the following theoretical discussion in general.

patent) market exposure either through direct-to consumer advertising (DTCA) or commercial/academic detailing targeting physicians or other prescribers.[14] However, some issues, such as potential allergies to excipients contained in generic drugs and patients' sociodemographic background, may also influence patients' beliefs and perceptions toward brand-name or generic drug.[15]

The highly asymmetric information is typical in the pharmaceutical market, as well as other markets of health products or health services.[16] The patients normally do not have the knowledge and expertise to make choices on which drugs to buy. Therefore, the physicians and pharmacists, acting on their patients' behalf, use their expertise to make decisions on which drugs to buy. In other words, the demand for pharmaceuticals is only indirectly derived from a patient's need or *induced* through his or her physician's prescription or pharmacist's counselling.

Insurers have natural incentives to encourage generic substitution for the expensive brand-name drugs to curb reimbursement cost. In practice, pharmacies may also have legitimate reasons to stock some generic drugs over others.[17] The demand for generic drugs can be induced by public/private insurers and/or pharmacies. The demand for brand-name drugs can be induced by either physicians or "indirect advertisements" that patients receive through cross-border televisions or online marketing.[18]

In the current setting, let me define the therapeutic variant to be on the $[0, 1]$ interval.[19] Naturally but without loss of generality, I assume that the locations of the

[14]In Canada, prescribers include physicians and other health professionals, such as nurse practitioners, optometrists, dentists, pharmacists, midwives and podiatrists under certain circumstances (Sketris, 2009). Physicians are the major prescribers for prescription drugs in Canada, although other health professionals can prescribe (Bell et al., 2010). Without loss of generality, I use physicians as the representative for all prescribers.

[15]Figueiras et al. (2008) summarize that patients' treatment choices are associated with beliefs about the perceived severity of their illness. Moreover, more serious or risky a consumer believes a medical condition to be, the less likely he or she would be to choose or accept a generic product. In addition, patients' views, knowledge, beliefs and choice of generic drugs are associated with sociodemographic factors such as ethnicity, education, income, age, risk perception, knowledge, and past experience.

[16]Asymmetric information is present when the knowledge gap existing between a health professional and a patient creates a situation of distinct advantage for the health professional.

[17]Pharmacies may receive rebates from generic manufacturers to stock their products. It may bring down managerial costs when pharmacies only stock limited drug brands (Bell et al., 2010). I discuss this in Chapter 2.

[18]I explain the incentives of the major stakeholders of the pharmaceutical system in Figure 2.4.

[19]A multi-dimensional therapeutic variant space may be appealing but complicates the discussion

two differentiated brand-name drugs are fixed at both ends of the $[0, 1]$ interval, drug 0 at 0 and drug 1 at 1, respectively.

Now suppose a representative patient's most-favourite drug variant (MFDV), if available in market, is uniformly distributed on the $[0, 1]$ interval along the therapeutic variant dimension.[20] Of course, the location of the MFDV, denoted by x, is random. In addition, it is not very likely that drug products available in the market exactly match what patients desire. When the location of the MFDV (x) does not match either 0 or 1, disutility arises, given the mismatch cost between the MFDV and the available drugs.[21] The distance between the location of each patient's MFDV and that of either brand-name drug determines the patient's preference ranking for the two available brand-name drugs. The farther the distance is, the less the patient prefers that drug. For example, if the patient's MFDV is closer to 0, i.e. $|x-0| < |x-1|$, the disutility generated from consuming drug 0 is less than that for drug 1. As a result, the patient prefers drug 0 to 1.

Due to the physiological and genetic diversity among human beings, patients' (induced) preference over the therapeutic variants is likely to be heterogeneous. The heterogeneity in patients' preference for therapeutic variant determines that patients will not rank the group of therapeutic variants in a unanimous way. For example, drug 0 lowers the cholesterol level more effectively in patient A than drug 1 does. While for patient B, drug 0 also lowers his or her cholesterol level only not as much as drug 1 does. This situation can be presented in the following schematic way within the $[0, 1]$ interval: for patient A, $|x_A - 0| < |x_A - 1|$; while for patient B, $|x_B - 0| < |x_B - 1|$. As such, patient A and B have opposite rankings over the two brand-name drugs 0 and 1. The way that the two brand-name drugs are differentiated in the therapeutic variant dimension is the horizontal product differentiation.

Now I turn to the differentiation in perceived quality. In contrast to the horizontal variant dimension, I assume that patients all agree on their assessment on drug

nevertheless.

[20] One can use different forms of distribution if necessary. In line with the standard literature, the uniform distribution is chosen for tractability purposes without losing explanation power.

[21] Disutility can be understood as "transportation cost" in absolute distance following Hotelling (1929). I adopt a quadratic form of disutility following d'Aspremont et al. (1979). I show them in detail in the next section.

(perceived) quality, i.e., the higher quality that a patient perceives for a drug, the better off he or she is. However, patients may still have different experiences in terms of perceived quality for the same drug with therapeutic quality q, depending on their types of preference. I use the parameter θ to measure the heterogeneity in patients' preference for (perceived) quality.

More specifically, all patients agree that the "one of a kind" brand-name drug 1 can offer them high perceived quality, thereby assigning a large θ to drug 1. In addition, all patients agree that the generic drug G carries low perceived quality, thereby assigning a small θ to drug G. It is drug 0, the brand-name original for the generic drug G, that truly divides patients: some patients with strong brand loyalty would assign a larger θ to the brand-name drug 0 than to the generic drug G, while others would just value the brand-name drug 0 and the generic drug G the same way.[22] The way that the generic drug G and its brand-name original drug 0 are differentiated in the perceived quality dimension is the vertical product differentiation.

In the setting, θ follows a Bernoulli distribution such that there are only two types of patients: either "selective" or "unselective" patients, with exogenous probabilities λ and $1-\lambda$, respectively.[23] On the one hand, all patients attach $\theta = \theta_H$ and $\theta = \theta_L$ to the brand-name drug 1 and to the generic drug G, respectively (both θ_H and θ_L are positive scalars and $\theta_H > \theta_L$). On the other hand, the selective patients (with a proportion of all, at λ), attach $\theta = \theta_H$ to the brand-name drug 0; while the unselective patients (with a proportion of all, at $1-\lambda$) value equally the brand-name drug 0 and its generic substitute G, by attaching $\theta = \theta_L$ to both the brand-name drug 0 and its generic substitute G.

It is clear that I model the heterogeneity of patients' perceptions on drug quality differently from Brekke et al. (2007). Specifically, in Brekke et al. (2007), both the brand-name drug 0 and 1 are assumed to have the same perceived quality ($\gamma\upsilon$) for the L-type patients, despite the difference between the brand-name drug 0 and 1. That is, the brand-name drug 0 has a generic substitute G, but the brand-name drug

[22] Patients' brand loyalty can also be interpreted as their high sensitivity to the health risk that may be caused during any product switch (Gumbs et al., 2007; Kesselheim et al., 2010).

[23] As I show next, θ follows a Bernoulli distribution only for the brand-name drug 0. All patients treat the brand-name drug 1 and the generic drug G in the same way in terms of perceived quality.

1 remains its market exclusivity. In addition, Brekke et al. (2007) use the discount factor γ, where $\gamma \in (0, 1)$, to differentiate the two types of patients. In my model, the heterogeneity in patients' perceived quality is embodied in the different attitudes for the brand-name drug 0, given the different types of patients. As such, γ is considered to be redundant and excluded from my model.

It should be noted that in the baseline model, there is no generic substitute for the brand-name drug 1 in the market yet. In other words, drug 1 still enjoys market exclusivity under its patent protection. As I show next, some unselective patients whose MFDV is closer to 1, eventually have to opt for the considerably more expensive brand-name drug 1. They do so because (1) the brand-name drug 1 offers them the (relatively) desirable drug variant that neither the brand-name drug 0 nor the generic drug G does, and (2) the generic (and cheaper) version of drug 1 is literally not available in the market.

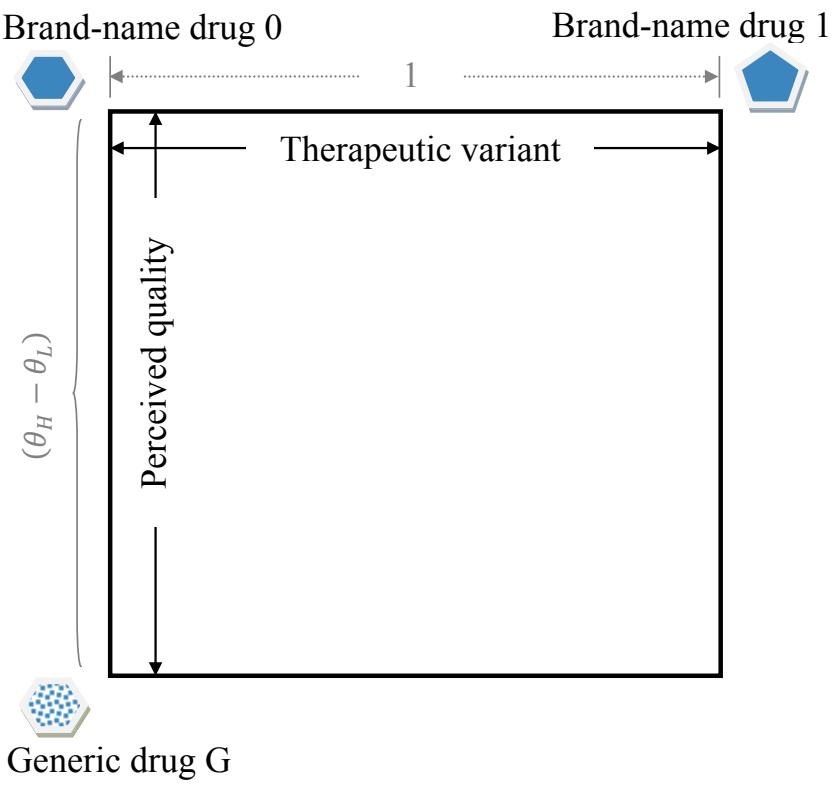
Let the dimension of therapeutic variant be on the horizontal axis and the dimension of perceived quality be on the vertical axis. In doing so, I can demonstrate how a representative selective patient may see the three drugs in a two-dimension box of drug characteristics.[24] The two brand-name drugs, 0 and 1 locate at the two extremes of the variant dimension on the $[0, 1]$ interval, respectively; whereas the generic drug G locates right below its brand-name original 0 in the perceived quality dimension, with the perceived quality difference $(\theta_H - \theta_L) \cdot q$. For simplicity, I can normalize the therapeutic quality q to 1. Again, the manufacturers differentiate the two brand-name drugs 0 and 1 by locating them on the extremes on the horizontal axis. The generic drug G that carries lower perceived quality is differentiated from the brand-name drug 0 on the vertical axis.[25] The locations of the three drugs on a two-dimension characteristic box are provided in Figure 3.1.

In the next section, I will formally define the utility function of a representative

[24] Of course, as I have explained, an unselective patient does not discriminate the generic drug G and its brand-name original 0 in the perceived quality dimension.

[25] This thesis focuses on what happens after manufacturers determine the product differentiation strategy, in the way that the drugs are differentiated both vertically and horizontally. Whether the two dimensions are limited to the current setting or can be extended indefinitely, or in other words, whether firms have chosen the strategies of maximum differentiation in one or both dimensions, is beyond the discussion of this thesis. Readers may refer to the relevant literature on why and to what extent products differentiate.

Figure 3.1: Locations for the Three Drugs in the Characteristics Box



patient and calculate the market shares for the three drugs.

3.3.2 A Representative Patient's Utility Function

I can define a representative patient's utility function as follows:

$$U_{ji} = \begin{cases} R + (1-t)\cdot\theta_{ji} - t\cdot(x-i)^2 - c_i & i = 0, 1; \\ R + (1-t)\cdot\theta_{ji} - t\cdot(x-0)^2 - c_i & i = G, \end{cases} \tag{3.3.1}$$

with

$$\theta_{ji} = \begin{cases} \theta_H & i = 0 \text{ and } j = \text{selective, or } i = 1; \\ \theta_L & i = 0 \text{ and } j = \text{unselective, or } i = G. \end{cases}$$

where j is the type of patients (j = selective *or* unselective); i is for drug i ($i = 0, 1, G$) the representative patient consumes; R is the basic reservation value, which can be

the utility derived from other sources. The reservation value is assumed large enough to guarantee the patient's utility is always positive. $t \in (0,1)$ is the weight that the patient attaches to the utility derived from drugs' variant dimension; $t \cdot (x-i)^2$, $(i = 0,1)$, measures patient's disutility from not having the drug with the ideal therapeutic variant. For tractability purposes, the disutility is measured in the way of "quadratic transportation cost" in line with d'Aspremont et al. (1979). This is different from the "absolute transportation cost" approach in Brekke et al. (2007). Accordingly, $(1-t)$ is the weight that the representative patient attaches to the utility derived from a drug's perceived quality dimension; $(1-t)\cdot\theta$ is the utility that the patient gets from a drug's perceived therapeutic quality. The utility function is additive to rule out any interaction between the vertical and horizontal differentiation.

Let p_0, p_1, and p_G be the prices for drugs 0, 1, and G, respectively, charged in the market.[26] The rate of copay is α. Accordingly, the copay level for drugs 0, 1, and G are c_0, c_1, or c_G, respectively, which are given by

$$\begin{aligned} c_0 &= \alpha \cdot p_G + (p_0 - p_G), \\ c_1 &= \alpha \cdot p_1, \quad \text{and} \\ c_G &= \alpha \cdot p_G. \end{aligned} \tag{3.3.2}$$

For simplicity, I assume the same percentage of copay (α) regardless of the patient's province of residence and regardless if the insurer is public or private.[27] Also without loss of generality, I do not include an additive term for deductibles. Since the generic substitute G is available for drug 0, the patient who purchases drug 0 has to pay out-of-pocket for the price differential between drug 0 and G, on top of his or her copay $\alpha \cdot p_G$. This "maximum-reimbursable-cost" type of policy is present in almost all public drug plans across the country. As Bell et al. (2010) summarizes, the provincial drug plans determines the appropriate formulary price — usually the

[26] Drug price may exist in various forms in practice. To focus on drug manufacturers' price setting behaviour, I refer to the drug price at the retail level. Therefore, manufacturer rebate or professional allowance, pharmaceutical distributor mark-up, and dispensing fee, etc. are excluded in the theoretical analysis in this chapter.

[27] As I have introduced in Chapter 2, in reality, the rate of copay has both between-regional disparities and between-program disparities. Bell et al. (2010) offers a comprehensive review on the rates of copay across Canada.

lowest price — for an interchangeable groups of drugs.[28]

Each patient needs to purchase one and only one of the three drugs (0, 1, or G) whichever offers him or her the highest utility.[29] In this sense, the market is fully covered by the three firms.

Given the above specification, it is clear that an unselective patient would consider the generic drug G over the brand-name drug 0, as long as $p_G < p_0$.[30] Nevertheless, as I show next, an unselective patient may still choose the brand-name drug 1 over the generic drug G in some situation.

For tractability, I assume that

$$(1-t)(\theta_H - \theta_L) > p_0 - p_G. \tag{3.3.3}$$

As such, a selective patient would only consider the brand-name drugs 0 or 1.[31]

Now I can use the unit box to describe the market in Figure 3.2. Horizontally, patients' ideal location for drug variant x lies on the interval $[0, 1]$. Vertically, the proportions of "selective" and "unselective" patients are λ and $1-\lambda$, respectively. As such, the area of the unit box, i.e. the total market share, is 1.

Now I consider the selective patients who are just indifferent between the two brand-name drugs 0 and 1, according to (3.3.1). For any patient type $x \in [0, 1]$, the marginal patient of this kind who is indifferent between the two drugs is defined by the vertical line in the unit box:

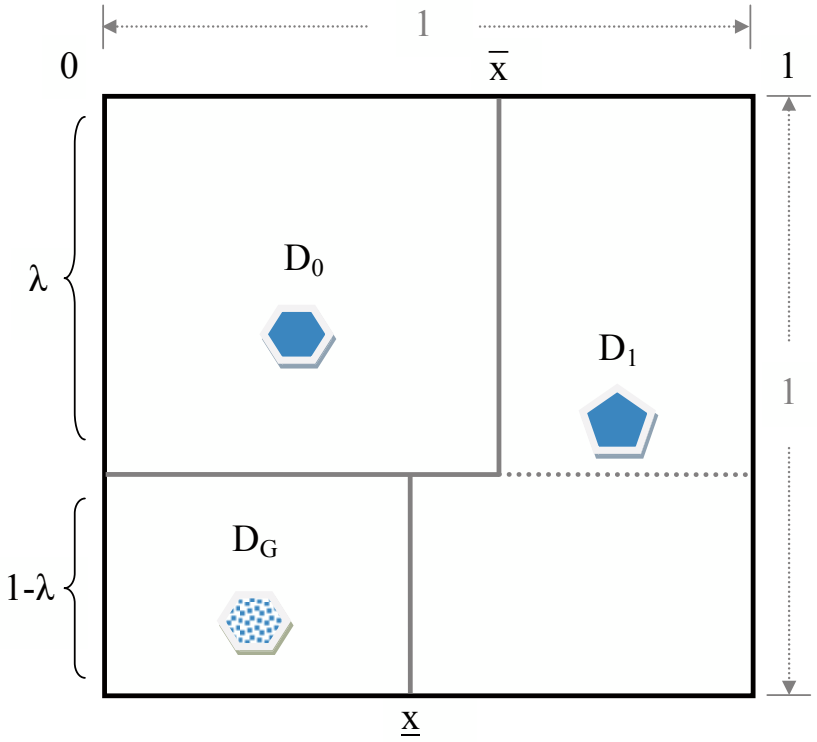
[28] The price information may be either requested by public drug plan or submitted from manufacturers. The way to define an interchangeable drug group varies across the provinces. Most provinces, such as the Atlantic provinces, Alberta, and Ontario etc., rely on the generic reference pricing (GRP) regime, in which only the lowest unit cost — the maximum-reimbursable cost — within a drug class is reimbursable. Some provinces may define an interchangeable drug group in a broad sense for many classes of drugs, such as the Special MAC policy in Nova Scotia (CIHI, 2010b). This is in line with Brekke et al. (2007)'s therapeutic reference pricing (TRP) regime, under which the maximum-reimbursable cost would apply to all drugs within the broader therapeutic group. The TRP regime tends to include many brand-name drugs as well as their bioequivalent generic drugs. Apparently it is likely to draw more intense competition among drug manufacturers. I first analyze the baseline model in the GRP regime, followed by the baseline extension in the TRP regime.

[29] The case that a patient takes no drug and lives with the consequences of non-treatment will not be considered.

[30] In this thesis, I take as given that a generic drug is cheaper than a brand-name drug, i.e., $p_G < p_0$ and $p_G < p_1$.

[31] A brief proof is provided in Appendix B.

Figure 3.2: Market Shares for the Three Drug Manufacturers



$$\overline{x} = \frac{c_1 - c_0 + t}{2t}. \tag{3.3.4}$$

Similarly, I consider the unselective patients who are just indifferent between drugs 1 and G, according to (3.3.1). For any patient type $x \in [0, 1]$, the marginal patient of this kind who is indifferent between the two drugs is defined by the vertical line in the unit box:

$$\underline{x} = \frac{c_1 - c_G + t - (1 - t) \cdot (\theta_H - \theta_L)}{2t}. \tag{3.3.5}$$

Demand for drugs 0 and G are separated by the parameter λ since I assume that the "selective" patients (with proportion λ) are only interested in the brand-name drug 0 even with the availability of generic drug G, whereas "unselective" patients (with proportion $1 - \lambda$) are only interested in the cheaper generic drugs, if available (drug G in this case).

3.3.3 Market Shares and Profits

In summary, the market shares for the three drug manufacturers can be depicted using the unit box in Figure 3.2, defined by the indifference lines (3.3.4), (3.3.5), and λ.

Let the difference in perceived quality between brand-name and generic drug be δ, where

$$\delta \equiv (\theta_H - \theta_L). \tag{3.3.6}$$

Based on (3.3.2), (3.3.4), (3.3.5), and (3.3.6), the market shares D_0, D_1, and D_G for drugs 0, 1, and G are, respectively,

$$\begin{aligned} D_0 &= \lambda \cdot \overline{x} \\ &= \frac{\lambda \cdot (c_1 - c_0 + t)}{2t} \\ &= \frac{\lambda \cdot [t + \alpha \cdot (p_1 - p_G) + p_G - p_0]}{2t}, \end{aligned} \tag{3.3.7}$$

$$\begin{aligned} D_1 &= 1 - D_0 - D_G \\ &= \frac{t - \alpha \cdot (p_1 - p_G) + \lambda \cdot (p_0 - p_G) + (1 - \lambda) \cdot (1 - t) \cdot \delta}{2t}, \quad \text{and} \end{aligned} \tag{3.3.8}$$

$$\begin{aligned} D_G &= (1 - \lambda) \cdot \underline{x} \\ &= \frac{(1 - \lambda) \cdot [c_1 - c_G + t - (1 - t) \cdot \delta]}{2t} \\ &= \frac{(1 - \lambda) \cdot [t + \alpha \cdot (p_1 - p_G) - (1 - t) \cdot \delta]}{2t}. \end{aligned} \tag{3.3.9}$$

The cost of manufacturing pharmaceuticals incurs disproportionally as fixed cost in the R&D stage and therefore only matters when firms decide whether or not to enter the market. The cost is considered as sunk cost when the three drug manufacturers compete in price in the one-shot game framework. I assume zero constraint on manufacturing capacity and manufacturing cost can be normalized to zero. For simplicity, I also assume zero marginal cost associated with manufacturers' endeavours

in developing therapeutic variant and/or brand-imaging.[32]

I need to study firms' price setting strategies when they face policy changes on drug pricing. To do so, I first define the profit functions for the three single-product firms:

$$\begin{aligned}\Pi_0 &= p_0 \cdot D_0 \\ &= \lambda \cdot \frac{[t + \alpha \cdot (p_1 - p_G) + p_G] \cdot p_0 - p_0^2}{2t},\end{aligned} \tag{3.3.10}$$

$$\begin{aligned}\Pi_G &= p_G \cdot D_G \\ &= (1-\lambda) \cdot \frac{(t + \alpha \cdot p_1 - (1-t) \cdot \delta) \cdot p_G - \alpha \cdot p_G^2}{2t}, \quad \text{and}\end{aligned} \tag{3.3.11}$$

$$\begin{aligned}\Pi_1 &= p_1 \cdot D_1 \\ &= \frac{[t + \lambda \cdot (p_0 - p_G) + \alpha \cdot p_G + (1-\lambda)(1-t) \cdot \delta] \cdot p_1 - \alpha \cdot p_1^2}{2t}.\end{aligned} \tag{3.3.12}$$

In the one-shot simultaneous game in price among the three firms, each firm sets its own price to maximize its profit given the optimal price setting strategies chosen by the remaining firms. The equilibrium is Nash.

3.3.4 Equilibrium price with a Binding Generic Price-cap

Canadian public and private insurers use the generic price-cap extensively to limit drug reimbursement cost. For example, some provincial drug plans, leveraging their purchasing power, only list the generic drug on the formulary if its price is at or below a predefined percentage of the reference brand-name drug price.[33] In the following sections, I discuss the equilibrium price with and without a binding generic drug price-cap, respectively.[34]

[32] Cost associated with the real product quality would diminish firms' incentive to improve quality or innovate for variant, and thereby reduce the extent of product differentiation (Neven and Thisse, 1990). In the setting, I discuss the pricing game given fixed (maximum) differentiation both in therapeutic variant and perceived quality.

[33] Alberta, Ontario, Quebec, and Newfoundland and Labrador use this approach (Bell et al., 2010).

[34] Canadian drug manufacturers often use non-price methods such as rebates to compete for shelf space in pharmacies. As a result, generic drug prices at the retail level tend to cluster, with or

When there is a binding generic price-cap, i.e.

$$p_G = \beta \cdot p_0, \tag{3.3.13}$$

where $\beta \in (0, 1)$ is the price-cap in percentage, I can only look at the equilibrium prices for the two brand-name firms. The generic drug price is solved given (3.3.13).

The first-order conditions of (3.3.10) and (3.3.12) are given by:

$$\frac{\partial \Pi_0}{\partial p_0} = 0 \quad \Leftrightarrow \quad p_0 = \frac{t + \alpha \cdot p_1 + (1-\alpha) \cdot p_G}{2} \quad \text{and} \tag{3.3.14}$$

$$\frac{\partial \Pi_1}{\partial p_1} = 0 \quad \Leftrightarrow \quad p_1 = \frac{t + \lambda \cdot (p_0 - p_G) + \alpha \cdot p_G + (1-\lambda) \cdot (1-t) \cdot \delta}{2\alpha}. \tag{3.3.15}$$

Second-order conditions are both satisfied to guarantee local maxima.[35] Substituting in p_G with (3.3.13), I have:

$$p_0 = \frac{t + \alpha p_1}{2 - \beta(1-\alpha)} \quad \text{and} \tag{3.3.16}$$

$$p_1 = \frac{[t + (1-\lambda)(1-t)\delta] \cdot [2 - \beta(1-\alpha)] + (\lambda + \beta\alpha - \beta\lambda)(t + \alpha p_1)}{2\alpha[2 - \beta(1-\alpha)]}. \tag{3.3.17}$$

Solve for p_0 and p_1 and let

$$\Gamma \equiv 4 - 2\beta + \alpha\beta - \lambda + \beta\lambda, \tag{3.3.18}$$

$$\Psi \equiv 2 - \beta + \alpha\beta, \quad \text{and} \tag{3.3.19}$$

$$\Phi \equiv 2 - \beta + 2\alpha\beta + \lambda - \beta\lambda. \tag{3.3.20}$$

without a price-cap. I do not discuss the case with a non-binding generic price-cap. The price clustering may also be the result of tacit collusion in the generic drug industry.

[35] Proof is straightforward and omitted.

The equilibrium prices for the two brand-name firms with the binding generic price-cap are, respectively,[36]

$$p_0 = \frac{t(\Gamma + \Phi) + (1-\lambda)(1-t)\delta\Psi}{\Gamma\Psi} \quad \text{and} \tag{3.3.21}$$

$$p_1 = \frac{t\Phi + (1-\lambda)(1-t)\delta\Psi}{\alpha\Gamma}. \tag{3.3.22}$$

3.3.4.1 Impact on Equilibrium Price with a Binding Generic Price-cap

Having solved the equilibrium prices for the three pharmaceutical firms under the copays defined in (3.3.2) and with a binding generic price-cap (β), now I discuss the impact of preference and policy changes on the firms' price setting strategies in the equilibrium. In the baseline model, there are three important parameters: λ, α, and β.

λ is a preference parameter defining the proportion of "selective" patients who display unanimous preference for brand-name drugs, whereas $(1-\lambda)$ is the proportion of "unselective" patients. λ is a measure of preference switch from brand-name to generic drug. The lower (higher) λ is, proportionally the more (less) patients switch from brand-name to generic drug.

α is a policy parameter defining the rate of copay. Insurers can raise α to control drug reimbursement costs.[37] A higher (lower) α means more (less) out-of-pocket spending for patients and this enhances (blunts) patients' price sensitivity.

β is the percentage of the brand-name drug price capping the generic drug price. A lower (higher) β means a lower (higher) generic drug price relative to the brand-name drug price,[38] which cuts drug reimbursement costs and would elicit price competition against the brand-name drugs.

In this model, I assume that all the above three parameters are exogenous. I study

[36] Note that Γ, Ψ, and Φ are all positive scalars given that α, β, and $\lambda \in (0,1)$. The proof is straightforward and is omitted.

[37] Public drug plans use copays to help supplement taxation as a source of funding (Bell et al., 2010).

[38] Failing to follow the price order means that the generic drugs would be taken off from the provincial formularies.

the impact of these exogenous shocks in the equilibrium prices.[39] As such, I analyze the comparative statics to understand the qualitative characteristics in the change of the equilibrium prices, given a shift in one parameter while holding everything else unchanged. I formally present and prove the propositions with respect to a change in each parameter as follows.

Proposition 1. *When the difference in perceived quality between brand-name drug and generic drug is large enough, ceteris paribus, a lower (higher) proportion of selective patients implies higher (lower) equilibrium prices for both brand-name drugs.*

Proof. First, the partial derivatives of p_1 with respect to λ is given by

$$\frac{\partial p_1}{\partial \lambda} = \frac{\alpha\Gamma[t(1-\beta)-(1-t)\delta\Psi]+\alpha(1-\beta)[t\Phi+(1-t)\delta\Psi(1-\lambda)]}{\alpha^2\Gamma^2}$$

$$= \frac{t\alpha(1-\beta)(\Gamma+\Phi)-\alpha(1-t)\delta\Psi}{\alpha^2\Gamma^2}$$

$$= \frac{\Psi}{\alpha\Gamma^2}[3t(1-\beta)-(1-t)\delta(3-\beta+\alpha\beta)]. \tag{3.3.23}$$

Second, from (3.3.16) and (3.3.23), the partial derivative of p_0 with respect to λ can be written as

$$\frac{\partial p_0}{\partial \lambda} = \frac{\alpha}{\Psi}\cdot\frac{\partial p_1}{\partial \lambda}$$

$$= \frac{1}{\Gamma^2}[3t(1-\beta)-(1-t)\delta(3-\beta+\alpha\beta)]. \tag{3.3.24}$$

Because $\Psi > 0$, also with (3.3.23) and (3.3.24), I have

$$Sign(\frac{\partial p_0}{\partial \lambda}) = Sign(\frac{\partial p_1}{\partial \lambda})$$
$$= Sign[3t(1-\beta)-(1-t)\delta(3-\beta+\alpha\beta)]. \tag{3.3.25}$$

[39] A dynamic analysis in the long run, which may involve chained effects in the parameters, brings considerable complexity to the model and will be left for future research.

Let

$$\overline{\delta} \equiv \frac{3t(1-\beta)}{(1-t)(3-\beta+\alpha\beta)}. \tag{3.3.26}$$

From (3.3.23), (3.3.24), (3.3.25), and (3.3.26) I conclude

$$\begin{cases} \frac{\partial p_0}{\partial \lambda} > 0, \frac{\partial p_1}{\partial \lambda} > 0, \quad if \quad \delta < \overline{\delta}; \\ \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} < 0, \quad if \quad \delta > \overline{\delta}. \end{cases} \tag{3.3.27}$$

□

The inequalities in (3.3.27) imply that when the difference in perceived quality between brand-name drugs 0, 1, and the generic drug G is greater than some threshold value, $\overline{\delta}$, with everything else being equal, a decrease (increase) in the proportion of selective patients has a positive (negative) impact on the equilibrium prices of both brand-name drugs 0 and 1. When the difference in perceived quality between brand-name drugs 0, 1, and the generic drug G is less than the threshold value, $\overline{\delta}$, with everything else being equal, a decrease (increase) in the proportion of selective patients has a negative (positive) impact on the equilibrium prices of both brand-name drugs 0 and 1.

The message from Proposition 1 is: the difference in the perceived quality between brand-name and generic drug matters when brand-name manufacturers price their products in response to a change in patients' preference. As long as patients believe the (perceived) quality difference between the brand-name original drug and its generic substitute is large enough, an increase in the proportion of the unselective patients would even stimulate the brand-name manufacturers to raise their prices to maximize profits.

Proposition 2. *When patients have to incur more (less) out-of-pocket spending for drugs in terms of a higher (lower) copay rate, ceteris paribus, both brand-name drug manufacturers would charge lower (higher) prices in equilibrium.*

Proof. Based on (3.3.22), the partial derivative of p_1 with respect to α is given by

$$\frac{\partial p_1}{\partial \alpha} = \frac{1}{\alpha^2\Gamma^2}\{\alpha\Gamma[2t\beta + (1-\lambda)(1-t)\beta\delta] - [t\Phi + (1-\lambda)(1-t)\delta\Psi][\Gamma + \alpha\beta]\}$$

$$= \frac{1}{\alpha^2\Gamma}[2t\alpha\beta + (1-\lambda)(1-t)\alpha\beta\delta - t(2-\beta+2\alpha\beta+\lambda-\beta\lambda)$$
$$- (1-\lambda)(1-t)(2-\beta+\alpha\beta)\delta] - \frac{\beta}{\alpha\Gamma^2}[t(2-\beta+2\alpha\beta+\lambda-\beta\lambda)$$
$$+ (1-\lambda)(1-t)(2-\beta+\alpha\beta)\delta]$$

$$= -\frac{1}{\alpha^2\Gamma}[t(2-\beta+\lambda-\beta\lambda) + (1-\lambda)(1-t)(2-\beta)\delta]$$
$$- \frac{\beta}{\alpha\Gamma^2}[t(2-\beta+2\alpha\beta+\lambda-\beta\lambda) + (1-\lambda)(1-t)(2-\beta+\alpha\beta)\delta]$$

$$< 0. \tag{3.3.28}$$

The last inequality is because the terms within both brackets in the previous step are always positive.

Also, based on (3.3.16) and (3.3.28), the partial derivative of p_0 with respect to α is given by

$$\frac{\partial p_0}{\partial \alpha} = \frac{(p_1 + \alpha\frac{\partial p_1}{\partial \alpha})(2-\beta+\alpha\beta) - \beta(t+\alpha p_1)}{\Psi^2}$$

$$= \frac{1}{\Psi^2}\left[(p_1 + \alpha\frac{\partial p_1}{\partial \alpha})(2-\beta) + \alpha^2\beta\frac{\partial p_1}{\partial \alpha} - t\beta\right]$$

$$= \frac{1}{\Psi^2}\{\left(\frac{2\beta}{\Gamma} - \frac{\beta^2}{\Gamma}\right)\left[2t + (1-\lambda)(1-t)\delta - \frac{t\Phi}{\Gamma} - \frac{(1-\lambda)(1-t)\delta\Psi}{\Gamma}\right]$$
$$- \frac{\beta}{\Gamma}[t(\Phi - 2\alpha\beta) + (1-\lambda)(1-t)\delta(\Psi - \alpha\beta)]$$
$$- \frac{\alpha\beta^2}{\Gamma^2}[t\Phi + (1-\lambda)(1-t)\delta\Psi] - t\beta\}. \tag{3.3.29}$$

Collecting terms and using (3.3.18), (3.3.20), and (3.3.19), (3.3.29) turns to

$$\begin{aligned}\frac{\partial p_0}{\partial \alpha} &= \frac{1}{\Psi^2}\{\frac{t\beta}{\Gamma^2}[(2-\beta-\lambda+\beta\lambda)\Gamma+(\beta-2-\alpha\beta)\Phi-\Gamma^2] \\ &\quad + \frac{\beta}{\Gamma^2}(\beta-2-\alpha\beta)(1-\lambda)(1-t)\delta(2-\beta+\alpha\beta)\} \\ &= \frac{1}{\Psi^2}\left[\frac{t\beta}{\Gamma^2}(\beta-2-\alpha\beta)(6-3\beta+3\alpha\beta)-\frac{\beta}{\Gamma^2}(1-\lambda)(1-t)\delta(\beta-2-\alpha\beta)^2\right] \\ &= -\frac{\beta}{\Gamma^2}[3t+(1-\lambda)(1-t)\delta] \\ &< 0. \end{aligned} \tag{3.3.30}$$

In summary, from (3.3.28) and (3.3.30), I obtain

$$\frac{\partial p_0}{\partial \alpha} < 0 \quad \textit{and} \quad \frac{\partial p_1}{\partial \alpha} < 0. \tag{3.3.31}$$

□

Proposition 2 suggests that a higher (lower) copay rate — a larger (smaller) α — with everything else being equal, leads to lower (higher) equilibrium prices for both the brand-name drugs 0 and 1.

When the insurer raises the percentage of patient copay, ceteris paribus, both the brand-name manufacturers for drugs 0 and 1 respond by lowering drug prices as they believe that the patients become more unselective as a whole. The two brand-name manufacturers always lower prices in response to the raise in the rate of copay no matter how patients view the brand-name drugs in terms of perceived quality. But as shown later, when the generic price-cap does not exist (i.e. there is no limit to generic drug price), the generic drug manufacturer plays a more active role in the pricing game and the difference in perceived quality, δ, will be again a pivotal factor in the outcome.

Proposition 3. *When the government lowers the generic price-cap, ceteris paribus, the corresponding brand-name manufacturer will respond by lowering the drug price*

in equilibrium; the reaction of the other brand-name drug firm is ambiguous: under certain circumstance, for example, with a large proportion of "selective" patients, the brand-name drug price in equilibrium goes up, ceteris paribus, even if a cheaper therapeutic substitute in the generic form is available.

Proof. Based on (3.3.22), the partial derivative of p_1 with respect to β is given by

$$\begin{aligned}\frac{\partial p_1}{\partial \beta} &= \frac{1}{\alpha^2\Gamma^2}\{[t(2\alpha-1-\lambda)+(1-\lambda)(1-t)\delta(\alpha-1)]\alpha(4-2\beta+\alpha\beta-\lambda+\beta\lambda) \\ &\quad -[t(2-\beta+2\alpha\beta+\lambda-\beta\lambda)+(1-\lambda)(1-t)\delta(2-\beta+\alpha\beta)]\alpha(\alpha-2+\lambda)\} \\ &= \frac{1}{\alpha\Gamma^2}\{t[(4-2\beta+\alpha\beta-\lambda+\beta\lambda)(2\alpha-1-\lambda) \\ &\quad -(2-\beta+2\alpha\beta+\lambda-\beta\lambda)(\alpha-2+\lambda)] \\ &\quad +(1-\lambda)(1-t)\delta[(\alpha-1)(4-2\beta+\alpha\beta-\lambda+\beta\lambda) \\ &\quad -(2-\beta+\alpha\beta)(\alpha-2+\lambda)]\} \\ &= \frac{1}{\alpha\Gamma^2}[3t(2\alpha-\alpha\lambda-\lambda)+(1-\lambda)(1-t)\delta(2\alpha-\alpha\lambda-\lambda)] \\ &= \frac{1}{\alpha\Gamma^2}[3t+(1-\lambda)(1-t)\delta](2\alpha-\alpha\lambda-\lambda), \end{aligned} \tag{3.3.32}$$

which implies

$$Sign(\frac{\partial p_1}{\partial \beta}) = Sign(2\alpha-\alpha\lambda-\lambda). \tag{3.3.33}$$

To understand the sign patterns of equation (3.3.33), I need to illustrate the relationships between α and λ. First, it is straightforward that $(2\alpha-\alpha\lambda-\lambda)$ increases with α.[40] Then let $\overline{\alpha}$ be the solution to $(2\alpha-\alpha\lambda-\lambda)=0$. That is,

$$\overline{\alpha} = \frac{2}{2-\lambda} - 1. \tag{3.3.34}$$

It is clear that $\overline{\alpha}$ monotonically increases in λ. A diagrammatic demonstration of equation 3.3.34 is shown in the Figure 3.3.

[40] It follows the fact that $2\alpha-\alpha\lambda-\lambda = (2-\lambda)\alpha-\lambda$ and $\lambda \in (0,1)$.

Now suppose the extreme case when λ is close to 1, implying that the root of equation (3.3.34) ($\overline{\alpha}$) is also close to 1. Bearing in mind that the rate of copay (α) in most drug insurance plans is rarely set above 50%,[41] which implies that $\alpha < \overline{\alpha} \approx 1$. This indicates $(2\alpha - \alpha\lambda - \lambda) < 0$ and therefore, $\frac{\partial p_1}{\partial \beta} < 0$.

When the value of λ drops, so does $\overline{\alpha}$ — the root of equation (3.3.34). It is not clear whether $\alpha < \overline{\alpha}$ or $\alpha > \overline{\alpha}$. As a result, the sign of $\frac{\partial p_1}{\partial \beta}$ is ambiguous.

Based on (3.3.16) and (3.3.32), the partial derivative of p_0 with respect to β is given by

$$\begin{aligned}
\frac{\partial p_0}{\partial \beta} &= \frac{1}{(2-\beta+\alpha\beta)^2}\left[\alpha\frac{\partial p_1}{\partial \beta}(2-\beta+\alpha\beta) + (t+\alpha p_1)(1-\alpha)\right] \\
&= \frac{1}{2-\beta+\alpha\beta}\{\frac{[3t+(1-\lambda)(1-t)\delta](2\alpha-\alpha\lambda-\lambda)}{\Gamma^2} \\
&\quad + \frac{1-\alpha}{\Gamma\Psi}[t(\Gamma+\Phi)+(1-\lambda)(1-t)\delta\Psi]\} \\
&= \frac{1}{\Gamma^2\Psi}\{(2\alpha-\alpha\lambda-\lambda)[3t+(1-\lambda)(1-t)\delta] \\
&\quad + (1-\alpha)(4-2\beta+\alpha\beta-\lambda+\beta\lambda)[3t+(1-\lambda)(1-t)\delta]\} \\
&= \frac{1}{\Gamma^2\Psi}[3t+(1-\lambda)(1-t)\delta](4-2\beta+3\alpha\beta-2\alpha-2\lambda+\beta\lambda-\alpha^2\beta-\alpha\beta\lambda) \\
&= \frac{1}{\Gamma^2\Psi}[3t+(1-\lambda)(1-t)\delta](2-\beta+\alpha\beta)(2-\lambda-\alpha) \\
&= \frac{1}{\Gamma^2}[3t+(1-\lambda)(1-t)\delta][(1-\lambda)+(1-\alpha)] \\
&> 0. \qquad (3.3.35)
\end{aligned}$$

The last inequality is justified because the terms within all parentheses in the

[41] See Bell et al. (2010) and CIHI (2010b).

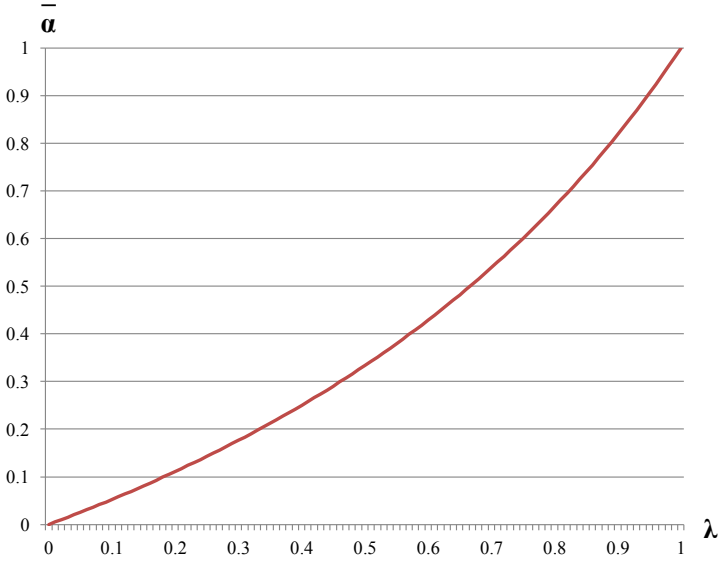
previous step are always positive.

From (3.3.33) and (3.3.35), I obtain

$$\frac{\partial p_0}{\partial \beta} > 0 \quad and \quad \begin{cases} \frac{\partial p_1}{\partial \beta} < 0, \quad if \quad \alpha < \overline{\alpha}; \\ \\ \frac{\partial p_1}{\partial \beta} > 0, \quad if \quad \alpha > \overline{\alpha}. \end{cases} \tag{3.3.36}$$

□

Figure 3.3: A Diagrammatic Demonstration of the Relationship between $\overline{\alpha}$ and λ



Proposition 3 suggests that with everything else being equal, a lower (higher) generic price-cap — a smaller (larger) β — leads to a lower equilibrium price for the brand-name drug 0, but its impact on the equilibrium price for the brand-name drug 1 is ambiguous.

On the one hand, the impact of a lower generic price-cap on the price of the brand-name drug 0 is definite, because a lower generic drug price brings increased competition to the brand-name drug in its own class. On the other hand, the impact of a lower generic price-cap on the price of the brand-name drug 1 remains unclear. The interaction between the other two parameters α and λ may play a role. Specifically, I find that when the proportion of the selective patients (λ) is arbitrarily high (close

to 1), a lower generic price-cap leads to a higher equilibrium price in brand-name drug 1, an undesirable result from the perspective of the policy-makers.[42] As generic substitution becomes common in the therapeutic market, the proportion of selective patients dwindles. As such, the undesirable price increase in brand-name drug 1 caused by the lower generic price-cap may or may not be reversed.

3.3.5 An Extension to the Baseline Model - Without a Generic Price-Cap

Four Canadian provinces explicitly require a price-cap on generic drugs, namely, Ontario, Quebec, Newfoundland and Labrador, and Alberta, while the rest of provinces do not. Now I examine the comparative statics of the equilibrium price when there is no generic price-cap, in contrast to the previous findings when there is a binding generic price-cap.

When there is no generic price-cap, the two first-order conditions (3.3.14) and (3.3.15) remain the same. In addition, the third first-order condition with respect to p_G is

$$\frac{\partial \Pi_G}{\partial p_G} = 0 \quad \Leftrightarrow \quad p_G = \frac{t + \alpha p_1 - (1-t)\delta}{2\alpha}. \tag{3.3.37}$$

Therefore, I have

$$p_0 = \frac{3(1+\alpha)t - (1+\alpha\lambda-2\alpha)(1-t)\delta}{6\alpha + \lambda(1-\alpha)}, \tag{3.3.38}$$

$$p_G = \frac{6t - (\lambda+2)(1-t)\delta}{6\alpha + \lambda(1-\alpha)}, \quad \text{and} \tag{3.3.39}$$

$$p_1 = \frac{(6\alpha - \lambda + \alpha\lambda)t + (2\alpha + \lambda - 3\alpha\lambda)(1-t)\delta}{\alpha[6\alpha + \lambda(1-\alpha)]}. \tag{3.3.40}$$

[42] This may not be an issue if the patented drug prices is also capped. For example, the PMPRB has tight regulations on the patented drug prices as I have introduced in Chapter 2.

3.3.5.1 Impact on Equilibrium Price without a Generic Price-Cap

Next, I discuss the impact of preference and policy changes on the firms' price setting strategies in the equilibrium by studying the comparative statics with respect to the preference/policy parameters, λ, α, and β, respectively.

Proposition 4. *When there is no generic price-cap, if the difference in perceived quality between brand-name drug and generic drug is not too large OR if the copay rate is above some certain threshold, ceteris paribus, a lower (higher) proportion of selective patients implies higher (lower) equilibrium prices for both the brand-name drugs and generic drug.*

Proof. Let

$$\Upsilon \equiv (1-4\alpha)(1-t)\delta - 3(1-\alpha)t. \tag{3.3.41}$$

Based on (3.3.40), the partial derivative of p_1 with respect to λ is given by

$$\begin{aligned}\frac{\partial p_1}{\partial \lambda} &= \frac{1}{\alpha[6\alpha+\lambda(1-\alpha)]^2}\{[-t+\alpha t+(1-t)\delta-3\alpha(1-t)\delta][6\alpha+\lambda(1-\alpha)] \\ &\quad -[(6\alpha-\lambda+\alpha\lambda)t+(2\alpha+\lambda-3\alpha\lambda)(1-t)\delta](1-\alpha)\} \\ &= \frac{-12t+4(1-t)\delta-16\alpha(1-t)\delta+12\alpha t}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{4[(1-4\alpha)(1-t)\delta-3(1-\alpha)t]}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{4\Upsilon}{[6\alpha+\lambda(1-\alpha)]^2}. \end{aligned} \tag{3.3.42}$$

Based on (3.3.39), the partial derivative of p_G with respect to λ is given by

$$\frac{\partial p_G}{\partial \lambda} = \frac{-(1-t)\delta[6\alpha+\lambda(1-\alpha)] - [6t-(\lambda+2)(1-t)\delta](1-\alpha)}{[6\alpha+\lambda(1-\alpha)]^2}$$

$$= \frac{2[(1-4\alpha)(1-t)\delta - 3(1-\alpha)t]}{[6\alpha+\lambda(1-\alpha)]^2}$$

$$= \frac{2\Upsilon}{[6\alpha+\lambda(1-\alpha)]^2}. \tag{3.3.43}$$

Based on (3.3.38), the partial derivative of p_0 with respect to λ is given by

$$\frac{\partial p_0}{\partial \lambda} = \frac{-\alpha(1-t)\delta[6\alpha+\lambda(1-\alpha)] - [3(1+\alpha)t-(1+\alpha\lambda-2\alpha)(1-t)\delta](1-\alpha)}{[6\alpha+\lambda(1-\alpha)]^2}$$

$$= \frac{-4\alpha^2(1-t)\delta - 3t + 3\alpha^2 t + (1-t)\delta(1-3\alpha)}{[6\alpha+\lambda(1-\alpha)]^2}$$

$$= \frac{(1+\alpha)[(1-4\alpha)(1-t)\delta - 3(1-\alpha)t]}{[6\alpha+\lambda(1-\alpha)]^2}$$

$$= \frac{(1+\alpha)\Upsilon}{[6\alpha+\lambda(1-\alpha)]^2}. \tag{3.3.44}$$

Note that

$$Sign(\frac{\partial p_1}{\partial \lambda}) = Sign(\frac{\partial p_G}{\partial \lambda}) = Sign(\frac{\partial p_0}{\partial \lambda}) = Sign(\Upsilon). \tag{3.3.45}$$

Let

$$\tilde{\delta} \equiv \frac{3t(1-\alpha)}{(1-t)(1-4\alpha)}. \tag{3.3.46}$$

To summarize the above results, I obtain

$$\begin{cases} \frac{\partial p_0}{\partial \lambda} > 0, \frac{\partial p_G}{\partial \lambda} > 0, \frac{\partial p_1}{\partial \lambda} > 0, & if \quad \delta > \tilde{\delta} \quad and \quad \alpha < 25\%; \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_G}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} < 0, & if \quad \delta < \tilde{\delta} \quad and \quad \alpha < 25\%; \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_G}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} < 0, & if \quad \alpha > 25\%. \end{cases} \tag{3.3.47}$$

□

Proposition 4 suggests that when the copay rate is relatively high ($\alpha > 25\%$ in the model), all three drug manufacturers, brand-name and generic, react to a lower (higher) proportion of the selective patients by raising (lowering) prices. When the copay rate is relatively low ($\alpha < 25\%$ in the model), the reaction from the three firms further depends on whether the difference in perceived quality between brand-name and generic drug is large. A small perceived quality differential will not change the direction of firms' price adjustment, while a large perceived quality would do. That is, with a low rate of copay and a large perceived quality differential, all three firms react to a lower (higher) proportion of selective patients by lowering (raising) prices.

Without any generic price-cap, in the first scenario, suppose that at an arbitrarily high rate of copay (i.e. $\alpha > 25\%$), a lower proportion of the selective patients, e.g. a preference switch from brand-name to generic drug, indicates higher brand-name drug prices in the equilibrium. Moreover, the increase in the proportion of unselective patients also offers the generic drug manufacturer more market power to charge a higher price, because there is no limit on generic drug price at all.

Without any generic price-cap, in the second scenario, suppose that the rate of copay is not high (i.e. $\alpha < 25\%$) and assume perceived quality between brand-name and generic drugs is not very different (i.e. $\delta < \tilde{\delta}$), all three drug firms would have the same reactions in price setting as in the first scenario. A lower proportion of the selective patients, for instance, a preference switch from brand-name to generic drug, leads to not only higher brand-name drug prices but higher generic drug price in the equilibrium.

The above two scenarios may not be as intuitive but the observation is consistent with profit maximization. They pose a dilemma for the policy-makers: on the one

hand, public/private insurers are glad to see the breakdown in patients' loyalty regarding those expensive brand-name drugs and in favour of the cheaper generic drug instead; on the other, the impact of this preference switch on the equilibrium drug prices is unexpected. With this dilemma, all drug manufacturers choose to raise their prices.

Without any generic price-cap, in the third scenario, suppose that the rate of copay is not high (i.e. $\alpha < 25\%$) and that the difference in the perceived quality between brand-name and generic drugs is very large (i.e. $\delta > \tilde{\delta}$). Under these conditions, both brand-name drug manufacturers will lower their prices in the equilibrium in response to patients' preference switch from brand-name to generic drug. The generic drug manufacturer will also lower its price to compete against its brand-name rivals with superior perceived quality.

Proposition 5. *When there is no price-cap on the generic drug, if the difference in perceived quality between brand-name drug and generic drug is large enough, ceteris paribus, a higher (lower) rate of copay leads to higher (lower) equilibrium prices for the brand-name drug* 0 *and the generic drug* G*. However, as long as the perceived quality differential between the brand-name drugs and the generic drug is not too small, ceteris paribus, a higher (lower) rate of copay leads to lower (higher) equilibrium price for the brand-name drug* 1*.*

Proof. Let

$$\Theta = (\lambda + 2)(1 - t)\delta - 6t. \tag{3.3.48}$$

Based on (3.3.38), the partial derivative of p_0 with respect to α is given by

$$\frac{\partial p_0}{\partial \alpha} = \frac{1}{[6\alpha + \lambda(1-\alpha)]^2}\{[3t + 2(1-t)\delta - \lambda(1-t)\delta][6\alpha + \lambda(1-\alpha)]$$
$$- [3(1+\alpha)t - (1 + \alpha\lambda - 2\alpha)(1-t)\delta](6-\lambda)\}$$

$$= \frac{6\lambda t - 18t + \lambda(1-t)\delta + 6(1-t)\delta - \lambda 2(1-t)\delta}{[6\alpha + \lambda(1-\alpha)]^2}$$

$$= \frac{(3-\lambda)[(\lambda+2)(1-t)\delta - 6t]}{[6\alpha + \lambda(1-\alpha)]^2}$$

$$= \frac{(3-\lambda)\Theta}{[6\alpha + \lambda(1-\alpha)]^2}. \tag{3.3.49}$$

Based on (3.3.39), the partial derivative of p_G with respect to α is given by

$$\frac{\partial p_G}{\partial \alpha} = \frac{(6-\lambda)[(\lambda+2)(1-t)\delta - 6t]}{[6\alpha + \lambda(1-\alpha)]^2}$$

$$= \frac{(6-\lambda)\Theta}{[6\alpha + \lambda(1-\alpha)]^2}. \tag{3.3.50}$$

I note that

$$Sign(\frac{\partial p_0}{\partial \alpha}) = Sign(\frac{\partial p_G}{\partial \alpha}) = Sign(\Theta). \tag{3.3.51}$$

When $\delta > \frac{t}{1-t}$, I show that $\frac{\partial p_1}{\partial \alpha} < 0$:

$$\begin{aligned}\frac{\partial p_1}{\partial \alpha} &= \frac{1}{\alpha^2[6\alpha+\lambda(1-\alpha)]^2}\{[6t+\lambda t+2(1-t)\delta-3\lambda(1-t)\delta]\alpha[6\alpha+\lambda(1-\alpha)] \\ &\quad -(12\alpha+\lambda-2\alpha\lambda)[(6\alpha-\lambda+\alpha\lambda)t+(2\alpha+\lambda-3\alpha\lambda)(1-t)\delta]\} \\ &= \frac{1}{\alpha^2[6\alpha+\lambda(1-\alpha)]^2}[-36\alpha^2 t-12\alpha^2(1-t)\delta+20\alpha^2\lambda(1-t)\delta-3\alpha^2\lambda^2(1-t)\delta \\ &\quad +\alpha^2\lambda^2 t+12\alpha\lambda t-12\alpha\lambda(1-t)\delta+-\lambda^2(1-t)\delta-2\alpha\lambda^2 t+2\alpha\lambda^2(1-t)\delta] \\ &= \frac{1}{\alpha^2[6\alpha+\lambda(1-\alpha)]^2}\{(6-\lambda)[3\lambda(1-t)\delta-\lambda t-2(1-t)\delta-6t]\alpha^2 \\ &\quad -2\lambda(6-\lambda)[(1-t)\delta-t]\alpha-\lambda^2[(1-t)\delta-t]\} \\ &< 0. \end{aligned} \tag{3.3.52}$$

When $\delta < \frac{t}{1-t}$, I show that the sign of $\frac{\partial p_1}{\partial \alpha}$ is indeterminant.[43]
Now define $\ddot{\delta}$ and $\dot{\delta}$, respectively, as

$$\begin{aligned}\ddot{\delta} &\equiv \frac{6t}{(\lambda+2)(1-t)} \quad \text{and} \\ \dot{\delta} &\equiv \frac{t}{1-t}. \end{aligned} \tag{3.3.53}$$

To summarize the above results, I have

$$\begin{cases} \frac{\partial p_0}{\partial \alpha} > 0, \frac{\partial p_G}{\partial \alpha} > 0, \quad if \quad \delta > \ddot{\delta}; \\ \\ \frac{\partial p_0}{\partial \alpha} < 0, \frac{\partial p_G}{\partial \alpha} < 0, \quad if \quad \delta < \ddot{\delta}. \end{cases} \tag{3.3.54}$$

and

$$\begin{cases} \frac{\partial p_1}{\partial \alpha} < 0, \quad if \quad \delta > \dot{\delta}; \\ \\ \frac{\partial p_1}{\partial \alpha} \lessgtr 0, \quad if \quad \delta < \dot{\delta}. \end{cases} \tag{3.3.55}$$

[43]The detailed proof is provided in Appendix B.

□

Proposition 5 suggests that if the difference in perceived quality between brand-name and generic drugs is not too large (i.e. $\delta < \ddot{\delta}$), with everything else being equal, an increase (decrease) in the rate of copay — a larger (smaller) α — would lead to lower (higher) prices for both the brand-name drug 0 and its generic version G in the equilibrium. However, when brand-name and generic drugs are perceived very different in quality (i.e. $\delta > \ddot{\delta}$), with everything else being equal, the opposite would occur.

If the difference in perceived quality between brand-name and generic drugs is not too small (i.e. $\delta > \dot{\delta}$), with everything else being equal, an increase (decrease) in the rate of copay — a larger (smaller) α — would lead to lower (higher) prices for the brand-name drug 1 in the equilibrium. But when the difference in perceived quality between brand-name and generic drugs is small (i.e. $\delta < \dot{\delta}$), the impact of changes in the copay rate on the price of brand-name drug 1 is ambiguous.

Consider the scenario in which patients' perceived quality between brand-name and generic drugs does not differ much (i.e. $\delta < \dot{\delta}$): when insurers increase the rate of copay, both the brand-name manufacturer 0 and its generic counterpart G react to lower their drug prices in the equilibrium, while the other brand-name manufacturer 1's price setting strategy is indeterminate. As the difference in perceived quality increases such that $\dot{\delta} < \delta < \ddot{\delta}$, the brand-name drug manufacturer 1 joins the other two manufacturers to lower their drug prices in the equilibrium in response to a rise in the rate of copay. If the difference in perceived quality is so large that $\delta > \ddot{\delta}$, the brand-name manufacturer 0 and its generic counterpart G react to increase their drug prices in the equilibrium in response to a rise in the rate of copay, while firm 1's price setting strategy remains the same no matter how large the difference in perceived quality is between brand-name and generic drugs.

A direct policy implication from the above proposition is that, if the difference in perceived quality between brand-name and generic drugs is not too large or not too small ($\dot{\delta} < \delta < \ddot{\delta}$), a copay rate increase initiated by a policy would be desirable for the policy-makers: all three drug manufacturers (brand-name and generic) would lower their drug prices in the equilibrium.

3.4 An Extension to the Baseline Model with Therapeutic Reference Pricing

The baseline model introduced above is characterized by the generic referencing pricing (GRP) reimbursement system. Under the GRP system, if a patient ends up purchasing the brand-name drug 0, one has to pay out-of-pocket, on top of his or her copay share, for the price differential between the brand-name original 0 and its generic version G. However, the GRP system does not require the other brand-name drug 1 to be included in the interchangeable drug category. Therefore, one who purchases the brand-name drug 1 does not need to pay any price differential on top his or her share of copay, as defined in (3.3.2). As such, the brand-name drug 1 is completely insulated from the competition from the cheaper drug G under the GRP system.

In this section, I introduce an extension to the baseline model characterized by the therapeutic referencing pricing (TRP) reimbursement system. Under the TRP system, the interchangeable therapeutic category is broadened to include not only the brand-name drug 0 and its generic substitute G but also the brand-name drug 1.[44] Note that brand-name drug 1 is still considered on patent thus without any direct generic substitute in the market. Now the patient *also* has to pay out-of-pocket for the price differential between the brand-name drug 1 and the generic drug G, on top of his or her share of copay. In a way, the TRP system elicits the price competition between the generic drug G and the brand-name drug 1, even if the latter does not have any generic substitute in principle.[45]

The TRP policy is also known as general therapeutic reference pricing. Under the assumption that there is only one generic drug in the therapeutic class, the TRP policy

[44]Similar policies can be found in the provincial drug plans across the country, such as the Special MAC policy for limited classes of drugs in Nova Scotia or reference-based pricing policy for selected classed of drugs in British Columbia (CIHI, 2010b).

[45]Empirically, drug 1 can be considered to be one with moderate, little or no improvement over existing medicines. The PMPRB applies the Therapeutic Class Comparison test to drug products like drug 1 such that its price cannot exceed the prices of other comparable drugs that treat the same disease or condition. Moreover, Canadian provincial government drug plans adopt standardized cost-effectiveness tests (for example, the Incremental Cost-effectiveness Ratio test, or ICER test) in such situations, which may similarly constrain the prices of these therapeutically similar brand-name drugs.

is equivalent as the reference-based pricing policy or the Special MAC policy.[46] By qualifying more drugs under the interchangeable therapeutic category, the TRP policy creates intense competition among these therapeutic substitutes.[47] Next, I discuss the impact of the change in the reimbursement system on the drug manufacturers' price setting behaviour.

3.4.1 Market Shares and Profits

The fundamental assumptions and model setup of the baseline model remain the same except that patients' copay shares for the three drugs are changed.

Let p_0, p_1, and p_G be the prices for drugs 0, 1, and G, respectively, charged in the market. α is the rate of copay. Now the patient who purchases the brand-name drug 0 or 1 has to pay out-of-pocket for the price differential between the brand-name drug and the generic drug G, on top of his or her copay αp_G. Accordingly, the copay level for drugs 0, 1, and G are c_0, c_1, or c_G, respectively, which are given by

$$\begin{aligned} c_0 &= \alpha p_G + (p_0 - p_G), \\ c_1 &= \alpha p_G + (p_1 - p_G), \quad \text{and} \\ c_G &= \alpha p_G. \end{aligned} \tag{3.4.1}$$

The market shares for the three drug manufacturers are:

[46] British Columbia was initially the only Canadian province that implemented the reference-based pricing policy, which provoked significant backlash from the pharmaceutical industry (Morgan, 2003). British Columbia currently implements the reference pricing policy for only five classes of drugs. But, in practice, the reference-based pricing is not exactly the same as the Special MAC policy. I have discussed this issue briefly in chapter 2. To avoid confusion, I only refer to the therapeutic reference pricing (TRP) in the theoretical discussion in this chapter.

[47] Note that the financial benefit from the intense price competition under the reference-based pricing regime may also come with health risks when patients switch to a cheaper interchangeable generic (Grootendorst and Holbrook, 1999). However, this thesis does not focus on the safety concern and its potential cost.

$$\begin{aligned} D_0 &= \frac{\lambda(c_1 - c_0 + t)}{2t} \\ &= \frac{\lambda[t + p_1 - p_0]}{2t}, \end{aligned} \tag{3.4.2}$$

$$\begin{aligned} D_G &= \frac{(1-\lambda)[c_1 - c_G + t - (1-t)\delta]}{2t} \\ &= \frac{(1-\lambda)[t + p_1 - p_G - (1-t)\delta]}{2t}, \quad \text{and} \end{aligned} \tag{3.4.3}$$

$$\begin{aligned} D_1 &= 1 - D_0 - D_G \\ &= \frac{t + p_G - p_1 + \lambda(p_0 - p_G) + (1-\lambda)(1-t)\delta}{2t}, \end{aligned} \tag{3.4.4}$$

respectively, where $\delta \equiv (\theta_H - \theta_L)q$ remains the difference in perceived quality between brand-name and generic drugs.[48]

In (3.4.2), (3.4.3), and (3.4.4), the parameter α does not appear because the identical components in the representative patient's copay cancel out in the derivation of market shares of the three firms. Due to the common term with α in the copay shares for all three drugs in (3.4.1), now only the difference between their drug prices matters.

Again, I assume zero marginal cost associated with manufacturers' endeavours in developing therapeutic variant and/or brand-imaging. Therefore the profit functions for the three firms are:

[48] The change in the copay of the brand-name drug 1 in (3.4.1) does not change the conclusion in the baseline model. That is, unselective patients prefer the generic drug G to its brand-name original 0 and that selective patients only consider the brand-name drugs 0 and 1, as long as $p_G < p_0$ and $(1-t)(\theta_H - \theta_L)q > p_0 - p_G$.

$$\begin{aligned}\Pi_0 &= p_0 D_0 \\ &= \lambda \frac{(t+p_1)p_0 - p_0^2}{2t},\end{aligned} \tag{3.4.5}$$

$$\begin{aligned}\Pi_G &= p_G D_G \\ &= (1-\lambda)\frac{[t+p_1-(1-t)\delta]p_G - p_G^2}{2t}, \quad \text{and}\end{aligned} \tag{3.4.6}$$

$$\begin{aligned}\Pi_1 &= p_1 D_1 \\ &= \frac{[t+\lambda(p_0-p_G)+p_G+(1-\lambda)(1-t)\delta]p_1 - p_1^2}{2t}.\end{aligned} \tag{3.4.7}$$

Same as the baseline model, the three firms are involved in a one-shot game in price in the above setting. The equilibrium is Nash.

3.4.2 Equilibrium Price with a Binding Generic Price-Cap

Now I discuss the equilibrium prices for the three firms when there is a binding price-cap for the generic drug.[49] I have

$$p_G = \beta p_0 \quad \text{from (3.3.13)}.$$

The first-order conditions for the two brand-name manufacturers are as follows:

$$\frac{\partial \Pi_0}{\partial p_0} = 0 \quad \Leftrightarrow \quad p_0 = \frac{t+p_1}{2} \quad \text{and} \tag{3.4.8}$$

$$\frac{\partial \Pi_1}{\partial p_1} = 0 \quad \Leftrightarrow \quad p_1 = \frac{t+\lambda(p_0-p_G)+p_G+(1-\lambda)(1-t)\delta}{2}. \tag{3.4.9}$$

Second-order conditions are both satisfied to guarantee local maxima.

Substituting in $p_G = \beta p_0$, I obtain:

[49] I will not extend the case when there is no generic price-cap.

$$p_0 = \frac{t + p_1}{2} \quad \text{and} \tag{3.4.10}$$

$$p_1 = \frac{t + (\lambda + \beta - \beta\lambda)p_0 + (1 - \lambda)(1 - t)\delta}{2}. \tag{3.4.11}$$

The equilibrium prices for the two brand-name firms with the binding generic price-cap are, respectively,

$$p_0 = \frac{3t + 2(1 - \lambda)(1 - t)\delta}{4 - \lambda - \beta + \beta\lambda} \quad \text{and} \tag{3.4.12}$$

$$p_1 = \frac{2t + 2(1 - \lambda)(1 - t)\delta + t(\lambda + \beta - \beta\lambda)}{4 - \lambda - \beta + \beta\lambda}. \tag{3.4.13}$$

3.4.2.1 Impact on Equilibrium Price with a Binding Generic Price-cap

With the equilibrium prices for the two brand-name firms under the TRP copay structure defined as (3.4.1) and a binding generic price-cap β, defined as (3.3.13), now I discuss the impact of preference and policy changes on the firms' price setting strategies in the equilibrium.

Proposition 6. *(1) When the difference in perceived quality between brand-name and generic drug is large enough (i.e. $\delta > 2\bar{\delta}$), ceteris paribus, both brand-name manufacturers respond by raising their drug prices, if there are proportionally less selective patients. (2) When the difference in perceived quality between brand-name and generic drug is small enough (i.e. $\delta < \bar{\delta}$), ceteris paribus, both brand-name manufacturers respond by raising their drug prices, if there are proportionally less selective patients. (3)When the difference in perceived quality between brand-name and generic drug is not too large or too small (i.e. $\bar{\delta} < \delta < 2\bar{\delta}$), ceteris paribus, firm* 0 *raises its price while firm* 1 *lowers its price.*

Proof. Based on (3.4.12) and (3.4.13), the partial derivatives of p_0 and p_1 with respect to λ are given by

$$\frac{\partial p_0}{\partial \lambda} = \frac{1}{[4-\lambda-\beta+\beta\lambda]^2}\{-2(1-t)\delta(4-\lambda-\beta+\beta\lambda) - [3t+2(1-\lambda)(1-t)\delta](-1+\beta)\},$$

$$= \frac{3[(1-\beta)t-2(1-t)\delta]}{[4-\lambda-\beta+\beta\lambda]^2} \tag{3.4.14}$$

and

$$\frac{\partial p_1}{\partial \lambda} = \frac{1}{[4-\lambda-\beta+\beta\lambda]^2}\{[-2(1-t)\delta+t-\beta t](4-\lambda-\beta+\beta\lambda) - [2t+2(1-\lambda)(1-t)\delta+t(\lambda+\beta-\beta\lambda)](-1+\beta)\}$$

$$= \frac{6[(1-\beta)t-(1-t)\delta]}{[4-\lambda-\beta+\beta\lambda]^2}, \tag{3.4.15}$$

respectively. Let

$$\bar{\delta} \equiv \frac{(1-\beta)t}{2(1-t)}. \tag{3.4.16}$$

Therefore, I have

$$\begin{cases} \frac{\partial p_0}{\partial \lambda} > 0, \frac{\partial p_1}{\partial \lambda} > 0, & if \quad \delta < \bar{\delta}; \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} > 0, & if \quad \bar{\delta} < \delta < 2\bar{\delta}; \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} < 0, & if \quad \delta > 2\bar{\delta}. \end{cases} \tag{3.4.17}$$

□

Under the TRP reimbursement regime, the brand-name drug 1 is directly involved in the price competition with the cheaper generic drug G. How the brand-name drug manufacturers' price setting behaviour responds to the changes in the preference parameter, λ, depends upon how much patients feel about the difference in perceived quality between brand-name and generic drugs.

More specifically, when the difference in perceived quality is large (i.e. $\delta > 2\bar{\delta}$), a switch of preference from brand-name to generic drug — a lower λ — leads to higher equilibrium prices for both brand-name drugs, with everything else being equal. The brand-name manufacturers can raise prices despite the fact that there are proportionally more unselective patients. The manufacturers leverage the facts that patients believe brand-name drugs have superior quality and that at least some patients do not mind paying a price premium for brand-name over generic drugs.

The exact opposite observations are found for the polar case. With everything else being equal, when the difference in perceived quality is small (i.e. $\delta < \bar{\delta}$), a switch of preference from brand-name to generic drug — a lower λ — leads to lower equilibrium prices for the two brand-name drugs.

Proposition 6 shows that the two brand-name manufacturers react differently in response to a preference switch from brand-name to generic drug (a lower λ), when the difference in perceived quality is in the intermediate range ($\bar{\delta} < \delta < 2\bar{\delta}$). Under this condition, the brand-name firm 0 raises it price while the other brand-name firm, also subject to generic competition with the TRP reimbursement policy, lowers its price. This strategy of lowering price, in response to the decreased proportion of selective patients, will be implemented by firm 0 only when the difference in perceived quality between brand-name and generic drug is further narrowed ($\delta < \bar{\delta}$). This intermediate state is new compared to what I find from the baseline model, where the equilibrium prices for both brand-name drugs always react in the same direction, whether the difference in perceived quality is large or small.

Proposition 7. *Under the TRP reimbursement policy, ceteris paribus, both brand-name manufacturers lower their drug prices in the equilibrium as the government lowers the generic price-cap.*

Proof. Based on (3.4.12) and (3.4.13), the partial derivatives of p_0 and p_1 with respect to β are given by the following, respectively,

$$\frac{\partial p_0}{\partial \beta} = \frac{1-\lambda}{(4-\lambda-\beta+\beta\lambda)^2}[3t + 2(1-\lambda)(1-t)\delta]$$

$$> 0 \tag{3.4.18}$$

and

$$\begin{aligned}\frac{\partial p_1}{\partial \beta} &= \frac{1}{(4-\lambda-\beta+\beta\lambda)^2}\{(t-t\lambda)(4-\lambda-\beta+\beta\lambda) \\ &\quad + [2t + 2(1-\lambda)(1-t)\delta + t(\lambda+\beta-\beta\lambda)](1-\lambda)\}\end{aligned}$$

$$= \frac{1}{(4-\lambda-\beta+\beta\lambda)^2}(1-\lambda)[6t + 2(1-\lambda)(1-t)\delta]$$

$$= \frac{2(1-\lambda)}{(4-\lambda-\beta+\beta\lambda)^2}[3t + (1-\lambda)(1-t)\delta]$$

$$> 0. \tag{3.4.19}$$

□

Proposition 7 shows that under the TRP reimbursement structure, when the government lowers the generic price-cap, both brand-name manufacturers unambiguously lower their drug prices. This finding cannot be observed from the baseline model.

Under the assumption of the GRP reimbursement regime in the baseline model, the price setting strategy of the brand-name manufacturer 1 is not certain, depending on the values of the other two parameters (α and λ). With an arbitrarily small rate of copay (i.e. $\alpha < \bar{\alpha}$), the brand-name drug manufacturer 1 would raise its price despite a lower generic price-cap (β) in the baseline model.

Apparently, this extension beyond the baseline model shows that the TRP regime is more effective than the GRP regime by eliciting generic competition to both the brand-name drugs under the interchangeable therapeutic category.

3.5 An Extension to the Baseline Model with Four Players

I introduce another extension beyond the baseline model in this section, in which there are four single-product drug manufacturers in one therapeutic market. Here the brand-name drug 1 has lost the patent protection and its generic version G_1 is available and covered in the formulary. More specifically, both brand-name drug 0 and 1 have their own generic substitutes, G_0 and G_1, respectively.[50] In the following, I discuss the equilibrium prices of the two brand-name firms. Both of them have their own generic substitutes, whose prices are capped.

3.5.1 Market Shares and Profits

The fundamental assumptions and model setup of the baseline model remain the same as the baseline model. But, I need to accommodate the brand-name drug 1's generic substitute G_1.

Let p_0, p_1, p_{G_0}, and p_{G_1} be the prices for drugs 0, 1, G_0, and G_1 charged in the market. The rate of copay is still α. Now the patient who purchases brand-name drug 1 has to pay out-of-pocket for the price differential between 1 and G_1, on top of his or her copay αp_{G_1}. The same as before, the patient who purchases brand-name drug 0 has to pay out-of-pocket for the price differential between 0 and G_0, on top of his or her copay αp_{G_0}. As such, patients' copay shares for the four drugs are, respectively,

$$\begin{aligned} c_0 &= \alpha p_{G_0} + (p_0 - p_{G_0}), \\ c_1 &= \alpha p_{G_1} + (p_1 - p_{G_1}), \\ c_{G_0} &= \alpha p_{G_0}, \quad \text{and} \\ c_{G_1} &= \alpha p_{G_1}. \end{aligned} \tag{3.5.1}$$

In the four-player model, the induced proportions of "selective" and "unselective" patients are still described by the proportions λ and $1-\lambda$, respectively. Adding a generic substitute G_1 for the brand-name drug 1 does not change the conclusion in

[50] Given the high degree of concentration in the Canadian generic industry, it is possible that G_0 and G_1 are manufactured by the same firm. For simplicity, I maintain the assumption that all drug manufacturers are single-product firm.

the baseline model. That is, unselective patients prefer generic drugs to their brand-name originals, respectively, and that selective patients only consider the brand-name drugs, as long as $p_{G_0} < p_0$, $p_{G_1} < p_1$, $(1-t)(\theta_H - \theta_L) > p_0 - p_{G_0}$, and $(1-t)(\theta_H - \theta_L) > p_1 - p_{G_1}$.[51]

As such, the proportion of selective patients, who prefer brand-name drugs only, is λ, regardless of which brand-name drug (0 or 1) that a selective patient purchases. In turn, the proportion of unselective patients, who prefer generic drugs only, is $1-\lambda$, regardless of which generic drug (G_0 or G_1) that an unselective patient purchases. I assume patients have homogeneous preference toward brand-name or generic drug within any given therapeutic market. Without loss of generality, this means a single λ for the therapeutic market composed of the four drugs, rather than having two distinct λs for each drug pairs, 0 vs. G_0 and 1 vs. G_1, respectively.

According to (3.3.1), I can rewrite the utility function of the representative patient as follows:

$$U_{ji} = \begin{cases} R + (1-t)\cdot\theta_{ji} - t\cdot(x-i)^2 - c_i & i = 0, 1; \\ R + (1-t)\cdot\theta_{ji} - t\cdot(x-0)^2 - c_i & i = G_0; \\ R + (1-t)\cdot\theta_{ji} - t\cdot(x-1)^2 - c_i & i = G_1, \end{cases} \tag{3.5.2}$$

with

$$\theta_{ji} = \begin{cases} \theta_H & i = 0, 1 \text{ and } j = \text{selective}; \\ \theta_L & i = G_0, G_1 \text{ and } j = \text{selective, or } j = \text{unselective}. \end{cases}$$

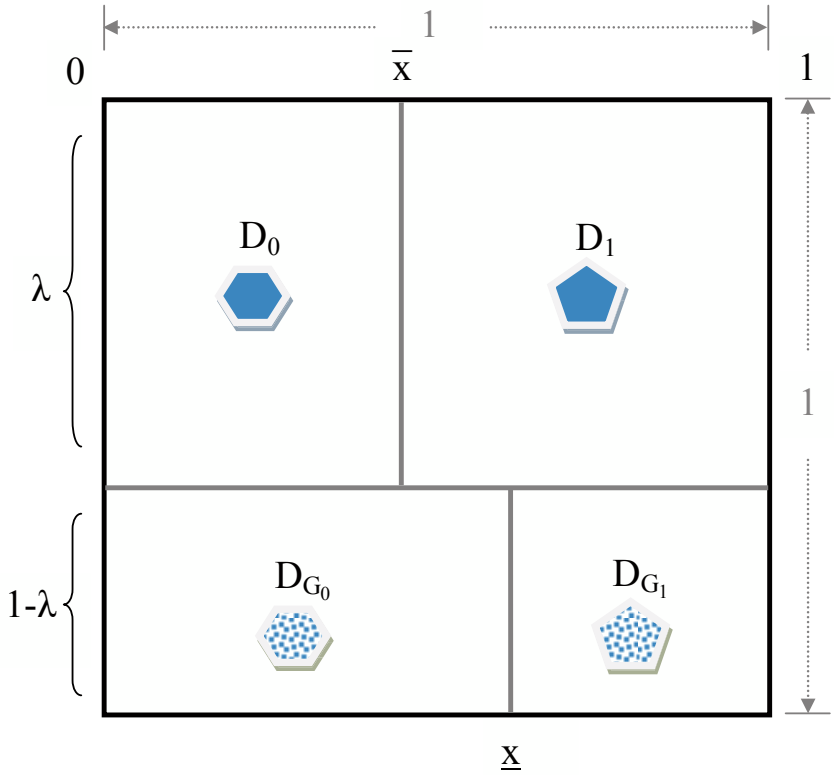
where c_i ($i = 0,\ 1,\ G_0,\ or\ G_1$) is defined by (3.5.1).

The market shares for the four drug manufacturers can be depicted in the unit box in Figure 3.4.

The market shares are calculated as follows:

[51] The proof is similar to that for the baseline model in Appendix B and therefore is omitted.

Figure 3.4: Market Shares for the Four Drug Manufacturers



$$D_0 = \frac{\lambda}{2t}[p_1 - p_0 - (1-\alpha)(p_{G_1} - p_{G_0})], \tag{3.5.3}$$

$$D_1 = \lambda - \frac{\lambda}{2t}[p_1 - p_0 - (1-\alpha)(p_{G_1} - p_{G_0})], \tag{3.5.4}$$

$$D_{G_0} = \frac{(1-\lambda)\alpha}{2t}(p_{G_1} - p_{G_0}), \quad \text{and} \tag{3.5.5}$$

$$D_{G_1} = (1-\lambda) - \frac{(1-\lambda)\alpha}{2t}(p_{G_1} - p_{G_0}). \tag{3.5.6}$$

Note that an unselective patient whose MFDV is close to 1 has to opt for brand-name drug 1 in the baseline model. As the patent of brand-name drug 1 expires,

now he or she can purchase the generic substitute G_1. By assumption, the brand-name and generic drugs market is completely segmented by the parameter λ. That is, selective patients only prefer and purchase brand-name drugs, while unselective patients only prefer and purchase generic drugs.

3.5.2 Equilibrium Price with a Binding Generic Price-cap

Now I discuss the equilibrium prices when there is a binding generic price-cap. In essence, each brand-name drug manufacturer sets its price to maximize its profit given the optimal price setting strategy chosen by the rivals. The prices of the generic substitutes are capped at a percentage of their brand-name original drugs' prices, respectively.

The generic drugs G_0 and G_1 may face different price-caps if they are introduced to the market at different points in time.[52] I assume

$$p_{G_0} = \beta_0 p_0 \quad \text{and}$$
$$p_{G_1} = \beta_1 p_1. \tag{3.5.7}$$

The demand functions for the two brand-name drugs, from (3.5.3) and (3.5.4), are, respectively,

$$D_0 = \frac{\lambda}{2t}[p_1 - p_0 - (1-\alpha)(\beta_1 p_1 - \beta_0 p_0)] \quad \text{and} \tag{3.5.8}$$

$$D_1 = \lambda - \frac{\lambda}{2t}[p_1 - p_0 - (1-\alpha)(\beta_1 p_1 - \beta_0 p_0)]. \tag{3.5.9}$$

Again with zero marginal cost associated with the endeavours in producing therapeutic variant and brand-imaging, the profit functions for the two brand-name firms are, respectively,

[52] Newer generic drugs may face an even lower price-cap if a new government policy on generic pricing is set in place before the generic drug is in market. Similar policies can be found in the Pharmaceutical Benefits Scheme in Australia, where tiered price-caps are applied to generic drugs in different categories (Löfgren, 2009). In addition, the solution where both generic price-caps are equal is trivial.

$$\Pi_0 = \frac{\lambda}{2t}[-p_0^2 + (1-\alpha)\beta_0 p_0^2 + p_1 p_0 - (1-\alpha)\beta_1 p_1 p_0] \quad \text{and} \tag{3.5.10}$$

$$\Pi_1 = \lambda p_1 - \frac{\lambda}{2t}[p_1^2 - (1-\alpha)\beta_1 p_1^2 - p_0 p_1 + (1-\alpha)\beta_0 p_1 p_0]. \tag{3.5.11}$$

I obtain the following first-order conditions:

$$\frac{\partial \Pi_0}{\partial p_0} = 0 \quad \Leftrightarrow \quad [2(1-\alpha)\beta_0 - 2]p_0 = [(1-\alpha)\beta_1 - 1]p_1 \quad \text{and} \tag{3.5.12}$$

$$\frac{\partial \Pi_1}{\partial p_1} = 0 \quad \Leftrightarrow \quad 2[1-(1-\alpha)\beta_1]p_1 = 2t - [1-(1-\alpha)\beta_0]p_0. \tag{3.5.13}$$

Second-order conditions are both satisfied to guarantee local maxima.

Therefore the equilibrium prices for the two brand-name firms with binding generic price-caps are, respectively,

$$p_0 = \frac{2t}{5[1-(1-\alpha)\beta_0]} \quad \text{and} \tag{3.5.14}$$

$$p_1 = \frac{4t}{5[1-(1-\alpha)\beta_1]}. \tag{3.5.15}$$

In this context, the entry of the generic drug G_1 establishes the market segmentation between the brand-name and the generic sector. The selective patients (λ in proportion) would now only prefer the two brand-name drugs, 0 and 1, while the unselective patients ($1-\lambda$ in proportion) would now only prefer the two generic drugs, G_0 and G_1.[53]

3.5.2.1 Impact on Equilibrium Price with a Binding Generic Price-cap

Since the proportion (λ) of the selective patients and the proportion ($1-\lambda$) of the unselective patients do not enter either (3.5.14) or (3.5.15), they do not play

[53] As it shows in Figure 3.2 and Figure 3.4.

any role in the optimal price setting decision for either brand-name firms in the current setup. That is, the brand-name manufacturers will not consider the preference switch between brand-name to generic drug as a factor in their price setting decisions, because of the market segmentation with the generic sector and the existence of the binding generic price-cap. The other two policy parameters, the copay rate and the generic price-cap, however, are still important for the price setting decisions of the brand-name manufacturers.

Proposition 8. *When both brand-named drugs have their own generic substitutes, if the prices of both generic drugs are capped, ceteris paribus, a higher (lower) copay rate leads both brand-name drug manufacturers to charge lower (higher) prices in the equilibrium.*

Proof. From (3.5.14) and (3.5.15), I derive the partial derivatives of p_0 and p_1 with respect to α as the following:

$$\frac{\partial p_0}{\partial \alpha} = -\frac{4t\beta_0}{5[1-(1-\alpha)\beta_0]^2} < 0 \tag{3.5.16}$$

and

$$\frac{\partial p_1}{\partial \alpha} = -\frac{4t\beta_1}{5[1-(1-\alpha)\beta_1]^2} < 0. \tag{3.5.17}$$

□

Proposition 8 suggests that a higher (lower) copay rate, with everything else being equal, leads to a lower (higher) price in the equilibrium for both brand-name drugs 0 and 1.

The finding here is consistent with that from the baseline model. When the government or private insurer raises the percentage of patient copay, ceteris paribus, both brand-name manufacturers respond by lowering drug prices. The manufacturers anticipate that patients would likely be more unselective with increased out-of-pocket spending. Again the two brand-name drug manufacturers always lower their prices in response to a copay rate increase regardless of the difference in patients' perceived quality between the brand-name and generic drugs.

Proposition 9. *When both brand-named drugs have their own generic substitutes, ceteris paribus, if the government lowers (raises) the generic price-caps, brand-name firms (*0 *and* 1*) will lower (raise) their drug prices correspondingly.*

Proof. From (3.5.14) and (3.5.15), I derive the partial derivatives of p_0 and p_1 with respect to β_0 and β_1 as the following:

$$\frac{\partial p_0}{\partial \beta_0} = \frac{4t(1-\alpha)}{5[1-(1-\alpha)\beta_0]^2} > 0, \tag{3.5.18}$$

$$\frac{\partial p_1}{\partial \beta_1} = \frac{4t(1-\alpha)}{5[1-(1-\alpha)\beta_1]^2} > 0, \tag{3.5.19}$$

and

$$\frac{\partial p_1}{\partial \beta_0} = \frac{\partial p_0}{\partial \beta_1} = 0. \tag{3.5.20}$$

□

Proposition 9 suggests that, in this four-player model, when the government lowers (raises) the price-cap for a generic drug, with everything else being equal, the manufacturer of the counterpart brand-name original will lower (raise) its price. There is no cross-price effect, for instance, a lower generic price-cap for G_0 does not lead to a lower brand-named drug price in drug 1.

The four-player model extends beyond the baseline model by introducing the generic substitute for the brand-name drug 1. The interesting finding here is: when different percentages of the price-cap is applied to different drug classes,[54] for instance, β_0 set for drugs G_0 and 0 and β_1 set for drugs G_1 and 1, a lower generic price-cap in one drug class has no effect on the price setting of the brand-name drug in the other drug class, everything else being equal.

[54]For example, in the Pharmaceutical Strategy-Phase 2 announced in October 2009, Alberta applies the policy of a lower generic price-cap only to the new generic drugs, in the provincial formulary after the introduction of the new policy. The information was retrieved from http://www.health.alberta.ca/initiatives/pharmaceutical-strategy-2.html, September 29, 2010.

3.6 Policy Implications

I have discussed the price setting behaviour of brand-name drug manufacturers in a typical Canadian prescription drug market with two-dimension product differentiation under different settings. I start with the baseline model characterized by two brand-name and one generic single-product drug manufacturers, both with and without a generic price-cap. I extend the baseline model by modifying the reimbursement structure: from the generic reference pricing (GRP) to the therapeutic reference pricing (TRP) system, such that both brand-name drugs are subject to the generic competition. I then extend the baseline model by adding a new generic manufacturer such that the model accommodates two brand-name manufacturers and their generic substitutes, respectively. Now I summarize the policy implications of the different model setups.

On the proportion of the "selective" (λ) patients, a decrease in λ means proportionally more patients switch their preference from brand-name to generic drug. I report mixed findings on λ from the different model setups.

First, in the baseline model, a decrease in λ could imply a lower brand-name drug price in the equilibrium. This is in line with the conventional wisdom that a firm lowers product price to expand its market share. But it only happens when the difference in perceived quality between the brand-name and generic drugs is not large. When patients are made to believe that the brand-name drug can bring more advanced therapeutic quality than the generic drug does, the brand-name drug manufacturers can raise their drug prices as a result. It is termed the "generic competition paradox" coined by Scherer (1993).[55]

Similar findings can also be identified in the extension of the baseline model with the therapeutic reference pricing reimbursement regime. Without a price-cap, the generic drug manufacturer uses the same price setting strategy as its brand-name

[55]Note that my theoretical models in this chapter are based on the assumption that a therapeutic market is defined at the 4^{th} level WHO-ATC code and that all drug manufacturers are single-product firms. In other words, if a therapeutic market can be defined in a much broader sense and if drug manufacturers are multi-product firms, I could possibly obtain other insights for explaining the generic competition paradox. I will further discuss this in the conclusions in Chapter 5.

counterpart. The generic competition paradox also appears under certain circumstances. In general, it is not a straightforward exercise to interpret the findings from the model without a generic price-cap.

Finally, the preference parameter λ does not matter in the brand-name drug manufacturers' price setting decisions in the extension with four players.

On the rate of drug insurance copay (α), when public/private insurers raise the copay rate, patients would have to pay more out-of-pocket to fill their prescriptions. In the baseline model and its extension with four manufacturers, the impact of a copay rate rise on the prices of brand-name drugs is clear and straightforward: both brand-name drug manufacturers choose to lower prices to attract the more unselective patients. It is the same under the model without a generic price-cap except that the brand-name drug 0 and its generic counterpart G could increase their prices in the equilibrium when there is a big difference in perceived quality between brand-name and generic drugs. The manufacturers can leverage this product differentiation in perceived quality to support their price setting strategies even if patients are more sensitive to price increases under the condition of a rising copay rate. The copay rate does not matter in brand-name drug manufacturers' price setting decisions in the extension with the therapeutic reference pricing regime.

On the generic price-cap (β), a lower price-cap on the generic drug means increased direct price competition between brand-name and generic drugs. The findings from the various model setups are quite consistent as expected. That is, when the government lowers the generic price-cap, both brand-name drug manufacturers will lower their prices. The only exception in the baseline model with a binding generic price-cap is that under some conditions (i.e. in a therapeutic market with more patients preferring brand-name drugs), the brand-name drug manufacturer 1 will respond to a lower generic price-cap by increasing its drug price.

3.7 Concluding Remarks

After an overview of the Canadian pharmaceutical market and the institutional background, this chapter uses oligopoly theory with product differentiation to address drug manufacturers' price setting behaviour in different settings.

In a typical therapeutic market, brand-name drugs are differentiated in terms of therapeutic variant in the horizontal dimension while generic drugs and their brand-name originals are differentiated in terms of perceived quality in the vertical dimension. The single-product pharmaceutical firms are involved in a one-shot simultaneous game in prices. Each firm sets its own price to maximize its profit given the optimal price setting strategies chosen by the other firms.

I solve the equilibrium prices and then study in detail the impact of the changes of the three preference/policy parameters on drug manufacturers' price setting behaviour, ceteris paribus, under four different model setups. The key findings include:

First, the differentiation in perceived quality between brand-name and generic drug is pivotal in the brand-name manufacturers' price setting decisions. As long as patients are made to believe that brand-name drugs can bring more advanced therapeutic quality than generic substitutes, brand-name drug manufacturers then leverage their market power to charge higher prices in the market. This may happen even when proportionally more patients become unselective, everything else being equal. In addition, this finding is robust under different reimbursement (GRP or TRP) systems.

Second, among others, the government/private drug insurers can use either raising the rate of copay or lowering the generic price-cap or both as optional policy tools to contain prescription drug reimbursement costs. Applying these policy tools in different situations may have distinct implications on drug manufacturers' price setting behaviour. It is clear and straightforward to see the dampening effect in the prices of the brand-name drugs if the rate of copay is raised, when there is a binding generic price-cap and everything else is equal. However, without a generic price-cap, a rise in the rate of copay may lead to higher equilibrium prices for both brand-name and generic drugs, under the condition that there is a big difference in patients' perceived quality between brand-name and generic drugs.

Third, given the fact that the Canadian generic drug market is heavily concentrated and that generic drug manufacturers traditionally use non-price methods to compete for shelf space in pharmacies, imposing generic price-caps to lower drug reimbursement cost is considered effective. In addition, a lower generic price-cap elicits

lower brand-name drug prices in the equilibrium, everything else being equal. Only under special circumstance, for example, in a relatively young therapeutic market with a predominant patients' preference for brand-name drugs, the patented brand-name manufacturer may respond to a lower generic price-cap by increasing its drug price. In this situation, price regulations on patented drugs may serve as a necessary policy complement.

It is interesting to note that the literature and the Canadian institutional background may offer other plausible explanations for the generic competition paradox besides the argument on perceived quality differences. For example, as I discussed in Chapter 2, brand-name drug manufacturer's stragegy to launch their own "authorized generic" alongside the "independent generics" can successfully segment the market of the price-sensitive and price-insensitive patients (Grootendorst, 2007). One may also argue that certain government's industry policy can reinforce the generic competition paradox. For example, in Chapter 2, I mentioned that to attract more pharmaceutical investment, Quebec reimburses the full brand-name drug costs for 15 years after they have been listed on the provincial formulary, despite there may have been generic versions in the market (Bell et al., 2010).

After a comprehensive overview of the Canadian pharmaceutical system and the relevant institutional background, this chapter studies drug manufacturers' price setting behaviour based on the oligopoly theory with product differentiation. The discussion provides theoretical underpinnings for the empirical study on drug price dynamics in the following chapter.

Chapter 4

A Multilevel Analysis of Price Dynamics for a Selected Cohort of Drugs

4.1 Introduction

The Canada Health Act ensures the provision of specific medical services (i.e. hospital and physician services) to all Canadians at little or no cost. Outpatient prescribed drug[1] expenditure is not universally covered by the public/private drug plans. Patients have to pay out-of-pocket partially or in full depending on their insurance coverages and the applicable cost-sharing systems. But, the majority of the expenditure is funded by the public and private insurers.

According to the Canadian Institute for Health Information (2010a), pharmaceuticals were the second-largest expenditure component in 2009 and continue to be one of the fastest growing expenditure components of the Canadian healthcare system. About $11.4 billion or 38%[2] of the total prescribed drug expenditure was funded by the public drug plans in Canada during 2008. Public drug plan managers face the challenge of containing drug cost inflation while ensuring the availability and accessibility of safe and effective drugs for their clients. The implications of the rapid growth of the prescribed drug expenditure on the sustainability of the healthcare system are profound.

Drug price, as one of the drivers of the overall drug expenditure, has received increasing attention recently. But it remains unclear how manufacturers compete in prices with rivals in certain market and policy contexts, how they set drug prices in response to policy changes, and how government legislations and policies may affect

[1] A prescribed drug is a substance considered to be a drug under the Food and Drugs Act, which is sold for human use as the result of a prescription from a health professional.

[2] Drug expenditure under the public drug plans is the leading category in the distribution of prescribed drug spending by source of finance in 2009. The other two categories in the top three are private insurance plans at 31.2% and out-of-pocket at 15.4%.

manufacturers' price setting behaviour.

While the marketing literature offers explanations to the changes of drug prices from the manufacturers' perspective, it does not relate the price setting behaviour to the underlying dynamic drug market structure. For example, Lu and Comanor (1998) and Comanor and Scheweitzer (2007) introduce the prototypes of marketing strategies: price skimming and price penetration. Skimming involves setting a high introductory price which is reduced over time. Penetration is the reverse, with a low introductory price to start but increased over time. However, we do not see why these price setting strategies take place because the authors did not link the trends of drug prices to the evolving drug market structure in the long run. For example, a brand-name drug manufacturer has monopolistic market power as long as its drug product is under patent protection. Once the patent expires, entry of generic drugs normally takes place. As such, the drug without patent protection may face the competition from multiple generic substitutes.

Would a brand-name manufacturer adjust its drug price as it loses the monopolistic market power? The conventional wisdom suggests that when the patent of a brand-name drug expires, the price of this drug will fall as its generic substitutes emerge in the market. However, a few studies find that the prices of some brand-name drugs go up after their patents expire. This generic competition paradox has also been indicated by my theoretical models in Chapter 3.

Grootendorst (2007), among others, looks at this counterintuitive phenomenon by examining the impact of the "authorized generics" on the brand-name drug price from the empirical perspective. Kong (2009), among others, uses game theory models to explain brand-name drug manufacturers' paradoxical price setting behaviour from the theoretical perspective.

Despite explanations offered by the above studies as to why the prices of some brand-name drugs rise in response to entries of generic substitutes, few studies on drug price dynamics have taken into account the Canadian context of both the pharmaceutical market structure and the health policy and legislation. It is important to control for these contextual variables to evaluate whether the generic competition paradox is still present in the marginal sense as shown in the regression model.

The Canadian legislations and the corresponding regulatory framework for pharmaceuticals gradually evolve with the changing environment of science and technology, international obligations, and the demands of various stakeholders. As I have shown in the previous chapters, the Canadian pharmaceutical system is complex because (1) multiple players are involved in the consumption of drug products; (2) drug manufacturers adopt product differentiation as one of the major strategies other than price competition; (3) patients' demand for prescription drugs is induced by other stakeholders in the system; and (4) the relevant policies on drug pricing and reimbursement mechanisms are fragmented across the country.[3]

At the federal level, the prices of patented drugs are regulated by the PMPRB. The PMPRB requires that the introductory price for patented drugs with breakthrough improvement never be the highest among seven comparator countries, including France, Germany, Italy, Sweden, Switzerland, the UK, and the US.[4] In addition, the annual price increases for patented drugs should be limited by the CPI. Drug manufacturers, on the other hand, may choose to exit or not to enter the Canadian market if they cannot obtain their desired prices under the PMPRB's price regulation. The PMPRB has no direct price control over non-patented drugs, including off-patent drugs and generic drugs that do not have any patents.

At the provincial level, provinces do not have jurisdiction in regulating drug price directly, but they develop various mechanisms to contain drug reimbursement costs covered by the public drug plans.

For example, Alberta and Ontario impose the policy of price-caps on generic drugs covered by their provincial drug plans. In October 2009, Alberta announced the new Pharmaceutical Strategy (Phase 2) requiring that the prices for new generic drugs be 45% of a brand-name drug price, down from 75% before the policy change.[5] The Ontario Drug Benefit Program (ODBP) imposes the price-caps on the generic drugs listed on the provincial formulary to set the maximum price for reimbursement. Under the policy, the prices of generic drugs are set at or below a predefined percentage of

[3]Detailed information on the provincial/territorial drug plans is available in Appendix A.

[4]Canadian patented drug prices were the third highest among the seven comparator countries in 2009 (PMPRB, 2010).

[5]The content of the Alberta Prescription Drug Program policies can be accessed at: http://www.health.alberta.ca/initiatives/pharmaceutical-strategy.html.

the the price of the brand-name original drug. The policy will also be phased in over time for drugs covered by private drug insurance plans and purchased out-of-pocket.[6]

In Quebec, the provincial drug plan stipulates the "most-favoured nation (MFN)" clause, under which the new generic drug pricing policy in Alberta automatically benefited Quebecers with the same lower generic drug prices (45% of the brand-name original). What is more, Ontario's even lower generic price-cap at 25% in July 2010 once again applies to Quebec simultaneously.

At the provincial level, there are also indirect drug cost containment policies in place, such as the maximum-reimbursable-cost type of policies and provincial drug formularies.[7] Maximum-reimbursable-cost type of policies and drug formularies indirectly promote drugs that are at or below the MAC/reference price and/or drugs covered by the formulary. They influence drug prices and shape the fundamental structure of the Canadian pharmaceutical market.

The consumption of pharmaceutical products is characterized by competing incentives, objectives, and interests. Patients have a limited role in drug selection, although they are the ultimate consumers. While those with the most knowledge about drugs, i.e., physicians[8] who diagnose and prescribe and pharmacists who dispense and provide counsel, do not pay for them. In addition, drugs are paid from multiple sources. The majority (98%) of Canadians have some form of insurance coverage for prescription drugs (Bell et al., 2010). The insurance coverage from the provincial or employer-based drug plans normally reduces consumers' sensitivity to drug prices.

As such, a comprehensive study on drug price dynamics requires an understanding of and a method to control the important contexts of the Canadian pharmaceutical market structures, health policies, and legislations. Underpinned by an extensive

[6] I discuss this in detail in Chapter 2.

[7] As discussed in detail in Chapter 2, maximum-reimbursable-cost type of policies include reference-based pricing policy, maximum allowable cost (MAC) policy, and least-cost alternative (LCA) policy. They require that the provincial drug plan only covers a predetermined level of cost, usually the least unit cost or the least expensive drug within a therapeutic class. Reference-based pricing and MAC/LCA policy are different in practice in terms of both the scope of the interchangeable drug class and the way provincial drug plans reimburse drug cost.

[8] As I have addressed in Chapter 2, in Canada, prescribing is not the privilege of physicians only but is extended to other health professionals under certain conditions. Physicians still write the majority of the prescriptions nevertheless. I use physicians as representatives of prescribers.

overview of the Canadian pharmaceutical system and the relevant institutional background in Chapter 2 and an in-depth study on drug manufacturers' price setting behaviour from the perspective of oligopoly theory in Chapter 3, this chapter examines the net impact of the market and policy changes on the drug price dynamics.

That is, I am able to explore and explain both the deterministic and random components of the drug price dynamics by running linear multilevel regressions of the drug prices on the contextual variables. More importantly, by controlling the important contextual variables from the empirical data, I am also able to examine the hypotheses related to the generic competition paradox as indicated from my theoretical models in Chapter 3. Specifically, I have three hypotheses: (1) More generic substitutes do not necessarily have a net effect of lowering drug prices. (2) More therapeutic substitutes also do not have a net effect of lowering drug prices. (3) Given the available generic substitution policy, brand-name drugs still maintain net price premiums over their generic substitutes. These hypotheses echo my theoretical propositions in Chapter 3. They help us gain a better understanding of drug manufacturers' price setting behaviour under certain government policies, which in turn will inform drug cost containment decision-making.

The rest of the chapter is organized as follows. Section 4.2 presents a review of the empirical and theoretical backgrounds on drug price studies. Section 4.3 shows the data and explains why the multilevel model is appropriate for modelling the drug price dynamics. Section 4.4 discusses two different multilevel model specifications and introduces multilevel modelling with endogeneity. The empirical findings are reported in Section 4.5. Finally, concluding remarks are offered in Section 4.6.

4.2 Empirical and Theoretical Backgrounds

4.2.1 Empirical Literature

The literature on drug price dynamics and drug manufacturers' price setting behaviours has developed rapidly since the 1990s with the advent of the more sophisticated pharmaceutical manufacturing technologies and escalating healthcare/pharma-

ceutical expenditures worldwide. In this section, I first introduce the empirical findings and then discuss the relevant theoretical literature.

One of the earliest empirical studies on drug price, Caves et al. (1991) present an exploratory analysis of the prices of brand-name and generic drugs in the prescription pharmaceutical markets in the US before the 1990s. They used the panel regression approach to control the variables of market shares, quantities sold, and brand-name drugs' advertising over time. These variables reflect the changes of the pharmaceutical market structures and conditions both within each drug's therapeutic class and in the industry as a whole. They discovered a downward rigidity in the prices of brand-name drugs after their patents expire.

The conventional wisdom suggests that when a brand-name drug is no longer protected by its patent, its price must fall as its generic substitutes are available at more competitive prices. Despite the erosion of market shares by the available generic drugs, brand-name drug price could nevertheless go up. Scherer (1993) attributes this "generic competition paradox" to the institutional regularities, including both the "risk-averse and price-insensitive" physicians and the "risk-avoiding and brand-superstitious" patients.

Since Scherer (1993), many other empirical studies have identified the generic competition paradox using different data for different time periods . For example, Frank and Salkever (1997) study 83 brand-name and associated generic drugs in the mid 1980s. They found that the brand-name drug prices are insulated from the increased competition from the generic drugs. A critical limitation of their research, however, is that the product competition between the brand-name drugs and their generic substitutes is limited to the same chemical compounds. The potential competition effect in a broader therapeutic class is excluded by design.

Lexchin (2004) examines the impact of the number of generic competitors on brand-name drug prices using a two-factor ANOVA approach. He found that when generic substitutes first became available, having four or more generic competitors was associated with a rise in brand-name drug prices compared to having one, two, or three generic competitors. Put differently, when facing product competition from more generic substitutes, brand-name drug manufacturers may respond by raising

drug prices. Of course, we should interpret this result with caution, since Lexchin (2004) includes the number of generic competitors as the only covariate. If missing contextual information is omitted in the regression model, it will be dumped to the disturbance term. This will bias the coefficient estimates.

One option for brand-name drug manufacturers to maintain the price premium over generic substitutes, while keeping or even increasing market shares, is to make confidential arrangements with their subsidiary company or some generic firm to release the "authorized generics" (Hollis, 2002; Hollis, 2005; Grootendorst, 2007).[9] In theory, an authorized generic drug could bring two offsetting effects to the market. First, the authorized generic drug is likely to compete with the independent generic drugs in price. Second, the authorized generic drug is likely to have an early market entry[10] and deter the independent generic manufacturers to follow up. By cannibalizing the low-end market, the brand-name drug may secure the high-end market and retain the price premium over the generics. Because the two effects are pro- and anti-competition effects respectively, the total effect of introducing the authorized generic drug remains unclear.

With mixed evidence on whether authorized generic drug is pro- or anti-competition from the previous literature, Grootendorst (2007) studies the prices of the available drugs in Canada during the period of 1998-2004. He reported that authorized generics are mildly pro-competitive through the quantitative approach. However, his qualitative study also shows anti-competition evidence. It should be noted that the information on authorized generic drugs is usually not publicly available. This adds difficulties to apply the research methodology to different drugs and/or in different periods.

[9]These brand-controlled generic drugs, also known as "pseudo" generic drugs or "ultra" generics, are different from the "independent" or "true" generics. I discuss this in Chapter 2.

[10]To acquire market entry, an authorized generic does not need to challenge the brand-name original's patent validity. I have discussed this in Chapter 2. Hollis (2002) examines the relationship between the timing of the entry of generic drugs and the pharmaceutical market structure for 31 drugs in nine Canadian provinces during the period of 1995-1999. The study confirms the early-mover advantage as the key to win over market shares in the generic drug market: the earlier a generic manufacturer enters the market, the larger market share it can take from its competitors. This finding, in addition to the fact that the generic sector in Canada is relatively small, can explain why the Canadian generic drug market is dominated by a few giants. The economic scale and lack of competition among Canadian generic drug manufacturers also explain why generic drugs are on average more expensive in Canada than in the US (Hollis, 2002).

4.2.2 Theoretical Literature

Besides the above empirical studies related to drug prices, the developing economic theories bring distinct perspectives to understanding drug manufacturers' price setting behaviour. In Chapter 3, I use oligopolistic models to demonstrate that pharmaceutical manufacturers strategically use product differentiation to soften price competition.

As Lancaster (1990) notes in his review on oligopoly theories, product differentiation can be the key to understand the generic competition paradox. In a oligopolistic market, firms face a tradeoff. Firms can produce goods that are very similar. As a result, they would share a potentially large pool of customers, but at the cost of harsh price competition. Alternatively, firms can produce goods that are very different. As a result, the price competition would be softened by the differentiated products, but at the same time firms may risk losing customers.

In the literature, there are two basic types of product differentiation, that is, horizontal and vertical product differentiation. The former can be traced to Hotelling (1929), in which products are broadly considered of equivalent quality, even though different consumers prefer different variants. The latter is proposed by Mussa and Rosen (1978), in which one product has more of all characteristics than another, or is universally ranked as a better product, therefore the consumers would rank the products in a universally accepted order of preference by product quality.

Neven and Thisse (1990) integrate the horizontal and vertical product differentiation in a unified setting and note that under certain circumstances, a firm would choose maximized differentiation only in one dimension and minimize differentiation in the other. Maximizing product differentiation in both dimensions is not an optimal solution for firms in such a context.

Brekke et al. (2007) use product differentiation theories to analyze the drug price setting behaviour under different reimbursement systems. In the setting, a brand-name original and its generic substitute are vertically differentiated in terms of perceived quality; brand-name drugs themselves are therapeutic substitutes and horizontally differentiated. These therapeutic substitutes offer different therapeutic variants to cater to patients' heterogeneous tastes for the most-favourite drug variant

(MFDV).

With a different approach for the US pharmaceutical market, Kong (2009) uses tiered consumer demand to explain drug manufacturers' price setting behaviour. Assuming that the consumers can be grouped by the degree of their drug insurance coverages, Kong (2009) employs a two-stage game model to show that the generic competition paradox is related to the share of the high-insurance-coverage consumers.[11]

The approach adopted by Kong (2009) makes sense to the US situation but does not apply to the Canadian setting because of significant institutional differences. In Canada, governments play important roles in the funding and provision of prescription drugs. In contrast, the US governments only play a limited role in the funding and provision of pharmaceuticals.[12] In addition, the direct-to consumer advertising (DTCA) of prescription drugs is allowed in the US but banned in Canada. As such, patients' demand for prescription drugs in Canada is induced by multiple players in a government-regulated market. The key players are physicians (prescribers), pharmacists, public/private drug plans, who all act as agents for patients and induce patients' demand for different types of drugs (brand-name or generic), as I have discussed in Chapter 2 and Section 4.1.

As a step further, I develop the theory of product differentiation in a typical Canadian prescription pharmaceutical market in Chapter 3. Recognizing the important roles that governments and health professionals play in shaping patients' demand for prescription drugs in the Canadian setting, I look at the impact of the changes of three preference/policy parameters on drug manufacturers' price setting strategies. I find that the differentiation in perceived quality between brand-name and generic drug can cause the generic competition paradox, with everything else being equal. Under certain circumstances, some government drug cost containment policies may have unintended effects in fuelling the price increase in brand-name drugs.

Despite the above discussion from the theoretical and empirical literature, there is a need for new empirical research on drug price dynamics taking into account

[11]That is, those patients with lower price sensitivity to a price increase in drugs tend to prefer purchasing brand-name drugs.

[12]The US government takes a more proactive stance in the public provision of health insurance under the Obama administration. Some Health Maintenance Organizations (HMO) in the US with considerable market powers can also play a big role.

the institutional background, including both the market structure and the Canadian health policy and legislation. In the following empirical study, I include drug classes from representative therapeutic categories of the Canadian pharmaceutical market. The existing literature cannot provide further evidence on my three hypotheses when taking the market structure and the unique Canadian context into consideration.

4.3 Data and Multilevel Modelling

4.3.1 Data Access and Data Structure

Recall that I examine three major research hypotheses in the following empirical study on drug price dynamics: (1) More generic substitutes do not have a net effect of lowering drug prices. (2) More therapeutic substitutes do not have a net effect of lowering drug prices. (3) Given that a generic substitution policy is available, brand-name drugs still maintain net price premiums over their generic substitutes. Before I use the multilevel (hierarchical) linear regression model to analyze the data, I need to introduce the data.

Quantitative research on the Canadian drug price dynamics faces several challenges. First, there is no single "perfect" measure for prescription drug prices in the Canadian market. The real transaction prices are veiled by many factors, e.g., the rebates/allowance off the invoice prices that pharmacies receive from generic drug manufacturers in return for maintaining certain drugs in the inventory.[13] Second, the conventional panel data models are often inadequate to model the pharmaceutical market because (1) the data are naturally clustered by hierarchies at different levels, and (2) the observations of drug prices are highly unbalanced in the time dimension. Ignoring these two aspects will result in inconsistent estimates. The following discussion focuses on the presentation of the data structure and introduces the multilevel modelling technique.

The longitudinal data on drug price, market structure, and generic substitution

[13]In 2006, Ontario passed Bill 102, the Transparent Drug System for Patients Act, to ban rebates generic manufacturers were paying to pharmacies. The recent reform in Ontario further banned the professional allowance (a variant of the manufacturer rebate) in the province. Other provinces did not follow. These policies are outside the time frame of this study but it leaves room for future research on drug price dynamics.

policy, etc. were accessed through the National Prescription Drug Utilization Information System (NPDUIS) at the Canadian Institute for Health Information (CIHI) for the period of 2000-2008. I use the manufacturers' list drug prices and the associated variables such as policy information submitted from Alberta, which exhibited the best overall data quality for this research.[14] The data were cleaned and then linked with drug patent data accessed from the Health Canada Patent Register.

To better answer the research questions, I use the following criteria to select the drug classes for analysis. First, I select the drug classes that contain the brand-name original drugs going off patent during the study period. As such, I am able to observe and analyze the drug price dynamics before and after the patents' expiry. Second, I select the drug classes that are representative of the therapeutic class in the Canadian drug market.[15]

Using the above criteria, I have selected three broad classes of drugs (WHO-ATC 4^{th} level) in this study. They include one class of cholesterol-lowering drugs (or statins) that target the cardiovascular system, one class of antifungal drugs (or triazoles) that target the antiinfectives for systemic use, and one class of migraine-relief drugs (or triptans) that target the nervous system. Each drug class contains both the brand-name original drug and its associated generic drugs at the drug molecule level (WHO-ATC 5^{th} level). All drug products in this study are defined by their unique Drug Identification Numbers (DINs),[16] The dataset for this study contains 105, 20, and 23 drugs under each selected drug class, respectively,[17] during the period from 2000 Q2 to 2008 Q2 (33 calendar quarters). In total, there are 148 drugs (DINs) in 14 drug molecules and manufactured by 19 drug firms. The panel data has 2,946

[14]Note that there are considerable regional disparities in drug prices at the reimbursement level across Canada due to the fragmented provincial policies. However, the list drug prices at the manufacturers' level are considered to be homogeneous nationwide.

[15]See Appendix C for detailed information on data access and manipulation as well as information on the selected drug products.

[16]Drug Identification Number (DIN) is the number located on the label of the prescription product and over-the-counter drug products that have been evaluated by Health Canada and approved for sale in Canada. A single DIN will be assigned for drugs with varying sizes, provided that all other product characteristics including drug name, manufacturer's name, dosage form, route of administration, medicinal ingredient(s), and corresponding strength(s) are identical.

[17]The selected drug classes are categorized under the 4^{th} level ATC code C10AA, J02AC, and N02CC, respectively.

unbalanced quarterly observations.[18]

Now I discuss the characteristics of the unique panel data. The structure of the panel data in my study has three levels. Level-1 is the repeated measurements (quarterly) over time for the drugs which are classified by their DINs at level-2. Drugs at level-2 can be further classified by the molecules (level-3) that they belong to. In addition, drugs at level-2 can also be classified by their manufacturers (level-3). That is, the data structure is complex in the way that the lower-level units (DINs at level-2) are cross-classified by the two higher-level units (molecules and manufacturers, both at level-3). For example, the brand-name original drug Zocor® and its generic substitute Apo-simvastatin (under the ATC code C10AA01) both belong to their drug molecule — simvastatin. Meanwhile, Zocor® and Apo-simvastatin are manufactured by the multinational firm Merck Frosst and the Canadian based Apotex Inc., respectively. Figure 4.1 sketches the relationships among the three levels.[19]

One might consider applying panel data models, but they are not suitable for the data structure here. First, panel data models would overlook the data classification above the drug (DIN) level. Second, they are often inadequate because the data are highly unbalanced caused by the late market entries of some drug products compared to others. Third, they cannot deal with the factors in the higher level that are cross-classified. Next, I discuss the multilevel modelling strategy.

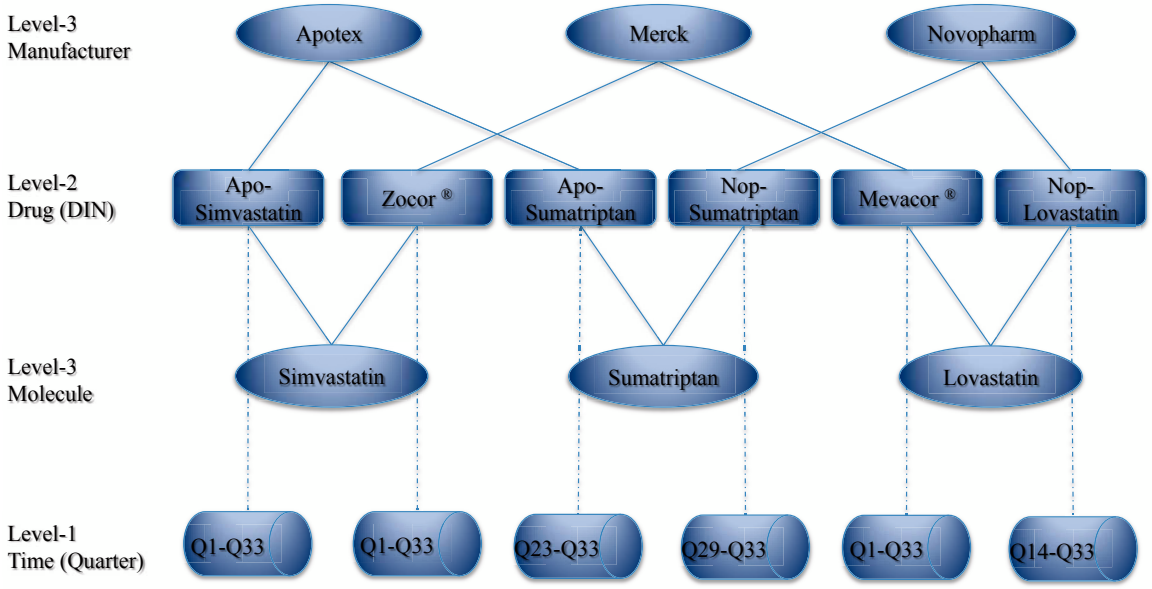
4.3.2 Multilevel Modelling

The multilevel model, also referred to as the hierarchical model, random-effects model, variance-components model, error-components model, random-coefficient model, or mixed model, is a class of statistical models with random parameters that vary at more than one level given the hierarchical data structures (for example, drugs nested within molecules or patients nested within hospitals). As noted above, the

[18]Section 4 includes a quarter-lag of drug price and two differenced instrumental variables on the right-hand side of the regression model. Therefore the effective sample size for the regression model is 2,502.

[19]Level-1 is the observations over time strictly nested within the Level-2 units (DINs). Level-1 (observations over time) is connected to and Level-2 (drugs) with dashed lines at the bottom of Figure 4.1. This figure demonstrates the data structure but does not include all products covered in this empirical study.

Figure 4.1: A Cross-classified Three-level Data Structure



multilevel model also comprises those with non-nested or other complex data structures such as cross-classified data or multiple membership data. In the cross-classified data, units in the lower level can belong to different categories at the higher level (for example, drugs categorized by molecules and by manufacturers; or students categorized by schools and by communities). In the multiple membership data, units in the lower level can shift their "membership" in the higher level (for example, in the study period, patients can attend multiple hospitals; or students are transferred between schools).

In fact, the random-effects (panel) model in econometrics can be seen as a specific type of the multilevel model.[20] A random-effects model has exactly two levels of random error terms, in which the level-2 error component is assumed to be random and independent from the regressors.[21]

The simplest multilevel model is one with random-intercepts only. That is, the randomness is only introduced to the intercept parameter. The slope parameters in

[20]For this reason, I do not use the term random-effects model interchangeably with multilevel model to avoid confusion.

[21]In the same way, a fixed-effects model can also be seen as a specific type of random-effects model, in which the level-2 "error term" has zero-variance.

the model remain non-random. In the following, I use a standard two-level model with only one intercept parameter and one slope parameter for demonstration.

I use the notation i for individual drug i, and j for the molecule j. Suppose y_{ji} is the price of drug i nested in molecule j, x_{ji} is a dummy variable indicating whether this drug i is a generic drug (in contrast to a brand-name drug), u_j is the number of generic substitutes in molecule j, respectively. Now I can write the two-level model separately, namely

$$y_{ji} = \alpha_j + \beta x_{ji} + \epsilon_{ji}, \qquad \text{for drugs } i = 1, ..., N \tag{4.3.1}$$

for level-1, where α_j and β are the intercept coefficient and the coefficient for x_{ji} respectively. ϵ_{ji} is the random error term at level-1, with

$$\epsilon_{ji} \sim N(0, \sigma_\epsilon^2); \tag{4.3.2}$$

and

$$\alpha_j = a + bu_j + \eta_j, \qquad \text{for molecules } j = 1, ..., J \tag{4.3.3}$$

for level-2, where a and b are the intercept coefficient and the coefficient for u_j respectively. η_j is the random error term at level-2, with

$$\eta_j \sim N(0, \sigma_\eta^2). \tag{4.3.4}$$

ϵ_{ji} and η_j are assumed to be independent. Also note that the level-2 equation decomposes α_j, the intercept coefficient at level-1. As such, I can write the two levels together, namely

$$y_{ji} = a + \beta x_{ji} + bu_j + (\eta_j + \epsilon_{ji}). \tag{4.3.5}$$

In (4.3.5), the constant intercept term a appears with the two random error terms in the parentheses, η_j and ϵ_{ji}. In comparison, a pooled OLS regression would completely ignore the existence of the level-2 error term η_j. Therefore, without taking account of the data structure, the coefficient estimates from an OLS regression model are unbiased (as long as η_j is uncorrelated with the regressors) but inefficient.

Now I also allow randomness in the slope coefficient, the multilevel model would have both a random-intercept and a random-slope. That is,

$$\begin{cases} y_{ji} = \alpha_j + \beta_j x_{ji} + \epsilon_{ji}, & \text{for drugs } i = 1, ..., N; \\ \alpha_j = a_0 + b_0 u_j + \eta_{j_1}, & \text{for molecules } j = 1, ..., J; \\ \beta_j = a_1 + b_1 u_j + \eta_{j_2}, & \text{for molecules } j = 1, ..., J. \end{cases} \tag{4.3.6}$$

Or alternatively,

$$y_{ji} = a_0 + a_1 x_{ji} + b_1 u_j x_{ji} + b_0 u_j + (x_{ji}\eta_{j_2} + \eta_{j_1} + \epsilon_{ji}), \tag{4.3.7}$$

where a_s and b_s $(s = 0, 1)$ represent the coefficients. In the parentheses of (4.3.7), the composite error term is the sum of $x_{ji}\eta_{j_2}$, η_j, and ϵ_{ji}, with

$$\begin{aligned} &\eta_{j_2} \sim N(0, \sigma^2_{\eta_2}), \\ &\eta_{j_1} \sim N(0, \sigma^2_{\eta_1}), \text{ and} \\ &\epsilon_{ji} \sim N(0, \sigma^2_{\epsilon}). \end{aligned} \tag{4.3.8}$$

Comparing (4.3.5) with (4.3.7), I note that the introduction of randomness to the slope coefficient β in (4.3.5) not only results in an additive random error term $(x_{ji}\eta_{j_2})$ but also creates a by-product — the interaction term between the regressors from the two levels (x_{ji} and u_j).

It is clear that the introduction of a level and/or a random slope term can substantially complicate the model. Nevertheless, the multilevel model has many advantages.

First of all, the multilevel model can be used to model for contextuality, which is critical for many research purposes. For example, drug price dynamics may follow certain patterns determined by the drug molecule and drug manufacturer in which each drug product is directly linked.

Second, the multilevel model can be used to interpret heterogeneity at various "between" and "within" levels. For example, a multilevel model can decompose the random variation in drug prices into (i) the variation between drug molecules, (ii) the variation within a molecule and between drugs, and (iii) the variation within a drug over time, etc.

Third, the multilevel model can capture unbalanced data structures, which results from natural imbalances in the data or come from natural hierarchies in the data.

For example, the generic entry often follows the expiry of the patent of the brand-name original. As I have shown in Figure 4.1, Apo-simvastatin and Zocor® are drugs nested within the molecule of simvastatin, which are used to treat high levels of cholesterol. Apo-sumatriptan and Nop-sumatriptan are drugs nested within the molecule of sumatriptan, which are used to treat migraine headaches.

In this thesis, I use the multilevel model to analyze the drug price dynamics with nested data structure for the following reasons. First, it produces statistically unbiased estimates of regression coefficients. Second, it uses the clustering information and therefore the standard errors, confidence intervals, and significance tests are generally more efficient than the model that ignores the clustering information. Third, by incorporating the covariates measured at different levels within the data hierarchy, the multilevel model can effectively explore the role of certain price setting factors (such as common drug characteristics or manufacturer practice).

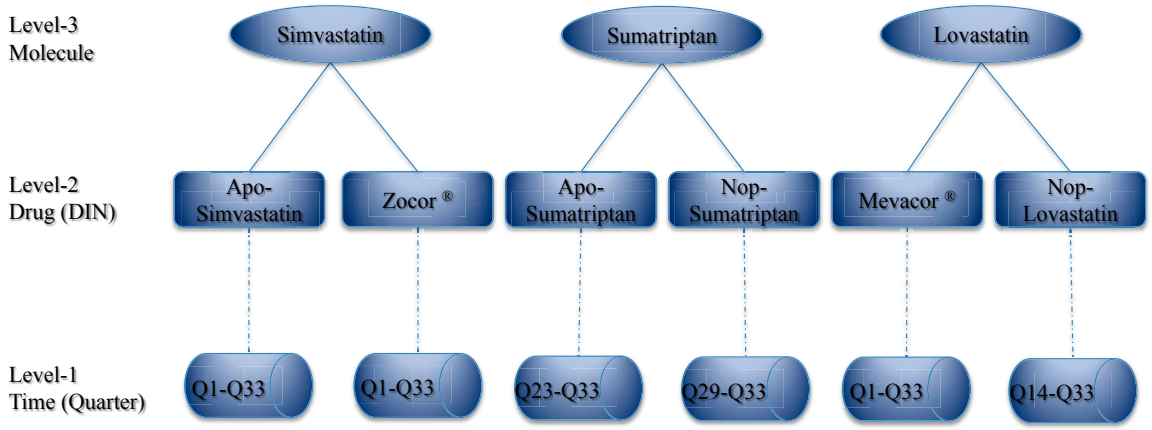
To examine the empirical research hypotheses, I need to evaluate the impact of contextual variables on drug prices. As I introduce the variables later, the contextual market structure and policy variables can exist at the drug level or at the molecule level. In the following analysis, I discuss random-intercept models for the analysis of the drug price dynamics in two different ways in order to address the research hypotheses.

The first model is a full representation of the cross-classified three-level random-intercept model mentioned above.

The second model is a reduced version in which I take out one of the cross-classified level-3 factors (i.e. manufacturer). In doing so, the reduced version becomes a strictly hierarchical three-level model, with the observations over time (level-1) strictly nested within drugs (level-2), and with the drugs strictly nested within the molecules (level-3) they belong to. Figure 4.2 sketches the relationship among the three hierarchies of the data.

The detailed specifications of the first and second models are given in the following section.

Figure 4.2: A Strictly Hierarchical Three-level Data Structure



4.4 Model Specifications

4.4.1 The Three-level Cross-classified Model

The structure of the data is demonstrated in Table 4.1, which decomposes the 2,946 observations by 14 molecules and by 19 manufacturers.

In Table 4.1, each row (column) stands for a drug molecule (manufacturer). The number in each cell of the table is the count of the drug (DIN) by quarter observations. Since the DIN contains information on drug's strength levels, each manufacturer-molecule combination may include multiple DINs. For example, Merck (FRS) manufactures Zocor® (simvastatin) with five versions — 5mg, 10mg, 20mg, 40mg, and 80mg pills. Accordingly there are five unique DINs and each DIN has 33 quarterly observations, giving a total of 165 observations in the cell of Merck-Zocor® (FRS-simvastatin). Another example is Pfizer (PFI) which manufactures Diflucan® (fluconazole) with three versions — 50mg, 100mg, and 150mg pills. Accordingly there are three unique DINs and each DIN has 33 quarterly observation, giving a total of 99 observations in the cell of Pfizer-Diflucan® (PFI-fluconazole).

Of the two tentative model specifications, the first model has two variance components at level-3 (molecules and manufacturers) and a single variance term at level-2 (drugs) and level-1 (time), respectively. Again for simplicity, I only introduce the random intercepts at each level in the model.

First, let $Y_{(j_1 j_2)it}$ be the vector of the price variable, with subscripts t, i, j_1, and j_2 denoting quarters (t), drugs (i), molecules (j_1), and manufacturers (j_2), respectively, where

$$\begin{aligned} & t = 1, 2, ..., N_{(j_1, j_2)i}, \\ & i = 1, 2, ..., N_{(j_1, j_2)}, \\ & j_1 = 1, 2, ..., 14, \text{ and} \\ & j_2 = 1, 2, ..., 19. \end{aligned} \tag{4.4.1}$$

Then, $Y_{(j_1 j_2)it}$ is the price of drug i at time t, with drug i grouped under molecule j_1 and manufactured by firm j_2.

Second, let $X_{(j_1 j_2)it}$ be the matrix of the explanatory variables, such as the number of generic firms within any molecule in any quarter, a dummy variable (0/1) indicating whether a drug is brand-name or generic, a dummy variable (0/1) indicating whether a generic substitution policy is in place, and an intercept term, etc. I use the multilevel model to examine the marginal impact of these explanatory variables on drug price.

Note I use the subscripts j_1 and j_2 to denote the two classifications at level-3 (molecule and manufacturer). They are grouped by parentheses, standing for classifications at the same level.

Third, let β be the vector of slope coefficients and $\varepsilon_{(j_1 j_2)it}$ be the composite random error term, which can be decomposed such that each level (manufacturer and molecule at level-3, drug at level-2, and time at level-1) has a random component, respectively. That is,

$$\varepsilon_{(j_1 j_2)it} = v^{(3)}_{j_1} + v^{(3)}_{j_2} + u^{(2)}_{(j_1 j_2)i} + e_{(j_1 j_2)it}, \tag{4.4.2}$$

where $v^{(3)}_{j_1}$ and $v^{(3)}_{j_2}$ are the random "molecule" effect and the random "manufacturer" effect at level-3, respectively; $u^{(2)}_{(j_1 j_2)i}$ is the random "drug" effect at level-2; and $e_{(j_1 j_2)it}$ is the residual random effect at level-1. The superscripts stand for the levels of each random error term. The superscript for level-1 is suppressed for simplicity.

Table 4.1: Number of Observations (DIN by quarter) in Each Molecule-by-Manufacturer Cell

	Manufacturer[b]																			
Molecule	JAN	APX	AZE	BRI	COB	FRS	GPM	GSK	JNJ	LIN	NOP	NVR	NXP	PFI	PMS	RAN	RPH	SDZ	TAR	**Totals**
Simvastatin		105			95	**165**	100				75				70		72	76	30	788
Lovastatin		66			28	66	56				40				44	20	44	38		402
Pravastatin		81		90	48		27			63	60		69		54	9	60	54		615
Fluvastatin												81								81
Atorvastatin														125						125
Rosuvastatin			71																	71
Fluconazole		99					66				66			**99**	66				18	414
Itraconazole	33																			33
Voriconazole														24						24
Sumatriptan		22			22		22	66			10				22		14	18		196
Naratriptan								66												66
Zolmitriptan			33																	33
Rizatriptan						66														66
Almotriptan									32											32
Totals[a]	33	373	104	90	193	297	271	132	32	63	251	81	69	248	256	29	190	186	48	2,946

[a] The 2,946 observations are spanned across 148 drugs (DINs). Each drug (DIN) has 1-33 quarterly observations.

[b] The manufacturers and their acronyms are: Janssen-Ortho Inc. (JAN), Apotex Inc. (APO), AstraZeneca Canada Inc. (AZE), Bristol-Myers Squibb Canada Co. (BRI), Cobalt Pharmaceuticals Inc. (COB), Merck Frosst Canada Ltd. (FRS), Genpharm Inc. (GPM), GlaxoSmithKline (GSK), Johnson & Johnson Inc. (JNJ), Linson Pharama Inc. (LIN), Novopharm Ltd. (NOP), Novartis Pharmaceuticals Canada Inc. (NVR), Nu-Pharm Inc. (NXP), Pfizer Canada Inc. (PFI), Pharmascience Inc. (PMS), Ranbaxy Pharmaceuticals Canada Inc. (RAN), Ratiopharm Inc. (RPH), Sandoz Canada Inc. (SDZ), and TaroPharma Inc. (TAR). More detailed information on each firm is offered in Appendix C.

Finally, the full model can be written as:

$$Y_{(j_1j_2)it} = X_{(j_1j_2)it}\beta + \varepsilon_{(j_1j_2)it}. \tag{4.4.3}$$

Expanding the composite term $\varepsilon_{(j_1j_2)it}$, I obtain

$$Y_{(j_1j_2)it} = X_{(j_1j_2)it}\beta + v^{(3)}_{j_1} + v^{(3)}_{j_2} + u^{(2)}_{(j_1j_2)i} + e_{(j_1j_2)it}. \tag{4.4.4}$$

Let $Y_{(j_1j_2)i}$ and $X_{(j_1j_2)i}$ be the $N_{(j_1j_2)i}$ observations for the $(j_1j_2)i^{th}$ drug and let $\varepsilon_{(j_1j_2)i}$ be associated with the $N_{(j_1j_2)i} \times 1$ vector of error terms. I obtain,

$$Y_{(j_1j_2)i} = X_{(j_1j_2)i}\beta + \varepsilon_{(j_1j_2)i}. \tag{4.4.5}$$

Stacking these terms ordered by the DIN (i), (4.4.4) can be expressed in the compact form:

$$Y = X\beta + \varepsilon. \tag{4.4.6}$$

where Y is the price vector with dimension $\left(\sum_{j_1=1}^{14}\sum_{i=1}^{N_{j_1}} N_{j_1i}\right)\times 1$; with k slope coefficients to be estimated, X is the $\left(\sum_{j_1=1}^{14}\sum_{i=1}^{N_{j_1}} N_{j_1i}\right) \times k$ matrix of explanatory variables, β is the $k \times 1$ vector of slope coefficients; ε is obtained by stacking the composite error term $\varepsilon_{(j_1j_2)it}$ in the same fashion.[22]

The random error terms at all three levels are assumed to be normally distributed with

$$\begin{aligned} &v^{(3)}_{j_1} \sim N(0, \sigma^2_{v_1}) \text{ and } v^{(3)}_{j_2} \sim N(0, \sigma^2_{v_2}), \\ &u^{(2)}_{(j_1j_2)i} \sim N(0, \sigma^2_u), \text{ and} \\ &e_{(j_1j_2)it} \sim N(0, \sigma^2_e). \end{aligned} \tag{4.4.7}$$

As a constant intercept is included in the matrix X, each random error term ($v^{(3)}_{j_1}$, $v^{(3)}_{j_2}$, $u^{(2)}_{(j_1j_2)i}$, and $e_{(j_1j_2)it}$) can be understood as a random intercept for each level, respectively.

[22]The dimension of Y can be expressed equivalently by $\left(\sum_{j_2=1}^{19}\sum_{i=1}^{N_{j_2}} N_{j_2i}\right) \times 1$, since there are two cross-classified groups at level-3. Similarly for X and ε.

In addition, I assume that the random terms at the same level and between different levels have zero pairwise covariances. The covariances between the error terms and the explanatory variables are also assumed to be zero. This condition can be relaxed later when the internal IV approach is adopted. As such, the variance-covariance structure for the error terms are given as follows:

$$\begin{aligned}
Var(Y_{(j_1j_2)it}|X) &= \sigma^2_{v_1} + \sigma^2_{v_2} + \sigma^2_u + \sigma^2_e, \\
Cov(Y_{(j_1j_2)it}, Y_{(j_1j_2)it'}|X) &= \sigma^2_{v_1} + \sigma^2_{v_2} + \sigma^2_u, \quad t \neq t' \\
Cov(Y_{(j_1j_2)it}, Y_{(j_1j_2)i't'}|X) &= \sigma^2_{v_1} + \sigma^2_{v_2}, \quad i \neq i' \\
Cov(Y_{(j_1j_2)it}, Y_{(j'_1j_2)i't'}|X) &= \sigma^2_{v_2}, \quad j_1 \neq j'_1 \\
Cov(Y_{(j_1j_2)it}, Y_{(j_1j'_2)i't'}|X) &= \sigma^2_{v_1}, \quad j_2 \neq j'_2 \\
Cov(Y_{(j_1j_2)it}, Y_{(j'_1j'_2)i't'}|X) &= 0, \quad \text{for all } i, i', t, \text{ and } t' \text{ if } j_1 \neq j'_1 \text{ and } j_2 \neq j'_2.
\end{aligned} \tag{4.4.8}$$

Given the above conditions and from (4.4.6), a block-diagonal variance-covariance matrix Ω can be formed and a Generalized Least Squares (GLS) estimator is possible.[23] [24] That is,

$$\hat{\beta} = (X^T\Omega^{-1}X)^{-1}X^T\Omega^{-1}Y. \tag{4.4.9}$$

Theoretically, the cross-classification model takes into account the variation in drug prices from both the "random molecule effect" and the "random manufacturer effect". It can also inform the relative importance of the two classifications in the drug price dynamics. The preliminary estimates from this model suggest that there is little evidence to support the cross-classified model with two random intercepts at level-3.[25] The random variation between manufacturers at level-3 is too small to be kept in the model due to the relatively homogeneous group of drug manufacturers in this sample. As a result, I drop the random intercept for the "manufacturer" factor at

[23] To form the multilevel block-diagonal variance-covariance matrix, I need to stack all time periods for the same drug i under molecule j_1 and manufactured by j_2; then stack all time periods for the next drug under the same molecule and manufactured by the same firm, ... , and so on.

[24] The demonstration of the block-diagonal matrix for the cross-classified model is lengthy, therefore omitted. The block-diagonal variance-covariance matrix for the three-level strictly hierarchical model is formally demonstrated in the following section.

[25] A different dataset with more heterogeneous manufacturer information, such as data with more classes of drugs or with a larger sample size, may result in different conclusions. The preliminary estimates of the cross-classified model is provided in Appendix C.

level-3 and reduce the model to a strictly hierarchical (three-level) specification. As shown in Figure 4.2, the repeated observations over time at level-1 are nested within each drug at level-2. In turn, the drugs at level-2 are nested within their molecule at level-3. Despite the lack of evidence for the random variation between manufacturers, I include the type of manufacturer (brand-name or generic) as an explanatory variable to control the manufacture effect.

4.4.2 The Three-level Strictly Hierarchical Model

The model remains the three-level model after dropping one of the cross-classified level-3 group factor. But the data structure is strictly hierarchical as seen in Figure 4.2. The notations of the three-level hierarchical model can be inherited from the above discussion, only to drop the manufacturer component at level-3.

Let Y_{jit} be the vector of the price variable, with subscripts t, i, and j denoting quarters (t), drugs (i), and molecules (j), respectively, where

$$\begin{aligned} &t = 1, 2, ..., N_{ji}, \\ &i = 1, 2, ..., N_j, \text{ and} \\ &j = 1, 2, ..., 14. \end{aligned} \tag{4.4.10}$$

Let X_{jit} be the matrix of the explanatory variables. Let β be the vector of slope coefficients and ε_{jit} be the composite random error term, which can be decomposed such that each level (molecule at level-3, drug at level-2, and time at level-1) has a random component, respectively. That is,

$$\varepsilon_{jit} = v_j^{(3)} + u_{ji}^{(2)} + e_{jit}, \tag{4.4.11}$$

where $v_j^{(3)}$ is the random "molecule" effect at level-3; $u_{ji}^{(2)}$ is the random "drug" effect at level-2; and e_{jit} is the residual random effect at level-1.

Finally, the full model in the three-level hierarchical specification can be written as:

$$Y_{jit} = X_{jit}\beta + v_j^{(3)} + u_{ji}^{(2)} + e_{jit}. \tag{4.4.12}$$

Let Y_{ji} and X_{ji} be the N_{ji} observations for the ji^{th} drug and let ε_{ji} be associated with the $N_{ji} \times 1$ vector of error terms. Then,

$$Y_{ji} = X_{ji}\beta + \varepsilon_{ji}. \tag{4.4.13}$$

Collecting these terms gives

$$\begin{bmatrix} Y_{11} \\ Y_{12} \\ \vdots \\ Y_{1N_1} \\ \vdots \\ \vdots \\ Y_{ji} \\ \vdots \\ Y_{jN_j} \\ \vdots \\ \vdots \\ Y_{14N_{14}} \end{bmatrix} = \begin{bmatrix} X_{11} \\ X_{12} \\ \vdots \\ X_{1N_1} \\ \vdots \\ \vdots \\ X_{ji} \\ \vdots \\ X_{jN_j} \\ \vdots \\ \vdots \\ X_{14N_{14}} \end{bmatrix} \cdot \beta + \begin{bmatrix} \varepsilon_{11} \\ \varepsilon_{12} \\ \vdots \\ \varepsilon_{1N_1} \\ \vdots \\ \vdots \\ \varepsilon_{ji} \\ \vdots \\ \varepsilon_{jN_j} \\ \vdots \\ \vdots \\ \varepsilon_{14N_{14}} \end{bmatrix} \tag{4.4.14}$$

or in the compact form as in (4.4.6).

The random error terms at all three levels are assumed to be normally distributed with

$$\begin{aligned} v_j^{(3)} &\sim N(0, \sigma_v^2), \\ u_{ji}^{(2)} &\sim N(0, \sigma_u^2), \text{ and} \\ e_{jit} &\sim N(0, \sigma_e^2). \end{aligned} \tag{4.4.15}$$

Each random error term ($v_j^{(3)}$, $u_{ji}^{(2)}$, and e_{jit}) can be understood as a random intercept for each level, respectively.

Again, I assume that the random terms at the same level and between different levels have zero pairwise covariances. The covariances between the error terms and

the explanatory variables are also assumed to be zero.[26] As a result, the variance-covariance structure for the error terms can be written as follows:

$$\begin{aligned} Var(Y_{jit}|X) &= \sigma_v^2 + \sigma_u^2 + \sigma_e^2, \\ Cov(Y_{jit}, Y_{jit'}|X) &= \sigma_v^2 + \sigma_u^2, \quad t \neq t' \\ Cov(Y_{jit}, Y_{ji't'}|X) &= \sigma_v^2, \quad i \neq i' \\ Cov(Y_{jit}, Y_{j'i't'}|X) &= 0 \quad \text{for all } i, i', t, \text{ and } t' \text{ if } j \neq j'. \end{aligned} \tag{4.4.16}$$

For the N_{ji} observations for drug i under molecule j, let $\prod_{ji} = E[\varepsilon_{ji}\varepsilon_{ji}^T]$.[27] Then,

$$\overset{N_{ji}\times N_{ji}}{\prod_{ji}} = \begin{bmatrix} \sigma_v^2 + \sigma_u^2 + \sigma_e^2 & \sigma_v^2 + \sigma_u^2 & \cdots & \sigma_v^2 + \sigma_u^2 \\ \sigma_v^2 + \sigma_u^2 & \sigma_v^2 + \sigma_u^2 + \sigma_e^2 & \cdots & \sigma_v^2 + \sigma_u^2 \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_v^2 + \sigma_u^2 & \sigma_v^2 + \sigma_u^2 & \cdots & \sigma_v^2 + \sigma_u^2 + \sigma_e^2 \end{bmatrix}. \tag{4.4.17}$$

Let $\bigwedge_{jii'} = E[\varepsilon_{ji}\varepsilon_{ji'}^T]$ for $i \neq i'$ and let $\boldsymbol{1}_k$ be a $k \times 1$ column of 1s. Then,

$$\overset{N_{ji}\times N_{ji'}}{\bigwedge_{jii'}} = \sigma_v^2 \cdot \boldsymbol{1}_{N_{ji}} \cdot \boldsymbol{1}_{N_{ji'}}^T. \tag{4.4.18}$$

With the above information, I can stack the components to form the matrix $\bigcap_j$ for molecule j $(j = 1, 2, ..., 14)$

$$\overset{\left(\sum_{i=1}^{N_j}\right)\times\left(\sum_{i=1}^{N_j}\right)}{\bigcap_j} = \begin{bmatrix} \prod_{j1} & \bigwedge_{j12} & \cdots & \bigwedge_{j1N_j} \\ \bigwedge_{j21} & \prod_{j2} & \cdots & \bigwedge_{j2N_j} \\ \vdots & \vdots & \ddots & \vdots \\ \bigwedge_{jN_j1} & \bigwedge_{jN_j2} & \cdots & \prod_{jN_j} \end{bmatrix}. \tag{4.4.19}$$

Let $0_{jj'} = E[\varepsilon_{ji}\varepsilon_{j'i}^T]$ for $j \neq j'$ and all i, where $0_{jj'}$ is the zero matrix with dimension $\left(\sum_{i=1}^{N_j} N_{ji}\right) \times \left(\sum_{i=1}^{N_{j'}} N_{j'i}\right)$.

Finally, by stacking the $\bigcap_j$ $(j = 1, 2, ..., 14)$ and $0_{jj'}$ $(j = 1, 2, ..., 14$ and $j \neq j')$ matrices,[28] I obtain the variance-covariance matrix for the full $\sum_{j=1}^{14}\sum_{i=1}^{N_j} N_{ji}$ observations

[26] As mentioned, this condition is relaxed later when the internal IV approach is adopted.
[27] ε_{ji}^T stands for the transpose of the vector ε_{ji}.
[28] For simplicity, I suppress all subscripts for the $0_{jj'}$ matrices in (4.4.20).

$$\Omega = \begin{pmatrix} \bigcap_1 & 0 & \cdots & 0 \\ 0 & \bigcap_2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & \bigcap_{14} \end{pmatrix}, \tag{4.4.20}$$

where the dimension of this block-diagonal matrix Ω is $\left(\sum_{j=1}^{14}\sum_{i=1}^{N_j} N_{ji}\right) \times \left(\sum_{j=1}^{14}\sum_{i=1}^{N_j} N_{ji}\right)$.

As such, the slope coefficients of the model β can be estimated using the GLS method. The GLS estimator can be written in the compact form as in (4.4.6):

$$\hat{\beta} = (X^T \Omega^{-1} X)^{-1} X^T \Omega^{-1} Y. \tag{4.4.21}$$

Note that the variances of the random error terms in a multilevel model in general are not known in empirical research. In this case, the variances (σ_v^2, σ_u^2, and σ_e^2), and therefore Ω, also need to be estimated. Given the large sample size in this study, I assume normal distribution for each of the error terms as in (4.4.15). I can use either the iterative generalized least squares (IGLS) or restricted maximum likelihood (REML) algorithm following Goldstein (1986), Goldstein and Rasbash (1992), and Rasbash and Goldstein (1994). When using these algorithms, generally one needs to specify starting values for the parameters to be estimated. The results of the 1^{st} round estimation will update the values of the parameters. This process is continued until convergence is achieved.

4.4.3 Multilevel Modelling with Endogenous Regressor

As noted above, an important condition to guarantee the consistency or unbiasedness of the β estimator is that the explanatory variables and the random error terms are uncorrelated. But this condition is often untenable in empirical research and as a result, endogeneity arises.[29] I discuss and deal with the endogeneity caused by correlation between regressor(s) and the random components at level-2 and level-3, which is more pronounced in the empirical estimation in this chapter. Endogeneity could cause inconsistency and bias in the generalized (or ordinary) least squares estimator.

[29] A regressor is said to be endogenous when there is a correlation between the regressor or variable and the error term.

The method of instrumental variables (IVs) is the standard approach for dealing with endogeneity in the econometric literature.

When specifying my model, I need to check whether or not the assumption that the unobserved individual random effects are uncorrelated with the included explanatory variables is satisfied. To address the endogeneity related to both level-2 and level-3 random error terms in the three-level context, I use the method of a IV-type maximum likelihood estimator (MLE). First, I create internal instrumental variables using both the first-differenced endogenous variable and its one-quarter lag. Then I run a maximum likelihood regression of the endogenous explanatory variable on the instrumental variables and the rest of exogenous explanatory variables. The predicted value from this regression is "purged" of the correlated unobservable individual effects. Next, I run another maximum likelihood regression of the dependant variable on the predicted value from the first regression and all other exogenous variables. A similar approach has been adopted in the literature. For example, Bollen et al. (1995) use a two-step probit (MLE) model to examine the effects of explanatory variables on binary outcomes, while controlling for the potential endogeneity of explanatory variables. River and Vuong (1988) also develop a two-step maximum likelihood procedure for estimating simultaneous probit models. They use the residuals from the first-stage regression as the additional explanatory variable in the second-stage estimation.

4.5 Empirical Analysis and Interpretation

Now I use the multilevel regression model to estimate the net impact of market structure and government policy on the drug price dynamics. By controlling these important contextual variables from the empirical data, I am also able to examine the hypotheses related to the generic competition paradox as indicated from my theoretical models in Chapter 3. Specifically, (1) more generic substitutes do not have a net effect of lowering drug prices. (2) More therapeutic substitutes do not have a net effect of lowering drug prices. (3) Given that a generic substitution policy is available, brand-name drugs still maintain net price premiums over their generic substitutes. With these research hypotheses, first I give detailed explanations to the variables included in the regression analysis, then report the estimation results using

the IV-MLE (three-level) model, and finally offer interpretations of the empirical results.

4.5.1 Description of Variables

The variable of interest is the price of drugs in the study sample. To understand the drug price dynamics, I let $logprice_{jit}$ be the logarithm of the price over time t, for drug i, under molecule j, which is defined as the dependent variable.

I use a number of variables to explain the dynamics of the drug prices or as the instrumental variables in the analysis. The summary of the above explanatory variables is provided in Table 4.2.[30]

Table 4.2: Description of Explanatory Variables in the Regression Analysis

Variable Name	Description
$logavgpricelag_{jit}$	Quarter-lag of average drug price (log)
$gennum_{it}$	Number of generic firms within molecule within quarter
$compnum_{jt}$	Total number of firms within each drug class within quarter
$brand_i$	Characteristic of a firm: brand-name firm dummy (generic)
$policy_{jit}$	Dummy variable indicating when generic substitution policy is in place (no generic substitution)
$policy \times brand$	Interaction term between policy and brand-name dummies
J_j	Dummy variable for antifungal drugs (cardiovascular)
N_j	Dummy variable for migraine-relief drugs (cardiovascular)
str_j	Relative strength (DDD) of a drug
$str \times J$	Interaction term between strength and antifungal drugs
$str \times N$	Interaction term between strength and migraine-relief drugs
$cq1_t$	Dummy variable for 1^{st} calendar quarter (2^{nd} quarter)
$cq3_t$	Dummy variable for 3^{rd} calendar quarter (2^{nd} quarter)
$cq4_t$	Dummy variable for 4^{th} calendar quarter (2^{nd} quarter)

* The baseline cases for the dummy variables are in parentheses.

$logavgpricelag_{jit}$ is the average historical (in quarter-lag) price (in logarithm) for all drugs with the same strength in molecule j in quarter t. Here this lagged variable reflects the price-setting anchor within each market niche, based on which drug prices are likely to be set for the next period. The inclusion of the lagged variable offers a control for the information that is not observable from the dataset so

[30]The detailed summary statistics of these variables are shown in Table C.5 in the Appendix.

that the bias caused by missing variables can be avoided.[31] When this price-setting anchor variable is included as an explanatory variable in the regression model, the endogeneity problem may arise.[32] I derive the first-differenced price-setting anchor variable ($\Delta lnavgpricelag_{jit}$) and its quarter-lag ($\Delta lnavgpricelag_{jit-1}$) as the instruments, which are both orthogonal to the time-invariant error components in this model. By using the instrumental variables, I am able to deal with the endogeneity problem.[33]

I let $gennum_{it}$ be the number of generic substitutes for drug i's molecule in quarter t. In general, the number of generic substitutes is different from one molecule to another. In addition, $gennum_{it}$ is derived in the way such that drugs with multiple strengths (therefore, different DINs) but from the same manufacturer, are counted as *one* generic substitute. It reflects the fact that different dosages of the same drug product normally do not compete among themselves. For example, different strengths of Apo-simvastatin in quarter t are all manufactured by Apotex. Therefore I record *one* more generic substitute in $gennum_{it}$ for the molecule simvastatin. I include $gennum_{it}$ to examine my first research hypothesis: whether more generic substitutes have a net effect of lowering drug prices, while other variables are controlled for.

Similarly, I let $compnum_{jt}$ be the total number of manufacturers that compete in the broad therapeutic market encompassing multiple drug molecules. For $compnum_{jt}$, I include all brand-name and generic drug manufacturers, within a group of molecules (js) in quarter t. For example, the total number of competitors ($compnum_{jt}$) for simvastatin in quarter t includes both the brand-name and generic drug manufacturers for the molecule simvastatin and both the brand-name and generic drug manufacturers

[31] For example, drug sales or volume factor likely play a role in determining drug prices. In addition, market share variable likely correlates with other market structure variables in the model. Without any control, the estimates can be biased.

[32] That is, in (4.4.12), the same factors shaping the dependent variable may also influence this explanatory variable through the time-invariant error components.

[33] Following Lewbel (1997) and Ebbes et al. (2004), I use the demeaned endogenous variables ($\Delta lnavgpricelag_{jit}$) and $\Delta lnavgpricelag_{jit-1}$) to derive two internal instrumental variables. Similarly, the internal IVs can also be derived using the orthogonality conditions inherent in the existing model. I only use the most recent two orthogonality conditions from the model. As Blundell and Bond (1998) point out, using orthogonality conditions far back in time from a dynamic panel may render weak instruments and also reduce the degrees of freedom from the model considerably.

for the rest of the five statin molecules, if available.[34] This variable records the number of all drugs competing within a broad therapeutic class. I include $compnum_{it}$ to examine my second research hypothesis: whether more therapeutic substitutes have a net effect of lowering drug prices, while other variables are controlled for.

$brand_i$ is the brand-name manufacturer dummy variable with generic manufacturer set as the baseline case. In the three-level hierarchical model, I do not include manufacturer in the random intercept at level-3, but I need to control the types of manufacturer in the regression. In doing so, I am able to statistically examine whether brand-name drugs are more expensive than the generic drugs after I control for other relevant variables.

$policy_{jit}$ is a dummy variable. It indicates whether or not a generic substitution policy is in place for drug molecule i in quarter t in the formulary. This variable is a proxy for generic competitors in the drug molecule in question.[35] As noted in Section 4.3.1, the manufacturers' list price and policy data were from Alberta public drug plans. Alberta adopts the Maximum Allowable Cost (MAC) or Least-cost Alternative (LCA) policies to contain drug reimbursement cost by encouraging generic drug substitution. As I discuss in Chapter 2, these policies require that the public drug plans only cover the cost of a predetermined, usually a less expensive drug (generic) within a drug molecule i. I include this variable to examine whether the generic substitution policy has a net effect of lowering drug prices. Note that there may be time lags in various degrees between market entry, the date of listing in the provincial formulary, and the date of the generic substitution policy in effect. For simplicity, I assume they all take place within a short time-frame.[36]

I let $brand \times policy$ be the interaction term between $brand_i$ and $policy_{jit}$. By

[34]Besides simvastatin, the other five statin molecules for my study are lovastatin, pravastain, fluvastain, atorvastatin, and rosuvastatin. Note that the molecule cerivastatin (ATC code: C10AA06) was voluntarily withdrawn from the market worldwide in 2001 due to serious side-effects, therefore it is not included in the analysis.

[35]However, it should be noted that there is generally a time-lag between the date a generic drug debuts in the market (marked by the issuance of Notice of Compliance by Health Canada) and the date the generic drug is listed in any provincial formulary. Also see Table 2.6.

[36]A generic drug first needs to acquire notices of compliances (NOCs) from Health Canada to gain market entry. Bioequivalency needs to be confirmed and approved by individual expert committees at the provincial level. Then the generic drug is approved to be listed in the provincial formulary and corresponding maximum-reimbursable-cost type of policy may start to apply.

including this interaction variable, I am able to evaluate the dynamics of the brand-name drug price when the generic substitution policy is in place compared to when there is no such policy. This is my third research hypothesis: whether brand-name drugs still maintain net price premiums over their generic substitutes when generic substitution policy is available, after all other variables are controlled for.

J_j and N_j are dummies for the groups of antifungal and migraine-relief drugs, with cardiovascular drugs being the baseline case (ATC group "J" and "N", and "C", respectively). I included these therapeutic group dummies to control for the systematic difference in setting drug prices across different ATC groups. The selected drug cohort under different ATC groups should be treated separately because they are grouped according to the human organs or systems on which they act, and/or their therapeutic and chemical characteristics.[37]

str_j is a derived variable indicating the *relative* strength of the drug in question. A common problem when comparing drugs is that different medication can be of different strengths and different potency. It can be confusing when one compares 1 gram of drug A with 1 milligram of drug B. The WHO Defined Daily Dose (DDD) is a solution to this problem by relating the drug use to a standardized unit which is analogous to one day's worth.[38] In addition, the DDD provides a fixed unit of measurement independent of price and dosage form (e.g. tablet strength), which allows me to evaluate the role of drug strength in the price-setting behaviour across drug classes. First, I retrieve the DDD information for all drug molecules included in this study.[39] For example, simvastatin has a DDD of 30mg, which means that

[37] I do not introduce a higher level at level-4 to my model because the three selected WHO-ATC groups are not random samples from the population of therapeutic group. Instead, they should be interpreted as the characteristics (variables) with respect to the drugs. Specifically, the statin drugs (ATC code at the 4^{th} level: C10AA) under the cardiovascular system group aim to lower the cholesterol level and to help alleviate chronic conditions in the cardiovascular system. The antifungal drugs (ATC code at the 4^{th} level: J02AC) under the group of anti-infectives for systemic use are used to treat fungal infections. The triptan drugs (ATC code at the 4^{th} level: N02CC) under the nervous system group are used to treat migraine headache, a type of neurological condition more common to women than to men. More background information on the three selected classes of drugs can be found in Appendix C.

[38] According to the WHO's definition, the DDD is a standardized statistical measure of drug consumption for comparison purposes. It defines the assumed average maintenance dose per day for a drug used for its main indication in adults.

[39] The DDD is subject to periodical review and therefore it may have different versions over time. For simplicity, I use the WHO DDD Index 2010, retrieved at http://www.whocc.no/atc_ddd_index

an average patient who takes simvastatin (for the treatment of hypercholesterolemia) uses 30mg per day; naratriptan has a DDD of 2.5mg, which means that an average patient who takes naratriptan (for pain relief) uses 2.5mg per day, etc. Then, the actual strength for each drug is divided by its DDD measure. As such, the outcome str_j is the relative strength level for each drug. It is standardized for comparison purposes, namely, a 20mg simvastatin tablet means two-thirds of a DDD and a 2.5mg naratriptan means 1 DDD, etc. I include str_j to control for the degree to which the dosage strengths may shape the drug price-setting behaviour.

I let $str \times J$ and $str \times N$ be the interaction terms between the relative strength variable (str_j) and the therapeutic class dummies (J_j and N_j), respectively. I include them to evaluate in this sample whether drug manufacturers use different price-setting strategies for stronger-dosage drugs across therapeutic classes.

Finally, drug prices in this study are deflated using the monthly CPI for prescribed medicines to rule out the inflation effect. Therefore in the regression model, I include three calendar quarter dummies, with the 2^{nd} quarter as the baseline case. In this way, I can control for the possible seasonality in the drug price dynamics net of inflation.

4.5.2 Empirical Results and Interpretation

4.5.2.1 Empirical Results for the Non-random Coefficient Estimates

The empirical regression estimates from the IV-MLE (three-level) model provides answers to my three research hypotheses. To evaluate the performance of the IV-MLE model, I include the estimates from the pooled ordinary least squares (OLS) model as the benchmark for comparison.[40]

The pooled OLS model does not take account of the special variance-covariance structure specified in (4.4.17), (4.4.19), and (4.4.20). As such, it gives less efficient yet unbiased (and consistent) estimates.[41]

Next, see Table 4.3 for the discussion of the coefficient estimates from both the

on Apr. 4, 2010.

[40]The OLS regression is a pooled two-stage least squares (2SLS) by using the same instrumental variables ($\Delta lnavgpricelag_{jit}$ and $\Delta lnavgpricelag_{jit-1}$) in the first-stage regression.

[41]Both regression models were estimated by Stata (Ver. 10.0). I use the Hausman-Taylor estimator (two-level) to verify the robustness of the estimation in the IV-MLE model.

OLS model and the IV-MLE model.

Table 4.3: Regression Results for the Drug Price Dynamics

	Pooled OLS	**IV-MLE**
$gennum_{it}$	0.0105(0.0147)	0.0111(0.0031)***
$compnum_{it}$	-0.0034(0.0037)	-0.0002(0.0002)
$brand_i$	0.1769(0.1258)	0.2939(0.0573)***
$policy_{jit}$	-0.0618(0.1157)	-0.0380(0.0202)*
$policy \times brand$	0.2843(0.1244)**	0.1717(0.0207)***
$lnavgpricelag_{jit}$	0.4610(0.5928)	0.5654(0.0796)***
J_j	0.3532(0.3627)	0.4235(0.3434)
N_j	1.1895(1.2958)	0.9675(0.3378)***
str_j	0.1019(0.1108)	0.0952(0.0317)***
$str \times J$	0.9309(1.0168)	0.8995(0.2810)***
$str \times N$	-0.1099(0.1154)	-0.0548(0.0971)
$cq1_t$	-0.0063(0.0091)	-0.0036(0.0018)**
$cq3_t$	-0.0087(0.0109)	-0.0048(0.0019)**
$cq4_t$	-0.0057(0.0100)	-0.0029(0.0019)
$constant$	0.0370(0.3375)	-0.1676(0.1871)
Random-effects Parameters		
Level-3 (Molecule): σ_v	-	0.4345(0.0927)*** [82.6%]
Level-2 (Drug): σ_u	-	0.1969(0.0123)*** [17.0%]
Level-1 (Time): σ_e	-	0.0321(0.0005)*** [0.4%]

***Statistically significant at 1% level, **significant at 5% level, *significant at 10% level

† Fractions of variance attributed to each specific level in brackets

The standard errors for the coefficient estimates in the pooled OLS model are all greater than those in the IV-MLE model. As a result, the more efficient IV-MLE specification renders more statistically significant estimates. Now I examine my research hypotheses as follows.

First of all, the coefficient estimate for *gennum* is positive and significant (at the $\alpha = 1\%$ level). This indicates that more generic substitutes within a drug molecule does not necessarily introduce a net effect of lowering drug prices, while other contextual variables are controlled for. In fact, it suggests that an additional generic drug in a molecule is associated with a 1% *increase* in the drug prices for the study sample. This finding provides direct support for my first research hypothesis.

Secondly, the coefficient for *compnum* is negative but not statistically significant, everything else being equal. Therefore, there is a lack of evidence to associate the

number of therapeutic substitutes across drug molecules and the drug price dynamics. This is in line with my second research hypothesis.

Thirdly, the coefficient estimate for the *brand* dummy is positive and statistically significant (at the $\alpha = 1\%$ level), indicating that brand-name drugs enjoy remarkable price premiums over their generic substitutes in general. In Chapter 3, I offer extensive discussions to explain this: brand-name manufacturers strategically differentiate their products from the generic substitutes in superior *perceived* quality. The regression estimates show that the brand-name drug manufacturers are able to charge almost 30% higher prices than generic drugs. Alternatively, the price premium may well be the result of the generic price-cap policy.[42] But note that the brand-name drugs in this study include both those with generic substitutes and those protected by patents. Without further examination, I am not able to disentangle which type of brand-name drugs contribute to the high prices.

The coefficient estimate for the *policy* dummy has a negative sign and is statistically significant (at the $\alpha = 10\%$ level). Nevertheless, this result does not tell us whether the generic substitution policy is associated with lower prices in brand-name drugs, in generic drugs, or in both.

I can find the answer from the interaction term $policy \times brand$. I note that the coefficient estimate for this interaction term is positive and statistically significant (at the $\alpha = 1\%$ level). In other words, brand-name drugs tend to maintain net price premiums over their generic substitutes by 18.7% on average,[43] despite the fact that the generic substitution policy is in place. But, the net price premium is decreased compared to the case where there is no such policy. This finding offers support for my third research hypothesis.

Brand-name manufacturers may strategically maintain the price premiums over generic drugs in the face of the generic competition. Nevertheless, it should be made clear that a generic substitution policy can offer considerable savings in drug reimbursement cost for public drug plans. By design, the generic substitution policy allows public drug plans to only cover the cost of generic drugs in an interchangeable

[42] It can also be explained as: high price is used as signals of quality in the literature, e.g. Fluet and Garella (2002).

[43] It is derived by applying the formula $e^{0.1717} - 1 \approx 0.187$.

drug class. Assuming the same prescribing patterns, the switch from brand-name to generic drugs would significantly bring down the drug reimbursement cost.[44]

The discussion of the rest of the control variables are as follows. First, the coefficient estimate for *logavgpricelag* is positive and statistically significant (at the $\alpha = 1\%$ level). Recall my assumption that drug manufacturers use the average drug price level within its market niche from the previous period as an anchor to set drug prices for the next period. The assumption obtains empirical support from the regression results: roughly 57% of the price dynamics in the current period can be explained by those in the previous period.

Second, the coefficients for J and N dummies are both positive but only the coefficient estimate for N dummy is statistically significant (at the $\alpha = 1\%$ level). It suggests that on the one hand, the prices of the antifungal drugs (under the ATC code J02AC) are not much different from the statin drugs — the baseline case (under the ATC code C10AA). On the other hand, the migraine-relief drugs (under the ATC code N02CC) are relatively more expensive compared to the baseline statin drugs. It is likely that drugs targeting chronic diseases generally entail a longer period of treatment than that for non-chronic diseases. Therefore the manufacturers may choose to charge a lower price on average for drug products used for chronic disease treatment. However, this observation cannot be confirmed until more classes of drugs are studied.

Third, the coefficient estimate for the relative strength variable str_j is positive and statistically significant (at the $\alpha = 1\%$ level). In general, the stronger dose each tablet/capsule contains, the more likely a drug manufacturer charges a high price for the drug, and vice versa. Everything else being equal, there is about a 10% increase in drug price per unit increase in the DDDs.

Fourth, the coefficient estimate for the interaction term $str \times J$ is positive and statistically significant (at the $\alpha = 1\%$ level). This suggests that an increase in drug

[44]For example, a preliminary estimate of extra dollars the Nova Scotia Pharmacare Programs could have reimbursed for statin drugs alone during 2000-2008 reaches $2.3 million (2002 constant CAD). In addition, a British study established the potential savings of the proprietary atorvastatin with generic simvastatin at approximately £2 billion over 5 years. Dutch studies determined the potential annual savings of therapeutic substitution of statins in two databases to be approximately €53 million and €52 million (Gumbs et al., 2007).

strength (DDD) for the antifungal drugs is associated with more pronounced price hikes than it is for the cardiovascular drugs (the baseline case). In the meantime, the coefficient estimate for $str \times N$ is negative but not statistically significant. It partly reflects the fact that some migraine-relief drugs in this study are relatively cheaper per DDD. This may provide decision-makers a valid reason for encouraging pill-splitting.[45]

Finally, the calendar quarter dummies all have negative coefficient estimates but only those for $cq1$ and $cq3$ are statistically significant (at the α =5% level). This represents that the upward price adjustment normally takes place in the 2^{nd} quarter when a new government budget starts.[46]

In summary, the empirical regression results based on the IV-MLE model provide sufficient support for all three research hypotheses. Namely, (1) more generic substitutes are not necessarily translated into a net effect of lowering drug prices, while other contextual variables are controlled. On the contrary, the results from the regression analysis suggest a *positive* impact of the number of generic substitutes on drug prices for the sample studied. (2) The number of therapeutic substitutes within each therapeutic market does not appear to be associated with the drug price dynamics, when everything else is controlled. (3) Brand-name drugs maintain net price premiums over their generic substitutes, even when a generic substitution policy is available. These empirical findings confirm and corroborate the generic competition paradox.

In addition, I want to take a second look at what I can learn from the generic competition paradox. There is a lack of coordination in drug price regulation between provincial governments and between different levels of governments. On the one hand, at the federal level, the prices of patented drugs are scrutinized by the PMPRB;[47]

[45]Dormuth et al. (2008) and Lexchin (2009) discuss perspectives in tablet-splitting practice in Canada.

[46]It should be noted that the price adjustment discussed here is in real terms rather than in nominal terms. It is informative since drug manufacturers also take the inflation effect into consideration when they set drug prices.

[47]The PMPRB did not regulate the prices of the drugs with dedicated patents initially. A dedicated patent means that the patentee has surrendered its proprietary interest and dedicated that interest to the Canadian public by so notifying the Commissioner of Patents. Through the act of dedication, a patentee also relinquishes its exclusive ownership of the patent. The PMPRB believed many patent dedications had been made to avoid the Board's

on the other, some provinces are able to set up price-caps for generic drugs. What is missing is an approach directed at the brand-name drugs whose patents have expired. There is no control on the prices of these off-patent drugs from either regulatory bodies.[48]

The brand-name drug manufacturers thereby can take advantage of the lack of coordinated price regulations to maintain higher prices, using their product differentiation strategies and market power derived from the entrenched brand-loyalty.[49] Given that the patents of many blockbuster drugs will expire in the years to come, the empirical findings may lend insights to the federal drug price regulatory agency, the PMPRB. The research results also provide useful information on the generic substitution policies for both Canadian public and private drug plan decision-makers.

4.5.2.2 Empirical Results for the Random Coefficient Estimates

Besides offering more efficient estimates, the IV-MLE model has the most obvious advantage over the OLS model: it provides estimates for the random coefficients. Specifically, the IV-MLE model suggests that the majority of heterogeneity in drug prices lies in the higher levels (level-2 and level-3). Inter-temporal variation in drug prices at level-1 accounts for only a very small proportion of the overall drug price randomness. That is, the between-drug random-effects at level-2 accounts for about 17% of the overall heterogeneity in the drug price dynamics, with only less than 1% taken by the level-1 inter-temporal random-effects. However, the between-molecule random-effects at level-3 absorbs the majority of the overall drug price heterogeneity at almost 83%. The empirical results strongly support the inclusion of the molecule factor at level-3 for this study.

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jurisdiction. As a result, since 1995, the PMPRB has begun to regulate the prices of the drug products whose patents have been "dedicated". The above information was retrieved at http://dsp-psd.pwgsc.gc.ca/Collection-R/LoPBdP/MR/mr136-e.htm on December 5, 2010.

[48] PMPRB (2007b) studies the markets for new off-patent drugs during the period of 2000-2005 using the IMS Health's MIDAS database for price and sales data. The report shows that regardless of generic entry, prices of brand-name drugs usually increased after patent expiry.

[49] PMPRB (2007a) investigates the market and price behaviour for 132 off-patent single-source drugs in Canada from 2001 to 2005 using the IMS database. The report reaches a conclusion that average prices for these off-patent single-source drugs have not increased faster than those of patented drugs, and have remained well below rates of CPI inflation, although some individual prices have risen or fallen by larger amounts.

The above findings echo what I have observed from the literature. First, looking at the limited inter-temporal random variation (level-1) in the drug price dynamics, I also note that drug prices over the study period are relatively stable in Canada (CIHI, 2010a).

Second, there is moderate random variation in drug prices between drugs (level-2). It can be interpreted by the fact that the prices of generic drugs within a molecule tend to cluster.[50] Therefore, the heterogeneity in price mainly exists between brand-name original and its generic substitutes but not among generic drugs themselves.

Third, when it comes to price-setting, manufacturers need to consider factors such as the treatment cycle of the drug product (for chronic or acute diseases), the type and size of the target patient population (for the senior or population in general), and the number of therapeutic competitors in the field, etc. As such, it is natural that the majority of the random-variation of the drug price dynamics lies in between molecules.

Note that the between-molecule random-effects may play different roles for different samples. The number and the heterogeneity of the drug classes that are included in the regression analysis may be associated with the results. In general, the more diverse drug classes that are in the sample, the more significant role the between-molecule effects will play in explaining the overall drug price heterogeneity.[51]

4.6 Concluding Remarks

With a comprehensive overview of the Canadian pharmaceutical system and the relevant institutional background in Chapter 2 and an in-depth study on drug manufacturers' price-setting behaviour from the perspective of oligopoly theory in Chapter 3, this chapter examines the relationship between the drug price dynamics and the changing drug market structure for the selected groups of drugs in the context of Canadian health policy and legislation.

[50] This could be a result of the regulation on generic drug prices or tacit collusion among the generic drug manufacturers in Canada. I discuss it in Chapter 2.

[51] The differences in the selected drug classes can be in terms of the target anatomical system, the target population, the stage of the product life-cycle, the size of the market, etc.

The Canadian pharmaceutical system is complex, in terms of the fragmented policy across the country, its dynamic and unique market structure, and the consumption process of pharmaceutical products.

The regulation on drug prices exists at both the federal and provincial levels. At the federal level, the PMPRB regulates the price for patented drugs but has no direct price control over non-patented drugs, including off-patent drugs and generic drugs that do not have any patents. At the provincial level, provinces develop various mechanisms to contain drug reimbursement cost covered by the public drug plans, including the maximum-reimbursable-cost policies and provincial formularies. These approaches indirectly promote drugs that are at or below a certain price and/or drugs that are covered by the formulary.

Several key stakeholders of the pharmaceutical system, with competing incentives, objectives, and interests, are involved in a complex consumption process of pharmaceutical products. Patients who consume drug products only have a limited role in drug selection; physicians who diagnose and prescribe, and pharmacists who dispense and provide counselling, do not pay for drugs; public or employer-based drug plans offer insurance coverage for prescription medication for the majority of Canadians to various degrees.

I have used the IV-MLE model to deal with endogeneity in the multilevel setting. The multilevel regression results suggest that the heterogeneity in drug prices predominantly resides in the higher hierarchies in the data structure (drug at level-2 and molecule at level-3). The empirical finding justifies the inclusion of the third level in the model to reflect the considerable random variation in drug prices at the drug molecule level. The share of the between-molecule random-effects at level-3 in the overall heterogeneity of drug prices may increase as more diverse drug classes are included in the sample.

I have presented three major research findings from the empirical regression: (1) More generic drugs in a molecule are not necessarily translated into lower drug prices. Instead, more generic substitutes indicate a net effect of price *increase* for this study, after other contextual variables are controlled for. (2) In addition, more therapeutic substitutes do not have a net effect of lowering drug prices either. (3) Given the

available generic substitution policy, brand-name drugs maintain net price premiums over their generic substitutes. But, the net price premium is decreased compared to the case where there is no such a policy. These empirical findings confirm and corroborate the generic competition paradox.[52]

It is clear that the lack of coordination in drug price regulation in the Canadian context offers latitude for brand-name drug manufacturers to maintain higher prices. The brand-name drug manufacturers can take advantage of the entrenched brand-loyalty and use product differentiation strategies to effectively soften the direct price competition for their drug products. It should be noted that this thesis focuses on the brand-name drug manufacturers' price-setting behaviours facing the generic drug competition. The literature offers a broader view assessing the nature of drug price competition in regulated markets, such as that of Canada. For example, Anis et al. (2003) studies the competition effect in the generic sector after the 70/90 generic price-cap policy was introduced in Ontario in the 1990s. The clustering of generic drug prices around the maximum allowable levels with little price dispersion identified in the previous decade can still be found today. Puig-Junoy (2010) surveys the literature on generic drug price competition in regulated European pharmaceutical markets, which is similar to that for the Canadian market. These discussions provide more interesting directions for future research.

Policy-makers at the federal and provincial level strive to contain drug reimbursement cost while ensuring the availability of safe and effective drugs for their clients. The empirical findings from this chapter provide useful information on the generic substitution policies to the decision-makers in both the Canadian public and private drug plans.

[52] As Hollis (2005) and Grootendorst (2007) show, the strategy launching "authorized generics" offers room for brand-name drug manufacturers to manipulate drug pricing. Ideally, the information on "authorized generics" can offer us additional insights to the generic competition paradox. Yet, data are not available for this research. I would consider the "authorized generic" variable in future research.

Chapter 5

Conclusion

Prescription drugs play an increasingly significant role in the Canadian healthcare system. Drug expenditure accounts for a considerable share in the total healthcare expenditure and continues to be one of the fastest growing expenditure components in Canada. But, drug manufacturers' price setting behaviours are not well understood in the literature. This leads to my research questions.

Why can brand-name drug manufacturers maintain a downward price rigidity for their off-patent drug products in spite of the generic drug competition? What is so special about the Canadian pharmaceutical industry? What economic theories can be used to explain the stories behind these observations?

To fill the knowledge gap between these questions about the Canadian pharmaceutical industry and our ability to understand and interpret these phenomena, I develop the oligopoly theory with two-dimension product differentiation based on an understanding of the key stylized facts about the Canadian pharmaceutical system. I analyze the impact of market structure and policy on the drug manufacturers' price setting strategies. Then I use the multilevel model to examine three hypotheses in the empirical research.

The research findings from my theoretical models and empirical studies corroborate the presence of the generic competition paradox after the contextual variables are properly controlled for. This thesis also contributes to the literature by offering new insights on drug manufacturer's price setting behaviours.

In the following, I summarize the major research findings and contributions of this thesis. I also discuss the limitations for future extension.

5.1 Major Research Findings and Contributions

To answer the above questions, I have identified unique factors that fundamentally shape and influence the drug prices. On the basis of a synthesis of the literature on the institutional history and development, I have summarized the major characteristics of the Canadian pharmaceutical system as follows.

First, unlike hospital and physician services, the Canada Health Act does not mandate universal coverage of prescription drugs for Canadians. Yet public drug plans remain one of the major stakeholders in the system. To maintain the sustainability of the Canadian health system, government policies and regulations are therefore present to contain soaring drug costs.

Second, there are both federal and provincial legislations on pharmaceutical prices and services. Provincial governments are responsible for the funding of pharmaceutical services and each province develops its own relevant policies. But there is a lack of full coordination between the federal and provincial governments, and among the provincial legislatures. The lack of a joint or coordinated national pharmaceutical strategy causes disparities in policies related to pharmaceutical services across the country.

Third, Canadian patients' demand for prescription drugs is largely induced by other stakeholders in the system (e.g. physicians, pharmacists, and public/private drug plans, etc.). The involvement of multiple stakeholders in the process of supplying and consuming prescription drugs is characterized by competing objectives and interests. As such, this institutional platform shapes the distinct marketing strategies for the two distinct sectors of the pharmaceutical industry, namely the brand-name and generic drug manufacturers.

The unique stylized facts of the Canadian pharmaceutical system serve as the solid foundation for my theoretical modelling and empirical study on drug manufacturers' price setting behaviour, in particular, the generic competition paradox.

The generic competition paradox has been noted widely in the literature, but few theoretical frameworks are proposed for exploring how market structures and legislations impact drug manufacturers' price setting strategies. I develop a framework of oligopoly theory with two-dimension product differentiation for the two-tier

structure of the pharmaceutical industry. In particular, I introduce three important parameters to the theoretical analysis, namely one patient preference parameter, one policy parameter for the copay, and another policy parameter for the generic price-cap. I demonstrate how these parameters affect drug manufacturers' price setting behaviours in different settings.

The major theoretical findings are as follows. (1) The differentiation in perceived quality between brand-name and generic drugs can be used to explain the generic competition paradox. In some circumstances, the degree of the product differentiation can be pivotal in shaping the brand-name drug manufacturers' price setting behaviour in response to the shift in patients' preference and changes in government policies. (2) Both copay and generic price-cap policies can be adopted by public drug plans to contain drug reimbursement cost, but policy-makers should use caution when applying these policies in combination or separately in order to reach their intended outcomes. (3) Generic price-cap is considered to be an effective tool to contain drug costs for public drug plans. This policy can also elicit competition among brand-name drug manufacturers, but it may need coordinated regulations on patented drug prices. In addition, without full coordination across the public and private sectors and across jurisdictions, the benefits of lowered prescription drug prices for some can become the additional costs for others.

My empirical analysis on the drug price dynamics using the multilevel model is another major contribution to the literature. Despite the discovery of the generic competition paradox for various drug classes, in various time periods, and in different countries, previous research rarely examines whether the paradox stays after the relevant contextual variables are properly controlled for. Moreover, for the first time in the literature, I use the multilevel model to analyze the "tree-like" pharmaceutical market data and evaluate the net effect of the paradox. The empirical study confirms my main research hypotheses. (1) More generic substitutes in a drug molecule are associated with a net effect of increases in drug prices, after other contextual variables are properly controlled for. (2) More therapeutic substitutes do not have a net effect of lowering drug prices either. (3) When a generic substitution policy is in place, brand-name drugs maintain net price premiums over their generic substitutes. But,

the net price premiums in the case when there is a generic substitution policy are lower than those where there is no such policy. These empirical findings are consistent with the predictions of the theory developed in this thesis.

5.2 Limitations and Future Research

As discussed in Chapter 2, the Canadian pharmaceutical market is complex. To focus on the research questions, I make assumptions for simplification in the theoretical discussion.

First, I assume zero marginal cost associated with manufacturers' endeavours in developing therapeutic variant and brand-imaging. This assumption is made in the setting of predetermined product differentiation. Costs related to product differentiation, such as advertisement for brand-imaging and detailing service for promoting drug products, may determine the extent of product differentiation and thereby shape different equilibrium prices from the solutions offered in this thesis. In addition, other hidden costs in practice, such as manufacturers' rebates and discounts, are directly related to drug manufacturers' price setting behaviours. It remains challenging to combine these additional factors into the theoretical work.

Second, the assumptions of dichotomous patients' preference and single-product firms in the theoretical work in Chapter 3 are examples of simplification of the reality. For example, brand-name drug manufacturers are likely to be multi-product multinational corporations. That is, a brand-name drug manufacturer may adopt different strategies when its new off-patent drug product faces generic competition. Other than competing with generic entrants in the price dimension, the brand-name drug manufacturer may opt for marketing a new line-extension drug with patent protection. A related assumption in Chapter 3 is associated with the scope of a therapeutic market, which I assume according to the standard WHO-ATC 5^{th} level code. If a therapeutic market can be broaden to include more substitutable therapeutic classes, we may gain new insights on the generic competition paradox.

Third, in practice, drug manufacturers may sell bundles of drugs to governments under certain risk-sharing schemes. These undisclosed transactions may significantly distort the market. It may also change the analysis and our understanding on drug

manufacturers' price setting behaviours.

Finally, there are certain limitations in the sample data. As mentioned in Chapter 4, more drug classes, longer study period, and more control variables such as market shares and age of drug molecules would offer a better understanding on the drug price dynamics.

For future theoretical research, I can consider a dynamic analysis in the long run regarding the oligopolistic models, based on the comparative statics exercises in the short run developed in Chapter 3. In doing so, I would be able to examine the interactions among the preference/policy parameters and obtain new insights on drug manufacturers' price setting strategies.

Empirically, the data issue can be addressed when better quality datasets with more variables are available. In addition, considering the ongoing drug reforms in the Canadian provinces, further examination on the drug price dynamics would allow researchers to evaluate the effectiveness of new policies and regulations.

My quantitative research methodology, the multilevel model, can be applied broadly in health economics and many other areas, including examining disparities in healthcare resource allocation, measuring health service quality, and economic evaluation.

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Appendix A

Detailed Information on Provincial and Territorial Drug Plans

The detailed information on provincial and territorial drug plans as of July 1, 2010 is retrieved from CIHI (2010b). Information is also available from the websites of provincial and territorial drug plans:[1]

British Columbia Pharmacare:
http://www.health.gov.bc.ca/pharmacare/index.html

Alberta Prescription Drug Program:
http://www.health.alberta.ca/AHCIP/prescription-program.html

Saskatchewan Drug Plan:
http://formulary.drugplan.health.gov.sk.ca/

Manitoba Pharmacare Program:
http://www.gov.mb.ca/health/pharmacare/index.html

Ontario Drug Benefits:
http://www.health.gov.on.ca/en/public/programs/drugs/funded_drug/default.aspx

New Brunswick Prescription Drug Program:
http://www.gnb.ca/0212/intro-e.asp

[1]The detailed information on the drugs plans/programs in Quebec, Northwest Territory, and Nunavut is not included in CIHI (2010b). I provide the corresponding websites below for interested readers. All websites are validated up to January 10, 2011.

Nova Scotia Pharmacare:
http://www.gov.ns.ca/health/pharmacare/

Prince Edward Island Pharmacy Services:
http://www.healthpei.ca/index.php3?number=1026180&lang=E

Newfoundland and Labrador Prescription Drug Program:
http://www.health.gov.nl.ca/health/prescription/index.html

Yukon Pharmacare:
http://www.hss.gov.yk.ca/pharmacare.php

First Nations and Inuit Health Branch:
http://www.hc-sc.gc.ca/fniah-spnia/nihb-ssna/benefit-prestation/drug-med/index-eng.php

Régime général d'assurance médicaments du Québec (RGAM):
http://www.ramq.gouv.qc.ca/en/citoyens/assurancemedicaments/index.shtml

Northwest Territories:
http://www.hlthss.gov.nt.ca/english/services/health_care_plan/default.htm

Nunavut:
http://www.drugcoverage.ca/p_benefit_nu.asp

Table A.1: Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia		
Eligibility	**Plan/Program**	**Fair PharmaCare**-All B.C. residents with active BC Medical Services Plan coverage
		Plan B-Permanent residents of licensed residential care facilities
		Plan C-Recipients of British Columbia Income Assistance Benefits
		Plan D-Cystic fibrosis
		Plan F-Children in the At-Home Program
		Plan G-No-Charge Psychiatric Medication Plan
		Plan P-Palliative care
	Beneficiary Group	Residents of British Columbia for at least three months
	Income Range	**Plan C** B.C. residents receiving medical benefits and income assistance through the Ministry of Housing and Social Development
		Plan G Low-income residents; an application for psychiatric medication coverage to a mental health service centre is required for approval
	Age Range	**Fair PharmaCare** Fair PharmaCare (Regular Assistance) - Residents born in 1940 or later Fair PharmaCare (Enhanced Assistance) - Residents born in 1939 or earlier
		Plan F Younger than age 18
	Disease Specific	Individuals with cystic fibrosis (plan D) Severely handicapped children- At-Home Program (plan F) Clients of mental health service centres (plan G) (meeting clinical and income criteria)

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Eligibility	**Other Eligibility Criteria**	Fair PharmaCare: An individual must -Have effective British Columbia Medical Services Plan (MSP) coverage; and -Have filed an income tax return for the relevant taxation year.
		Criteria for Fair PharmaCare Enhanced Assistance: An individual must -Have been born in 1939 or earlier; -Have effective British Columbia Medical Services Plan (MSP) coverage; and -Have filed an income tax return for the relevant taxation year.
		Plan B recipients are enrolled and receive coverage through the care facility.
		Plan C recipients must be registered in MSP and receiving medical benefits and income assistance through the Ministry of Housing and Social Development.
		Plan D individuals with cystic fibrosis are registered with a provincial cystic fibrosis clinic.
		Plan F recipients must be -Age 17 or younger; -A resident of B.C.; -Living at home with a parent or guardian; and -Assessed as dependent in at least three of four areas of daily living.
		Plan G -The patient's physician or psychiatrist must submit an application for psychiatric medication coverage to a mental health service centre for approval. -Patient must qualify for premium assistance under the Medical Services Plan.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Eligibility	**Other Eligibility Criteria**	Plan P recipients must be -Enrolled in MSP, living at home; -Diagnosed as being in the terminal stage of a lifethreatening illness; and -Have a life expectancy of up to six months. The physician submits an application, certifying the individual meets the criteria.
Cost-Sharing Mechanism	**Premium**	None
	Copayment / Coinsurance	Fair PharmaCare -After meeting their annual deductible, families pay 30% of the eligible prescription drug costs for the remainder of the calendar year (or until reaching their annual maximum, whichever comes first).
		Fair PharmaCare Enhanced Assistance -After meeting their annual deductible, families pay 25% of the eligible prescription drug costs for the remainder of the calendar year (or until reaching their annual maximum, whichever comes first).
	Deductible	Fair PharmaCare Net family income<$15,000 Deductible = $0 Net family income $15,000 to $30,000 Deductible = 2% of net income Net family income>$30,000 Deductible = 3% of net income
		Fair PharmaCare Enhanced Assistance Net family income<$33,000 Deductible = $0 Net family income $33,000 to $50,000 Deductible = 1% of net income Net family income>$50,000 Deductible = 2% of net income

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Cost-Sharing Mechanism	**Deductible (Cont'd)**	For a family registered for Fair PharmaCare whose income cannot be verified OR For a person actively enrolled in the Medical Services Plan but not registered for Fair PharmaCare deductible = $10,000 Note: The deductible is based on income bands so the percentages provided are approximate. **No deductible is applied to the remaining plans/programs.**
	Maximum Beneficiary Contribution	Fair PharmaCare Net family income<$15,000 Maximum = 2% of net income Net family income $15,000 to $30,000 Maximum = 3% of net income Net family income>$30,000 Maximum = 4% of net income
		Fair PharmaCare Enhanced Assistance Net family income<$33,000 Maximum = 1.25% of net income Net family income $33,000 to $50,000 Maximum = 2% of net income Net family income>$50,000Maximum = 3% of net income Note: The maximum is based on income bands so the percentages provided are approximate. **No maximum beneficiary contribution is applied to the remaining plans/programs.**
Policy-Related Information	**Prescription Cost Components**	PharmaCare will pay the pharmacy's actual acquisition cost (AAC), including freight costs, up to a maximum of 7% above the manufacturer's list price for wholesale drugs, plus the professional/dispensing fee. PharmaCare coverage is subject to **Low-Cost Alternative Policy:** If several drugs contain identical active ingredients, PharmaCare sets a maximum

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Policy-Related Information	**Prescription Cost Components (Cont'd)**	low-cost alternative (LCA) price that it will pay for any of the drugs in that group. The LCA price is set at the lowest average cost claimed by B.C. pharmacies for the drugs in the group. Drugs in the group within one percent of that LCA price are fully covered.
		Reference Drug Program: If there is more than one drug in a therapeutic class, PharmaCare provides full coverage of only those drugs considered to be the most medically effective and the most cost effective in that category – the reference drug. Five classes of drugs are included in the Reference Drug Program: 1. Histamine 2 receptor blockers (H2 blockers) 2. Non-steroidal antiinflammatory drugs (NSAIDS) 3. Nitrates 4. Angiotensin converting enzyme inhibitors (ACE inhibitors) 5. Dihydropyridine calcium channel blockers (dihydropyridine CCBs)
	Professional Fees	PharmaCare reimburses up to $8.60 for dispensing fees.
		Effective February 1, 2009, the **Frequency of Dispensing Policy** limits the number of dispensing fees that PharmaCare will pay for drugs dispensed in less than a 28 days' supply: -PharmaCare will pay a maximum of three dispensing fees for drugs dispensed daily. -PharmaCare will pay a maximum of five dispensing fees for drugs dispensed in 2-to-27 days' supplies.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Policy-Related Information	**Professional Fees (Cont'd)**	Plan B dispensing pharmacies are paid a capitation fee (per long-term care bed).
		Methadone (maintenance) interaction fee: $7.70.
		Special services fee – Remuneration to pharmacists if they choose not to fill a prescription based on their professional opinion (fee of twice the dispensing fee).
		Emergency contraceptive honorarium: $15.
		The following interim policy was negotiated as part of an interim agreement between the Province of British Columbia and the BC Pharmacy Association. The interim agreement expires on December 31, 2009. However, the parties have agreed to seek a longer-term agreement under which this, or a similar, policy may continue. **Interim Policy – Pharmacist Clinical Services Associated With Prescription Adaptation:** Pharmacists will be reimbursed for prescription adaptation services, defined as follows: 1. Renewing a prescription; 2. Changing the dose, formulation or regimen of a prescription to enhance patient outcomes; and 3. Making a therapeutic drug substitution within the same therapeutic class. For renewing and/or changing the dose, formulation or regimen of a prescription, pharmacists will be paid $8.60.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Policy-Related Information	**Professional Fees (Cont'd)**	For making a therapeutic drug substitution, pharmacists will be paid $17.20. Clinical services fees are paid in addition to the usual dispensing fee to which the pharmacy may be entitled. Special services fees are not paid for any prescription for which a clinical service fee is paid. Clinical services fees are paid in the quarter following the one in which the clinical service was provided. The ministry will pay a maximum of two clinical services fees per drug, per person during a sixmonth period. A transition agreement came into effect January 1, 2010, to bridge the six-month period required to develop a long-term agreement to ensure the continuation of benefits specified in the interim policy. Regulatory changes effective October 21, 2009, expanded B.C. pharmacists' scope of practice to include the administration of vaccinations. Authorized pharmacists are paid $10 for each publicly funded vaccination they provide.
	Markup	PharmaCare does not cover (pay for) retail markup.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Policy-Related Information	**Markup (Cont'd)**	PharmaCare does not cover (pay for) retail markup. Insulins, with the exception of Humalog, and needles and syringes for insulin therapy are reimbursed at the regular retail price, which includes markup. However, no dispensing fee may be charged.
	Ingredient Pricing	PharmaCare payment is based on the actual acquisition cost (AAC) up to a maximum price of 7% above the manufacturer's price for wholesale drugs. AAC is adjusted to reflect the true cost to the pharmacy and is net of any cash discounts, volume discounts, rebates or performance allowances. PharmaCare coverage is subject to **Low-Cost Alternative Policy:** If several drugs contain identical active ingredients, PharmaCare sets a maximum LCA price that it will pay for any of the drugs in that group. The LCA price is set at the lowest average cost claimed by B.C. pharmacies for the drugs in the group. Drugs in the group within one percent of that LCA price are fully covered. **Reference Drug Program:** If there is more than one drug in a therapeutic class, PharmaCare provides full coverage of only those drugs considered to be the most medically effective and the most cost effective in that category – the reference drug. Five classes of drugs are included in the Reference Drug Program: 1. Histamine 2 receptor blockers (H2 blockers) 2. Non-steroidal antiinflammatory drugs (NSAIDS) 3. Nitrates 4. Angiotensin converting enzyme inhibitors (ACE inhibitors) 5. Dihydropyridine calciumchannel blockers (dihydropyridine CCBs)

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Policy-Related Information	**Coordination of Benefits (Public/Private)**	With the exception of B.C. residents covered by Veterans Affairs Canada, Royal Canadian Mounted Police, Canadian Forces, Workers' Compensation or the federal Non-Insured Health Benefits Program, PharmaCare covers every individual. PharmaCare will consider coverage first and private insurance will consider coverage second.
	Coordination of Benefits (Intra-Jurisdictional)	For PharmaCare claims, the rules of plan adjudication are as follows, by plan priority. If patients don't meet the criteria of one plan, they will move on to the next until a plan is selected. If one plan only offers partial coverage (for example, based on medication) then patients could have claims and payments for multiple plans. The order of adjudication is as follows: Plan B, Plan P, Plan D, Plan G, Plan F, Plan C, Fair PharmaCare Fair PharmaCare Enhanced Assistance
	Restricted Benefit Process	Special authority forms are completed by practitioners on behalf of their patients. These forms can be forwarded to PharmaCare by mail, fax or telephone. The special authority requests are adjudicated on an individual basis, according to established criteria. Approved requests are entered into a patient's PharmaNet record. The special authority coverage is then available through any B.C. pharmacy. Special authorities are valid from the effective date for various periods of time, depending on the medication and use. Information regarding requests is returned to the practitioner by fax or mail.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Policy-Related Information	**Restricted Benefit Process (Cont'd)**	If appropriate, expired special authority coverage may be renewed. The requests for renewal should be submitted at least two weeks before the expiry date.
	Reimbursement Policy	Every time an enrolled Fair PharmaCare beneficiary purchases medication at a registered B.C. pharmacy,a claim is automatically submitted for coverage. As of January 1, 2008, PharmaCare no longer reimburses prescription or medical supply costs paid before the date a family registers for Fair PharmaCare. Costs continue to count towards the Fair PharmaCare deductible and annual family maximum, but costs above the deductible that occurred before registration are not reimbursed. Special authorities are prioritized by date received and the urgency of the request. On average, most requests are processed within two weeks. To ensure PharmaCare coverage, approval must take place prior to purchasing or dispensing a prescription drug. Retroactive coverage is not provided. The province does not reimburse for most out-of-province claims.
	Miscellaneous	**Prescription Quantities** PharmaCare limits coverage of all prescription drugs to a maximum 30-day supply (for short-term medications and first-time prescriptions for maintenance drugs) or a 100-day supply (for repeat prescriptions of maintenance drugs) Exemptions to the 30-day supply limit are available for

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

British Columbia (Cont'd)		
Policy-Related Information	**Miscellaneous (Cont'd)**	Plan B patients; Consumers in rural or remote areas; and Prescriptions under the Trial Prescription Program (where a 14-day trial has been dispensed). **Travel Supply** As of May 1, 2008, PharmaCare covers out-of-province travel supplies of medication up to the PharmaCare maximum allowable days' supply. Under the new policy, once every six months (180 days), a patient can ask for an out-of-province travel supply. Patients are required to sign a PharmaCare travel declaration form and the pharmacy is required to retain this form on file for the normal record retention periods specified by the College of Pharmacists of B.C.
Alberta		
Eligibility	**Plan/Program**	**Seniors** **Widows** **Palliative** **Non-Group** **Rare Diseases Drug Program**
	Beneficiary Group	**Seniors** Alberta residents age 65 or older and eligible dependants **Widows** Alberta residents age 55 to 64 who qualify for Alberta Widows Pension and eligible dependants

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Alberta (Cont'd)		
Eligibility	**Beneficiary Group**	**Palliative** Palliative residents treated at home **Non-Group** Alberta residents younger than age 65 and eligible dependants **Rare Diseases Drug Program** Albertans with rare diseases who have government-sponsored drug coverage and whose physician has applied for coverage will be considered; an individual or family must reside in Alberta for five years to be eligible for the program; the residency requirement will be waived for individuals moving to Alberta from another province in Canada if they were covered by that province's program
	Income Range	None
	Age Range	**Seniors** Alberta residents age 65 or older, or their spouse/partner, or their eligible dependent(s) **Widows** 55 to 64 **Non-Group** Younger than 65
	Disease Specific	Alberta Health and Wellness provides additional coverage for prescription drugs: **Specialized High-Cost Drugs** provides funding to Alberta Health Services for high-cost drugs: immunosuppressants for prevention of solid organ and bone marrow transplant rejection; HIV drugs; Pulmozyme (for cystic fibrosis); human growth hormone (for pediatric growth hormone deficiency and chronic renal failure); Flolan,

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Alberta (Cont'd)		
Eligibility	**Disease Specific (Cont'd)**	Tracleer, Revatio and Remodulin (for primary pulmonary hypertension); Visudyne (for classic form of wet age-related macular degeneration); bone marrow transplant adjunctive agents (Neupogen); and Copaxone, Avonex, Rebif and Betaseron for pediatric multiple sclerosis. The Alberta Cancer Board may provide medically required cancer drugs.
	Other Eligibility Criteria	**Seniors** In order to be registered, seniors must complete a proof-of-age declaration, which Alberta Health and Wellness mails to them; registration with the Alberta Health Care Insurance Plan (AHCIP) is required **Widows** Recipients of the Alberta Widows Pension **Palliative** Be registered with the AHCIP; diagnosed by a physician as being palliative and receiving treatments at home **Non-Group** Be registered with AHCIP and not eligible to receive the Alberta Widows Pension or be in premium arrears for the plan
Cost-Sharing Mechanism	**Premium**	**Non-Group, July 2010** Single: $63.50/month; Family: $118.00/month Subsidized rates are available to those who qualify, based on information reported on their prior year's income tax returns. Subsidized rates are: Single: $44.45/month; Family: $82.60/month

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Alberta (Cont'd)		
Cost-Sharing Mechanism	**Copayment/ Co-Insurance**	**Seniors** 30% per prescription up to a maximum of $25 **Widows** 30% per prescription up to a maximum of $25 **Palliative** 30% per prescription up to a maximum of $25; the lifetime maximum amount the patient pays out of pocket is $1,000 **Non-Group** 30% per prescription up to a maximum of $25
	Deductible	None
	Maximum Beneficiary Contribution	Palliative: $1,000
Policy-Related Information	**Prescription Cost Components**	Actual acquisition cost + professional fees + inventory allowance There are three drug price policies: least-cost alternative (LCA), maximum allowable cost (MAC) and actual acquisition cost (AAC). The LCA price is the lowest unit cost established for a drug product within a set of interchangeable drug products. Alberta's supplemental health plans will only pay for the lowest-priced drug product where interchangeable (generic) products can be used to fill a prescription. Beneficiaries who choose highercost alternatives are responsible for paying the difference.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Alberta (Cont'd)		
Policy-Related Information	**Prescription Cost Components (Cont'd)**	The MAC price is the maximum unit cost established for a specific drug product or a group of drug products. A small number of products are subject to MAC pricing. Pursuant to the pharmacy agreement, pharmacists are expected to charge the AAC of a drug product. For interchangeable drug products, pharmacists can only charge the AAC to a maximum of the lowest LCA or MAC price.
	Professional Fees	Alberta has two types of professional fees: dispensing fees and additional inventory allowance. The additional inventory allowance pricing component was implemented effective July 1, 2000. The fees from April 1, 2010, to March 31, 2011, are Acquisition Cost<$74.99, Dispensing Fee $10.22, Add'l Inventory Allowance $3.71* Acquisition Cost ($75, $149.99), Dispensing Fee $15.53, Add'l Inventory Allowance $2 Acquisition Cost>$150, Dispensing Fee $20.94, Add'l Inventory Allowance $5.03 For insulin and oral contraceptives, the prescription charge must not exceed the acquisition cost of the drug product times 5/3. For injectable drugs other than insulin, the prescription charge must not exceed the acquisition cost of the injectable drugs times 5/3, to a maximum of $100 more than the acquisition cost of the injectable drug. For compounded prescriptions that require more than seven minutes for preparation, the additional charge for compounding must not exceed 75 cents per minute for each minute in excess of seven minutes.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Alberta (Cont'd)		
Policy-Related Information	**Professional Fees (Cont'd)**	The transitional allowance applies to prescriptions with an AAC of between $0.00 and $74.99, with the exception of insulin, oral contraceptives, injectables, diabetic supplies, Alberta Public Health Activities Program drugs and Pharmacy Practice Models Initiative drugs. * The additional inventory allowance field was increased to allow for a transitional allowance to be incorporated. The transitional allowance will apply as follows: April 1, 2010, to March 31, 2011: $3.71 April 1, 2011, to March 31, 2012: $2.71 April 1, 2012, to March 31, 2013: $1.71 April 1, 2013, to March 31, 2014: $0.71
	Markup	Prices listed in the Alberta Health and Wellness Drug Benefit List include a wholesaler markup, but only if the drug manufacturer distributes through a wholesaler. In such cases, it is asked to include a distribution allowance of up to 7.5%. This includes both single-source and interchangeable products.
	Ingredient Pricing Policy	All prices printed in the Alberta Health and Wellness Drug Benefit List are based on responses to an Alberta price confirmation for the period of time during which the list is in effect.
	Coordination of Benefits (Public/Private)	Alberta Health and Wellness allows coordination of benefits between its Alberta Blue Cross non-group plans and private plans. The payment is shared pursuant to the Canadian Life and Health Insurance Association rules regarding coordination of benefits.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Alberta (Cont'd)		
Policy-Related Information	**Coordination of Benefits (Intra-Jurisdictional)**	Alberta Health and Wellness does not permit coordination of benefits across its public plans. It is intended that Albertans only be enrolled in one government plan at a time. As such, coordination of benefits is not necessary. Generally, Albertans eligible for coverage under federal plans do not seek coverage under another Alberta government plan.
	Restricted Benefit Process	Special authorization request forms are completed by providers and reviewed by clinical pharmacists of the program. Prior approval must be granted to ensure coverage by special authorization. Special authorization is granted for a maximum of 12 months. If continued treatment is necessary the providers must re-apply for coverage before the expiry date. A small number of drugs is restricted to specific age groups.
	Reimbursement Policy	When beneficiaries pay out of pocket, reimbursement claims are permitted. Claims from out of province and out of country are permitted but coverage is restricted to comparable benefits on the Alberta Health and Wellness Drug Benefit List. To be eligible for reimbursement, claims must be received by Alberta Blue Cross within 12 months of the service date. The service must have been provided after the effective date of coverage.
	Miscellaneous	**Prescription Quantities** No limitation on the quantities of drugs that may be prescribed.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Alberta (Cont'd)		
Policy-Related Information	**Miscellaneous (Cont'd)**	In most cases, Alberta Health and Wellness will not pay benefits for more than a 100-day supply of a drug at one time. Drugs considered maintenance or long-term therapy in the following therapeutic classes should be dispensed for 100 days: Anticoagulants Anticonvulsants Digitalis and digitalis glycosides Hypoglycemic agents Thyroid drugs Vitamins Oral contraceptives Antihypertensive agents Conjugated estrogens Anti-arthritics The Seniors and Widows, Non-Group and Palliative programs do not cover prescription costs exceeding $25,000 per beneficiary per year. On an exception basis, this amount can be modified by Alberta Health and Wellness.
Saskatchwan		
Eligibility	**Plan/Program**	Universal Program
	Beneficiary Group	Families/individuals applying for and approved for the drug plan's Special Support Program (income tested)

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Eligibility	**Beneficiary Group (Cont'd)**	Supplementary Health Program – People nominated for coverage by Saskatchewan Social Services Guaranteed Income Supplement (GIS) recipients – Government of Canada program for low-income seniors Saskatchewan Income Plan recipients –Provincial program to provide a monthly supplement to low-income seniors Seniors Drug Plan (income tested) – Seniors age 65 or older who have applied and qualified based on income Families/individuals approved for Family Health Benefits (eligibility is established by Saskatchewan Social Services, based on the number of children in the family and the family's annual income) Saskatchewan Aids to Independent Living (SAIL) beneficiaries (paraplegics, cystic fibrosis and chronic renal disease) Persons approved for the drug plan's palliative care coverage (residents who are in the late stages of a terminal illness) Government wards Inmates of provincial correctional institutions Families' granted emergency assistance (residents who require immediate treatment with covered prescription drugs and are unable to cover their share of the cost; this is a one-time benefit and individuals are encouraged to apply for income-tested coverage for future assistance) **Workers' Health Benefits Program** (Note: As of March 19, 2008, the Saskatchewan Workers' Health Benefits Program

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Eligibility (Cont'd)	**Beneficiary Group (Cont'd)**	was discontinued. Working adults without children who are currently enrolled and receiving benefits will maintain coverage until June 2010, if they continue to meet the original criteria.) – Single: income less than $21,000; married or common law: income less than $26,000 –**In addition applicant must be** A Saskatchewan resident with a valid Saskatchewan health card; Single or a couple, without dependent children; Younger than age 65; and Employed or self-employed –**and not be** Receiving benefits under a private or employer-sponsored health plan or the federal government's Non-Insured Health Benefits program; and nor Attending a post-secondary education institution on a full-time basis (university or technical school). **Children's Insulin Pump Program** –Applicants must be age 17 or younger. –Applicants must have type 1 diabetes and require a pump to adequately stabilize blood sugar levels. **Children's Drug Program** –Children age 14 or younger Not eligible: Citizens whose health services are covered under First Nations and Inuit Health, Health Canada, Veterans Affairs Canada, Royal Canadian Mounted Police, Canadian Forces, Workers' Compensation or federal penitentiaries are

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Eligibility (Cont'd)	**Beneficiary Group (Cont'd)**	not eligible for drug plan benefits under Saskatchewan Health. Note: Residents may qualify and be covered under more than one program at the same time. The better benefit applies at the time a prescription is filled.
	Income Range	**Seniors Program** Individual annual net income must be below the limit for the federal age credit.
	Age Range	Children's Drug Program: Children age 14 or younger Seniors Program: 65 or older
	Disease Specific	N/A
	Other Eligibility Criteria	N/A
Cost-Sharing Mechanism	**Premium**	None
	Copayment/ Co-Insurance	**Special Support Program** Income tested (based on benefit drug costs, to help spread cost out evenly over the year) Up to $15 per prescription for the Seniors Drug Plan for drugs listed on the Saskatchewan formulary and those approved under exception drug status; no charge for seniors who have SAIL or Palliative Care coverage 35% for seniors receiving the Saskatchewan Income Plan supplement or receiving the federal Guaranteed Income Supplement (automatically receive this copayment once the deductible has been met but may also apply for income-tested coverage); 35% for Family Health Benefits once the deductible has been met; no charge for benefit prescriptions for FHB children younger than 18 35% for Workers' Health Benefits

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Cost-Sharing Mechanism	**Copayment/ Co-Insurance (Cont'd)**	Up to $2 per prescription for Supplementary Health (persons nominated by Saskatchewan Social Services for special coverage, including persons on social assistance, wards, inmates, etc.); some drugs covered at no charge; individuals younger than 18 and certain other categories receive benefit prescriptions at no charge For the Emergency Assistance Program, the level of assistance provided is in accordance with the consumer's ability to pay Up to $15 per prescription for the Children's Drug Plan for drugs listed on the Saskatchewan formulary and those approved under exception drug status
	Deductible	**Special Support Program** Income tested (annual threshold based on 3.4% of adjusted family income) $100 semi-annual family deductible for seniors receiving the Saskatchewan Income Plan supplement or receiving the federal Guaranteed Income Supplement and residing in a special care home (automatically receive this deductible but may also apply for incometested coverage) $200 semi-annual family deductible for seniors receiving the Guaranteed Income Supplement and living in the community (automatically receive this deductible but may also apply for incometested coverage) $100 semi-annual family deductible for Family Health Benefits $100 semi-annual deductible for Workers? Health Benefits No deductible for people covered under the Palliative Care Drug Program

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Cost-Sharing Mechanism (Cont'd)	**Maximum Beneficiary Contribution**	Eligible seniors pay no more than $15 per prescription for drugs listed under the Saskatchewan formulary and those approved under exception drug status (MAC and LCA policies apply). Children up to age 14 will pay no more than $15 per prescription for drugs listed under the Saskatchewan formulary and those approved under exception drug status (MAC and LCA policies apply).
Policy-Related Information	**Prescription Cost Components**	**Low-Cost Alternative** Benefits are based on the lowestpriced interchangeable brand as listed in the formulary. **Maximum Allowable Cost** Classes of drugs are reviewed by the province's expert drug review committees to determine which products are equally safe, beneficial and cost effective. The price of the most cost-effective drugs are used as a guide to set the maximum price that the drug plan will cover for other similar drugs used to treat the same condition. **Prescription Cost** The prescription cost is calculated by adding the actual acquisition cost of the drug material (which can include an allowable wholesale markup), the pharmacy markup (up to a maximum) and dispensing fee (up to a maximum). Extemporaneous preparations add a compounding fee of $0.75/minute to a maximum of 60 minutes; a maximum of 20 minutes applies for most methadone compounds.
	Professional Fees	The maximum dispensing fee is $9.15 (effective August 1, 2009).

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Policy-Related Information	**Professional Fees**	Trial prescriptions – Specific list of drugs; trial for 7 or 10 days; follow-up by pharmacist required; the usual and customary professional fee (to a maximum of $9.15) is paid for the trial quantity; if the medication is continued, no fee may be claimed on the "remainder" prescription, but an alternative reimbursement fee of $7.50 is paid even if the balance of the prescription is not dispensed; subsequent refills are subject to usual reimbursement Methadone managed care – Pharmacists supply a daily quantity of methadone; the managed care fee is $3.50 per day ($24.50 per week) and is paid only for face-to-face interactions between the patient and the pharmacist Emergency contraception prescribing – Pharmacists who have the required training may charge a prescribing fee equal to two times the usual dispensing fee; this is in addition to the usual cost plus fee for the dispensed product Refusal to dispense – Specific list of drugs; may charge 1.5 times the pharmacy's usual and customary dispensing fee Seamless care fee – For services related to medication reconciliation for clients who are transferred from an institution to a community setting; may charge 1.5 times the pharmacy's usual and customary dispensing fee Compliance packaging – Effective January 15, 2010; as set out in the Medication Assessment and Compliance Packaging Policy; currentlyeligible/nominated home care clients: $6.25 for each 7-day supply ($25 for a 28-day supply or $31.25 for a 35-day supply) Medication assessment – Effective January 15, 2010; as set out in the Medication Assessment and Compliance Packaging Policy; fee – no more than $60, restricted to payment once per calendar year

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Policy-Related Information	**Markup**	The maximum pharmacy markup allowance calculated on the prescription drug cost is 30% for drug costs up to $6.30; 15% for drug costs between $6.31 and $15.80; 10% for drug costs of $15.81 to $200; and Maximum markup of $20 for drug costs higher than $200; For urine-testing agents, the pharmacy receives the acquisition cost along with the markup and a 50% markup in place of the dispensing fee. For insulin, the pharmacy receives the acquisition cost plus a negotiated markup.
	Ingredient Pricing Policy	Manufacturers are required to guarantee the prices of their listed products during the fiscal year (April to March). The prices published in the formulary include the maximum allowable wholesale markup. Pharmacies are required by contract to submit their actual acquisition cost of the drug, which may be less than the published formulary price. **Standing Offer Contract (SOC)** The drug plan tenders the drugs in certain interchangeable groups to obtain the lowest possible price. An accepted tender, called a SOC, requires the manufacturer to guarantee delivery of the specific drug to pharmacies through approved distributors at the contracted price. In return, the manufacturer's product will be used almost exclusively. Only the accepted tendered drug can be used to fill a prescription in a SOC-interchangeable group.
	Coordination of Benefits (Public/Private)	The drug plan is the first payer on eligible claims for eligible beneficiaries. Costs not covered by the drug plan are either sent electronically by the pharmacy or manually by the patient to the private insurance carrier (where applicable).

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Policy-Related Information	**Coordination of Benefits (Intra-Jurisdictional)**	Citizens whose health services are covered under First Nations and Inuit Health, Health Canada, Veterans Affairs Canada, Royal Canadian Mounted Police, Canadian Forces, Workers' Compensation or federal penitentiaries are not eligible for drug plan benefits under Saskatchewan Health.
	Restricted Benefit Process	**Exception Drug Status** Criteria-based coverage for drug products where regular benefit listing may not be appropriate or possible: Physicians, dentists, duly qualified optometrists (or authorized office staff), nurse practitioners, midwives and pharmacists may apply for Exception Drug Status (EDS). Requests can be submitted by telephone, mail or fax. Patients are notified by letter if coverage has been approved and the time period for which coverage has been approved. If a request has been denied, letters are sent to the patient and prescriber notifying them of the reason for the denial. For pharmacist-initiated EDS requests, the diagnosis, which must be obtained from the physician or physician's agent, is to be consistently documented within the pharmacy, whether the documentation is on the original prescription, computer file or EDS fax form.
	Reimbursement Policy	An online computer network transmits prescription information from the pharmacy to the central computer where it is checked against stored data to determine whether it can be approved for payment. The prescription claim is adjudicated and cost information is then transmitted back to the pharmacy, detailing the consumer share and drug plan share. Beneficiaries can submit claims if they have had to pay out of pocket for various reasons (system down, EDS coverage not in place at time of dispensing, etc.).

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Saskatchwan (Cont'd)		
Policy-Related Information	**Reimbursement Policy (Cont'd)**	Beneficiaries are eligible for the same drug benefits out of province as in Saskatchewan, according to Saskatchewan prices and an individual's coverage level. Original receipts for prescriptions purchased in another province or territory can be submitted to the drug plan.
	Miscellaneous	**Prescription Quantities** With some exceptions, the drug plan places no limitation on the quantities of drugs that may be prescribed. Prescribers shall exercise their professional judgment in determining the course and duration of treatment for their patients. However, in most cases, the drug plan will not pay benefits or credit deductibles for more than a three-month supply of a drug at one time. A pharmacist may charge one dispensing fee for each prescription for most drugs listed in the formulary. If a prescription is for a duration of one month or more, the pharmacist is entitled to charge a dispensing fee for each 34-day supply; however, the contract the drug plan has with pharmacies does not prohibit the pharmacist from dispensing more than a 34- day supply for one fee. The contract also contains a list of two-month and 100-day supply drugs. Prescribing and dispensing should be in these quantities once the medical therapy of a patient is in the maintenance stage, unless there are unusual circumstances that require these quantities not to be dispensed.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Manitoba		
Eligibility	**Plan/Program**	**FS03** – Employment and Income Assistance Program **NH02** – Personal Care Home/Nursing Homes **PA04** – Palliative Care Drug Access Program **PC01** – Pharmacare
	Beneficiary Group	**FS03** Individual Manitobans who are receiving drug benefits pursuant to the Employment and Income Assistance Program **NH02** Manitoba residents of personal care homes **PA04** Residents who are terminally ill and wish to remain at home **PC01** All provincial residents who are eligible for benefits under The Prescription Drugs Cost Assistance Act Persons who meet the following qualifications are designated as eligible individuals to receive benefits under the act: A person must be a resident as defined in The Health Services Insurance Act and be registered and eligible for benefits under that act; A person must be a member of a family unit whose members have, in a benefit year, collectively spent more on specified drugs than the deductible amount determined; and

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Manitoba (Cont'd)		
Eligibility (Cont'd)	**Beneficiary Group (Cont'd)**	An application to become eligible must be made to the minister by the person's family unit, and the minister must be satisfied that the members of the family unit have, in a benefit year, collectively spent more on specified drugs than the deductible amount determined. Not eligible are citizens whose health services are covered under First Nations and Inuit Health, Health Canada, Veterans Affairs Canada, Royal Canadian Mounted Police, Canadian Forces, Workers' Compensation, federal penitentiaries or private drug benefit plans as per sections 2(2) (a) and (b) in The Prescription Drugs Cost Assistance Act.
	Income Range	N/A
	Age Range	N/A
	Disease Specific	N/A
	Other Eligibility Criteria	N/A
Cost-Sharing Mechanism	**Premium**	None
	Copayment/ Co-Insurance	None
	Deductible	Income based – Annual threshold based on total adjusted family income (total adjusted family income is total annual income on line 150 of the Notice of Assessment, less $3,000 for a spouse and each eligible dependent, if applicable) **Deductible rates for adjusted family incomes for 2010–2011:** 2.69% – income between (0, $15,000] 3.82% – income between ($15,000, $21,000]

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Manitoba (Cont'd)		
Cost-Sharing Mechanism (Cont'd)	**Deductible (Cont'd)**	3.86% – income between ($21,000, $22,000] 3.92% – income between ($22,000, $23,000] 3.98% – income between ($23,000, $24,000] 4.02% – income between ($24,000, $25,000] 4.07% – income between ($25,000, $26,000] 4.11% – income between ($26,000, $27,000] 4.15% – income between ($27,000, $28,000] 4.19% – income between ($28,000, $29,000] 4.22% – income between ($29,000, $40,000] 4.59% – income between ($40,000, $42,500] 4.70% – income between ($42,500, $45,000] 4.79% – income between ($45,000, $47,500] 4.86% – income between ($47,500, $75,000] 6.08% – income more than $75,000 No deductible for people covered under the Palliative Care Drug Access Program
	Maximum Beneficiary Contribution	The maximum beneficiary contribution is based on the beneficiary deductible. Once a family's deductible has been met, all eligible drug costs are reimbursed.
Policy-Related Information	**Prescription Cost Components**	**Prescription Cost** The prescription cost is equal to the cost of the specified drug (the price of the specified drug (the price of the specified drug to the pharmacist or holder of the pharmacy license) and a professional fee (the professional fee is equal to the amount regularly charged by a pharmacist to persons who are responsible for paying the fee without reimbursement).

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Manitoba (Cont'd)		
Policy-Related Information	**Prescription Cost Components (Cont'd)**	**Lowest Cost Pricing** Benefits are based on the lowest priced interchangeable brand as listed in the formulary whether or not the specified drug is prescribed with a "no sub" or "no substitution" instruction.
	Professional Fees	The professional fee for Pharmacare is equal to the amount regularly charged by a pharmacist to persons who are responsible for paying the fee without reimbursement. The Employment and Income Assistance Program has a maximum professional fee of $6.95. Effective April 1, 2008, monthly capitation fee for personal care homes: $36.76 per bed/month for Winnipeg and $37.46 per bed/month for rural areas
	Markup	N/A
	Ingredient Pricing Policy	The specified drug as listed in the Specified Drug Regulations is equal to the cost for the lowest-priced interchangeable product prescribed in the formulary Or in any other case, the lowest usual price of the specified drug as charged from time to time by wholesalers or manufacturers that supply pharmaceuticals to pharmacists or holders of pharmacy licenses
	Coordination of Benefits (Public/Private)	For each benefit year beginning on or after April 1, the amount of the benefits payable to a family unit is the cost of specified drugs incurred collectively by the family unit in the benefit year that exceeds the deductible amount determined. A person is not considered to have spent an amount on the cost of a specified drug in the following cases: The person is entitled to be reimbursed for the cost of the specified drug from a source other than the government to the extent of the reimbursement.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Manitoba (Cont'd)		
Policy-Related Information (Cont'd)	**Coordination of Benefits (Public/Private) (Cont'd)**	The person is entitled to have the cost of the specified drug paid from a fund or pursuant to a program established under a law enacted by Parliament or a legislature in Canada or elsewhere. Citizens whose health services are covered under First Nations and Inuit Health, Health Canada, Veterans Affairs Canada, Royal Canadian Mounted Police, Canadian Forces, Workers' Compensation, federal penitentiaries or private drug benefit plans are not eligible for provincial drug plan benefits as per sections 2(2) (a) and (b) in The Prescription Drugs Cost Assistance Act.
	Coordination of Benefits (Intra-Jurisdictional)	Citizens whose health services are covered under First Nations and Inuit Health, Health Canada, Veterans Affairs Canada, Royal Canadian Mounted Police, Canadian Forces, Workers' Compensation, federal penitentiaries or private drug benefit plans are not eligible for provincial drug plan benefits as per sections 2(2) (a) and (b) in The Prescription Drugs Cost Assistance Act.
	Restricted Benefit Process	A drug or other item not listed in Part 1, or a specified drug listed in Part 2 for use in a different condition, may be considered for eligibility if It is ordinarily administered only to hospital inpatients and is being administered outside of a hospital; It is not ordinarily prescribed or administered in Manitoba but is being prescribed because it is required in the treatment of a patient having an illness, disability or condition rarely found in Manitoba; or Evidence, including therapeutic and economic evidence, provided to the minister in accordance with the criteria established by him or her, supports a specific treatment regimen which includes use of the drug or other item.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Manitoba (Cont'd)		
Policy-Related Information (Cont'd)	**Restricted Benefit Process (Cont'd)**	Process: Exception Drug Status, Part 2 – Adjudicated for payment by the DPIN system automatically if the pharmacist or prescriber indicates on the prescription that the patient meets the established Part 2 criteria Part 3 – The prescriber must contact Manitoba Health to request eligibility for prescription; eligibility is from date of approval
	Reimbursement Policy	An online computer network transmits prescription information from the pharmacy to the central computer where it is checked against stored data to determine whether the prescription can be approved for payment. The prescription information is then transmitted back to the pharmacy, detailing the customer's cost share and the drug plan cost share. The cost of a specified drug when purchased in a province or territory of Canada other than Manitoba, incurred to a maximum amount that is considered reasonable by the minister. The original receipts for prescriptions purchased in another province or territory can be submitted to the drug plan for reimbursement.
	Miscellaneous	**Prescription Quantities** In any 90-day period, no benefit is payable for more than the following number of days' supply (number of days' supply of a specified drug is equal to the quantity of the specified drug dispensed divided by the person's daily dosage requirements for that drug) of a specified drug: –100; and Up to an additional 100, if - the prior approval of the minister has been obtained; and - the person will be outside of Canada for more than 90 consecutive days.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Ontario		
Eligibility	**Plan/Program**	**Ontario Drug Benefit Program (ODB)** **Trillium Drug Program** **Special Drugs Program** **New Drug Funding Program for Cancer Care**
	Beneficiary Group	**Ontario Drug Benefit Program (ODB)** Drug benefits for Ontarians age 65 or older, residents of long-term care homes and homes for special care, recipients of professional home services and social assistance, and recipients of the Trillium Drug Program **Trillium Drug Program** Drug benefits for Ontario residents who have high drug costs in relation to their household income; any Ontario resident who does not qualify under any of the other plans can apply for the Trillium Drug Program **Special Drugs Program** Drug benefits for Ontarians with a valid health card for certain expensive outpatient drugs used to treat specific diseases or conditions **New Drug Funding Program for Cancer Care** Drug benefits for newer, intravenous drugs, typically administered in hospitals and cancer care facilities; the ministry provides about 75% of the overall funding for intravenous cancer drugs in Ontario and hospitals fund the remaining 25% through their operating budgets
	Income Range	N/A
	Age Range	N/A

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Ontario (Cont'd)		
Eligibility (Cont'd)	**Disease Specific**	Special Drugs Program covers specific drugs for Cystic fibrosis and thalassemia; HIV; Erythropoietin (EPO) for end-stage renal disease; Cyclosporine for solid organ or bone marrow transplant; Human growth hormone for children with growth failure; Clozapine for treatment of schizophrenia; and Alglucerase for people with Gaucher's Disease
	Other Eligibility Criteria	N/A
Cost-Sharing Mechanism	**Premium**	None
	Copayment/ Co-Insurance	ODB recipients pay up to $2 per prescription (copayment) if they are –A senior single person with an annual net income of less than $16,018; – A senior couple with acombined annual net income of less than $24,175; – Receiving benefits under the Ontario Works Act or the Ontario Disability Support Program Act; – Receiving professional services under the Home Care Program; – Residents of long-term care facilities and homes for special care; or – Eligible under the Trillium Drug Program. ODB recipients each pay their first annual $100 (that is, prorated deductible based on number of months) in prescription costs each year. After that, they pay up to $6.11 (copayment) toward the ODB dispensing fee on each prescription if they are – A senior single person with an annual net income equal to or greater than $16,018; or – A senior couple with a combined annual net income equal to or greater than $24,175.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Ontario (Cont'd)		
Cost-Sharing Mechanism (Cont'd)	**Copayment/ Co-Insurance (Cont'd)**	The Ontario Drug Benefit (ODB) Program benefit year runs from August 1 to July 31 of the following year. Copayment of $2.83 for prescriptions dispensed in outpatient hospital pharmacies
	Deductible	$100 deductible for Single seniors (65 or older) with annual income of $16,018 or more Senior couples with acombined a nnual income of $24,175 or more Trillium Drug Program applicants must pay a quarterly or prorated deductible that is based on income No deductible for other ODB-eligible people
	Maximum Beneficiary Contribution	N/A
Policy-Related Information	**Prescription Cost Components**	Drug benefit price (DBP) + markup + professional fee Effective March 2007: Cost-to-operator claims are restricted to cases where a pharmacy is unable to acquire an interchangeable generic product and must dispense the original product or an interchangeable generic product with a higher drug benefit price.
	Professional Fees	The maximum dispensing fee is $7. Effective August 1, 2008: Dispensing fee shall be set at a maximum of two fees per medication per patient per month; exceptions are for patients in long-term care homes and/or drugs in exemption medication list Effective April 2007: Introduction of professional allowance for a medication review program, MedsCheck; residents of Ontario with three or more chronic conditions are eligible to receive annual MedsCheck reviews; followup MedsCheck reviews were introduced in November 2007

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Ontario (Cont'd)		
Policy-	**Markup**	Maximum 8% where permitted
Related Information (Cont'd)	**Ingredient Pricing Policy**	Since October 2006, through implementation of the Transparent Drug System for Patients Act (Bill 102), the OPDP may enter into listing agreements with manufacturers. Before a product is approved for listing, the ministry and the manufacturer must agree on its drug benefit price (DBP). The price of multiple-source drugs must be at no more than 50% of the original brand product. Price increases may be considered for drug products that have been listed on the formulary as a benefit under the Ontario Drug Benefit (ODB) Program for at least five years and where the manufacturer is able to submit evidence of substantial raw material cost increases during the previous year. When a pharmacy is not able to purchase a formulary-listed drug at a price less than or equal to its OPDB reimbursement mount (that is, the drug benefit price + 8% markup), payment of the acquisition cost to the pharmacy of the least-expensive listed drug product in the pharmacy's inventory may be claimed. This is referred to as a "costto-operator" (CTO) claim. CTO claims may be submitted for eligible drug products only.
	Coordination of Benefits (Public/Private)	Claims for seniors with both private insurance and public provincial coverage are processed under their provincial plan first. Individuals or families can apply to the Trillium Drug Program if private insurance does not cover 100% of their prescription drug costs and if they are not eligible for drug coverage under the ODB program.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Ontario (Cont'd)		
Policy-Related Information (Cont'd)	**Coordination of Benefits (Intra-Jurisdictional)**	A person cannot be on more than one provincial public drug plan at the same time.
	Restricted Benefit Process	**Limited-Use Products** limited-use (LU) prescription forms are no longer required from the physician. LU prescriptions now require a reason-for-use (RFU) code to be handwritten on the prescription or provided electronically or verbally by the physician. The LU prescription is valid for one year from the initial date unless otherwise stated in the LU note. **Exceptional Access (EAP)** To apply for special coverage for drug products not listed on the formulary, the physician must send a written request to the Drug Programs Branch. Ministry staff coordinates the review process, which includes obtaining a recommendation from the Committee to Evaluate Drugs (CED). The CED requires full details of an individual's case in order to make a recommendation. The ministry's decision on individual coverage in a particular patient's case will be communicated via letter to the physician making the request. If coverage is approved, the physician may provide a copy of the approval notice for the patient to take to the pharmacy. Effective November 27, 2008, EAP introduced a Telephone Request Service (TRS) for select drugs. In most cases, the requests will be assessed in real time. Requests for approximately 40 drugs for specific, often urgent, indications will be considered. Requests for drugs/indications not currently considered through TRS should apply via written request.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Ontario (Cont'd)		
Policy-Related Information (Cont'd)	**Reimbursement Policy**	Claims are only reimbursed when dispensed from an Ontario pharmacy, written by a physician licensed in Ontario and the recipient is an eligible Ontario resident. If patients meet all the above criteria and pay cash at the pharmacy, they may submit receipts for reimbursement to the Ontario Drug Program.
	Miscellaneous	**Prescription Quantities** The normal quantity dispensed shall be the entire quantity of the drug prescribed. The maximum quantity that may be charged under the ODB program must not exceed that required for a 100-day course of treatment. Beginning November 14, 2002, the 30-Day Prescription Program was implemented by ODB. All new prescriptions for ODB recipients are subjected to a 30-day maximum prescription limit if they have not been taken in the preceding 12 months. If the newly prescribed drug helps a patient after the initial 30-day supply and the patient is not having any problems with it, the remainder of the prescription can be dispensed up to the maximum 100-day supply. Some recipients are exempt from this program (that is, travel out of province for extended periods, samples from physician, insulin prescriptions). For recipients covered under the Ontario Works Act, the maximum quantity of medication claimed under the ODB program must not exceed that required for a 35-day course of treatment.
New Brunswick		
Eligibility	**Plan/Program**	A–Seniors Program B–Cystic Fibrosis E–Adults in Licensed Residential Facilities F–Department of Social Development

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

New Brunswick (Cont'd)		
Eligibility (Cont'd)	**Plan/Program (Cont'd)**	G–Children in the Care of the Minister of Social Development H–Multiple Sclerosis R–Organ Transplant T–Human Growth Hormone Deficiency U–HIV/AIDS V–Nursing Home
	Beneficiary Group	A–Seniors who receive the Guaranteed Income Supplement (GIS) or who qualify for benefits based on an annual income as follows: – A single senior with an annual income of $17,198 or less; – A senior couple (both age 65 or older) with a combined annual income of $26,955 or less; or – A senior couple with one spouse younger than 65 with a combined annual income of $32,390 or less. B–Cystic fibrosis patients or patients with juvenile or infant sclerosis of the pancreas E–Individuals residing in a licensed adult residential facility who hold a valid health card for prescription drugs issued by the Department of Social Development F–Individuals holding a valid health card for prescription drugs issued by the Department of Social Development G–Special needs children and children under the care of the Minister of Social Development H–Residents in possession of a prescription written by a neurologist for the medications Avonex, Rebif, Betaseron or Copaxone are eligible to apply for assistance

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

New Brunswick (Cont'd)		
Eligibility (Cont'd)	**Beneficiary Group (Cont'd)**	R–Recipients of an organ or bone marrow transplant who are registered with and qualify for the NBPDP T–Individuals with growth hormone deficiency or hypopituitarism who are registered with and qualify for the NBPDP U–Individuals diagnosed with HIV/AIDS and who are registered with the NBPDP through a provincial infectious disease specialist V–Individuals who reside in a registered nursing home
	Income Range	A–For seniors without the Guaranteed Income Supplement (GIS): single senior with an annual income of $17,198 or less; senior couple (both age 65 or older) with a combined annual income of $26,955 or less; or senior couple with one spouse younger than 65 with a combined annual income of $32,390 or less
	Age Range	A–65 or older
	Disease Specific	B–Cystic fibrosis or juvenile or infant sclerosis of the pancreas C–H1N1 influenza H–Multiple sclerosis R–Organ transplant T–Human growth hormone U–HIV/AIDS
	Other Criteria	N/A
Cost-Sharing Mechanism	**Premium**	B–$50 yearly registration fee H–$50 yearly registration fee R–$50 yearly registration fee T–$50 yearly registration fee U–$50 yearly registration fee

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

New Brunswick (Cont'd)		
Cost-Sharing Mechanism (Cont'd)	**Copayment/ Co-insurance**	A–Seniors with GIS: $9.05 for each prescription, up to a maximum of $250 in one calendar year; seniors without GIS: $15 per prescription B–20% of the costs for each prescription up to a maximum of $20 E–$4 for each prescription F–$4 for each prescription for adults (18 or older) and $2 for children (younger than 18) H–Ranges from zero to 100% of the prescription cost, depending on discretionary income; the copay is determined annually during the re-qualification period R–20% of the costs for each prescription up to a maximum of $20 T–20% of the costs for each prescription up to a maximum of $20 U–20% of the costs for each prescription up to a maximum of $20
	Deductible	None
	Maximum Beneficiary Contribution	A–Seniors with the Guaranteed Income Supplement (GIS): $250 in one calendar year B–$500 per family unit in one fiscal year + premium (see above) E–$250 per person in a fiscal year F–$250 per family unit in a fiscal year R–$500 per family unit in a fiscal year + premium (see above) T–$500 per family unit in one fiscal year + premium (see above) U–$500 per family unit in one fiscal year + premium (see above)
Policy-Related Information	**Prescription Cost Components**	Actual acquisition cost (AAC) or maximum allowable price (MAP) + dispensing fee

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

New Brunswick (Cont'd)				
Policy-Related Information (Cont'd)	**Professional Fees**	**Ingredient Cost/ Prescription**	**Dispensing Fee**	**Dispensing Fee for Compounds**
		$0.00–$99.99	$9.40	$14.10
		$100.00–$199.99	$11.90	$17.85
		$200.00–$499.99	$17.00	$18.00
		$500.00–$999.99	$22.00	$22.00
		$1,000.00–$1,999.99	$62.00	$62.00
		$2,000.00–$2,999.99	$82.00	$82.00
		$3,000.00–$3,999.99	$102.00	$102.00
		$4,000.00–$4,999.99	$122.00	$122.00
		$5,000.00–$5,999.99	$142.00	$142.00
		Greater Than or Equal to $6,000.00	$162.00	$162.00
		Note: Dispensing physicians are reimbursed 80% of the applicable fee listed in the above table.		
	Markup	None		
	Ingredient Pricing Policy	The NB Prescription Drug Program MAP list establishes the maximum amount payable to pharmacies for interchangeable and certain single-source drugs.		
	Coordination of Benefits (Public/Private)	N/A		

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

New Brunswick (Cont'd)		
Policy-Related Information (Cont'd)	**Coordination of (Intra-Jurisdictional)**	N/A
	Restricted Benefit Process	Drugs not listed as regular benefits may be eligible for reimbursement under New Brunswick Prescription Drug Program (NBPDP) through special authorization. Drugs eligible for consideration through special authorization: Drugs listed as special authorization benefits have specific criteria for coverage which must be met in order to be approved Under exceptional circumstances, requests for drugs without specific criteria may be reviewed case-by-case and assessed based on the published medical evidence Drugs not eligible for consideration through special authorization: New drugs not yet reviewed by the expert advisory committee Drugs excluded as eligible benefits further to the expert advisory committee's review and recommendation Drugs not licensed or marketed in Canada (for example, drugs obtained through Health Canada's Special Access Programme) Products specifically excluded as benefits as identified on the exclusion list Special authorization requests must be submitted in writing by a prescriber to the NB Prescription Drug Program Special Authorization Unit.
	Reimbursement Policy	If a beneficiary pays out of pocket, he or she may submit the claim for coverage if it is a benefit product and was purchased at a pharmacy within New Brunswick.
	Miscellaneous	**Prescription Quantities** 100 days' supply/35 days' supply for narcotics, controlled drugs and benzodiaze -pines or the limit as set for specific medications by the NBPDP Quantitative limits established for a number of products listed as benefits.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Nova Scotia		
Eligibility	**Plan/Program**	A–Family Pharmacare Program C–Drug Assistance for Cancer Patients D–Nova Scotia Diabetes Assistance Program F–Department of Community Services Programs S–Seniors Pharmacare Program
	Beneficiary Group	A–Families, including families of one, who apply for the program; any permanent Nova Scotia resident with a valid Nova Scotia health card number is eligible to enrol; must not have coverage through Department of Community Services Programs, Seniors Pharmacare, Diabetes Assistance Program or 65 Long-Term Care Pharmacare Plan C–Permanent Nova Scotia residents with a valid Nova Scotia health card number who have a gross family income no greater than $15,720 per year and are not eligible for coverage under other drug programs, except Family Pharmacare D–Permanent Nova Scotia residents with a valid Nova Scotia health card number younger than age 65 who have a confirmed diagnosis of diabetes and who do not have drug coverage through Veterans Affairs Canada, First Nations and Inuit Health, Nova Scotia Family Pharmacare or any other drug insurance plan for medications and supplies for diabetes F–Eligible clients and their dependents in receipt of income assistance who do not have access to another drug plan, be it from a public or private entity S–Permanent Nova Scotia residents who are age 65 or older with a valid Nova Scotia health card number and who do not have drug coverage through Veterans Affairs Canada, Non-Insured Health Benefits, NS Family Pharmacare or any other public or private plan that covers most medications and supplies after age 65

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Nova Scotia (Cont'd)		
Eligibility (Cont'd)	**Income Range**	A–No income-based criteria for eligibility; however, family deductible is based on income; see section on deductible C–Gross family income no greater than $15,720 D–No income-based criteria for eligibility; however, deductible is based on income; see section on deductible F–As determined by Department of Community Services S–No income-based criteria for eligibility, however, premium is based on income; see section on premium
	Age Range	A–No age range criteria for eligibility; all adults (age 18 or older) must register as their own family C–Younger than 65 D–Younger than 65 F–Younger than 65 S–65 or older
	Disease Specific	C–Cancer D–Diabetes
	Other Eligibility Criteria	A–Family members must agree to provide family size information and annual family income verification through Canada Revenue Agency (CRA) D–Residents must agree to provide family size information and to allow family income verification through Canada Revenue Agency (CRA)
Cost-Sharing Mechanism	**Premium**	For Program A/C/D/F: no premium S–No premium for people who receive the GIS; for those who do not receive the GIS, they must pay a premium of up to $424 a year; some low-income seniors who do not get the GIS may qualify for reduced premiums

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Nova Scotia (Cont'd)		
Cost-Sharing Mechanism (Cont'd)	**Copayment/ Co-insurance**	A–20% copayment with annual copayment maximum; annual family copayment maximum based on adjusted family income C–No copayment D–20% of the total prescription cost F–$5 per prescription unless the client or dependent is eligible for copayment exemption S–30% of the total prescription cost (minimum of $3 per prescription); maximum annual copayment of $382
	Deductible	A–Annual family deductible is a sliding scale percentage based on adjusted family income C–No deductible D–Annual deductible is a sliding scale percentage based on adjusted family income F–No deductible S–No deductible
	Maximum Beneficiary Contribution	A–Annual family copayment plus annual family deductible S–Annual maximum copayment of $382 + premium (see above)
Policy-Related Information	**Prescription Cost Components**	Actual acquisition cost (AAC) or maximum allowable cost (MAC), MAC Less the Pharmacare Allowance, or Special MAC + 2% markup (from Apr. 1, 2009, to Mar. 31, 2010, to a maximum of $50 perprescription) + applicable professional fee (to a maximum of $10.42). In the case of injectable products (except insulin) and ostomy supplies: AAC or, where applicable, MAC or Special MAC + 10% markup (to a maximum of $250 per prescription) + applicable professional fee (to a maximum of $10.42)

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Nova Scotia (Cont'd)		
Policy-Related Information (Cont'd)	**Professional Fees**	For prescriptions the maximum fee is $10.42
	Markup	10% for injectable products and ostomy supplies and 2% for all other prescriptions
	Ingredient Pricing Policy	Actual acquisition cost (AAC) means the net cost to the provider after deducting all rebates, allowances, free products, etc. No markup or buying profit is to be included in the calculation of AAC. The net cost to the provider is defined as the drug ingredient (or supply) costs based on date of purchase and inventory flow, even though the current prices available may be lower or higher when the product is dispensed. Incentives for prompt payment (payment within 15 days up to a maximum of 2%) will not be included in the calculation. MAC is the maximum allowable cost established by the Pharmacare programs for an interchangeable drug category. A MAC price is applied to those drugs which are Pharmacare benefits, have multiple suppliers and have been deemed interchangeable (for example, brand name drugs and their generic equivalents). For each interchangeable category, a maximum allowable cost per unit (tablet, capsule, millilitre, etc.) is determined by examining costs available from each manufacturer. The MAC is based on the lowest price available to the pharmacy, including prices available from direct ordering if the manufacturer is a direct order company. Exemptions to a MAC are available for beneficiaries who have experienced side effects with lower-cost alternatives. A request must be received from the prescriber detailing the reaction. Exemptions will not be considered when there is an "ultrageneric" alternative available (that is, where the brand name company manufacturers its own identical generic). MAC Less the Pharmacare Allowance is a discount from the MAC of the top 20 (by cost) interchangeable, multi-source, generic categories billed to the

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Nova Scotia (Cont'd)		
Policy-Related Information (Cont'd)	**Ingredient Pricing Policy (Cont'd)**	Pharmacare programs. The product categories to which the Pharmacare Allowance applies are updated twice a year with the Pharmacare Reimbursement List and are based on the utilization over the six months previous to the Reimbursement List calculations. The Pharmacare Allowance pursuant to the Tariff Agreement is 15%, effective August 15, 2007. Special MAC is the special maximum allowable cost assigned to certain groups of drugs that are similar in therapeutic effect; specific services for which coverage is established; certain unit dose and special delivery formats that are also available in less expensivebulk formats; and certain supplies that are used for the same function.
	Coordination of Benefits (Public/Private)	A–Program is payer of last resort. Any out-of-pocket costs to client after private plans are used can be applied to Family Pharmacare. S–If the copayments a senior pays to his or her private insurance exceed the amount of the annual maximum premium plus the annual maximum copayment he or she would have paid if enrolled in Seniors Pharmacare, he or she may request a reimbursement of the difference. See Eligibility–Beneficiary Group above for coordination of benefits
	Coordination of Benefits (Intra-Jurisdictional)	A–Program is payer of last resort. Any out-of-pocket costs to client after private plans are used can be applied to Family Pharmacare. See Eligibility–Beneficiary Group above for coordination of benefits.
	Restricted Benefit Process	Exception Status Drugs are those which are only eligible for coverage under the Pharmacare programs when an individual meets criteria developed by the Atlantic or Canadian Expert Advisory Committees or the Cancer Systemic Therapy Policy Committee (CSTPC).

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Nova Scotia (Cont'd)		
Policy-Related Information (Cont'd)	**Restricted Benefit Process (Cont'd)**	To request coverage, the physician should mail or fax a completed standard request form or letter to the Pharmacare office. Physicians may also contact the Pharmacare office and speak directly to a pharmacist consultant to request coverage. Every effort is made to process requests within seven days. A letter notifies clients if the request is approved. Clients may bring this letter to the pharmacy to verify that coverage has been approved or the pharmacist may simply bill the claim online for immediate response for a limited list of products. The physician is notified if coverage is authorized, if the request is refused because the criteria for coverage are not met or if more information is required. Selected exception status drugs can be billed online without prior approval if criteria codes are provided during the billing process. For most of the drugs that canbe billed using criteria codes, the criteria codes are supplied directly by an authorized prescriber. By supplying a code, the prescriber is verifying that he or she is prescribing the drug for an indication approved under the Pharmacare programs. The prescriber may provide diagnostic information on the prescription (instead of the actual code) but it must clearly indicate to the pharmacist which code should be used.
	Reimbursement Policy	If beneficiary paid cash at the pharmacy he or she has up to six months from date of purchase to send original receipts to Pharmacare for reimbursement. Prescriptions filled at a pharmacy outside Nova Scotia, but inside Canada, will be reimbursed in medical emergencies only. There is no reimbursement, emergency or otherwise, for prescriptions filled outside Canada.
	Miscellaneous	**Prescription Quantities** 100 days' supply maximum, if prescribed

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Nova Scotia (Cont'd)		
Policy-Related Information (Cont'd)	**Miscellaneous (Cont'd)**	Seniors Pharmacare Program beneficiaries travelling outside the province for more than 100 days will be allowed to obtain two prescriptions for the same medication before leaving Nova Scotia. Neither prescription shall exceed a 90 days' supply (maximum 180 days' supply for the two prescriptions). The usual copayment and professional fee will apply to each of the prescriptions. There is a 28-day minimum supply for maintenance medications.
Prince Edward Island		
Eligibility	**Plan/Program**	A–AIDS/HIV Program B–Community Mental Health Program C–Cystic Fibrosis Program D–Diabetes Control Program E–Erythropoietin Program F–Family Health Benefit Program G–Growth Hormone H–Hepatitis Program I–Immunization Program J–Intron A (Interferon alfa-2b) Program K–Meningitis Program M–High-Cost Drug Program N–Institutional Pharmacy/Nursing Home Program O–Nutrition Services Program P–Phenylketonuria (PKU) Program R–Rabies Program S–Seniors Drug Cost Assistance Plan

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Prince Edward Island (Cont'd)		
Eligibility (Cont'd)	**Plan/Program (Cont'd)**	T–Transplant Program U–Rheumatic Fever Program V–Sexually Transmitted Diseases (STD) Program W–Children-In-Care/Financial Assistance Program X–Tuberculosis (TB) Drug Program Z–Quit Smoking Program
	Beneficiary Group	A–Persons diagnosed as HIV positive, diagnosed with AIDS or with a needlestick injury and registered with the program through the chief health officer B–Approved long-term psychiatric patients living in the community C–Persons eligible for P.E.I. Medicare, diagnosed with cystic fibrosis and who are registered with the program D–Persons eligible for P.E.I. Medicare, diagnosed with diabetes and registered with the program E–Persons eligible for P.E.I. Medicare, diagnosed with chronic renal failure or receiving kidney dialysis and registered with the program F–Families (parents, guardians and children younger than 18 or younger than 25 and in full-time attendance at a postsecondary educational institution), eligible for P.E.I. Medicare with a total net family income less than the threshold (see Income Range section below); families must apply for coverage on an annual basis and provide income information to the program G–Children eligible for P.E.I. Medicare with a proven growth hormone deficiency or Turner Syndrome and who are registered with the program H–Persons diagnosed with hepatitis; persons who have been in close contact with a person diagnosed with hepatitis or are at risk of infection; persons with an occupational risk of infection

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Prince Edward Island (Cont'd)		
Eligibility (Cont'd)	**Beneficiary Group (Cont'd)**	I–Children and persons at risk for exposure to various communicable diseases J–For the treatment of patients diagnosed with hairy cell leukemia, AIDSrelated Kaposi's sarcoma and basal cell carcinoma; the person's physician must request coverage from the chief health officer of the Department of Health and Social Services K–Persons who have been in close contact with a person diagnosed with meningitis or are at risk of infection M–Persons eligible for P.E.I. Medicare and approved for coverage of one or more of the medications included in the program; patients must apply for coverage on an annual basis and provide income information to the program N–Residents in government manors or private nursing homes eligible for coverage under the Long-Term Care Subsidization Act O–High-risk pregnant women diagnosed with a nutritional deficiency P–Persons eligible for P.E.I. Medicare, diagnosed with phenylketonuria and registered with the program R–Persons with exposure to or at risk for exposure to rabies through an animal bite S–Persons eligible for P.E.I. Medicare and age 65 or older T–Persons eligible for P.E.I. Medicare, who have had an organ or bone marrow transplant and are registered with the program U–Persons eligible for P.E.I. Medicare and who have a well-documented history of rheumatic fever or rheumatic heart disease and are registered with the program V–Persons diagnosed with a sexually transmitted disease or identified contacts of a person diagnosed with a sexually transmitted disease W–Persons eligible under the Social Assistance Act and persons in the temporary or permanent care of the director of child welfare

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Prince Edward Island (Cont'd)		
Eligibility (Cont'd)	**Beneficiary Group (Cont'd)**	X–Patients must have a diagnosis of tuberculosis confirmed by the chief health officer of the Department of Health and Social Services Z–Persons eligible for P.E.I. Medicare and who have registered with the program
	Income Range	F–Family Health Benefit Program: 1 Child with Net Annual Family Income less than $24,800 2 Children with Net Annual Family Income less than $27,800 3 Children with Net Annual Family Income less than $30,800 4 Children with Net Annual Family Income less than $33,800 More than 4 children, add $3,000 per additional child to Net Annual Family Income M–Prescription copay is based upon total net family income
	Age Range	G–younger than 18 S–65 or older
	Disease Specific	A–AIDS/HIV; B–Mental health; C–Cystic fibrosis; D–Diabetes; G–Growth hormone; H–Hepatitis; I–Immunization; J–Intron A (Interferon alfa-2b); K–Meningitis; M–High-cost drugs; P–Phenylketonuria (PKU); R–Rabies; T–Transplant; U–Rheumatic; V–Sexually transmitted diseases (STDs); X–Tuberculosis (TB)
	Other Eligibility Criteria	N/A
Cost-Sharing Mechanism	**Premium**	None
	Copayment/ Co-insurance	D–Insulin: $10 per 10 mL vial of insulin or box of 1.5 mL insulin cartridges; $20 per box of 3 mL insulin cartridges; Blood Glucose Test strips: $11 per prescription to a maximum of 100 strips every 30 days

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Prince Edward Island (Cont'd)		
Cost-Sharing Mechanism (Cont'd)	**Copayment/ Co-insurance (Cont'd)**	Oral medications and urine-testing materials: $11 per prescription High-cost diabetes medications: An incomebased portion of the medication plus the professional fee for each high-cost medication obtained F–The pharmacy professional fee per prescription M–Income-based portion of the drug plus the pharmacy professional fee for each prescription S–First $11 of the medication cost plus the pharmacy professional fee for each prescription; reducing to $8.25 as of September 1, 2010 Z–Patients are responsible for all medication costs approved, except for the first $75, which will be paid by the program
	Deductible	None
	Maximum Beneficiary Contribution	N/A
Policy-Related Information	**Prescription Cost Components**	Maximum allowable cost (MAC) + professional fee Where no MAC exists the cost is based upon the manufacturer's net catalogue price and professional fee for manufacturers defined as direct. If the manufacturer is not defined as direct, the cost is the manufacturer's net catalogue price plus a markup to a maximum of 13% plus the professional fee.
	Professional Fees	The professional fees for the Children in Care, Diabetes (oral medications and test strips only), Financial Assistance, Quit Smoking and STD programs is $8.20 for prescription drugs, $7.96 for non-prescription drugs and $12.30 for extemporaneous compounds.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Prince Edward Island (Cont'd)		
Policy-Related Information (Cont'd)	**Professional Fees (Cont'd)**	The surcharge for the Family Health Benefit, Nursing Home and Seniors programs for medications with defined ingredient cost equal to or greater than $45 is 9.5% to a maximum of $60. The high-cost drug surcharge for MS drugs and other high-cost drugs is 7.5% of defined ingredient cost to a maximum of $150. The monthly capitation fee for the Nursing Home Program is $51.59. There is no maximum fee on all the other programs
	Markup	See Prescription Cost Components and Ingredient Pricing Policy
	Ingredient Pricing Policy	P.E.I. Drug Programs creates a maximum allowable cost (MAC) list, which is published and distributed to pharmacies on a monthly basis. For products with a MAC, the ingredient cost is based on the manufacturer's net catalogue price of the lowest product within an interchangeable category plus a markup to a maximum of 5%. Where no MAC exists and the manufacturer is defined as being direct, the cost is based upon the manufacturer's net catalogue price. If there is no MAC and the manufacturer is not defined as direct, the cost is based upon the manufacturer's net catalogue price plus a markup to a maximum of 13%.
	Coordination of Benefits (Public/Private)	N/A
	Coordination of Benefits (Intra-Jurisdictional)	N/A
	Restricted Benefit Process	Prescribers may apply for special authorization coverage by mailing or faxing a completed special authorization form.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Prince Edward Island (Cont'd)		
Policy-Related Information (Cont'd)	**Restricted Benefit Process (Cont'd)**	Allow two to four weeks for the processing of exceptional drug requests. A letter will be sent notifying the patient and prescriber if coverage has been approved. If the request is denied, letters are sent to the patient and prescriber notifying them of the reason for the denial. Payment of the medication is the responsibility of the patient in these cases. If the request is approved, patients may be reimbursed for one fill of the prescription received during the assessment period after all of the requested information has been received.
	Reimbursement Policy	If a beneficiary paid cash at the pharmacy he or she has six months to submit receipts for reimbursement.
	Miscellaneous	**Program Maximum Allowable Days' Supply** Nursing Home Program: 35 days Institutional Pharmacy Program: 35 days AIDS/HIV Program: 60 days Children-In-Care Program: 30 days-regular drugs; 60 days-maintenance drugs Note: Prescriptions introducing a medication, strength, dosage or dosage form shall be filled for a maximum of 30 days for the first two prescriptions or refills. Cystic Fibrosis Program: 60 days Diabetes Control Program: 30 days-insulin, 100 blood glucose test strips; 90 days-oral medications and test strips Note: Prescriptions introducing a medication, strength, dosage or dosage form shall be filled for a maximum of 30 days for the first two prescriptions or refills.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Prince Edward Island (Cont'd)		
Policy-Related Information (Cont'd)	**Miscellaneous (Cont'd)**	Family Health Benefit Program: 30 days-regular drugs; 60 days-maintenance drugs; 30 days-drugs under EDS coverage Note: Prescriptions introducing a medication, strength, dosage or dosage form shall be filled for a maximum of 30 days for the first two prescriptions or refills. Financial Assistance Program: 30 days-regular drugs; 60 days-maintenance drugs; 30 days-drugs under EDS coverage Note: Prescriptions introducing a medication, strength, dosage or dosage form shall be filled for a maximum of 30 days for the first two prescriptions or refills. Growth Hormone Program: 30 days Hepatitis Program: 30 days Intron A Program: 30 days Multiple Sclerosis Drug Program: 30 days Phenylketonuria Program: 60 days Rheumatic Fever Program: 60 days Seniors Drug Cost Assistance Plan: 30 days-regular drugs; 90 days-maintenance drugs; 30 days-drugs under EDS coverage. Note: Prescriptions introducing a medication, strength, dosage or dosage form shall be filled for a maximum of 30 days for the first two prescriptions or refills. Transplant Drugs Program: 60 days Tuberculosis Drug Program: 60 days
Newfoundland and Labrador		
Eligibility	**Plan/Program**	The Foundation Plan (Previously Income Support Drug Program or plan E) The Access Plan (Previously Low Income Drug Program or plan L) The 65Plus Plan (Previously Senior Citizen's Drug Subsidy Plan or plan N)

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Newfoundland and Labrador (Cont'd)		
Eligibility (Cont'd)	**Plan/Program (Cont'd)**	The Assurance Plan (plan H) The Select Needs Plan
	Beneficiary Group	**The Foundation Plan** provides 100% coverage of eligible prescription drugs for those who need the greatest support. This includes persons and families in receipt of income support benefits through the Department of Human Resources, Labour and Employment, and certain individuals receiving services through the regional health authorities, including children in the care of Child, Youth and Family Services and individuals in supervised care. **The Access Plan** offers individuals and families with low incomes access to eligible prescription medications. The amount of coverage is determined by net income level and family status (see Income Range section). **The 65Plus Plan** provides coverage for eligible prescription drugs to residents age 65 or older who receive Old Age Security benefits and the Guaranteed Income Supplement (GIS). **The Assurance Plan** offers protection for individuals and families against the financial burden of eligible high drug costs, whether it be from the cost of one extremely high-cost drug or the combined cost of different drugs. **The Select Needs Plan** provides 100% coverage for disease-specific medications and supplies for residents with cystic fibrosis and growth hormone deficiency.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Newfoundland and Labrador (Cont'd)		
Eligibility (Cont'd)	**Income Range**	**The Access Plan:** Families with children, including single parents: net annual incomes of $30,000 or less Couples without children with net annual incomes of $21,000 or less Single individuals with net annual incomes of $19,000 or less **The Assurance Plan** maximum out of pocket is based on the following net income ranges: –Up to $39,999 –$40,000 to $74,999 –$75,000 to $149,999
	Age Range	The 65Plus Plan for those age 65 or older The Select Needs Plan for beneficiaries with growth hormone deficiency age 18 or younger
	Disease Specific	The Select Needs Plan– Cystic fibrosis and growth hormone deficiency
	Other Criteria	N/A
Cost-Sharing Mechanism	**Premium**	None
	Copayment/ Co-insurance	The 65Plus Plan–Markup and professional fee The Access Plan– Copayments are based on income as follows: Families (With Children) Copay: 20% for Income less than $21,000 Copay: 25.6% for Income less than $22,000 Copay: 31.1% for Income less than $23,000 Copay: 36.7% for Income less than $24,000 Copay: 42.2% for Income less than $25,000

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Newfoundland and Labrador (Cont'd)		
Cost-Sharing Mechanism (Cont'd)	**Copayment/ Co-insurance (Cont'd)**	Copay: 47.8% for Income less than $26,000 Copay: 53.3% for Income less than $27,000 Copay: 58.9% for Income less than $28,000 Copay: 64.4% for Income less than $29,000 Copay: 70.0% for Income less than $30,000 Couples (With No Children) Copay: 20.0% for Income less than $15,000 Copay: 28.3% for Income less than $16,000 Copay: 36.7% for Income less than $17,000 Copay: 45.0% for Income less than $18,000 Copay: 53.3% for Income less than $19,000 Copay: 61.7% for Income less than $20,000 Copay: 70.0% for Income less than $21,000 Single Individuals Copay: 20.0% for Income less than $13,000 Copay: 28.3% for Income less than $14,000 Copay: 36.7% for Income less than $15,000 Copay: 45.0% for Income less than $16,000 Copay: 53.3% for Income less than $17,000 Copay: 61.7% for Income less than $18,000 Copay: 70.0% for Income less than $19,000 The Assurance Plan–Beneficiaries can have a copayment between 0% and 99%

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Newfoundland and Labrador (Cont'd)		
Cost-Sharing Mechanism (Cont'd)	**Deductible**	None
	Maximum Beneficiary Contribution	The Assurance Plan maximums are based on net income as follows: Max: 5.0% for Net Income up to $39,999 Max: 7.5% for Net Income between $40,000 and $74,999 Max: 10.0% for Net Income between $75,000 and $149,999
Policy-Related Information	**Prescription Cost Components**	Total prescription price = (defined cost) + (up to the maximum professional fee) + (up to the maximum surcharge) **Defined Cost** Products listed in the NIDPF will be the published price. Products specified under reasonable-based pricing will be the lesser of the reasonable-based pricing published price or manufacturer's list price (MLP) plus 8.5%. Extemporaneous preparations will be the MLP plus 8.5% for each covered product used in the extemporaneous preparation. All other cases (except methadone) will be MLP plus 8.5%. Methadone, when used for the purposes of addiction only and billed under the specific PIN 967211, shall have a defined cost set at $1.50 per dose for the duration of the agreement (July 10, 2007, to March 31, 2011).
	Professional Fees	Professional Fee $7.15 from January 1, 2008, to March 31, 2011 Extemporaneous Preparations Fee $10.73 from January 1, 2008, to March 31, 2011 This applies to compounds that contain three or more ingredients. Additionally, 10 cents per powder paper will be paid on compounded prescriptions where the pharmacist compounds powder papers.
	Markup	Maximum Surcharge 10% of the defined cost (chargeable only when the defined cost exceeds $30)

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Newfoundland and Labrador (Cont'd)		
Policy-Related Information (Cont'd)	**Ingredient Pricing Policy**	As of July 10, 2007, there are no longer three definitions for manufacturer up-charge: direct, wholesale and tendered wholesale price. Reimbursement will be as noted under defined cost. Diabetic supplies and insulin will no longer be reimbursed at a 33 1/3% markup. Reimbursement will be as noted under defined cost. Birth control fee will be reimbursed at the maximum professional fee as noted above, instead of the previous $4.10.
	Coordination of Benefits (Public/Private)	**The Foundation Plan** Private insurers must be billed first. Government will pay the balance provided it does not exceed the cost government would have paid if there was no private insurance. **The Access Plan** Private insurers must be billed first. Government will pay the balance provided it does not exceed the cost government would have paid if there was no private insurance. **The 65Plus Plan** Private insurers must be billed first. Government will pay the balance provided it does not exceed the cost government would have paid if there was no private insurance. **The Assurance Plan** Private insurers must be billed first. Government will pay a percentage of the balance as defined by the beneficiary's calculated copayment. **The Select Needs Plan** Private insurers must be billed first. Government will pay the balance provided

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Newfoundland and Labrador (Cont'd)		
Policy-Related Information (Cont'd)	**Coordination of Benefits (Public/Private) (Cont'd)**	it does not exceed the cost government would have paid if there was no private insurance.
	Coordination of Benefits (Intra-Jurisdictional)	**The Foundation Plan** Other federal public plans are to be used before this plan. **The 65Plus Plan** Other federal public plans are to be used before this plan. **The Access Plan** Other federal public plans are to be used before this plan. **The Assurance Plan** Other federal public plans are to be used before this plan. **The Select Needs Plan** Other federal public plans are to be used before this plan.
	Restricted Benefit Process	A special authorization request form has been prepared at the request of pharmacists and physicians, which may be used to facilitate the approval process. While staff of the division try to accommodate verbal requests where possible, requests are assessed in the order received (fax, mail or verbal) and must be subject to a review of the patient's medication claims summary. The use of the form, while not mandatory, is encouraged to expedite the approval process.
	Reimbursement Policy	**The Foundation Plan** Reimbursement can be considered under exceptional circumstances; out-of-province claims are only considered if a patient is referred out of province for medical reasons and approval is obtained prior to leaving the province

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Newfoundland and Labrador (Cont'd)		
Policy-Related Information (Cont'd)	**Reimbursement Policy (Cont'd)**	**The Access Plan** The program only applies to benefits obtained within the province of Newfoundland and Labrador **The 65Plus Plan** For medications purchased in the province only **The Select Needs Plan** The program applies only to benefits obtained through the Health Sciences Centre Pharmacy of the Eastern Regional Health Authority; out-of-province claims are considered only if a patient is referred out of province for medical reasons and approval is obtained prior to leaving the province
	Miscellaneous	**Prescription Quantities** 90 days' supply 30 days' supply for narcotics
Yukon		
Eligibility	**Plan/Program**	**Children's Drug and Optical Program** **Chronic Disease Program** **Pharmacare**
	Beneficiary Group	**Children's Drug and Optical Program** Children younger than age 19 from lowincome families **Chronic Disease Program** Residents who have a chronic disease or a serious functional disability as provided under the Chronic Disease and Disability Benefits Regulations and not having coverage through First Nations and Inuit Health; program may also include clients receiving palliative care

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Yukon (Cont'd)		
Eligibility	**Beneficiary Group**	**Pharmacare** Seniors age 65 or older (and seniors spouses age 60 or older) registered with Yukon Health Care Insurance Plan (YHCIP) and not having coverage through First Nations and Inuit Health; program may also include clients receiving palliative care **For all programs:** Benefits are not covered if they are already available through a federal or territorial drug program, such as First Nations and Inuit Health and Veterans Affairs Canada. Residents with private or group insurance plans must submit claims to those plans first and will then be eligible for top-up benefits. The Pharmacare program is the insurer of last resort.
	Income Range	Tables with family income and family size are used to determine deductibles for Chronic Disease and Children's Drug and Optical programs; the table for Children's Drug and Optical indicates income ranges that would not be eligible for the program
	Age Range	**Children's Drug and Optical Program** Children age 0 to 18 years **Pharmacare** Seniors age 65 or older (and seniors spouses age 60 or older)
	Disease Specific	**Chronic Disease Program** Residents who have a chronic disease or a serious functional disability as provided under the Chronic Disease and Disability Benefits Regulations (residents must use private insurance plans first)

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Yukon (Cont'd)		
Eligibility (Cont'd)	**Other Criteria**	Absence from the territory for more than 183 consecutive days (six months) will result in suspension of drug and benefit cost reimbursement starting the date of departure. A one-month extension will be considered on application to the director of health care insurance where the Yukon is the location of the applicant's only principal residence. On return to the territory, the resident may re-apply for coverage under the respective program.
Cost-Sharing Mechanism	**Premium**	None
	Copayment/ Co-insurance	None
	Deductible	**Children's Drug and Optical Program** Maximum $250 per child and $500 per family; deductible may be waived or reduced depending on income **Chronic Disease Program** Maximum $250 per individual and $500 per family, waived for palliative care recipients; deductible may be waived or reduced depending on income
	Maximum Beneficiary Contribution	N/A
Policy-Related Information	**Prescription Cost Components**	AAC + markup + professional fee
	Professional Fees	The professional fee maximum is $8.75.
	Markup	Pharmacies are allowed a 30% markup. In addition, if AAC includes a wholesale up charge, this can be included up to a maximum of 14%.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Yukon (Cont'd)		
Policy-Related Information (Cont'd)	**Ingredient Pricing Policy**	Yukon Drug Programs formulary benefits will be based on the lowestpriced interchangeable brand available as negotiated with the Pharmacy Society of Yukon. Prices listed in the formulary are based on McKesson wholesale prices.
	Coordination of Benefits (Public/Private)	For all Yukon government plans, residents must access private insurance plans first.
	Coordination of Benefits (Intra-Jurisdictional)	Residents must access all other drug insurance plans first. Coordination between Yukon government plans: Children who are eligible for Chronic Disease Program will use that plan before Children's Drug and Optical Plan.
	Restricted Benefit Process	Application process: Yukon physicians only may apply for exception drug status. Applications must be submitted in writing. Criteria for exception drugs–Refer to EDS Table Initial 30-Day Approval. When an exception drug is prescribed the pharmacist may request a 30-day approval. The pharmacist must phone the respective drug program advising that the patient is active; the exception drug will be covered for 30 days providing the drug is listed in the formulary. If the drug requires a specialist recommendation according the product's criteria, the 30-day coverage will not be granted unless the specialist information is provided.
	Reimbursement Policy	When beneficiaries pay out of pocket, receipts may be submitted for reimbursement if eligible under the program. Receipts will be assessed using formulary-listed prices. Exception drugs will require approval and these may be backdated. Payment will not be made for any drug or supply receipt that is mailed from an address outside of the Yukon.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

Yukon (Cont'd)		
Policy-Related Information (Cont'd)	**Miscellaneous**	**Prescription Quantities** The respective drug programs will not pay for more than 100 days' supply. There must be an interval of 75 days before a further 100-day supply can be given. Physicians shall exercise their professional judgment in determining the course and duration of treatment for their patients.
First Nations and Inuit Health Branch (FNIHB)		
Eligibility	**Plan/Program**	NIHB–Non-Insured Health Benefits
	Beneficiary Group	Registered Indian according to the Indian Act; or Inuk recognized by one of the Inuit Land Claim organizations; or An infant younger than one year of age whose parent is an eligible recipient; and Is currently registered or eligible for registration under a provincial or territorial health insurance plan; and Is not covered under a separate agreement with federal, provincial or territorial governments.
	Income Range	N/A
	Age Range	N/A
	Disease Specific	Special formularies for chronic renal failure patients and palliative care
	Other Criteria	NIHB program is the payer of last resort; that is, resident must use private, provincial or territorial health plan first if eligible for any of those.
Cost Sharing Mechanism	**Premium**	None
	Copayment/ Co-insurance	None
	Deductible	None

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

FNIHB (Cont'd)		
Cost Sharing Mechanism	**Maximum Beneficiary Contribution**	N/A
Policy-Related Information	**Prescription Cost Components**	Drug benefit list price + professional fee + markup (if applicable)
	Professional Fees	Pharmacists can charge dispensing fees. They are negotiated between NIHB and pharmacists' associations in a number of provinces/territories and will differ in each jurisdiction.
	Markup	Markups, if applicable, are negotiated as part of the pharmacy agreements between NIHB and the pharmacists' associations in the different jurisdictions. If a markup exists, it will be submitted by the pharmacy in a separate field in the electronic claim document. The markups are not built into the price file.
	Ingredient Pricing Policy	NIHB pays the amount identified on the price file that is created and maintained on NIHB's behalf by the claims processor. The principles guiding the price file are the following: If an item is listed on both a provincial formulary and the NIHB benefits list, NIHB pays the same. If an item is unique to NIHB, the program will pay according to the price list of a national wholesaler. Exceptions exist in Atlantic Canada and Quebec.
	Coordination of Benefits (Public/Private)	When beneficiary is covered by a private health care plan, claims must be submitted to it first.

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

FNIHB (Cont'd)		
Policy-Related Information	**Coordination of Benefits (Intra-Jurisdictional)**	When beneficiary is covered by another public health care plan, claims must be submitted to it first.
	Restricted Benefit Process	There are four types of limited-use benefits: Limited-use benefits, which do not require prior approval Limited-use benefits, which require prior approval (using the Limited-Use Drugs Request Form) Benefits with an exception status, which require prior approval (using the Benefit Exception Questionnaire) Benefits which have a quantity and frequency limit Upon receipt of a prescription for a limiteduse drug or a non-listed drug, the pharmacist must initiate the prior approval process by calling the Health Canada NIHB Drug Exception Centre. A benefit analyst will request prescriber and client information. An electronically generated Exception or Limited-Use Drugs Request Form will be immediately faxed, if possible, to the prescribing physician. The physician will complete and return the form using the toll-free fax number indicated on the form. The Drug Exception Centre will review the information and the pharmacist will be notified of the decision by fax. If approved, the provider should retain this faxed confirmation for billing purposes.
	Reimbursement Policy	Submissions for retroactive coverage must be received by FNIHB on an NIHB Client Reimbursement Request Form within one year from the date of service or date of purchase. The regional office assesses appropriateness of claims and acts accordingly. The vast majority of the claims are paid directly online to the

Table A.1: (Cont'd) Comparison of Provincial and Territorial Drug Subsidy Programs as of July 2010

FNIHB (Cont'd)		
Policy-Related Information (Cont'd)	**Reimbursement Policy**	pharmacist via electronic transactions. Effective December 1, 2009, ESI Canada will administer the Health Information and Claims Processing Services (HICPS) for pharmacy benefits covered by the NIHB Program.
	Miscellaneous	**Prescription Quantities** The normal quantity dispensed shall be the entire quantity of the drug prescribed. A maximum 100-day supply should be considered for those circumstances where the patient has been stabilized on a medication and the prescriber feels that further adjustment during the prescribed period is unlikely. The physician may continue to prescribe a smaller quantity with repeats at certain intervals when it is in the patient's best interest. However, effective September 9, 2008, prescriptions for most chronic medications should be refilled no sooner than 28 days. NIHB will reduce the professional fee on most chronic medications that are dispensed less than 28 days apart.

Table A.2: Glossary of Terms for Table A.1

Category	Terminology	Definition
Eligibility	**Age group**	Age-specific requirements for beneficiaries to be eligible for coverage under a provincial, territorial or federal drug program.
	Beneficiary group	Recipients of benefits under a specified provincial, territorial or federal plan/program.
	Disease specific	Disease-specific requirements for beneficiaries to be eligible for coverage under a provincial, territorial or federal drug program.
	Income range	Family or individual income-specific requirements for beneficiaries to be eligible for coverage under a specific provincial, territorial or federal drug program.
	Plan/program	A provincial, territorial or federal program that provides coverage for drugs for a set population. Programs have defined rules for eligibility, payment, etc.
Cost-Sharing Mechanism	**Copayment/ co-insurance**	The portion of the drug cost that the beneficiary must pay each time a drug is dispensed. This may be a fixed amount or a percentage of the total cost. When calculated as a percentage of the total cost, this is also known as co-insurance.
	Deductible	The amount of total drug spending a beneficiary must pay in a defined time period before any part of his or her drug costs will be paid by the drug benefit plan/ program. A deductible may be a fixed amount or a percentage of income (income-based deductible).
	Maximum beneficiary contribution	The maximum amount of drug spending a beneficiary is required to pay in a defined time period. Once the maximum contribution has been reached, the drug program will pay 100% of eligible drug costs for the remainder of the year or time period.
	Premium	The amount a beneficiary is required to pay to enrol in a provincial, territorial or federal drug plan/program.

Table A.2:(Cont'd) Glossary of Terms for Table A.1

Category	Terminology	Definition
Policy-Related Information	**Coordination of benefits**	Coordination of benefits is a process whereby payments are coordinated through two or more drug plans (public/private, intra-jurisdictional). One plan is considered the primary insurer. The primary insurer is defined in the policies of the insurance plan/drug program. The portion of the drug cost not paid for by the primary insurer is claimed through the secondary insurer.
	Ingredient Pricing Policy	A set of conditions related to the repayment of the ingredient cost portion of a prescription under a specific provincial, territorial or federal drug program.
	Markup	An amount added to the cost price of a drug or ingredient, usually based on a percentage of the cost price.
	Prescription cost components	The categories of costs that, when added together, make up the total cost of dispensing a prescription drug to a patient; usually includes the cost of the drug (or ingredients), a markup on the drug or ingredient cost and a professional fee.
	Professional fees	The amount paid for the services provided by a service provider, such as a pharmacist; may also be referred to as a dispensing fee, compounding fee or any other special service fee.
	Reimbursement Policy	A set of conditions regarding the repayment to a beneficiary of the incurred prescription drug cost under a specific provincial, territorial or federal drug program.
	Restricted Benefit Process	The steps by which prescribers request coverage for drug products where approval for coverage requires prior authorization by the specific provincial, territorial or federal drug program.

Appendix B

Proofs:

B.1 Proof for the Preference of a Representative Selective Patient in Section 3.3.2

In the baseline model of chapter 3, I have introduced that a selective patient would only consider the brand-name drugs 0 or 1, under the assumption (3.3.3).

Proof. From (3.3.1), I am able to show that for a representative selective patient,

$$U_0 > U_G, \tag{B.1.1}$$

as long as the assumption (3.3.3), i.e. $(1-t)(\theta_H - \theta_L)q > p_0 - p_G$ holds. U is the total utility the patient derives from consuming drug 0 or drug G as indicated in the subscripts.

That is, a selective patient would choose the brand-name drug 0 over its generic substitute G.

Now suppose some selective patient is indifferent between the generic drug G and the other brand-name drug 1. Therefore, for these patients, I have

$$U_G = U_1. \tag{B.1.2}$$

Solve for (B.1.2) given (3.3.1), I obtain

$$\underline{x}^* = \frac{\alpha(p_1 - p_G) + t - (1-t)(\theta_H - \theta_L)q}{2t}. \tag{B.1.3}$$

In the meantime, I have the indifference line between the two brand-name drugs 0 and 1 defined as the following

$$\overline{x}^* = \frac{\alpha(p_1 - p_G) - (p_0 - p_G) + t}{2t}. \tag{B.1.4}$$

Using (3.3.3) again, I obtain

$$\overline{x}^* > \underline{x}^*. \tag{B.1.5}$$

Now I use Figure B.1 which is similar to Figure 3.2 to continue my proof.

Figure B.1: Preference of selective Patients for the Three Drugs

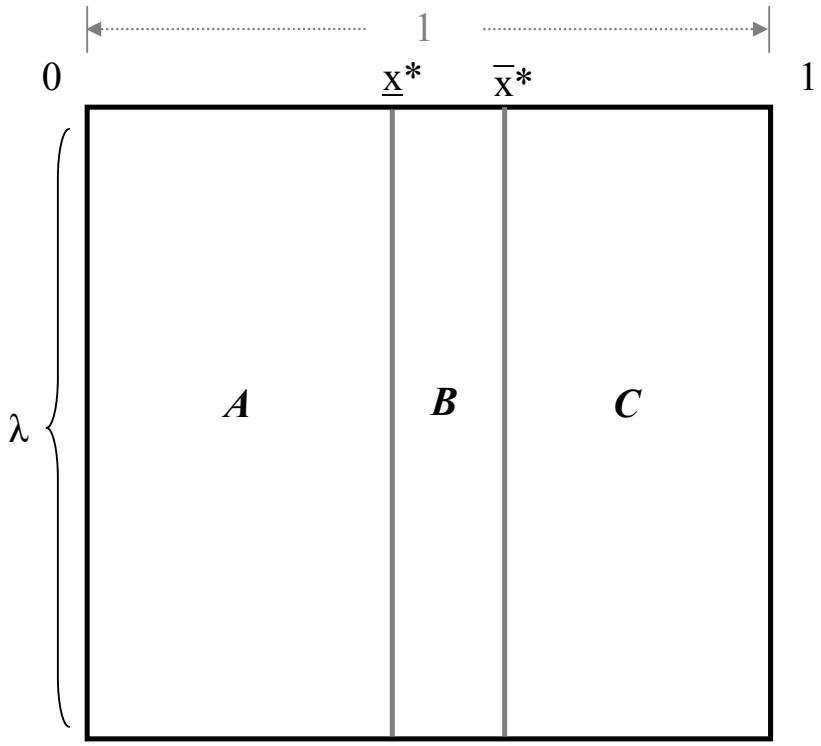

Figure B.1 demonstrates the preference of the selective patients (only) for the three drugs, 0, 1, and G.

From the above diagram, the two indifference lines ($\overline{x}^*$ and $\underline{x}^*$) separate the box into three regions, labelled A, B, and C, respectively.

Firstly, region A is to the right of both indifference lines. This indicates that the brand-name drug 1 is strictly preferred to both the brand-name drug 0 and the

generic drug G. As a result, in region A, the selective patients only consider the brand-name drug 1.

Secondly, region B is to the left of $\overline{x}^*$ but to the right of $\underline{x}^*$. This indicates that the brand-name drug 1 is strictly preferred to the generic drug G and that the brand-name drug 0 is strictly preferred to the brand-name drug 1. As a result, in region B, the selective patients only consider the brand-name drug 0.

Finally, region A is to the left of both indifference lines. This indicates that both the brand-name drug 0 and the generic drug G are strictly preferred to the brand-name drug 1. Now, with (B.1.1) under the assumption (3.3.3), I conclude that in region A, the selective patients only consider the brand-name drug 0.

In summary, a selective patient would only consider the two brand-name drugs (0 and 1), when (3.3.3) holds. □

B.2 Detailed Proofs for Proposition 5 in Section 3.3.5.1

From (3.3.53), I need to show the sign of the following:

$$\frac{\partial p_1}{\partial \alpha} = \frac{1}{\alpha^2[6\alpha + \lambda(1-\alpha)]^2}\{(6-\lambda)[3\lambda(1-t)\delta - \lambda t - 2(1-t)\delta - 6t]\alpha^2 - 2\lambda(6-\lambda)[(1-t)\delta - t]\alpha - \lambda^2[(1-t)\delta - t]\}. \tag{B.2.1}$$

Proof. I will only focus on the terms in the brackets to show the sign of $\frac{\partial p_1}{\partial \alpha}$, i.e.

$$f(\alpha) = a\alpha^2 + b\alpha + c, \tag{B.2.2}$$

where

$$a \equiv (6-\lambda)[3\lambda(1-t)\delta - \lambda t - 2(1-t)\delta - 6t], \tag{B.2.3}$$

$$b \equiv -2\lambda(6-\lambda)[(1-t)\delta - t], \tag{B.2.4}$$

$$c \equiv -\lambda^2[(1-t)\delta - t]. \tag{B.2.5}$$

First look at the discriminant of the quadratic equation $f(\alpha)$:

$$\begin{aligned}\Delta &= b^2 - 4ac \\ &= 4\lambda^2(6-\lambda)^2[(1-t)\delta - t]^2 \\ &\quad + 4\lambda^2[(1-t)\delta - t](6-\lambda)[3\lambda(1-t)\delta - \lambda t - 2(1-t)\delta - 6t] \\ &= 8\lambda^2(6-\lambda)[(1-t)\delta - t][2(1-t)\delta - 6t + \lambda(1-t)\delta] \\ &= 8\lambda^2(6-\lambda)\{(2+\lambda)[(1-t)\delta]^2 - (2+\lambda)t(1-t)\delta \\ &\quad - 6t(1-t)\delta + 6t^2\}. \end{aligned} \tag{B.2.6}$$

Again, the sign of the discriminant Δ is determined by the sign of the terms within the brackets in (B.2.6).

Now, let the terms in the brackets be

$$g(A) = (2+\lambda)A^2 - (8+\lambda)tA + 6t^2, \tag{B.2.7}$$

where

$$A \equiv (1-t)\delta. \tag{B.2.8}$$

The roots of $g(A) = 0$ are t and $\frac{6}{2+\lambda}t$, respectively. Accordingly, I discuss the following cases:

1. When $A \leq t$:

$$Sign(g(A)) = Sign(\Delta) > 0, \tag{B.2.9}$$

$f(\alpha) = 0$ has two distinct real roots.

Also,

$$b = -2\lambda(6-\lambda)(A-t) > 0, \tag{B.2.10}$$

and

$$c = -\lambda^2(A - t) > 0. \tag{B.2.11}$$

Rearrange terms for a

$$a = (6 - \lambda)[(3\lambda - 2)A - (\lambda + 6)t]. \tag{B.2.12}$$

I need to examine the sign of $K \equiv (3\lambda - 2)A - (\lambda + 6)t$ within the brackets in (B.2.12).

If $(3\lambda - 2) > 0$, K monotonically increases in A and reaches its maximum $2t(\lambda - 4) < 0$ at $A = t$, which implies $a < 0$.

If $3\lambda - 2 \leq 0$, it is obviously that $a < 0$. Therefore, I have

$$a < 0. \tag{B.2.13}$$

From (B.2.10) and (B.2.13), we have

$$-\frac{b}{2a} > 0. \tag{B.2.14}$$

Since

$$-2a - b = 2(6 - \lambda)[2A(1 - \lambda) + 6t] > 0, \tag{B.2.15}$$

and (B.2.14), I have

$$0 < -\frac{b}{2a} < 1. \tag{B.2.16}$$

Also from

$$f(0) = c > 0, \quad \text{and} \tag{B.2.17}$$

$$\begin{aligned} f(1) &= a + b + c \\ &= 2\lambda A(4 - \lambda) + 12t(\lambda - 3) - 12A \\ &= -2A[(2 - \lambda)^2 + 2] - 12t(3 - \lambda) \\ &< 0, \end{aligned} \tag{B.2.18}$$

I can determine the location of the parabola (B.2.2). $f(\alpha) > 0$ at $\alpha = 0$ and increases to the maximum at $\alpha = -\frac{b}{2a}$. $f(\alpha)$ then decreases till it becomes negative at $\alpha = 1$. In summary, the sign of $f(\alpha)$ is indefinite over $\alpha \in (0, 1)$ when $A \leq t$.

2. When $t < A \leq \frac{6t}{2+\lambda}$:

$$Sign(g(A)) = Sign(\Delta) < 0, \tag{B.2.19}$$

$f(\alpha) = 0$ has no real roots.

Similar to (B.2.12), we can only look at the sign of $K \equiv (3\lambda - 2)A - (\lambda + 6)t$.

If $(3\lambda - 2) > 0$, K monotonically increases in A and reaches its maximum $-\frac{(6-\lambda)^2}{2+\lambda}(4 - \lambda)t < 0$ at $A = \frac{6t}{2+\lambda}$, which implies $a < 0$;

If $3\lambda - 2 \leq 0$, it is obviously that $a < 0$. Therefore, I have

$$a < 0. \tag{B.2.20}$$

With both (B.2.19) and (B.2.20), I can determine the location of the parabola (B.2.2). Specifically, $f(\alpha) < 0$ over $\alpha \in (0, 1)$.

3. When $A > \frac{6t}{2+\lambda}$:

$$Sign(g(A)) = Sign(\Delta) > 0, \tag{B.2.21}$$

$f(\alpha) = 0$ has two distinct real roots. As $A > \frac{6}{2+\lambda}t$,

$$\begin{aligned} b &= -2\lambda(6 - \lambda)(A - t) < 0, \\ c &= -\lambda^2(A - t) < 0, \end{aligned} \tag{B.2.22}$$

whereas a may be negative or positive as A increases.

When $a < 0$, I have,

$$\begin{aligned} -\frac{b}{2a} &< 0, \\ f(0) &= c < 0, \\ f(1) &= a + b + c < 0. \end{aligned} \tag{B.2.23}$$

Combining (B.2.21) and (B.2.23), I can determine the location of the parabola (B.2.2). Specifically, $f(\alpha) < 0$ over $\alpha \in (0, 1)$.

When $a > 0$, I have,

$$\begin{aligned} -\frac{b}{2a} &> 0, \\ f(0) &= c < 0. \end{aligned} \tag{B.2.24}$$

Also since

$$2a - (-b) = -2(6 - \lambda)[2A(1 - \lambda) + 6t] < 0, \tag{B.2.25}$$

I have

$$-\frac{b}{2a} > 1. \tag{B.2.26}$$

Finally, with $f(1) < 0$ by (B.2.18), I can determine the location of the parabola (B.2.2). $f(\alpha) < 0$ at $\alpha = 0$ and decreasing till $\alpha = 1$. $f(\alpha)$ keeps decreasing to its minimum at $\alpha = -\frac{b}{2a}$. In summary, $f(\alpha) < 0$ over $\alpha \in (0, 1)$ when $A > \frac{6t}{2+\lambda}$.

I can summarize the results as follows:

$$\begin{cases} \frac{\partial p_1}{\partial \alpha} \lessgtr 0, & A \leq t; \\ \frac{\partial p_1}{\partial \alpha} < 0, & t < A \leq \frac{6t}{2+\lambda}; \\ \frac{\partial p_1}{\partial \alpha} < 0, & A > \frac{6}{2+\lambda}. \end{cases} \tag{B.2.27}$$

□

Appendix C

Background Information for the Empirical Research in Chapter 4

C.1 ATC Classification System — 1^{st} Level

Table C.1: Drug Groups at the 1^{st} Level of the ATC Classification System

Code†	Contents
A	Alimentary tract and metabolism
B	Blood and blood forming organs
C	Cardiovascular system
D	Dermatologicals
G	Genito-urinary system and sex hormones
H	Systemic hormonal preparations, excluding sex hormones and insulins
J	Antiinfectives for systemic use
L	Antineoplastic and immunomodulating agents
M	Musculo-skeletal system
N	Nervous system
P	Antiparasitic products, insecticides and repellents
R	Respiratory system
S	Sensory organs
V	Various

Source: World Health Organization (http://www.whocc.no/atc_ddd_index)

† The code refers to the 1^{st} level ATC code.

C.2 Data Manipulation

Data on off-patent brand-name drugs were accessed at the Health Canada Patent Register in July 2008.[1] The Patent Register contains information on prescription drugs that have been granted patents in the Canadian pharmaceutical market. Patent-related information for both patented and off-patent drugs is maintained and updated in the Register on a monthly basis.

Other drug related information, including drug price data, for the public drug plans were accessed through the National Prescription Drug Utilization Information System (NPDUIS) maintained at the Canadian Institute for Health Information (CIHI). The NPDUIS database, managed by CIHI's Pharmaceuticals department, contains the claims-level data on prescription drugs. The data are collected from publicly financed drug benefit programs in Canada. In addition, the database contains supporting information to help provide context for drug claims data which include formulary and drug products information, and information on policies of public drug plans in Canada.[2]

The drug price data accessed from the NPDUIS is the manufacturers' list price. In practice, drug manufacturers may use various measures, such as rebates, discounts, or allowances, to offer off-invoice monetary incentives to pharmacies. The manufacturers' list price is the market price that is net of these hidden measures.[3] In addition, the manufacturers' list price is considered the same across Canada,[4] despite the fact that drug costs at claims-level and individual out-of-pocket spending can vary significantly across the country. The list price is submitted by drug manufacturers to the public drug plan/program and may be used by the public drug plan/program to determine the drug cost that would be payable by a patient when the price for the dispensed drug is higher than the reimbursable cost. The manufacturers' list drug price data used in this research is contained in the public drug plans of Alberta.[5]

[1] I only accessed and kept the data for drugs for human use. Veterinary drugs are not considered in the research.

[2] The above information was accessed at http://www.cihi.ca on November 29, 2010.

[3] Drug price is measured in unit price, in Canadian dollars per capsule/tablet.

[4] Ward Health Strategies (2007).

[5] Alberta submits drug list price data to the NPDUIS consistently during the study period. The data exhibit the best data quality overall for this research.

The information on drug patents and the list drug price data were merged by the Drug Identification Number (DIN). Drug price data were converted to 2002 constant dollars using Statistics Canada's monthly CPI for prescribed medicines to rule out the inflation effect.

Each drug is defined uniquely by the DIN. As a result, the original dataset contains 3,543 drugs (DINs), including all dosage forms, in 245 WHO-ATC groups (4^{th} level). The study period has 33 quarters, starting from April 2000 to June 2008. Among them, 115 brand-name drugs in 39 WHO-ATC groups went off patent during the period of 2002-2007.

The data were transformed into the longitudinal format. The quarterly datasets starts in 2000 Quarter 2 (1^{st}) and ends in 2008 Q2 (33^{rd}). If each DIN were associated with 33 observations over time in the setting of a balanced panel, I would have 116,919 price records in total. However, the panel is highly unbalanced. Among them, some drugs were delisted from the formulary and therefore the drug price records were discontinued; some drug products had late market entries and therefore were listed in the formulary late during the study period. As such, the unbalanced panel for this study includes 82,772 effective price records.

Among them, I exclude drugs with non-oral-solid dosage forms for measuring convenience. I select the drug classes that contain the brand-name original drugs going off patent during the study period. As such, I am able to observe and analyze the drug price dynamics before and after the patents' expiry. I also select the drug classes that are representative of the therapeutic class in the Canadian drug market.

C.3 Data Access

Data including the manufacturers' list drug price were accessed from the NPDUIS database maintained at the CIHI through the Graduate Student Data Access Program (GSDAP). The dataset also contains information on drug dosage form, strength, and manufacturer information etc. Table C.2 shows the major sources of the data accessed for this research.

Table C.2: Sources of Data Access

Data Element	**Data Sources**
Drug patent status/ Drug off-patent dates etc.	1. Health Canada Patent Register 2. Health Canada Drug Product Database
Detailed drug information, including: Drug plan, DIN, WHO-ATC code, strength, dosage form, generic or brand-name manufacturer, and manufacturer list price, etc.	1. Health Canada Drug Product Database 2. National Prescription Drug Utilization Information System (NPDUIS)
Consumer Price Index	Statistics Canada CPI for prescribed drugs

C.4 Background of the Selected Drug Classes

1. WHO-ATC code C10AA–:
   The drugs under WHO-ATC code (4^{th} level) — C10AA–, also known as statins (or HMG-CoA reductase inhibitors), are a class of drugs that lower cholesterol levels in human.

2. WHO-ATC code J02AC–:
   The drugs under WHO-ATC code (4^{th} level) — J02AC– are the triazole anti-fungal drugs, used to treat fungal infections such as athlete's foot, ringworm, candidiasis (thrush), serious systemic infections such as cryptococcal meningitis, and others.

3. WHO-ATC code N02CC–:
   The drugs under WHO-ATC code (4^{th} level) — N02CC–, also known as triptans (or serotonin agonists or 5-hydroxytryptamine receptor agonists), are a class of drugs that are used in the treatment of migraine headaches.

The following table displays the information of the three selected drug classes.

Table C.3: Information on the Three Selected Drug Classes

ATC Code*	ATC Sub-group	Brand Name	Generic Name	Manufacturer	NOC†	DDD‡
C10AA-	C10AA01	Zocor®	Simvastatin	Merck	1990-08-29	30
	C10AA02	Mevacor®	Lovastatin	Merck	1988-06-30	45
	C10AA03	Pravachol®	Pravastatin	Bristol-Myers Squibb	1995-03-30	30
	C10AA04	Lescol®	Fluvastatin	Novartis	1996-05-31	60
	C10AA05	Lipitor®	Atorvastatin	Pfizer	1997-02-19	20
	C10AA07	Crestor®	Rosuvastatin	AstraZeneca	2003-02-16	10
J02AC-	J02AC01	Diflucan®	Fluconazole	Pfizer	1995-09-22	200
	J02AC02	Sporanox®	Itraconazole	Janssen	1996-01-30	200
	J02AC03	Vfend®	Voriconazole	Pfizer	2004-08-20	400
N02CC-	N02CC01	Imitrex®	Sumatriptan	GlaxoSmithKline	1995-03-31	50
	N02CC02	Amerge®	Naratriptan	GlaxoSmithKline	1998-04-28	2.5
	N02CC03	Zomig®	Zolmitriptan	AstraZeneca	1998-08-24	2.5
	N02CC04	Maxalt®	Rizatriptan	Merck	1999-07-16	10
	N02CC05	Axert®	Almotriptan	Johnson&Johnson	2003-09-29	12.5

* The versions of all listed ATC codes are verified to reamin the same during the study period of 2000-2008.

† Dates of notices of compliance (NOC) are retrieved from the Drug Product Database held at Health Canada on November 27, 2010.

‡ The unit of the Defined Daily Doses is milligram. Information on the DDD is retrieved from WHO DDD Index 2010, at http://www.whocc.no/atc_ddd_index on Apr. 4, 2010.

C.5 Acronyms for Drug Product Manufacturers

Table C.4: Acronyms Table for Drug Product Manufacturers

Acronym	Manufacturer	Product Characteristic
JAN	Janssen-Ortho Inc.	Brand-name
APX	Apotex Inc.	Generic
AZE	AstraZeneca Canada Inc.	Brand-name
BRI	Bristol-Myers Squibb Canada Co.	Brand-name
COB	Cobalt Pharmaceuticals Inc.	Generic
FRS	Merck Frosst Canada Ltd.	Brand-name
GPM	Genpharm Inc.	Generic
GSK	GlaxoSmithKline	Brand-name
JNJ	Johnson & Johnson Inc.	Brand-name
LIN	Linson Pharama Inc.	Generic[†]
NOP	Novopharm Ltd.	Generic
NVR	Novartis Pharmaceuticals Canada Inc.	Brand-name
NXP	Nu-Pharm Inc.	Generic
PFI	Pfizer Canada Inc.	Brand-name
PMS	Pharmascience Inc.	Generic
RAN	Ranbaxy Pharmaceuticals Canada Inc.	Generic
RPH	Ratiopharm Inc.	Generic
SDZ	Sandoz Canada Inc.	Generic
TAR	TaroPharma Inc.	Generic

[†] Linson Pharma Inc. is a subsidiary of Bristol-Myers Squibb Canada Co.

C.6 Summary Statistics of the Major Variables in the Regression Analysis

Table C.5: Summary Statistics of the Major Variables by Molecules

Drug class (ATC Code)	Molecule	Variable	Obs	Mean	Std. Dev.	Min	Max
Statin (C10AA–)	Simvastatin	*price*	659	1.3085	0.4577	0.5341	2.3477
		gennum	659	6.8209	2.2364	0	8
		compnum	659	28.0683	5.9909	7	32
		strength	659	30	0	30	30
		brand	659	0.2276	0.4196	0	1
		generic	659	0.7724	0.4196	0	1
		policy	659	0.9317	0.2524	0	1
	Lovastatin	*price*	348	1.6954	0.6395	1.0273	3.4074
		gennum	348	6.6207	1.9753	1	8
		compnum	348	26.0460	7.5323	7	32
		strength	348	45	0	45	45
		brand	348	0.1724	0.3783	0	1
		generic	348	0.8276	0.3783	0	1
		policy	348	1	0	1	1
	Pravastatin	*price*	516	1.2098	0.3157	0.8976	2.2262
		gennum	516	7.8372	2.1390	2	10
		compnum	516	26.8779	6.5462	9	32
		strength	516	30	0	30	30
		brand	516	0.1570	0.3641	0	1
		generic	516	0.8430	0.3641	0	1
		policy	516	1	0	1	1

† The detailed description of these variables is provided in Table 4.2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

Table C.5: (Cont'd) Summary Statistics of the Major Variables by Molecules

Drug class (ATC Code)	Molecule	Variable	Obs	Mean	Std. Dev.	Min	Max
Statin (C10AA–)	Fluvastatin	*price*	72	1.0420	0.2158	0.7568	1.4837
		gennum	72	0	0	0	0
		compnum	72	23.2222	9.3405	7	32
		strength	72	60	0	60	60
		brand	72	1	0	1	1
		generic	72	0	0	0	0
		policy	72	0	0	0	0
	Atorvastatin	*price*	113	2.0400	0.2460	1.5707	2.3323
		gennum	113	0	0	0	0
		compnum	113	22.5664	9.1621	7	32
		strength	113	20	0	20	20
		brand	113	1	0	1	1
		generic	113	0	0	0	0
		policy	113	0	0	0	0
	Rosuvastatin	*price*	59	1.5572	0.2663	1.2151	1.9599
		gennum	59	0	0	0	0
		compnum	59	29.6271	2.4276	24	32
		strength	59	10	0	10	10
		brand	59	1	0	1	1
		generic	59	0	0	0	0
		policy	59	0	0	0	0

† The detailed description of these variables is provided in Table 4.2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

Table C.5: (Cont'd) Summary Statistics of the Major Variables by Molecules

Drug class (ATC Code)	Molecule	Variable	Obs	Mean	Std. Dev.	Min	Max
Triazole (J02AC–)	Fluconazole	*price*	363	6.7342	3.3808	2.9450	15.1837
		gennum	363	4.0083	1.2647	1	5
		compnum	363	6.5372	1.6287	3	8
		strength	363	200	0	200	200
		brand	363	0.2479	0.4324	0	1
		generic	363	0.7521	0.4324	0	1
		policy	363	0.9890	0.1045	0	1
	Itraconazole	*price*	30	3.7851	0.0836	3.6097	4.0338
		gennum	30	0	0	0	0
		compnum	30	5.9	1.9538	3	8
		strength	30	200	0	200	200
		brand	30	1	0	1	1
		generic	30	0	0	0	0
		policy	30	0	0	0	0
	Voriconazole	*price*	18	30.3568	18.7397	12.0292	49.3837
		gennum	18	0	0	0	0
		compnum	18	8	0	8	8
		strength	18	400	0	400	400
		brand	18	1	0	1	1
		generic	18	0	0	0	0
		policy	18	0	0	0	0

† The detailed description of these variables is provided in Table 4.2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

Table C.5: (Cont'd) Summary Statistics of the Major Variables by Molecules

Drug class (ATC Code)	Molecule	Variable	Obs	Mean	Std. Dev.	Min	Max
Triptan (N02CC–)	Sumatriptan	*price*	148	11.0629	2.4900	8.5385	16.6092
		gennum	148	5.0405	3.0212	0	7
		compnum	148	9.8514	3.3470	4	12
		strength	148	50	0	50	50
		brand	148	0.4054	0.4926	0	1
		generic	148	0.5946	0.4926	0	1
		policy	148	0.7770	0.4177	0	1
	Naratriptan	*price*	60	12.9228	0.4815	12.2179	14.8569
		gennum	60	0	0	0	0
		compnum	60	6.8333	3.4941	4	12
		strength	60	2.5	0	2.5	2.5
		brand	60	1	0	1	1
		generic	60	0	0	0	0
		policy	60	0	0	0	0
	Zolmitriptan	*price*	30	12.8152	0.1673	12.5588	13.1385
		gennum	30	0	0	0	0
		compnum	30	6.8333	3.5241	4	12
		strength	30	2.5	0	2.5	2.5
		brand	30	1	0	1	1
		generic	30	0	0	0	0
		policy	30	0	0	0	0

† The detailed description of these variables is provided in Table 4.2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

Table C.5: (Cont'd) Summary Statistics of the Major Variables by Molecules

Drug class (ATC Code)	Molecule	Variable	Obs	Mean	Std. Dev.	Min	Max
Triptan (N02CC–)	Rizatriptan	*price*	60	12.9487	0.2619	12.4241	13.8185
		gennum	60	0	0	0	0
		compnum	60	6.8333	3.4941	4	12
		strength	60	10	0	10	10
		brand	60	1	0	1	1
		generic	60	0	0	0	0
		policy	60	0	0	0	0
	Almotriptan	*price*	26	13.2790	0.1463	13.1131	13.5655
		gennum	26	0	0	0	0
		compnum	26	10.3077	2.5420	5	12
		strength	26	12.5	0	12.5	12.5
		brand	26	1	0	1	1
		generic	26	0	0	0	0
		policy	26	0	0	0	0

† The detailed description of these variables is provided in Table 4.2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

C.7 The Regression Result of the Cross-classified Random-effect Specification

As shown in Table C.6, the random intercept for "Between Manufactures" can be ignored. This indicates that the variation between drug molecules is more prevalent in the sample for this research. This can also be proved in the unconditional model.[6] As a result, I drop the "manufacturer" as a random intercept component in the multilevel analysis in Chapter 4 to simplify the analysis. As noted, I include the type of manufacturer (brand-name or generic) as an explanatory variable to control the manufacture effect.

Table C.6: Cross-classified Three-Level Regression Analysis for the Drug Price Dynamics

Fixed Effect	**Coefficient**	**Std.Err**	**t-Ratio**
Intercept	0.1823	0.0640	2.85
logavgpricelag	0.5892	0.0122	48.28
compnum	0.0001	0.0001	0.69
gennum	-0.0022	0.0007	-3.25
generic	-0.2646	0.0297	-8.91
metoo	-0.0219	0.0465	-0.47
$brand \times gennum$	0.0327	0.0006	55.87
hi_str	0.1513	0.0180	8.39
J	0.6600	0.0997	6.62
N	0.8923	0.0887	10.07
$hi\_str \times J$	0.2171	0.0470	4.62
$hi\_str \times N$	-0.1157	0.0403	-2.87
Random Intercepts	**Variance**	**Std.Dev.**	
Level 1			
Inter-temporal variation	0.000589	0.024272	
Level 2			
Drugs within Molecules	0.007528	0.086767	
Level 3			
Between Molecules	0.015991	0.126455	
Between Manufacturers	0.000000	0.000000	

[6] An unconditional model is the regression model only with an intercept term, with the same variance-covariance structure as the conditional model.