Brand-Name and Generic Drug Pricing in a Regulated Environment: Findings from Canada Data

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Abstract

The "generic competition paradox" refers to the phenomenon that off-patent brand-name drug manufacturers appear to be able to insulate themselves from generic drug competition in maintaining their market shares and profitability. While the existing theoretical work provides some plausible explanations for this paradox based on so-called product differentiation, we note that this literature does not pay full attention to changes in a regulated environment. Canada provides the context for studying drug manufacturers' price-setting and product differentiation decisions in a regulated market. In this paper, we attempt to fill the void in the literature by incorporating changes in patient preference and government reimbursement policies into our theoretical analysis. We conduct empirical analysis of the relationship between the drug price dynamics and the complex institutions and changing market places of the pharmaceutical industry. The theoretical and empirical work show that the difference in perceived quality between brand-name and generic drugs, rate of copay, and generic-substitution policy can influence brand-name drug price premiums.

Keywords: patented brand-name drug, off-patent brand-name drug, generic drug, product differentiation, drug pricing, market structure, patient preference, government reimbursement policies, multilevel modelling

JEL Classification: C23, I18, L11

1 Introduction

Prescription drug spending accounts for a considerable share of total healthcare expenditure in virtually all developed economies. Drug manufacturers' price setting behaviour, prevailing within complex institutions and changing market places, are critically important to the total healthcare expenditure.

Market structures in the pharmaceutical industry range from pure monopoly to monopolistic competition and can experience the flux of constant change. At any point in time, patented brand-name drugs may coexist with off-patent brand-name and/or generic substitutes in the same therapeutic market. As existing patented brand-name drugs go off-patent, generic substitutes emerge and new patented brand-name drugs also arrive.

The "generic competition paradox" refers to the phenomenon that, contrary to the common belief that more generic substitutes drive down drug prices, off-patent brand-name drug manufacturers can insulate themselves from generic drug competition and maintain their market shares and profitability.¹ Hurwitz and Caves (1988) note that off-patent brandname drug manufacturers can increase their market shares by promotional activities thus maintaining price premiums over generic substitutes for some time. Caves et al. (1991) discover a downward rigidity in the prices of brand-name drugs with expired patents even after taking into account market structures, advertising and drug's therapeutic class. Grabowski and Vernon (1992) confirm this phenomenon even when a policy change facilitates the introduction of generic substitution. Scherer (1993) suggests this paradox exists because of institutional regularities such as "risk-averse and price-insensitive" physicians and "risk-avoiding and brand-superstitious" patients. Frank and Salkever (1997) find some brand-name drugs are able to insulate themselves from the increased competition from the generic drugs within the same chemical compounds. Wiggins and Maness (2004) note that the generic competition paradox appears in some cases but not in others. Although there has been ongoing

 $^{^{1}}$ Comanor (1986) provides an insightful discussion on the facts and political economy of the pharmaceutical industry.

efforts to identify and explain this paradox, as Berndt (2002) notes it is unclear as to why this paradox persists in many cases.

Indeed, most pharmaceutical markets in developed economies are regulated and characterized by competing incentives from various players: physicians who prescribe drugs do not consume and pay for them; patients who consume drugs do not prescribe and pay full prices for them if they are covered by public/private insurance; and government/insurance agencies who regulate drug pricing and may pay for a significant portion of full prices do not prescribe and consume them. In the backdrop of a regulated pharmaceutical market with multiple stakeholders, we focus on the concept of product differentiation to gain a better understanding of the generic competition paradox.

Consider the oligopolistic market.² Instead of producing similar products at the cost of harsh price competition, oligopolistic firms tend to differentiate their products to dampen price competition even though their products may only appeal to a smaller pool of customers. There are different forms of product differentiation. According to Hotelling (1929), a form of differentiation, often called horizontal product differentiation, appears in a market where products are considered to be of equivalent quality, even though different consumers prefer different variants. Another form of differentiation proposed by Mussa and Rosen (1978), often called vertical product differentiation, appears in a market where one product has more of all characteristics than any other products, or is ranked as a better product by consumers in a universally accepted order by some dimension of quality. Neven and Thisse (1990) integrate horizontal product differentiation with vertical product differentiation in a unified setting, noting that under certain circumstances a firm would choose to maximize 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. Based on these concepts, Brekke et al. (2007) further theorize that an off-patent brand-name drug and its generic substitute are vertically differentiated in perceived quality³ while patented

²See Lancaster (1990).

³According to Hollis (2002), the earlier the market entry, the greater market share a generic manufacturer

brand-name drugs that are therapeutic substitutes, are horizontally differentiated. These therapeutic substitutes offer different therapeutic variants to cater to patients' heterogeneous tastes. Grootendorst (2007) notes that division between off-patent drugs and their substitutes may be less clear in reality as some brand-name manufacturers may participate in the generic market by making confidential arrangements with their subsidiary company or a generic firm to release "authorized generics". Kong (2009) uses tiered consumer demand based on drug insurance coverage to explain drug manufacturers' price setting behaviour and finds that the generic competition paradox is related to the fact that some patients with high insurance coverage are less sensitive to price premiums on off-patent brand-name drugs. However, Kong (2009) does not discuss the role played by governments in the funding and provision of prescription drugs.⁴

With the oligopolistic firms on the supply side, patients' demand for prescription drugs is induced by multiple players in a government-regulated market. The key players are patients (consumers), physicians (professional agents for patients), pharmacists (professional agents for both patients and physicians), and public/private drug plan administrators (regulators and funding agents). All regulators and agents, based on relevant health information, induce patients' demand for different types of drugs (brand-name or generic).

In this paper, we extend the two-dimension product differentiation model proposed by Brekke et al. (2007) to a regulated environment such as the one in Canada, where there are multiple players—regulators and public and private insurance plans, physicians, patients and pharmacists. In our model, we evaluate the impacts of the shift in patient preference and the change in government policies on drug manufacturers' price setting behaviour. We find that the differentiation in perceived quality between brand-name and generic drugs can be

gets. However, being the earliest may be costly because the generic drug firm that challenges the patent would likely be involved in patent litigation. To encourage early generic entry, in Ontario, the first listed generic drug that challenges a brand-name drug's patent can 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).

⁴This is particularly relevant to Canada where direct-to-consumer advertising of prescription drugs is banned but there is easy access to American TV advertising via satellite cable in Canada.

pivotal in the brand-name manufacturers' price setting decisions. As long as patients believe (or are made to believe) that brand-name drugs are "superior" in therapeutic quality than generic substitutes, brand-name drug manufacturers are able to leverage their market power to charge higher prices in the market. This may happen even when there are proportionally more patients become less "selective" on perceived quality, everything else being equal. This finding is robust under different reimbursement systems.

In addition to our theoretical work, we empirically explore the following three hypotheses: (1) More generic substitutes do not have any net effect of lowering drug prices. (2) More therapeutic substitutes do not have any net effect of lowering drug prices. (3) Given the available generic substitution policy, brand-name drugs do not have any net price premiums over their generic substitutes. To ensure a rigorous evaluation of these hypotheses, we confine our analysis of the existing consumer preferences between brand-name and generic drugs and existing policy parameters within a specific set of drugs in the Canadian market. When the regulated environment and drug market "ecology" are properly controlled for, we have evidence to reject the first and third hypotheses but cannot reject the second hypothesis.

The paper is organized as follows. In Section 2 we propose the two-dimension product differentiation models in different settings. In Section 3 we explain the data and empirical research methodology. We discuss our empirical findings in Section 4. Finally, we conclude in Section 5.

2 Theoretical Analysis

2.1 The Baseline Model

We assume the baseline model has 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 off patent and therefore, has a generic substitute or its bioequivalent counterpart, named G. The other brand-name drug in this therapeutic market, named 1, is still on patent.⁵ The price of the generic drug G is capped by a predetermined percentage of the price of its brand-name original, drug 0.

In this model, all patients are covered by some form of drug insurance,⁶ under which patients at the pharmacies are only responsible for out-of-pocket insurance deductibles and copays while the public/private drug plans reimburse the rest of the drug cost.⁷ 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.

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

We characterize drug products along two dimensions, namely, therapeutic variant and perceived quality. First, drugs within a therapeutic market may exist 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 brandname drugs 0 and 1 are differentiated in therapeutic variant dimension, denoted $q \in [0, 1]$. Second, the perceived quality by patients and health professionals may or may not have anything to do with the actual therapeutic variant scale of the drug, q. It is, rather, based on the manufacturer's (or brand's) promotion, patient's (or family/friends') experience, and health professionals' belief.⁸ Patients' knowledge and perception are shaped by educational efforts via mass media, financial incentives, and communication among patients and health professionals (Hassali et al., 2009). To some patients, brand-name drugs are perceived to possess

⁵It 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.

⁶We assume that 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.

⁷When the generic version of a brand-name drug is available but the prescription is filled by the brandname drug instead, the patient needs to pay a copay for the generic drug plus the price differential between the generic drug and its brand-name original.

⁸Generic drugs and their brand-name counterparts are bioequivalent in terms of medicinal ingredient but they may differ in peripheral features such as non-medicinal ingredient and packaging. 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.

superior quality compared to their generic counterparts because the former has longer market exposure either through direct-to-consumer advertising (DTCA) or commercial/academic detailing targeting physicians or other prescribers.⁹ 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 drugs.¹⁰

The demand for generic drugs can be induced by public/private insurers and/or pharmacists because of their budgetary considerations and professional knowledge. Insurers have natural incentives to encourage generic substitution for expensive brand-name drugs to curb reimbursement costs. Pharmacists may also have financial incentives and professional considerations to fill generic drugs over brand-name drugs for patients.¹¹ In addition, the demand for brand-name drugs can be induced by either physicians, because of their professional knowledge, or "indirect advertisements" that patients receive through cross-border televisions or online marketing.¹²

In the current setting with the therapeutic variant dimension (q) reflected by the [0, 1] interval, we assume that the two differentiated brand-name drugs are fixed at both ends of the [0, 1] interval. That is, drug 0 (1) is located at 0 (1). Suppose the patient's most-favourite drug variant (MFDV) is located at point x, which is uniformly distributed on the [0, 1] interval of the therapeutic variant dimension.¹³ When the MFDV (x) is not located at either 0 or 1, disutility measured as the distance between x and a drug (either drug 0 or drug 1) arises.¹⁴ The smaller (greater) the distance between the location of each patient's

⁹Prescribers include physicians and other health professionals (Sketris, 2009). Without loss of generality, we use physicians as the representative for all prescribers in this paper.

¹⁰Figueiras et al. (2008) summarize that patients' treatment choices are associated with beliefs about the perceived severity of their illness. Moreover, the 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.

¹¹Pharmacies 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).

¹²Only the United States and New Zealand allow DTCA.

¹³One can use different forms of distribution if necessary. In line with the standard literature, uniform distribution is chosen for tractability purposes without losing explanation power.

¹⁴Disutility can be understood as "transportation cost" in absolute distance following Hotelling (1929). We adopt the quadratic form of disutility following d'Aspremont et al. (1979).

MFDV and that of a brand-name drug (either drug 0 or drug 1), the more (less) the patient prefers the drug as the drug generates less (more) disutility. 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 physiological and genetic diversity, patients' (induced) preference over the therapeutic variants is bound to be heterogeneous. This heterogeneity of patients dictates that the ranking of therapeutic variants is not unanimous among patients. 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 but not as much as drug 1 does. That is, 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.

In contrast to the above-mentioned *horizontal* product differentiation (therapeutic variant dimension), in the *vertical* product differentiation patients all agree on their assessment on drug (perceived) quality. However, patients may still have different preferences for perceived quality. We use $\theta > 0$ to measure the heterogeneity in patients' preferences for perceived quality. 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.¹⁵ On the one hand, all patients attach $\theta = \theta_H$ to the brand-name drug 1 and $\theta = \theta_L$, where $\theta_H > \theta_L$). 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.¹⁶

 $^{^{15}\}theta$ 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.

¹⁶Note that we model the heterogeneity of patients' perceptions on drug quality differently from Brekke et al. (2007). In Brekke et al. (2007), both the brand-name drugs 0 and 1 have the same perceived quality (γv) for the L-type patients, despite the difference between the brand-name drugs 0 and 1. That is, the brand-name drug 0 has a generic substitute G, but the brand-name drug 1 remains its market exclusivity. In addition, Brekke et al. (2007) use a discount factor γ , where $\gamma \in (0, 1)$, to differentiate the two types of patients. In our 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 the model.

In the baseline model, there is no generic substitute for the brand-name drug 1, which is still on patent. Some "unselective" patients whose MFDV is closer to 1, eventually opt for the considerably more expensive brand-name drug 1. They do so because (1) the brandname 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.¹⁷

Figure 1 shows the characteristic box for these drugs in which, the therapeutic variant dimension is shown by the horizontal axis and the perceived quality dimension is shown by the vertical axis. The two brand-name drugs, drugs 0 and 1, are located respectively at the top left and right corners of the unit box whereas the generic drug G is located at the lower left corner of the unit box with the perceived quality difference being $(\theta_H - \theta_L) \cdot q$. The generic drug G is differentiated from the brand-name drug 0 on the vertical axis as having a lower perceived quality.¹⁸ Among the two types of patients, the "selective" ones observe and discriminate the three drugs in the unit box while the "unselective" ones do not discriminate the generic drug G and its brand-name original 0.

2.1.2 Patient's Utility Function

Now we define the utility function of the patient and calculate the market shares for the three drugs. Let the utility function of patient type j from consuming drug i (i = 0, 1, G) be:

$$U_{ji} = \begin{cases} R + (1-t) \cdot \theta_{ji} - t \cdot (x-i)^2 - c_i & i = 0, 1; \\ R + (1-t) \cdot \theta_{ji} - t \cdot (x-0)^2 - c_i & i = G, \end{cases}$$
(2.1)

¹⁷Drummond et. al (2005) introduce a third dimension on drug choice - how likely a patient would opt out the drug market till a less expensive drug is finally available. For simplicity, this paper does not study the case that a patient takes no drug and lives with the consequences of non-treatment.

¹⁸We focus on what happens after manufacturers determine their 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 paper. Readers may refer to the relevant literature on why, and to what extent, products differentiate.





Generic drug G

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 patient type (j = "selective" or "unselective"); i is drug type (i = 0, 1, G) consumed; R is the basic reservation utility derived from other sources;¹⁹ $(1 - t) \in (0, 1)$ is the weight attached to the utility derived from drug *i*'s perceived quality by patient type *j*, θ_{ji} ;²⁰ $t \in (0, 1)$ is the weight attached to the disutility from not having the drug with the ideal therapeutic variant x, $(x - i)^2$, (i = 0, 1);²¹ and c_i is the disutility of consuming drug

 $^{^{19}}R$ is assumed large enough to guarantee the patient's utility is always positive.

 $^{^{20}{\}rm The}$ utility function is additive to rule out any interaction between the vertical and horizontal differentiation.

 $^{^{21}}$ For tractability purposes, this disutility is measured in the form of "quadratic transportation cost" in line with d'Aspremont et al. (1979). This is different from the "absolute transportation cost" approach in

i, measured by patient's copay level.

Let p_0 , p_1 , and p_G be the market prices for drugs 0, 1, and G, respectively.²² Let the rate of copay be α . Accordingly, the copay levels for drugs 0, 1, and G are respectively,

$$c_{0} = \alpha \cdot p_{G} + (p_{0} - p_{G}),$$

$$c_{1} = \alpha \cdot p_{1}, \text{ and}$$

$$c_{G} = \alpha \cdot p_{G}.$$
(2.2)

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 Canadian public drug plans. This is also referred to as the generic reference pricing (GRP) reimbursement system.

The unit box in Figure 2 can be used to analyze patient preference. 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. 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.²³

According to equation (2.1), for any patient type $x \in [0, 1]$, the marginal "selective" patient who is just indifferent between the two brand-name drugs 0 and 1 is defined by the vertical line in the unit box:

$$\overline{x} = \frac{c_1 - c_0 + t}{2t}.$$
(2.3)

Brekke et al. (2007).

²²Drug price may take various forms in reality compared to a unified single "market price". To focus on drug manufacturers' price setting behaviour, we refer to the drug price at the retail level. Therefore, manufacturer rebate or professional allowance, pharmaceutical distributor mark-up, and dispensing fee, etc. can be excluded in the theoretical analysis.

²³The case that a patient takes no drug and lives with the consequences of non-treatment will not be considered.



Figure 2: Market Shares for the Three Drug Manufacturers

Similarly, for any patient type $x \in [0, 1]$, the marginal "unselective" patient who is just indifferent between the two drugs 1 and G is defined by the vertical line in the unit box:

$$\underline{x} = \frac{c_1 - c_G + t - (1 - t) \cdot (\theta_H - \theta_L)}{2t}.$$
(2.4)

Demand for drugs 0 and G are separated by the parameter λ since we 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).

2.1.3 Market Shares and Profits

In summary, the market shares for the three drug manufacturers can be depicted using the unit box in Figure 2, defined by the indifference lines \overline{x} , \underline{x} , and λ . Let the difference in perceived quality between brand-name and generic drug be δ :

$$\delta \equiv (\theta_H - \theta_L). \tag{2.5}$$

Based on equations (2.2), (2.3), (2.4), and (2.5), the market shares D_0 , D_1 , and D_G for drugs 0, 1, and G are, respectively,

$$D_0 = \lambda \cdot \overline{x}$$

$$= \frac{\lambda \cdot (c_1 - c_0 + t)}{2t}$$

$$= \frac{\lambda \cdot [t + \alpha \cdot (p_1 - p_G) + p_G - p_0]}{2t},$$
(2.6)

$$D_{1} = 1 - D_{0} - D_{G}$$

= $\frac{t - \alpha \cdot (p_{1} - p_{G}) + \lambda \cdot (p_{0} - p_{G}) + (1 - \lambda) \cdot (1 - t) \cdot \delta}{2t}$, and (2.7)

$$D_G = (1 - \lambda) \cdot \underline{x}$$

$$= \frac{(1 - \lambda) \cdot [c_1 - c_G + t - (1 - t) \cdot \delta]}{2t}$$

$$= \frac{(1 - \lambda) \cdot [t + \alpha \cdot (p_1 - p_G) - (1 - t) \cdot \delta]}{2t}.$$
(2.8)

For simplicity, we assume manufacturing cost is normalized to zero such that there is no production capacity constraint. We also assume zero marginal cost associated with manufacturers' endeavours in developing therapeutic variant and/or brand-imaging.²⁴ The profit

 $^{^{24}}$ 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, we discuss the pricing game given fixed (maximum) differentiation both in therapeutic variant and perceived quality.

functions for the three single-product firms are, respectively,

$$\Pi_{0} = p_{0} \cdot D_{0}$$

= $\lambda \cdot \frac{[t + \alpha \cdot (p_{1} - p_{G}) + p_{G}] \cdot p_{0} - p_{0}^{2}}{2t},$ (2.9)

$$\Pi_G = p_G \cdot D_G$$

= $(1 - \lambda) \cdot \frac{(t + \alpha \cdot p_1 - (1 - t) \cdot \delta) \cdot p_G - \alpha \cdot p_G^2}{2t}$, and (2.10)

$$\Pi_{1} = p_{1} \cdot D_{1}$$

$$= \frac{[t + \lambda \cdot (p_{0} - p_{G}) + \alpha \cdot p_{G} + (1 - \lambda)(1 - t) \cdot \delta] \cdot p_{1} - \alpha \cdot p_{1}^{2}}{2t}.$$
(2.11)

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.

2.1.4 Equilibrium Price with a Binding Generic Price-cap

Public and private insurers use the generic price-cap extensively to limit drug reimbursement cost. Now we discuss the equilibrium price with and without a binding generic drug price-cap, respectively.²⁵

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

$$p_G = \beta \cdot p_0, \tag{2.12}$$

where $\beta \in (0,1)$ is the price-cap in percentage, we can only look at the equilibrium prices

²⁵Note that 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 without a price-cap. We 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.

for the two brand-name firms. The generic drug price is derived from equation (2.12).

The first-order conditions for equations (2.9) and (2.11) are given by:

$$\frac{\partial \Pi_0}{\partial p_0} = 0 \quad \Leftrightarrow \quad p_0 = \frac{t + \alpha \cdot p_1 + (1 - \alpha) \cdot p_G}{2} \quad \text{and} \tag{2.13}$$

$$\frac{\partial \Pi_1}{\partial p_1} = 0 \quad \Leftrightarrow \quad p_1 = \frac{t + \lambda \cdot (p_0 - p_G) + \alpha \cdot p_G + (1 - \lambda) \cdot (1 - t) \cdot \delta}{2\alpha}.$$
 (2.14)

The second-order conditions are both satisfied to guarantee local maxima. Substituting p_G with $\beta \cdot p_0$ into equations (2.13) and (2.14), we have:

$$p_0 = \frac{t + \alpha p_1}{2 - \beta(1 - \alpha)} \quad \text{and} \tag{2.15}$$

$$p_1 = \frac{[t + (1 - \lambda)(1 - t)\delta] \cdot [2 - \beta(1 - \alpha)] + (\lambda + \beta\alpha - \beta\lambda)(t + \alpha p_1)}{2\alpha[2 - \beta(1 - \alpha)]}.$$
 (2.16)

 $p_0 \ {\rm and} \ p_1 \ {\rm can} \ {\rm be solved} \ {\rm from equations} \ (2.15) \ {\rm and} \ (2.16).$ Let

$$\Gamma \equiv 4 - 2\beta + \alpha\beta - \lambda + \beta\lambda, \qquad (2.17)$$

$$\Psi \equiv 2 - \beta + \alpha \beta, \quad \text{and} \tag{2.18}$$

$$\Phi \equiv 2 - \beta + 2\alpha\beta + \lambda - \beta\lambda.$$
(2.19)

The equilibrium prices for the two brand-name drugs with the binding generic price-cap are, respectively, 26

²⁶Note 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.

$$p_0 = \frac{t(\Gamma + \Phi) + (1 - \lambda)(1 - t)\delta\Psi}{\Gamma\Psi} \quad \text{and}$$
(2.20)

$$p_1 = \frac{t\Phi + (1-\lambda)(1-t)\delta\Psi}{\alpha\Gamma}.$$
(2.21)

Now we 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, which are explained below. 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; α is the rate of copay established by public/private insurance plans; and β is the percentage of the brand-name drug price capping the generic drug price.

By altering these three parameters, we can observe the impact of these changes on the equilibrium drug prices.²⁷

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.

Proposition 1 suggests that the difference in the perceived quality between brand-name and generic drugs 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 drug and its generic substitute is large enough, an increase in the proportion of the "unselective" patients would 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

²⁷The proofs are straightforward and are available upon request.

would charge lower (higher) prices in equilibrium.

Proposition 2 suggests that 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 patients become more "unselective" as a whole.²⁸

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 in which there is a large proportion of "selective" patients, the equilibrium brand-name drug price goes up, ceteris paribus, even if a cheaper therapeutic substitute in the generic form is available.

Proposition 3 suggests that with everything else being equal, a lower (higher) generic price-cap 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 because the interaction between the other two parameters α and λ may play a role. We find that when the proportion of "selective" patients (λ) is very 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.²⁹

2.1.5 An Extension to the Baseline Model without a Generic Price-cap

When there is no generic price-cap, the two first-order conditions (2.13) and (2.14) remain the same. In addition, the third first-order condition with respect to p_G is

$$\frac{\partial \Pi_G}{\partial p_G} = 0 \quad \Leftrightarrow \quad p_G = \frac{t + \alpha p_1 - (1 - t)\delta}{2\alpha}.$$
(2.22)

²⁸As 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.

²⁹This may be less of an issue if the patented drug prices are also capped. For example, in Canada the Patented Medicine Prices Review Board set Maximum Non-Excessive price (MNE) for patented drugs.

Therefore, we have

$$p_0 = \frac{3(1+\alpha)t - (1+\alpha\lambda - 2\alpha)(1-t)\delta}{6\alpha + \lambda(1-\alpha)},$$
(2.23)

$$p_G = \frac{6t - (\lambda + 2)(1 - t)\delta}{6\alpha + \lambda(1 - \alpha)}, \quad \text{and}$$
(2.24)

$$p_1 = \frac{(6\alpha - \lambda + \alpha\lambda)t + (2\alpha + \lambda - 3\alpha\lambda)(1 - t)\delta}{\alpha[6\alpha + \lambda(1 - \alpha)]}.$$
(2.25)

Now we 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 and generic drugs 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.

Proposition 4 suggests that when the copay rate is relatively high ($\alpha > 25\%$ in the model), all three drug manufacturers, brand-name and generic, will raise (lower) prices in response to a lower (higher) proportion of the "selective" patients. 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 drugs is large enough. With a low rate of copay and a large enough perceived quality differential, all three firms will lower (raise) prices in response to a lower (higher) proportion of "selective" patients.

Without any generic price-cap, in the first scenario, when there is 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) leads to higher brand-name drug prices in the equilibrium. Moreover, an 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 the generic drug price.

Without any generic price-cap, in the second scenario, where the rate of copay is not high (i.e. $\alpha < 25\%$) and perceived quality between brand-name and generic drugs is not very different, all three drug firms would have the same reactions in price setting as in the first scenario. If there is a lower proportion of the "selective" patients, 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 intuitive but the observations are consistent with profit maximization. They pose a dilemma for the policy-makers: on the one hand, public/private insurers are willing to see the breakdown in patients' loyalty regarding expensive brand-name drugs and gain favour for the less expensive 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, where the rate of copay is not high (i.e. $\alpha < 25\%$) and the difference in the perceived quality between brand-name and generic drugs is very large, 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 and generic drugs is very large, 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 and generic drugs is very small, ceteris paribus, a higher (lower) rate of copay leads to lower (higher) equilibrium price for the brand-name drug 1.

Proposition 5 suggests that if the difference in perceived quality between brand-name and generic drugs is very large, with everything else being equal, an increase (decrease) in the rate of copay would lead to higher (lower) prices for both the brand-name drug 0 and its generic version G in the equilibrium.

If the difference in perceived quality between brand-name and generic drugs is very large, with everything else being equal, an increase (decrease) in the rate of copay would lead to lower (higher) prices for brand-name drug 1 in the equilibrium. But when the difference in perceived quality between brand-name and generic drugs is very small, 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 differential between brandname and generic drugs is not large: 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, 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 sufficiently large, 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 extreme, 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.

2.2 An Extension to the Baseline Model with Therapeutic Reference Pricing

We introduce an extension to the baseline model characterized by the therapeutic referencing pricing (TRP) reimbursement system, which differs from the GRP reimbursement system. The GRP system excludes the brand-name drug 1 in the interchangeable drug category but in the TRP system, the interchangeable therapeutic category is broadened to include the brand-name drug 1, which is on patent and doe not have any generic substitute, in addition to the brand-name drug 0 and its generic substitute G. 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. Clearly, the TRP system elicits price competition between the generic drug G and the brand-name drug 1, even if the latter does not have any generic substitute. By qualifying more drugs under the interchangeable therapeutic category, the TRP policy creates intense competition among these therapeutic substitutes.

2.2.1 Market Shares and Profits

Now we discuss the impact of the change in the reimbursement system on the drug manufacturers' price-setting behaviour. 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 levels for drugs 0, 1, and G are, respectively,

$$c_0 = \alpha \cdot p_G + (p_0 - p_G),$$

$$c_1 = \alpha \cdot p_G + (p_1 - p_G), \text{ and } (2.26)$$

$$c_G = \alpha \cdot p_G.$$

The market shares for the three drug manufacturers are, respectively,

$$D_{0} = \frac{\lambda(c_{1} - c_{0} + t)}{2t}$$

= $\frac{\lambda[t + p_{1} - p_{0}]}{2t}$, (2.27)

$$D_G = \frac{(1-\lambda)[c_1 - c_G + t - (1-t)\delta]}{2t}$$

= $\frac{(1-\lambda)[t+p_1 - p_G - (1-t)\delta]}{2t}$, and (2.28)

$$D_1 = 1 - D_0 - D_G$$

= $\frac{t + p_G - p_1 + \lambda(p_0 - p_G) + (1 - \lambda)(1 - t)\delta}{2t}$, (2.29)

where $\delta \equiv (\theta_H - \theta_L)q$ represents the difference in perceived quality between brand-name and generic drugs.³⁰

In equations (2.27), (2.28), and (2.29), 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 equations (2.26), only the difference between their drug prices matters.

Again, for simplicity, we assume zero marginal cost associated with manufacturers' endeavours in developing therapeutic variant and/or brand-imaging. Therefore the profit func-

³⁰The change in the copay of the brand-name drug 1 in (2.26) 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 $(1-t)(\theta_H - \theta_L)q > p_0 - p_G$.

tions for the three firms are, respectively,

$$\Pi_0 = p_0 D_0$$

= $\lambda \frac{(t+p_1)p_0 - p_0^2}{2t}$, (2.30)

$$\Pi_G = p_G D_G$$

= $(1 - \lambda) \frac{[t + p_1 - (1 - t)\delta]p_G - p_G^2}{2t}$, and (2.31)

$$\Pi_1 = p_1 D_1$$

= $\frac{[t + \lambda(p_0 - p_G) + p_G + (1 - \lambda)(1 - t)\delta]p_1 - p_1^2}{2t}$. (2.32)

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

2.2.2 Equilibrium Price with a Binding Generic Price-cap

Recall that generic price-cap given in equation (2.12) is $P_G = \beta \cdot p_0$. The first-order conditions for the two brand-name manufacturers are, respectively,

$$\frac{\partial \Pi_0}{\partial p_0} = 0 \quad \Leftrightarrow \quad p_0 = \frac{t+p_1}{2} \quad \text{and}$$
 (2.33)

$$\frac{\partial \Pi_1}{\partial p_1} = 0 \quad \Leftrightarrow \quad p_1 = \frac{t + \lambda(p_0 - p_G) + p_G + (1 - \lambda)(1 - t)\delta}{2}.$$
(2.34)

The second-order conditions are both satisfied to guarantee local maxima. Substituting p_G with $\beta \cdot p_0$ in equations (2.33) and (2.34), we obtain

$$p_0 = \frac{t+p_1}{2}$$
 and (2.35)

$$p_{1} = \frac{t + (\lambda + \beta - \beta \lambda)p_{0} + (1 - \lambda)(1 - t)\delta}{2}.$$
(2.36)

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

$$p_0 = \frac{3t + 2(1 - \lambda)(1 - t)\delta}{4 - \lambda - \beta + \beta\lambda} \quad \text{and}$$
(2.37)

$$p_1 = \frac{2t + 2(1 - \lambda)(1 - t)\delta + t(\lambda + \beta - \beta\lambda)}{4 - \lambda - \beta + \beta\lambda}.$$
(2.38)

With the equilibrium prices for the two brand-name firms under the TRP copay structure defined in equations (2.26) and a binding generic price-cap $p_G = \beta \cdot p_0$, we can evaluate 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 drugs is either large enough or small enough, 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 drugs is neither too large nor too small, ceteris paribus, firm 0 raises its price while firm 1 lowers its price.

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 set prices in response to preference changes (more or less "selective") depends upon how patients feel about the difference in perceived quality between brand-name and generic drugs.

When the difference in perceived quality is very large or very small, a switch of patients' preference from brand-name to generic drug — "selective" patients becoming "unselective" patients — leads to higher equilibrium prices for both brand-name drugs, with everything else being equal. The brand-name manufacturers raise prices to maximize profits because there are proportionally less "selective" patients whom the manufacturers must leverage, regardless of the difference in perceived quality.

However, when the difference in perceived quality is in an intermediate range, a switch of patients' preference from brand-name to generic drugs leads to a higher equilibrium price for drug 0 but a lower equilibrium price for brand-name drug 1. The brand-name drug 1 manufacturer lowers its price in response to the smaller proportion of "selective" patients only when the difference in perceived quality between brand-name and generic drug is further narrowed. This intermediate state differs from what we find from the baseline model, where the equilibrium prices for both brand-name drugs always move in the same direction regardless of the difference in perceived quality being 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 generic price-cap becomes smaller.

Proposition 7 shows that, under the TRP system, if the generic price-cap becomes smaller, then both brand-name manufacturers unambiguously lower their drug prices. This is because the TRP system is more effective than the GRP system in eliciting generic competition to both the brand-name drugs under the interchangeable therapeutic category. This finding is unique in this extension with the TRP system and not observed in the baseline model.

The key predictions from the above theoretical work are summarized as follows:

First, the difference in perceived quality between brand-name and generic drugs is pivotal in brand-name manufacturers' price setting decisions regardless of which reimbursement (GRP or TRP) is in place. As long as patients believe (or are made to believe) that brandname drugs are "superior" in therapeutic quality than generic substitutes, brand-name drug manufacturers are able to leverage their market power to charge higher prices in the market. This may happen even when proportionally more patients become "unselective".

Second, the public/private drug insurers can either raise the rate of copay or lower the generic price-cap or do both to control prescription drug reimbursement costs. These policy tools used in different situations may have distinct implications on drug manufacturers' price setting behaviour. It is clear that prices of the brand-name drugs will fall if the rate of copay is raised significantly and a binding generic price-cap is in place.

Third, imposing generic price-caps to lower drug reimbursement costs is considered effective. Only under special circumstances, for example, in a relatively young therapeutic market with predominant patients' preference for brand-name drugs, those patented brandname manufacturers may respond to a lower generic price-cap by increasing their drug prices. In this situation, price regulations on patented drugs may serve as a necessary policy complement.

In the following, we use the data on the representative therapeutic drugs of the Canadian pharmaceutical market to test three hypotheses while taking into account of the market structure and the unique Canadian context.

3 Data and Empirical Research Methodology

The longitudinal data on key information of prescription drug products, including drug price, market structure, and generic substitution 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. The manufacturers' list drug prices and the associated variables such as policy information submitted from the province of Alberta, which exhibited the best overall data quality, were used for this research.³¹ The data were cleaned and then linked with drug patent data accessed from the Health Canada

³¹Note 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.

Patent Register.

To include on- and off-patent brand-name drugs and generic drugs, the data of three broad classes of drugs (WHO-ATC 4^{th} level) were selected for the period from 2000 Q2 to 2008 Q2 (33 calendar quarters). 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).³² The dataset for this study contains 105, 20, and 23 drugs under each selected drug class, respectively.³³ In total, there are 148 drugs (DINs) in 14 drug molecules and manufactured by 19 drug firms. The unbalanced panel data has 2,946 quarterly observations.³⁴

The panel data has a tree-like or nested structure with 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 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 Canada-based Apotex Inc., respectively. Figure 3 sketches the relationships among the three levels.³⁵

³²Drug 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.

 $^{^{33}\}mathrm{The}$ selected drug classes are categorized under the 4^{th} level ATC code C10AA, J02AC, and N02CC, respectively.

 $^{^{34}}$ We include 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. Ren (2011) contains more details on the data collection.

³⁵Level-1 is the observations over time strictly nested within the Level-2 units (DINs). Level-1 (observa-



Figure 3: A Cross-classified Three-level Data Structure

The distribution of the data is demonstrated in Table 1, which decomposes the 2,946 observations by 14 molecules and by 19 manufacturers.

tions over time) is connected to and Level-2 (drugs) with dashed lines at the bottom of Figure 3. This figure demonstrates the data structure but does not include all products covered in this empirical study.

	Tal	ble 1:	Num	ber of	Observ	vations	(DIN	by qu	larter)) in Ea	ch Mo	lecule-	by-Ma	unufact	urer C	Jell			
									Manu	lfactur	\mathbf{er}^b								
Molecule JAN	APX	AZE	BRI	COB	FRS	GPM	GSK	ſŊſ	LIN	NOP	NVR	NXP	ΡFΙ	\mathbf{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	00		69		54	6	60	54		615
Fluvastatin											81								81
Atorvastatin													125						125
Rosuvastatin		71																	71
Fluconazole	66					66				66			66	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
\mathbf{Totals}^{a} 33	373	104	00	193	297	271	132	32	63	251	81	69	248	256	29	190	186	48	2,946
^{a} The 2,946 observ	ations .	are spa	mned .	across 1	l48 dru	gs (DIN	s). Eac	th drug	g (DIN	V) has]	l-33 qua	arterly	observ	ations.					
b The manufacture.	rs and	their a	cronyı	ns are:	Janssei	n-Ortho	Inc. (JAN),	A pote	ex Inc.	(APO)	, Astra	Zeneca	Lanad	la Inc.	(AZE)			
Bristol-Myers Squi	bb Can	ada Cc	o. (BR	I), Cot	alt Ph	armaceu	tticals I	nc. (C	(OB),	Merck	Frosst	Canada	Ltd.	(FRS),	Genpł	ıarm In	c. (GPN	М),	
GlaxoSmithKline (GSK),	$_{ m Johnso}$	m & J	ohnson	Inc. (J	INJ), Li	nson P]	haram	a Inc.	(LIN),	Novop	harm I	Ltd. (1	(OP),					
Novartis Pharmace	uticals	Canad	la Inc.	(NVR), Nu-P	harm Iı	ıc. (NX	(P), P	fizer C	Janada	Inc. (P	FI), PI	narma	science	Inc. (F	MS),			

Ranbaxy Pharmaceuticals Canada Inc. (RAN), Ratiopharm Inc. (RPH), Sandoz Canada Inc. (SDZ), and TaroPharma Inc. (TAR).

In Table 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 the 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).

We select the multilevel modelling strategy to handle the special data structure for the following reasons: (1) A multilevel model can be used to model a complex market context. (2) It 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. (3) It can capture unbalanced data structures resulting from natural imbalances and natural hierarchies in the data. (4) It utilizes the clustering information and therefore produces statistically unbiased estimates and corresponding standard errors.

To test our hypotheses, we use 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 sketches the hierarchical three-level data structure.³⁶

The multilevel model can be parameterized in the form of the GLS model, which can

³⁶In principle, the cross-classification model represented in Figure 3 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. However, 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, we drop the random intercept for the "manufacturer" factor at level-3 and reduce the model to a strictly hierarchical (three-level) specification. As shown in Figure 4, 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, we include the type of manufacturer (brand-name or generic) as an explanatory variable to control the manufacturer effect.



Figure 4: A Strictly Hierarchical Three-level Data Structure

be estimated by either the iterative generalized least squares (IGLS) or restricted maximum likelihood (REML) algorithm if the explanatory variables and the random error terms are uncorrelated. However the correlations between some endogenous explanatory variables and the random components at level-2 and level-3 cannot be ruled out and cause bias and inconsistency in the estimation. To address this problem, we use the IV-type maximum likelihood estimation (MLE), in which we first run the maximum likelihood estimation of the regression of the endogenous explanatory variable on the instrumental variables (both the first-differenced endogenous explanatory variable and its one-quarter lag, and, then, we run the maximum likelihood estimation of the regression of the dependant variable on the predicted values of endogenous variables and all other exogenous variables. A similar approach has been adopted in the literature. For example, River and Vuong (1988) develop a two-step maximum likelihood procedure for estimating simultaneous probit models; and 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.

4 Empirical Findings

Because the difference in perceived quality between brand-name and generic drugs, the lower rate of copay and generic price-cap will sustain the price premiums of brand-name drugs even if they are off patent, we now wish to test the following hypotheses by taking into consideration the market structure and existing public policy.

The *first* hypothesis is that more generic substitutes do not have any net effect of lowering drug prices. The *second* hypothesis is that more therapeutic substitutes do not have any net effect of lowering drug prices. The *third* hypothesis is that, given the generic substitution policy in place, brand-name drugs do not have any net price premiums over their generic substitutes.

The variable of interest is the price of drugs in the study sample. To understand the drug price dynamics, 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.

We 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 2.

The variable $logavgpricelag_{jit}$ is the average historical (in quarter-lag) price (in logarithm) for all drugs *i* with the same strength in molecule *j* in quarter *t*. The lagged value of this variable can be viewed as the price-setting anchor within each market niche for the next period. It is also used to control for the unobservable information resulting from missing variables.³⁷ When this price-setting anchor variable is included as an explanatory variable in the regression model, the endogeneity problem may arise. We 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, we are able to deal with the endogeneity

³⁷For example, drug sales or volume factor likely play a role in determining drug prices. In addition, a market share variable likely correlates with other market structure variables in the model. Without any control, the estimates can be biased.

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)	
$policy_{jit} \times brand_i$	Interaction term between policy and brand-name dummy variables	
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	
$str_j \times J_j$	Interaction term between strength and antifungal drugs	
$str_j \times N_j$	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)	

Table 2: Description of Explanatory Variables in the Regression Analysis

* The baseline cases for the dummy variables are in parentheses.

problem.³⁸

The variable $gennum_{it}$ is 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

³⁸Following Lewbel (1997) and Ebbes et al. (2004), we 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. We 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.

among themselves.³⁹ We include in our models $gennum_{it}$ to examine the *first* hypothesis that more generic substitutes do not have any net effect of lowering drug prices, while other variables are appropriately controlled for.

The variable $compnum_{jt}$ is the total number of brand-name and generic drug manufacturers that compete in the broad therapeutic market encompassing multiple drug molecules j's in quarter t.⁴⁰ This variable records the number of all drugs competing within a broad therapeutic class. We include into our models $compnum_{it}$ to examine the *second* hypothesis that more therapeutic substitutes do not have have any net effect of lowering drug prices, while other variables are appropriately controlled for.

The variable $brand_i$ is the brand-name manufacturer dummy variable for drug *i* with generic manufacturer being the baseline case. In the three-level hierarchical model, we include in our models $brand_i$ to test for brand-name price premiums after appropriately controlling for other relevant variables.

The variable $policy_{jit}$ is a dummy variable indicating whether or not a generic substitution policy is in place for drug i's molecule j in quarter t in the formulary. This variable is a proxy for generic competitors in the drug molecule in question.⁴¹ As noted in Section 3, 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 costs by encouraging generic drug substitution. 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 j. We include this variable in our model to

³⁹For example, different strengths of Apo-simvastatin in quarter t are all manufactured by Apotex. Therefore we record *one* more generic substitute in $gennum_{it}$ for the molecule simvastatin.

⁴⁰For 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 for the rest of the five statin molecules, if available. Besides simvastatin, the other five statin molecules for this 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.

⁴¹However, 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.

examine whether the generic substitution policy has a net effect of lowering drug prices.

The variable $policy_{jit} \times brand_i$ is the interaction term between $policy_{jit}$ and $brand_i$. By including this variable in our model, we are able to evaluate the dynamics of the brandname drug price with and without a generic substitution policy in place. That is, we can test the *third* hypothesis that brand-name drugs do not have any net price premiums over their generic substitutes when generic substitution policy is in place, after all other variables are controlled for.

The variables J_j and N_j are dummy variables for the groups of antifungal and migrainerelief drugs js, with cardiovascular drugs being the baseline case (ATC group "J" and "N", and "C", respectively). We include these therapeutic group dummy variables in our regression model to appropriately control for systematic price differences 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.⁴²

The variable str_j is a derived variable indicating the *relative* strength of the drug in question. We relate the drug dosage to a standardized unit, the WHO Defined Daily Dose (DDD).⁴³ The DDD provides a fixed unit of measurement independent of price and dosage form (e.g. tablet strength), which allows us to evaluate the role of drug strength.⁴⁴ We in-

 $^{^{42}}$ We do not introduce a higher level at level-4 to the model because the three selected WHO-ATC groups are not random samples from the population of a 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.

⁴³According 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. The DDD is subject to periodical review and therefore it may have different versions over time. For simplicity, we use the WHO DDD Index 2010, retrieved at http://www.whocc.no/atc_ddd_index on Apr. 4, 2010.

⁴⁴First, we retrieve the DDD information for all drug molecules included in this study. For example, simvastatin has a DDD of 30mg, which means that 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_i is the relative strength level for

clude str_j in our models to appropriately control for the degree to which the dosage strengths may shape the drug price-setting behaviour.

The variables $str_j \times J_j$ and $str_j \times N_j$ are two interaction terms between the relative strength variable (str_j) and therapeutic class dummy variables, J_j and N_j , respectively. We include them to evaluate in this sample whether drug manufacturers use different pricesetting 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, we include three calendar quarter dummy variables, with the 2^{nd} quarter as the baseline case. In this way, we can control for the possible seasonality in the drug price dynamics net of inflation.

The regression coefficient estimates from the IV-MLE (three-level) estimation are given in Table 3. To evaluate the estimates of the IV-MLE estimation, we also include in Table 3 the pooled 2SLS estimates as the benchmark.⁴⁵ The pooled 2SLS estimation does not take into account of the complex variance-covariance structure in the multilevel model. As such, it gives less efficient yet unbiased coefficient estimates.⁴⁶ As a result, the more efficient IV-MLE estimation allows for more reliable statistical inference.

Specifically, the results of the IV-MLE estimation suggest 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 volatility. 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% for the level-1 inter-temporal random-effect. However, the between-molecule random-effect at level-3 absorbs the overall drug price heterogeneity about 83%. The empirical results strongly support the inclusion of the molecule factor at level-3 for this study.

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.

⁴⁵The pooled 2SLS estimation uses the same instrumental variables $\Delta lnavgpricelag_{jit}$ and $\Delta lnavgpricelag_{jit-1}$.

⁴⁶We use the Hausman-Taylor estimator (two-level) to verify the robustness of the IV-MLE estimation.

	Pooled 2SLS	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)*
$policy_{jit} \times brand_i$	$0.2843(0.1244)^{**}$	$0.1717(0.0207)^{***}$
$lnavgpricelag_{jit}$	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)	$0.0952(0.0317)^{***}$
$str_j \times J_j$	0.9309(1.0168)	$0.8995(0.2810)^{***}$
$str_j \times N_j$	-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 Para	meters	
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%]
R^2	0.9742	-
Log-likelihood	_	4572.5606

 Table 3: Regression Results for the Drug Price Dynamics

***Statistically significant at 1% level, **
significant at 5% level, *
significant at 10% level

 † Fractions of variance attributed to each specific level in brackets

Our three hypotheses based on the results of the IV-MLE estimation are examined as follows.

First, the coefficient estimate for gennum is positive and significant at the 1% significance

level. This indicates that more generic substitutes within a drug molecule does not lower drug prices, when other contextual variables are appropriately 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 provides the evidence for rejecting the *first* hypothesis.

Second, although the coefficient estimate for *compnum* is negative, it is not statistically significant. Therefore, there is no statistically significant evidence to associate the number of therapeutic substitutes across drug molecules and the drug price dynamics. This provides no evidence for rejecting the *second* hypothesis.

Third, the coefficient estimate for *brand* is positive and statistically significant at the 1% significance level, indicating that brand-name drugs enjoy remarkable price premiums over their generic substitutes in general. As predicted by our theoretical work, the regression estimate confirms that brand-name drug manufacturers are able to maintain a 29% price premium over generic drugs as the result of the difference in perceived quality between brand-name and generic drugs. In addition, the coefficient estimate for *policy* is negative and statistically significant at the 10% significance level. Clearly, when there is a generic substitution policy in place, all drug prices will fall about 3.8%. This supports the effectiveness of the generic substitution policy.

Fourth, the coefficient estimate for the interaction term $policy \times brand$ is positive and statistically significant at the 1% significant level. Brand-name drugs tend to maintain net price premiums over their generic substitutes by about 18.7% on average,⁴⁷ even when the generic substitution policy is in place, although the net price premium (18.7%) is less than the case (29%) where there is no such policy by the 12% percentage point difference. This finding rejects the *third* hypothesis.

Indeed, a generic substitution policy by design allows public drug plans to cover only the cost of generic drugs in an interchangeable drug class and ensures considerable savings for these plans.⁴⁸

⁴⁷It is derived by applying the formula $e^{0.1717} - 1 \approx 0.187$.

⁴⁸For example, a preliminary estimate of extra dollars the Nova Scotia Pharmacare Programs could

In addition to the above key empirical findings, we now discuss other empirical findings based on the coefficient estimates associated with the rest of the control variables.

First, the coefficient estimate for *logavgpricelag* is positive and statistically significant at the 1% significance level. The empirical evidence supports that about 57% of the price dynamics in the current period can be explained by the price anchors in the previous period.

Second, the coefficient estimates for J and N are both positive but that of N is statistically significant at the 1% significance level. This suggests that while 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), the migraine-relief drugs (under the ATC code N02CC) are more expensive compared to the baseline statin drugs.

Third, the coefficient estimate for str is positive and statistically significant at the 1% significance level. In general, the stronger (weaker) dose each tablet/capsule contains, the higher (lower) price premium a drug manufacturer would charge for the drug. Everything else being equal, there is about a 10% increase for 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 1% significance level. This suggests that an increase in drug strength (DDD) is associated with a higher price premium for the antifungal drugs than for the cardiovascular drugs.

Finally, the calendar quarter dummy variables all have negative coefficient estimates but only those of cq1 (first quarter) and cq3 (third quarter) are statistically significant at the 5% level. This reflects that the upward price adjustment normally takes place in the 2^{nd} quarter when a new government budget starts.⁴⁹

have reimbursed for statin drugs alone during 2000-2008 reaches \$2.3 million (2002 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 \in 53 million and \in 52 million (Gumbs et al., 2007).

⁴⁹It should be noted that the price adjustment discussed here is in real terms. It is informative since drug manufacturers also take the inflation effect into consideration when they set drug prices.

5 Concluding Remarks

In this paper, we use the two-dimension product differentiation model to analyze the impact of changes in patient preference and government policies on drug manufacturers' price setting behaviour. Our theoretical work suggests that the greater difference in perceived quality between brand-name and generic drugs leads to higher brand-name drug prices and that a higher rate of copay with a binding generic price-cap can reduce brand-name drug price premiums.

To evaluate the theoretical predictions, we examine Canadian drug price data. Because of the unbalanced and hierarchical panel data, we use the multilevel model to appropriately capture the complex contextuality of the data and implement the IV-MLE estimation to deal with endogeneity issues and produce unbiased and efficient estimates. 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 findings based on the IV-MLE estimation are as follows. First, more generic drugs in a molecule do not necessarily translate 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. Second, more therapeutic substitutes do not have any net effect of lowering drug prices either. Third, when the generic substitution policy is in place, brand-name drugs still maintain some price premiums over their generic substitutes, albeit the price premium is lower than the case without this policy. These empirical findings give us some indirect evidence for the difference in perceived quality in brand-name and generic drugs and for the limited role of copay and generic price-cap policies.

Given the nature of the pharmaceutical industry/market, policy-makers at the federal and provincial levels strive for a balance between the containment of drug reimbursement costs and the encouragement of innovation in providing effective and safe drugs. The empirical findings from this paper provide useful information to decision-makers of both public and private drug plans.

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