Brand-name and Generic Drug Pricing in A Regulated Environment: Findings from Canadian 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 it does not pay full attention to changes in a regulated market. Canada provides the context for studying drug manufacturers' price-setting and product differentiation decisions in such an environment. To fill the void in the literature, we first incorporate changes in patient preference and government reimbursement policies into our theoretical analysis. Then we conduct empirical analysis of the relationship between the drug price dynamics and the complex institutions in changing market places of the pharmaceutical industry. Our theoretical and empirical work provides new predictions and evidence on the brand-name drug price premiums. More specifically, the difference in perceived quality between brand-name and generic drugs, rate of copay, and generic-substitution policy do influence brand-name drug manufacturers' price-setting decisions.

Keywords: drug patent, brand-name drug, generic drug, product differentiation, drug pricing, market structure, patient preference, government reimbursement policies, rate of copay, generic price-cap, generic-substitution policy, multilevel modelling
JEL Classification: C23, I18, L11

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Abstract

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1 Introduction

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

Market structures in the pharmaceutical industry range from pure monopoly to monopolistic competition and can experience constant changes. At any point in time, patented brand-name drugs may coexist with off-patent brand-name and/or their generic substitutes in the same therapeutic market. As existing patented brand-name drugs are expected to 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 brand-name 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 efforts to identify and explain this paradox, as Berndt (2002) notes it is unclear as to why this paradox persists in many cases.

Indeed, pharmaceutical markets in most 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 with generic price-caps and may pay for a significant portion of full prices through copay rates do not prescribe and consume them. We attempt to take into account the regulated pharmaceutical market with multiple stakeholders when analyzing the generic competition paradox.

Brekke et al. (2007) theorize that an off-patent brand-name drug and its generic substitute are vertically

[1] Comanor (1986) provides an insightful discussion on the facts and political economy of the pharmaceutical industry.

differentiated in perceived quality[2] in the fashion of Mussa and Rosen (1978), while patented brand-name drugs that are therapeutic substitutes,[3] are horizontally differentiated in the fashion of Hotelling (1929). Grootendorst (2007) notes that the division between off-patent drugs and their substitutes may be less clear in reality as some brand-name drug manufacturers may participate in the generic market by making confidential arrangements with their subsidiary company or a generic drug 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. Drug firms actively adopt price discrimination given the existence of the tiered consumer groups, in a market setting that systematically raising prices is allowed. In an environment where drug price is regulated such as in Canada, it is more realistic to maintain the price premium than raising prices. The focus of Kong (2009) is not on the role played by governments in the funding and provision of prescription drugs, which is one of the focal points of this paper.[4]

In this paper, we extend the two-dimension product differentiation model proposed by Brekke et al. (2007) for the regulated environment, where there are multiple stakeholders with various copay rates and generic price-caps in generic or therapeutic referencing reimbursement systems. Our model incorporate patient preference, government policies, market structure, and firms' profit optimization under the regulated market setting. The model makes predictions relevant to policy making in such markets. For example, the differentiation in perceived quality between brand-name and generic drugs can be 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 their generic substitutes, brand-name drug manufacturers are able to leverage their market power to charge higher prices in the market (see Proposition 1 below). This may happen even when there are proportionally less patients are "selective" on perceived quality, everything else being equal. This finding is robust under different reimbursement systems (see Propositions 3 and 6 below).

In addition to the predictions of our theoretical model, we also use a unique data set to test the following three hypotheses: (1) More generic substitutes do not have any net effect of lowering drug prices (checking the evidence against the prediction of Proposition 1 discussed below). (2) More therapeutic drug substitutes

[2]Hollis (2002) finds that the earlier the market entry, the greater market share a generic manufacturer 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).

[3]These substitutes offer different therapeutic variants with different pharmacokinetic and pharmacodynamic properties which may be needed for some patients.

[4]This 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.

do not have any net effect of lowering drug prices (checking the evidence for the combination of several pricing strategies of brand-name drug manufacturers predicted by Proposition 6 discussed below). (3) Given the available generic substitution policy, brand-name drugs do not have any net price premiums over their generic substitutes (checking the evidence against the prediction of Proposition 3 discussed below). To ensure a rigorous evaluation of these hypotheses, we take the existing consumer preferences between brand-name and generic drugs and existing policy as given. We use the multilevel model to reflect the regulated environment and drug market "ecology" where different drugs appear at different points in time. In addition, the drug price dynamics needs to be anchored to the historical prices which may be endogenous. Hence, we use this multilevel model with the instrumental variable estimation in our identification strategy. We have found the evidence to reject the first and third hypotheses but not the second one. These findings imply that the difference in the perceived quality between brand-name drugs and their generic substitutes diminishes as more generic substitutes become available. But it is not the case for more therapeutic drug substitutes. With the existing generic substitution policy, brand-name drugs can still have premiums and be priced at about 18.7% higher on average.

The remainder of the paper is organized as follows. In Section 2 we propose the two-dimension product differentiation models in various regulatory settings. In Section 3 we explain the data and empirical research methodology. We discuss our empirical findings in Section 4. Finally, concluding remarks are offered in Section 5.

2 Theoretical Analysis

2.1 The Baseline Model

Our 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 government caps the price of the generic drug G with 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 premiums, deductibles and copays while the public/private drug plans reimburse patients the rest of the drug cost.[7] With the knowledge of patients'

[5]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.

[6]We assume that the drugs are used to treat chronic conditions in the seniors. The majority of Canadian seniors are fully covered by public drug plans, but with varying degrees of patient cost-sharing.

[7]When the generic version of a brand-name drug is available but the prescription is filled by the brand-name drug instead,

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 the drug products in our model along two dimensions in the similar spirit of Brekke et. al. (2007), namely, therapeutic variant and perceived quality. First, drugs within a therapeutic market may exist in rather distinct therapeutic variants, e.g., in terms of their interactions with certain kinds of food and other medications, their mechanism of action, and/or their pharmacokinetics, etc. The two brand-name 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 superior quality compared to their generic counterparts because the former has longer market exposure either through direct-to-consumer advertising (DTCA) or commercial detailing targeting physicians or other prescribers.[9] However, some issues, such as potential allergies to excipients contained in generic drugs and patients' socio-demographic 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, out of their professional knowledge, or "indirect advertisements" that patients receive through cross-border televisions

patient needs to pay a copay for the generic drug plus the price differential between the generic drug and its brand-name original.

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

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

[10] Figueiras 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 socio-demographic factors such as ethnicity, education, income, age, risk perception, knowledge, and past experience.

[11] 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).

or online marketing.[12]

In the current setting with the therapeutic variant dimension (q) reflected by the $[0,1]$ interval, the two differentiated brand-name drugs are located at both ends of the $[0,1]$ interval. That is, drug 0 (1) is located at 0 (1). Let the typical patient's most-favourite drug variant (MFDV) be 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 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) preferences over the therapeutic variants are 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 with less side effects in patient A than drug 1 does. But for patient B, it may be the other way around. In other words, for patient A, $|x_A-0| < |x_A-1|$; while for patient B, $|x_B-0| < |x_B-1|$. As such, patient A and patient B have exactly 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. We assume that θ follows the 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 $\theta = \theta_L$ to the generic drug G (both θ_H and θ_L are positive scalars and $\theta_H > \theta_L$). On the other hand, the "selective" patients attach $\theta = \theta_H$ to the brand-name drug 0; while the "unselective" patients 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.

Our model is different from Brekke et al. (2007) in treating the heterogeneity of patients' perceptions on drug quality. In Brekke et al. (2007), both the brand-name drugs 0 and 1 have the same perceived quality ($\gamma\upsilon$) for the "L-type" patients, despite the difference between the brand-name drugs 0 and 1 (that is, the

[12] Only the United States and New Zealand allow DTCA.

[13] One 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.

[14] Disutility 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).

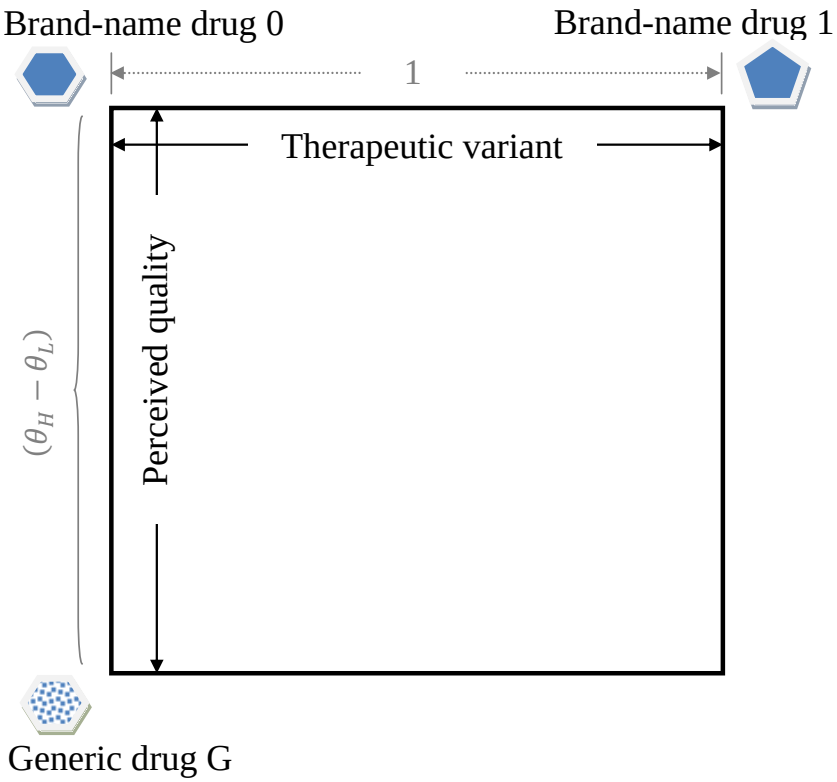
[15] θ follows a Bernoulli distribution only for the brand-name drug 0. All patients treat the brand-name drug 1 and the generic drug G in the same way in terms of perceived quality.

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 our model.

In the baseline model, there is no generic substitute for the brand-name drug 1, the drug 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 brand-name drug 1 offers them the more desirable drug variant that neither the brand-name drug 0 nor the generic drug G does, and (2) a generic (and cheaper) version of drug 1 is not yet available in the market.[16]

Figure 1 shows a box characterizing these drugs, where 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,

Figure 1: Locations of the Three Drugs



[16] Drummond 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.

drugs 0 and 1, are located respectively at the top left and right corners of the box whereas the generic drug G is located at the lower left corner of the 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.[17] Among the two types of patients, the "selective" ones observe and discriminate the three drugs in the 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:

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

with

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

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;[18] $(1 - t) \in (0, 1)$ is the weight attached to the utility derived from drug i's perceived quality by patient type j, θ_{ji};[19] $t \in (0, 1)$ is the weight attached to the disutility from not having the drug with the ideal therapeutic variant x, $(x - i)^2$, $(i = 0, 1)$;[20] and c_i is the disutility of consuming drug 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.[21] Let the rate of copay be α.

[17] We 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. Interested readers may refer to the relevant literature on why, and to what extent, products differentiate.

[18] R is assumed large enough to guarantee the patient's utility is always positive.

[19] The utility function is additive to rule out any interaction between the vertical and horizontal differentiation.

[20] 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 Brekke et al. (2007).

[21] Drug 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.

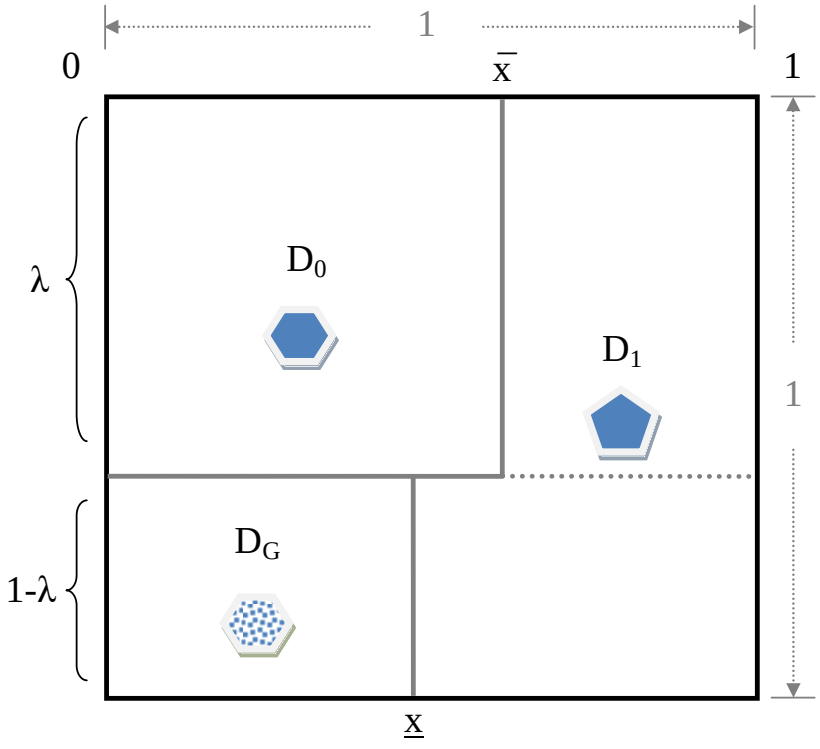
Accordingly, the copay levels for drugs 0, 1, and G are given, respectively, by

$$\begin{aligned} c_0 &= \alpha \cdot p_G + (p_0 - p_G), \\ c_1 &= \alpha \cdot p_1, \quad \text{and} \\ c_G &= \alpha \cdot p_G. \end{aligned} \tag{2.2}$$

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.

We use the unit square in Figure 2 to analyze patient preference and drugs' market shares. Horizontally, a patient's 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.[22]

Figure 2: Market Shares for the Three Drug Manufacturers



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

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, also called the indifference line, in the unit square:

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

The market shares of drugs 0 and 1 (D_0 and D_1) are separated by the indifference line $\overline{x}$ along the horizontal axis of the unit square.

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, also called the indifferent line, in the unit square:

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

The market shares of drug 1 and G (D_1 and D_G) are separated by the indifference line $\underline{x}$ along the horizontal axis of the unit square.

On the vertical axis of the unit square, the market shares of drugs 0 and G (D_0 and D_G) are separated by the indifferent line determined by the preference parameter λ since 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

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

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

From the conditions given in equations (2.2), (2.3), (2.4), and (2.5), we can derive the market shares of

drugs 0, 1, and G (D_0, D_1, and D_G), respectively,

$$\begin{aligned} D_0 &= \lambda \cdot \overline{x} \\ &= \frac{\lambda \cdot (c_1 - c_0 + t)}{2t} \\ &= \frac{\lambda \cdot [t + \alpha \cdot (p_1 - p_G) + p_G - p_0]}{2t}, \end{aligned} \tag{2.6}$$

$$\begin{aligned} D_1 &= 1 - D_0 - D_G \\ &= \frac{t - \alpha \cdot (p_1 - p_G) + \lambda \cdot (p_0 - p_G) + (1 - \lambda) \cdot (1 - t) \cdot \delta}{2t}, \quad \text{and} \end{aligned} \tag{2.7}$$

$$\begin{aligned} D_G &= (1 - \lambda) \cdot \underline{x} \\ &= \frac{(1 - \lambda) \cdot [c_1 - c_G + t - (1 - t) \cdot \delta]}{2t} \\ &= \frac{(1 - \lambda) \cdot [t + \alpha \cdot (p_1 - p_G) - (1 - t) \cdot \delta]}{2t}. \end{aligned} \tag{2.8}$$

For tractability, we impose some simplicity assumptions such as manufacturing cost is normalized to zero and marginal cost associated with manufacturers' endeavours in developing therapeutic variant and/or brand-imaging is also zero.[23] Under these simplification assumptions, the profit functions for the three single-product firms (Π_0, Π_G, and Π_1) are, respectively,

$$\begin{aligned} \Pi_0 &= p_0 \cdot D_0 \\ &= \lambda \cdot \frac{[t + \alpha \cdot (p_1 - p_G) + p_G] \cdot p_0 - p_0^2}{2t}, \end{aligned} \tag{2.9}$$

$$\begin{aligned} \Pi_G &= p_G \cdot D_G \\ &= (1 - \lambda) \cdot \frac{(t + \alpha \cdot p_1 - (1 - t) \cdot \delta) \cdot p_G - \alpha \cdot p_G^2}{2t}, \quad \text{and} \end{aligned} \tag{2.10}$$

$$\begin{aligned} \Pi_1 &= p_1 \cdot D_1 \\ &= \frac{[t + \lambda \cdot (p_0 - p_G) + \alpha \cdot p_G + (1 - \lambda)(1 - t) \cdot \delta] \cdot p_1 - \alpha \cdot p_1^2}{2t}. \end{aligned} \tag{2.11}$$

In the one-shot simultaneous game in prices among the three firms, each firm sets its own price to

[23] 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.

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 can use the generic price-cap to limit drug reimbursement cost. Now we discuss the equilibrium price with and without a binding generic drug price-cap, respectively.[24]

The binding generic price-cap is the percentage ($\beta \in (0,1)$) of the price of drug 0 (p_0) that is used to set the price of drug G; that is

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

Because of this binding price-cap, we need to examine only the equilibrium prices for the two brand-name firms and the generic drug price can be derived directly from equation (2.12).

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

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

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

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:

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

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

p_0 and p_1 can be solved from equations (2.15) and (2.16). Let

[24] Note 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.

$$\Gamma \equiv 4 - 2\beta + \alpha\beta - \lambda + \beta\lambda, \tag{2.17}$$

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

$$\Phi \equiv 2 - \beta + 2\alpha\beta + \lambda - \beta\lambda. \tag{2.19}$$

The equilibrium prices for the two brand-name drugs with the binding generic price-cap can be rewritten as, respectively,[25]

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

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

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: the preference parameter λ is the proportion of "selective" patients who display unanimous preference for brand-name drugs, whereas $(1-\lambda)$ is the proportion of "unselective" patients; the copay parameter α is the rate of copay established by public/private insurance plans; and the pricing-cap parameter β is the percentage of the original brand-name drug 0's price set as the generic drug G's price.

The impacts out of changes in these three parameters on the equilibrium drug prices can be stated in the following propositions.[26]

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 difference in (perceived) quality between the brand-name drug and its generic substitute is large enough, even an increase in the proportion of the "unselective" patients could stimulate the brand-name manufacturers to raise their prices to maximize profits.

[25] 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.
[26] The proofs for all propositions in this paper can be found in Appendix A.

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.*

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.[27]

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.[28]

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

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

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

Therefore, we have the following equilibrium prices for drugs 0, G, and 1, respectively.

[27] 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.

[28] This 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.

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

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

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

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 (e.g. $\alpha > 25\%$ in the current model setting), all three drug manufacturers, brand-name and generic, would raise (lower) prices in response to a lower (higher) proportion of the "selective" patients. When the copay rate is relatively low (e.g. $\alpha < 25\%$ in the current model setting), 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 would 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 the difference in perceived quality between brand-name and generic drugs is not huge, 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 hand, 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 the difference in perceived quality between brand-name 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 would react by increasing their drug prices in the equilibrium in response to a rise in the rate of copay, while firm 1's price-setting strategy would remain 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 effective from the policy-makers' perspective: all three drug manufacturers (brand-name and generic) would lower their drug prices in the equilibrium.

2.1.6 An Extension to the Baseline Model with Therapeutic Reference Pricing

The GRP system excludes the brand-name drug 1 in the interchangeable drug category. But the TRP system broadens the interchangeable therapeutic category to include the brand-name drug 1, which is on patent and does not have any generic substitute, in addition to the other brand-name drug 0 and its generic drug 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 brand-name drug 1 and the generic drug G, even if the former 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.[29]

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 much difference in perceived quality exists 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

[29] The derivation of the market equilibrium is straightforward and can be found in Appendix B.

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 is lowered, 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 regime (GRP or TRP) is in place. As long as patients believe (or are made to believe) that brand-name drugs are "superior" in therapeutic quality than their 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 "unselective" patients.

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 brand-name 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.

Next, we use a unique data set to test the following three hypotheses: (1) More generic substitutes do not have any net effect of lowering drug prices (checking the evidence against the prediction of Proposition 1). (2) More therapeutic drug substitutes do not have any net effect of lowering drug prices (checking the evidence for the combination of several pricing strategies of brand-name drug manufacturers predicted by

Proposition 6). (3) Given the available generic substitution policy, brand-name drugs do not have any net price premiums over their generic substitutes (checking the evidence against the prediction of Proposition 3).

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.[30] The data were cleaned and then linked with drug patent data accessed from the Health Canada 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).[31] The dataset for this study contains 105, 20, and 23 drugs under each selected drug class, respectively. 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.[32] Table 1 decomposes the 2,946 observations by the 14 molecules and by the 19 manufacturers.

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

[31]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.

[32]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.

Table 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).

The variable of interest is the dynamics of drug price. We use $logprice_{jit}$ to denote the logarithm of the price in quarter t, for drug i, under molecule j. The drug prices are affected by a number of explanatory variables. We also construct instrumental variables from some explanatory variables for our identification strategy. The summary of the above explanatory variables is provided in Table 2.

Table 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)
$policy_{jit} \times brand_i$	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)

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

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 following period. It is also used to control for the unobservable information resulting from missing variables.[33] However, it is highly likely that this variable is endogenous. We must find a strategy, which is explained below, to deal with it.

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

[33]For 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.

drug product normally do not compete among themselves.[34] The variable $gennum_{it}$ is used 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.[35]

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.[36] This variable records the number of all drugs competing within a broad therapeutic class. The variable $compnum_{it}$ is used to examine the *second hypothesis* that more therapeutic substitutes do not 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 drugs being the reference. In the three-level hierarchical model, the variable $brand_i$ is used to test the existence of brand-name drug 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.[37] The public drug plan[38] 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. This variable is used to 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 $brand_i$. We use it to evaluate the dynamics of the brand-name drug price with and without a generic substitution policy in place. In other words, we are able to test the *third hypothesis* that brand-name drugs do not have any net price premiums over their generic substitutes when the 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 migraine-relief drugs

[34] For 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.

[35] Some may argue the number of generic drugs for a given drug molecule can be endogenous, in the sense that drug price may be a factor for a generic firm to consider before its market entry. Because of the lack of drug price variation in Canada, however, drug price is hardly an entry decision factor. In contrast, market share and timing of market entry are arguably more essential for Canadian generic firms (Hollis, 2002). Note it is not to deny that drug price might shape the market structure. Recent changes in generic price-cap policies across the provinces since 2008 are probably a force shaping the market structure in the long run. Our empirical analysis pre-dated this period.

[36] 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 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 (WHO-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.

[37] 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.

[38] As noted in Section 3, the manufacturers' list price and policy data were from Alberta public drug plans.

js, with cardiovascular drugs being the baseline case (WHO-ATC group "J" and "N", and "C", respectively). They are included to control for the systematic price differences across different WHO-ATC groups. The selected drug cohort under different WHO-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.[39]

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).[40] 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.[41] The variable str_j is used to appropriately control for the degree to which the dosage strengths may influence the drug price-setting.

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 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. We also include three calendar quarter dummy variables in the regression model, with the 2^{nd} quarter being the baseline case. This way, we can control for the possible seasonality in the drug price dynamics net of inflation.

With the above variables, we select the multilevel modelling strategy to handle the special data structure for the following reasons: (1) A multilevel model is a good fit for the complex pharmaceutical market structure. (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 fully explore the unbalanced data structures resulting from the natural imbalances and natural hierarchies in the data. (4) It utilizes the clustering information and therefore produces statistically

[39] 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 (WHO-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 (WHO-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 (WHO-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.

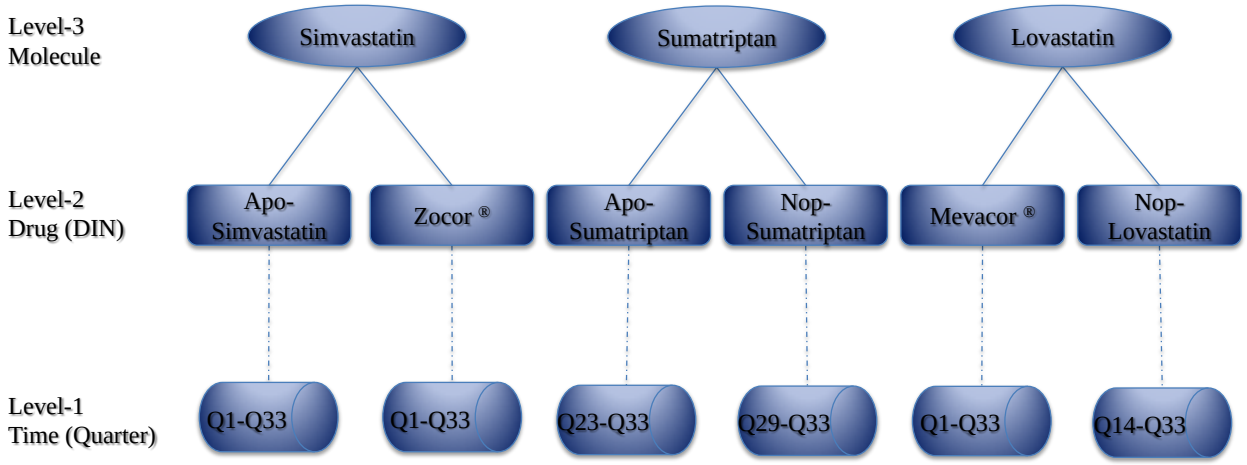
[40] According to the WHO's definition, the DDD is a standardized statistical measure of drug consumption for comparison purposes. It defines the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD is subject to periodical review and therefore it may have 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.

[41] First, 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_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.

unbiased estimates and corresponding standard errors.

We use a three-level strictly hierarchical 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 3 sketches the three-level hierarchical data structure.[42]

Figure 3: A Strictly Hierarchical (Three-level) Data Structure



The multilevel model can be parameterized in the form of the Generalized Least Squares (GLS) model, which can 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 variable (such as the historical price anchor) and the random components at level-2 and level-3 in drug prices cannot be ruled out and cause bias and inconsistency in the estimation. This limitation will affect our ability to identify any causal relationship correctly. To form a better identification strategy, we use the IV-type maximum likelihood estimation (MLE) in two steps. In the first step, we run the maximum likelihood estimation of the regression of the endogenous explanatory variable on a set of suitable instrumental variables. More specifically, we select the first-differenced price-setting anchor variable ($\Delta lnavgpricelag_{jit}$) and its quarter-lag ($\Delta lnavgpricelag_{jit-1}$) as the instrumental variables because they are both orthogonal to the time-invariant error components.[43] In

[42] In principle, the cross-classification model with manufacturers and molecules cross-classified at level-3 maybe an appropriate choice. 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 Appendix C, 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.

[43] Following 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

the second step, we run the maximum likelihood estimation of the regression of the dependant variable on the predicted value of the endogenous variable 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

In our theoretical models, we have shown that the difference in perceived quality between brand-name and generic drugs, the lower rate of copay and generic price-cap can sustain the price premiums of brand-name drugs even if they face competitions from the generic substitutes. Empirically, we wish to test the following hypotheses by taking account of the market structure and existing public policy variables.

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. And 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 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.[44] In comparison to the multilevel model, the pooled 2SLS estimation does not take account of the variance-covariance matrix reflecting the hierarchical market structures. As such, it gives less efficient yet unbiased coefficient estimates.[45] 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.

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

render weak instruments and also reduce the degrees of freedom from the model considerably.

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

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

Table 3: Regression Results for the Drug Price Dynamics

	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 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%]
R^2	0.9742	-
Log-likelihood	-	4572.5606

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

† Fractions of variance attributed to each specific level in brackets

First, the coefficient estimate for *gennum* is positive and significant at the 1% 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 an empirical evidence for rejecting the *first hypothesis*. Moreover, the *first hypothesis* echoes with *Proposition 1* in the theoretical section under certain conditions.[46] In a therapeutic market with more and more generic substitutes, the proportion of "unselective" patients is expected to be on the rise. If the difference in perceived quality between brand-

[46]It is noted that our theoretical model only deals with a single generic drug manufacturer, which can be conceived as a "standardized" generic firm in the sense that patients do not (or are not able to) differentiate various generic drug firms in a given therapeutic market.

name drug and generic drug is large enough, *ceteris paribus*, this higher proportion of "unselective" patients can result in higher brand-name drugs.

Second, although the coefficient estimate for *compnum* is negative, it is not statistically significant. There is no empirical evidence to associate the number of therapeutic substitutes across drug molecules and the drug price dynamics. We cannot reject the *second hypothesis*. If we revisit *Proposition 6* in the theoretical discussion, in a drug market characterised with therapeutic competition (such as that under the TRP system), the brand-name drug firms could either raise or lower the drug prices in response to the increasing number of therapeutic substitutes under certain conditions.[47] This may be a sign of strong market segmentation where drugs in other molecules (including both brand-name and generic drugs) have limited roles in influencing drug prices after all.

Third, the coefficient estimate for *brand* is positive and statistically significant at the 1% level, indicating that brand-name drugs enjoy remarkable price premiums over their generic substitutes in general. As predicted by the 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% 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% level. Brand-name drugs tend to maintain net price premiums over their generic substitutes by about 18.7% on average,[48] 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* and is consistent with the theoretical discussion. As *Proposition 3* predicts, despite the public drug plan lowers the generic price-cap, in a therapeutic market with a large proportion of "selective" patients who believe brand-name drugs carry superior quality than the generic substitutes, it is still better off for some brand-name drug manufacturer to raise price, *ceteris paribus*.

In addition to the above key empirical findings with reference to the three hypotheses, 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% level. The empirical evidence supports that about 57% of the price dynamics in the current period can be explained

[47] The unobservable "perceived quality" between different drugs play a role in the theoretical discussion. As much as it is interesting if we are able to quantify it or find a proxy, it is not the focus of this paper and we shall leave the discussion for future research.

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

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% level. This suggests that while the prices of the antifungal drugs (under the WTO-ATC code J02AC) are not much different from the statin drugs — the baseline case (under the WHO-ATC code C10AA), the migraine-relief drugs (under the WHO-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% 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% 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]

5 Concluding Remarks

In this paper, we use the two-dimension product differentiation model to analyse the impact of changes in patient preference and government policies on drug manufacturers' price-setting behaviour. Our theoretical model 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 the Canadian drug price data. The unbalanced and hierarchical panel data motivate us to use the multilevel model to appropriately capture the complex contextuality of the data. To deal with the issue of endogeneity, we implement the IV-MLE estimation in our identification strategy. 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).

Based on the key theoretical predictions, we investigate the empirical evidence. 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

[49] It 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.

therapeutic substitutes in a more segmented market do not have any net effect of lowering drug prices either as the result of off-setting market forces. Third, when the generic substitution policy is in place, brand-name drugs still maintain price premium 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 Canadian 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 in Canada.

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A Appendix: Proofs

A.1 Proof for the Preference of the "Selective" Patient in Section 2.1.2

In the baseline model, for tractability, we assume

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

As such, the "selective" patient would only consider the brand-name drug 0 or 1, under the above assumption (A.1).

Proof. From (2.1), we can show that for the "selective" patient,

$$U_0 > U_G, \tag{A.2}$$

as long as the assumption (A.1) holds. U is the total utility the patient derives from consuming drug 0 or drug G as indicated in the subscripts.

That is, the "selective" patient will choose the brand-name drug 0 over its generic substitute G.

If the "selective" patient is indifferent between the generic drug G and the brand-name drug 1, then for this patient,

$$U_G = U_1. \tag{A.3}$$

From (A.3), (2.1) and (2.2), we obtain the indifference line between brand-name drug 1 and generic drug G

$$\underline{x}^* = \frac{\alpha(p_1 - p_G) + t - (1-t)(\theta_H - \theta_L)}{2t}. \tag{A.4}$$

and the indifference line between brand-name drugs 0 and 1

$$\overline{x}^* = \frac{\alpha(p_1 - p_G) - (p_0 - p_G) + t}{2t}. \tag{A.5}$$

Using (A.1) again, we have

$$\overline{x}^* > \underline{x}^*. \tag{A.6}$$

Use Figure 4 similar to Figure 2 to continue our proof:

Figure 4 demonstrates the preference of the "selective" patient (only) for drugs 0, 1, and G. The two indifference lines ($\overline{x}^*$ and $\underline{x}^*$) separate the box into three regions, labelled A, B, and C, respectively.

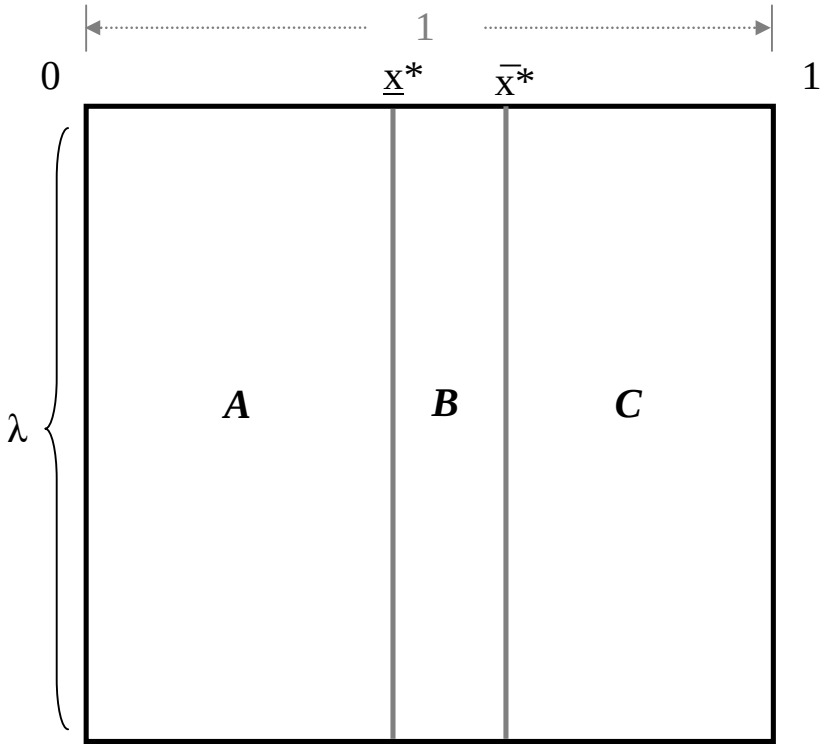
Firstly, region C, the area to the right of both indifference lines, indicates that brand-name drug 1 is strictly preferred to both brand-name drug 0 and generic drug G. As such, in region A, the "selective" patient only considers brand-name drug 1.

Secondly, region B, between $\overline{x}^*$ and $\underline{x}^*$, indicates that brand-name drug 1 is strictly preferred to generic drug G and that brand-name drug 0 is strictly preferred to brand-name drug 1. As such, in region B, the "selective" patient only considers brand-name drug 0.

Finally, region A, to the left of both indifference lines, indicates that both brand-name drug 0 and generic drug G are strictly preferred to brand-name drug 1. Combining (A.2) with (A.1), we conclude that in region A, the "selective" patient only considers brand-name drug 0.

In summary, the "selective" patient considers only brand-name drugs 0 and 1, when (A.1) holds. ■

Figure 4: Preference of "Selective" Patient for Three Drugs



A.2 Proof for Proposition 1

Proof.

First, the partial derivative of p_1 with respect to λ, in (2.21), is given by

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

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

$$= \frac{\Psi}{\alpha\Gamma^2}[3t(1-\beta)-(1-t)\delta(3-\beta+\alpha\beta)]. \tag{A.7}$$

Second, from (2.15), (2.18) and (A.7), the partial derivative of p_0 with respect to λ can be written as

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

$$= \frac{1}{\Gamma^2}[3t(1-\beta)-(1-t)\delta(3-\beta+\alpha\beta)]. \tag{A.8}$$

Because $\Psi > 0$, also with (A.7) and (A.8),

$$Sign(\frac{\partial p_0}{\partial \lambda}) = Sign(\frac{\partial p_1}{\partial \lambda})$$
$$= Sign[3t(1-\beta) - (1-t)\delta(3-\beta+\alpha\beta)]. \tag{A.9}$$

Let

$$\overline{\delta} \equiv \frac{3t(1-\beta)}{(1-t)(3-\beta+\alpha\beta)}. \tag{A.10}$$

From (A.7), (A.8), (A.9), and (A.10) we conclude

$$\begin{cases} \frac{\partial p_0}{\partial \lambda} > 0, \frac{\partial p_1}{\partial \lambda} > 0, \quad if \quad \delta < \overline{\delta}; \\ \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} < 0, \quad if \quad \delta > \overline{\delta}. \end{cases} \tag{A.11}$$

■

A.3 Proof for Proposition 2

Proof.

Based on (2.21), the partial derivative of p_1 with respect to α is given by

$$\begin{aligned}
\frac{\partial p_1}{\partial \alpha} &= \frac{1}{\alpha^2\Gamma^2}\{\alpha\Gamma[2t\beta + (1-\lambda)(1-t)\beta\delta] - [t\Phi + (1-\lambda)(1-t)\delta\Psi][\Gamma + \alpha\beta]\} \\
&= \frac{1}{\alpha^2\Gamma}[2t\alpha\beta + (1-\lambda)(1-t)\alpha\beta\delta - t(2-\beta+2\alpha\beta+\lambda-\beta\lambda) \\
&\quad - (1-\lambda)(1-t)(2-\beta+\alpha\beta)\delta] - \frac{\beta}{\alpha\Gamma^2}[t(2-\beta+2\alpha\beta+\lambda-\beta\lambda) \\
&\quad + (1-\lambda)(1-t)(2-\beta+\alpha\beta)\delta] \\
&= -\frac{1}{\alpha^2\Gamma}[t(2-\beta+\lambda-\beta\lambda) + (1-\lambda)(1-t)(2-\beta)\delta] \\
&\quad - \frac{\beta}{\alpha\Gamma^2}[t(2-\beta+2\alpha\beta+\lambda-\beta\lambda) + (1-\lambda)(1-t)(2-\beta+\alpha\beta)\delta] \\
&< 0. \qquad \text{(A.12)}
\end{aligned}$$

The last inequality is because the terms within both brackets in the previous step are always positive. Also, based on (2.15) and (A.12), the partial derivative of p_0 with respect to α is given by

$$\begin{aligned}
\frac{\partial p_0}{\partial \alpha} &= \frac{(p_1 + \alpha\frac{\partial p_1}{\partial \alpha})(2-\beta+\alpha\beta) - \beta(t+\alpha p_1)}{\Psi^2} \\
&= \frac{1}{\Psi^2}\left[(p_1 + \alpha\frac{\partial p_1}{\partial \alpha})(2-\beta) + \alpha^2\beta\frac{\partial p_1}{\partial \alpha} - t\beta\right] \\
&= \frac{1}{\Psi^2}\left\{\left(\frac{2\beta}{\Gamma} - \frac{\beta^2}{\Gamma}\right)\left[2t + (1-\lambda)(1-t)\delta - \frac{t\Phi}{\Gamma} - \frac{(1-\lambda)(1-t)\delta\Psi}{\Gamma}\right]\right. \\
&\quad - \frac{\beta}{\Gamma}[t(\Phi - 2\alpha\beta) + (1-\lambda)(1-t)\delta(\Psi - \alpha\beta)] \\
&\quad \left. - \frac{\alpha\beta^2}{\Gamma^2}[t\Phi + (1-\lambda)(1-t)\delta\Psi] - t\beta\right\}. \qquad \text{(A.13)}
\end{aligned}$$

Collecting terms and using (2.17), (2.19), and (2.18), (A.13) turns to

$$\begin{aligned}\frac{\partial p_0}{\partial \alpha} &= \frac{1}{\Psi^2}\Big\{\frac{t\beta}{\Gamma^2}[(2-\beta-\lambda+\beta\lambda)\Gamma+(\beta-2-\alpha\beta)\Phi-\Gamma^2] \\ &\quad + \frac{\beta}{\Gamma^2}(\beta-2-\alpha\beta)(1-\lambda)(1-t)\delta(2-\beta+\alpha\beta)\Big\} \\ &= \frac{1}{\Psi^2}\left[\frac{t\beta}{\Gamma^2}(\beta-2-\alpha\beta)(6-3\beta+3\alpha\beta)-\frac{\beta}{\Gamma^2}(1-\lambda)(1-t)\delta(\beta-2-\alpha\beta)^2\right] \\ &= -\frac{\beta}{\Gamma^2}[3t+(1-\lambda)(1-t)\delta] \\ &< 0. \end{aligned} \tag{A.14}$$

In summary, from (A.12) and (A.14), we obtain

$$\frac{\partial p_0}{\partial \alpha} < 0 \quad and \quad \frac{\partial p_1}{\partial \alpha} < 0. \tag{A.15}$$

■

A.4 Proof for Proposition 3

Proof.

Based on (2.21), the partial derivative of p_1 with respect to β is given by

$$\begin{aligned}\frac{\partial p_1}{\partial \beta} &= \frac{1}{\alpha^2\Gamma^2}\{[t(2\alpha-1-\lambda)+(1-\lambda)(1-t)\delta(\alpha-1)]\alpha(4-2\beta+\alpha\beta-\lambda+\beta\lambda) \\ &\quad -[t(2-\beta+2\alpha\beta+\lambda-\beta\lambda)+(1-\lambda)(1-t)\delta(2-\beta+\alpha\beta)]\alpha(\alpha-2+\lambda)\} \\ &= \frac{1}{\alpha\Gamma^2}\{t[(4-2\beta+\alpha\beta-\lambda+\beta\lambda)(2\alpha-1-\lambda) \\ &\quad -(2-\beta+2\alpha\beta+\lambda-\beta\lambda)(\alpha-2+\lambda)] \\ &\quad +(1-\lambda)(1-t)\delta[(\alpha-1)(4-2\beta+\alpha\beta-\lambda+\beta\lambda) \\ &\quad -(2-\beta+\alpha\beta)(\alpha-2+\lambda)]\} \\ &= \frac{1}{\alpha\Gamma^2}[3t(2\alpha-\alpha\lambda-\lambda)+(1-\lambda)(1-t)\delta(2\alpha-\alpha\lambda-\lambda)] \\ &= \frac{1}{\alpha\Gamma^2}[3t+(1-\lambda)(1-t)\delta](2\alpha-\alpha\lambda-\lambda), \end{aligned} \tag{A.16}$$

which implies

$$Sign(\frac{\partial p_1}{\partial \beta}) = Sign(2\alpha-\alpha\lambda-\lambda). \tag{A.17}$$

To understand the sign patterns of equation (A.17), we need to illustrate the relationship between α and λ. First, it is straightforward that $(2\alpha-\alpha\lambda-\lambda)$ increases with α.[50] Then let the threshold copay rate $\overline{\alpha}$ be the solution to $(2\alpha-\alpha\lambda-\lambda)=0$. That is,

$$\overline{\alpha} = \frac{2}{2-\lambda} - 1. \tag{A.18}$$

It is clear that $\overline{\alpha}$ monotonically increases in the proportion of "unselective" patients λ. A diagrammatic demonstration of equation (A.18) is shown in Figure 5.

Now suppose the extreme case when λ is close to 1, implying that the root of equation (A.18) ($\overline{\alpha}$) is also close to 1. Bearing in mind that the rate of copay (α) in most drug insurance plans is rarely set above 50%,[51] which implies that $\alpha < \overline{\alpha} \approx 1$. This indicates $(2\alpha-\alpha\lambda-\lambda) < 0$ and therefore, $\frac{\partial p_1}{\partial \beta} < 0$.

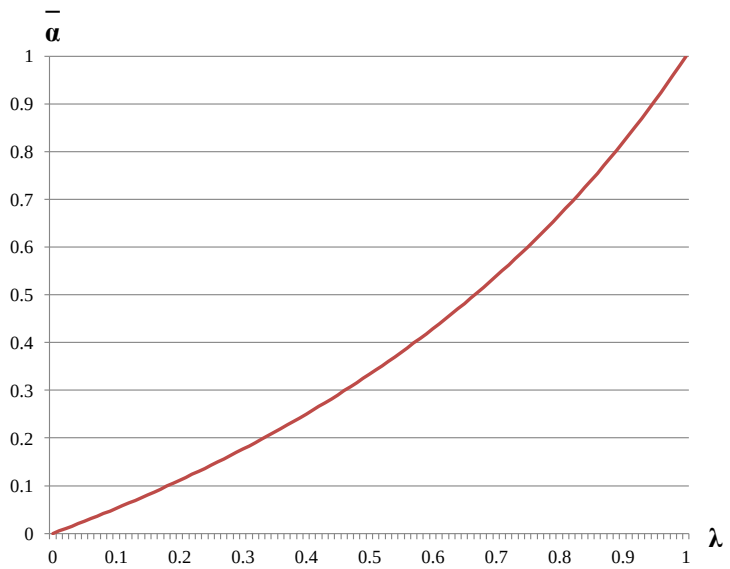
When the value of λ drops, so does $\overline{\alpha}$ — the root of equation (A.18). It is not clear whether $\alpha < \overline{\alpha}$ or $\alpha > \overline{\alpha}$. As a result, the sign of $\frac{\partial p_1}{\partial \beta}$ is ambiguous.

Based on (2.15) and (A.16), the partial derivative of p_0 with respect to β is given by

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

[51] See Bell et al. (2010).

Figure 5: A Diagrammatic Demonstration of the Relationship between $\overline{\alpha}$ and λ



$$\frac{\partial p_0}{\partial \beta} = \frac{1}{(2-\beta+\alpha\beta)^2}\left[\alpha\frac{\partial p_1}{\partial \beta}(2-\beta+\alpha\beta)+(t+\alpha p_1)(1-\alpha)\right]$$

$$= \frac{1}{2-\beta+\alpha\beta}\left\{\frac{[3t+(1-\lambda)(1-t)\delta](2\alpha-\alpha\lambda-\lambda)}{\Gamma^2} + \frac{1-\alpha}{\Gamma\Psi}[t(\Gamma+\Phi)+(1-\lambda)(1-t)\delta\Psi]\right\}$$

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

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

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

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

$$> 0. \tag{A.19}$$

The last inequality is justified because the terms within all parentheses in the previous step are always positive.

From (A.17) and (A.19), we obtain

$$\frac{\partial p_0}{\partial \beta} > 0 \quad and \quad \begin{cases} \frac{\partial p_1}{\partial \beta} < 0, & if \quad \alpha < \overline{\alpha}; \\ \\ \frac{\partial p_1}{\partial \beta} > 0, & if \quad \alpha > \overline{\alpha}. \end{cases} \tag{A.20}$$

■

A.5 Proof for Proposition 4

Proof.
Let

$$\Upsilon \equiv (1-4\alpha)(1-t)\delta - 3(1-\alpha)t. \tag{A.21}$$

Based on (2.25), the partial derivative of p_1 with respect to λ is given by

$$\begin{aligned}\frac{\partial p_1}{\partial \lambda} &= \frac{1}{\alpha[6\alpha+\lambda(1-\alpha)]^2}\{[-t+\alpha t+(1-t)\delta-3\alpha(1-t)\delta][6\alpha+\lambda(1-\alpha)] \\ &\quad -[(6\alpha-\lambda+\alpha\lambda)t+(2\alpha+\lambda-3\alpha\lambda)(1-t)\delta](1-\alpha)\} \\ &= \frac{-12t+4(1-t)\delta-16\alpha(1-t)\delta+12\alpha t}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{4[(1-4\alpha)(1-t)\delta-3(1-\alpha)t]}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{4\Upsilon}{[6\alpha+\lambda(1-\alpha)]^2}.\end{aligned} \tag{A.22}$$

Based on (2.24), the partial derivative of p_G with respect to λ is given by

$$\begin{aligned}\frac{\partial p_G}{\partial \lambda} &= \frac{-(1-t)\delta[6\alpha+\lambda(1-\alpha)]-[6t-(\lambda+2)(1-t)\delta](1-\alpha)}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{2[(1-4\alpha)(1-t)\delta-3(1-\alpha)t]}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{2\Upsilon}{[6\alpha+\lambda(1-\alpha)]^2}.\end{aligned} \tag{A.23}$$

Based on (2.23), the partial derivative of p_0 with respect to λ is given by

$$\begin{aligned}\frac{\partial p_0}{\partial \lambda} &= \frac{-\alpha(1-t)\delta[6\alpha+\lambda(1-\alpha)]-[3(1+\alpha)t-(1+\alpha\lambda-2\alpha)(1-t)\delta](1-\alpha)}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{-4\alpha^2(1-t)\delta-3t+3\alpha^2 t+(1-t)\delta(1-3\alpha)}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{(1+\alpha)[(1-4\alpha)(1-t)\delta-3(1-\alpha)t]}{[6\alpha+\lambda(1-\alpha)]^2} \\ &= \frac{(1+\alpha)\Upsilon}{[6\alpha+\lambda(1-\alpha)]^2}.\end{aligned} \tag{A.24}$$

Note that

$$Sign(\frac{\partial p_1}{\partial \lambda}) = Sign(\frac{\partial p_G}{\partial \lambda}) = Sign(\frac{\partial p_0}{\partial \lambda}) = Sign(\Upsilon). \tag{A.25}$$

Let

$$\tilde{\delta} \equiv \frac{3t(1-\alpha)}{(1-t)(1-4\alpha)}. \tag{A.26}$$

To summarize the above results, we obtain

$$\begin{cases} \frac{\partial p_0}{\partial \lambda} > 0, \frac{\partial p_G}{\partial \lambda} > 0, \frac{\partial p_1}{\partial \lambda} > 0, \quad if \quad \delta > \tilde{\delta} \quad and \quad \alpha < 25\%; \\ \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_G}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} < 0, \quad if \quad \delta < \tilde{\delta} \quad and \quad \alpha < 25\%; \\ \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_G}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} < 0, \quad if \quad \alpha > 25\%. \end{cases} \tag{A.27}$$

■

A.6 Proof for Proposition 5

Proof.
Let

$$\Theta = (\lambda + 2)(1 - t)\delta - 6t. \tag{A.28}$$

Based on (2.23), the partial derivative of p_0 with respect to α is given by

$$\begin{aligned}\frac{\partial p_0}{\partial \alpha} &= \frac{1}{[6\alpha + \lambda(1-\alpha)]^2}\{[3t + 2(1-t)\delta - \lambda(1-t)\delta][6\alpha + \lambda(1-\alpha)] \\ &\quad - [3(1+\alpha)t - (1 + \alpha\lambda - 2\alpha)(1-t)\delta](6-\lambda)\} \\ &= \frac{6\lambda t - 18t + \lambda(1-t)\delta + 6(1-t)\delta - \lambda 2(1-t)\delta}{[6\alpha + \lambda(1-\alpha)]^2} \\ &= \frac{(3-\lambda)[(\lambda+2)(1-t)\delta - 6t]}{[6\alpha + \lambda(1-\alpha)]^2} \\ &= \frac{(3-\lambda)\Theta}{[6\alpha + \lambda(1-\alpha)]^2}. \end{aligned} \tag{A.29}$$

Based on (2.24), the partial derivative of p_G with respect to α is given by

$$\begin{aligned}\frac{\partial p_G}{\partial \alpha} &= \frac{(6-\lambda)[(\lambda+2)(1-t)\delta - 6t]}{[6\alpha + \lambda(1-\alpha)]^2} \\ &= \frac{(6-\lambda)\Theta}{[6\alpha + \lambda(1-\alpha)]^2}. \end{aligned} \tag{A.30}$$

We note that

$$Sign(\frac{\partial p_0}{\partial \alpha}) = Sign(\frac{\partial p_G}{\partial \alpha}) = Sign(\Theta). \tag{A.31}$$

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

$$\begin{aligned}
\frac{\partial p_1}{\partial \alpha} &= \frac{1}{\alpha^2[6\alpha+\lambda(1-\alpha)]^2}\{[6t+\lambda t+2(1-t)\delta-3\lambda(1-t)\delta]\alpha[6\alpha+\lambda(1-\alpha)] \\
&\quad -(12\alpha+\lambda-2\alpha\lambda)[(6\alpha-\lambda+\alpha\lambda)t+(2\alpha+\lambda-3\alpha\lambda)(1-t)\delta]\} \\
&= \frac{1}{\alpha^2[6\alpha+\lambda(1-\alpha)]^2}[-36\alpha^2 t-12\alpha^2(1-t)\delta+20\alpha^2\lambda(1-t)\delta-3\alpha^2\lambda^2(1-t)\delta \\
&\quad +\alpha^2\lambda^2 t+12\alpha\lambda t-12\alpha\lambda(1-t)\delta+-\lambda^2(1-t)\delta-2\alpha\lambda^2 t+2\alpha\lambda^2(1-t)\delta] \\
&= \frac{1}{\alpha^2[6\alpha+\lambda(1-\alpha)]^2}\{(6-\lambda)[3\lambda(1-t)\delta-\lambda t-2(1-t)\delta-6t]\alpha^2 \\
&\quad -2\lambda(6-\lambda)[(1-t)\delta-t]\alpha-\lambda^2[(1-t)\delta-t]\} \\
&< 0. \qquad (A.32)
\end{aligned}$$

When $\delta < \frac{t}{1-t}$, the sign of $\frac{\partial p_1}{\partial \alpha}$ is indeterminant.[52]
Now define $\ddot{\delta}$ and $\dot{\delta}$, respectively, as

$$\begin{aligned}
\ddot{\delta} &\equiv \frac{6t}{(\lambda+2)(1-t)} \quad \text{and} \\
\dot{\delta} &\equiv \frac{t}{1-t}. \qquad (A.33)
\end{aligned}$$

To summarize the above results, we have

$$\begin{cases} \frac{\partial p_0}{\partial \alpha} > 0, \frac{\partial p_G}{\partial \alpha} > 0, \quad if \quad \delta > \ddot{\delta}; \\ \\ \frac{\partial p_0}{\partial \alpha} < 0, \frac{\partial p_G}{\partial \alpha} < 0, \quad if \quad \delta < \ddot{\delta}. \end{cases} \qquad (A.34)$$

and

$$\begin{cases} \frac{\partial p_1}{\partial \alpha} < 0, \quad if \quad \delta > \dot{\delta}; \\ \\ \frac{\partial p_1}{\partial \alpha} \lessgtr 0, \quad if \quad \delta < \dot{\delta}. \end{cases} \qquad (A.35)$$

■

A.6.1 Proof for the indeterminant sign of $\frac{\partial p_1}{\partial \alpha}$

Proof.
We focus on the terms in the brackets to show the sign of $\frac{\partial p_1}{\partial \alpha}$, i.e.

$$f(\alpha) = a\alpha^2 + b\alpha + c, \qquad (A.36)$$

[52] The proof is provided in Section A.6.1 below.

where

$$a \equiv (6-\lambda)[3\lambda(1-t)\delta - \lambda t - 2(1-t)\delta - 6t], \tag{A.37}$$

$$b \equiv -2\lambda(6-\lambda)[(1-t)\delta - t], \tag{A.38}$$

$$c \equiv -\lambda^2[(1-t)\delta - t]. \tag{A.39}$$

First look at the discriminant of the quadratic equation $f(\alpha)$:

$$\begin{aligned}
\Delta &= b^2 - 4ac \\
&= 4\lambda^2(6-\lambda)^2[(1-t)\delta - t]^2 \\
&\quad + 4\lambda^2[(1-t)\delta - t](6-\lambda)[3\lambda(1-t)\delta - \lambda t - 2(1-t)\delta - 6t] \\
&= 8\lambda^2(6-\lambda)[(1-t)\delta - t][2(1-t)\delta - 6t + \lambda(1-t)\delta] \\
&= 8\lambda^2(6-\lambda)\{(2+\lambda)[(1-t)\delta]^2 - (2+\lambda)t(1-t)\delta \\
&\quad - 6t(1-t)\delta + 6t^2\}.
\end{aligned} \tag{A.40}$$

Again, the sign of the discriminant Δ is determined by the sign of the terms within the brackets in (A.40). Now, let the terms in the brackets be

$$g(A) = (2+\lambda)A^2 - (8+\lambda)tA + 6t^2, \tag{A.41}$$

where

$$A \equiv (1-t)\delta. \tag{A.42}$$

The roots of $g(A) = 0$ are t and $\frac{6}{2+\lambda}t$, respectively. Accordingly, we discuss the following cases:

1. When $A \leq t$:

$$Sign(g(A)) = Sign(\Delta) > 0, \tag{A.43}$$

$f(\alpha) = 0$ has two distinct real roots.

Also,

$$b = -2\lambda(6-\lambda)(A-t) > 0, \tag{A.44}$$

and

$$c = -\lambda^2(A-t) > 0. \tag{A.45}$$

Rearrange terms for a

$$a = (6-\lambda)[(3\lambda-2)A - (\lambda+6)t]. \tag{A.46}$$

We need to examine the sign of $K \equiv (3\lambda-2)A - (\lambda+6)t$ within the brackets in (A.46).

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, we have

$$a<0. \tag{A.47}$$

From (A.44) and (A.47), we have

$$-\frac{b}{2a}>0. \tag{A.48}$$

Since

$$-2a-b=2(6-\lambda)[2A(1-\lambda)+6t]>0, \tag{A.49}$$

and (A.48), we have

$$0<-\frac{b}{2a}<1. \tag{A.50}$$

Also from

$$f(0)=c>0, \quad \text{and} \tag{A.51}$$

$$\begin{aligned} f(1) &= a+b+c \\ &= 2\lambda A(4-\lambda)+12t(\lambda-3)-12A \\ &= -2A[(2-\lambda)^2+2]-12t(3-\lambda) \\ &< 0, \end{aligned} \tag{A.52}$$

we can determine the location of the parabola (A.36). $f(\alpha)>0$ 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 $t<A\leq\frac{6t}{2+\lambda}$:

$$Sign(g(A))=Sign(\Delta)<0, \tag{A.53}$$

$f(\alpha)=0$ has no real roots.

Similar to (A.46), 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, we have

$$a<0. \tag{A.54}$$

With both (A.53) and (A.54), we can determine the location of the parabola (A.36). Specifically, $f(\alpha)<0$ over $\alpha\in(0,1)$.

3. When $A>\frac{6t}{2+\lambda}$:

$$Sign(g(A))=Sign(\Delta)>0, \tag{A.55}$$

$f(\alpha) = 0$ has two distinct real roots. As $A > \frac{6}{2+\lambda}t$,

$$\begin{aligned} b &= -2\lambda(6-\lambda)(A-t) < 0, \\ c &= -\lambda^2(A-t) < 0, \end{aligned} \tag{A.56}$$

whereas a may be negative or positive as A increases.

When $a < 0$, we have,

$$\begin{aligned} -\frac{b}{2a} &< 0, \\ f(0) &= c < 0, \\ f(1) &= a + b + c < 0. \end{aligned} \tag{A.57}$$

Combining (A.55) and (A.57), we can determine the location of the parabola (A.36). Specifically, $f(\alpha) < 0$ over $\alpha \in (0, 1)$.

When $a > 0$, we have,

$$\begin{aligned} -\frac{b}{2a} &> 0, \\ f(0) &= c < 0. \end{aligned} \tag{A.58}$$

Also since

$$2a - (-b) = -2(6-\lambda)[2A(1-\lambda) + 6t] < 0, \tag{A.59}$$

We have

$$-\frac{b}{2a} > 1. \tag{A.60}$$

Finally, with $f(1) < 0$ by (A.52), we can determine the location of the parabola (A.36). $f(\alpha) < 0$ 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 $A > \frac{6t}{2+\lambda}$.

We summarize the results as follows:

$$\begin{cases} \frac{\partial p_1}{\partial \alpha} \lessgtr 0, & A \le t; \\ \frac{\partial p_1}{\partial \alpha} < 0, & t < A \le \frac{6t}{2+\lambda}; \\ \frac{\partial p_1}{\partial \alpha} < 0, & A > \frac{6}{2+\lambda}. \end{cases} \tag{A.61}$$

■

A.7 Proof for Proposition 6

Proof.

Based on (B.12) and (B.13), the partial derivatives of p_0 and p_1 with respect to λ are given by

$$\begin{aligned}\frac{\partial p_0}{\partial \lambda} &= \frac{1}{[4-\lambda-\beta+\beta\lambda]^2}\{-2(1-t)\delta(4-\lambda-\beta+\beta\lambda) \\ &\quad -[3t+2(1-\lambda)(1-t)\delta](-1+\beta)\}, \\ &= \frac{3[(1-\beta)t-2(1-t)\delta]}{[4-\lambda-\beta+\beta\lambda]^2} \end{aligned} \tag{A.62}$$

and

$$\begin{aligned}\frac{\partial p_1}{\partial \lambda} &= \frac{1}{[4-\lambda-\beta+\beta\lambda]^2}\{[-2(1-t)\delta+t-\beta t](4-\lambda-\beta+\beta\lambda) \\ &\quad -[2t+2(1-\lambda)(1-t)\delta+t(\lambda+\beta-\beta\lambda)](-1+\beta)\} \\ &= \frac{6[(1-\beta)t-(1-t)\delta]}{[4-\lambda-\beta+\beta\lambda]^2}, \end{aligned} \tag{A.63}$$

respectively. Let

$$\bar{\delta} \equiv \frac{(1-\beta)t}{2(1-t)}. \tag{A.64}$$

Therefore, we have

$$\begin{cases} \frac{\partial p_0}{\partial \lambda} > 0, \frac{\partial p_1}{\partial \lambda} > 0, & if \quad \delta < \bar{\delta}; \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} > 0, & if \quad \bar{\delta} < \delta < 2\bar{\delta}; \\ \frac{\partial p_0}{\partial \lambda} < 0, \frac{\partial p_1}{\partial \lambda} < 0, & if \quad \delta > 2\bar{\delta}. \end{cases} \tag{A.65}$$

■

A.8 Proof for Proposition 7

Proof.

Based on (B.12) and (B.13), the partial derivatives of p_0 and p_1 with respect to β are given by the following, respectively,

$$\begin{aligned}\frac{\partial p_0}{\partial \beta} &= \frac{1-\lambda}{(4-\lambda-\beta+\beta\lambda)^2}[3t+2(1-\lambda)(1-t)\delta] \\ &> 0 \end{aligned} \tag{A.66}$$

and

$$\begin{aligned}\frac{\partial p_1}{\partial \beta} &= \frac{1}{(4-\lambda-\beta+\beta\lambda)^2}\{(t-t\lambda)(4-\lambda-\beta+\beta\lambda) \\ &\quad + [2t+2(1-\lambda)(1-t)\delta + t(\lambda+\beta-\beta\lambda)](1-\lambda)\} \\ &= \frac{1}{(4-\lambda-\beta+\beta\lambda)^2}(1-\lambda)[6t+2(1-\lambda)(1-t)\delta] \\ &= \frac{2(1-\lambda)}{(4-\lambda-\beta+\beta\lambda)^2}[3t+(1-\lambda)(1-t)\delta] \\ &> 0. \end{aligned} \tag{A.67}$$

■

B Appendix: Derivation of Equilibrium for the Extension to the Baseline Model with Therapeutic Reference Pricing

B.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,

$$\begin{aligned} c_0 &= \alpha \cdot p_G + (p_0 - p_G), \\ c_1 &= \alpha \cdot p_G + (p_1 - p_G), \quad \text{and} \\ c_G &= \alpha \cdot p_G. \end{aligned} \tag{B.1}$$

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

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

$$\begin{aligned} D_G &= \frac{(1-\lambda)[c_1 - c_G + t - (1-t)\delta]}{2t} \\ &= \frac{(1-\lambda)[t + p_1 - p_G - (1-t)\delta]}{2t}, \quad \text{and} \end{aligned} \tag{B.3}$$

$$\begin{aligned} D_1 &= 1 - D_0 - D_G \\ &= \frac{t + p_G - p_1 + \lambda(p_0 - p_G) + (1-\lambda)(1-t)\delta}{2t}, \end{aligned} \tag{B.4}$$

where $\delta \equiv (\theta_H - \theta_L)q$ represents the difference in perceived quality between brand-name and generic drugs.[53]

In equations (B.2), (B.3), and (B.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 equations (B.1), 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 functions for the three firms are,

[53] The change in the copay of the brand-name drug 1 in (B.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 $(1-t)(\theta_H - \theta_L)q > p_0 - p_G$.

respectively,

$$\begin{aligned}\Pi_0 &= p_0 D_0 \\ &= \lambda \frac{(t+p_1)p_0 - p_0^2}{2t},\end{aligned} \tag{B.5}$$

$$\begin{aligned}\Pi_G &= p_G D_G \\ &= (1-\lambda)\frac{[t+p_1-(1-t)\delta]p_G - p_G^2}{2t}, \quad \text{and}\end{aligned} \tag{B.6}$$

$$\begin{aligned}\Pi_1 &= p_1 D_1 \\ &= \frac{[t+\lambda(p_0-p_G)+p_G+(1-\lambda)(1-t)\delta]p_1 - p_1^2}{2t}.\end{aligned} \tag{B.7}$$

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.

B.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,

$$\frac{\partial \Pi_0}{\partial p_0} = 0 \quad \Leftrightarrow \quad p_0 = \frac{t+p_1}{2} \quad \text{and} \tag{B.8}$$

$$\frac{\partial \Pi_1}{\partial p_1} = 0 \quad \Leftrightarrow \quad p_1 = \frac{t+\lambda(p_0-p_G)+p_G+(1-\lambda)(1-t)\delta}{2}. \tag{B.9}$$

The second-order conditions are both satisfied to guarantee local maxima. Substituting p_G with $\beta \cdot p_0$ in equations (B.8) and (B.9), we obtain

$$p_0 = \frac{t+p_1}{2} \quad \text{and} \tag{B.10}$$

$$p_1 = \frac{t+(\lambda+\beta-\beta\lambda)p_0+(1-\lambda)(1-t)\delta}{2}. \tag{B.11}$$

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

$$p_0 = \frac{3t+2(1-\lambda)(1-t)\delta}{4-\lambda-\beta+\beta\lambda} \quad \text{and} \tag{B.12}$$

$$p_1 = \frac{2t+2(1-\lambda)(1-t)\delta+t(\lambda+\beta-\beta\lambda)}{4-\lambda-\beta+\beta\lambda}. \tag{B.13}$$

With the equilibrium prices for the two brand-name firms under the TRP copay structure defined in equations (B.1) 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.

C Appendix: Background Information for the Empirical Research in Section 3

C.1 ATC Classification System — 1^{st} Level

Table 4: 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.[54] 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.[55]

The drug price data accessed from the NPDUIS are the manufacturers' list prices. 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.[56] In addition, the manufacturers' list price is considered the same across Canada,[57] 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.[58]

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, we 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, we exclude drugs with non-oral-solid dosage forms for measuring convenience. We select the drug classes that contain the brand-name original drugs going off patent during the study period. As such, we are able to observe and analyze the drug price dynamics before and after the patents' expiry. We also select the drug classes that are representative of the therapeutic class in the Canadian drug market.

[54] We only accessed and kept the data for drugs for human use. Veterinary drugs are not considered in the research.

[55] The above information was accessed at http://www.cihi.ca on November 29, 2010.

[56] Drug price is measured in unit price, in Canadian dollars per capsule/tablet.

[57] Ward Health Strategies (2007).

[58] 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.

C.3 Data Access

Data including the manufacturers' list drug prices 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 5 shows the major sources of the data accessed for this research.

Table 5: 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 antifungal 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 6: 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 7: 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 8: 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 2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

Table 8: (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 2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

Table 8: (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 2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

Table 8: (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 2.

‡ The price variable is measured in 2002 Canadian dollars. The strength variable is measured in Defined Daily Doses (DDDs).

Table 8: (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

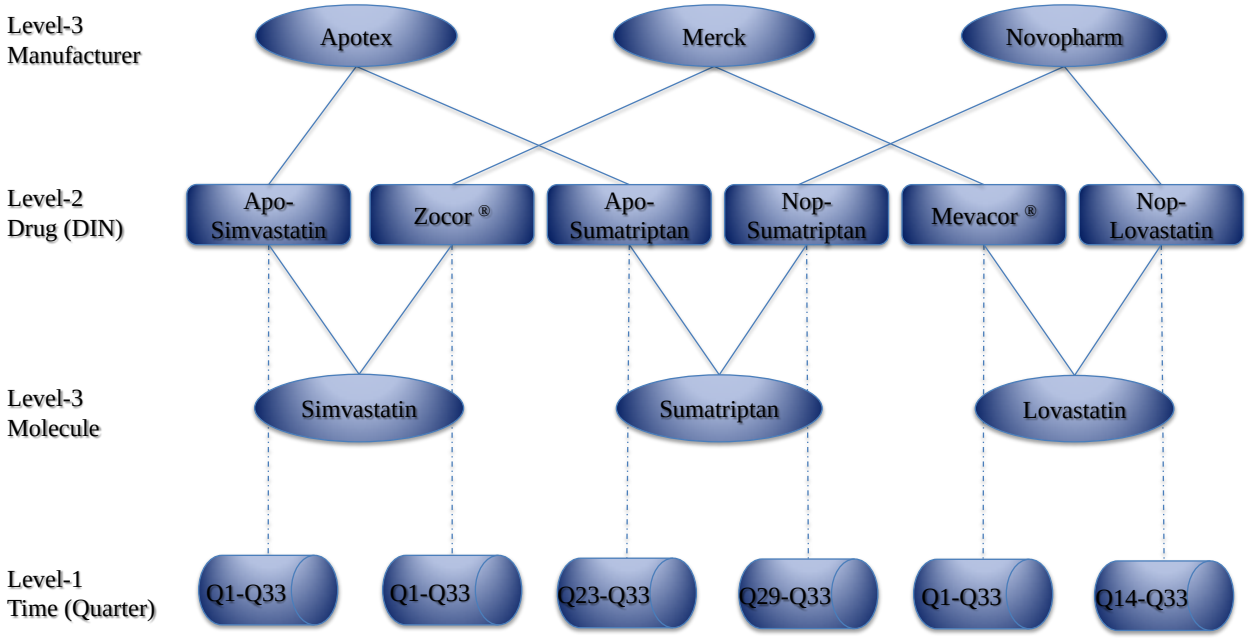
† The detailed description of these variables is provided in Table 2.

‡ 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

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 6 sketches the relationships among the three levels.[59]

Figure 6: A Cross-classified Three-level Data Structure



As shown in Table 9, 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.[60] As a result, we drop the "manufacturer" as a random intercept component in the multilevel analysis in Chapter 4 to simplify the analysis. As noted, we include the type of manufacturer (brand-name or generic) as an explanatory variable to control the manufacture effect.

[59] 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 6. This figure demonstrates the data structure but does not include all products covered in this empirical study.

[60] An unconditional model is the regression model only with an intercept term, with the same variance-covariance structure as the conditional model.

Table 9: 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	