Essays in Regulation of Pharmaceutical Markets

**Dissertation**
**submitted to the Faculty of Economics,**
**Business Administration and Information Technology**
**of the University of Zurich**

to obtain the degree of
Doctor of Philosophy
in Management and Economics

presented by

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approved in October 2013 at the request of

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The Faculty of Economics, Business Administration and Information Technology of the University of Zurich hereby authorizes the printing of this dissertation, without indicating an opinion of the views expressed in the work.

Zurich, 23.10.2013

Chairman of the Doctoral Board: Prof. Dr. Josef Zweimüller

# Acknowledgements

In writing this dissertation I benefited much from the interaction with a number of people who deserve and have my appreciation.

First and foremost, I am grateful to my advisor Uli Kaiser for his support and encouragement during the whole time of my dissertation. I greatly appreciate his generosity and his efforts in making this a successful project. I am also specially thankful to Armin Schmutzler for having my back in repeated occasions and for co-advising my thesis.

I am most indebted to Dani Halbheer, with whom I have had the pleasure to spend many instructive and amusing coffee breaks. I would like to thank him for his constant support, his helpful advice, and for reading and commenting on many of my drafts.

Many thanks go to my coauthors: Thomas Rønde, for hosting me in Copenhagen in severals occasions and to Hannes Ullrich, whom I owe the answers to a good deal of questions. It was a great opportunity to learn from them and a pleasure to work with them. I also want to thank Michelle Sovinsky for all the inspiring discussions and for bringing me closer to the Empirical IO community. Special thanks go to my colleagues Donja Darai, Nicole Ehrsam, Dennis Gärtner, Betti Klose, and Michael Ribbers for all the joy and cake they brought into the office.

Finally, I wish to express my gratitude to my family for their unconditional help and to my partner Kevin Staub for his patience, his encouragement, and his constant and caring support. Without his love none of this would have been possible.

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# Chapter 1

# Introduction

Pharmaceuticals play a key role in working towards achieving the "human right of everyone to the enjoyment of the highest attainable standard of physical and mental health.[1]" As required by the United Nations, governmental health care agencies attempt to provide innovative, safe, effective, and affordable pharmaceuticals given their financial resources. Cost containment policies to influence consumers' purchase decisions, physicians' prescription behavior, and firms' pricing strategies have been widely used to control public budgets in health care systems, but preventing rises in expenditures has proven to be a difficult task. Reasons are e.g. an aging population, the introduction of new and expensive medicines and treatments, a strongly represented and influential pharmaceutical industry, and consumers' low price sensitivity due to insurance coverage.

This dissertation empirically examines two highly debated topics in the pharmaceutical industry. The first chapter analyzes the argument that parallel trade promotes price competition and generates substantial savings to consumers as well as to the government, which is the provider of public health insurance. The second and the third chapters explore the effects of reference pricing, a regulatory policy widely used in Europe to control expenditures for pharmaceuticals.

[1] As stated in the preamble of the 1946 Constitution of the World Health Organization and Article 25. of the 1948 Universal Declaration of Human Rights.

Chapter 1 investigates parallel trade, a practice where products are legally marketed in one country but distributed in another country without authorization of the property rights holder. Parallel trade deals with topics in the related fields of international trade, intellectual property, and competition policy. Opponents of parallel trade argue that parallel imports weaken intellectual property protection, thereby reducing innovation incentives (Li and Maskus 2006, Szymanski and Valletti 2006, and Valletti 2006). On the other hand, politicians and regulatory agencies alike typically propose parallel trade to promote (price) competition (Ganslandt and Maskus 2004), which generates savings to consumers and insurers. In an attempt to reduce high prices for pharmaceutical products, the European Union has allowed parallel imports within its area. The aim of this chapter is to investigate and empirically quantify the impact of parallel trade in markets for pharmaceuticals.

The first part of Chapter 1 develops a structural model of demand and supply (Berry 1994) using Danish data on prices, sales and characteristics of medicines used in the treatment of hypercholesterolemia (presence of high levels of cholesterol in the blood). These products are top selling medicines worldwide in terms of volume and revenue. Furthermore, the Danish pharmaceutical market provides a clean empirical setting to study these effects due to its unique market structure and the availability of very rich data. The second part of the chapter uses the estimates of the model parameters from the first part and provides a framework to simulate outcomes under a complete ban of parallel imports, keeping other regulatory schemes unchanged.

There are two sets of key results from prohibiting parallel imports. The first set focuses on price effects, which differ substantially along two dimensions: the patent protection status of the molecule (on-patent or off-patent) and the type of the firm (original firms, generic firms, and parallel importers). On average, prices increase more in markets where the molecule is off-patent. On the other dimension, both generic firms and original producers increase their pharmacy purchase prices when competition from parallel importers is removed.

The second set of empirical results reports the effects on market participants. My model takes into consideration consumers' preferences allowing them to substitute between products. Prohibiting parallel imports induces consumers to substitute towards original products for which they have stronger preferences. Removing parallel imports leads to (i) an increase in profits for original producers and a decrease for generic firms, (ii) an increase in consumers expenditures and governmental health care expenditures, and (iii) to an overall decrease in welfare driven by a decrease in consumer surplus.

Chapter 2 and Chapter 3 examine the effects of reference pricing, a particularly widely embraced tool to control expenditures (López-Casasnovas and Puig-Junoy 2000). With this approach the maximum reimbursement obtained by a consumer is determined using prices of similar drugs as reference. Reference pricing aims at benefiting patients that prefer cheaper products over more expensive ones. Thus, inducing more price sensitivity on consumers and competitive pressure on firms.

While existing studies have shown that reference pricing effectively curtails prices of prescription drugs (Aronsson et al. 2001; Brekke et al. 2009, 2011; Kanavos et al. 2008; Pavcnik 2002; Puig-Junoy 2007), a hitherto empirically unanswered issue is to what extent differences in the *design* of reference pricing systems affect market outcomes. Specifically, we study the effects of a change from an "external" (based on a basket of prices in other countries) to an "internal" (based on comparable domestic products) reference price system. We address that question by exploiting a reform in Denmark, a country that switched from external to internal reference pricing in April 2005.

Chapter 2 conducts a thorough analysis of the reform effects on market participants using data on anti-cholesterol products. Specifically, we first estimate a flexible logit-type demand model (Berry 1994; Berry et al. 1995) that allows for both horizontal and vertical product differentiation, as well as for consumer-specific heterogeneity that determines substitution patterns between products. Second, we estimate pricing equations to predict the counterfactual prices of products had the reform taken place before it actually did. Finally,

we use our estimated pricing and structural demand parameters to compute a counterfactual demand which allows us to calculate total changes in demand, consumer expenditures, producer revenues as well as consumer welfare.

We find that while our estimated consumer compensating variation is small, the reform led to substantial reductions in pharmacy purchase prices and reference prices as well as in copayment prices —the final price paid by consumers—, and to sizeable decreases in overall producer revenues, health care expenditures, and consumer expenditures. These effects differ markedly between original products, generic products, and parallel imports, with health care expenditures and producer revenues decreasing and consumer expenditures increasing most for original products. The reform also induced consumers to substitute from original products — for which they have strong preferences — to generics and parallel imports. This substitution also explains the small increase in consumer welfare despite a substantial decrease in expenditures.

Chapter 3 extends the analysis to other pharmaceuticals and focuses only on price effects of the reform. Specifically, we use Danish data on the following three therapeutic markets that differ in the severity of the condition: For the treatment of a chronic condition we continue using anti-cholesterol drugs, for a semi-chronic condition we use antiulcerants, and for the treatment of an acute condition we use antibiotics.

We expect the intensity of the effects from the reform to differ between these therapeutic groups because patients with a chronic condition generally face higher health care expenditures, their treatment time is longer and they might be more experienced and better informed about their substitution options.

We base our analysis in Pavcnik (2002). Our results show that the switch from external to internal reference pricing led to a substantial reduction in pharmacy purchase prices. Moreover, the effects are stronger for the chronic condition than for the acute condition and the reform affects generic firms and parallel importers more than original firms. Finally, we find that the reform reinforces the effects of competition, specially for generic firms.

# References


Aronsson, Thomas, Bergman, Mats A. and Niklas Rudholm (2001), The Impact of Generic Drug Competition on Brand Name Market Shares – Evidence from Micro Data, *Review of Industrial Organization*, 19 (4), 423-433.

Berry, Steven T. (1994), Estimating Discrete-Choice Models of Product Differentiation, *The RAND Journal of Economics*, 25 (2), 242-262.

Berry, Steven T., Levinsohn, James, and Ariel Pakes (1995), Automobile Prices in Market Equilibrium, *Econometrica*, 63 (4), 841-890.

Brekke, Kurt R., Grasdal, Astrid L., and Tor H. Holmås (2009), Regulation and Pricing of Pharmaceuticals: Reference Pricing or Price Cap Regulation, *European Economic Review*, 53 (2), 170-185.

Brekke, Kurt R., Holmås, Tor H., and Odd Rune Straume (2011), Reference Pricing, Competition, and Pharmaceutical Expenditures: Theory and Evidence from a Natural Experiment, *Journal of Public Economics*, 95 (7-8), 624-638.

Ganslandt, Mattias and Keith E. Maskus (2004), Parallel Imports and the Pricing of Pharmaceutical Products: Evidence from the European Union, *Journal of Health Economics*, 23 (5), 1035-1057.

Kanavos, Panos, Costa-Font, Joan, and Elizabeth Seeley (2008), Competition in Off-Patent Drug Markets: Issues, Regulation and Evidence, *Economic Policy*, 23 (55), 499-544.

Li, Changying and Keith E. Maskus (2006), The Impact of Parallel Imports on Investments in Cost–Reducing Research and Development, *Journal of International Economics*, 68 (2), 443–455.

López-Casasnovas, Guillem and Jaume Puig-Junoy (2000), Review of the Literature on Reference Pricing, Universitat Pompeu Fabra, mimeo.

Pavcnik, Nina (2002), Do Pharmaceutical Prices Respond to Potential Patient Out-of-pocket Expenses?, *The RAND Journal of Economics*, 33 (3), 469-487.

Puig-Junoy, Jaume (2007), The Impact of Generic Reference Pricing Interventions in the Statin Market, *Health Policy*, 84, 14-29.

Szymanski, Stefan and Tommaso M. Valletti (2006), Parallel Trade, International Exhaustion and Intellectual Property Rights: A Welfare Analysis, *The Journal of Industrial Economics*, 54 (4), 499–526.

Valletti, Tommaso M. (2006), Differential Pricing, Parallel Trade, and the Incentive to Invest, *Journal of International Economics*, 70 (1), 314–324.

# Chapter 2

# Parallel Trade of Pharmaceuticals: The Danish Market for Statins

*Acknowledgements*: I would like to thank Daniel Halbheer, Ulrich Kaiser, Katja Seim, Kevin Staub, Hannes Ullrich, and seminar participants at at the University of Zurich, and at the 7th. Competition Law and Economics European Network "CLEEN" workshop for helpful comments and suggestions. Financial support from the Swiss National Science Foundation through grant PBZHP1-138689 is gratefully acknowledged.

## 2.1 Introduction

Parallel trade refers to the practice where products are legally marketed in one country but distributed in another country without authorization of the property rights holder. In the European market for pharmaceuticals, governmental health care agencies attempt to provide innovative, safe, effective and affordable pharmaceuticals keeping their financial resources. To reach this goal different regulatory policies across nations are in use. However, it has been argued that these differences in regulatory strategies generate significant price dispersion and hence induce arbitrage opportunities and a profitable market for parallel trade (Danzon 1998, Danzon and Chao 2000). Whether or not parallel imports in the pharmaceutical industry are beneficial for market participants has been an intensely debated issue. Opponents of parallel trade argue that parallel imports weaken intellectual property protection and therefore firms have less incentives to innovate, which generates dynamic inefficiency. Supporters on the other hand emphasize that allowing parallel trade benefits consumers because it increases competition leading to lower prices, which in turn generates savings to consumers and insurers. In an attempt to reduce high prices for pharmaceutical products, the European Union has allowed parallel imports within its area.[1]

The goal of this paper is to investigate the impact of parallel trade in markets for pharmaceuticals. More specifically, this paper attempts to identify and understand the effects of parallel imports on consumers' consumption choices, government expenditures for pharmaceuticals, and producers' strategies.

I empirically quantify these effects on the market participants using data on prices, sales and characteristics of statins in Denmark. Statins are used in the treatment of hypercholesterolemia—presence of high levels of cholesterol in the blood—, a chronic condition that, if left unattended, can have severe consequences like heart attacks and strokes, which are both leading causes of death in developed countries. The best known statins sell

[1]The United States currently referred bill S.319, Pharmaceutical Market Access and Drug Safety Act of 2011, to Senate committee on 2/10/2011 to allow parallel imports.

under the tradename *Lipitor* (by *Pfizer*) and *Zocor* (by MSD Sharp & Dohme) and are top selling medicines worldwide in terms of volume and revenue. The Danish pharmaceutical market provides a clean empirical setting to study these effects due to its unique market structure and the availability of very rich data. A particularly attractive feature of my data is that it allows me to distinguish between the price set by the firm, the price set by the pharmacy, and the price paid by consumers.

The paper consists of two parts. The first part develops and estimates a structural model of demand and supply under current regulation laws and market structure. The second part uses estimates of the model parameters and the provided framework to construct counterfactuals allowing a welfare evaluation under a complete ban of parallel imports.

Eliminating parallel trade yields the following results. First, a prohibition of parallel trade reduces average prices but results in higher prices for both original products and generic products. Second, eliminating parallel trade leads to substitution from parallel imported products towards original products. Third, consumer expenditures as well as government expenditures increase absent parallel trade. Finally, banning parallel imports reduces consumer surplus and increases firm profits, leading to an overall decrease in welfare.

Finally, while beyond the scope of this paper, the long-term effects of parallel trade, particularly on generating dynamic inefficiencies that can reduce welfare, remain a highly controversial and unresolved question. Because the industry heavily relies on R&D and innovation is an important driver of consumer welfare, the subject constitutes an important issue for further research.

This paper is organized as follows. Section 2.2 provides a review of the relevant literature. Section 2.3 offers an overview of the Danish pharmaceutical market. Section 4.3 describes the data. Section 2.5 describes the empirical framework and describes the simulation strategy. Section 4.5 presents the results and welfare implications. Section 4.6 concludes.

## 2.2 Literature Review

This section offers a summary of the literature on parallel imports. First, I present the legal framework on parallel trade in the European Union. Next, I review the literature that has address parallel imports in the pharmaceutical industry from an economics perspective.

### A Legal Perspective

Parallel trade deals with topics in three related fields: intellectual property law, international trade, and competition law.[2]

International research intensive firms rely strongly on intellectual property rights to protect their investments. One important policy is the legal principle of exhaustion of patent rights, which determines the markets where the property right owner can prevent unauthorized trade. Under the Trade-Related Aspects of Intellectual Property Rights Agreement (TRIPS) each country is free to determine a national or an international policy of exhaustion of patent rights (Article 6 of the TRIPS Agreement). The European Union has adopted a policy of community exhaustion, such that property right owners can prevent resale of products first sold outside the area but cannot interfere in the trade of its products within members states of the European Union.

Furthermore, in an effort to achieve and protect an European Common Market the European Commission and the European Court of Justice strictly enforce the principle of free movement of goods within the European Union (Article 28 of the consolidated version of the Treaty on the Functioning of the European Union (TFEU)).

Original firms have used different strategies to limit parallel trade, like challenging restrictive distribution agreements with wholesalers, setting supply restrictions in exporter countries or challenging trademark protection[3] but parallel trade within the European

[2]See Kyle (2009) for an overview of the literature related to parallel trade in pharmaceuticals

[3]See for example: GlaxoSmithKline Services Unlimited v. Commission of the European Communities Case C-501/06, 2009 ECR I-9291; GlaxoGroup Ltd. v. Dowelhurst Ltd. & Anor Case HC 03 00464, 2003

Union has been enabled and protected through these laws, that prioritize the principle of a Common Market over the possible welfare looses generated through reduced incentives to innovate. More recent cases have shed light into the importance of considering dynamic inefficiencies (Petrucci 2010, Tsouloufas 2011) and the necessity of revising the goals of the EU competition laws.

**An Economic Perspective**

Most of the empirical studies on parallel imports in the pharmaceutical industry have almost exclusively focused on price effects. For instance, Ganslandt and Maskus (2004) use a regulatory change after Sweden joined the European Union in 1995. They estimate a 19 percent price reduction due to parallel imports for the top 50 molecules in Sweden.[4] In contrast, Kanavos and Costa-Font (2005) study six molecules during 1997 to 2002 in 11 European countries. They do not attribute price decreases in import countries to parallel trade, but rather to generic substitution and find evidence for entry of parallel importers to be determined by price differences between countries. A more related study is Enemark et al. (2006). The authors use data on four European countries including the top 50 products in Denmark in 2004. Following the strategy of West and Mahon (2003) they find that parallel trade generated 168 million Danish krones savings. My results contribute to the view that parallel trade does generate substantial savings to consumers and health care agencies, however the magnitude of the savings is much higher (on average 242.6 million Danish krones) than the results in Enemark et al. even when my sample includes only two of their products.

Another issue investigated is the fact that given the heavily regulated industry, firms are usually limited in their price setting strategies to compete with parallel trade. The only empirical paper that studies non-price responses to parallel trade is Kyle (2011). Her

EWHC 2015; Hoffman-La Roche v. Centrafarm Case C-1 02/77, 1978 ECR 1139.

[4]A molecule in this context is the active ingredient of a pharmaceutical product defined by its bottom-level Anatomical Therapeutic Chemical (ATC) classification code.

study reveals that firms are indeed using other strategies to hinder parallel trade, typically differentiating products across countries by altering the brand name, dosage form, and strength.

The theoretical literature has gone beyond studying price effects and explore the impact of parallel trade on R&D. Li and Maskus (2006), Szymanski and Valletti (2006), and Valletti (2006) conclude that parallel imports have detrimental effects on incentives to innovate in the long run but can be beneficial to consumers in the short run. However, Grossman and Lai (2008) show that allowing international parallel trade can benefit innovation, since governments will use different price control tools if international parallel trade were permitted. This issue, while beyond the scope of my paper, is still a relevant question.

## 2.3 The Danish Pharmaceutical Industry

This section offers an overview of the pharmaceutical industry and discusses the main regulatory framework in effect during the time period covered by my data (May 2003 to March 2005).

### 2.3.1 Industry Description

The pharmaceutical industry in Denmark has a typical vertical structure. First, at the upstream level there are three types of firms: Original firms, generic firms, and parallel importers. Original firms engage in R&D and manufacture new medicines using intellectual property rights to protect their innovations. Generics firms produce bioequivalent copies of original products and are only allowed to enter the market after the relevant patents have expired. In contrast, parallel importers do not engage in manufacturing. Instead, they supply products that are imported from markets outside of Denmark. Typically, parallel importers repackage, relabel, and redistribute (original and generic) products. Since 1990, parallel imports are legal in Denmark—even for products under patent protection.

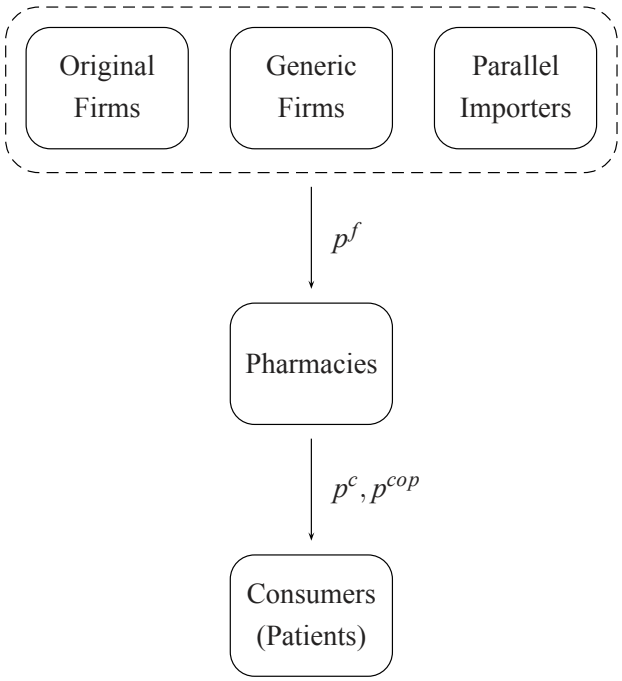


Figure 2.1: Overview of vertical industry structure

Second, at the wholesale level, pharmacies purchase pharmaceuticals from upstream firms that are supplied to consumers (patients). Pharmacies operate in a highly regulated market environment, as I detail below. The most important features of the regulation are: generic substitution and retail price regulation.

Finally, at the downstream level, consumers purchase prescription-only pharmaceuticals from the pharmacies. At the consumer level, the regulator implemented a system of reference pricing that sets reimbursement rules. Importantly, the reimbursement price determines copayment prices, which govern consumers' purchase decision. Figure 2.1 illustrates the vertical structure.

### 2.3.2 Regulatory Framework

Governmental safety concerns and budget constrains generate a high degree of regulation on pharmaceutical markets. In Europe, price regulation and reimbursement rules of phar-

maceuticals is a national competence. Denmark's regulatory body has adopted a policy of free pricing at the upstream level. However, the upstream firms must report their prices to the Danish Medicines Agency (DKMA). Every second week, the DKMA updates prices and product availability in a publicly available list. This list is used by doctors when issuing prescriptions, by hospitals for their electronic patient records, by pharmacies to ensure availability of products, and by consumers to obtain information about (copayment) prices of available substitutes. Next, I discuss pharmacy regulation and follow it with a description of the reimbursement rules that determine copayment prices.

### Pharmacy Regulation

Pharmacies face two types of regulation: generic substitution and retail price regulation. Danish pharmacists are required by law to dispense the cheapest product among available substitutes, unless the consumer or the doctor explicitly requests another product. Generic substitution for off-patent products has been encouraged since 1991.

Pharmacy retail prices $p^c$ for prescription-only pharmaceuticals are identical nationwide and can be decomposed as follows:

$$p^c = \mu p^f + k, \tag{2.1}$$

where $p^f$ is the pharmacy purchase price (at the wholesale level), $\mu$ is the regulated markup above the pharmacy purchase price, and $k$ is the prescription fee (including value added tax).[5] Notice that, in effect, retail price regulation determines pharmacies' unit margins.

### Reimbursement Rules

The final price paid by consumers is the copayment price, that is, the pharmacy retail price adjusted for reimbursement. Specifically, the copayment price $p^{cop}$ is given by:

$$p^{cop} = p^c - 0.8 * p^r, \tag{2.2}$$

[5]The exact rules and yearly adjustments to compute pharmacy retail prices from pharmacy purchase prices are detailed in Appendix A.

where $p^c$ is the pharmacy retail price and $p^r$ is the reference price. The reference price in a given substitution group is set equal to the lowest price of the Danish pharmacy retail price and the average price in EU-15 (excluding Greece, Luxembourg, Spain, and Portugal). The 80% reimbursement of the reference price applies for consumers with yearly expenditures exceeding 2,950 Danish krones (DKK) (€395).[6]

Substitution groups are defined by DKMA guidelines. Products are assigned to the same substitution group if they have the same active ingredient, administration form, strength, and similar package size. Importantly, consumers can freely choose among products in the same substitution group.

This reimbursement rule, while allowing consumers some freedom in their choices, does influence consumers' price sensitivity by covering only a fraction of their expenditures. Therefore, reference pricing is a widely used measure for cost containment (López-Casasnovas and Puig-Junoy 2000; Espín et al. 2011).[7] Brekke et al. (2007, 2009, 2011), Kaiser et al. (2013), and Pavcnik (2002) empirically investigate the impact of reference pricing on consumers and government expenditures.

## 2.4 The Data

I use data from the market of statins during the time period May 2003 to March 2005. Price data and product characteristics were obtained from DKMA. Sales data was made available from the Danish Association of the Pharmaceutical Industry (LIF). I observe fortnightly prices and sales for 213 products sold in Denmark, which belong to the molecules in the therapeutic group of HMG CoA reductase inhibitors (commonly known as statins).

[6]The medical condition explored below is a chronic condition for which this minimum expenditure is reached.

[7]The WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies (online access at *http://whocc.goeg.at*) offers an overview of the countries that currently use reference pricing to control expenditures.

A product is defined by four attributes: active substance, strength, package size, and firm. The active substance is captured by the molecule classified by the 5-level ATC code. Strength measures the amount of the active substance in milligram per pill. Package size is simply the number of pills per package.

There are six molecules, out of which three are off-patent (Simvastatin, Lovastatin, and Pravastatin). The other molecules are on-patent (Fluvastatin, Atorvastatin, and Rosuvastatin). Table 2.1 provides an overview and indicates the ATC codes. In addition, the table provides information about brand names, patent owners and the average number of firms and products in each molecule. The best known statins sell under the tradenames *Lipitor* (*Pfizer*) and *Zocor* (*MSD Sharp & Dohme*) and are top selling medicines in terms of quantity and revenue.

Generic firms sell version of the first three molecules (C10AA01-C10AA03). In contrast, the molecules Fluvastatin (C10AA04), Atorvastatin (C10AA05), and Rosuvastatin (C10AA07) are protected by an active patent and sold by original firms. Importantly there is more than one active firm in these groups because of the presence of parallel importers.

To make different products comparable I normalize prices and quantities using defined daily doses (DDD). This measure is proposed by the World Health Organization and widely used in the pharmaceutical industry.

Table 2.2 shows average pharmacy purchase prices $p^f$, pharmacy retail prices $p^c$, reference prices $p^r$ and copayment prices $p^{cop}$. All prices are deflated using consumer price index with 2005 as basis year. The summary is organized as follows: Part A shows averages for all products, Part B presents the results by molecule, Part C by firm type, and Part D by the patent status. Pharmacies buy one DDD for around DKK 6 (around €0.80) and consumers copayment is on average DKK 3.2 (€0.40). As noted in Kanavos and Costa-Font (2005), pharmacy purchase price for parallel imports lies just below the price for original firms and significantly above generic prices. Copayments seem to be substantially higher for original products than for parallel imports or generics. Also, consumers pay more for

off-patent products than for on-patent products. This is due to the reimbursement rules and the lack of substitutes in the on-patent segment.

Finally, Table 2.3 summarizes average sales and revenues, and expenditures. Fortnightly sales are in volume and amount to about 2.4 million DDD on average for a period of 14-days. The most popular products are Simvastatin (C10AA01) and Atorvastatin (C10AA05) selling fortnightly on average around 1.7 million DDD and 0.5 million DDD respectively. Furthermore, most sales come from generic products. Revenues are calculated as pharmacy purchase price times sold DDDs. The statins markets generates fortnightly on average DKK 9 million. Original firms account for the highest revenues, while revenues for generics and parallel imports are substantially lower. Government expenditures are reimbursement costs and amount to DKK 10.3 million on average for a period of 14-days. Finally, consumers pay only a fraction of their cost (copayment price times consumed DDDs). Their expenditures are fortnightly on average DKK 3.3 million.

## 2.5 Empirical Framework

The empirical framework has two main components: demand estimation and supply estimation. The estimation draws on Berry (1994), Stern (1996), and Verboven (1996), and is closely related to recent work by Branstetter et al. (2011), Dutta (2011), and Dunn (2012). The first part of this paper specifies a discrete choice model to estimate consumer demand. These estimates are used in the second part to recover the marginal cost of production from the firms' profit maximizing conditions. Ultimately, the goal of the analysis is to use the estimates to generate policy implications from a hypothetical ban of parallel imports.

### 2.5.1 Demand Estimation

I consider a market with a set of consumers that are indexed by $i$. Each consumer chooses the product $j$ ($j = 1, \ldots, J$) that maximizes her utility $U_{ij}$. Consumer choice has a nested

logit structure (Berry 1994). The nests ($g = 1, \ldots, G$) follow from substitution groups defined by the DKMA. Importantly, consumers can freely choose among products in the same substitution group.[8]

The utility of a consumer as a function of observed and unobserved product characteristics is:

$$U_{ij} = X_j\beta - \alpha p_j^{cop} + \xi_j + \sum_g [d_{jg}\zeta_{ig}] + (1-\sigma)\varepsilon_{ij}. \tag{2.3}$$

The terms that are invariant across consumers are captured by mean utility $\delta_j \equiv X_j\beta - \alpha p_j^{cop} + \xi_j$, which depends on observed product characteristics $X_j$, copayment price $p_j^{cop}$ and product characteristics $\xi_j$ (that are unobserved to the econometrician).

The nesting structure is reflected in $d_{jg}$, a dummy equal to one if product $j$ belongs to the set of products $J$ in nest $g$ ($J_g$) and zero otherwise. $\zeta_{ig}$ is common to all products in nest $g$ and its distribution depends on the nesting parameter $\sigma$. The random utility term $\varepsilon_{ij}$ represents unobserved consumer-specific heterogeneity. Each $\varepsilon_{ij}$ is assumed to be identically, independently distributed extreme value across consumers and products. Cardell (1997) shows that if $\varepsilon_{ij}$ is i.i.d. extreme value, then $\zeta_{ig} + (1-\sigma)\varepsilon_{ij}$ is also an extreme value random variable.

The nesting parameter measures correlation of consumer choices between substitution groups. Products are considered closer substitutes the closer $\sigma$ gets to one. If $\sigma = 1$ the model reduces to a simple logit model where there is perfect substitutability of products between nests. On the contrary, if $\sigma = 0$ there is no substitution across nests. McFadden (1978) shows that for the nested logit to be consistent with random-utility maximization, the estimated value for $\sigma$ must lie between 0 and 1.

The model also includes one nest that is explicitly modeled as the outside option. It allows consumers with high cholesterol to be treated with drugs other than statins or where no medication but rather life style changes like more sports and a low-fat diet are

[8]Consumers can choose a product that belongs to a different substitution group only after consulting the practitioner. I allow for this possibility in my estimation.

recommended. In absence of the outside option a change in prices of the inside goods, statins, will not have an effect on aggregate output. The price of the outside good is assumed not to be set in response to the prices of the inside goods and its mean utility is normalized to zero ($\delta_0 \equiv 0$).

If each consumer selects the product that provides them with the highest utility and using the distributional assumptions, Berry (1994) shows how to solve for mean utility levels as a function of observed market shares. The market share of product $j$ $s_j$ can be decomposed as follows:

$$s_j(\delta, \sigma) = s_{j|g}(\delta, \sigma) s_g(\delta, \sigma), \tag{2.4}$$

where $s_{j|g}$ is the share of product $j$ in nest $g$ and $s_g$ is the share of nest $g$ in the market. Following Berry (1994), these terms are:

$$s_{j|g}(\delta, \sigma) = \frac{\exp(\delta_j/(1-\sigma))}{D_g} \text{ and } s_g(\delta, \sigma) = \frac{D_g^{(1-\sigma)}}{\sum_g D_g^{(1-\sigma))}},$$

where $D_g$ is:

$$D_g \equiv \sum_{j \in J_g} \exp(\delta_j/(1-\sigma)).$$

The nest containing the outside good has only one element ($D_o = 1$), thus the market share of the outside good is:

$$s_o(\delta, \sigma) = \frac{1}{\sum_g D_g^{(1-\sigma)}}.$$

Finally, solving for mean utility levels the linear equation to be estimated is:

$$ln(s_j) - ln(s_o) = X_j\beta - \alpha p_j^{cop} + \sigma ln(s_{j|g}) + \xi_j. \tag{2.5}$$

The variables included in the vector of observed product characteristics are the strength, package size, a dummy variable indicating if the product is on-patent and the number of products in the same nest. I further include firm and time period dummy variables in the specification. More important, I obtain the coefficient on price $\alpha$ and the nesting parameter $\sigma$. These are the parameters that will determine elasticities of demand and thereby influence the substitution patterns of consumers and the price setting of firms. My

prior is that $\alpha$ has a negative sign such that higher prices are associated with a decrease in mean utility. The nesting parameter $\sigma$ should lie between 0 and 1 to be consistent with random-utility maximization.

### Instrumental Variables

To control for endogeneity arising from potential correlation between unobserved product characteristics and $p_j^{cop}$ and $s_{j|g}$ Berry et al. (1995) propose the use of characteristics of other firms as valid instruments. Since characteristics of product $k$ are not included in the utility function for product $j$ but are correlated with the price and conditional shares of product $j$ through the markup in the first-order conditions of the profit maximizing firm in oligopolistic competition. Additionally, Nevo (2001) proposes exploiting the panel structure of the data and uses the price of the same label in other markets as instrument, because the price of product $j$ in two different markets will be correlated due to the common marginal cost, but market specific valuations are independent across markets. Accordingly, the instruments I use are the number of products of rival firms, the average price of products from the same firm in other substitution groups, the sum of characteristics of rival firms, and squares of own products' characteristics.

### Market Size and the Outside Good

Longstanding elevated levels of cholesterol in the blood induce the formation of plaque in the arteries causing narrowing or even blockage of arteries. This condition is asymptomatic and can go undetected for a long period of time generating life-threatening problems like heart attacks or strokes. Total market size includes consumption of both, consumers in treatment and potential consumers with high cholesterol levels. In a similar way as Dunn(2012) or Ching et al. (2012) I use different sources to determine total market size.

The first step is to define the fraction of the population with elevated levels of cholesterol. Guidelines recommend for a healthy adult to have less than 5 millimoles per liter

of blood (mmol/L) of total cholesterol and less than 3 mmol/L of low-density lipoprotein cholesterol. According to the Danish Association of Heart Patients (Madsen and Videbæk, 2004) and the Danish Institute for Rational Pharmacotherapy (IRF, 2006) around 60% of the Danish population between 40 and 80 years of age exceed these thresholds.This estimate goes in line with a report from the World Health Organization (Roth, 2010) that shows disease prevalence statistics for similar countries to Denmark, where the percentage of total population aged 40-79 years with high levels of cholesterol lies between 35% and 61%.

Second, total consumption of statins from consumers in treatment is obtained from the Danish Health Data and Disease Control Institute (www.medstat.dk). I assume that if potential consumers were prescribed with statins, they will consume the same dosage as the average actual consumer. The sum of actual consumption and hypothetical consumption from potential consumers gives total market size.

**Price Elasticities**

Finally, the price paid by consumers ($p^{cop}$) is the relevant price to calculate the associated elasticities. Using $\alpha$ and $\sigma$ from the demand estimation the own price elasticity for product $j$ in a nested logit is:

$$\eta_{jj} = \frac{\partial s_j}{\partial p_j^{cop}} \frac{p_j^{cop}}{s_j} = -\alpha \frac{1}{(1-\sigma)} p_j^{cop} [1 - \sigma s_{j|g} - (1-\sigma) s_j].$$

Cross-price elasticities are expected to be smaller if the products are consider less substitutable. If product $j$ and product $k$ are in the same substitution group their respective cross-price elasticity is:

$$\eta_{jk} = \frac{\partial s_j}{\partial p_k^{cop}} \frac{p_k^{cop}}{s_j} = \alpha \frac{1}{(1-\sigma)} p_k^{cop} [\sigma s_{k|g} + (1-\sigma) s_k].$$

If product $j$ and product $l$ are not in the same substitution group, the cross-price elasticity is:

$$\eta_{jl} = \frac{\partial s_j}{\partial p_l^{cop}} \frac{p_l^{cop}}{s_j} = \alpha p_l^{cop} s_l.$$

### 2.5.2 Supply Estimation

On the supply side of the market there are multiproduct firms that are free to choose their pharmacy purchase price ($p^f$). Assuming that prices are set in a Bertrand-Nash equilibrium, the profit-maximization conditions can be used to recover markups and marginal cost of production.

Each firm $f$, with $f = 1, \ldots, F$, produces some subset $\vartheta_f$ of the $J$ products. The profit function of firm $f$ can then be written as:

$$\Pi_f = \sum_{j \in \vartheta_f} (p_j^f - c_j) s_j M - K \tag{2.6}$$

Where $p_j^f$, $c_j$, and $s_j$ are product $j$'s respective pharmacy purchase price, marginal cost, and market share. $M$ is total market size including consumption from actual and potential consumers, and $K$ are the firm's fixed cost.

The first order condition for product $j$ is:

$$\frac{\partial \pi_j}{\partial p_j^f} = M \left( s_j + \sum_{h \in \vartheta_f} (p_h^f - c_h) \frac{\partial s_h}{\partial p_j^f} \right) = 0$$

Each firm sets prices for each product considering the price of all of its other products. The set of $J$ first order conditions characterize equilibrium prices and can be rewritten in vector form as $S(p^{cop}, x, \xi) - \Delta(p^{cop}, x, \xi)(P - C) = 0$, where $S$ is the vector of shares, $\Delta$ is a $J \times J$ matrix with $\Delta = -\partial s_h / \partial p_j^f$ if $h$ and $j$ are produced by the same firm and $\Delta = 0$ otherwise, $P$ is the vector of pharmacy purchase prices ($p^f$), and $C$ a vector of marginal cost.

Finally, the $J$ pricing equations can be express as marginal cost and markup, where the term $\Delta^{-1} S$ is a measured of predicted markups:

$$P = C + \Delta^{-1} S \tag{2.7}$$

### 2.5.3 Counterfactual Calculation

Removing parallel importers from the market affects the market participants in different ways. Firms face less competition which is associated with an increase in prices. Consumers, additionally to facing higher expenditures due to the increase in prices, are confronted with less variety. Consumers that consumed parallel imports substitute towards generics, original products or to the outside option. Finally, the effect of a ban of parallel imports on governmental expenditures depends on the magnitude of changes in prices and the new choices of consumers. If, for example, ex-buyers of parallel imports choose original products and those prices rise, then government expenditures would most likely increase, since prices for original products are on average higher than prices for parallel imports even before the prohibition.

To calculate the new equilibrium I use the following three equations. First, I follow the Danish rules and regulations and use equation (2.1) and (2.2) to obtain the counterfactual copayment prices as follows:

$$p^{cop}_{j_{counter}} = \mu p^{f}_{j_{counter}} + k - 0.8 * p^{r}_{j}. \tag{2.8}$$

Second, eliminating parallel imports does not affect consumers tastes, therefore I use equation (2.4) to obtain counterfactual shares for each product:

$$s_{j_{counter}}(\delta_{counter}, \sigma) = \frac{\exp(\delta_{j_{counter}}/(1-\sigma))}{D_g} \frac{D_g^{(1-\sigma)}}{\sum_g D_g^{(1-\sigma))}}, \tag{2.9}$$

where $\delta_{j_{counter}} = X_j\beta - \alpha p^{cop}_{j_{counter}} + \xi_j$. Finally, removing parallel imports does not affect marginal cost of production of the remaining firms. Using the same Bertrand-Nash equilibrium assumptions for the price setting behavior of the firms, I calculate counterfactual pharmacy purchase prices using the marginal cost implied by the demand estimates as follows:

$$P^{f}_{counter} = C + \Delta^{-1}_{counter} S_{counter} \tag{2.10}$$

Solving equations (2.8), (2.9), and (2.10) simultaneously yields the counterfactual market equilibrium prices and shares.

### 2.5.4 Consumer Surplus and Welfare

Consumer surplus is (Small and Rosen 1981):

$$CS = \frac{1}{\alpha} M \ln \left[ 1 + \sum_{g=1}^{G} \left( \sum_{j \in G_g} exp^{\delta_j/(1-\sigma)} \right)^{(1-\sigma)}. \right] \tag{2.11}$$

I use equation (2.11) to calculate yearly consumer surplus with the real data and with the counterfactual data. The difference $CS_{real} - CS_{counterfactual}$ measures the effects on consumer surplus generated by prohibiting parallel imports. This measure not only accounts for possible harm induced by price increases, but, because it takes consumers' preferences into consideration, it also captures losses generated by reducing the market variety.

Finally, I define total welfare as the sum of consumer surplus and firms' profits. The difference between real total welfare and counterfactual total welfare mirrors the changes in total welfare from a prohibition in parallel trade.

## 2.6 Results

This section reports three sets of empirical findings. First, it presents estimates of the utility parameters and the implied elasticities. Second, it reports cost estimates for the different firm types. Third, the section provides policy implications from a counterfactual analysis.

### 2.6.1 Demand

Estimating the demand side in (2.5) yields the empirical counterparts of the utility parameters and the substitution parameters. The following finding reports the empirical insights concerning the utility parameters.

**Empirical Finding 1 (Utility Parameters)** *The coefficient on copayment price is negative and the nesting parameter is positive.*

Estimates are provided in Table 2.4. The estimated OLS coefficient on copayment price $\alpha$ is close to zero (-0.053). When controlling for endogeneity, the estimate is clearly negative, as expected. This means that a higher copayment price reduces consumers' mean utility. Specifically the IV - nested logit estimate of $\alpha$ is -0.832. These estimates are in line with previous findings: Dunn (2012) finds a price coefficient of -1.61 for anti-cholesterol drugs based on US data covering the period 1996 to 2007. Similarly, Branstetter et al. (2011) obtain a price coefficient of -0.30 for the market of hypertension drugs in the United States between 1997 and 2008.

The OLS estimate of the nesting parameter $\sigma$ is 0.803, which shows a relatively high degree of substitution across different product groups. The degree of substitution is lower when controlling for endogeneity. In this case the estimate of $\sigma$ is 0.315. Both estimates lie between zero and one (which is consistent with random-utility maximization) and are slightly higher than the value 0.24 reported in Dutta (2011).

The estimation of the utility parameters yields further insides. First, products with less strength (-0.807) and more pills per package (0.018) are associated with higher market shares. The coefficient on products in groups with patent protection is positive (1.697), while the coefficient on the number of products in each substitution group is negative (-0.212), suggesting that a less competitive environment has a positive impact on market shares. Second, the firm dummies coefficients indicate that consumers have a strong preferences for original firms.

Next, I report the empirical insights regarding the substitution patterns.

**Empirical Finding 2 (Elasticities)** *The own-price elasticities are negative and the cross-price elasticities are positive.*

Table 2.5 summarizes the mean own and cross-price elasticities of demand associated with the coefficient estimated from the IV - nested logit. Part A reports the average elasticities for all products. The mean own-price elasticity is -3.608 and is very similar to the obtained result in Dunn (2012) of -3.11. The results on cross-price elasticities are as

expected small and much lower if products belong to different substitution groups. Part B of Table 2.5 reports average elasticities for products in each molecule group. Part C of the table reports elasticities for products in each type of firm. Original firms and parallel importers, which charge higher prices, have higher elasticities than generics. Finally, Part D summarizes the results for products off-patent and on-patent. Mean own-price elasticities are higher if the product is off-patent, which is expected to be more competitive segment.

### 2.6.2 Supply

This section uses the results from the demand side to estimate the supply side in (2.7). The estimated average marginal cost of production for a unit of DDD is DKK 5.28 (see Table 2.6). This cost estimate is below the average pharmacy purchase price of DKK 5.93 (reported in Table 2.2), implying an average unit margin of DKK 0.65. Part B of Table 2.6 also reports average production cost at the molecule level and confirms that all markups are positive. Interestingly, the table shows that markups differ by the patent status of the molecules.

**Empirical Finding 3 (Competition Effect)** *Markups are lower for off-patent molecules and higher for on-patent molecules.*

This result nicely mirrors that competition from generics erodes unit markups: the on-patent molecules generate higher markups than the off-patent molecules because there is only competition due to parallel imports but not from generics (see Part D of Table 2.6). Further, the analysis shows that original firms have higher average markups (0.74) than both parallel importers (0.63) and generic firms (0.58).

### 2.6.3 The Impact of Parallel Trade

To investigate the impact of parallel trade, I first calculate the counterfactual market equilibrium when parallel imported products are eliminated from the consumers' choice set.

Next, I compare the market outcome when parallel imports are present to the counterfactual market outcome and derive policy implications.

### Counterfactual Market Equilibrium

Solving the system of equations in Section 2.5.3 yields the new market equilibrium prices and shares, which are used to find the new markups, firm profits, government expenditures and consumer expenditures. In this section I compare these results with their counterparts and summarize my findings due to parallel trade as follows.

**Empirical Finding 4 (Trade Effect)** *Eliminating parallel trade reduces average prices but results in higher prices for both original products and generic products.*

Intuitively, average prices decrease because parallel traded products—the cheaper alternative to the original product— are removed from the market. However, as can be expected, this results in higher average prices for original products. Because prices are strategic complements, average prices for generic products increase as well. Furthermore, the copayment prices increases more for original products than for generics, which is caused by the prevailing reimbursement rules. On another dimension, prices for off-patent products decrease, while prices for on-patent increase. This result provides evidence supporting the conjecture of Enemark et al. (2006), that firms producing on-patent products do not engage in competition with parallel importers if there is no generic available, because the price-sensitive market segment that will switch to parallel imports is small or the parallel importer faces capacity constraints. These results on price effects due to parallel trade are reported in Table 2.7.

Next, I analyze the change on market shares that mirrors substitution patterns.

**Empirical Finding 5 (Substitution Patterns)** *Eliminating parallel trade leads to substitution from parallel imported products towards original products.*

Original firms benefit from a ban of parallel imports while generic firms lose market share (see Table 2.8). Intuitively, these substitution patterns can be attributed to the strong preferences that consumers have toward original products. Moreover, off-patent products gain substantially on shares from a prohibition of parallel imports.

The competitive pressure from generic products is also present when parallel trade is prohibited. Similar to Empirical Finding 3, I identify the following effect of competition on markups.

**Empirical Finding 6 (Competition Effect)** *Markups are lower for off-patent molecules and higher for on-patent molecules even absent parallel trade.*

Specially, through the lack of competition of any kind in on-patent markets, original firms increase their markups substantially more than generic firms. The changes in markups are reported in Table 2.9.

Further, I analyze the impact of banning parallel trade on profits, government expenditures and consumers expenditures, the results are presented in Table 2.10. Eliminating parallel trades generates an increase in profits and an increase in expenditures. The average profit for original firms in a 14-day period is DKK 0.57 million, this profit amounts to DKK 4.19 million after eliminating parallel imports. On the contrary, the profits generated by generic firms decrease. Government expenditures and consumers expenditures follow the same path. Both, government expenditures and consumer expenditures increase substantially more for original products than for generic products.

### Policy Implications

The results from the counterfactual analysis with respect to consumer surplus and welfare are summarized in Table 2.11. Eliminating parallel importers yield the following result:

**Empirical Finding 7 (Welfare)** *Eliminating parallel trade reduces consumer surplus and increases firm profits, leading to an overall decrease in welfare.*

Consumer surplus decreases on average by DKK 111.41 million (around $ 18.2 million) when parallel importers are removed from the sample.[9] The decrease in consumer surplus is driven by two effects. First, consumers face less variety of products and because parallel imports are regarded closer substitutes to original products than generics, consumers substitute towards original products in the absence of parallel imports. Second, a less competitive environment is associated with an increase in copayment prices, specially consumers consuming original products face a higher increase in prices. Finally, total welfare is given by the sum of consumer surplus and profits. The average yearly welfare lost from a prohibition of parallel importers is on average DKK 54.9 million per year (around $ 8.9 million).

Furthermore, removing parallel imports generates the following results with respect to government expenditures and consumer expenditures:

**Empirical Finding 8 (Expenditures)** *Eliminating parallel trade increases consumer expenditures as well as government expenditures.*

On average, yearly government expenditures increase by DKK 182.7 million (see Table 2.12). Consumer expenditures increase yearly on average DKK 75 million and differs substantially from the results on consumer surplus. This shows that using only consumer expenditures as a measure of welfare, as is done in previous studies, might underestimate the total welfare loss.

## 2.7 Conclusions

This paper analyzes the effects of parallel trade in the Danish market for statins. It develops a structural model of demand and supply and uses these estimates to simulate new market

[9]The observed data covers a period of three years, but only 2004 accounts for the whole 12 months, therefore each part of the table shows the average for each year. The yearly average at the bottom is constructed for any period of 12 months.

outcomes under a hypothetical ban of parallel imports. There are two key results from prohibiting parallel imports. The first set focuses on price effects, which differ along two dimensions: the type of firm and the patent protection status of the molecule. Eliminating parallel trade reduces average prices but results in higher prices for both original products and generic products. Furthermore, average prices for off-patent products decrease, while average prices for on-patent products are positively affected by excluding parallel imports. The second set of results reports the effects on market participants: Firms, government and consumers. On average, firms profits increase, but the effect is positive for original firms and negative for generic firms. Consumer surplus decreases due to a decrease in variety and an increase in expenditures. Moreover, government expenditures increase due to a prohibition of parallel trade. Finally, total welfare is defined as the sum of consumer surplus and profits. Eliminating parallel trade leads to an overall decrease in welfare.

My model takes into consideration consumers' preferences, that determine substitution patterns, in the measure of consumer surplus, as opposed to previous studies that use only consumers expenditures as welfare measure. My results support the view that parallel trade generates significant savings to consumers and insurers. Furthermore, the analysis carefully follows the rules and regulation in Denmark. To expand these results to other geographical markets, albeit not difficult, it is necessary to consider these rules, which play an important role in determining the results.

Finally, while beyond the scope of this paper, the long-term effects of parallel trade, particularly on incentives to innovate, remain a highly controversial and unresolved question. Because innovation is an important driver of consumer welfare, the subject constitutes an important issue for further research.

# References


Berry, Steven T. (1994), Estimating Discrete–Choice Models of Product Differentiation, *The RAND Journal of Economics*, 25 (2), 242–262.

Berry, Steven T., James Levinsohn, and Ariel Pakes (1995), Automobile Prices in Market Equilibrium. *Econometrica*, 63 (4), 841–890

Berndt, Ernst and Pierre Dubois (2012), Impacts of Patent Expiry and Regulatory Policies on Daily Cost of Pharmaceutical Treatments: OECD Countries, 2004-2010, IDEI Working Paper 702.

Branstetter, Lee G. , Chirantan Chatterjee, and Matthew Higgins (2011), Regulation and Welfare: Evidence from Paragraph IV Generic Entry in the Pharmaceutical Industry, NBER Working Paper 17188.

Brekke, Kurt R., Grasdal, Astrid L., and Tor H. Holmås (2009), Regulation and Pricing of Pharmaceuticals: Reference Pricing or Price Cap Regulation, *European Economic Review*, 53 (2), 170-185.

Brekke, Kurt R., Holmås, Tor H., and Odd Rune Straume (2011), Reference Pricing, Competition, and Pharmaceutical Expenditures: Theory and Evidence from a Natural Experiment, *Journal of Public Economics*, 95 (7-8), 624-638.

Cardell, N. Scott (1997), Variance Components Structures for the Extreme–Value and Logistic Distributions with Applications to Models of Heterogeneity, *Econometric Theory*, 13 (2), 185–213.

Danzon, Patricia M. (1998), The Economics of Parallel Trade, *Pharmacoeconomics*, 13 (3), 293–304.

Danzon, Patricia M. and Li-Wei Chao (2000), Cross-National Price Differences for Pharmaceuticals: How Large and Why?, *Journal of Health Economics*, 19 (2), 159–195.

Dunn, Abe (2012), Drug Innovations and Welfare Measures Computed from Market Demand: The Case of Anti-Cholesterol Drugs, *American Economic Journal: Applied Economics*, 4 (3), 167–189.

Dutta, Antara (2011), From Free Entry to Patent Protection: Welfare Implications for the Indian Pharmaceutical Industry, *The Review of Economics and Statistics*, 93 (1), 160–178.

Enemark, Ulrika, Møller, Kjeld, and Jan Sørensen (2006), The Economic Impact of Parallel Import of Pharmaceuticals, CAST - Centre for Applied Health Services Research and Technology Assessment, University of Southern Denmark.

Espín, Jaime, Rovira, Joan, and Antonio Olry de Labry (2011), WHO/HAI Project on Medicine Prices and Availability, Review Series on Pharmaceutical Pricing Policies and Interventions, Working Paper 1: External Reference Pricing;
URL: http://www.haiweb.org/medicineprices/24072012/ERPfinalMay2011.pdf

Ganslandt, Mattias and Keith E. Maskus (2004), Parallel Imports and the Pricing of Pharmaceutical Products: Evidence from the European Union, *Journal of Health Economics*, 23 (5), 1035–1057.

Ganslandt, Mattias and Keith E. Maskus (2008), Intellectual Property Rights, Parallel Imports and Strategic Behavior, in Frontiers of Economic and Globalization.

Grossman, Gene M. and Edwin L.-C. Lai (2008), Parallel Imports and Price Controls, *the RAND Journal of Economics*, 2008, 39 (2), 378–402.

Kaiser, Ulrich, Susan J. Mendez, Rønde, Thomas, and Hannes Ullrich (2013), Regulation of Pharmaceutical Prices: Evidence from a Reference Price Reform in Denmark, University of Zurich, Business working paper 330.

Kanavos, Panos and Joan Costa-Font (2005), Pharmaceutical Parallel Trade in Europe: Stakeholder and Competition Effects, *Economic Policy*, 20 (44), 751–798.

Kyle, Margaret (2009), Parallel Trade in Pharmaceuticals: Firm Responses and Competition Policy, in B. Hawk (Ed.), International Antitrust Law & Policy: Fordham Competition Law, Juris Publishing, New York.

Kyle, Margaret (2011), Strategic Responses to Parallel Trade, *The B.E. Journal of Economic Analysis & Policy*, 11 (2).

Madsen, Mette and Jørgen Videbæk (2004), Hjertestatistik - Heart Statistics 2004, Hjerteforeningen og Institut for Folkesundhed. http://www.hjerteforeningen.dk

McFadden, Daniel (1978), Modelling the Choice of Residential Location, in A. Karlqvist, L. Lundqvist, F. Snickars, and J. Weibull (eds.), Spatial Interaction Theory and Planning Models, Amsterdam: North-Holland.

Li, Changying and Keith E. Maskus (2006), The Impact of Parallel Imports on Investments in Cost–Reducing Research and Development, *Journal of International Economics*, 68 (2), 443–455.

López-Casasnovas, Guillem and Jaume Puig-Junoy (2000), Review of the Literature on Reference Pricing, Universitat Pompeu Fabra, mimeo.

Pavcnik, Nina (2002), Do Pharmaceutical Prices Respond to Potential Patient Out-of-pocket Expenses?, *The RAND Journal of Economics*, 33 (3), 469–487.

Petrucci, Carlo (2010), Parallel Trade of Pharmaceutical Products: The ECJ Finally Speaks – Comment on GlaxoSmithKline, *European Law Review*, 35 (2), 275–286.

Stern, Scott (1996), Market Definition and the Returns to Innovation: Substitution Patterns in Pharmaceutical Markets, MIT Sloan School & NBER working paper.

Szymanski, Stefan and Tommaso M. Valletti (2006), Parallel Trade, International Exhaustion and Intellectual Property Rights: A Welfare Analysis, *the Journal of Industrial Economics*, 54 (4), 499–526.

Tsouloufas, Georgios (2011), Limiting Pharmaceutical Parallel Trade in the European Union: Regulatory and Economic Justifications, *European Law Review*, 36 (3), 385–404.

Valletti, Tommaso M. (2006), Differential Pricing, Parallel Trade, and the Incentive to Invest, *Journal of International Economics*, 70 (1), 314–324.

Verboven, Frank (1996), International Price Discrimination in the European Car Market, *the RAND Journal of Economics*, 27 (2), 240–268.

West, Peter and James Mahon (2003), Benefits to Payers and Patients From Parallel Trade, University of York, York health economics consortium.

Table 2.1: **Danish Market for Statins**

| ATC Code | Molecule | Brand name | Original Firm | Obs. | Average Number of | |
|---|---|---|---|---|---|---|
| | | | | | Firms | Products |
| C10AA01 | Simvastatin | Zocor | *MSD Sharp & Dohme* | 3,323 | 11.85 | 69.51 |
| | | | | | (1.02) | (10.85) |
| C10AA02 | Lovastatin | Mevacor | *MSD Sharp & Dohme* | 829 | 5.39 | 17.44 |
| | | | | | (0.81) | (2.72) |
| C10AA03 | Pravastatin | Pravachol | *Bristol-Myers Squibb* | 766 | 5.94 | 19.28 |
| | | | | | (2.06) | (8.13) |
| C10AA04 | Fluvastatin | Lescol | *Novartis* | 490 | 2.00 | 10.00 |
| | | | | | (0.00) | (0.00) |
| C10AA05 | Atorvastatin | Lipitor | *Pfizer* | 611 | 3.03 | 12.57 |
| | | | | | (0.44) | (1.11) |
| C10AA07 | Rosuvastatin | Crestor | *AstraZeneca* | 369 | 1.59 | 8.10 |
| | | | | | (0.75) | (1.37) |
| All | | | | 6,388 | 19.71 | 130.76 |
| | | | | | (1.96) | (7.05) |

Notes: Average number of firms and average number of products in each molecule group for a 14-days period. Products are characterized by the combination of molecule (5-level ATC code), strength, package size and firm. Standard deviation in parentheses

Table 2.2: **Average Prices**

| | Pharmacy Purchase Price ($p^f$) | Reference Price ($p^r$) | Copayment Price ($p^{cop}$) |
|---|---|---|---|
| A. *All Products* | | | |
| | 5.93 | 7.31 | 3.21 |
| | (4.53) | (5.34) | (4.42) |
| B. *By ATC Code* | | | |
| C10AA01 | 4.63 | 4.42 | 3.76 |
| | (4.94) | (3.91) | (5.77) |
| C10AA02 | 7.08 | 9.16 | 3.47 |
| | (3.78) | (4.30) | (3.04) |
| C10AA03 | 7.71 | 11.10 | 2.57 |
| | (4.41) | (6.20) | (1.81) |
| C10AA04 | 8.27 | 12.66 | 2.56 |
| | (2.14) | (3.56) | (0.72) |
| C10AA05 | 7.91 | 11.53 | 2.31 |
| | (2.99) | (4.50) | (0.90) |
| C10AA07 | 4.92 | 7.19 | 1.44 |
| | (1.35) | (2.05) | (0.41) |
| C. *By Firm Type* | | | |
| Original Firm | 8.68 | 10.35 | 4.63 |
| | (3.62) | (4.91) | (4.84) |
| Generic Firm | 2.62 | 3.86 | 1.31 |
| | (2.03) | (2.32) | (1.77) |
| Parallel Importer | 7.64 | 8.92 | 4.4 |
| | (5.04) | (6.07) | (5.50) |
| D. *By Patent Status* | | | |
| Off-Patent | 5.69 | 6.67 | 3.46 |
| | (4.78) | (5.31) | (4.82) |
| On-Patent | 7.00 | 10.29 | 2.06 |
| | (2.85) | (4.34) | (0.87) |

Notes: Fortnightly average prices for a defined daily dose in Danish krones. All figures deflated using consumer prices index with June 2005 as basis. $p^f$ is the pharmacy purchase price, $p^r$ is the reference price, and $p^{cop} = p^c - 0.8 * p^r$ is the copayment price. The results are summarized as follows: A. All products, B. Products in the same ATC code, C. Products from the same firm type, and D. Products on-patent and off-patent. Exchange rates in June 2005: DKK 1 = $ 0.1634 = € 0.1343. Standard deviation in parentheses.

Table 2.3: **Average Sales, Average Revenues, and Average Expenditures**

| | Sales | Revenues | Expenditures | |
|---|---|---|---|---|
| | | | Government | Consumers |
| A. *All Products* | | | | |
| | 2,446.127 | 9.139 | 10.342 | 3.315 |
| | (520.621) | (1.891) | (2.075) | (0.627) |
| B. *By ATC Code* | | | | |
| C10AA01 | 1,669.324 | 2.516 | 2.729 | 1.344 |
| | (550.280) | (0.498) | (0.579) | (0.224) |
| C10AA02 | 24.420 | 0.186 | 0.188 | 0.087 |
| | (4.845) | (0.103) | (0.123) | (0.037) |
| C10AA03 | 182.748 | 1.554 | 1.776 | 0.472 |
| | (45.749) | (0.803) | (0.951) | (0.202) |
| C10AA04 | 23.021 | 0.178 | 0.211 | 0.053 |
| | (4.910) | (0.041) | (0.049) | (0.012) |
| C10AA05 | 470.609 | 4.312 | 4.982 | 1.246 |
| | (76.914) | (0.897) | (1.052) | (0.263) |
| C10AA07 | 79.241 | 0.409 | 0.477 | 0.119 |
| | (33.288) | (0.166) | (0.191) | (0.048) |
| C. *By Firm Type* | | | | |
| Original Firms | 694.424 | 6.176 | 6.615 | 2.325 |
| | (167.741) | (1.793) | (2.018) | (0.593) |
| Generic Firms | 1,498.947 | 1.639 | 2.182 | 0.584 |
| | (633.574) | (0.527) | (0.691) | (0.176) |
| Parallel Imports | 252.757 | 1.324 | 1.545 | 0.406 |
| | (149.244) | (0.100) | (0.444) | (0.141) |
| D. *By Patent Status* | | | | |
| Off-Patent | 1,890.991 | 4.367 | 4.823 | 1.935 |
| | (525.779) | (1.165) | (1.238) | (0.411) |
| On-Patent | 555.136 | 4.772 | 5.519 | 1.380 |
| | (72.161) | (0.868) | (1.020) | (0.255) |

Notes: Sales are fortnightly averages 1,000 defined daily dosages. Revenues and expenditures are fortnightly averages in million Danish krones. The results are summarized as follows: A. All products, B. Products in the same ATC code, C. Products from the same firm type, and D. Products on-patent and off-patent. Exchange rates in June 2005: DKK 1 = $ 0.1634 = € 0.1343. Standard deviation in parentheses.

Table 2.4: **Demand Estimation**

| | OLS - Nested Logit | | IV - Nested Logit | |
|---|---|---|---|---|
| | Coef. | Std. Error | Coef. | Std. Error |
| Copayment price | -0.053*** | (0.004) | -0.831*** | (0.051) |
| Conditional share | 0.880*** | (0.007) | 0.315* | (0.123) |
| Strength in ddd | 0.347*** | (0.022) | -0.807*** | (0.067) |
| Package size | 0.024*** | (0.0004) | 0.018*** | (0.001) |
| On-Patent | 0.979*** | (0.064) | 1.697*** | (0.119) |
| No. prod. in nest | 0.239*** | (0.005) | -0.212*** | (0.051) |
| Constant | -11.416*** | (0.609) | -10.669*** | (0.952) |
| *Firm Dummy Variables* | | | | |
| *Original Firms* | | | | |
| *AstraZeneca* | 0.589 | (0.609) | 2.813** | (0.939) |
| *Bristol-Myers Squibb* | 2.601*** | (0.611) | 6.183*** | (0.957) |
| *MSD Sharp & Dohme* | 1.897** | (0.609) | 9.207*** | (1.036) |
| *Novartis* | 0.415 | (0.610) | 2.244* | (0.940) |
| *Pfizer* | 2.147*** | (0.611) | 5.056*** | (0.947) |
| *Generic Firms* | | | | |
| *1A Farma* | 1.768** | (0.611) | 2.614* | (1.024) |
| *Actavis* | 0.21 | (0.612) | 0.742 | (0.937) |
| *Alpharma* | 2.186*** | (0.610) | 2.084* | (0.942) |
| *Alternova* | 1.401* | (0.608) | 1.336 | (0.934) |
| *Arrow* | 1.002 | (0.632) | 4.330*** | (0.947) |
| *Durascan* | 1.987** | (0.609) | 0.663 | (0.952) |
| *Genthon* | 1.283* | (0.617) | 1.066 | (0.971) |
| *Gevita* | 1.702** | (0.612) | 0.634 | (0.956) |
| *Hexal* | 2.052*** | (0.609) | 2.143* | (0.947) |
| *Ranbaxy* | 1.186 | (0.620) | 0.915 | (0.964) |
| *Ratiopharm* | 1.198* | (0.609) | 0.349 | (0.959) |
| *Sandoz* | 1.270* | (0.611) | -0.073 | (0.970) |
| *Parallel Importers* | | | | |
| *Copyfarm* | 2.013** | (0.622) | 0.618 | (0.984) |
| *EuroPharma* | 1.261* | (0.616) | 1.941 | (0.998) |
| *Orifarm* | 1.454* | (0.609) | 4.207*** | (0.968) |
| *Paranova* | 1.230* | (0.609) | 2.237* | (0.964) |
| *PharmaCoDane* | 1.411* | (0.608) | 4.729*** | (1.065) |
| *Recept Pharma* | 1.230* | (0.621) | 1.138 | (0.957) |
| *Stada* | 0.082 | (0.612) | 0.522 | (0.979) |

Notes: Table 2.4 reports OLS and IV - nested logit estimates of equation (2.5). The number of observations is 6,388. The specification also includes firm, and time period dummy variables. The reference category for firm dummy variables is the parallel importer *Universal Pharma*. Robust standard errors in parenthesis. ***, ** and * indicate statistical significance at the one, five, and ten percent level. The instruments for the IV - nested logit are: the number of products of rival firms, average price of products from the same firm in other substitution groups, the sum of characteristics of rival firms, and squares of own products' characteristics.

Table 2.5: **Average Own- and Cross-Price Elasticities of Demand**

| | Own-price elasticities | Cross-price elasticities | |
|---|---|---|---|
| | | Same nest | Different nest |
| A. *All Products* | | | |
| | -3.608 | 0.179 | 0.0014 |
| | (5.263) | (0.245) | (0.0004) |
| B. *By ATC Code* | | | |
| C10AA01 | -4.398 | 0.074 | 0.0015 |
| | (6.878) | (0.193) | (0.0004) |
| C10AA02 | -3.816 | 0.359 | 0.0014 |
| | (3.380) | (0.268) | (0.0003) |
| C10AA03 | -2.854 | 0.191 | 0.0013 |
| | (2.077) | (0.137) | (0.0003) |
| C10AA04 | -2.559 | 0.536 | 0.0014 |
| | (0.845) | (0.222) | (0.0004) |
| C10AA05 | -2.190 | 0.256 | 0.0014 |
| | (0.732) | (0.132) | (0.0003) |
| C10AA07 | -1.325 | 0.272 | 0.0014 |
| | (0.412) | (0.188) | (0.0003) |
| C. *By Firm Type* | | | |
| Original Firm | -5.043 | 0.273 | 0.0014 |
| | (5.906) | (0.259) | (0.0004) |
| Generic Firm | -1.542 | 0.101 | 0.0014 |
| | (2.150) | (0.139) | (0.0004) |
| Parallel Importer | -5.016 | 0.230 | 0.0015 |
| | (6.558) | (0.317) | (0.0004) |
| D. *By Patent Status* | | | |
| Off-patent | -3.962 | 0.162 | 0.0015 |
| | (5.727) | (0.245) | (0.0004) |
| On-patent | -1.959 | 0.316 | 0.0014 |
| | (0.806) | (0.200) | (0.0004) |

Notes: Table 2.5 reports mean own and cross-price elasticities of demand using the results from the IV - nested logit. The results are summarized as follows: A. All products, B. Products in the same ATC code, C. Products from the same firm type, and D. Products on-patent and off-patent. Standard deviation in parentheses.

Table 2.6: **Average Marginal Cost and Average Markups**

| | Marginal Cost | Markups |
|---|---|---|
| A. *All Products* | | |
| | 5.277 | 0.648 |
| | (4.486) | (0.137) |
| B. *By ATC Code* | | |
| C10AA01 | 4.038 | 0.589 |
| | (4.906) | (0.135) |
| C10AA02 | 6.428 | 0.651 |
| | (3.761) | (0.074) |
| C10AA03 | 7.052 | 0.655 |
| | (4.395) | (0.087) |
| C10AA04 | 7.537 | 0.732 |
| | (2.184) | (0.076) |
| C10AA05 | 7.141 | 0.774 |
| | (2.957) | (0.110) |
| C10AA07 | 4.080 | 0.840 |
| | (1.324) | (0.058) |
| C. *By Firm Type* | | |
| Original Firm | 7.940 | 0.745 |
| | (3.673) | (0.114) |
| Generic Firm | 2.035 | 0.584 |
| | (2.003) | (0.125) |
| Parallel Importer | 7.014 | 0.631 |
| | (4.992) | (0.114) |
| D. *By Patent Status* | | |
| Off-Patent | 5.077 | 0.617 |
| | (4.740) | (0.125) |
| On-Patent | 6.208 | 0.789 |
| | (2.855) | (0.099) |

Notes: Table 2.6 reports average marginal cost and markups calculated from the first order conditions in equation (2.7) in Danish krones per defined daily dose. The results are summarized as follows: A. All products, B. Products in the same ATC code, C. Products from the same firm type, and D. Products on-patent and off-patent. Standard deviation in parentheses.

Table 2.7: **Average Change in Prices**

| | Pharmacy purchase price ($p^f$) | | | Reference price ($p^r$) | | | Copayment price ($p^{cop}$) | | |
|---|---|---|---|---|---|---|---|---|---|
| | real | counter. | change in % | real | counter. | change in % | real | counter. | change in % |
| A. *All Products* | | | | | | | | | |
| | 5.92 | 5.33 | -10.08 | 7.31 | 6.70 | -8.37 | 3.21 | 2.84 | -11.50 |
| | (4.53) | (4.17) | | (5.34) | (4.88) | | (4.42) | (3.93) | |
| B. *By ATC Code* | | | | | | | | | |
| C10AA01 | 4.63 | 3.70 | -19.96 | 4.42 | 3.69 | -16.71 | 3.76 | 2.99 | -20.58 |
| | (4.94) | (4.03) | | (3.91) | (2.29) | | (5.77) | (4.99) | |
| C10AA02 | 7.08 | 6.70 | -5.41 | 9.16 | 8.09 | -11.62 | 3.47 | 3.83 | 10.60 |
| | (3.78) | (4.14) | | (4.30) | (4.03) | | (3.04) | (3.68) | |
| C10AA03 | 7.71 | 6.56 | -14.92 | 11.10 | 9.13 | -17.69 | 2.57 | 2.46 | -4.19 |
| | (4.41) | (4.27) | | (6.20) | (5.66) | | (1.81) | (2.13) | |
| C10AA04 | 8.27 | 8.27 | 0.01 | 12.66 | 12.65 | -0.07 | 2.56 | 2.57 | 0.32 |
| | (2.14) | (2.14) | | (3.56) | (3.56) | | (0.72) | (0.72) | |
| C10AA05 | 7.91 | 8.54 | 7.90 | 11.53 | 12.41 | 7.72 | 2.31 | 2.56 | 10.66 |
| | (2.99) | (3.49) | | (4.50) | (5.29) | | (0.90) | (1.04) | |
| C10AA07 | 4.92 | 5.04 | 2.47 | 7.19 | 7.37 | 2.41 | 1.44 | 1.49 | 3.27 |
| | (1.35) | (1.30) | | (2.05) | (2.00) | | (0.41) | (0.39) | |
| C. *By Firm Type* | | | | | | | | | |
| Original Firm | 8.69 | 8.79 | 2.49 | 10.35 | 10.34 | 0.15 | 4.63 | 4.79 | 3.45 |
| | (3.62) | (3.63) | | (4.91) | (4.90) | | (4.84) | (4.94) | |
| Generic Firm | 2.62 | 2.63 | 3.55 | 3.86 | 3.86 | 1.54 | 1.31 | 1.33 | 1.14 |
| | (2.03) | (2.01) | | (2.32) | (2.28) | | (1.77) | (1.78) | |
| Parallel Importer | 7.64 | | | 8.92 | | | 4.40 | | |
| | (5.04) | | | (6.07) | | | (5.50) | | |
| D. *By Patent Status* | | | | | | | | | |
| Off-Patent | 5.69 | 4.90 | -14.01 | 6.67 | 5.79 | -13.16 | 3.46 | 3.01 | -13.04 |
| | (4.78) | (4.27) | | (5.31) | (4.45) | | (4.82) | (4.33) | |
| On-Patent | 7.00 | 7.15 | 2.16 | 10.29 | 10.52 | 2.27 | 2.06 | 2.14 | 4.05 |
| | (2.85) | (3.11) | | (4.34) | (4.74) | | (0.87) | (0.95) | |

Notes: Fortnightly average prices for a defined daily dose in Danish krones and average percentage change. All figures deflated using consumer prices index with June 2005 as basis. The results are summarized as follows: A. All products, B. Products in the same ATC code, C. Products from the same firm type, and D. Products on-patent and off-patent. Exchange rates in June 2005: DKK 1 = $ 0.1634 = €0.1343. Standard deviation in parentheses

Table 2.8: **Average Change in Shares**

| | Real | Counterfactual | Change in % |
|---|---|---|---|
| A. *All Products* | | | |
| | 0.124 | 0.243 | 96.337 |
| | (0.429) | (1.539) | |
| B. *By ATC Code* | | | |
| C10AA01 | 0.161 | 0.355 | 120.109 |
| | (0.567) | (2.103) | |
| C10AA02 | 0.010 | 0.168 | 1621.355 |
| | (0.014) | (0.637) | |
| C10AA03 | 0.079 | 0.086 | 8.888 |
| | (0.176) | (0.148) | |
| C10AA04 | 0.016 | 0.019 | 21.171 |
| | (0.015) | (0.030) | |
| C10AA05 | 0.254 | 0.283 | 11.385 |
| | (0.284) | (0.268) | |
| C10AA07 | 0.066 | 0.063 | -3.295 |
| | (0.044) | (0.059) | |
| C. *By Firm Type* | | | |
| Original Firm | 0.113 | 0.481 | 324.499 |
| | (0.214) | (2.299) | |
| Generic Firm | 0.184 | 0.058 | -68.189 |
| | (0.625) | (0.137) | |
| Parallel Importer | 0.048 | | |
| | (0.165) | | |
| C. *By Patent Status* | | | |
| Off-Patent | 0.116 | 0.264 | 127.819 |
| | (0.460) | (1.708) | |
| On-Patent | 0.161 | 0.156 | -3.295 |
| | (0.234) | (0.215) | |

Notes: Fortnightly average shares per product in percentage. The results are summarized as follows: A. All products, B. Products in the same ATC code, C. Products from the same firm type, and D. Products on-patent and off-patent. Standard deviation in parentheses.

Table 2.9: **Average Change in Markups**

| | Real | Counterfactual | Change in % |
|---|---|---|---|
| A. *All Products* | | | |
| | 0.648 | 0.706 | 9.031 |
| | (0.137) | (0.215) | |
| B. *By ATC Code* | | | |
| C10AA01 | 0.589 | 0.645 | 9.567 |
| | (0.135) | (0.241) | |
| C10AA02 | 0.651 | 0.741 | 13.875 |
| | (0.074) | (0.256) | |
| C10AA03 | 0.655 | 0.699 | 6.713 |
| | (0.087) | (0.119) | |
| C10AA04 | 0.732 | 0.733 | 0.109 |
| | (0.076) | (0.079) | |
| C10AA05 | 0.774 | 0.875 | 13.148 |
| | (0.110) | (0.010) | |
| C10AA07 | 0.840 | 0.859 | 2.226 |
| | (0.058) | (0.004) | |
| C. *By Firm Type* | | | |
| Original Firm | 0.745 | 0.852 | 14.336 |
| | (0.114) | (0.255) | |
| Generic Firm | 0.584 | 0.593 | 1.576 |
| | (0.125) | (0.049) | |
| Parallel Importer | 0.631 | | |
| | (0.114) | | |
| D. *By Patent Status* | | | |
| Off-Patent | 0.617 | 0.674 | 9.103 |
| | (0.125) | (0.225) | |
| On-Patent | 0.789 | 0.844 | 6.968 |
| | (0.099) | (0.061) | |

Notes: Table 2.9 reports average markups per defined daily dose in Danish krones. The results are summarized as follows: A. All products, B. Products in the same ATC code, C. Products from the same firm type, and D. Products on-patent and off-patent. Standard deviation in parentheses.

Table 2.10: **Changes in Profits and Expenditures**

| | Variable Profits | | | Government Expenditures | | | Consumer Expenditures | | |
|---|---|---|---|---|---|---|---|---|---|
| | real | counter. | change in % | real | counter. | change in % | real | counter. | change in % |
| A. *All Products* | | | | | | | | | |
| | 1.54 | 4.48 | 189.84 | 10.34 | 18.48 | 78.70 | 3.32 | 7.04 | 112.29 |
| | (0.41) | (6.59) | | (2.08) | (7.23) | | (0.63) | (5.58) | |
| B. *By ATC Code* | | | | | | | | | |
| C10AA01 | 0.91 | 3.75 | 312.10 | 2.73 | 9.62 | 252.40 | 1.34 | 4.51 | 235.42 |
| | (0.42) | (6.78) | | (0.58) | (8.18) | | (0.22) | (6.18) | |
| C10AA02 | 0.02 | 0.25 | 1,365.12 | 0.19 | 3.38 | 1,700.00 | 0.09 | 1.10 | 1,173.99 |
| | (0.00) | (0.41) | | (0.12) | (5.88) | | (0.04) | (1.53) | |
| C10AA03 | 0.14 | 0.10 | -31.52 | 1.78 | 1.32 | -25.94 | 0.47 | 0.35 | -25.41 |
| | (0.04) | (0.06) | | (0.95) | (0.92) | | (0.20) | (0.24) | |
| C10AA04 | 0.02 | 0.02 | 14.94 | 0.21 | 0.25 | 20.55 | 0.05 | 0.06 | 20.98 |
| | (0.00) | (0.02) | | (0.05) | (0.25) | | (0.01) | (0.06) | |
| C10AA05 | 0.39 | 0.30 | -23.47 | 4.98 | 3.47 | -30.28 | 1.25 | 0.90 | -27.66 |
| | (0.07) | (0.15) | | (1.05) | (1.66) | | (0.26) | (0.43) | |
| C10AA07 | 0.07 | 0.06 | -8.96 | 0.48 | 0.47 | -2.08 | 0.12 | 0.12 | -1.85 |
| | (0.03) | (0.03) | | (0.19) | (0.25) | | (0.05) | (0.06) | |
| C. *By Firm Type* | | | | | | | | | |
| Original Firm | 0.57 | 4.19 | 633.50 | 6.61 | 17.50 | 164.55 | 2.32 | 6.78 | 191.47 |
| | (0.14) | (6.67) | | (2.02) | (7.36) | | (0.59) | (5.65) | |
| Generic Firm | 0.81 | 0.29 | -64.44 | 2.18 | 0.98 | -55.05 | 0.58 | 0.26 | -55.14 |
| | (0.43) | (0.14) | | (0.69) | (0.40) | | (0.18) | (0.12) | |
| Parallel Importer | 0.17 | | | 1.54 | | | 0.41 | | |
| | (0.10) | | | (0.53) | | | (0.14) | | |
| D. *By Patent Status* | | | | | | | | | |
| Off-Patent | 1.08 | 4.11 | 279.95 | 4.82 | 14.41 | 198.77 | 1.94 | 5.99 | 209.36 |
| | (0.41) | (6.67) | | (1.24) | (8.03) | | (0.41) | (5.83) | |
| On-Patent | 0.46 | 0.37 | -19.81 | 5.52 | 4.07 | -26.18 | 1.38 | 1.05 | -23.76 |
| | (0.06) | (0.18) | | (1.02) | (1.90) | | (0.26) | (0.49) | |

Notes: Total variable profits, total government expenditures and total consumer expenditures are fortnightly average in million Danish krones. The results are summarized as follows: A. All products, B. Products in the same ATC code, C. Products from the same firm type, and D. Products on-patent and off-patent. Exchange rates in June 2005: DKK 1 = $ 0.1634 = €0.1343. Standard deviation in parentheses

Table 2.11: **Average Welfare Effects**

| | real | counterfactual | change | change in % |
|---|---|---|---|---|
| A. *Consumer Surplus* | | | | |
| May 2003 - Dec. 2003 | 120.32 | 56.37 | -63.95 | -53.15 |
| Jan. 2004 - Dec. 2004 | 365.55 | 188.27 | -177.28 | -48.50 |
| Jan. 2005 - Mar. 2005 | 28.95 | 16.85 | -12.11 | -41.81 |
| Yearly average | 232.35 | 119.78 | -111.41 | -49.29 |
| B. *Variable Profits* | | | | |
| May 2003 - Dec. 2003 | 21.67 | 36.50 | 14.83 | 71.44 |
| Jan. 2004 - Dec. 2004 | 47.32 | 171.68 | 124.37 | 251.41 |
| Jan. 2005 - Mar. 2005 | 6.69 | 11.15 | 4.47 | 76.08 |
| Yearly average | 38.03 | 94.54 | 56.51 | 167.50 |
| C. *Total Welfare* | | | | |
| May 2003 - Dec. 2003 | 141.99 | 92.87 | -49.11 | -34.59 |
| Jan. 2004 - Dec. 2004 | 412.87 | 359.96 | -52.91 | -12.82 |
| Jan. 2005 - Mar. 2005 | 35.64 | 28.00 | -7.64 | -21.43 |
| Yearly average | 270.38 | 214.32 | -54.90 | -20.73 |

Notes: All figures are in million Danish krones. Exchange rates in June 2005: DKK 1 = $ 0.1634 = € 0.1343. The average yearly difference in consumer surplus is -111.41 million Danish krones. The average yearly difference in variable profits is 56.51 million Danish krones

Table 2.12: **Average Yearly Expenditures**

| | real | counterfactual | change | change in % |
|---|---|---|---|---|
| A. *Government Expenditures* | | | | |
| May 2003 - Dec. 2003 | 207.23 | 330.43 | 123.20 | 62.45 |
| Jan. 2004 - Dec. 2004 | 251.24 | 507.05 | 255.81 | 101.96 |
| Jan. 2005 - Mar. 2005 | 48.27 | 68.10 | 19.83 | 41.95 |
| Yearly average | 271.51 | 454.22 | 182.71 | 80.90 |
| B. Consumers Expenditures | | | | |
| May 2003 - Dec. 2003 | 65.92 | 97.10 | 31.17 | 48.28 |
| Jan. 2004 - Dec. 2004 | 80.76 | 225.74 | 144.98 | 190.85 |
| Jan. 2005 - Mar. 2005 | 15.76 | 22.04 | 6.28 | 41.14 |
| Yearly average | 87.29 | 162.29 | 75.00 | 123.06 |

Notes: All figures are in million Danish krones. Exchange rates in June 2005: DKK 1 = $ 0.1634 = € 0.1343.

# A. From pharmacy purchase price to pharmacy retail price

| | | |
|---|---|---|
| **BEK nr. 133** | Mar. 14 2003<br>Jun. 09 2003 | From the pharmacy purchase price per package pay 60.1% of the following amounts:<br>if $p^f \leq$ DKK 30 : 60% of $p^f$ + DKK 1.80<br>if DKK 30 $< p^f \leq$ DKK 60: 40% of $p^f$ + DKK 7.80<br>if $p^f >$ DKK 60: 20% of $p^f$ + DKK 19.80<br>Prescription's fee excl. VAT: DKK 6.15. |
| **BEK nr. 368** | Jun. 09 2003<br>Mar. 26 2004 | From the pharmacy purchase price per package pay 64.1% of the following amounts:<br>if $p^f \leq$ DKK 30 : 60% of $p^f$ + DKK 1.80<br>if DKK 30 $< p^f \leq$ DKK 60: 40% of $p^f$ + DKK 7.80<br>if $p^f >$ DKK 60: 20% of $p^f$ + DKK 19.80<br>Prescription's fee excl. VAT: DKK 6.15. |
| **BEK nr. 270** | Mar. 26 2004<br>Apr. 12 2004 | From the pharmacy purchase price per package pay 61% of the following amounts:<br>if $p^f \leq$ DKK 30 : 60% of $p^f$ + DKK 1.80<br>if DKK 30 $< p^f \leq$ DKK 60: 40% of $p^f$ + DKK 7.80<br>if $p^f >$ DKK 60: 20% of $p^f$ + DKK 19.80<br>Prescription's fee excl. VAT: DKK 6.15. |
| **BEK nr. 231** | Apr. 12 2004<br>Feb. 28 2005 | From the pharmacy purchase price per package pay 64.3% of the following amounts:<br>if $p^f \leq$ DKK 30 : 60% of $p^f$ + DKK 1.80<br>if DKK 30 $< p^f \leq$ DKK 60: 40% of $p^f$ + DKK 7.80<br>if $p^f >$ DKK 60: 20% of $p^f$ + DKK 19.80<br>Prescription's fee excl. VAT: DKK 6.15. |
| **BEK nr. 123** | Feb. 28 2005<br>Apr. 01 2005 | From the pharmacy purchase price per package pay 59.4% of the following amounts:<br>if $p^f \leq$ DKK 30 : 60% of $p^f$ + DKK 1.80<br>if DKK 30 $< p^f \leq$ DKK 60: 40% of $p^f$ + DKK 7.80<br>if $p^f >$ DKK 60: 20% of $p^f$ + DKK 19.80<br>Prescription's fee excl. VAT: DKK 6.15. |
| **BEK nr. 122** | Apr. 01 2005<br>Jul. 18 2005 | From the pharmacy purchase price per package pay 59.4% of the following amounts:<br>if $p^f \leq$ DKK 30 : 44.6% of $p^f$ + DKK 8.29<br>if DKK 30 $< p^f \leq$ DKK 60: 31.3% of $p^f$ + DKK 12.29<br>if $p^f >$ DKK 60: 18% of $p^f$ + DKK 20.29<br>Prescription's fee excl. VAT: DKK 6.76. |

Notes: Using the information in the table below, the pharmacy retail price including VAT (25%) and fees for a product in the most expensive category before June 2003 is: $p^c = 1.25 * (6.15 + 0.601 * (0.2 * p^f + 19.8) + p^f)$. These rules and regulations can be found under: *www.retsinformation.dk*

# Chapter 3

# Regulation of Pharmaceutical Prices: Evidence from a Reference Price Reform in Denmark

This chapter is joint work with Ulrich Kaiser, Thomas Rønde, and Hannes Ullrich. It is a revised version of UZH Business Working Paper No. 330, Department of Business Administration, University of Zurich and it is forthcoming in *Journal of Health Economics*.

*Acknowledgements*: The authors would like to thank Friedrich Breyer, Jean-Pierre Dubé, Tomaso Duso, Werner Güth, Felix Höffler, Marc Rysman, Andrew Toole, and Peter Zweifel for helpful comments. We also benefited from comments received at the Symposium of the

German Economic Association of Business Administration in Vallendar, the Economics Seminar Ottobeuren, the European conference on Health Economics, Helsinki, the European Association for Research in Industrial Economics, Istanbul, the International Industrial Organization Conference, Boston, as well as seminar presentations in Düsseldorf, Konstanz, Mannheim and Zurich. The paper also gained greatly from extensive discussions with Kurt Brekke, Jaime Espín, Margaret Kyle, and Saul Lach. We are very much indebted to Jørgen Clausen of the Danish Association of the Pharmaceutical Industry (Lægemiddel Industri Foreningen, LIF) for data provision and data advice. Excellent medical advice was provided to us by the MDs Marit Otto, Roland Knudsen, and in particular Johannes Schmid. Financial support from the Economic Policy Research Network and the Swiss National Science Foundation (grants 100018-135257 and PBZHP1-143346) is gratefully acknowledged.

## 3.1 Introduction

A steadily growing life expectancy, aging populations, and the increasing cost of medical treatments have induced policy makers to introduce various cost containment tools. Reference pricing, where patients are reimbursed a fraction of the retail price when buying a prescription drug, constitutes a particularly widely embraced approach (Berndt and Dubois 2012; Espín et al. 2011; López-Casasnovas and Puig-Junoy 2000).

While existing studies have shown that reference pricing effectively curtails prices of prescription drugs (Aronsson et al. 2001; Brekke et al. 2009, 2011; Kanavos et al. 2008; Pavcnik 2002; Puig-Junoy 2007), a hitherto empirically unanswered issue is to what extent differences in the *design* of reference pricing systems affect market outcomes. A particularly relevant question here is whether reference prices should be determined "externally", through a basket of similar products in other countries, or "internally", through prices of similar domestic products.

We address that question by estimating the effects of a reference pricing reform in Denmark, a country that switched from external to internal reference pricing in April 2005. In Denmark, patients are reimbursed 80% of the reference price. The difference between the retail price and the reimbursement — the copayment — is paid by the consumers. Danish patients always co-pay and the reform did not change the 80% reimbursement rate.

Since the Danish reference pricing reform affected all drugs equally — original drugs (on– and off–patent), generics, and parallel imports[1] — we study to what extent these different types of products were differently affected by the reference pricing reform. We confine our analysis to statins which currently constitute the best-selling drugs in terms of sales both in Denmark and worldwide. Statins treat high levels of cholesterol and are used to decrease mortality and morbidity of patients with cardiovascular diseases.

[1]Parallel imports are drugs that parallel importers, independent commercial agents, buy in a low-price country, re-package, re-label, and distribute in a high-price country. Parallel importing is legal in the European Union.

We find that the *design* of reference price systems matters substantially for prices and demand. In particular, the switch from external to internal reference pricing reduced both retail prices, reference prices, and consumer copayments by around 22%. There are substantial differences between the three types of drugs we consider: prices fall most for generics followed by parallel imports and original drugs, where in the latter case consumer copayments actually increased. Overall producer revenue and public expenditures both decrease by around 19% while consumer expenditures decrease by 17% as a consequence of the reform.

As the first paper to apply a structural demand estimation that is based on a consumer utility function we are able to calculate a proper measure of consumer welfare changes induced by a modification of pharmaceutical pricing regulation. We estimate an annual total consumer compensating variation (the amount government would need to pay consumers for them to accept foregoing the reform) of six million Danish krones (DKK) — around one million US dollars per year. The relatively small increase in consumer welfare seems at odds with our finding of a dramatic decrease in total patient copayments. Using changes in copayments as a welfare measure alone, however, ignores that the reform makes consumers more price sensitive due to increasing copayments for the more expensive original drugs which in turn leads them to substitute away from their otherwise preferred original drugs. Such consumer welfare-decreasing substitution effects go unnoticed if total patient copayments alone are used as a welfare measure as in previous studies (e.g. Brekke et al. 2011; Granlund 2010).

The paper closest to ours is Brekke et al. (2011) who exploit a quasi-experimental transition from price cap regulation to endogenous reference pricing that affected a subset of high volume off-patent drugs in Norway in 2003. They find that the switch from price cap regulation to reference pricing significantly decreased both prices for original products and generics and that the change lead to reductions in the market shares of original products. Brekke et al. (2011) constitutes one of few papers that study both price and demand effects

of a pharmaceutical pricing reform. Their demand estimation is, however, restrictive in that it employs linear market share equations relying on the implicit assumption that all products under consideration are perfect substitutes.

We attempt to generate more flexible and hence more reliable estimates of the causal effects that the reform of Danish reference price design may have entailed on the demand for statins. The counterfactual experiment we conduct is to ask what the reform effects would have been had it occurred in the period before it was actually put in place. The advantage of this strategy is that we can effectively "filter out" factors other than the reform that may have simultaneously affected pharmaceutical market outcomes. Specifically, we first estimate a flexible logit-type demand model (Berry 1994; Berry et al. 1995) that allows for both horizontal and vertical product differentiation as well as for arbitrary substitution patterns between products by allowing for consumer-specific heterogeneity in drug demand. Second, we estimate pricing equations to predict the counterfactual prices of drugs had the reform taken place before it actually did. Finally, we use our estimated pricing and structural demand parameters to compute counterfactual demand which allows us to calculate total changes in demand, consumer expenditures, producer revenues as well as consumer welfare.

The paper proceeds as follows: Section 3.2 offers an overview of the Danish pharmaceutical market and the institutional settings of the reference price reform, Section 4.3 describes our data set, Section 3.4 presents the empirical strategy, Section 4.5 provides our estimation results, and Section 4.6 concludes.

## 3.2 The Danish market for pharmaceutical products

As in other European countries, the market for pharmaceutical products in Denmark is regulated. Denmark follows EU regulations regarding product authorization. Product pricing, reimbursement rules, and the regulation of pharmacies are national matters.

The pricing of pharmaceutical products in Denmark is free.[2] Changes in pharmacy purchase prices are notified to and evaluated by the Danish Medicines Agency (DKMA). The agency updates prices every 14 days and makes them publicly available online. Prices are identical nationwide.

In Denmark, pharmacists must first offer the patient the cheapest product within a group of substitutes unless the prescription explicitly requires no substitution, which is the case for just five percent of all prescriptions. The patient may then decide herself whether or not she buys the cheapest product or a substitute at a higher price and a higher copayment. Other relevant market features are that (i) Denmark maintains a universal health care system that is financed through general tax revenues, (ii) that advertising prescription drugs to patients is prohibited and (iii) that detailing is regulated. Detailing it is mainly used for new products and not for established drugs, such as the ones in our analysis.

The reform that this paper investigates involves the change in the way reference prices are calculated. On April 1, 2005, Denmark changed from external to internal reference pricing for all prescription-only pharmaceuticals independent of their patent status. The classification of products into substitution groups remained unchanged. In Denmark, patients may only substitute among products with the same active substance, administration form, strength, and similar package size, where package size may not vary by more than ten percent within substitution groups.

Before the reform reference prices were based on average prices in the EU-15 member states, excluding Greece, Luxembourg, Spain, and Portugal. The reference price for a given product was the lowest cross-state average price among products belonging to the same substitution group. However, if a product's retail price was below the EU average, the reference price was set equal to the retail price. After the reform, the reference price

[2]There exists one fairly loose restriction, however, by that drugs for which an analogous product exists cannot be reimbursed if its price is more than 20 per cent higher than the price of the analogous drug.

was set equal to the lowest domestic retail price out of all products belonging to the same substitution group.

Around the time of the reform there were other events happening that might have influenced the behavior of the market participants. We grouped these events and divided our observed data into six different periods, which are summarized in Appendix A. Our main relevant dates were set by the Danish government. In May 2004, the Danish parliament ratified the new reimbursement law making it public in June 2004. On April 1, 2005, the law was implemented. However, it is likely that information regarding changes in reimbursement rules had been at the disposal of market participants prior to these two legislatively determined dates. On September 17, 2003, the Danish Minister of Health announced the assembly of a group of experts with the aim of changing the existing reimbursement system to strengthen competition. Moreover, as a member of the working group, the Danish Association of the Pharmaceutical Industry (Lægemiddel Industri Foreningen, LIF) launched the idea of changing the way reference prices are calculated, as was eventually adopted in April 2005. Between May 2001 and April 2003, LIF maintained a voluntarily agreement on price ceilings. However, not all members complied with the agreement. After its expiration in 2003, LIF announced a continuation of the price ceiling for another two years. This was a unilateral announcement on the side of LIF rather than an official agreement with the Danish Ministry of Health.[3] Finally, the Danish Ministry of Health and LIF again signed an agreement on a price ceiling in October 2006.

Our analysis focuses on the base period (May 03, 2001 until April 14, 2003) and the implementation period (April 01, 2005 to September 25, 2006). Our base period is the

[3]Notwithstanding, we cannot exclude the possibility that the LIF announcement allowed producers in the market to coordinate on higher prices levels (Knittel and Stango 2003). However, uncertainty regarding the credibility of the LIF announcement, as well as the volatile market structure following the patent expiration of a popular product, *Zocor*, in 2001, suggest that price coordination was difficult to sustain. For this reason, we interpret the price development as being the result of the announced reform, but we are not able to separate the effects of the reform from the possible effects of the LIF announcement.

time between the working group assembly and the ratification in parliament. It serves as a base because no reliable information about prospective changes in the reimbursement system was publicly or privately available and because the number of firms as well as prices remained stable. Our treatment period covers the actual implementation of the reform. We discard the two LIF agreement periods as well as the adjustment period after the expiration of the first LIF agreement to avoid including effects other than the actual reform. We also discard the announcement period because firms were informed about the new legislation which allowed them to prepare for a new competitive setting.

## 3.3 Data

Our data set contains fortnightly prices and sales of statins for the period between February 2003 and June 2006. We downloaded the publicly available price data from http://*www.medicinpriser.dk*. The sales data are proprietary and were made available to us by LIF. They come with the same periodicity as the price data.

The site http://*www.medicinpriser.dk* contains a list of all authorized pharmaceutical products marketed in Denmark. Prices are updated every second Monday based on changes reported by producers during the last two weeks. The data base is used by general practitioners when issuing prescriptions, by hospitals for their electronic patient records, and by pharmacies to ensure nationally uniform prices for prescription drugs.

A pharmaceutical product is characterized by its name, package size, form of administration, strength, 5-level anatomical therapeutic chemical classification code (ATC code), and producer name. The ATC code is a combination of letters and digits that precisely

describes a product's active substance.

Appendix B contains a characterization of statins in terms of their ATC code. Statins are divided into eight different ATC classes, of which six are marketed in Denmark. Three of them (Simvastatin, Lovastatin, and Pravastatin) lost patent protection before our data set starts which induced generic entry to the market. Fluvastatin lost patent protection by the end of 2003 and the remaining two molecules, Atorvastatin and Rosuvastatin, are on-patent during the whole period we analyze. The post-reform reference price for these two on-patent drugs is then determined by parallel imports.[4]

Medical practitioners in Denmark tend to regard all statins as close substitutes, at least with respect to their effects on cholesterol levels and slightly less so with respect to their resorption. When treating a patient, they follow the recommendations issued by the Institut for Rational Farmakoterapi (IRF, an institution under the Danish Medicines Agency that seeks to promote the most rational use of medical products) and simultaneously choose the active ingredient and dosage. It is not clear a priori if and to what extent Danish medical doctors and patients are price sensitive. IRF does, however, issue recommendations to substitute one product by another if (i) it has been demonstrated in clinical studies that the effects are identical, and (ii) one of the products is substantially cheaper than the other.

Table 3.1 presents a descriptive overview of prices and sales of statins. To make the different strengths, package sizes, and active ingredients comparable we converted prices and quantities into Defined Daily Dosages (DDD).[5]

[4]Although parallel importing of generics is possible, most parallel imports in our data are original products.

[5]We cannot exclude that our DDD normalization suppresses potential non-linearities in pricing. It is unclear,, however, how that would affect our analysis. In addition, such a problem would only materialize

Prices are in Danish crowns (DKK) and are deflated using the consumer price index with the year 2005 as the basis. The average retail price of statins is DKK 7.8 per DDD across all periods and products. Average reference prices are DKK 6.1 and consumer copayments are DKK 2.9. These prices differ substantially across the three different types of drugs. original products are most expensive with an average retail price of DKK 12.2. Generics are cheapest and cost on average DKK 3.6, while parallel imported drugs cost on average DKK 11.

All prices decreased from the base to the implementation period on average. This decrease was stronger for retail prices than for copayments. The decline in retail prices from the base to the implementation period is smaller for original drugs than for generics or parallel imports. Copayments even increased for original drugs, on average from DKK 4.6 to DKK 5.8 per DDD.

Sales are on average highest for generics, followed by original products and parallel imports. From the base to implementation period, sales for generics and parallel imports increased on average and decreased for original products.

Appendix C summarizes other market and product characteristics such as the number of products on the market, the number of firms active in the market, average package size, and average strength. It shows that half of the products are generics and that there are more producers of generics than original firms or parallel importers. We observe an increase in the number of generic products from the base to implementation period (from 54.5 to 70.3 on average) and a decrease in the number of original and parallel imported products.

if pricing strategies changed with the reform, an issue for which we do not find any evidence. Moreover, any time-invariant differences in pricing strategies will be accounted for by our product fixed effects.

The products we consider are all pills, coated pills or capsules. The median package size is 98 pills, and the median strength is 20 milligram of active substance per pill. These characteristics do not vary much between the base and the implementation period.

## 3.4 Empirical strategy

Our empirical strategy to identify the effects of the reimbursement reform on prices and demand proceeds in three steps. We first estimate a structural demand model that maps observed and unobserved product and consumer characteristics to product sales. Second, we estimate a reduced-form pricing equation that studies to what extent prices changed due to the reform. This estimation generates the prices that would have been observed had the reform taken place in the base period already. Third, we use our estimated counterfactual prices and plug them into our demand model for the base period, the period before the reform. This generates counterfactual demand for the base period given our predicted counterfactual prices for the base period. The reform effects are identified by comparing these counterfactuals with observed base period market outcomes.

### 3.4.1 Demand Model

Lipid Modifying Agents (LMA), as many other drugs, are both vertically and horizontally differentiated products. In our model, we account for vertical differentiation by including product brand names and package size as observable characteristics. An idiosyncratic error term allows for horizontal differentiation.

To estimate the demand for statins we employ a random coefficients logit model due to

Berry et al. (1995). This model assumes that in every time period each individual consumer $i$ chooses product $j$ that maximizes her utility.[6] Omitting the time index $t$ for notational convenience, her utility function is:

$$U_{ij} = \delta_j + \sigma_p p_j^{cop} \nu_{ij} + \varepsilon_{ij}, \tag{3.1}$$

where all consumers obtain mean utility $\delta_j$, which is common to all consumers and individual-specific utility $\sigma_p p_j^{cop} \nu_i + \varepsilon_{ij}$. The term $p_j^{cop}$ denotes patient copayment. Importantly, we allow for variation of consumer preferences for price in the population by including the term $\sigma_p p_j^{cop} \nu_i$. Own-price and cross-price elasticities may hence vary across individuals which generates much more plausible price elasticity estimates compared to the computationally less burdensome simple logit and nested logit models for differentiated products demand (Berry et al. 1995). To identify consumer preferences regarding price, we assume $\nu_{ij}$ to be drawn from a standard normal distribution with standard deviation $\sigma_p$, a parameter that is to be estimated. If $\sigma_p$ is insignificantly different from zero, the model collapses into the simple logit model (Berry 1994). The idiosyncratic random error term $\varepsilon_{ij}$ is assumed to be i.i.d. Gumbel distributed.

We decompose mean utility into

$$\delta_j = \boldsymbol{x_j}\boldsymbol{\beta} - \alpha p_j^{cop} + \xi_j, \tag{3.2}$$

where $\boldsymbol{x_j}$ denotes a vector of observed product characteristics and $\xi_j$ is an unobservable

[6] Due to the aggregate nature of our product-level data, we assume that the consumer entity is a joint physician-patient unit and, consequently, abstract from possible agency problems. The assumption holds if physicians act in the interest of their individual patients. See Dunn (2012) for a recent example using a similar assumption in modeling demand for statins.

product characteristic.[7]

Vector $\boldsymbol{x_j}$ includes sets of dummy variables for product names, strength of the active ingredient, and package size. These three characteristics implicitly define substitution groups which are set by the regulator and hence impose a soft restriction on the choice set. We further include monthly dummy variables to control for seasonal variation as discussed by Ockene et al. (2004) and Tung et al. (2009) as well as time period dummies.

The assumption that consumers are utility-maximizers combined with the assumption that $\varepsilon_{ij}$ is i.i.d. Gumbel distributed leads to the following market share equation (Berry 1994):

$$s_j(\boldsymbol{x_i}; \boldsymbol{\theta}) = \int_\nu \frac{exp(\delta_j + \sigma_p p_j^{cop} \nu_i)}{1 + \sum_J exp(\delta_j + \sigma_p p_j^{cop} \nu_i)} dF_\nu(\nu), \tag{3.3}$$

where vector $\boldsymbol{\theta}$ contains the coefficient vector $\boldsymbol{\beta}$, identical for all individuals, and parameter $\sigma_p$.

To close the model, we need to define potential market size and implicitly the share of outside good $j = 0$. Consumption of the outside good provides consumers with a mean utility that we normalize to 0 ($\delta_0 = 0$). In our setting, the composite outside good consists of products that are not statins and that may reduce cholesterol level including, for example, non-statin LMAs, homeopathic products, a bicycle, or a pair of running shoes.

The price of our outside good is not set in response to the prices of the inside goods, the statins. We define total market size as the amount of DDDs sold if all *potential* patients had received statins as medication. We infer the number of potential patients based on a claim by the Danish Association of Heart Patients (Hjerteforeningen, 2007) that 60% of all

[7]Note that the mapping between the copayment and consumer utility follows from the combination of the mean, $p_j^{cop}\alpha$, and individual-specific utility terms, $p_j^{cop}\sigma_p\nu_{ij}$: $p_j^{cop}(\sigma_p\nu_{ij} - \alpha)$.

Danish residents between ages of 40 and 80 years have an elevated cholesterol level. At a total Danish population of 5.5 million this fraction matches well with IRF's (IRF, 2006) estimate that 2.1 million Danish residents above the age of 35 have a total cholesterol level of more than 5 mmol/l, the critical threshold above which treatment with statins is started. As we base our estimates on DDD, a daily per-patient unit, the potential market size can be computed simply as 60% of all Danish residents between the ages of 40 and 80. We employ this broad market definition to provide conservative demand estimates. Decreasing potential market size, for example, by assuming a lower fraction of people with elevated cholesterol levels, increases absolute elasticities of substitution.

The term $\xi_j$ is unobserved by the econometrician but observed by both consumers and producers. In our setting, we think of this characteristic as quality perception in the market which might deviate from the time-invariant mean product name effect we explicitly control for. This quality perception may vary over time and can be influenced by changes in consumer information through channels such as producer publicity, post-entry clinical testing, and population product experience. Profit-maximizing producers will adjust prices to changes in $\xi_j$ which leads to omitted variable bias in the estimated price coefficient. We address the resulting endogeneity problem by employing a set of instruments and estimating the model using GMM. Following Dubé et al. (2012) we write the objective function as a constrained optimization problem for numerical robustness:

$$\begin{aligned} \min_{\boldsymbol{\theta}, \boldsymbol{x_j}} \quad & \boldsymbol{x_j}' \boldsymbol{Z} \boldsymbol{W} \boldsymbol{Z}' \boldsymbol{x_j} \\ & \text{subject to } s(\boldsymbol{x_j}; \boldsymbol{\theta}) = \boldsymbol{S}, \end{aligned} \tag{3.4}$$

where the vector $\boldsymbol{Z}$ denotes a set of optimal instrumental variables, the vector $\boldsymbol{W}$ denotes a weighting matrix, and $\boldsymbol{S}$ are the observed market shares. In the construction of the vec-

tor of optimal instruments, which closely follows Reynaert and Verboven (2012), we rely on identification arguments in Berry et al. (1995) who include variables containing information about the competitive environment. These covariates, termed "BLP instruments" hereafter, are the sums of other firms' products' characteristics (package size and strength of active ingredient) as well as the number of competitors in the market and in the relevant substitution groups. A detailed description of the identification and estimation of our model is relegated to Appendix D.

With a fully specified demand model and counterfactual prices at hand we can compute a simple monetary measure of reform effects on consumer utility, the Hicksian compensating variation. Formally, we obtain consumer compensation variation measure by solving the integral over the differences in maximum expected utilities via numerical simulation (see Small and Rosen, 1981):

$$CV = \int \frac{1}{\alpha + \nu_i} \left\{ \ln \sum_j \exp\left(\delta_j^{pre} + \sigma_p p_j^{c,pre} \nu_i\right) - \ln \sum_j \exp\left(\delta_j^{post} + \sigma_p p_j^{c,post} \nu_i\right) \right\} f\left(\boldsymbol{\nu} \mid \theta^{pre}\right) d(\boldsymbol{\nu}) \tag{3.5}$$

We will use the parameters of our demand model to predict counterfactual demand (superscript "post") for statins based on the counterfactual prices whose estimation we discuss in the subsequent paragraph.

### 3.4.2 Reduced-form Price Equation

The idea behind our pricing regression is to infer price changes due to the reform by regressing actual retail prices on a large set of control variables, fixed effects, and a set of dummy variables for the reform. This allows us to calculate the prices that would have been observed had the reform happened in the base period.

We could in principle also compare prices in the base and the reform period to infer what products would have cost in the absence of the reform. That would, however, imply to discard products that were unavailable either in the base or in the reform period. It would also imply forgoing to control for confounding factors such as the competitive environment in the counterfactual reform, the base period.

To identify our pricing equation we exploit the panel structure of our data. In particular, we rely on within-variation for identification by using time-invariant product name fixed effects. These fixed effects also capture important product-level market characteristics such as the time a product has been on the market. In addition, we control for seasonal within-year trends using month fixed effects and for time-invariant cost of active ingredient strength and package size by including substitution fixed effects as well as pulp and paper prices. Pulp and paper prices are input prices and affect prices but not the unobserved quality $\xi_j$. In addition, we include the set of BLP instruments discussed in Subsection 3.4.1.

We interact the reform dummy with dummy variables for the type of product, namely if it is an original product, generic, or parallel imported drug. While Pavcnik (2002), Granlund (2010), and Brekke et al. (2009, 2011) find strongest price decreases for original products, some earlier studies provide evidence for non-decreasing prices for original products that goes along with increased competition (Frank and Salkever, 1997, Grabowski and Vernon, 1992, Regan, 2008). This has been labeled the "generic competition paradox" (Scherer, 1993). The intuition here is that original products may themselves differentiate even further and only target low-elasticity consumers to avoid facing tougher competition.

While many studies explore the link between reference pricing and competition between

original products and generics, we are able to identify and differentiate a third group, parallel imports. The efficacy of parallel importing as a tool to improve price competition has been a highly debated topic.

We consider retail prices as the relevant price outcome as these are the prices producers set. They mechanically define copayments and reference prices after the reform. We use the linear panel specification

$$\ln p_{jt} = \gamma_1 D_t + \gamma_2 D_t * \mu_b + \gamma_3 D_t * \mu_{PI} + \mu_j + \mu_m + \mu_s + \gamma_4 N_t + \gamma_5 N_{st} + \boldsymbol{z_{jt}\gamma} + \varepsilon_{jt}, \quad (3.6)$$

where the dependent variable is the log retail price per DDD of product $j$ at time $t$. $D_t$ equals one in the implementation period and zero in the base period. Further indicator variables are denoted by $\mu$, where subscript $b$ indexes original products (brand), $PI$ parallel imports, $j$ products, $m$ months, and $s$ substitution groups. The specification also controls for the number of products in the market, $N_t$, the number of products in product $j$'s substitution group, $N_{st}$, the set of BLP instruments, and production cost factors. The latter variables are stacked in vector $\boldsymbol{z_{jt}}$. The term $\varepsilon_{jt}$ denotes an idiosyncratic shock.

From our estimation of Equation (3.6) we calculate counterfactual product prices in the base period, period $BP$:

$$\hat{p}_{jBP} = exp(\hat{\gamma}_1 + \hat{\gamma}_2 * \hat{\mu}_b + \hat{\gamma}_3 * \hat{\mu}_{PI} + \hat{\mu}_j + \hat{\mu}_m + \hat{\mu}_s + \hat{\gamma}_4 N_{BP} + \hat{\gamma}_5 N_{sBP} + \boldsymbol{z_{jBP}\hat{\gamma}}). \quad (3.7)$$

## 3.5 Estimation results

Our estimation results fall in three parts. We first discuss our demand model, proceed with our price estimations, and finally evaluate the reform effects on prices, demand, and consumer surplus.

### 3.5.1 Demand Parameters

Table 3.2 reports the estimated coefficients and the implied price elasticities with respect to consumer copayment for three alternative specifications of our demand model. The left columns present OLS logit results where we assume that consumers have homogeneous preferences with respect to patient copayment ($\sigma_p = 0$) and that prices are exogenous to demand. The middle columns show IV logit results where we instrument prices. The right column displays random coefficients logit model results, our main and preferred specification.

We estimate a negative and significant copayment coefficient in the OLS Logit model and a mean own-price elasticity of -.22. We refer to Berry (1994) for a derivation of the price elasticities for our three models. While low in absolute terms, this simple model obtains the correct negative sign for the copayment coefficient. Once we instrument prices, identification of the copayment improves, as measured in terms of $t$-values, substantially and the coefficient more than doubles as opposed to the non-instrumented estimates. The corresponding mean own-price elasticity is -.59. We report our first stage regression results, our regression of our endogenous variable retail price on the instruments and the exogenous variables, in Appendix E. The tests for joint instrument significance are all substantially above the critical value of ten that Stock et al. (2002) suggest.

As we have little reason to believe that all individuals in Denmark are equally sensitive to price changes, we drop the assumption that $\sigma_p = 0$ in the RC Logit model. This full model reveals significantly more price elastic demand with a mean estimate of -1.54 and a corresponding standard deviation of .54. The implied mean elasticities are double the IV Logit ones.

Our specification does not include a single dummy for original products. We include a set of 42 product name dummies instead, the corresponding coefficient estimates are, however, not displayed for brevity. Averaging over these brand name dummies for original products, parallel imports, and generics shows that the coefficients related to original products are four times larger than for the other two drugs types, whose coefficients on name dummies are fairly similar.

Our estimates suggest that consumers are more price elastic than what is found in most of the existing literature on pharmaceuticals demand (Gemmill et al. 2007, for a survey). This is not surprising as an external reference price mechanism was in place in Denmark before the reform. Even with external reference prices, consumers were faced with the choice between buying either cheaper generics and parallel imported drugs or the more expensive original products and, hence, they were more price-sensitive than in markets with little copayment.

In all three models, the coefficient estimates on month indicator variables are in line with first evidence by Ockene et al. (2004) and Tung et al. (2009), who find that lipid levels are low in the summer and high in the winter. The corresponding coefficient estimates are not displayed in the table for brevity.

### 3.5.2 Prices

Our next step is to calculate the change in prices the reform induced. We run a total of six alternative pricing regressions. Table 3.3 presents the coefficient estimates in the order of increasing numbers of control variables. We shall use the full specification, depicted in column (6), to compute all reform effects in the following subsections. The estimation

sample contains observations on all products on the market in the base period and the implementation period. To take into account potential serial correlation we compute standard errors that are robust to autocorrelation and heteroskedasticity and clustered at the product level.

In all specifications, we obtain a negative average effect of the reform on retail prices. Specification (6) implies that, on average, the reform decreases prices for generics by 35.8%, original products prices by 7.3%, and parallel import prices by 18.7%.[8] Specification (5) excludes only the original product and parallel import interaction terms. It estimates the reform effect on retail prices over all types of products at -21.4%.

Specification (1) comes with a minimum of control variables and significantly overestimates the average reform effect with -40.6%. Adding BLP instruments as basic controls for the competitive environment in specification (2) reduces the bias to some extent. Both coefficients of the numbers of products in the market and in substitution groups as a further competition control variable in specification (3) are significant and negative, as expected based on standard oligopoly theory. Here, the estimated reform effect doubles to -78.8% which is a sign for substitution group specific effects of the reform on product entry and exit, i.e. selective entry and exit. Including these continuous control variables, however, we cannot discriminate between changes and time-invariant levels in the numbers of products in substitution groups. Therefore, we include further substitution group fixed effects in specification (4). The latter almost nullify the estimates of $\gamma_4$ and $\gamma_5$ in specification (3) and the bias of the reform effect estimate is further reduced. Finally, in specifications (5)

[8]We use a log-linear specification with dummy explanatory variable $D_t$ and so the percentage effect of the reform on retail prices is defined as $\exp\left(\hat{\gamma}_1 - \frac{1}{2}V(\hat{\gamma}_1) - 1\right) \times 100$ (see Kennedy, 1981).

and (6), we add an input cost index (pulp and paper) and product name fixed effects to control for time-invariant levels of product quality. The latter should alleviate concerns that selection may confound our estimates of the reform effect.

Our results can be explained by the mechanisms similar to the ones suggested by Brekke et al. (2011). The Danish reform strengthened firms incentives to decrease prices by giving price setters the possibility to influence the market reference price. As the Danish reform entailed a change within an existing reference price system, the size of its impact on retail prices and consumer copayments had been an open empirical question. Our results provide a first attempt to quantify these effects.

### 3.5.3 Reform Effects on Prices, Demand, and Consumer Surplus

Our demand estimates and our estimates for counterfactual prices form the backbone of our calculation of counterfactual demand and consumer surplus. The flexibility of our demand model allows us to take into account consumers' substitution behavior caused by our estimated retail price changes from which we infer the induced reference price changes and patient copayments.

Recall that, after the reform, the reference price is defined by the lowest price in a given substitution group. A strong price decrease for low-price generics paired with a weaker price decrease for high-price original products will lead to an increase in consumer copayment for original products. Hence, we expect the reform to be highly effective in pushing consumers to substitute away from original products towards generics and parallel imports.

Table 3.4 reports absolute and percentage differences between our observed market outcomes in the base period and our predicted counterfactual market outcomes had the reform

already been implemented in the base period. It shows that overall retail prices decrease by 21.9%, where the largest decrease is accounted for by generics with 46.4%. retail prices for parallel imports decrease significantly less with 22.1% but, most remarkably, pharmacy retail prices for original products decrease only by 7.2%. While the latter finding falls short of the generic competition paradox whereby increased competition causes increasing prices of original products (Frank and Salkever, 1997; Grabowski and Vernon, 1992; Regan, 2008), our results run counter to the findings of Pavcnik (2002) and Brekke et al. (2009, 2011) who find a stronger decrease in retail prices for original products products. We should keep in mind, however, that the Danish reform has not been a full switch to reference pricing but only a change in the design of an existing reference price system.

Copayments decrease significantly both for generics and parallel imports while they increase for original products. As the final purchase decision is with the consumer facing copayments, these predicted effects should induce a significant shift in demand away from original products. This mechanism helps reducing expenditures even if pharmacy retail prices for original products do not decrease significantly after the reform. Consumers substitute towards generics that witnessed large price decreases from consistently more expensive original products. This asymmetric change in copayments is due to the asymmetric changes in retail prices but comparably uniform changes in reference prices across drug types. The quite uniform reference price changes are due to the fact that, in the market for statins, most substitution groups include both original products and generic products.

Indeed, we find that the demand for generics increases by 30% and for parallel imports by 28.4%. Demand for original products decreases by 26.1%. These results are in

line with Brekke et al. (2011) and demonstrate the power of a market-based competition-strengthening mechanism in inducing consumer switching to cheaper products.

Overall government and consumer expenditures decrease by 18.8% and 17%, respectively. Producers obtain 19.5% less revenue. The largest loss in revenues of 29.2% is incurred by original firms. As the revenues for parallel imports increase by 14.1%, the reform has had a beneficial impact for parallel importers.

The significant decrease in consumer expenditures can be explained mostly by consumers' switching from original products to generics and parallel imports. In addition, the population of potential consumers experienced a utility gain of DKK 6,142,571 ($ 1,013,524) per year. Given that the reform entailed a substantial total copayment decrease for generic drugs and parallel imports, this may seem surprising. However, the reform led to copayment increases for original products drugs which forced consumers to substitute away from original products, for which they have strong preferences as indicated by the large coefficients on the name dummies for original products, towards generics and parallel imports. Our finding of relatively small changes in consumer welfare shows that using consumer expenditures, as in Brekke et al. (2011) or Granlund (2010), as a proxy for patient welfare may lead to an overestimation of the reform effects. Patient expenditures do, however, not account for welfare losses due to substitution away from an otherwise preferred product.

We hence find that the Danish pricing reform has been largely successful in decreasing public expenditures and consumer expenditures. It also incentivized consumers to switch to generics or parallel imports. While significant utility gains are realized on the national level, patient welfare gains are low. Producers of original products incur substantial revenue losses. We approximate the associated loss in *total* welfare by the sum of the compensating

variation and changes in producer revenue as DKK 56,473,530 ($ 9,318,132).

## 3.6 Conclusions

Reference pricing constitutes a widely adopted cost containment tool used by governments to curb expenditures for pharmaceuticals. While it is well documented that reference pricing drives down pharmaceutical prices, little is known about the design of such systems.

This paper demonstrated that the design of reference price systems may substantially impact market outcomes. It analyzed the extent to which a switch from external reference pricing, where reference prices are determined based on prices of similar products in other countries, to internal reference pricing, where the price of the cheapest domestic substitute constitutes the reference price, matters for prices and demand.

We used product-level data to study the effects of a reference pricing reform in Denmark in April 2005 when the country substituted external for internal reference pricing. This reform affected all prescription drugs independent of patent status. The focus of our analysis were statins which constitute blockbuster drugs both in Denmark and worldwide.

Our analysis showed that retail prices, reference prices, and consumer copayments all decrease by around 22% due to the switch to internal reference pricing. These changes are quite unevenly distributed across different types of drugs. Prices decreased most substantially for generics where consumer copayments declined by as much as 56%. Prices for parallel imported drugs also decreased significantly while prices for original products changed comparatively little. Consumer copayments for original products increased by seven percent — a result which can be explained by a more pronounced decrease in refer-

ence prices relative to retail prices for this type of drugs.

We used these predicted reform-induced changes in prices to analyze changes in drug demand caused by the reform. To this end we derived a structural model of the demand for statins that allowed us to predict counterfactual drug demand and to calculate consumer welfare effects due to the reform.

Our estimates indicate an overall increase in statins demand associated with the reform. These demand changes were again unevenly distributed across alternative drug types. Demand increased most for generic drugs, by 27%. Parallel imported drugs encountered a similarly large increase while the demand for original products decreased by 26%. The switch to internal reference pricing hence induced patients to substitute towards generic and parallel imported drugs.

Combining price and demand effects we estimated an overall average decrease in producer revenue by 19%, a decrease in health care expenditures by 19%, and a decrease in consumer expenditures by 17%. Parallel importers benefited most from the reform. Their overall revenues increased by 14% which reflects the relatively small decrease in prices combined with a relatively large increase in demand. The revenues of generic producers decrease slightly by nine percent while those of original products decreased by as much as 29%.

We also found that health care expenditures decreased by 20% for generics and by 27% for original products while they increased by 12% for parallel imported products. These results indicate that the reduction in reference prices, which constitutes a key determinant of pharmaceutical cost reimbursement, compensates the associated increase in demand. We come to an opposite conclusion for parallel imported drugs while the reduction in health

expenditures for original products follows directly from falling prices and demand.

Consumer expenditures also decreased as a consequence of the reform, by 17% on average. This reduction is primarily driven by the massive decrease in consumer expenditures for original products (35%). Consumer expenditures increased, however, by a quarter for generic drugs and by 22% for parallel imported drugs. In both cases, an increase in demand for the respective type of drugs over-compensates the reform-associated reductions in reference prices.

Our structural estimation of drug demand allows us to calculate consumers' compensating variation, our measure of consumer welfare. It represents the amount patients would need to be compensated for to maintain their level of utility after foregoing the reform. Our estimate for the compensating variation is six million DKK (one million USD) per year. This may seem small given the comparatively large reductions in consumer expenditures, but approximating consumer welfare by patient expenditures ignores welfare losses induced by substitution from a preferred product (original products) to cheaper alternatives (generics and parallel imports).

The key result of our analysis is that not only the introduction of reference pricing as such — as shown by previous empirical studies such as Brekke et al. (2011) — may have dramatic consequences for market outcomes but that the *design* of reference pricing systems may also have substantial impacts on producers, patients, and government health care expenditures. In particular, our paper shows that a switch from external to internal reference pricing may effectively stimulate substitution away from original products and reduce health care expenditures. It may, however, not lead to a substantial increase in consumer surplus.

While the present paper confined itself to the analysis of a chronic disease, future research will extent the analysis to an acute treatment like an infectious disease. We speculate that the reform effects may be considerably smaller for an acute treatment since patients may be substantially less price elastic.

Furthermore, adverse regulatory impacts on producers' static profits may lead to dynamic firm reactions, for example a reduction of research and development expenditures. Innovation is an important driver of consumer welfare in pharmaceutical markets. While beyond the scope of this paper, investigating the trade-off between static and dynamic objectives in regulatory policies for research-intensive industries is an important research agenda.

# References


Aronsson, Thomas, Bergman, Mats A. and Niklas Rudholm (2001), The Impact of Generic Drug Competition on Brand Name Market Shares – Evidence from Micro Data, *Review of Industrial Organization*, 19 (4), 423-433.

Berndt, Ernst and Pierre Dubois (2012), Impacts of Patent Expiry and Regulatory Policies on Daily Cost of Pharmaceutical Treatments: OECD Countries, 2004-2010, IDEI Working Paper 702.

Berry, Steven T. (1994), Estimating Discrete-Choice Models of Product Differentiation, *The RAND Journal of Economics*, 25 (2), 242-262.

Berry, Steven T., Levinsohn, James, and Ariel Pakes (1995), Automobile Prices in Market Equilibrium, *Econometrica*, 63 (4), 841-890.

Berry, Steven T., Levinsohn, James, and Ariel Pakes (1999), Voluntary Export Restraints on Automobiles: Evaluating a Trade Policy, *American Economic Review*, 89 (3), 400-430.

Brekke, Kurt R., Grasdal, Astrid L., and Tor H. Holmås (2009), Regulation and Pricing of Pharmaceuticals: Reference Pricing or Price Cap Regulation, *European Economic Review*, 53 (2), 170-185.

Brekke, Kurt R., Holmås, Tor H., and Odd Rune Straume (2011), Reference Pricing, Competition, and Pharmaceutical Expenditures: Theory and Evidence from a Natural Experiment, *Journal of Public Economics*, 95 (7-8), 624-638.

Bresnahan, Timothy F. (1987), Competition and Collusion in the American Automobile Industry: The 1955 Price War, *Journal of Industrial Economics*, 35 (4), 457-482.

Chamberlain, Gary (1987), Asymptotic Efficiency in Estimation with Conditional Moment Restrictions, *Journal of Econometrics*, 34 (3), 305-334.

Dubé, Jean-Pierre, Fox, Jeremy T., and Che-Lin Su (2012), Improving the Numerical Performance of Static and Dynamic Aggregate Discrete Choice Random Coefficients Demand Estimation, *Econometrica*, 80 (5), 2231-2267.

Dunn, Abe (2012), Drug Innovations and Welfare Measures Computed from Market Demand: The Case of Anti-Cholesterol Drugs, *American Economic Journal: Applied Economics*, 4 (3), 167-189.

Espín, Jaime, Rovira, Joan, and Antonio Olry de Labry (2011), WHO/HAI Project on Medicine Prices and Availability, Review Series on Pharmaceutical Pricing Policies and Interventions, Working Paper 1: External Reference Pricing;
URL: http://www.haiweb.org/medicineprices/24072012/ERPfinalMay2011.pdf

Frank, Richard G. and David S. Salkever (1997), Generic Entry and the Pricing of Pharmaceuticals, *Journal of Economics and Management Strategy*, 6 (1), 75-90.

Gemmill, Marin C., Costa-Font, Joan, and Alistair Mcguire (2007), In Search of a Corrected Prescription Drug Elasticity Estimate: A Meta-regression Approach, *Health Economics*, 16, 627-643.

Goeree, Michelle S. (2008), Limited Information and Advertising in the U.S. Personal Computer Industry, *Econometrica*, 76 (5), 1017-1074.

Grabowski, Henry G. and John M. Vernon (1992), Brand Loyalty, Entry, and Price Competition in Pharmaceuticals after the 1984 Drug Act, *Journal of Law and Economics*, 35, 331-350.

Granlund, David (2010), Price and Welfare Effects of a Pharmaceutical Substitution Reform, *Journal of Health Economics*, 29 (6), 856-865.

Hess, Stephane, Train, Kenneth E., and John W. Polak (2006), On the Use of a Modified Latin Hypercube Sampling (MLHS) Method in the Estimation of a Mixed Logit Model for Vehicle Choice, *Transportation Research: Part B*, 40 (2), 147-163.

Hjerteforeningen (2007), Danskerne har for højt kolesteroltal; http://www.hjerteforeningen.dk/sw19716.asp

Institut for Rationel Farmakoterapi (2006), Lipidsænkende behandling, http://www.irf.dk/dk/publikationer/rationel_farmakoterapi/maanedsblad/2006/lipidsaenkende_behandling.htm

Kanavos, Panos, Costa-Font, Joan, and Elizabeth Seeley (2008), Competition in Off-Patent Drug Markets: Issues, Regulation and Evidence, *Economic Policy*, 23 (55), 499-544.

Kennedy, Peter E. (1981), Estimation with Correctly Interpreted Dummy Variables in Semilogarithmic Equations, *American Economic Review*, 71 (4), 801.

Knittel, Christopher R. and Victor Stango (2003), Price Ceilings as Focal Points for Tacit Collusion: Evidence from Credit Cards, *American Economic Review*, 93 (5), 1703-1729.

Knittel, Christopher R. and Konstantinos Metaxoglou (2012), Estimation of Random Coefficient Demand Models: Two Empiricists' Perspective, Working paper.

López-Casasnovas, Guillem and Jaume Puig-Junoy (2000), Review of the Literature on Reference Pricing, Universitat Pompeu Fabra, mimeo.

Ockene, Ira S., David E. Chiriboga, Edward J. Stanek III, Morton G. Harmatz, Robert Nicolosi, Gordon Saperia, Arnold D. Well, Patty Freedson, Philip A. Merriam, George Reed, Yunsheng Ma, Charles E. Matthews, and James R. Hebert (2004), Seasonal Variation in Serum Cholesterol Levels: Treatment Implications and Possible Mechanisms, *Archives of Internal Medicine*, 164 (8), 863-870.

Pavcnik, Nina (2002), Do Pharmaceutical Prices Respond to Potential Patient Out-of-pocket Expenses?, *The RAND Journal of Economics*, 33 (3), 469-487.

Puig-Junoy, Jaume (2007), The Impact of Generic Reference Pricing Interventions in the Statin Market, *Health Policy*, 84, 14-29.

Regan, Tracy L. (2008), Generic Entry, Price Competition, and Market Segmentation in the Prescription Drug Market, *International Journal of Industrial Organization* 26 (4), 930-948.

Reynaert, Mathias and Frank Verboven (2012), Improving the Performance of Random Coefficients Demand Models: The Role of Optimal Instruments, CEPR Discussion Paper No. 9026.

Scherer, Frederic M. (1993), Pricing, Profits, and Technological Progress in the Pharmaceutical Industry, *Journal of Economic Perspectives* 7, 97-115.

Small, Kenneth A. and Harvey S. Rosen (1981), Applied Welfare Economics with Discrete Choice Models, *Econometrica*, 49 (1), 105-130.

Stock, James H., Wright, Jonathan H., and Motohiro Yogo (2002), A Survey of Weak Instruments and Weak Identification in Generalized Method of Moments, *Journal of the American Statistical Association*, 20 (4), 518-529.

Su, Che-Lin and Kenneth L. Judd (2012), Constrained Optimization Approaches to Estimation of Structural Models, *Econometrica*, 80 (5), 2213-2230.

Tung, Patricia, Stephen D. Wiviott, Christopher P. Cannon, Sabina A. Murphy, Carolyn H. McCabe, and C. Michael Gibson (2009), Seasonal Variation in Lipids in Patients Following Acute Coronary Syndrome on Fixed Doses of Pravastatin (40 mg) or Atorvastatin (80 mg) (from the Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis In Myocardial Infarction 22 [PROVE IT-TIMI 22] Study), *The American Journal of Cardiology*, 103 (8), 1056-1060.

Table 3.1: **Prices and sales for statins**

| | All | | | Original Products | | | Generics | | | Parallel Imports | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | Median | Std. Dev. | Mean | Median | Std. Dev. | Mean | Median | Std. Dev. | Mean | Median | Std. Dev. |
| *All periods* | | | | | | | | | | | | |
| Retail price | 7.79 | 5.18 | 6.78 | 12.15 | 11.28 | 5.98 | 3.61 | 2.52 | 3.28 | 11.00 | 9.76 | 7.81 |
| Reference price | 6.09 | 3.43 | 6.16 | 8.91 | 7.38 | 6.20 | 2.91 | 1.90 | 3.00 | 9.11 | 6.90 | 7.51 |
| Consumer copayment | 2.92 | 1.47 | 4.17 | 5.02 | 2.78 | 5.37 | 1.28 | 0.72 | 1.70 | 3.71 | 2.67 | 4.68 |
| Quantities (in 1,000 DDD) | 24.44 | 2.19 | 114.30 | 20.06 | 5.73 | 36.46 | 34.48 | 1.44 | 157.31 | 9.53 | 0.63 | 55.59 |
| Obs. | 13,861 | | | 3,907 | | | 6,633 | | | 3,321 | | |
| *Base period* | | | | | | | | | | | | |
| Retail price | 9.37 | 7.57 | 6.51 | 12.56 | 11.57 | 5.38 | 5.10 | 3.64 | 4.06 | 12.69 | 13.05 | 6.87 |
| Reference price | 7.19 | 4.33 | 5.93 | 9.95 | 9.21 | 5.46 | 3.84 | 2.45 | 3.59 | 9.51 | 10.07 | 6.70 |
| Consumer copayment | 3.62 | 2.09 | 4.82 | 4.60 | 2.75 | 5.38 | 2.02 | 1.15 | 2.61 | 5.08 | 3.40 | 6.00 |
| Quantities (in 1,000 DDD) | 18.77 | 2.41 | 61.01 | 18.98 | 6.47 | 31.40 | 25.09 | 1.36 | 85.80 | 8.57 | 0.74 | 27.67 |
| Obs. | 2,524 | | | 744 | | | 1,090 | | | 690 | | |
| *Implementation period* | | | | | | | | | | | | |
| Retail price | 5.81 | 3.41 | 6.11 | 11.57 | 9.57 | 6.23 | 2.58 | 1.95 | 2.25 | 7.32 | 4.09 | 7.23 |
| Reference price | 4.21 | 2.03 | 5.39 | 7.26 | 6.75 | 6.58 | 2.01 | 1.38 | 2.07 | 6.63 | 3.73 | 7.19 |
| Consumer copayment | 2.44 | 1.06 | 3.67 | 5.75 | 2.92 | 5.42 | 0.97 | 0.60 | 1.02 | 2.02 | 1.30 | 2.14 |
| Quantities (in 1,000 DDD) | 26.54 | 1.60 | 125.80 | 18.18 | 4.83 | 34.17 | 35.72 | 1.05 | 164.81 | 9.52 | 0.44 | 32.38 |
| Obs. | 4,963 | | | 1,340 | | | 2,781 | | | 842 | | |

Notes: Prices are per Defined Daily Dose (DDD) and are deflated using consumer prices index with June 2005 as basis. Exchange rates in June 2005: DKK 1 = $ 0.1634 = €0.1343. Quantities measure as sold DDD.

Table 3.2: **Logit and random coefficient logit demand**

| | OLS Logit | IV Logit | RC Logit - MPEC | |
|---|---|---|---|---|
| | | | Mean | Std. dev. |
| Copayment | -.14*** | -.39*** | -1.54*** | .54*** |
| | (.006) | (.033) | (.271) | (.086) |
| Package Size | .02*** | .02*** | .02*** | |
| | (.001) | (.0006) | (.001) | |
| Strength | .01*** | -.003 | -.004 | |
| | (.001) | (.003) | (.003) | |
| Constant | -9.85*** | -6.52*** | -6.14*** | |
| | (.133) | (.471) | (.594) | |
| $R^2$ | .42 | .35 | | |
| # obs. | 13,861 | 13,861 | 13,861 | |
| $\eta_j$ (mean) | -.22 | -.59 | -1.19 | |

Notes: Robust standard errors in parentheses. Product name, month, and time period dummies are included. F-value in the first-stage regression of IV Logit: 136.16. 5,000 modified latin hypercube sampling draws used to simulate market shares in the random coefficients logit model. Elasticities $\eta_j$ are market share weighted mean elasticities in the base period.

Table 3.3: **Price Regressions**

| | $\ln$ *retail price* ($N = 7,487$) | | | | | |
|---|---|---|---|---|---|---|
| | (1) | (2) | (3) | (4) | (5) | (6) |
| Reform ($\gamma_1$) | -.52*** (.057) | -.48*** (.111) | -1.53*** (.194) | -.46*** (.061) | -.24*** (.046) | -.44*** (.072) |
| Reform × Original Product ($\gamma_2$) | | | | | | .37*** (.077) |
| Reform × Parallel Import ($\gamma_3$) | | | | | | .24** (.094) |
| No. Products in Market ($\gamma_4$) | | | -.10*** (.023) | -.001 (.004) | -.002 (.004) | -.001 (.004) |
| No. Products in Subst. group ($\gamma_5$) | | | -.12*** (.012) | -.07*** (.015) | -0.007 (.013) | -0.02* (.012) |
| Pulp & Paper × Product name | No | No | No | No | Yes | Yes |
| BLP Instruments | No | Yes | Yes | Yes | Yes | Yes |
| Fixed effects | | | | | | |
| Product name | No | No | No | No | Yes | Yes |
| Substitution group | No | No | No | Yes | Yes | Yes |
| Month | Yes | Yes | Yes | Yes | Yes | Yes |
| Constant | 2.10*** (.064) | 2.02*** (.402) | 4.35*** (.526) | 1.64*** (.254) | -4.798*** (1.592) | -5.25** (1.728) |
| $R^2$ | .10 | .13 | .35 | .57 | .89 | .89 |

Notes: The table reports linear dummy variable regression estimates of the coefficients in Equation (1). Values between parentheses are robust standard errors clustered at the product level. The estimation sample contains only the base and the implementation period. *** p< 0.01, ** p< 0.05, * p < 0.1

Table 3.4: **Reform effects on market shares, expenditures, and consumer welfare**

| | All | | Generics | | Parallel Imports | | Original Products | |
|---|---|---|---|---|---|---|---|---|
| | Δ | Δ% | Δ | Δ% | Δ | Δ% | Δ | Δ% |
| *In DKK (2005) per DDD* | | | | | | | | |
| Retail price | -2.05 | -21.91 | -2.36 | -46.37 | -2.80 | -22.10 | -.90 | -7.20 |
| Reference price | -1.61 | -22.36 | -1.54 | -40.33 | -1.80 | -18.94 | -1.52 | -15.23 |
| Consumer copayment | -.77 | -21.21 | -1.12 | -55.53 | -1.36 | -26.84 | .31 | 6.71 |
| *In 1,000 DDD per year* | | | | | | | | |
| Quantities | 5,819 | 9.43 | 9,212 | 26.98 | 1,299 | 28.37 | -4,691 | -26.08 |
| *In 1,000 DKK (2005) per year* | | | | | | | | |
| Producer revenue | -67,834 | -18.83 | -7,277 | -8.97 | 7,282 | 14.07 | -67,839 | -29.23 |
| Government expenditures | -52,556 | -19.48 | -10,766 | -20.24 | 4,641 | 11.76 | -46,431 | -27.17 |
| Consumer expenditures | -15,277 | -16.99 | 3,488 | 24.83 | 2,641 | 22.42 | -21,407 | -34.91 |
| Consumer surplus | 6,142.57 | | | | | | | |

Notes: Price changes are computed from base to implementation period, based on predicted prices from specification (6) in Table 5. All other changes from base period to counterfactual implementation in base period, using estimated parameters of random coefficient logit to predict counterfactual market shares and consumer surplus. All figures in June 2005. Exchange rates in June 2005: DKK 1 = $ 0.1634 = € 0.1343.

# A. Summary of events related to changes in the Danish reimbursement system

| | | |
|---|---|---|
| **LIF Agreement** | May 03 2001<br>Apr. 14 2003 | Since 2001 LIF members and the Danish Ministry of Health have an agreement on price ceiling running until 2005. Not all LIF members comply with the agreement. |
| **Adjustment** | Apr. 28 2003<br>Sep. 01 2003 | The Danish Medicine Agency starts updating pharmaceutical prices every 14 days. Before, reimbursement prices were set every 6 months |
| **Base:**<br>**Working group** | Sep. 15 2003<br>Jun. 07 2004 | The Danish Ministry of Health announces to assemble a working group that is asked to submit proposals regarding reimbursement rules with the aim to increase competition.<br>The Association of Danish Pharmacies launches the idea that reimbursements should be based on the cheapest domestic product within substitute groups. The idea earns widespread support among leading politicians |
| **Announcement** | Jun. 21 2004<br>Mar. 28 2005 | The law regarding the new reimbursement system is passed by the Danish parliament |
| **Treatment:**<br>**Implementation** | Apr. 01 2005<br>Sep. 25 2006 | The new law is implemented |
| **New**<br>**LIF agreement** | since<br>Oct. 29 2006 | The LIF and the government agree upon on a price ceiling corresponding to the price on 30 Aug. 2006 |

# B. characterization of statins in terms of their ATC code

| 2-Level | 3-Level | 4-Level | 5 - Level | |
|---|---|---|---|---|
| C10 Lipid Modifying Agents | C10A | C10AA HMG CoA reductase inhibitors (Statins) | C10AA01 | **simvastatin** |
| | | | C10AA02 | **lovastatin** |
| | | | C10AA03 | **pravastatin** |
| | | | C10AA04 | **fluvastatin** |
| | | | C10AA05 | **atorvastatin** |
| | | | C10AA06 | cerivastatin |
| | | | C10AA07 | **rosuvastatin** |
| | | | C10AA08 | pitavastatin |
| | | C10AB Fibrates | C10AB01 | clofibrate |
| | | | C10AB02 | bezafibrate |
| | | | C10AB03 | aluminium clofibrate |
| | | | C10AB04 | **gemfibrozil** |
| | | | C10AB05 | fenofibrate |
| | | | C10AB06 | simfibrate |
| | | | C10AB07 | ronifibrate |
| | | | C10AB08 | ciprofibrate |
| | | | C10AB09 | etofibrate |
| | | | C10AB10 | clofibride |
| | | C10AC Bile acid sequestrants | C10AC01 | **colestyramine** |
| | | | C10AC02 | **colestipol** |
| | | | C10AC03 | colextran |
| | | | C10AC04 | **colesevelam** |
| | | C10AD Nicotinic acid and derivatives | C10AD01 | niceritrol |
| | | | C10AD02 | nicotinic acid |
| | | | C10AD03 | nicofuranose |
| | | | C10AD04 | aluminium nicotinate |
| | | | C10AD05 | nicotinyl alcohol (pyridylcarbinol) |
| | | | C10AD06 | **acipimox** |
| | | | C10AD52 | nicotinic acid, combinations |
| | | C10AX Other lipid modifying agents | C10AX01 | dextrothyroxine |
| | | | C10AX02 | probucol |
| | | | C10AX03 | tiadenol |
| | | | C10AX05 | meglutol |
| | | | C10AX06 | omega-3-triglycerides incl. other esters and acids |
| | | | C10AX07 | magnesium pyridoxal 5-phosphate glutamate |
| | | | C10AX08 | policosanol |
| | | | C10AX09 | **ezetimibe** |
| | | | C10AX10 | alipogene tiparvovec |
| | C10B | C10BA combinations | C10BA01 | lovastatin and nicotinic acid |
| | | | C10BA02 | **simvastatin and ezetimibe** |
| | | C10BX combinations | C10BX01 | simvastatin and acetylsalicylic acid |
| | | | C10BX02 | pravastatin and acetylsalicylic acid |
| | | | C10BX03 | atorvastatin and amlodipine |

Notes: Table B displays a detailed classification of lipid modifying agents with their respective ATC codes. Only boldfaced chemical substances are marketed in Denmark. Source: WHO Collaborating Centre for Drug Statistics Methodology.

# C. Market and product characteristics

| | All | | | Original Products | | |
|---|---|---|---|---|---|---|
| | Mean | Median | Std. Dev. | Mean | Median | Std. Dev. |
| *All periods* | | | | | | |
| Number of products | 122.27 | 127 | 14.16 | 34.42 | 35 | 3.79 |
| Number of firms | 20.00 | 19 | 3.12 | 4.92 | 5 | 0.27 |
| Package size | 67.75 | 98 | 35.79 | 67.84 | 98 | 34.77 |
| Strength in mg. | 28.62 | 20 | 18.56 | 33.92 | 20 | 23.67 |
| Obs. | 13,861 | | | 3,907 | | |
| *Base period* | | | | | | |
| Number of products | 126.39 | 127 | 4.85 | 37.23 | 38 | 0.97 |
| Number of firms | 19.01 | 19 | 0.44 | 5 | 5 | 0 |
| Package size | 65.97 | 98 | 34.96 | 64.62 | 98 | 35.06 |
| Strength in mg. | 26.70 | 20 | 16.55 | 34.35 | 20 | 22.85 |
| Obs. | 2,524 | | | 744 | | |
| *Implementation period* | | | | | | |
| Number of products | 126.03 | 132 | 15.07 | 33.70 | 35 | 2.57 |
| Number of firms | 22.17 | 23 | 2.30 | 5 | 5 | 0 |
| Package size | 67.49 | 98 | 34.69 | 69.87 | 98 | 34.47 |
| Strength in mg. | 30.70 | 20 | 19.97 | 33.41 | 20 | 24.19 |
| Obs. | 4,963 | | | 1,340 | | |

| | Generics | | | Parallel Imports | | |
|---|---|---|---|---|---|---|
| | Mean | Median | Std. Dev. | Mean | Median | Std. Dev. |
| *All periods* | | | | | | |
| Number of products | 60.81 | 60 | 11.73 | 32.08 | 29 | 9.41 |
| Number of firms | 9.95 | 10 | 1.71 | 5.64 | 5 | 1.75 |
| Package size | 67.61 | 98 | 37.16 | 67.93 | 84 | 34.17 |
| Strength in mg. | 27.77 | 20 | 15.99 | 24.09 | 20 | 14.60 |
| Obs. | 6,633 | | | 3,321 | | |
| *Base period* | | | | | | |
| Number of products | 54.59 | 55 | 2.24 | 35.28 | 35 | 5.24 |
| Number of firms | 10.01 | 10 | 0.44 | 5 | 5 | 0 |
| Package size | 66.24 | 98 | 35.04 | 66.98 | 84 | 34.72 |
| Strength in mg. | 23.85 | 20 | 12.20 | 22.93 | 20 | 10.70 |
| Obs. | 1,090 | | | 690 | | |
| *Implementation period* | | | | | | |
| Number of products | 70.34 | 72 | 7.24 | 23.00 | 26 | 6.01 |
| Number of firms | 10.83 | 11 | 1.22 | 7.07 | 8 | 1.48 |
| Package size | 66.75 | 98 | 35.13 | 66.17 | 60 | 33.43 |
| Strength in mg. | 29.79 | 20 | 17.68 | 29.38 | 20 | 19.31 |
| Obs. | 2,781 | | | 842 | | |

Notes: Fortnightly average prices for a defined daily dose in Danish krones. All figures are deflated using consumer prices index with June 2005 as basis, where DKK 1 = $ 0.1634 = € 0.1343. Quantities measure as sold defined daily doses.

# D. Identification and estimation of the demand model

In the discussion of identification we closely follow recent propositions in Reynaert and Verboven (2012) about the benefits of using optimal instruments in random coefficient logit models. Subsequently, we sketch out our estimation procedure.

The unobserved characteristics of product $j$, $\xi_{jt}$, are known to both producers and patients, which implies that prices are endogenous in equilibrium and must be instrumented. Not instrumenting prices leads to downward biased estimates of the price coefficient $\alpha_i$. We take two steps to remedy the problem of price endogeneity. First, we employ product name fixed effects to control for time-invariant quality levels. Second, a set of time-varying instruments accounts for variation around time-invariant means. Hence, identification relies on the conditional moment restrictions

$$E\left[\xi_{jt}|\boldsymbol{X_t}\right] = 0, \tag{3.8}$$

which is the mean independence of unobserved product quality $\xi_{jt}$ of observed product characteristics $\boldsymbol{X}$.

These conditional moment restrictions can be transformed into unconditional moment restrictions

$$E\left[\xi_{jt}\boldsymbol{z_{jt}}\right] = 0, \tag{3.9}$$

where $\boldsymbol{z_{jt}}$ are the instruments. Reynaert and Verboven (2012) have shown that Chamberlain's (1987) optimal instruments work extremely well in random coefficient logit models, most importantly in identifying the nonlinear parameters. The set of optimal instruments is defined as the set of derivatives of the unobserved characteristic with respect the estimated parameters:

$$\boldsymbol{z_{jt}} = E\left[\frac{\partial \xi_{jt}(\theta)}{\partial \theta'}\middle| \boldsymbol{X_t}, \boldsymbol{w_{jt}}\right], \tag{3.10}$$

where we include an input price index as cost shifter $w_{jt}$. The intuition is equivalent to standard instruments with the difference that the derivatives make use of the functional forms assumed in the model whereas the standard instruments are simple linear projections. To see this, Reynaert and Verboven (2012) show that the set of derivatives with respect to the linear parameters $\beta$ and $\alpha$ are simply the set of observed product characteristics and cost shifters. The derivative with respect to the nonlinear parameter $\sigma$ is a nonlinear

function of all competing products' characteristics. Hence, the biggest gain is achieved for the nonlinear parameter $\sigma$ since the market share equation taking into account consumer heterogeneity can be exploited. Berry et al. (1999) and Goeree (2008) have previously approximated the expectation in equation (3.10) to construct optimal instruments. They evaluate the derivative at the mean of the disturbance vector (that is at $\xi_{jt} = 0$) while Reynaert and Verboven (2012) form the exact expectation by computing the mean of the derivative over $\hat{\xi}_{jt}$. The latter is the approach we follow.

Note that in order to compute $\boldsymbol{z_{jt}}$ in equation (3.10), we require initial estimates for $\boldsymbol{\theta}$ the very parameter vector we aim to ultimately estimate. One option would be to estimate the computationally expensive heterogenous logit model using standard instruments and using the results obtain therein as initial estimates for the optimal instruments. Reynaert and Verboven (2012) propose a simpler approach and show that it performs equally well as running the more general model twice. The idea is to estimate a homogenous IV logit model first. This is a linear IV regression and, hence, very fast. We choose three sets of standard instruments for this preliminary estimation. First, the sums of own other products' observed characteristics and sums of other firms' product characteristics which follows the arguments in Bresnahan (1987) and Berry et al. (1995) that the crowdedness in characteristics space should have an impact on equilibrium markups. Second, we include own product characteristics which are assumed to be exogenous. We follow Dubé et al. (2012) by also including squared and interaction terms of the product characteristics active ingredient strength and package size. Third, we make use of a cost-side variable to account mainly for packaging costs. We interact an index for pulp and paper prices with product name fixed effects. This model does not obtain an estimate for $\sigma$ so we must guess an initial value. We set this value equal to the absolute mean price coefficient $|\alpha|$. With these initial estimates at hand we can now compute the complete set of optimal instruments $\boldsymbol{z_{jt}}$ in equation (3.10).[9]

We estimate the random coefficient logit model using a sample that includes all products marketed between February 2003 and June 2007. In this sample, we observe 115 bi-weekly time-periods and approximately 100 products per period. Using our optimal instruments,

[9]See page 10 in Reynaert and Verboven (2012) for the exact algorithm we use.

we estimate the model by solving a mathematical program with equilibrium constraints (MPEC) as introduced by Su and Judd (2012) and Dubé et al. (2012):

$$\begin{aligned} \min_{\theta,\xi} \quad & \boldsymbol{g}(\boldsymbol{\xi})' \boldsymbol{W} \boldsymbol{g}(\boldsymbol{\xi}) \\ & \text{subject to} \quad \boldsymbol{s}(\boldsymbol{\xi};\boldsymbol{\theta}) = \boldsymbol{S}, \end{aligned}$$

where $\boldsymbol{g}(\boldsymbol{\xi})$ is the sample analogue to $E(\boldsymbol{z_{jt}}\boldsymbol{\xi})$. The main advantage of this approach as compared to the nested fixed point algorithm in Berry et al. (1995) is that the first and second derivatives of this problem are highly sparse in cases with many markets and not too many products. This can be exploited by numerical solvers and substantially increase computational speed. It also avoids numerical error propagation by circumventing the nesting of loops for optimization. We adapt and use Matlab code provided online by Dubé et al. (2012).

To obtain the constraints $\boldsymbol{s}(\boldsymbol{\xi};\boldsymbol{\theta}) = \boldsymbol{S}$ we solve the market share equation in (3.3) numerically. We assume $\nu$ to follow a standard normal distribution and draw 5000 modified latin hypercube sampling draws for estimation, as proposed in Hess et al. (2006), which have shown to be an improvement over frequently used Halton draws.[10] We further follow the proposition in Knittel and Metaxoglu (2012) to use 50 different starting values to increase confidence that the numerical solver stops at the true solution. The majority out of these 50 estimation runs converge, and those that do, converge to the same solution. The Knitro 8.0 solver's exit flag confirms convergence (as opposed to pre-mature stopping).

We compute changes in Marshallian consumer surplus. Our assumption of linear utility implies the absence of income effects so that consumer surplus and compensating variation coincide. The absence of income effects is a reasonable assumption if the change in consumer surplus is small relative to household income, which is the case for the Danish reform.

[10]Consumer demographics such as the income distribution in Denmark are likely to explain some of this unobserved heterogeneity with respect to price sensitivities. Ideally, we would include the income distribution when estimating the distribution parameters for the price coefficient. However, given the shortness of the analyzed time period we do not observe much variation in the national income distribution in Denmark and, hence, including it will not lead to improved identification of the model. Furthermore, the fact that Denmark has a comparatively flat income distribution reduces the potential of including this observed consumer demographic.

# E. First stage results for IV Logit specification

| | | | | | |
|---|---|---|---|---|---|
| Strength of other firms' products | .0003*** | Package size | -.017**** | Strength | -.067*** |
| | (.00007) | | (.002) | | (.005) |
| Strength of own products | -. 0007*** | Package size$^2$ | .0001*** | Strength$^2$ | -.0001* |
| | (.00002) | | (.00001) | | (.00006) |
| Strength × package size | .0001*** | | | | |
| | (.00004) | | | | |
| *Dummy variables* | | | | | |
| Atorvastatin Ranbaxy | -99.24 | Pravastatin Sandoz | -16.30*** | Zarator | -13.60*** |
| | (94.84) | | (3.493) | | (2.936) |
| Canef | -13.55*** | Pravastatin Stada | -44.58*** | Zocolip | -12.23*** |
| | (3.264) | | (16.06) | | (3.370) |
| Crestor | -8.48*** | Simvacop | -31.33*** | January | .03 |
| | (2.776) | | (9.030) | | (.111) |
| Lescol | -5.76** | Simvastatin 1A Farma | 8.57** | February | .14 |
| | (2.835) | | (3.935) | | (.122) |
| Lescol depot | -4.77* | Simvastatin Actavis | -6.09** | March | -.08 |
| | (2.810) | | (3.040) | | (.120) |
| Lipitor | -8.91*** | Simvastatin Alpharma | -2.03 | April | -.06 |
| | (2.942) | | (2.978) | | (.123) |
| Lovacodan | -4.21 | Simvastatin Alternova | -4.78 | May | -.28** |
| | (3.053) | | (2.945) | | (.124) |
| Lovastatin Actavis | -5.13* | Simvastatin Arrow | -.46 | June | -.19 |
| | (2.839) | | (3.261) | | (.124) |
| Lovastatin Alternova | -2.52 | Simvastatin Genthon | -10.14 | July | -.04 |
| | (2.875) | | (11.07) | | (.134) |
| Lovastatin Universal Farma | -9.83*** | Simvastatin Gevita | -5.59 | August | -.03 |
| | (2.849) | | (3.936) | | (.125) |
| Lovastatin ratiopharm | .82 | Simvastatin Hexal | -9.87*** | September | -.12 |
| | (4.928) | | (2.917) | | (.128) |
| Mevacor | -15.58** | Simvastatin Merck NM | -19.15*** | October | -.19 |
| | (7.595) | | (7.145) | | (.121) |
| Perichol | -5.00 | Simvastatin Orifarm | -24.96** | November | -.16 |
| | (3.422) | | (10.62) | | (.117) |
| Pravachol | -38.73*** | Simvastatin Paranova | -78.24*** | LIF Agreement | -2.23*** |
| | (3.583) | | (14.20) | | (.241) |
| Pravastatin 1A Farma | -14.57*** | Simvastatin Ratiopharm | -25.34*** | Adjustment | -.78*** |
| | (3.533) | | (4.482) | | (.211) |
| Pravastatin Alternova | -4.36 | Simvastatin Sandoz | -12.50*** | Working group | -.48*** |
| | (3.260) | | (3.025) | | (.165) |
| Pravastatin HEXAL | -19.09*** | Sortis | -3.10 | Announcement | -.76*** |
| | (3.529) | | (3.884) | | (.152) |
| Pravastatin Nycomed | -9.62*** | Statinacop | -2.98 | Implementation | -.13 |
| | (2.858) | | (4.002) | | (.133) |
| Pravastatin Ranbaxy | -15.39*** | Tahor | -7.00** | P&P × Name | Yes |
| | (3.875) | | (3.384) | | |
| Pravastatin Recept | -9.35** | Torvast | -12.49*** | Constant | 12.44*** |
| | (4.083) | | (3.822) | | (3.156) |
| *F-test results* | | | | | |
| All instruments | | | | | 136.16 |
| BLP instruments | | | | | 30.91 |
| Pulp & Paper (P&P) instruments | | | | | 16.35 |
| Squares and interactions instruments | | | | | 13.70 |
| $R^2$ | | | | | .59 |

Notes: First stage regression coefficients of IV Logit. Robust standard errors in parentheses. The reference categories for dummy variables are: Product name *Zocor*, Month December, and Period 'New LIF agreement'.
*** p< 0.01, ** p< 0.05, * p < 0.1

# Chapter 4

# How Do Drug Prices Respond to a Change from External to Internal Reference Pricing? Evidence from a Danish Regulatory Reform

This chapter is joint work with Ulrich Kaiser.

*Acknowledgements*: The authors are greatly indebted to Hannes Ullrich. Financial support from the Swiss National Science Foundation through grants 100018-135257 and PBZHP1-143346 is gratefully acknowledged.

## 4.1 Introduction

Reference pricing systems, where patients are reimbursed a fraction of the retail price when buying a prescription drug, constitute a particularly widely embraced tool to curb medical expenses across the world (Berndt and Dubois 2012; Espín et al. 2011; López-Casasnovas and Puig-Junoy 2000). These systems aim at benefiting patients that prefer cheaper products over more expensive ones, thus inducing more price sensitivity on consumers and more competitive pressure on firms.

There exists a large body of empirical evidence that shows that such systems indeed are effective in bringing down retail prices of prescription drugs (Aronsson et al. 2001; Brekke et al. 2007, 2009, 2011; Danzon and Liu 1998; Kanavos et al. 2008; Pavcnik 2002; Puig-Junoy 2007). It is also observed that different countries apply different rules as to how the reference price is determined. However, much less is known about the consequences of the *design* of such reference price systems. In April 2005, Denmark switched from external reference pricing (where the reference price was calculated as the average price of similar products in other European countries) to internal reference pricing (where the reference price is calculated as the cheapest price of a similar product in the country). A switch from an external to an internal reference price system creates incentives for patients to buy the cheapest product within a set of substitutes, since the price wedge between the cheapest substitute and a preferred products becomes larger due to the reform, unless there is only a single product in a group of substitutes. This argument is theoretically formalized by Brekke et al. (2009, 2011). We empirically study the effects on prices of a change in the *design* of the reference price system using a comprehensive panel set that covers around 23,600 observations of 640 unique products that we track for 59 fortnightly time periods.

We speculate that the effect of the reform on prices varies by the severity of the condition and by the type of the firm. Specifically, we distinguish between drugs that treat a chronic disease, a semi-chronic disease, and an acute disease. For the chronic condition we use anti-cholesterol drugs (statins). For the semi-chronic condition we use drugs for peptic

ulcer and gastro-oesophageal reflux disease (antiulcerants). And for the acute condition we use antibiotics. Our prior is that patients with a chronic condition are more price sensitive than patients with an acute condition because health expenditures are generally substantially higher, treatment time is longer and patients might be more experienced and better informed about their substitution options.

In addition, we differentiate between three types of firms: original firms, generic firms and parallel importers. Original firms engage in R&D using intellectual property rights to protect their innovations. Generic firms produce drugs that are bioequivalent copies of original products and may only legally enter the market after the patents have expired. Parallel importers do not engage in manufacturing. Instead, they buy products in low-price countries, repackage, relabel, and sell them in high-price countries. Parallel importing is legal within the European Union and in Denmark it is permitted for both on-patent and off-patent pharmaceuticals. We explicitly allow the reform to affect each type of firm differently to account for the evidence supported by a large body of literature suggesting that generics are perceived to be different from original products. Previous studies find that original firms keep high prices and are able to retain substantial market shares despite the presence of low-price generic substitutes. This is associated with consumer heterogeneity with respect to their price sensitivity and consumers brand-loyalty generated by first-mover advantage (Caves et al. 1991; Grabowski and Vernon 1992; Frank and Salkever 1997; Aronsson et al. 2001; Coscelli 2000). Specifically, after generics enter the market, the price sensitive consumers switch and original producers are left with consumers that are even less price sensitive and probably brand-loyal. We expect that the switch from external to internal reference pricing affects generics more than original products, because these are consumed by more price sensitive patients. In addition, parallel imports are closer substitutes to original firms because they are not copies but exactly the same product in another package. Therefore, we expect parallel importers to react similarly to original firms.

Our paper is most closely related to the seminal work of Pavcnik (2002). She studies

a switch from price cap to external reference pricing in Germany, one of the countries that first introduced this policy. She uses reduced-form pricing regressions where she maps dummy variables for the time period after the regulatory change to retail prices. Our findings suggest that producers substantially reduced prices after the reform. In particular, she finds that the effects are stronger for original products, specially for those that faced generic competition. We also explore the latter finding and control for competition. We expect the reform to reinforce the effects of competition, such that prices decrease more in markets facing more competitors after the reform is introduced.

Other related work includes Brekke et al. (2009, 2011) and Kaiser et al. (2013). The first two papers study a switch from price cap to reference price regulation in Norway, confirming the previous results. In Kaiser et al. (2013) we conduct a welfare analysis of the Danish change from external to internal reference pricing. This analysis focuses on anti-cholesterol products only and it also includes reduced–form pricing equations similar to Pavcnik. The main finding is that the substitution from external to internal reference pricing yield a substantial decrease in prices, but opposite to Pavcnik, the effects are stronger for generics. The present analysis extends our earlier analysis by including treatments for a semi-chronic and an acute condition.

In our paper we find that the switch from external to internal reference pricing has effectively impacted pharmacy purchase prices negatively, more so for chronic conditions than for acute conditions. We also show that the reform affected prices for generics and parallel imports more than for original products. Finally, competition plays an important role and we show that the change in the design of reference pricing reinforced the effects of competition in reducing prices, inducing strongest price changes for markets with many substitute products.

This paper is organized as follows. Section 4.2 offers an overview of the Danish pharmaceutical market. Section 4.3 describes the data. Section 4.4 describes the empirical framework. Section 4.5 presents the results. Section 4.6 concludes.

## 4.2 Institutional Background

This section offers a short overview of the Danish pharmaceutical industry and describes the main regulatory framework. In Denmark the pricing of pharmaceutical products is free in the sense that firms can set any price. However these prices must be reported to the Danish Medicines Agency (DKMA) every 14 days. DKMA makes them publicly available online under URL *http://medicinpriser.dk*, a website that also contains information on all authorized pharmaceutical products in Denmark and was designed to ensure that prices for pharmaceuticals are identical nationwide.

Second, pharmacies operate in a highly regulated environment. The number and location of pharmacies, as well as their markups are regulated by the government. The regulation of the markup implicitly sets the pharmacy retail price $p^c$, such that $p^c = p^f + k$, where $p^f$ is the price set by the firm (pharmacy purchase price) and $k$ is the prescription fee (including value added taxes, (VAT)). Moreover, Danish pharmacists are required to dispense the cheapest product among available substitutes, unless the consumer or the doctor explicitly requests another product.

Third, consumers are entitled to free and equal access to health care services. The reimbursement that consumers obtain when buying pharmaceuticals depends on her annual health care expenditures and the choice of the product. The final price paid by consumers $p^{cop}$ is given by:

$$p^{cop} = p^c - \tau * p^r, \tag{4.1}$$

where $p^c$ denotes the pharmacy retail price, $p^r$ is the reference price and $\tau$ is the fraction of the reference price that will be reimbursed. Consumers in long term treatments with high prices can obtain as much as 80 percent of their cost reimbursed.

The reform affecting reference prices took effect on April 1, 2005. Denmark changed from external to internal reference pricing for all prescription-only pharmaceuticals independent of their patent status. No other changes were made to the reimbursement system.

Before the reform, the reference price for a given product was defined as the pharmacy retail price of the chosen product up to the average price of the same product in the EU-15 member states, excluding Greece, Luxembourg, Spain, and Portugal. Once the retail price exceeded the EU average price, the reference price was set equal to the EU average price.

The reimbursement reform originated from an assembly of a group of experts from the Danish Ministry of Health on September 15, 2003, who wanted to collect ideas for a reform of the existing reimbursement system to strengthen competition and cost awareness. The Danish Association of the Pharmaceutical Industry (Lægemiddel Industri Foreningen, LIF) — the Danish assembly of original drugs producers — launched the idea of using the domestic Danish price of the cheapest available product within a substitution group as the reference price instead of EU averages. In June 2004, the Danish parliament ratified the new reimbursement law making it public and implementing it in April 1, 2005.

These government–determined dates are important for our analysis as they define the time periods before and after the reform. Other events that may have affected drug prices include a voluntarily agreement on price ceilings that was established by LIF members between May 2001 and April 2003 and a new agreement on price ceilings that the Danish Ministry of Health and LIF ratified in October 2006. The voluntary price ceilings agreement was not respected by most LIF members, and probably neither by generic firms or parallel importers, since they are not represented by LIF.

In order to separate the reform effects from the price ceiling agreements before and after the reform, we define and focus our analysis to a *base period* and an *implementation period*. The base period includes the time between September 15, 2003 and June 7, 2004 — the time between the working group assembly and the ratification of the reform in parliament. We choose these dates because, during that time, no reliable information about prospective changes in the reimbursement system was publicly or privately available. Moreover, the number of firms as well as prices remained stable, an issue that we discuss in more detail in Section 4.3. The implementation period covers the time between April 1, 2005 and

September 25, 2006, the time span between the reform implementation and the beginning of the new price ceiling agreement. We discard all other time periods for our empirical analysis.

## 4.3 Data

Our data set contains fortnightly prices and other characteristics of pharmaceuticals in three therapeutic markets: Anti-cholesterol drugs, drugs for acid-related gastrointestinal conditions, and antibiotics. These products are used in the treatment of diseases that vary in their severity and length of therapy with anti-cholesterol drugs constituting the longest and with more severe consequences and antibiotics constituting the shortest and least severe therapy.

We differentiate these markets because we expect the reform to have different effects in each one. Our prior is that patients with a chronic condition are more price sensitive than patients in an acute treatment, due to the fact that their health care expenditures are generally substantially higher, treatment time is longer and they might be more experienced and better informed about their substitution options.

A product is defined by four attributes: active substance, strength, package size, and firm. The active substance is captured by the 5-level anatomical therapeutic chemical classification code (ATC Code). Strength measures the amount of the active substance in milligram per pill. Package size is the number of pills per package. Importantly, products with similar ATC codes are closer substitutes than products in other ATC codes. DKMA classifies products with the same 5-level ATC code, strength, administration form, and similar package size into substitution groups. Products within a substitution group are perfect substitutes and consumers can freely choose among products in the same substitution group.

To make products from different strength or package size comparable we normalize

prices and quantities using defined daily doses (DDD). This measure is proposed by the World Health Organization and widely used in the pharmaceutical industry. One DDD is defined as the average maintenance dose per day for a drug used for its main indication in adults.

Our dependent variable is the pharmacy purchase price in Danish krones (DKK) per defined daily dose (DDD), i.e. the price that is actually set by the producers for a unit of DDD. Prices are deflated using the consumer price index with the year 2005 as basis.

Table 4.1 provides information on turnover, reimbursement, the number of patients in treatment and sales for each therapeutic group. This information is not based on the product-level data that we use in our econometric analysis but was downloaded from *www.medstat.dk*, a website that contains yearly statistics on consumption and utilization of pharmaceuticals in Denmark. The table shows that turnover (pharmacy retail price $\times$ DDDs sold) is relatively similar to all products but slightly higher for antiulcerants. However, the chronic conditions account for a higher share of reimbursement than the acute condition. Moreover, the number of patients differs enormously between the treatments. In 2005 almost 1.7 million patients were treated with antibiotics. In the same year the number of patient treated with antiulcerants was around 380,000 and 307,000 patients were treated with anti-cholesterol drugs. The increase in the number of patient using anti-cholesterol drugs is remarkable (170 percent from 2002 to 2006). Utilization per patient (sales in DDD relative to number of patients) is much higher for anti-ulcerant and anti-cholesterol drugs than for antibiotics.

Finally, Table 4.1 also gives an estimate of the duration of treatment indicated by the measure at the bottom of the table. If we convert it into sales in DDD per inhabitant per year, the measure constitutes an estimate of the number of days for which each resident is annually treated on average. If each person in Denmark was treated with anti-cholesterol drugs, the treatment length in 2006 would be around 22 days. The treatment for antiulcerants would be between 11 and 14 days, and the treatment with antibiotics would only take

five days. These figures are approximations and are just meant to illustrate differences in treatment durations. Actual treatment with anti-cholesterol drugs can be lifelong, while a treatment with antiulcerants lasts between six weeks and six months.

Our data is consists of information on 253 antiulcerants, 228 statins, and 157 antibiotics that we observe for 58 fortnightly time periods.[1] Table 4.2 displays descriptive statistics on prices and variables that mirror the respective competitive situation. Reported are fortnightly average prices for a DDD in DKK. A DDD of antibiotics costs on average more than a DDD of anti-cholesterol products or antiulcerants. Note that average reference prices are higher than average pharmacy purchase prices, because the latter do not include prescription fees or VAT.

Furthermore, the average number of products and average number of firms is relatively stable and very similar for all groups, which helps us mitigate attributing effects to the reform that could have arisen from entry and exit. In contrast, the average number of substitution groups and the average number of products in a substitution group differs significantly. For anti-cholesterol drugs there are on average 40 substitution groups, each with around five to seven products to choose from. In the case of anti-ulcerants there are only around three products in each substitution group, and in the antibiotics group, there are only two products in each substitution group. We expect the reform to have stronger effects on the chronic condition, since this is the therapy that faces more competition.

Finally, the table presents the share of original products, generic products, and parallel imports in each group. The share of generics in the chronic and semi-chronic condition is higher than the share of original products. Parallel imports are also well represented in these groups (28 percent of anti-cholesterol drugs and 12 percent of antiulcerants) but not in the group of antibiotics, where they only make one percent of all observations. Antibiotics is a group dominated by original products.

[1] Appendix A displays the exact classification of the products in terms of their ATC code.

## 4.4 Empirical Approach

This section describes our empirical framework. Our aim is to identify the effect of the reimbursement reform on pharmacy purchase prices. To this end, and like Pavcnik (2002), we estimate standard fixed effects regressions of dummy variables for the reform and variables that represent competition on the natural logarithm of pharmacy purchase prices. Our regression equation take the following form:

$$\ln p_{jt}^{f} = \rho R + \alpha_1 R * d_{op} + \alpha_2 R * d_{pi} + \gamma_1 z_j + \gamma_2 R * z_j + \beta_1 R * z_j * d_{op} + \beta_2 R * z_j * d_{pi} + \mu_j + \nu_t + \epsilon_{jt},$$

where $p_{jt}^{f}$ is the pharmacy purchase price of a product $j$ in time $t$. $R$ denotes a dummy variable that is coded one for the implementation and zero for the base period. It is our variable of main interest and its corresponding parameter $\rho$ is to be interpreted as the approximate percentage difference between the pharmacy purchase price before and after the reform. $d_{op}$ and $d_{pi}$ are dummy variables equal to one if the product is an original product (op) or if the product is a parallel import (pi) respectively. We interact these dummy variables with the reform dummy to allow for different impacts in different types of firms. The variable $z_j$ is the number of products in a substitution group and measures the the current competitive situation of product $j$. We interact $z_j$ with the reform dummy to allow competition to have different effects on prices before and after the reform and in addition, we permit these effects to differ for each firm type by interacting them with the firm type dummy variables. The term $\mu_j$ lumps together all product-specific time-invariant characteristics of product $j$. Since all drug characteristics — strength, active ingredient, package size and substitution group — are time-invariant, we do not need to additionally account for them. Finally, we include a full set of time dummy variable $\nu_t$ and the term $\epsilon_{jt}$ is an iid Normal distributed error term.

## 4.5 Results

This section reports our empirical findings from a change in the design of reference pricing. The results are summarized separately for each therapeutic treatment. Table 4.3 presents the results for anti-cholesterol drugs, Table 4.4 the results for antiulcerants, and Table 4.5 the results for antibiotics.

**Empirical Finding 9 (Price Effect)** *A switch from external to internal reference pricing yields a substantial reduction in pharmacy purchase prices. The effects are stronger for chronic conditions than for acute conditions.*

Importantly, the effects of the reform are stronger the more severe the condition is. We find that prices decrease by 47 percent ($= \exp(-0.633) - 1$) for statins, by 22.9 percent for anti-ulcerants and 5.3 percent for antibiotics. These are the results from a specification that includes only a dummy variable for the reform and product-specific fixed effects (see Specification (1) in all tables). This pattern is robust to the inclusion of more explanatory variables. These results support the view that consumers with a chronic condition are more price sensitive than those with an acute condition and as expected, the reaction to the reform in chronic groups is stronger.

We additionally study differences in reform effects for each type of firm. In Specification (2) we introduce two variables that measure the effect of the reform on original products and the effect of the reform on parallel imports. Generics constitute the base category and the coefficient on the reform dummy corresponds to the reform effect on generics.

**Empirical Finding 10 (Effects by Type of Firm)** *A switch from external to internal reference pricing affects generic firms and parallel importers stronger than original firms.*

The effects on generics and parallel imports is stronger than for original products in all therapeutic groups. Specially in the group of statins, where the negative effect on original products (-0.23 = $\exp(-0.907+0.648)-1$) is substantially lower than the effects on generics

(-59.6 percent) or parallel imports (-60 percent). Furthermore, in all therapeutic groups, the differences in effects between generics and parallel imports are small and not statistically significant. Contrary to our findings, Pavcnik (2002), Granlund (2010), and Brekke et al. (2011) find stronger price decreases for original products. However, these studies analyze the introduction of reference pricing, while in our setting, a policy of reference pricing was already in place and we expect patients to be already more price sensitive.

Next, we use the number of products in a substitution group as a measure for competitiveness and allow it to affect prices differently before and after the reform.

**Empirical Finding 11 (Effects of competition)** *A switch from external to internal reference pricing reinforces the effects of competition. Specially for generic products and chronic conditions.*

The results correspond to Specification (3) and indicate that it is ambiguous how more products in a substitution group affect prices. The effects for statins is almost zero, for antiulcerants is negative, while the effect for antibiotics is positive. However, we show that the reform reinforces the expected effect of competition and this result is consistent in all three markets. The coefficient of *Reform* $\times$ *# of products in substitution group* is negative and significant for all therapeutic groups, suggesting that more competition after the reform is associated with lower prices. This result also holds if we further allow the reform effects to be different for products from different types of firms (Specification (4)). These findings reflect the differences in the structure of the therapeutical markets. Products in the same substitution group are closer substitutes to each other, than products outside the substitution group. While for antibiotics there are many substitution groups each with few products, the structure for statins is the opposite: few substitution groups each with more products (as reported in Table 4.2). The reform reinforces the effects of competition more for chronic conditions, where there are many substitution options, than for acute conditions, where there are fewer substitution options. Furthermore, in Specification (5)

we allow competition to have a different effect, not only before and after the reform, but also for different types of firms. The results suggest that the reform reinforces competition effects particularly for generic products.[2]

To summarize our results, we find that the switch from external to internal reference pricing has effectively impacted pharmacy purchase prices negatively, mostly so for chronic conditions than for acute conditions. We also show that the reform affected prices for generics and parallel imports more than for original products. Finally, competition plays an important role and we show that the change in the design of reference pricing reinforced competitive pressure, inducing strongest price changes for markets with many substitute products.

## 4.6 Conclusion

While it is undisputed that reference pricing effectively brings down prices of pharmaceutical products, much less is known how a reference price system should ideally be designed. We focus our analysis on one particularly question: should reference prices be externally determined or internally determined? To provide an answer, we use a Danish reform for reimbursement of expenditures for pharmaceuticals.

As Pavcnik (2002) we estimated reduced-form pricing equations where we linked the reform to pharmaceutical purchase prices for three types of therapeutic groups that differ in the severity of the condition: anti-cholesterol drugs, that treat a chronic condition, antiulcerants, that treat a semi-chronic condition, and antibiotics for the treatment of an acute condition. We allow for different effects in these groups because consumers differ in their price sensitivity by the type of condition. Consumers with a more prevalent disease face regular and higher expenditures, thus we expect them to be better informed with regard to their substitution alternatives, than consumers that are treated occasionally and

[2]Appendix B presents the results from specification (5) separately for each type of firm, in each therapeutic group.

for a short period of time, as is usually the case of antibiotics.

We find that the switch from external to internal reference prices substantially reduced pharmacy purchase prices. The effects are stronger for chronic conditions and for generics products and parallel imports. Furthermore, the reform reinforces the effects of competition.

# References


Aronsson, Thomas, Bergman, Mats A. and Niklas Rudholm (2001), The Impact of Generic Drug Competition on Brand Name Market Shares – Evidence from Micro Data, *Review of Industrial Organization*, 19 (4), 423-433.

Berndt, Ernst and Pierre Dubois (2012), Impacts of Patent Expiry and Regulatory Policies on Daily Cost of Pharmaceutical Treatments: OECD Countries, 2004-2010, IDEI Working Paper 702.

Brekke, Kurt R., Grasdal, Astrid L., and Tor H. Holmås (2009), Regulation and Pricing of Pharmaceuticals: Reference Pricing or Price Cap Regulation, *European Economic Review*, 53 (2), 170-185.

Brekke, Kurt R., Holmås, Tor H., and Odd Rune Straume (2011), Reference Pricing, Competition, and Pharmaceutical Expenditures: Theory and Evidence from a Natural Experiment, *Journal of Public Economics*, 95 (7-8), 624-638.

Brekke, Kurt R., Königbauer, Ingrid, and Odd Rune Straume (2007), Reference Pricing of Pharmaceuticals, *Journal of Health Economics*, 26 (3), 613-642.

Caves, Richard E. , Whinston, Michael D., and Mark A. Hurwitz (1991), Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry. *Brookings Papers on Economic Activity, Microeconomics*, 1, 1-48.

Coscelli, Andrea (2000), The Importance of Doctors' and Patients' Preferences in the Prescription Decision, *Journal of Industrial Economics*, 48 (3), 349-369.

Danzon, Patricia M. and Hong Liu (1998), Reference Pricing and Physician Drug Budgets: The German Experience in Controlling Pharmaceutical Expenditures. Working paper, The Wharton School, University of Pennsylvania.

Espín, Jaime, Rovira, Joan, and Antonio Olry de Labry (2011), WHO/HAI Project on Medicine Prices and Availability, Review Series on Pharmaceutical Pricing Policies and Interventions, Working Paper 1: External Reference Pricing;
URL: http://www.haiweb.org/medicineprices/24072012/ERPfinalMay2011.pdf

Frank, Richard G. and David S. Salkever (1997), Generic Entry and the Pricing of Pharmaceutical, *Journal of Economics and Management Strategy*, 6 (1), 75-90.

Grabowski, Henry G. and John M. Vernon (1992), Brand Loyalty, Entry, and Price Competition in Pharmaceuticals after the 1984 Drug Act, *Journal of Law and Economics*, 35, 331-350.

Granlund, David (2010), Price and Welfare Effects of a Pharmaceutical Substitution Reform, *Journal of Health Economics*, 29 (6), 856-865.

Kaiser, Ulrich, Mendez, Susan J., Rønde, Thomas, and Hannes Ullrich (2013), Regulation of Pharmaceutical Prices: Evidence from a Reference Price Reform in Denmark, IZA Discussion Paper No. 7248.

Kanavos, Panos, Costa-Font, Joan, and Elizabeth Seeley (2008), Competition in Off-Patent Drug Markets: Issues, Regulation and Evidence, *Economic Policy*, 23 (55), 499-544.

López-Casasnovas, Guillem and Jaume Puig-Junoy (2000), Review of the Literature on Reference Pricing, Universitat Pompeu Fabra, mimeo.

Pavcnik, Nina (2002), Do Pharmaceutical Prices Respond to Potential Patient Out-of-pocket Expenses?, *The RAND Journal of Economics*, 33 (3), 469-487.

Puig-Junoy, Jaume (2007), The Impact of Generic Reference Pricing Interventions in the Statin Market, *Health Policy*, 84, 14-29.

Table 4.1: **Market Overview**

| Variable | Type of treatment | 2002 | 2003 | 2004 | 2005 | 2006 |
|---|---|---|---|---|---|---|
| Turnover in DKK 1,000 | Anti-cholesterol | 489,240 | 457,672 | 334,291 | 280,264 | 301,282 |
| | Antiulcerants | 613,756 | 613,876 | 618,724 | 622,886 | 596,833 |
| | Antibiotics | 338,624 | 331,975 | 338,262 | 352,013 | 376,395 |
| Reimbursement in DKK 1,000 | Anti-cholesterol | 362,503 | 326,350 | 224,843 | 189,755 | 208,073 |
| | Antiulcerants | 389,119 | 376,426 | 368,650 | 381,571 | 362,280 |
| | Antibiotics | 137,805 | 138,012 | 142,850 | 149,669 | 169,837 |
| Number of patients in treatment | Anti-cholesterol | 138,464 | 189,821 | 250,111 | 307,080 | 374,839 |
| | Antiulcerants | 327,317 | 341,323 | 358,808 | 379,164 | 407,389 |
| | Antibiotics | 1,621,397 | 1,625,345 | 1,636,340 | 1,666,884 | 1,684,154 |
| Sales in DDD/1,000 inhabitants/day | Anti-cholesterol | 15.6 | 23.9 | 34.9 | 46.7 | 60.8 |
| | Antiulcerants | 31.8 | 33.1 | 35.1 | 37.6 | 40.8 |
| | Antibiotics | 13.4 | 13.7 | 14.2 | 14.9 | 15.3 |

**Source:** *www.medstat.dk*

Table 4.2: **Summary statistics**

| Type of treatment | Variable | Base period | | Implementation period | |
|---|---|---|---|---|---|
| | | Mean | Std. Dev. | Mean | Std. Dev. |
| Anti-cholesterol | Pharmacy purchase price $p^f$ | 6.20 | 4.48 | 3.88 | 4.27 |
| | Reference price $p^r$ | 7.37 | 5.50 | 4.31 | 5.29 |
| | Number of products | 127.19 | 4.11 | 127.06 | 14.53 |
| | Number of firms | 19.01 | 0.45 | 22.27 | 2.31 |
| | Number of substitution groups | 39.92 | 0.62 | 39.04 | 0.92 |
| | Products in substitution group | 6.95 | 4.55 | 5.01 | 2.55 |
| | Original product (=1 if original) | 0.29 | 0.45 | 0.27 | 0.44 |
| | Generic product (=1 if generic) | 0.43 | 0.50 | 0.56 | 0.50 |
| | Parallel import (=1 if parallel import) | 0.28 | 0.45 | 0.17 | 0.38 |
| | Total Observations | 2,541 | | 4,759 | |
| Antiulcerants | Pharmacy purchase price $p^f$ | 7.61 | 11.02 | 7.86 | 11.68 |
| | Reference price $p^r$ | 12.1 | 19.41 | 11.91 | 20 |
| | Number of products | 143.16 | 2.99 | 152.98 | 14.77 |
| | Number of firms | 22.66 | 0.47 | 21.44 | 0.91 |
| | Number of substitution groups | 69 | 0.77 | 63.26 | 1.07 |
| | Products in substitution group | 3.57 | 2.55 | 3.61 | 1.90 |
| | Original product (=1 if original) | 0.31 | 0.46 | 0.20 | 0.40 |
| | Generic product (=1 if generic) | 0.58 | 0.49 | 0.59 | 0.49 |
| | Parallel import (=1 if parallel import) | 0.12 | 0.32 | 0.21 | 0.41 |
| | Total Observations | 2,862 | | 5,909 | |
| Antibiotics | Pharmacy purchase price $p^f$ | 18.78 | 74.22 | 19.04 | 76.03 |
| | Reference price $p^r$ | 30.03 | 106.35 | 29.53 | 105.42 |
| | Number of products | 141.05 | 2.68 | 117.71 | 3.44 |
| | Number of firms | 14.97 | 1.11 | 13.07 | 0.35 |
| | Number of substitution groups | 96.53 | 1.97 | 86.70 | 1.56 |
| | Products in substitution group | 2.07 | 1.31 | 1.81 | 1.09 |
| | Original product (=1 if original) | 0.62 | 0.49 | 0.61 | 0.49 |
| | Generic product (=1 if generic) | 0.37 | 0.48 | 0.37 | 0.48 |
| | Parallel import (=1 if parallel import) | 0.01 | 0.12 | 0.02 | 0.13 |
| | Total Observations | 2,820 | | 4,587 | |

Notes: Table 4.2 reports summary statistics for all variables in each therapeutic group. Prices are fortnightly averages for a defined daily dose in Danish krones. All figures deflated using consumer prices index with June 2005 as basis.DDD

Table 4.3: **Estimation Results – Anti-Cholesterol**

| | (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|---|
| Reform | -0.633*** | -0.907*** | -0.316*** | -0.848*** | -0.828*** |
| | (0.053) | (0.052) | (0.055) | (0.059) | (0.065) |
| Reform × Original | | 0.648*** | | 0.624*** | 0.557*** |
| | | (0.024) | | (0.029) | (0.052) |
| Reform × PI | | -0.013 | | -0.008 | 0.111 |
| | | (0.035) | | (0.036) | (0.080) |
| # Products in subs. group | | | 0.001 | -0.031*** | -0.032*** |
| | | | (0.004) | (0.004) | (0.004) |
| Reform × # Products in subs. group | | | -0.079*** | -0.038*** | -0.042*** |
| | | | (0.004) | (0.004) | (0.006) |
| Reform × # Products in subs. group × Original | | | | | 0.016* |
| | | | | | (0.009) |
| Reform × # Products in subs. group × PI | | | | | -0.024* |
| | | | | | (0.013) |
| N=7,300 | | | | | |
| $R^2$ | 0.202 | 0.285 | 0.246 | 0.300 | 0.301 |

Notes: Table 4.3 reports linear regression estimates of the coefficients in our pricing equation for the therapeutic market of anti-cholesterol products. The variable *PI* stands for parallel import, the variable *Original* stands for original product. Robust standard errors in parentheses. The estimation sample contains only the base and the implementation period. Statistical significance: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Table 4.4: **Estimation Results – Antiulcerants**

| | (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|---|
| Reform | -0.260*** | -0.253*** | -0.237*** | -0.251*** | -0.160*** |
| | (0.026) | (0.027) | (0.027) | (0.028) | (0.028) |
| Reform × Original | | -0.008 | | 0.036*** | -0.174*** |
| | | (0.013) | | (0.014) | (0.022) |
| Reform × PI | | -0.030* | | 0.034* | -0.263*** |
| | | (0.017) | | (0.018) | (0.042) |
| # Products in subs. group | | | -0.031*** | -0.033*** | -0.046*** |
| | | | (0.003) | (0.003) | (0.003) |
| Reform × # Products in subs. group | | | -0.006*** | -0.007** | -0.046*** |
| | | | (0.003) | (0.003) | (0.004) |
| Reform × # Products in subs. group × Original | | | | | 0.079*** |
| | | | | | (0.006) |
| Reform × # Products in subs. group × PI | | | | | 0.079*** |
| | | | | | (0.009) |
| N=8,771 | | | | | |
| $R^2$ | 0.102 | 0.102 | 0.120 | 0.121 | 0.138 |

Notes: Table 4.4 reports linear regression estimates of the coefficients in our pricing equation for the therapeutic market for antiulcerants. PI stands for parallel import, Original stands for original products. Robust standard errors in parentheses. The estimation sample contains only the base and the implementation period. Statistical significance: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Table 4.5: **Estimation Results – Antibiotics**

| | (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|---|
| Reform | -0.055*** | -0.071*** | -0.006 | -0.010 | -0.000 |
| | (0.009) | (0.009) | (0.009) | (0.010) | (0.010) |
| Reform × Original | | 0.025*** | | 0.006 | -0.009 |
| | | (0.004) | | (0.004) | (0.007) |
| Reform × PI | | -0.019 | | 0.024* | 0.009 |
| | | (0.014) | | (0.014) | (0.080) |
| # Products in subs. group | | | 0.018*** | 0.017*** | 0.017*** |
| | | | (0.003) | (0.003) | (0.003) |
| Reform × # Products in subs. group | | | -0.027*** | -0.027*** | -0.031*** |
| | | | (0.002) | (0.002) | (0.003) |
| Reform × # Products in subs. group × Original | | | | | 0.008** |
| | | | | | (0.003) |
| Reform × # Products in subs. group × PI | | | | | 0.006 |
| | | | | | (0.021) |
| N=7,407 | | | | | |
| $R^2$ | 0.065 | 0.072 | 0.108 | 0.108 | 0.109 |

Notes: Table 4.5 reports linear regression estimates of the coefficients in our pricing equation for the therapeutic market for antibiotics. PI stands for parallel import, Original stands for original products. Robust standard errors in parentheses. The estimation sample contains only the base and the implementation period. Statistical significance: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

# A. Characterization of Products in Terms of Their ATC Code

| Type of treatment | ATC 4-Level | ATC 5-Level | Molecule name |
|---|---|---|---|
| Anti-cholesterol | C10AA HMG CoA reductase inhibitors (Statins) | C10AA01 | Simvastatin |
| | | C10AA02 | Lovastatin |
| | | C10AA03 | Pravastatin |
| | | C10AA04 | Fluvastatin |
| | | C10AA05 | Atorvastatin |
| | | C10AA07 | Rosuvastatin |
| Antiulcerants | A02BA H2-receptor antagonists | A02BA01 | Cimetidine |
| | | A02BA02 | Ranitidine |
| | | A02BA03 | Famotidine |
| | | A02BA04 | Nizatidine |
| | A02BC Proton pump inhibitors | A02BC01 | Omeprazole |
| | | A02BC02 | Pantoprazole |
| | | A02BC03 | Lansoprazole |
| | | A02BC04 | Rabeprazole |
| | | A02BC05 | Esomeprazole |
| Antibiotics | J01CA Penicillins with extended spectrum | J01CA01 | Ampicillin |
| | | J01CA02 | Pivampicillin |
| | | J01CA04 | Amoxicillin |
| | | J01CA08 | Pivmecillinam |
| | | J01CA11 | Mecillinam |
| | | J01CA12 | Piperacillin |
| | J01CE Beta-lactamase-sensitive penicillins | J01CE01 | Benzylpenicillin |
| | | J01CE02 | Phenoxymethylpenicillin |
| | J01CF Beta-lactamase resistant penicillins | J01CF01 | Dicloxacillin |
| | | J01CF05 | Flucloxacillin |
| | J01CR Combinations of penicillins | J01CR02 | Amoxicillin and enzyme inhibitor |
| | | J01CR05 | Piperacillin and enzyme inhibitor |

Notes: Table A displays a detailed classification of the products considered in the analysis in terms of their Anatomical Therapeutical Chemical classification code and the average number of products for a period of 14-days in each molecule group for the base and the implementation period. Source for classification: WHO Collaborating Centre for Drug Statistics Methodology.

# B. Estimation Results by Product Type

| | Original Products | Generic Products | Parallel Imports |
|---|---|---|---|
| A. *Anti-cholesterol* | | | |
| Reform | -0.071*** | -0.952*** | -0.821*** |
| | (0.021) | (0.112) | (0.095) |
| # Products in subs. group | 0.018*** | -0.077*** | -0.028*** |
| | (0.001) | (0.008) | (0.008) |
| Reform × # Products in subs. group | -0.014*** | -0.054*** | -0.101*** |
| | (0.001) | (0.008) | (0.009) |
| Const | 2.003*** | 1.626*** | 2.265*** |
| | (0.014) | (0.108) | (0.065) |
| $N$ | 2024 | 3760 | 1516 |
| $R^2$ | 0.226 | 0.312 | 0.554 |
| B. *Antiulcerants* | | | |
| Reform | -0.153*** | -0.289*** | -0.210*** |
| | (0.012) | (0.044) | (0.017) |
| # Products in subs. group | 0.005*** | -0.088*** | 0.003* |
| | (0.001) | (0.005) | (0.002) |
| Reform × # Products in subs. group | 0.008*** | -0.043*** | 0.008*** |
| | (0.001) | (0.005) | (0.002) |
| Const | 2.356*** | 1.388*** | 2.352*** |
| | (0.008) | (0.036) | (0.014) |
| $N$ | 2032 | 5136 | 1603 |
| $R^2$ | 0.392 | 0.204 | 0.531 |
| C. *Antibiotics* | | | |
| Reform | -0.017* | 0.007 | . |
| | (0.009) | (0.019) | . |
| # Products in subs. group | 0.031*** | 0.004 | 0.006 |
| | (0.004) | (0.006) | -0.011 |
| Reform × # Products in subs. group | -0.022*** | -0.031*** | -0.013** |
| | (0.002) | (0.003) | -0.005 |
| Const | 0.812*** | -1.042*** | 1.637*** |
| | (0.009) | (0.018) | -0.041 |
| $N$ | 4536 | 2749 | 122 |
| $R^2$ | 0.116 | 0.109 | 0.876 |

Notes: Table B reports linear regression estimates of the coefficients in our pricing equation and summarizes the results by the therapeutic market. Robust standard errors in parentheses. The estimation sample contains only the base and the implementation period. Statistical significance: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

# Curriculum Vitae

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