Parallel Imports and Mandatory Substitution Reform

*A Kick or A Muff for Price Competition in Pharmaceuticals?**

David Granlund[1] and Miyase Yesim Köksal[2]

April 2011

Abstract

What has been the effect of competition from parallel imports on prices of locally-sourced on-patent drugs? Did the 2002 Swedish mandatory substitution reform increase this competition? To answer these questions, we carried out difference-in-differences estimation on monthly data for a panel of all on-patent prescription drugs sold in Sweden during the 40 months from January 2001 through April 2004. On average, facing competition from parallel imports caused a 15-17% fall in price. While the reform increased the effect of competition from parallel imports, it was only by 0.9%. The reform, however, did increase the effect of therapeutic competition by 1.6%.

JEL Classification: I11, L51, L65.

Keywords: parallel imports; pharmaceutical drugs; price competition; reference pricing; therapeutic competition.

*The authors would like to thank Douglas Lundin, Niklas Rudholm, Johan Stennek, Måns Söderbom, Joakim Westerlund and seminar participants at the Economics Department of the University of Gothenburg and at the Third Swedish Workshop on Competition Research for helpful comments and suggestions. We are grateful to IMS Sweden for providing the dataset and to the Swedish Competition Authority for a research grant that supported the work.

[1] Corresponding author. The Swedish Retail Institute (HUI), SE-103 29 Stockholm, Sweden; and Department of Economics, Umeå. University, SE-901 87 Umeå, Sweden. E-mail: david.granlund@econ.umu.se, Tel.: 46 90 786 99 40, Fax: 46 90 786 99 95.

[2]Department of Economics, School of Business, Economics and Law, University of Gothenburg, SE-405 30 Gothenburg, Sweden. E-mail: Miyase.Yesim@economics.gu.se

Introduction

During the period 1998-2008, average annual real growth in pharmaceutical spending has exceeded that in overall health spending in the EU. Spending on pharmaceuticals averaged 4.7% growth per year, while overall health spending grew 4% (OECD, 2010). Pharmaceutical spending accounted for 1.7% of GDP on average across the EU countries in 2008.[1] The largest part of pharmaceutical spending, about 50%, is for on-patent locally-sourced drugs, i.e. drugs with patent protection that are directly supplied by the manufacturer via authorized wholesalers. Until the patent expires and generics enter the market – unless parallel trade is allowed – these drugs are only subject to competition from therapeutic alternatives. We here analyze the price-effects of competition for these drugs, focusing on competition from parallel imports and the effects of a mandatory substitution reform on the intensity of such competition.

Parallel imported drugs are legally produced goods bought in low price countries for resale in high price countries without the authorization of the patent holder. They have the same active ingredient in the same amount and the same dosage form (e.g., tablet or capsule) as the locally-sourced drugs. However, they might differ in packaging as, depending on the requirement of the importing country, they might be repackaged or relabeled, and the brand name might even differ slightly. Parallel trade of pharmaceuticals is legally allowed within the EU towards fulfilling the objective of creating a single market. But, in the United States, for example, allowing parallel trade of pharmaceuticals has for many years, since the Clinton administration, been a hot topic in debate on rising pharmaceutical costs. Advocates have claimed that allowing parallel imports from Canada, for example, would reduce the pharmaceutical costs substantially, while opponents have stated that the safety of parallel imported drugs cannot be guaranteed (Pecorino, 2002).

Medical insurance is likely to reduce the price competition in pharmaceuticals by making consumers' less price sensitive. To counteract this, substitution policies, giving the right to or obliging the pharmacists to substitute the prescribed drug with a cheaper alternative, have been introduced in many European countries and American states. These are intended to make

[1] The share of pharmaceutical spending in GDP ranged from below 1% in Luxembourg, Norway, and Denmark, to more than 2% in Lithuania, Greece, Bulgaria, Hungary, Portugal, and the Slovak Republic. The share in Sweden was 1.2%.

consumers react more to prices, decreasing cost both directly, as prescribed drugs are replaced with cheaper versions, and indirectly, through increased price competition. Sweden introduced a mandatory substitution reform in October 2002, requiring pharmacists to dispense, with the consent of the consumer, the cheapest available generic or parallel-imported drug, unless the prescribing physician opposed substitution for medical reasons. The reform brought in a special form of "reference pricing", whereby drugs with the same active substance – e.g., an off-patent drug and its generics, or an on-patent drug and its parallel imported versions – are grouped together and the price of the cheapest drug in each group is set as the reference price for reimbursement. Maximum reimbursement is fixed at a percentage of that price, but the amount consumers actually pay depends on which drug they buy. Consumers who choose a drug with the reference price pay only a certain "deductible", while consumers who choose a drug with a higher price still pay that deductible but, in addition, also pay the full price difference.

The 2002 reform changed the Swedish reference price system which had been introduced in January 1993. Before 2002, the reference price system only covered off-patent drugs and their generics with the reference price set at 110% of the price of the cheapest available substitute. The reform, however, required substitution not only between off-patent drugs and their generics but also between on-patent drugs and their parallel imported versions, and set the reference price at 100% of the price of the cheapest available substitute. The reform also made it mandatory for pharmacists – who otherwise have no incentive for substitution – to dispense the cheapest available substitute.[2] The new system thus both increased consumers' information about available alternative drugs and their prices and also exposed them more to the prices.

Such conditional reimbursement is expected to increase consumer price sensitivity and thus competition as well. This is consistent with both theoretical results (Mestre-Ferrandiz, 2003; Brekke et al., 2007, and Miraldo, 2009) and empirical results (Pavcnik, 2002; Aronsson, Bergman, and Rudholm, 2001; Bergman and Rudholm, 2003; Brekke et al., 2009; Granlund, 2010; Granlund and Rudholm, 2011) that reference pricing type policies promote substitution

[2] For example, the UK, Netherlands and Norway provide financial incentives for pharmacists to dispense parallel imported drugs (Kyle, 2009). However, other than an annual ex post payment by the county councils, responsible for reimbursement, to the Swedish pharmacy state monopoly (the National Corporation of Swedish Pharmacies, Apoteket AB) to compensate it for purchasing and dispensing parallel imports and generics, there are no explicit financial incentives to Swedish pharmacies to dispense parallel imports (Kanavos et al., 2005).

and increase price competition between brand-name drugs and their generics. Regarding substitution reforms in general, Buzzelli et al. (2006) estimated that they lowered pharmaceutical prices by 3% on average across 16 OECD countries. In country specific analyses, Granlund (2010) and Granlund and Rudholm (2011) estimated that the Swedish mandatory substitution reform reduced average unweighted prices by 4%, and average weighted prices by 10%.

Despite the attention that substitution reforms and reference pricing have received, there have been, to the best of our knowledge, no empirical studies on how they affect competition from parallel imports. This paper attempts to fill this gap. There is, however, a theoretical paper by Köksal (2009) showing that reference pricing should increase price competition from parallel imports. The theoretical literature regarding parallel trade also includes Pecorino (2002), Ganslandt and Maskus (2004), Maskus and Chen (2004), Jelovac and Bordoy (2005), and Chen and Maskus (2005), which show, among other things, that parallel imports should create price competition and cause prices to fall in the destination country. The empirical literature about the effects of competition from parallel imports is limited to Ganslandt and Maskus (2004), Kanavos and Costa-Font (2005), and Kyle (2010), none of which addressed reference pricing or substitution reforms in general.

Ganslandt and Maskus (2004) used Swedish data from 1994-1999 to study the effect of competition from parallel imports on the prices of the 50 molecules with largest sales values. Using instrumental variable method to account for potential endogeneity in the entry decisions of parallel traders, they found that competition from parallel imports reduced prices by 12-19%. Using OLS, they found that competition from three or more parallel traders was associated with 5% lower prices, while no statistically significant association was found between prices and competition from only one or two parallel traders. Using data on 30 countries, Kyle (2010) examined the effect of both potential and actual entry of parallel imports on prices of locally-sourced drugs, and reported results consistent with the OLS results of Ganslandt and Maskus (2004). On the other hand, Kanavos and Costa-Font (2005) estimated the effect of the market share of parallel imports on price competition and found no statistically significant effect.

The analyses in this paper were carried out using a product level panel dataset covering all on-patent prescription drugs sold in Sweden during January 2001 through April 2004. To identify

the effects of competition from parallel imports and how these effects were influenced by the mandatory substitution reform, following Pavcnik (2002) and Brekke et al. (2009), we used difference-in-differences estimation. Following Ganslandt and Maskus (2004), we also used instrumental variable estimation to address potential endogeneity in the entry decisions of parallel traders.

This study adds to the limited knowledge of competition from parallel imports by analyzing how the price effects of competition from parallel imports is affected by a mandatory substitution reform as well as how it depends on the length of time the parallel imports have been available in the market. The dataset also allowed us to control for competition from therapeutic alternatives – drugs with different active ingredients but similar therapeutic effects in treating a particular disease – including indirect generic competition from off-patent therapeutic alternatives themselves facing generic competition.

The present study thus complements Ganslandt and Maskus (2004) by controlling for both "therapeutic competition" (inter-brand competition) and "indirect generic competition" (intra-brand competition), as well as by analyzing a period when parallel trade had been legal in Sweden for many years (it became legal when Sweden joined the EU in 1995) and investigating a somewhat different segment of the market. We restricted our attention to on-patent drugs, but not just to big sellers. Like Ganslandt and Maskus (2004), we confined our analyses to the price-effects of facing competition from parallel imports; that is, for example, we did not analyze entry and exit decisions of parallel traders, or how those decisions might have been affected by the mandatory substitution reform.

We found that facing competition from parallel imports caused prices of locally-sourced drugs to fall on average with 15-17%. The mandatory substitution reform increased this effect causing prices to fall further, but only by one percentage point. The full effect of competition from parallel imports was not realized immediately, but instead prices kept decreasing over time.

Our analysis has implications for the effect of reform on therapeutic competition as well. We found that the prices of drugs facing therapeutic competition would have been 1.5% less on average than if they had not faced such competition. The mandatory substitution reform

increased the effect of therapeutic competition by 1.6 percentage points. The effect of therapeutic competition depended on whether the therapeutic alternatives were subject to generic competition. Facing therapeutic competition led to a statistically significant fall in prices if the therapeutic alternatives were themselves subject to generic competition. The mandatory substitution reform increased this fall, indicating that the reform increased the effects of generic competition.

The next section presents the institutional structure of the Swedish pharmaceutical market, focusing first on reimbursement for prescription drugs and the implications of mandatory substitution reform in this regard, and then on price setting and distribution of pharmaceuticals. The following two sections first provide a theoretical framework, and then an overview of the dataset including descriptive statistics. A section then explains the empirical strategy based on which the econometric analysis is carried out, followed by a section which reports and discusses the estimation results. Finally, the last section summarizes and concludes the paper.

The Institutional Structure of the Swedish Pharmaceutical Market

Reimbursement and Mandatory Substitution Reform

Statutory health insurance has covered the whole Swedish population and also subsidized a large part of pharmaceutical costs ever since pharmaceutical benefits scheme was introduced in 1955.[3] The subsidy for prescription drugs increases stepwise over any 12-month period. Since June 1999, consumers pay 100% of the cost up to SEK 900; 50% of the cost from SEK 900 to 1700; 25% from SEK 1700 to 3300; 10% from SEK 3300 to 4300; and then are fully subsidized during the remainder of the 12-month period. During the study period, about 70% of total pharmaceutical costs were borne publicly, specifically by the 21 county councils (Köping Höggård and Redman, 2007; National Board on Health and Welfare, 2006). The county councils – also responsible for providing health care – are required to have at least one "drug and therapeutic committee", the purpose of which is to promote safe and cost effective use of

[3] This section refers to law SFS (1981:49) on control of pharmaceutical costs and subsequent changes in this law, listed at www.notisum.se/rnp/sls/fakta/a9810049.htm, accessed 30 October 2008.

pharmaceuticals, e.g., by writing recommendations to physicians regarding choices of pharmaceuticals (Anell and Persson, 2005).

Reference pricing was introduced as reimbursement scheme in Sweden in 1993. Each off-patent drug and its generics were grouped together, with substitution allowed only within groups. A reference price was set for each group at 110% of the price of the cheapest available drug within the group, usually a generic. Costs exceeding the reference price were not included in the maximum annual copayment limit (RFFS 1992:20, 1996:31). Thus consumers who bought an expensive drug had to pay the entire difference between it and the reference price, in addition to a certain percentage (the coinsurance rate) of the reference price.

This reference price system was reformed with the introduction of mandatory substitution in October 2002. The rule for setting the reference price was changed so that it now was set at 100% of the price of the cheapest available drug within the group. Still drugs with the same active ingredient are grouped together, but since October 2002 on-patent drugs and their parallel imported versions are also part of the reference price system (SOU 2000:86, Medical Products Agency, 2002).[4,5] The reform made substitution compulsory within the group of interchangeable drugs, requiring pharmacists to inform consumers of such drugs and to dispense the cheapest available generic instead of the off-patent brand-name drug, or the parallel import instead of the on-patent brand-name drug (with the consent of the consumer) unless the prescribing physician prohibited the substitution for medical reasons.[6] The pharmacist must also inform consumers that they can buy the more expensive prescribed drug instead of the cheapest substitute if they pay

[4] Läkemedelsverket – The Medical Products Agency (MPA) – defines a product as a substitute if it has the same active substance, strength, and form (e.g., pills or fluid) as the prescribed product, and if its package size is approximately the same as that of the prescribed one.

[5] Parallel imported drugs are covered within the reference pricing system only in Sweden and Denmark (see Lopez-Casasnovas and Puig-Junoy (2000) for an extensive review on reference pricing).

[6] If the physician prohibits the substitution for medical reasons, the consumer is still reimbursed based on the full price of the more expensive prescribed drug. Physicians only prohibited substitution for 3% of the prescriptions during October 2002 to December 2003 (National Corporation of Swedish Pharmacies et al., 2004). The corresponding figure for January 2003 to October 2006 for physicians in the county of Västerbotten was 2%(Granlund, 2009). Andersson et al. (2005) reports that during the one-year period from October 2002 to October 2003 physicians in Västra Götaland region prohibited substitution in 1-8% of prescriptions for selected indicator drugs.

the difference. The reform clearly makes pharmacists substitute the available cheapest alternative within the reference price system where there had previously been no incentive for pharmacists to initiate substitution. Before the reform, Apoteket AB – the National Corporation of Swedish Pharmacies – recommended that pharmacists dispense parallel imported drugs only if the responsible drug and therapeutic committee had not recommended differently and if the prescribing physician had only written the name of the drug and thus had not specified either a locally-sourced package or a parallel import; and those committees only recommended dispensing parallel imports that had a record of reliable supply (Persson, Anell and Persson, 2001).

Three characteristics of the mandatory substitution reform may have contributed to making consumers more price sensitive, resulting in increased substitution and hence lower pharmaceutical prices. The reform lowered the transaction cost of substitution, since previously it had been recommended that physicians be contacted first if they had not explicitly consented to substitution on the prescription. Then, when substitution is offered (as it always should be after the reform), consumers gain information about the availability of cheaper substitutes, which might enhance their willingness to switch. Finally, only costs up to 100% of the cheapest substitutable product are now covered, compared with 110% previously.

Price Setting and Distribution

Pharmaceutical manufacturers and parallel traders need approval from Läkemedelsverket – the Medical Products Agency (MPA) – to sell their products in Sweden.[7] Manufacturers are free to set their own prices, but in order to be included in the pharmaceutical benefits scheme they must then be approved by Läkemedelsförmånsnämnden (LFN) – the Pharmaceutical Benefits Agency – which replaced the National Social Insurance Board as part of the mandatory substitution

[7] The Medical Products Agency has as objective to send a first response to firms applying for approval for parallel import of pharmaceuticals within 120 days from when all necessary pharmaceutical information is received from the authorities in the source country (http://www.lakemedelsverket.se, accessed 101020).

reform in 2002.[8] Before that, prices had been negotiated between the manufacturer and the authority, but on the grounds of efficiency in the market the authority abolished negotiations and started to consider price setting as an integrated part of cost-effectiveness analysis.

Manufacturers can change price after the launch of a product in Sweden by getting approval from LFN.[9] During the study period, price comparisons played a crucial role in price-setting decisions. Both before and after the mandatory substitution reform, applications for price increases were required to include motivations for the price increase as well as information about the prices and treatment costs of comparable drugs (RFFS 1996:31, LFNFS 2003:1). An exception is if the requested price is the same as or less than the price of the most expensive substitutable product in the reference group: In this case no motivation is needed and the price increase is always accepted (LFNAR 2006:1). This is of little help for locally-sourced brand-name drugs, however, which are generally the most expensive in their reference group. In fact, price comparisons have probably made it harder for these drugs to get approval for price increases if they face competition. Even though a drug faces competition from parallel imports, the authority might still allow a price increase, since the supply of parallel imports is limited, and sometimes unreliable. If the drug would be removed from the market unless the price increase were approved and if supply of parallel imports was limited, patients would then face the risk of remaining untreated.

Unlike the regulations before the mandatory substitution reform (RFFS 1996:31), the regulations after the reform (LFNFS 2003:1) clearly state that the authority should consider marginal benefits and marginal costs of a drug when deciding whether or not to include it in the reimbursement scheme at the requested price. Hence competition between therapeutically equivalent drugs should be fiercer after the reform, not because of more price sensitive consumers – since the reform didn't allow substitution between therapeutic alternatives – but

[8] The name of the Pharmaceutical Benefits Agency (LFN) was changed to the Dental and Pharmaceutical Benefits Agency (TLV) on September 1, 2008, since a dental care reform went into effect in July, 2008 and a new Dental Care Benefits Board was established.

[9] The National Social Insurance Board was allowed 90 days (or under some circumstances 180 days) to decide whether to approve price changes (RFFS 1996:31). The Pharmaceutical Benefits Board is required to decide whether to approve price cuts as soon as possible, but is allowed 90 days (or under some circumstances 150 days) to handle applications for price increase (SFS 2002:687).

because of the requirement that marginal benefits and marginal costs should be considered to be included in the reimbursement system.

During the first few months of the study-period, the National Social Insurance Board applied a specific rule for pricing parallel imports, approving an application only if the price was at least 10% below that of the locally-sourced drug. After the EU Commission ruled this discriminatory, the Board changed this rule in the spring of 2001. However, both before and after this change, a large majority of the prices of parallel imports were set about 10% below the price of the locally-sourced drug (National Social Insurance Board, 2002).

Retail pharmacies are the only legal entities in Sweden to dispense prescription drugs for outpatient care. Throughout the study period, all pharmacies were owned by the government monopoly, Apoteket AB – the National Corporation of Swedish Pharmacies – which paid and charged uniform prices nationwide for each drug. In July 2009, the pharmacy market was deregulated and private pharmacies were allowed to enter, but still the retail prices of prescription drugs remain uniform across the country.

Theoretical Framework

There are few studies examining the effects of parallel trade on prices in pharmaceuticals. Ganslandt and Maskus (2004) show the price-effect of parallel trade by setting up a model where each parallel trader supplies a limited quantity of drugs to the destination country and where the parallel imports are assumed to be sold at lower prices than locally-sourced drugs to guarantee that the entire quantity of parallel imports is sold, while price in the source country is held fixed. In this model, the residual demand that a locally-sourced drug faces, and hence its price, fall with the number of parallel traders.

Ganslandt and Maskus provide convincing reasons why parallel traders will not supply unlimited amounts, e.g., that the amounts they can buy in the low price countries are limited.[10] Still, they show that, if parallel traders could supply an unlimited amount without affecting the margin

[10] Supply of pharmaceuticals in source countries is limited, so the marginal cost of supply is likely to increase more, and to vary more, for parallel traders than for generic producers.

between the price they pay and the price they charge, then potential competition would result in price convergence up to the cost of trade. Similarly, Pecorino (2002) argues that there is no reason for the law of one price not to hold for pharmaceuticals if parallel trade is allowed and trade cost is zero. Jelovac and Bordoy (2005) analyze the case where consumers consider parallel imports inferior to locally-sourced drugs, e.g., due to differences in packing. Allowing parallel trade again leads to price convergence with lower prices in the destination country, though prices do not fully converge because of the perceived inferiority of the parallel imports.[11]

Different from the above mentioned studies, Frank and Salkever (1992) model competition from generics. Parallel imports differ from generics in terms of supply conditions and variation in marginal cost, but their model is general enough to derive effects of competition from parallel imports as well as effects of mandatory substitution on competition. The model includes one brand name producer, *n* identical generic producers, and two types of consumers: price-insensitive loyal consumers, whose demand is unaffected by the price of generics; and cross-price sensitive consumers, whose demand is influenced by both the brand-name and generic prices. Frank and Salkever show that the brand-name price would fall with entry of generic producers, unless entry leads to a fall in both demand for the brand-name drug and the own-price elasticity of its demand. So, unless a fall in demand also leads to less price-sensitive marginal consumers, entry of generics is likely to reduce brand-name price. Frank and Salkever also show that, under reasonable conditions, an increase in the share of price-sensitive consumers will enhance the downward pressure exerted by entry of generics on brand-name prices. This result should also apply for the effect of entry of parallel imports on prices of locally-sourced drugs. Hence, as mandatory substitution is likely to make consumers more price sensitive, it is likely to enhance the downward pressure exerted on brand-name prices by competition from both generics and parallel imports.

Demand models, like that of Frank and Salkever (1992), have implications for therapeutic competition as well. If demand is sensitive to relative prices among therapeutic alternatives, the price of a drug whose therapeutic alternatives gain generic competition would also fall. Given that price is a positive function of demand, this would happen: (i) if the price of the brand-name

[11] Maskus and Chen (2004) and Chen and Maskus (2005) provide theoretical analyses of parallel trade in general, not focusing just on pharmaceuticals.

drug facing generic competition falls and brand name therapeutic alternatives are substitutes; (ii) if the generics are substitutes for therapeutically equivalent brand-name drugs. Also, entry of therapeutic alternatives should reduce the price of a drug if it reduces demand for that drug (and again, if price is a positive function of demand). Mandatory substitution reform, by making consumers more price sensitive, has increased price competition in Sweden and reduced the prices of both generics and brand-name drugs facing generic competition (Granlund and Rudholm, 2011). Therefore, given that demand is sensitive to relative prices among therapeutic alternatives, we expect the effect of therapeutic alternatives gaining generic competition to be larger after the substitution reform.

Köksal (2009) also strengthens our expectation that mandatory substitution increases competition from parallel imports. Based on the two-country model of Jelovac and Bordoy (2005), where consumers perceived parallel imports as inferior, she examined theoretically the extent to which healthcare reimbursement policies should affect the results of parallel trade. It is assumed that a monopoly manufacturer produces a patented drug and supplies the two countries. The manufacturer price differentiates since the two countries are assumed to differ in their consumers' valuations of the drug, as well as in the share of the price paid directly by the consumers. Given the price difference between the two countries, parallel traders – in a perfectly competitive market with no cost of trade – buy the drug in low price country and resell it in the high price country. Parallel trade then causes greater price reduction under reference pricing than under simple coinsurance at a constant rate regardless of the price of the drug chosen. As the 2002 reform aimed to strengthen the effect of reference pricing by making substitution mandatory for the pharmacist and increasing out-of-pocket costs for the consumer, we expect it to have increased the competition from parallel imports.

Overview of the Data

The study is based on a panel-data set covering all prescription drugs sold in Sweden during 1992-2007. An observation in the dataset represents a product with a certain active ingredient, strength, form, and package size, supplied by a certain firm and sold in a certain month (though

only quarterly data for 1992-1994). For each observation the dataset includes information about whether the product is brand-name or generic, locally-sourced or parallel imported, as well as total units sold and the total value. In order to efficiently isolate the effect of the 2002 mandatory substitution reform on competition from parallel imports, only data from January 2001 through April 2004 was used. Using older data, due to adjustments to the existence of parallel imports, might have distorted the estimations. Parallel imports were allowed starting in 1995 when Sweden joined the European Union, but their extent was very limited the first two years, and Ganslandt and Maskus (2004) expressed the belief that the market was not in long-run equilibrium even at the end of their study period, in 1998.[12] Data after April 2004 was not used since 10 countries – new potential source countries for parallel imports – joined the EU in May 2004, possibly distorting the results.

Table 1. The Swedish prescription pharmaceutical market, 1997-2007

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
GDP	1927001	2012091	2123971	2249987	2326176	2420761	2515150	2624964	2735218	2900790	3063145
TPS	13984	16270	18148	19934	21301	22872	23301	23807	24819	25943	23067
PI	272	1008	1402	1754	2012	2090	2100	2527	3018	3012	2707
PI/TPS	2%	6%	7,7%	8,8%	9,4%	9,1%	9%	10,6%	12,1%	11,6%	11,7%
# PI Firms	2	8	10	9	9	10	11	11	9	12	14

Notes: GDP, TPS and PI are in million SEK and expressed in nominal terms. TPS and PI are abbreviations for total pharmaceutical sales and total sales value of parallel imports respectively. PI/TPS represents the share of parallel imports in total pharmaceutical sales.
Source: Intercontinental Medical Statistics (IMS)

Prescription pharmaceutical sales constituted about 0.9% of GDP during 2001-2004 (Table 1). Both the share of parallel imports in total pharmaceutical sales (PI/TPS) and the number of parallel traders increased substantially in 1998, due to the integration of Sweden in the EU (Ganslandt and Maskus, 2004). While the share of parallel imports was 2% in 1997, it was 6% in

[12] It is possible that pharmacists and consumers changed their attitudes as they learned more about parallel imports during the first few years they were in the market. This might have changed the effect of competition from parallel imports in the years prior to our study period.

1998 and the number of parallel traders increased from 2 in 1997 to 8 in 1998. There was no similar change in the share of parallel imports or in the number of parallel traders during 2001-2004.

The empirical analysis focuses only on locally-sourced on-patent prescription drugs. Off-patent and parallel imported drugs were used to create the relevant variables for the analysis but were excluded in the final dataset. No information on the dates of patent expiration was available. Instead, we defined pharmaceuticals as off-patent starting the first time any generic with the same active ingredient was sold in Sweden.

Table 2. Descriptive statistics for variables used in estimations

Variable	Mean	Std. Dev.	Min	Max
ln*p*	5.7571	1.5356	1.9201	11.7574
Picomp	0.1309	0.3373	0	1
Pifirms	0.3257	1.0297	0	9
Mpi	4.0016	11.6196	0	79
Thcomp	0.8437	0.3631	0	1
Nthcomp	3.1403	2.4750	0	12
Thgencomp	0.2071	0.3404	0	1
Ref	0.4666	0.4988	0	1
*Ref*Picomp*	0.0662	0.2487	0	1
*Ref*Pifirms*	0.1541	0.6863	0	8
*Ref*Mpi*	2.3156	9.6610	0	79
*Ref*Thcomp*	0.3847	0.4888	0	1
Ref Nthcomp*	1.4818	2.3239	0	12
*Ref*Thgencomp*	0.1040	0.2609	0	1
Time	20.2653	11.5346	1	40
Timepi	2.7899	8.3111	0	40
EURO/SEK	9.1794	0.1485	8.8963	9.6670
Lnlong	4.1716	0.7975	-0.6931	4.6868

Table 2 presents the variables used in the econometric analysis and the descriptive statistics on the data. The variable $\ln p_{it}$ is the natural logarithm of the real price (wholesale price in month t deflated by consumer price index). $Picomp_{it}$ is an indicator for whether drug i is subject to competition from parallel imports (hereafter pi-competition) and $Pifirms_{it}$ is the number of

parallel traders drug i faces competition from.[13] Mpi_{it} is defined as the number of months drug i had faced competition from parallel imports before month t. $Thcomp_{it}$ is a dummy controlling for whether a drug has any therapeutic competitors, $Nthcomp_{it}$ is the number of therapeutic competitors and $Thgencomp_{it}$ is the share of product i's therapeutic competitors facing generic competition.[14] Ref_t is a dummy variable taking the value one for the months after the mandatory substitution reform and the following six variables are interaction variables between Ref_t and the variables mentioned above. $Time_t$ is the number of the month, starting from January 2001, and $Timepi_{it}$ is an interaction variable between this variable and $Picomp_{it}$. The last two variables are instruments used in instrumental variable regressions: the Euro/SEK exchange rate and the logarithm of the number of months the product has been sold in Sweden ($Lnlong_{it}$).[15]

Of the 3,339 on-patent prescription drugs with different active ingredient, strength, and form (102,235 observations) 84% faced therapeutic competition while only 13% faced pi-competition (Table 2). Descriptive statistics, not presented in the table, show that for drugs that face pi-competition, the average market share in units for parallel imports is 39%.

Econometric Analysis

A difference-in-differences strategy was used to identify the effects of competition from parallel imports (hereafter pi-competition) on prices of locally-sourced drugs and how these effects were influenced by the 2002 mandatory substitution reform. The effects of facing pi-competition were identified by comparing changes in prices of drugs that gained or lost pi-competition with those of drugs that did not face changes in pi-competition. The effect of the reform was identified by comparing the price-effects of changes in pi-competition before the reform with those after, as

[13] A parallel imported drug is considered to be a pi-competitor to the locally sourced drug if it has the same substance (i.e., 7-digit ATC code), strength, and form (e.g. pill or fluid) as that drug and are sold in Sweden the same month. Since, for example, a 100-pill package can substitute for two 50-pill packages, it is not required that the parallel import be of the same package size as the locally-sourced drug.

[14] Following Brekke et al. (2008) and Pavcnik (2002) pharmaceuticals with the same 5-digit ATC code were classified as therapeutic competitors.

[15] In order to be able to take the natural logarithm we defined $long_{it}$ equal to 0.5 the first month a product was sold, and so on. $Lnlong_{it}$ is the natural logarithm of a variable truncated at 108.5 months due to lack of older data.

well as by comparing differences in prices before and after the reform for drugs that always faced pi-competition with those for drugs that never faced pi-competition.

In a difference-in-differences setting one or several parameters capture fixed differences among the drugs, while one or several other parameters capture changes over time that are common to all drugs. We included drug specific fixed effects, α_i, to control for fixed differences among individual drugs. For example, the fixed effects control for differences in severity of side effects and other aspects of the drugs themselves that might affect their price. The fixed effects also control for most of the variation in demand across observations, in fact for 87% of the variation in units sold. To control for changes over time that are common to all drugs we included a linear time-trend; a dummy variable taking the value one after the mandatory substitution reform; and dummy variables for calendar months.[16] We also included variables to control for price changes as a result of being subject to competition from parallel imports; number of parallel trading firms importing the drug; number of months a drug had faced such competition; being subject to competition from therapeutic alternatives; number of therapeutic alternatives; and share of therapeutic alternatives facing generic competition. Then the main specifications are

$$\begin{aligned}\ln p_{it} = {} & \beta_1 Picomp_{it} + \beta_2 Pifirms_{it} + \beta_3 Mpi_{it} + \beta_4 Timepi_{it} + \beta_5 Ref * Picomp_{it} + \beta_6 Ref * Pifirms_{it} \\ & + \beta_7 Ref * Mpi_{it} + \beta_8 Thcomp_{it} + \beta_9 Nthcomp_{it} + \beta_{10} Thgencomp_{it} + \beta_{11} Ref * Thcomp_{it} \\ & + \beta_{12} Ref * Nthcomp_{it} + \beta_{13} Ref * Thgencomp_{it} + \beta_{14} Time_t + \beta_{15} Ref_t \\ & + \sum_{m=2}^{12} \gamma_m Month_t + \alpha_i + \varepsilon_{it}\end{aligned} \tag{1}$$

$$\begin{aligned}\ln p_{it} = {} & \beta_1 Picomp_{it} + \beta_3 Mpi_{it} + \beta_4 Timepi_{it} + \beta_5 Ref * Picomp_{it} + \beta_7 Ref * Mpi_{it} + \beta_8 Thcomp_{it} \\ & + \beta_9 Nthcomp_{it} + \beta_{10} Thgencomp_{it} + \beta_{11} Ref * Thcomp_{it} + \beta_{12} Ref * Nthcomp_{it} \\ & + \beta_{13} Ref * Thgencomp_{it} + \beta_{14} Time_t + \beta_{15} Ref_t + \sum_{m=2}^{12} \gamma_m Month_t + \alpha_i + \varepsilon_{it}.\end{aligned} \tag{2}$$

The difference between specifications (1) and (2) is that $Pifirms_{it}$ and $Ref*Pifirms_{it}$ are not included in (2), to facilitate the use of an instrumental variable method. If these two variables

[16] As discussed in the Appendix, similar results were obtained using year-month dummies to control for common price changes. Year-month dummies were not included in the main specifications, however, in order to use time-variation in the instruments for identification.

were in the estimation, there would be too many endogenous variables to instrument. Specification (1) was estimated with fixed-effects OLS estimator, while specification (2) was estimated with fixed-effects OLS and a fixed-effects IV estimator, resulting in three estimations. To check the robustness of the results and to verify what the estimates describe, we also estimated many other specifications, described briefly in the Appendix and in footnotes where we also discuss their results.

The parameters β_1-β_4 describe the effects of competition from parallel imports before the mandatory substitution reform and, together with β_5-β_7, the effects after the reform. β_1 and β_4 describe the effect of facing pi-competition at all and how this effect changed over time. β_2 describes how the effect relates to the number of parallel trading firms importing the drug, and β_3 shows the effect of the number of months a drug had already faced competition from parallel imports.[17] The identifying assumption for these parameters is that no other variables, except those included in the specification, caused price changes that are correlated with facing competition from parallel imports. Since therapeutic competition can have important effects on prices and might be correlated with pi-competition, we included $Thcomp_{it}$, $Nthcomp_{it}$ and $Thgencomp_{it}$ in the specifications as well.[18,19]

The parameters β_5-β_7 for the interaction variables describe how the reform has influenced the price effect of competition from parallel imports. A requirement for these parameters to be correctly estimated is that no excluded variable influenced the price effect of facing pi-competition differently before the reform relative to after the reform. This requirement is one important motive for including Mpi_{it} and $Ref*Mpi_{it}$ in the specifications. There are several reasons why Mpi_{it} – which is correlated with the reform – could influence prices.[20] First, before the reform, the pharmaceutical committees recommended pharmacists dispense only parallel

[17] Separate effects of Mpi_{it} and $Timepi_{it}$ were identified by data on drugs changing from facing pi-competition to not facing it, or vice versa, at different times during the study period. For drugs that faced pi-competition none or all months of the study-period, Mpi_{it} and $Timepi_{it}$ are perfectly correlated.

[18] The share of drugs facing therapeutic competition is statistically significantly higher among the drugs facing competition from parallel imports than those not facing such competition at all, but the difference is small in size: only 5 percentage points.

[19] Ellison et al. (1997), Brekke et al. (2009), and Lichtenberg and Philipson (2002) provide evidence on therapeutic competition.

[20] The mean of Mpi_{it} is statistically significantly larger after the reform than before, and for drugs facing pi-competition this difference is large: 7.74 (std. err. 0.30).

imports that had a record of reliable supply (Persson, Anell and Persson, 2001). Second, the longer a parallel imported drug had been in the market, the more familiar consumers, physicians, and pharmacists would be with it, making it a stronger competitor for the locally-sourced drug.[21] Third, if a parallel import had been sold in Sweden for a long time, without any supply shortages, or even interruptions due to possible strategic response of manufacturers like supply rationing in the source countries, then the price approving authority might consider the parallel import a reliable alternative for the locally-sourced drug and therefore dare to be tougher in its decisions regarding approval of price increases for the locally-sourced drug.

The identifying requirement for the parameters β_5-β_7 was also the main reason why we included $Timepi_{it}$ in the specifications, to capture changes over time in the effect of facing pi-competition not caused by the substitution reform but perhaps by changed consumer attitudes toward parallel imports.[22] Lastly, interaction variables between the reform and controls for therapeutic competition were included since, as discussed before, there are reasons to expect that the effects of facing therapeutic competition were increased by the reform.

An obvious problem is that entry decisions of parallel traders are determined by the prices of pharmaceuticals. In other words, the variables controlling for pi-competition might be endogenous, and hence the OLS estimator might be biased. This problem is reduced by inclusion of fixed effects, since parallel traders then must react to price changes within the study-period for the OLS estimator to be endogenous. Still, we cannot rule out the possibility of endogeneity, and therefore also conducted an instrumental variable estimation.[23]

---

[21] Using data on on-patent prescription drugs sold in the county of Västerbotten, Sweden, during 2003-2006 (see Granlund and Rudholm (2008) for details of the dataset), we found that patients were statistically significantly less likely to oppose substitution by a parallel import the larger Mpi_{it} was. Controlling for Mpi_{it}, however, the patients became more likely to oppose substitution over time. Since Mpi_{it} is correlated with sales volume of the parallel import, we estimated the fixed-effects IV specification including the market share of parallel imports, but got similar results regarding Mpi_{it}, suggesting that this is not the explanation to its effect.

[22] $Timepi_{it}$ accounts for the differences in the time trend of drugs subject to pi-competition and drugs not subject to it. Before the reform, the time trend of drugs subject to pi-competition was different from that of drugs not subject to it. Even though the time trend differs between the two groups, the difference in time trend is stable over time, implying that the difference could be captured by $Timepi_{it}$.

[23] The therapeutic competition variables might be endogenous to some degree as well, since high prices for a drug can make competing pharmaceutical firms more likely to invest in R&D for therapeutic alternatives. Moreover, firms could choose not to launch their products in Sweden if the prices of therapeutic alternatives in Sweden are low. The first source of endogeneity is likely to be small, since firms make their investment decision based on expectation of future prices around the world without having perfect foresight, and since the Swedish market, for

The five possible endogenous variables, $Picomp_{it}$, Mpi_{it}, $Ref*Picomp_{it}$, $Ref*Mpi_{it}$, and $Timepi_{it}$, are all functions of *Picomp* and highly correlated; with correlations among the five ranging from 0.54 to 0.91. To overcome the difficulties this creates for finding strong instruments, we employed a three-stage instrumental variable estimation. In the first stage, OLS estimation was employed to explain and predict *Picomp*, using the exogenous variables of specification (2), including fixed effects, and a set of instruments (explained below). Drugs with no variation in *Picomp* during the study period were not included in this regression since the instruments have no predictive power for *Picomp* for them, and since the inclusion of fixed effects means that there is no endogeneity problem for them either. Instead, true values were used as predictions for *Picomp* for these drugs. Then, the predictions for *Picomp* were used to create predictions for Mpi_{it}, $Timepi_{it}$, $Ref*Picomp_{it}$, and $Ref*Mpi_{it}$.[24] Lastly, the predictions for all five possible endogenous variables are used as instruments for their actual values in a 2SLS estimation, using the xtivreg2 command by Schaffer (2010).

This method has two advantages over a standard two-stage IV-method where all endogenous variables are instrumented directly, using the same set of instruments. First, this method will predict similar drugs to face pi-competition both before and after the reform, which means that the estimated effect of the reform on pi-competition will not be affected by changes in the drugs facing pi-competition. Second, and more importantly, it yields robust estimates for the possible endogenous variables. When predicting all endogenous variables directly, the instrument sets were found to be weak for at least one of the possible endogenous variables, resulting in unreliable estimates which were not robust even to small changes in the instrument sets.

---

most drugs, constitutes a relatively small share of the entire market (Pharmaceutical consumption in Sweden constituted 0.7% of the total pharmaceutical consumption in the OECD in 2005, OECD, 2008). The second source of endogeneity is likely to be small as well since the prices of pharmaceuticals in Sweden are about the average of the large markets in the European Union (Lundkvist, 2002).

[24] The first stage regression also used only data from the period January 2001 through April 2004. Thus, only variations in Mpi_{it} within this period could be predicted for each product. With fixed effects, subtracting a product specific constant from Mpi_{it} did not affect the estimates for this variable. However, this prevented us from including Mpi_{it} nonlinearly, e.g., Mpi^2_{it}. OLS results including Mpi^2_{it} were, however, very similar to those excluding it, suggesting that it is not important to include it. OLS estimation using dummy variables for each value of Mpi_{it} also indicated that the effect of Mpi_{it} was nearly linear up to values of 50 months, but no additional effect was found for even higher values. Only 1.5% of the observations in the dataset had values of *Mpi* exceeding 50. These results are available from the authors upon request.

Several sets of instruments were tested, nearly all inspired by Ganslandt and Maskus (2004). We report the full results obtained when using the Euro/SEK exchange rate as instrument but also the key results obtained when using the logarithm of the number of months the product had been sold in Sweden ($Lnlong_{it}$), as well as key results obtained when using both the exchange rate and $Lnlong_{it}$ as instruments. The Euro/SEK exchange rate is the instrument thought most likely to be exogenous, though $Lnlong_{it}$ should also be exogenous since we controlled for therapeutic competition. Other instrument sets tested include interaction between *Euro/SEK* and sales values in 1995 and transformations of *Lnlong*.[25]

During the study period, important source countries such as Italy, Greece, and Spain switched to the Euro as currency or fixed their exchange rate towards the Euro. The Euro/SEK exchange rate therefore affected price differences between locally-sourced drugs in Sweden and the source countries, an important determinant for parallel traders' entry decisions. $Lnlong_{it}$ could also be a good instrument since the probability that a drug is also sold in low price countries increased with the number of months it had been sold in Sweden, and since it might take a few months after it was first sold in both Sweden and a source country before parallel traders could establish relevant contacts and get the approval from the Medical Products Agency. We used the natural logarithm since the effect of the number of months on entry of parallel traders was thought likely to decrease. Also, an untransformed variable representing the number of months from first sale would be perfectly correlated with $Time_{it}$ and therefore unusable as an instrument.

Results

The three main sets of full estimation results are presented in Table 3, while Table 4 presents the key results from regressions with other instruments. All reported coefficients and standard errors in the tables and elsewhere are the estimates multiplied by 100. In the Appendix we report the results of the robustness analyses, showing that the results are quite insensitive to changes in the specifications.

[25] As mentioned above, $Lnlong_{it}$ is the natural logarithm of a variable truncated at 108.5 months due to lack of older data. Including a dummy variable for those with a value of 108.5 or higher did not contribute to explaining $Picomp_{it}$, however, so it was not included as an instrument.

Differentials are also presented at the bottom of the Table 3 and in Table 4 describing the average effect of the variables of main interest on prices. The differential d*lnP/*d*Picomp* was calculated using the estimates for the seven pi-variables as well as the average value of these variables when *Picomp* equals one. For the IV estimation (Table 3), the differential indicates that drugs facing pi-competition had 15% lower prices on average compared to what they would have had if they had never faced pi-competition.[26] Similar results were obtained from estimations 4 and 5 (Table 4) and for other, not reported, IV estimations with different instruments. For the OLS estimations, the corresponding figures are less than 4%, indicating that endogeneity bias is considerable.

Pifirms and *Ref*Pifirms* both had positive coefficients in estimation 1, possibly caused by endogeneity, but perhaps because manufacturing firms might have increased prices to extract as much as possible from price-insensitive loyal consumers if competition from parallel imports became too fierce.[27] The coefficients for *Mpi* in all estimations indicate that the full effect of facing pi-competition was not felt immediately.[28] Compared to the estimates from the OLS regression (estimation 2 in table 3), that for *Mpi* from the IV regression is lower (i.e., more negative), but that for *Timepi* is approximately as much higher. These differences might not be caused by endogeneity, but perhaps by correlation between these variables, as high as 0.8, which means that the differences between the coefficients are estimated imprecisely (Greene 2003: Chapter 4). However, the joint effect of these variables is not affected by this high correlation.

The differential dln*P/*d (*Ref*Picomp)* indicates that mandatory substitution had increased the effect of pi-competition, but by less than one percentage point. For the OLS regressions the result is driven by the effect of *Ref*Picomp*, but for the IV regression it is mainly explained by the negative estimate for *Ref*Mpi*.

[26] Since the dependent variable is in logarithmic form, the exact change in price (in percent) should be calculated using the formula $100*[\exp(\beta)-1]$.

[27] Frank and Salkever (1992) discuss the similar so called "generic paradox" that brand name producers might react to generic competition by increasing their prices.

[28] For observations with *Picomp* equal to one, the average values for *Mpi* and *Ref*Mpi* are 27.26 and 15.49, respectively. The Mpi-variables thus account for more than 75% of the estimates for d*lnP/*d*Picomp* in all three estimations.

Table 3. Estimation results, multiplied by 100

	(1) OLS	(2) OLS	(3) IV
$Picomp_{it}$	0.041	0.323**	-11.076***
	(0.187)	(0.150)	(1.595)
$Pifirms_{it}$	0.197***		
	(0.072)		
Mpi_{it}	-0.145***	-0.135***	-0.444***
	(0.011)	(0.011)	(0.054)
$Timepi_{it}$	0.002	-0.004	0.360***
	(0.012)	(0.011)	(0.059)
$Ref*Picomp_{it}$	-1.247***	-1.043***	-0.028
	(0.314)	(0.252)	(0.410)
$Ref*Pifirms_{it}$	0.051		
	(0.082)		
$Ref*Mpi_{it}$	0.013**	0.010	-0.027**
	(0.005)	(0.006)	(0.011)
$Thcomp_{it}$	-0.395	-0.404	-0. 316
	(0.340)	(0.340)	(0.343)
$Nthcomp_{it}$	0.121**	0.126**	0.106**
	(0.050)	(0.050)	(0.051)
$Thgencomp_{it}$	-3.142***	-3.167***	-3.012***
	(0.360)	(0.360)	(0.365)
$Ref*Thcomp_{it}$	-0.826***	-0.819***	-0.726***
	(0.209)	(0.207)	(0.210)
$Ref*Nthcomp_{it}$	-0.185***	-0.185***	-0.189***
	(0.027)	(0.027)	(0.027)
$Ref*Thgencomp_{it}$	-0.521***	-0.542***	-0.649***
	(0.162)	(0.161)	(0.164)
Ref_t	1.146***	1.147***	1.155***
	(0.158)	(0.158)	(0.160)
$Time_t$	-0.037***	-0.037***	-0.038***
	(0.005)	(0.005)	(0.005)
d ln*P*/d *Picomp*	-3.776***	-3.848***	-16.066***
	(0.221)	(0.213)	(1.765)
d ln*P*/d (*Ref*Picomp)*	-0.733***	-0.735***	-0.867***
	(0.182)	(0.185)	(0.207)
d ln*P*/d *Thcomp*	-1.494***	-1.490***	-1.413***
	(0.357)	(0.357)	(0.361)
d ln*P*/d (*Ref*Thcomp)*	-1.659***	-1.659***	-1.606***
	(0.154)	(0.153)	(0.155)
Sample size	102,187	102,187	102,187
Log likelihood	148,563.8	148,558.8	147,868.2

Notes: The asterisks ***, ** and * denote that the coefficient is significantly different from zero at the 1%, 5%, and 10% levels. Standard errors that are robust against heteroskedasticity and autocorrelation are shown in parentheses. For the IV-specifications, F value for significance of the instrument (the Euro/SEK exchange rate) in the first stage regression was 17.70. The differentials were evaluated at the mean of each variable when the relevant explanatory variable, i.e., *Picomp, Ref*Picomp, Thcomp*, *or Ref*Thcomp*, took the value one. Estimation results for calendar months are suppressed to save space, but are available from the author upon request.

Table 4. Estimation results from IV regressions with instruments *Lnlong*, and both *EURO/SEK* and *Lnlong*, multiplied by 100

	(4) IV	(5) IV
d ln*P*/d *Picomp*	-18.720***	-17.461***
	(1.984)	(1.871)
d ln*P*/d (*Ref*Picomp)*	-0.855***	-0.861***
	(0.209)	(0.208)
Sample size	102,187	102,187
Log likelihood	147,567.9	147,728.2

Notes: For estimation 4, the F value for significance of the instrument (*Lnlong*) in the first stage regression was 108.32. For estimation 5, the F value for significance of the instruments (the Euro/SEK exchange rate and *Lnlong*) in the first stage regression was 65.26. See also notes to Table 3.

The estimates for the therapeutic competition variables, *Thcomp*, *Nthcomp*, and *Thgencomp*, indicate that, before the reform, the effect of facing such competition was small if the therapeutic alternatives did not face generic competition, but the effect increased substantially if they gained generic competition. The reform increased the importance of whether therapeutic competitors face generic competition, reflecting that the reform led to lower generic prices and lower prices of brand-name drugs facing generic competition. The reform also substantially increased the effect of *Thcomp*, probably because the Pharmaceutical Benefits Agency (LFN), unlike its predecessor prior to the reform, had a clear instruction to consider marginal benefits and costs of a drug before deciding whether or not to approve its suggested price and list it for reimbursement. The average effect of facing therapeutic competition during the study-period was a price reduction of 1.5% and the reform increased the effect of therapeutic competition by 1.6 percentage points. This means that the reform more than tripled this effect from 0.7% to 2.3%. Our results on therapeutic competition are consistent with Brekke et al. (2009) and Ellison et al. (1997) showing that drugs with the same active ingredient − generics in their case − are closer substitutes than drugs with different active ingredients but similar therapeutic effects.

Lastly, the estimates for $Time_t$ show that the prices of drugs not facing pi-competition fell over time. The estimates for Ref_t indicate that the prices of drugs not subject to pi- or therapeutic competition were positively associated with the reform, but this coefficient might capture something besides causal effects of the reform.

Conclusions

We analyzed the effects of competition from parallel imports on prices of all locally-sourced on-patent prescription drugs sold in Sweden during January 2001-April 2004 and whether 2002 mandatory substitution reform affected this competition.

Using an instrumental variable method, we found that drugs facing competition from parallel imports had 15-17% lower prices on average compared to what they would have had if they had never faced such competition. The corresponding estimate from OLS regressions was only 4%. The results are of similar magnitude to those of Ganslandt and Maskus (2004) despite that we controlled for therapeutic competition and indirect generic competition, covered all the on-patent prescription drugs, and analyzed a different period. Thus, our results confirm their conclusion that parallel imports substantially reduce prices of locally-sourced drugs.

The large difference between the IV and the OLS results indicates that it is important to account for endogeneity caused by simultaneous determination of prices and entry decisions of parallel traders. The OLS result describes the association between prices and pi-competition which was affected both by high prices encouraging entry of parallel traders, causing more positive (or less negative) association, and by the causal effect of competition from parallel imports itself. Therefore, OLS result gives only a lower bound on the absolute causal effect of pi-competition.

The mandatory substitution reform increased the effect of pi-competition, but by less than one percentage point in absolute value. Thus, the effect of pi-competition was large also when substitution was not mandatory. One reason could be that many pharmacies already before the mandatory substitution reform dispensed parallel imports to consumers whose physicians had not specified either a locally-sourced or parallel imported package. The full effect of parallel imports was not realized immediately, but rather the prices of locally-sourced drugs fell continuously as they faced competition from parallel imports. The IV-results indicate that the reform has increased the intensity of competition from parallel imports mainly by strengthening this gradual effect.

Our empirical strategy made it possible to analyse the full effect of competition from parallel imports over time. The same strategy could be used to analyze the full effect of generic competition, which is a subject for future research.

Our analysis has implications for the effect of mandatory substitution reform on therapeutic competition as well. The prices of drugs facing such competition were 1.5% less on average than they would have been otherwise. The reform increased the effect of therapeutic competition by 1.6%. The results also show that the effect of therapeutic competition depended on whether the therapeutic competitors were subject to generic competition. Facing therapeutic competition led to a substantial fall in prices if the therapeutic competitors themselves were subject to generic competition. The reform increased the effect of generic competition and thus this effect as well.

Lichtenberg and Philipson (1997) showed that between-patent competition (therapeutic competition), most of which occurs while a drug is under patent, costs the patent holder at least as much as within-patent competition (generic competition), which cannot occur until a drug is off-patent. The results of this paper are in line with theirs by showing that patent holders are significantly hurt by competition, both from parallel imports and therapeutic alternatives, and also by showing that these forms of competition, particularly therapeutic competition, was strengthened by the reform. This evidence points at the debate on potential drawback of parallel trade and substitution policies, that is, they might cause patent holders to lose profits and hence to invest less in innovation.

Appendix: Robustness analysis of key results

We conducted OLS regressions including Mpi^2 and $Ref*Mpi^2$ as well as specifications including 40 year-month dummies instead of 11 month dummies (*Month*), the time trend (*Time*) and the dummy for the reform (*Ref*). Including Mpi^2 and $Ref*Mpi^2$ reduced d*lnP/*d*Picomp* by a half percentage point and d*lnP/*d (*Ref*Picomp)* by about 0.1 percentage point in absolute terms. Including year-month dummies reduced the average estimated effect of pi-competition by about 0.6 percentage point, but changed the estimate for d*lnP/*d(*Ref*Picomp)* by less than 0.1 percentage point. Thus, *Time* and *Ref* seem to have captured changes over time common to all drugs sufficiently well that such changes had little effect on the key results.

We also estimated specifications 1 and 2 separately for drugs that never, or always, faced pi-competition. The estimates for d*lnP/*d (*Ref*Picomp)* for this restricted sample was -0.432 (0.257) and -0.430 (0.250) for specifications 1 and 2, that is, slightly smaller compared to the estimates for the whole sample: -0.773 (0.182) and -0.735 (0.185), respectively.

As argued in the section on econometric analysis, including *Mpi* and *Timepi* might be important for estimating the effect of the mandatory substitution reform correctly. To test this, we ran regression 3 excluding *Mpi* and *Ref*Mpi*; excluding *Timepi*; and excluding all three simultaneously. Excluding only *Mpi* and *Ref*Mpi*, or only *Timepi*, had very little impact on the estimates for d*lnP/*d(*Ref*Picomp)*, but excluding all three simultaneously led to an estimate of -3.061 (0. 202) , compared to the estimate from regression 3 (-0.867 (0.207)).

As noted earlier, the identifying assumption for the effect of the mandatory substitution reform on the price-effect of pi-competition (d*lnP/*d(*Ref*Picomp)*) was that no excluded variable influence the price-effect of facing pi-competition differently before and after the reform. By including the interaction variable between time trend and dummy for facing pi-competition ($Timepi_{it}$), we allowed drugs facing such competition to have a different time trend relative to those not facing it, without this biasing the estimator of the effect of the reform on pi-competition. Still, this estimator might be biased if factors not accounted for in the regressions affected the two groups differently, and if these factors increased or decreased over time in an unstable manner so that their effects could not be captured by *Timepi*, for example, if something

affecting the two groups differently occurred only during a certain part of the study-period. To test the importance of this problem we ran regression 3 for different periods: January 2000-April 2004, January 2002-April 2004, and January 2001-June 2003. We also ran regression 3 using the normal study period but excluding observations from April 2002, when the law regarding mandatory substitution was passed by parliament, through October 2002; and excluding observations from January 2002, when the bill was presented to parliament, through October 2002. Besides functioning as sensitivity analyses, these latter two regressions were designed to give an idea whether firms started to adjust their prices even before the reform came into effect. We also ran regression 3 excluding the first 3, 6, or 9 months after the reform.

For these regressions, the estimated average reform-effect on pi-competition was in the range -1.279 to -0.830 and different from zero at the 5%-level of statistical significance. These results indicate that the estimates for d*lnP/*d(*Ref*Picomp)* are stable to changes in the study-period. No evidence was found of firms adjusting prices before the reform came into effect.

Would variation in *Mpi* in the distant past matter less than in the recent past? To examine this, we ran regression 2 including the following variables $Mpid01_{it}$, $Mpid13_{it}$, $Mpid36_{it}$, $Mpid612_{it}$, $Mpid1224_{it}$, $Mpid2436_{it}$ – where $Mpid01_{it}=Mpi_{it}-Mpi_{i,t-1}$, $Mpid13_{it}=Mpi_{i,t-1}-Mpi_{i,t-3}$, and so on – as well as interaction variables between the reform and each of these variables. We found no evidence that variation in *Mpi* in the distant past mattered less than more recent variation, since the differential with respect to $Mpid01_{it}$ was of similar magnitude to that with respect to $Mpid2436_{it}$.

We also investigated whether the relationship between *Mpi* and pharmaceutical prices might be explained by that drugs facing pi-competition were less able to adjust their prices to keep up with inflation. Since the Pharmaceutical Benefits Agency approves nominal prices, not real prices, this could be the case if the agency were less willing to allow price increases for drugs with pi-competition. To investigate this we ran a regression with the *Mpi* variables replaced by a variable describing the consumer price index (CPI) and variables describing changes in it that occurred during months when a drug faced pi-competition; as well as regressions including both the *Mpi* and the CPI variables. The likelihood values were lower when CPI variables were included instead of the *Mpi* variables, suggesting that the *Mpi* variables better explain the variations in

prices. Also, the estimates for the *Mpi* variables were relatively robust against inclusion of the CPI variables as well, while the estimates for several of the CPI variables became statistically non-significant when the *Mpi* variables were included. Therefore, we conclude that the relationship between *Mpi* and pharmaceutical prices is not explained by the Pharmaceutical Benefits Agency being less willing to approve price increases for drugs facing pi-competition. Instead, the relationship is likely explained by consumers and pharmacists becoming less reluctant to use parallel imports the longer they have been in the market, as discussed earlier.

Finally, we ran several regressions including $Pifirms^2$ (squared) or using dummy variables to account for the number of parallel traders. However, unlike Ganslandt and Maskus (2004), we found no evidence of prices being reduced more when additional parallel traders entered the market after the first, unless we simultaneously excluded the *Mpi* variables and *Timepi*. Since specifications including the number of parallel traders only could be estimated with OLS, we cannot interpret this as showing that there is no additional price reducing effect. But our results suggest that any additional effect might be exaggerated if one has not accounted for the lagged effect of entry of parallel traders. The correlations between *Pifirms* and *Mpi* and *Timepi*, respectively, is 0.67 and 0.80, so it is not surprising that controlling for *Mpi* and *Timepi* affects the estimates for *Pifirms*. Full results from all estimations mentioned here are available from the authors upon request.

References

Anell, A., and U. Persson (2005), Reimbursement and clinical guidance for pharmaceuticals in Sweden: Do health-economic evaluations support decision making? *The European Journal of Health Economics* 6(3): 274–279.

Andersson, K., G. Bergström, M.G. Petzold, and A. Carlsten (2005), What are the obstacles to generic substitution? An assessment of the behaviour of prescribers, patients and pharmacies during the first year of generic substitution in Sweden, *Pharmacoepidemiology and Drug Safety* 14(5): 341-348.

Aronsson, T., M.A. Bergman, and N. Rudholm (2001), The impact of generic drug competition on brand name market shares: Evidence from micro data, *Review of Industrial Organization* 19(4): 425-435.

Bergman, M.A., and N. Rudholm (2003), The relative importance of actual and potential competition: Empirical evidence from the pharmaceuticals market, *Journal of Industrial Economics* 51(4): 455-467.

Brekke, K.R., A.L. Grasdal, and T.H. Holmås (2009), Regulation and pricing of pharmaceuticals: Reference pricing or price cap regulation, *European Economic Review* 53(2): 170-185.

Brekke, K.R., I. Königbauer, and O.R. Straume (2007), Reference pricing of pharmaceuticals, *Journal of Health Economics* 26(3): 613-642.

Buzzelli, C., A. Kangasharju, I. Linnosmaa, and H. Valtonen (2006), Impact of generic substitution on pharmaceutical prices and expenditures in OECD countries, *Journal of Pharmaceutical Finance, Economics and Policy* 15: 41-62.

Chen, Y., and K.E. Maskus (2005), Vertical pricing and parallel imports, *Journal of International Trade and Economic Development* 14 (1): 1-18.

Colombo, F., and D. Morgan (2006), Evolution of health expenditures in OECD countries, *Revue Francaise des Affaires Sociales* 6-7(6): 19-42.

Ellison, S.F., I. Cockburn, Z. Griliches, and J. Hausman (1997), Characteristics of Demand for Pharmaceutical Products: An examination of Cephalosporins, *RAND Journal of Economics* 28(3): 426-446.

Frank, R.G., and D.S. Salkever (1992), Pricing, patent loss and the market for pharmaceuticals, *Southern Economic Journal* 59(2): 165-179.

Ganslandt, M., and K.E. Maskus (2004), Parallel imports and the pricing of pharmaceutical products: Evidence from the European Union, *Journal of Health Economics* 23(5): 1035-1057.

Granlund, D. (2009), Are private physicians more likely to veto generic substitution of prescribed pharmaceuticals?, *Social Science & Medicine* 69(11): 1643-1650.

Granlund, D. (2010), Price and welfare effects of a pharmaceutical substitution reform, *Journal of Health Economics* 29(6): 856-865.

Granlund, D., and N. Rudholm (2008), Consumer loyalty in the Swedish pharmaceutical market, *Umeå Economic Studies 742*, Umeå University.

Granlund, D., and N. Rudholm (2011), Consumer information and pharmaceutical prices: Theory and evidence, *Oxford Bulletin of Economics and Statistics* 73(2): 230-254.

Greene, W.H. (2003), Econometric Analysis, Fifth Edition, New York: Prentice Hall.

Jelovac, I., and C. Bordoy (2005), Pricing and welfare implications of parallel imports in the pharmaceutical industry, *International Journal of Health Care Finance and Economics* 5(1): 5-21.

Kanavos, P., and J. Costa-Font, (2005), Pharmaceutical parallel trade in Europe: Stakeholder and competition effects, *Economic Policy* 20(44): 751–798.

Kanavos, P., D. Gross, and D. Taylor (2005), Parallel trading in medicines: Europe's experience and its implications for commercial drug importation in the United States, *AARP Public Policy Institute Issue Paper* 2005-7.

Köksal, M.Y. (2009), Reference pricing: Making parallel trade in pharmaceuticals work, *Working Papers in Economics* 367.

Kyle, M. K. (2011), Strategic responses to parallel trade, *B.E. Journal of Economic Analysis and Policy* 11(2).

Köping Höggård, M., and T. Redman (2007), Pharmaceutical pricing and reimbursement information, Sweden Pharma Profile, EU.

LFNFS 2003:1, Läkemedelsförmånsnämndens föreskrifter om ansökan och beslut hos Läkemedelsförmånsnämnden. [The Pharmaceutical Benefits Board's regulations about applications and decisions at the Pharmaceutical Benefits Board] (in Swedish), Sweden.

LFNAR 2006:1, General Guidelines Concerning Price Increases of Pharmaceuticals from the Pharmaceutical Benefits Board, Sweden.

Lichtenberg, F.R., and T.J. Philipson (2002), The dual effects of intellectual property regulations: Within- and between-patent competition in the U.S. pharmaceuticals industry, NBER Working Paper Series 9303.

Lopez-Casosnovas, G., and J. Puig-Junoy (2000), Review of the literature on reference pricing, *Health Policy* 54(2): 87-123.

Lundkvist, J. (2002), Pricing and reimbursement of drugs in Sweden, *The European Journal of Health Economics* 3(1): 66-70.

Maskus, K.E., and Y. Chen (2004), Vertical price control and parallel imports: Theory and evidence, *Review of International Economics* 12(4): 551-570.

Medical Products Agency (2002) Utbytbara läkemedel [Substitutable Medicinal Products] (in Swedish).

Mestre-Ferrandiz, J. (2003), Reference prices: The Spanish way, *Investigaciones Economicas* 27(1): 125-149.

Miraldo, M. (2009), Reference pricing and firms' pricing strategies, *Journal of Health Economics* 28(1): 176-197.

National Board on Health and Welfare (2006), Läkemedelsförsäljningen i Sverige – Analys och prognos [Pharmaceutical sales in Sweden: Analysis and forecast], Stockholm (in Swedish).

National Corporation of Swedish Pharmacies, The Federation of Swedish County Councils, and the Pharmaceutical Benefits Board (2004), Utbyte av läkemedel – En uppföljning av de första 15 månaderna med läkemedelsreformen [Substitution of pharmaceuticals: The first 15 months of the substitution reform], Stockholm (in Swedish).

National Social Insurance Board (2002), Prissättningen av parallellimporterade läkemedel i Sverige [Price setting of parallell imported pharmaceuticals in Sweden], RFV Redovisar 2002:4.

OECD (2008), Pharmaceutical pricing policies in a global market, *OECD Health Policy Studies*, OECD.

OECD (2010), Health at a glance: Europe 2010, OECD Publishing, http://dx.doi.org/10.1787/health-glance-2010-en

Pavcnik, N. (2002), Do pharmaceutical prices respond to potential patient out of pocket expenses, *RAND Journal of Economics* 33(3): 469-487.

Pecorino, P. (2002), Should the U.S. allow prescription drug reimports from Canada?, *Journal of Health Economics* 21(4): 699-708.

Persson, U., A. Anell, and M. Persson (2001), Parallellhandel med läkemedel i Sverige – En ekonomisk analys [Parallel trade with pharmaceuticals in Sweden – An economic analysis], Lund: The Swedish Institute for Health Economics.

RFFS 1992:20 Riksförsäkringsverkets föreskrifter om fastställande av pris på läkemedel [The National Social Insurance Board's regulations for establishing prices for pharmaceuticals] (in Swedish).

RFFS 1996:31 Riksförsäkringsverkets föreskrifter om fastställande av pris på läkemedel m.m. [The National Social Insurance Board's regulations for establishing prices for pharmaceuticals etc.] (in Swedish).

Schaffer, M.E. (2010), xtivreg2: Stata module to perform extended IV/2SLS, GMM, and AC/HAC, LIML, and k-class regression for panel data models. http://ideas.repec.org/c/boc/bocode/s456

SFS 2002:687 Förordning om läkemedelsförmåner m.m. [Ordinance 2002:687 on Pharmaceutical Benefits, etc.] (in Swedish).

SOU 2000:86 Den nya läkemedelsförmånen [The new pharmaceutical benefits scheme] (in Swedish).