Reference Pricing, Generic Entry, and Pharmaceutical Prices

Kurt R. Brekke*, Chiara Canta†, Odd Rune Straume‡

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Abstract

In this paper we study the impact of reference pricing (RP) on entry of generic firms in the pharmaceutical market. For given prices, RP increases generic firms' expected profit, but since RP also stimulates price competition the impact on generic entry is theoretically ambiguous. In order to empirically test the effects of RP, we exploit a policy reform in Norway in 2005 that exposed a subset of drugs to RP. Having detailed product-level data for a wide set of substances from 2003 to 2013, we find that RP increases the number of generic drugs. We also find that RP increases market shares of generic drugs and reduces prices of both branded and generic drugs with a significant part of these effects being caused by increased generic entry. Despite price reductions, we find no effect of RP on pharmaceutical expenditures, but show that this is due to an increase in total demand.

Keywords: Pharmaceuticals; Reference pricing; Generic entry

JEL classifications: I11; I18; L13; L65

*Department of Economics, Norwegian School of Economics (NHH), Helleveien 30, N-5045 Bergen, Norway. E-mail: kurt.brekke@nhh.no

†Department of Economics, Norwegian School of Economics (NHH), Helleveien 30, N-5045 Bergen, Norway. E-mail: chiara.canta@nhh.no

‡Department of Economics/NIPE, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal; and Department of Economics, University of Bergen, Norway. E-mail: o.r.straume@eeg.uminho.pt.

1 Introduction

Reference pricing (RP) of pharmaceuticals has become a widely used regulatory scheme. According to Carone et al. (2012) at least 20 member states in the EU has introduced reference pricing.[1] In the US many federal states practice RP through the Medicaid Maximum Allowable Cost programmes. A RP scheme defines a maximum price that will be reimbursed by the insurer for a set of drugs with similar therapeutic effects. Consumers can purchase a drug priced above the reference price, but will then have to pay out-of-pocket the difference between the reference price and the actual drug price. The intention of RP is to curb pharmaceutical expenditures by increasing the demand elasticity and stimulating price competition between drug producers. In this paper we study whether RP has the intended effects.

RP schemes apply in most cases to substances where the original brand-name drug has lost patent protection and faces competition from generic drug versions.[2] Given that RP enhances price competition between brand-name and generic drug producers, then RP can in principle have a negative effect on the expected profits of generic producers and thus reduce generic entry.[3] If the negative effect on generic entry is sufficiently large, then RP may in fact *dampen* price competition and potentially *increase* pharmaceutical expenditures.[4] Clearly, in the extreme case where generic entry is deterred by the expectation of fierce price competition, RP would be counterproductive in containing medical costs. Thus, knowledge about the effects of RP on generic entry has major policy implications.

In this paper we conduct an empirical analysis of the impact of RP on generic entry and the corresponding effects on drug prices, sales, and expenditures. To motivate our empirical analysis, we develop a general theoretical model that allows us to identify the key effects of RP on generic entry. The theoretical analysis shows that the impact of RP on generic entry depends on the relative strength of two counteracting effects. On the one hand, for given prices, RP increases the demand for generic drugs due to a higher brand-name copayment, which provides

[1] As described in Carone et al. (2012), the exact details of the RP schemes vary across countries both in terms of the formula for fixing the reference price and the cluster of drugs that are subject to reference pricing.

[2] In some countries, such as Germany or the Netherlands, RP is applied more broadly including also drugs with similar therapeutic effects but different substances (see, e.g., Carone et al., 2012).

[3] The idea that potential ex post competition may reduce entry is well illustrated in Dasgupta and Stiglitz (1988).

[4] Danzon and Chao (2000) was perhaps the first paper to make this argument, but focused mainly on the effect of direct price regulation on generic competition.

the generic producers with an incentive to set higher prices and thus makes generic entry more profitable. On the other hand, RP triggers the brand-name producer to reduce its price to counteract the (expected) reduction in demand. If the brand-name producer's price response to RP is sufficiently aggressive, so that the generic producers also reduce their prices, then the net effect on generic entry may be negative. Thus, the impact of RP on generic entry is theoretically ambiguous and consequently an empirical question.

To estimate the effect of RP on generic entry, we exploit a policy reform in Norway that introduced a RP scheme called *Trinnpris* in 2005.[5] Importantly, the scheme was gradually implemented due to administrative reasons, and included initially only a limited set of off-patent substances. This allows us to use a difference-in-difference approach to estimate the effect of RP on generic entry. The effect is identified by selecting a sample of substances which all had generic competition prior to the policy reform in 2005, and comparing the change in the number of generic firms for the substances that were exposed to RP with those that were not exposed to RP. Estimating a fixed-effect model making use of detailed product-level data from 2003 to 2013, we find that the introduction of RP (i) substantially *increased* the number of generic producers, (ii) *intensified* price competition resulting in lower prices of both brand-name and generic drugs, and (iii) *increased* the market share of generic producers. Thus, our results suggest that the RP leads to a demand increase for generic drugs that outweighs the corresponding price reductions, and therefore stimulates generic entry. Despite the price reductions, we find no negative effect of RP on pharmaceutical expenditures, but show that this is due to an increase in total demand.

The literature on the effects of RP on pharmaceutical prices, sales, and expenditures is fairly large.[6] The empirical studies tend find that RP intensifies price competition between brand-name and generic producers, with the price response being stronger for brand-name drugs than generic drugs (see e.g., Pavcnik, 2002, Brekke et al., 2009, 2011, Kaiser et al., 2014). Most empirical studies also report that the brand-name market share is reduced by the introduction of RP (see e.g., Aronsson, 2001, Brekke et al. 2011, Kaiser et al., 2014). Despite the findings of intensified price competition, this literature tends to ignore the effect of RP on generic entry. The contribution of our study in relation to this literature is two-fold: First, we directly estimate the

[5] For details about this scheme, see the website of the Norwegian Medicines Agency; www.legemiddelverket.no/trinnpris.

[6] See Galizzi et al. (2011) for a review of the literature on RP in pharmaceutical markets.

impact of RP on generic entry per se. Second, we estimate the effect of RP on market outcomes explicitly accounting for generic entry. Our results show that RP has a positive effect on generic entry, which reinforces the direct effect of RP on prices and sales.

Despite the rich empirical literature on generic entry in pharmaceutical markets[7], very few papers investigate the impact of RP on generic entry. Ekelund (2001), Rudholm (2001), and Moreno-Torres et al. (2009) are, to our knowledge, the only studies that address the relationship between RP and generic entry.[8] Ekelund (2001) and Rudholm (2001) analyse the introduction of RP in the Swedish pharmaceutical market. While Ekelund (2001) reports a (weak) negative effect of RP on generic entry, Rudholm (2001) finds no effect of RP.[9] A more recent study by Moreno-Torres et al. (2009) on the Spanish pharmaceutical market finds a negative effect of RP on generic entry. Our study reports the opposite result, namely that RP stimulates generic entry. This is due to the fact that the positive demand effect on generic sales more than offsets the negative price effect induced by RP. However, as pointed out above, the impact of RP on generic entry is theoretically ambiguous, and this may explain the diifferent results. Our study also contributes to the existing studies in that we exploit the gradual implementation of RP in Norway, which enables us to estimate the causal effect of RP on generic entry using a difference-in-difference approach.

The remainder of the paper is structured as follows. In Section 2 we present a general framework to illustrate the main theoretical mechanisms which determine the relationship between RP and generic entry. In Section 3 we describe the institutional framework of the Norwegian pharmaceutical market. In Section 4 we present our data and descriptive statistics. In Section 5 we explain our empirical strategy and report our results. Section 6 concludes the paper.

[7] See, for instance, Grabowski and Vernon (1992), Frank and Salkever (1997), Scott Morton (1999, 2000), Reiffen and Ward (2005) for generic entry in the more unregulated US pharmaceutical market, and Rudholm (2001) and Iizuka (2009) for generic entry in the more regulated Swedish and Japanese markets, respectively.

[8] There is also a cross-country study by Danzon and Ketcham (2004) on the effects of different RP schemes on generic competition using one-year cross-sectional data.

[9] Bergman and Rudholm (2003) also study the impact of RP in Sweden, but focus on the impact of actual and potential generic competition on pharmaceutical prices.

2 Theoretical framework

To motivate our empirical analysis, we present a general theoretical framework for assessing the impact of different reimbursement schemes on pharmaceutical price setting, which in turn affect incentives for generic entry. Consider a pharmaceutical market with a brand-name drug (denoted b) which has lost patent protection and potentially faces competition from generic producers (denoted g and indexed by $i = 1, ..., n$) that can enter the market by incurring a fixed cost f. Without loss of generality, we abstract from other production costs.

Consumers are partially insured and face copayments c_b if purchasing the brand-name drug and c_g^i if purchasing generic drug i. Demand for the two drug versions are given by $D_b\left(c_b, c_g^1, ..., c_g^n, n\right)$ and $D_g^i\left(c_b, c_g^1, ..., c_g^n, n\right)$, with $\partial D_b/\partial c_b < 0$, $\partial D_b/\partial c_g^i > 0$, $\partial D_g^i/\partial c_g^i < 0$, $\partial D_g^i/\partial c_b > 0$, $\partial D_b/\partial n \leq 0$ and $\partial D_g^i/\partial n < 0$, and where all demand functions for generic drugs are symmetric. Finally, we assume that $D_b > D_g^i$ if $c_b = c_g^i$, implying that (at least some) consumers strictly prefer the brand-name drug over a generic alternative if copayments are identical. The profits of brand-name and generic producers, respectively, are then given by

$$\pi_b = p_b D_b\left(c_b, c_g^1, ..., c_g^n, n\right), \tag{1}$$

$$\pi_g^i = p_g^i D_g^i\left(c_b, c_g^1, ..., c_g^n, n\right) - f, \quad i = 1, ..., n. \tag{2}$$

where p_b and p_g^i are the prices set by the brand-name producer and generic producer i, respectively. We consider a two-stage game where the generic entry decisions are followed by simultaneous price setting.

2.1 Fixed percentage reimbursement (FPR)

Suppose first that the copayment is a fixed percentage of the price of the demanded product. If we let $\alpha \in (0, 1)$ be the coinsurance rate, the copayments for the brand-name and the generic drug i are $c_b^F = \alpha p_b$ and $c_{g_i}^F = \alpha p_g^i$, respectively. Suppose that n generic firms have entered the market. Because of the assumed symmetry among the generic producers, the Nash equilibrium in the price game has equal prices (and therefore equal demand) for all generic drugs. Let us denote the equilibrium brand-name and generic prices by p_b^F and p_g^F, respectively. These prices

are implicitly defined by the following system of equations:[10]

$$D_b\left(c_b^F\left(p_b^F\right), c_g^F\left(p_g^F\right), n\right) + c_b^F \frac{\partial D_b\left(c_b^F\left(p_b^F\right), c_g^F\left(p_g^F\right), n\right)}{\partial c_b^F} = 0, \tag{3}$$

$$D_g\left(c_b^F\left(p_b^F\right), c_g^F\left(p_g^F\right), n\right) + c_g^F \frac{\partial D_g\left(c_b^F\left(p_b^F\right), c_g^F\left(p_g^F\right), n\right)}{\partial c_g^F} = 0. \tag{4}$$

Defining $\varepsilon_j := -\frac{\partial D_j}{\partial c_j}\frac{c_j}{D_j}$ as the copay-elasticity of demand for drug j, the equilibrium conditions (3)-(4) imply

$$\varepsilon_b\left(c_b^F\left(p_b^F\right), c_g^F\left(p_g^F\right), n\right) = \varepsilon_g\left(c_b^F\left(p_b^F\right), c_g^F\left(p_g^F\right), n\right) = 1. \tag{5}$$

Thus, in equilibrium, each producer will price its drug such that the copay-elasticity of demand is equal to one. We assume that $\varepsilon_b < \varepsilon_g$ for $c_b = c_g$, which implies that the brand-name drug is higher priced than the generic drugs in equilibrium ($p_b^F > p_g^F$).

2.2 Exogenous reference pricing (RP)

Let us now consider a reference pricing scheme where the insurer defines a maximum reimbursement r, which is assumed to be exogenous in the sense that it does not depend on the pricing of the brand-name and generic producers. This is arguably the best approximation to reimbursement schemes where the reference price is not frequently updated or where updates are not based on predefined rules.

Assuming that the reference price is set such that $p_g^i < r < p_b$, copayments are given by $c_{g_i}^R = \alpha p_g^i$ and $c_b^R = \alpha r + p_b - r$.[11] By applying this copayment scheme and maximising (1)-(2) with respect to p_b and p_g^i, respectively, we derive the Nash equilibrium in the price game under RP, for a given number (n) of generic producers. Once more, because of symmetry, all generic prices (and market shares) are equal. Let us denote the equilibrium brand-name and generic

[10] Assuming the second-order conditions

$$\frac{\partial^2 \pi_b}{\partial p_b^2} = 2\alpha\frac{\partial D_b}{\partial c_b} + c_b\frac{\partial^2 D_b}{\partial c_b^2} < 0,$$

$$\frac{\partial^2 \pi_g^i}{\partial\left(p_g^i\right)^2} = 2\alpha\frac{\partial D_g^i}{\partial c_g} + c_g^i\frac{\partial^2 D_g^i}{\partial\left(c_g^i\right)^2} < 0, \quad i = 1, ..., n$$

are fulfilled.

[11] A reference price outside this interval would either imply that there is no difference between FPR and RP (if $r > p_b$) or that patients are not insured (if $r < p_g^i$). We consider both of these cases to be irrelevant.

prices by p_b^R and p_g^R, respectively. These prices are implicitly given by

$$D_b\left(c_b^R\left(p_b^R\right), c_g^R\left(p_g^R\right), n\right) + p_b^R \frac{\partial D_b\left(c_b^R\left(p_b^R\right), c_g^R\left(p_g^R\right), n\right)}{\partial c_b^R} = 0 \tag{6}$$

and

$$D_g\left(c_b^R\left(p_b^R\right), c_g^R\left(p_g^R\right), n\right) + c_g^R \frac{\partial D_g\left(c_b^R\left(p_b^R\right), c_g^R\left(p_g^R\right), n\right)}{\partial c_g^R} = 0. \tag{7}$$

Using once more the definition of copay-elasticity of demand, the equilibrium prices are such that

$$\varepsilon_b\left(c_b^R\left(p_b^R\right), c_g^R\left(p_g^R\right), n\right) = 1 - \frac{(1-\alpha)\, r}{p_b^R} < \varepsilon_g\left(c_b^R\left(p_b^R\right), c_g^R\left(p_g^R\right), n\right) = 1. \tag{8}$$

Thus, in equilibrium prices are set such that the copay-elasticity of demand is lower for brand-name than for generic drugs.[12]

2.3 FPR versus RP

Let us now compare equilibrium pricing under the two reimbursement regimes and deduce the potential implications for generic entry. When comparing the two equilibria, implicitly given by (5) and (8), notice that $c_g^R\left(p_g\right) = c_g^F\left(p_g\right)$, whereas $c_b^R\left(p_b\right) > c_b^F\left(p_b\right)$.

Consider first the pricing of the brand-name drug. Comparing (5) and (8), it is straightforward to see that RP gives the brand-name producer an incentive to reduce its price, compared with FPR. For given prices, RP reduces demand for the brand-name drug while simultaneously making demand more price-elastic. The first effect implies that RP increases the copay-elasticity of brand-name drug demand, whereas the second effect implies that brand-name profits are maximised when the copay-elasticity is less than one. Thus, both effects contribute towards a lower price for the brand-name drug under RP than under FPR.

The price response of generic producers to RP is more ambiguous. On the one hand, RP reduces the copay-elasticity of generic drug demand for given prices, since $c_b^R\left(p_b\right) > c_b^F\left(p_b\right)$ and therefore $D_g^R\left(p_b, p_g\right) > D_g^F\left(p_b, p_g\right)$, which gives generic producers an incentive to increases prices. On the other hand, the negative price response to RP by the brand-name producer implies that $c_b^R\left(p_b^R\right) < c_b^R\left(p_b^F\right)$, which has the opposite effect on the copay-elasticity of generic demand and

[12] This does not imply that the brand-name price is lower than generic prices in equilibrium, since, for equal copayments, the copay-elasticity is lower for brand-name than for generic drugs.

thus generic pricing. Thus, RP has both a positive direct (demand) effect and a negative indirect effect (due to prices being strategic complements) on the pricing of generic drugs. The relative strength of these two counteracting effects determine whether equilibrium generic prices are higher or lower under RP, compared with FPR. Since equilibrium generic prices imply a copay-elasticity equal to one under both reimbursement regimes, and since $c_g^R(p_g) = c_g^F(p_g)$, the effect of RP on generic prices depends ultimately on how RP affects the brand-name copayment, and how this in turn affects the copay-elasticity of generic drug demand. Given the assumption that $\partial\varepsilon_g/\partial c_b < 0$,[13] we can conclude that $p_g^R < (>)\, p_g^F$ if and only if $c_b^R\left(p_b^R\right) < (>)\, c_b^F\left(p_b^F\right)$. In words, if RP implies a lower brand-name copayment in equilibrium, it also implies lower generic drug prices.

Are incentives for generic entry higher under RP than under FPR? The answer to this question depends on the equilibrium profit difference (for a given number of generic producers) under the two reimbursement regimes. This profit difference can be written as

$$\pi_g^R(n) - \pi_g^F(n) = \left[D_g^R - D_g^F\right] p_g^R + \left[p_g^R - p_g^F\right] D_g^F. \tag{9}$$

The first term represents the demand effect, whereas the second term represents the price effect. Since both effects are *a priori* ambiguous, we can distinguish between four different scenarios:

1. If $p_g^R > p_g^F$ and $D_g^R > D_g^F$, RP unambiguously stimulates generic entry.
2. If $p_g^R > p_g^F$ and $D_g^R < D_g^F$, the effect of RP on generic entry is theoretically ambiguous.
3. If $p_g^R < p_g^F$ and $D_g^R > D_g^F$, the effect of RP on generic entry is theoretically ambiguous.
4. If $p_g^R < p_g^F$ and $D_g^R < D_g^F$, RP unambiguously discourages generic entry.

Since most empirical studies find that RP leads to lower generic prices, we consider the last two scenarios to be the most likely ones. If so, it follows that a necessary (but not sufficient) condition for RP to stimulate generic entry is that it leads to a lower brand-name market share.

[13] Since

$$\frac{\partial\varepsilon_g}{\partial c_b} = -\frac{c_g}{D_g}\left(\frac{\partial^2 D_g}{\partial c_b \partial c_g} - \frac{\partial D_g}{\partial c_g}\frac{\partial D_g/\partial c_b}{D_g}\right),$$

a sufficient (but not necessary) condition for $\partial\varepsilon_g/\partial c_b < 0$ is $\partial^2 D_g/\partial c_b \partial c_g \geq 0$.

3 Institutional background

The total sales of pharmaceuticals in Norway are around 20 billion NOK, where prescription drugs have a market share of around 80 percent.[14] As in most other European markets, the Norwegian pharmaceutical market is subject to regulation.[15] On the supply side, prices of prescription drugs are subject to price cap regulation. The price regulation scheme is based on international reference pricing (or external referencing), where prices are collected from nine Western European countries.[16] The maximum price of a given drug on the Norwegian market is set as the average of the three lowest prices of the (original brand-name) product in the reference countries. Generic drugs obtain the same price cap as the original brand-name product. In practice, this usually implies that the price cap is binding for the original drug, but not for the generic drugs. The price caps are usually revised annually, and change depending on the price development in the reference countries and/or the movements in the exchange rates.

On the demand side, there is cost-sharing of medical expenditures between the National Insurance Scheme and the patients for prescription drugs on the reimbursement list.[17] For these drugs, patients pay a standard coinsurance, which is currently 38 percent of the price of the drug, up to an annual expenditure cap (at NOK 2105). If the medical expenditures exceed this cap, patients receive 100 percent insurance coverage for any additional medical costs within the given calender year.

To increase demand elasticity and curb pharmaceutical expenditures, Norway introduced in 2005 a reference pricing scheme called *Trinnpris*. This scheme applies to prescription drugs on the reimbursement list that have lost patent protection and thus are subject to competition from generic drugs. The reference price, which is the maximum reimbursement from the National Insurance Scheme, is set as a fixed discount on the price cap of the original brand-name drug in the period prior to patent expiration and generic entry. The initial discount is 35 percent and effective immediately when generic competition takes place. After six months the discount is

[14] 1 Euro is about 8 NOK, 1 US dollar is about 6 NOK, and 1 British pound about 10 NOK.

[15] For details about the regulation of the Norwegian pharmaceutical market, see the website of the Norwegian Medicines Agency; *www.legemiddelverket.no.*

[16] The reference countries for Norway are Austria, Belgium, Denmark, Finland, Germany, Ireland, the Netherlands, Sweden, and the UK

[17] Over-the-counter drugs and prescription drugs not listed for reimbursement, which usually are pharmaceutical aimed at treating short-term conditions, the patients have to pay out-of-pocket 100 percent of the medical costs.

increased to around 60 or 80 percent depending on the sales value of the drug. Eventually, after (at least) 18 months the regulator can increase the markup up to a maximum of 90 percent for the substances with the highest sales value.[18]

Patients that purchase a product that is priced higher than the reference price have to pay the full price difference out-of-pocket in addition to the standard coinsurance payment. Notably, this part of the patients' copayment have to be paid irrespectively of whether the accumulated medical costs exceed the annual expenditure cap described above. Moreover, pharmacies are through the generic substitution law obliged to offer patients lower priced (generic) products. If patients refuses to accept the generic substitute, then they are charged the price difference between the actual price of the product and the reference price.

The *Trinnpris* scheme, which was effective from 1st of January 2005, was announced by the government in May 2004 and later approved by the Norwegian Parliament in October 2004. However, the implementation of the reference pricing scheme was gradual. This was mainly due to practical reasons and the administrative workload related to computing the reference prices for the relevant products. Thus, from 1 January 2005 the Norwegian Medicines Agency included only 20 off-patent substances that had lost patent protection and faced competition from generic drugs.[19] The scheme has been gradually extended and includes now more than 100 substances. In the empirical part, we will exploit this policy reform and its gradual implementation in order to identify effects on generic entry and pricing.

4 Data and descriptive statistics

To study the effects of RP on the entry of generic products and, in turn, on pricing and sales of pharmaceuticals, we have collected information about generic entry, pricing and sales of the 222 best selling molecules from the database of the Norwegian Pharmacy Association, which contains detailed sales information of all transactions (purchases) made at every pharmacy in Norway.[20] We could retrieve monthly information about sales revenues and volumes (number of packs and

[18] For more details see the webpage of the Norwegian Medicines Agency www.legemiddelverket.no.

[19] For the list of substances subject to *Trinnpris*, with details about when they were included, see www.legemiddelverket.no/trinnpris.

[20] Sales that are channeled through the hospitals to hospitalized patients and over-the-counter drugs sales taking place outside pharmacies (at, say, grocery stores) are not covered by this database. For more details, see the website of the Norwegian Pharmacy Association; www.apotek.no.

defined daily doses (DDDs)) for all products over the eleven year period 2003-2013. The data also contains information about producer (seller), pack size, dosage strength, and whether the drug is branded or generic.

Using the information about actual generic sales in our data, we can identify the date entry of each generic firm. The data also allows us to measure the intensity of generic competition, as we can observe the number of active generic products at each date during the sample period.[21] By dividing sales revenues by sales volumes measured in DDDs, we obtaines a monthly (sales-) weighted average price per DDD of the brand-name and generic drugs for each month. This measure enables us to study the impact of reference pricing and generic entry on the firms' pricing strategies as well as the corresponding effects on sales and market shares.

Data on reference prices for all products in our sample over the period 2003-2013 was collected from the Norwegian Medicines Agency. From this dataset, we used the date in which the reference price was applied to each specific market (if ever).

We only include in the analysis markets with generic competition before the reform was announced, in May 2004. This allows us to exclude molecules under patent protection. In absence of reliable patent data, our study focuses on the effect of RP on competition at the intensive margin, rather than at the extensive margin. We dropped 7 molecules subject to a previous, experimental version of reference pricing (which was an endogenous RP scheme called *Indekspris*). Moreover, we dropped all all non-tablets products. The reason to focus on tablets only is twofold. First, no molecules commercialized in non-tablet form only have been subject to RP over the 2003-2013 period. Second, this ensures that the market defined by each molecule includes comparable producs. Within the same molecule one can have non-tablet and tablet products, and they may not be substitutable. We are left with an unbalanced panel of 36 molecules for a total of 4,686 month-molecule observations over the period 2003-2013. Of the 36 molecules in our sample, 19 were subject to RP in some period after the reform was introduced, in January 2005. This group will be our treatment group. Conversely, 17 molecules were never subject to RP, and they will constitute our control group.

In Table 1, we report the mean and the standard deviations of the dependent variables in our empirical models, for drugs with generic competition. For drugs subject to reference pricing,

[21] We consider as a unique product all packages differing only in dosage (number of tabs or grams per tabs).

we calculate these measure for the periods before and after these drugs were included in the RP scheme. For drugs never subject to reference pricing, we calculate averages before and after the reform was introduced, in 2005, in order to provide some comparison. The drugs in the treatment group display an increase in the number of generics present on the market after the introduction of reference pricing (from 1.6 to 2.5 per market). For drugs in the control group, the number of generics actually decreased over time (from 2.4 to 1.7). Drug prices in the treatment group before the introduction of RP are relatively high compared with the ones in the control group. However, the average price for treated drugs decreases after the introduction of reference pricing, whereas the average price of drugs in the control group does not decline substantially over time. A similar pattern can be found for the market shares of the originator. Figures 2-8 display the trends of the variables of interest for the control and treatment groups.

[Insert Table 1 here]

5 Empirical Strategy and results

Our aim is to test for the effect of RP on the number of generic products in the market. As mentioned above, we limit our analysis to markets with some generic competition prior to the announcement of the RP reform. Thus, our estimates of the effect of RP are conditional on competition being already present in the market. As discussed in Section 2, a necessary condition for RP to stimulate generic entry in the case where RP leads to lower generic prices, is that demand shifts away from the originator. For this reason, we also test the effect of RP on market shares and on market prices.

Our strategy relies on a comparison of the molecules affected by RP (treatment group) to similar molecules that were never subject to RP (control group). The effect of the regulatory change can be evaluated with a difference-in-difference approach. Because of the panel structure of the data, we can compare inter-temporal variation in the number of generic competitors before and after the imposition of the reform for each molecule. The identification does not only rely on a before and after comparison, but also on a comparison of variations in the number of generic products for molecules subject to RP with variation in outcomes for molecules not subject to this reform.

The model to be estimated is

$$Y_{it} = \beta \mathbf{X}_{it} + \rho D_{it} + \delta_t + a_i + \epsilon_{it}, \tag{10}$$

where Y_{it} is the variable of interest (number of generics, prices, sales or market shares) at time t in market i. D_{it} is a dummy variable equal to one if molecule i is subject to RP at time t, and the vector $\mathbf{X}_{it}$ contains observed time-varying characteristics. In the baseline model these include the number of therapeutic substitutes in the same ATC3 group and market size (captured by the log of sales revenues of all the product in the therapeutic group). a_i is a molecule fixed effect, whereas δ_t is a month-specific effect common to all molecules. The coefficient of interest is ρ, which captures the effect of reference pricing.

5.1 Pre-reform test

For our approach to be valid in identifying the causal effect of RP on generic entry, the treatment and the control group need to be comparable. While differences in characteristics that are constant over time can be controlled for by fixed effects, systematic differences in trends in the pre-reform period are more problematic. In other words, for our parameter ρ to estimate causal effects, the trend of the number of generic products before the introduction of RP should be similar in the treatment and control group. We cannot implement the usual pre-reform tests, due to the fact that RP is introduced at different points in time to the molecules in the treatment group. However, we run the test on the period before the reform was announced, in May 2004. By that point, the producers of molecules soon to be included in the RP scheme could have been already informed (at least informally).[22]

The plots of the pre-reform trends are presented in Figure 1. The figure suggests that the evolutions in the number of generics are fairly similar across the two groups in the pre-reform period. To test our assumption of common trends, we also run a fixed effects regression where the dependent variable is the number of generics. We only consider pre-reform observations (January 2003-May 2004) and we include interactions between monthly dummies and a dummy indicating treated molecules. If these interactions do not have a significant coefficient, this

[22] Of the 19 molecules in the treatment group, 14 were included in the RP scheme already in 2005, while 5 were included later on.

indicates that pre-reform trends are not significantly different, and that the control group is legitimate. The results of the test are presented in Table 2. All interactions are non-significant, both individually and jointly.

[Insert Figure 1 here]

[Insert Table 2 here]

5.2 Effects of reference pricing on generic entry

The main results on generic entry is reported in Table 3, in column (1). The number of generics in a given market is significantly higher after the introduction of RP. The effect (1.4) is quite high if compared with average number of entrants in the pre-reform period (1.6). As our descriptive statistics and Figure 2 illustrate, this positive and strongly significant effect is due to both an increase in the number of generics for molecules subject to RP, and a decline in the number of generics for molecules in the control group.

In order to be consisted with our pre-reform test, we also consider the possibility that producers may be informed early about the inclusion in the RP scheme. Thus, we define a different treatment dummy, taking value one in all periods with RP and in the 7 months prior to the inclusion of the drug in the RP scheme. The results, presented in column (2) of Table 2, indicate that our parameter of interest is robust to this alternative specification.

Our results are robust to different criteria of inclusion in the sample. First, we exclude from the sample molecules belonging to the treatment group that are included in the RP scheme after 2006 (5 molecules). This robustness check is meant to exclude the possibility that our previous results are driven by molecules included late in the scheme. For these molecules, our pre-reform test may fail to detect differences in trends occurring immediately before the introduction of RP. The results, reported in the first column of Table 4, rule out this possibility. To check whether the results are specific to tablets, we also run the regressions on the full set of products, including non-tablets. In this case, the treatment group is the same as in our main sample, but the control group is now larger, including 29 molecules. Again, the main results, reported in the second column, are confirmed, and the coefficient of interest has a similar magnitude. Finally, we consider the sample including non-tablets, but we exclude the 5 molecules for which the RP

was introduced after 2006. Again, the results are robusts to this specification.

Controlling for RP inclusion, we do not find any significant effect of the number of therapeutic substitutes and of the market size (captured by market revenues) on the number of generics on each market. While this is somehow surprising, if compared with the previous literature (see Grabowski and Vernon, 1992, and Scott-Morton, 1999 and 2000), it is probably due to the fact that these variables display little variation over time. The effects of molecule-specific market conditions may thus be captured by the fixed effects.

[Insert Table 3 here]

[Insert Table 4 here]

5.3 Effects of reference pricing on market shares and prices

Based on our main result reported above, that RP increases the number of generics, we expect RP to affect negatively the market share of brand-name drugs. Theoretically, the effect of RP on brand-name prices is unambiguously negative, whereas the effect on generic prices is ambiguous. Below we explore these two issues by analysing the effect of RP on market shares and prices. We estimate two groups of models similar to the previous one, but where the dependent variables are market shares and prices, respectively.

The results on the effect of RP on the originator's market share are presented in Table 5. In columns (1) and (2) we do not control for the number of generics, and we find that the introduction of RP reduces the market shares of the originators by 38 percentage points (36 points if we lag the introduction of reference pricing to take announcement effects into account). This coefficient is statistically and economically significant. However, it may capture two effects. On the one hand, RP shifts demand from the brand-name drugs to generics, and this may lead to a reduction in brand-name market shares for a given number of generics. On the other hand, we have shown in the previous section that RP also encourages entry, and this may also have a negative effect on the originators' market shares. In order to disentangle these two effects, in columns (3) and (4) we control for the number of generics. Not surprisingly, the coefficient is negative and significant. In line with our economic intuition, controlling for the number of generics reduces the estimated coefficient for the RP dummy. This result is comparable with

the one of the literature, that takes the number of generics as given in assessing the impact of RP.

[Insert Table 5 here]

We now turn to analysing the effect of RP on prices. The results for the price model, for both brand-name drugs and generics, are presented in Table 6. The dependent variables are logged prices, so that the coefficients can be interpreted in terms or relative changes. In columns (1) and (4) we do not control for the number of generics. The estimated effect of RP on prices is negative for both the brand-name drugs (an estimated 34% reduction) and generics products (an estimated 43% reduction). The fact that generic prices drop more than the prices of brand-name drugs does not imply that the decline for generics is higher in absolute terms, since generics typically have lower prices (see Figures 5 and 6). In columns (2) and (5) we control for the number of generics on the market. We do not find a significant coefficient associated with this variable, and the estimated effect of RP on prices does not seem to be strongly affected by its inclusion in the regression.

In columns (3) and (5) we use the dummy associated with the announcement of RP. The coefficient associated with this dummy has a slightly lower coefficient than the dummy associated with the introduction of RP in the market. Thus, it seems that price adjustments are not fully implemented at the time of the policy announcement, but take place once the new regulation is in place in the market.

In Table 7, we present estimates on the effect of RP on average prices. Not surprisingly, the effect is negative. This is due both to the shift in demand towards cheaper generic drugs, and to price responses of both brand-name and generic firms.

[Insert Table 6 here]

[Insert Table 7 here]

The empirical evidence described above allows us to better interpret the evidence on generic entry. RP leads to lower prices but higher demand for generic drugs. Thus, RP shifts demand from brand-name to generic drugs, even after prices have been adjusted. This is a necessary condition for RP to encourage entry in the case where RP leads to lower generic prices. Indeed,

our results on the effect of RP on generic entry show that the positive demand effect is sufficiently large to outweigh the negative price effect. Even if post-RP prices are lower, the expected profit of selling a generic drug increases because of the demand effect.

5.4 Effects of reference pricing on expenditures and profits

In the previous sections, we have shown that reference pricing reduces prices, and shifts demands towards generics. Overall, the effect on generic entry is positive. We now turn to analysing the effect of RP on total pharmaceutical expenditures (born both by the government and by consumers) and on the profitability of selling brand-name and generic drugs. The effect on expenditures is *a priori* ambiguous: since prices have been reduced for molecules with RP, demand might have increased, thus offsetting potential savings. Concerning profitability, we expect the profits of the originator to decline, and the joint profits of generics' producers to increase, once we control for the number of generics in the market. If this was not the case, it would be difficult to explain the positive effect of RP on generics' entry.

Our measure of expenditures is the total sales (prices multiplied by volumes) of all drugs in the therapeutic group. Our measure of profitability is also the sales of brand-name drugs and generics. We assume that the variable costs of producing all drugs have not changed over time, so that sales revenues can be interpreted as a proxy for profits.

Table 8 summarises the results. In columns (1) and (2) we report the results for the expenditures. There appears to be no significant effect of RP on overall (log) expenditures. Despite the reduction in prices, expenditures do not decline. As reported in Table 9, this seems to be due to the fact that RP is associated with an increase in the total volume of drugs sold (in DDDs). The increase is non-negligible, amounting to approximately 30%.

However, when we decompose sales between brand-name and generic drugs, the results are quite different. The coefficients are presented in columns (3) and (4) of Table 8. As expected, the profits (proxied by sales) of the originators are negatively affected by RP. The coefficient is very high, 85%, even controlling for the number of generics. The joint profits of generics' producers are positively affected by RP (the increase equals 185%), for a given number of generics present in the market. This is direct evidence of the fact that expected profits (for a given number of generics) are higher in markets with RP, implying that RP stimulates generic entry.

[Insert Table 8 here]

[Insert Table 9 here]

6 Conclusion

This paper constitutes an attempt to generate predictions on the effect of reference pricing on the number of generics and ultimately on prices. Theoretically, the effect of RP on generic entry is ambiguous and depends on the relative strength of two opposing effects. Whereas RP shifts demand towards generic drugs for given drug prices, which (all else equal) stimulates generic entry, RP also induces the brand-name producer to reduce its price, which has the opposite effect on the profitability of selling generic drugs.

Using Norwegian data, we compare drugs subject and not subject to RP, and find that the introduction of a RP scheme has a positive effect on the number of generic products present in the market. Although RP leads to lower prices for all drugs, the positive effect on demand for generic drugs is sufficiently large to stimulate generic entry. Thus, our results suggest that focusing on short-term price responses to RP might lead to an underestimation of the pro-competitive effects of reference pricing, since the initial price reductions caused by RP (for a given number of generics) are reinforced by increased generic entry. Nevertheless, our empirical results also show that the price reductions caused by RP did not translate into a reduction in overall drug expenditures, since these price reductions were offset by an increase in the total demand for prescription drugs.

One important limitation of our study is that we only consider generic entry/exit in markets where generic competition is already present. An interesting line of future research would be to include in the analysis all off-patent drugs, in order to look at the effect of RP on the probability and lags of entry. To this purpose, detailed patent data would be needed.

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Appendix

[Insert Figures 2-8 here]

Tables and Figures

Table 1: Descriptive statistics

VARIABLES	RP. Before	RP. During	No RP. Before 2005	No RP. After 2005
N. of generics	1.643 (1.1863)	2.497 (1.2689)	2.364 (2.0512)	1.692 (1.6985)
Average Price	14.715 (24.1303)	7.714 (12.4324)	5.486 (3.8217)	4.561 (3.0436)
Market share of orig.	.756 (.2824)	.391 (.2132)	.681 (.3546)	.694 (.3673)
N. of markets	19	19	17	17

Figure 1: Average number of generics. Pre-reform trend for substances subject to reference pricing (RP) and not subject to reference pricing (CR)

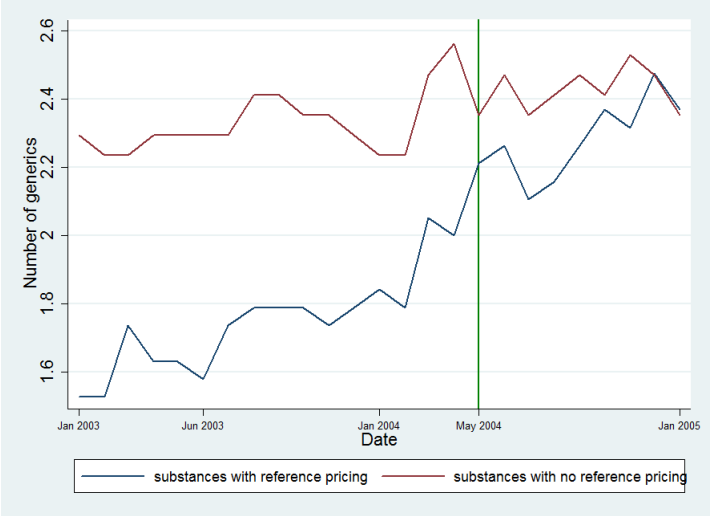

Table 2: Pre-reform test, fixed effects with model with robust standard error.

	Number of generics
Interaction 1	-.294
	(.3386)
Interaction 2	-.231
	(.3116)
Interaction 3	-.012
	(.2809)
Interaction 4	-.1808
	(.3137)
Interaction 5	-.179
	(.2967)
Interaction 6	-.231
	(.3139)
Interaction 7	-.070
	(.2698)
Interaction 8	-.136
	(.2635)
Interaction 9	-.138
	(.2209)
Interaction 10	-.082
	(.1922)
Interaction 11	-.132
	(.2552)
Interaction 12	-.026
	(.1931)
Interaction 13	.091
	(.1959)
Interaction 14	-.038
	(.1701)
Interaction 51	.063
	(.1690)
Number of terapeutic substitutes	-.036
	(.2214)
Log Revenues	.092
	(.2029)
Joint Significance (Ftest)	.1105
Time dummies	Yes
Molecule dummies	Yes
Number of markets	36
Observations	575
R^2	0.0734

Table 3: Estimated effects of reference pricing on the number of generics. Fixed effect models

	(1)	(2)
Reference Pricing	1.420***	
	(.4196)	
Reference Pricing, 7 month lagged		1.528***
		(.3589)
Number of therapeutic substitutes	-.252	-.268
	(.2171)	(.2169)
LogRevenues	-.042	-.073
	(.1915)	(.2012)
Constant	4.920*	5.5022*
	(2.7658)	(2.9663)
Time dummies	Yes	Yes
Molecule dummies	Yes	Yes
Number of markets	36	36
Observations	4686	4686
R^2	.1797	.1857

Table 4: Estimated effects of reference pricing on the number of generics. Robustness checks

	(1) Treatment: RP before 2006	(2) All molecules	(3) All molecules. Treatment: RP before 2006
Reference Pricing	1.266*	1.355***	1.280*
	(.635)	(.501)	(.759)
Number of therapeutic substitutes	-0.284	-0.372	-0.400
	(.220)	(.282)	(.304)
LogRevenues	-0.00146	0.135	0.246
	(.194)	(.320)	(.335)
Constant	4.709*	2.759	1.390
	(2.725)	(5.258)	(5.223)
Time dummies	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes
Number of markets	31	48	43
Observations	4026	6335	5675
R-squared	.191	.112	.110

Table 5: Estimated effects of reference pricing on the originator's market shares. Fixed effect models

	(1)	(2)	(3)	(4)
Reference Pricing	-.386***		-.313***	
	(.0700)		(.0657)	
Reference Pricing, 7 month lagged		-.367***		-.285***
		(.0666)		(.0652)
Number of therapeutic substitutes	.035	.036	.024	.025
	(.0321)	(.0320)	(.0304)	(.0303)
LogRevenues	-.034	-.020	-.039	-.027
	(.0412)	(.0469)	(.0362)	(.0404)
Number of generics			-.055***	-.057***
			(.0098)	(.0112)
Constant	.952	.672	1.125*	.940
	(.6144)	(.6820)	(.5605)	(.6131)
Time dummies	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes
Number of markets	36	36	36	36
Observations	4486	4486	4486	4486
R^2	.4844	.4465	.5574	.5245

Table 6: Estimated effects of reference pricing on prices (logged). Fixed effect models

	(1)	(2)	(3)	(4)	(5)	(6)
	Originator	Originator	Originator	Generics	Generics	Generics
Reference Pricing	-.343***	-.321***		-.421***	-.417***	
	(.0670)	(.0730)		(.0702)	(.0712)	
Reference Pricing, 7 month lagged			-.255***			-.320***
		(.0740)				(.0784)
Number of therapeutic substitutes	.021	.018	.017	.048	.046	.047
	(.0321)	(.0337)	(.0369)	(.0310)	(.0319)	(.0352)
Number of generics		-.016	-.022		-.006	-.012
		(.0182)	(.0216)		(.0137)	(.0163)
Constant	1.289***	1.428***	1.415***	1.327***	1.358***	1.365***
	(.2644)	(.2958)	(.3274)	(.2701)	(.2919)	(.3225)
Time dummies		Yes	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes	Yes	Yes
Number of markets	36	36	36	36	36	36
Observations	4484	4484	4484	3850	3850	3850
R^2	.5443	.5480	.5103	.4806	.4811	.4244

Table 7: Estimated effects of reference pricing on average prices (logged). Fixed effect models

	(1)	(2)	(3)
Reference Pricing	-570***	-.510***	
	(.0813)	(.0676)	
Reference Pricing, 7 month lagged			-.430***
			(.0708)
Number of therapeutic substitutes	.032	.022	.022
	(.0274)	(.0268)	(.0311)
Number of generics		-.042 **	-.049**
		(.0171)	(.0217)
Constant	1.472***	1.654***	.1.379***
	(.2334)	(.2414)	(.2799)
Time dummies	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes
Number of markets	36	36	36
Observations	4686	4686	4686
R^2	.7125	.7304	.6765

Table 8: Estimated effects of reference pricing on expenditures (logged). Fixed effect models

	(1)	(2)	(3)	(4)
	Total	Total	Originator	Generics
Reference Pricing	-.228		-.851***	1.836*
	(.1366)		(.2060)	(.9823)
Reference Pricing, 7 month lagged		-.162		
		(.1227)		
Number of therapeutic substitutes	.002	.001	.045	-.344
	(.0658)	(.0672)	(.1232)	(.2903)
Number of generics	-007	-.013	-.102**	.242***
	(.0328)	(.0346)	(.0471)	(.0650)
Constant	14.373***	13.820***	13.087***	14.355***
	(.5860)	(.3197)	(1.1055)	(2.5472)
Time dummies	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes
Number of markets	36	36		
Observations	4686	4686	4484	3845
R^2	.3381	.3321	.4420	.1976

Table 9: Estimated effects of reference pricing on volumes (measured in DDD, logged). Fixed effect models

	(1)	(2)
Reference Pricing	.282**	
	(.1208)	
Reference Pricing, 7 month lagged		.268**
		(.1132)
Number of therapeutic substitutes	-.020	-.022
	(.0603)	(.0607)
Number of generics	.035	.036
	(.0334)	(.0344)
Constant	12.720***	12.441***
	(.5295)	(.5573)
Time dummies	Yes	Yes
Molecule dummies	Yes	Yes
Number of markets	36	36
Observations	4686	4686
R^2	.1652	.1602

Figure 2: Average number of generics. Trend for substances subject to reference pricing (RP) and not subject to reference pricing (CR)

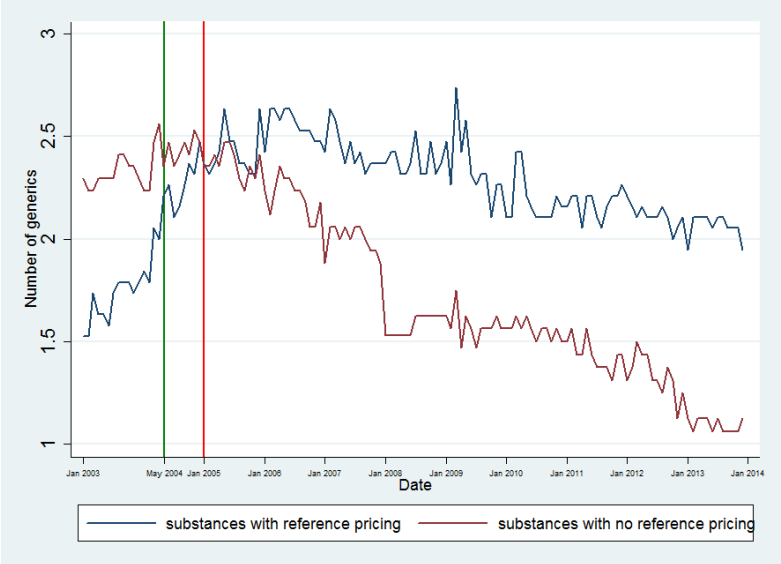

Figure 3: Average market shares of the originator. Trend for substances subject to reference pricing (RP) and not subject to reference pricing (CR)

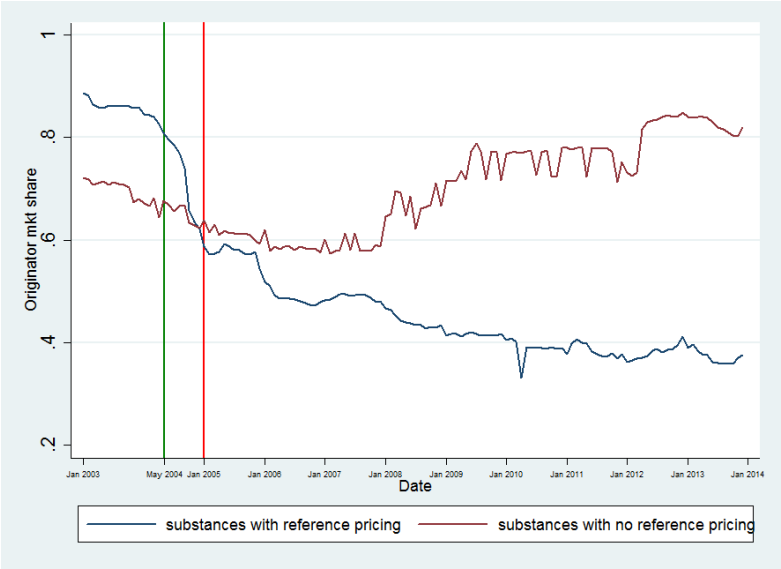

Figure 4: Average prices. Trend for substances subject to reference pricing (RP) and not subject to reference pricing (CR)

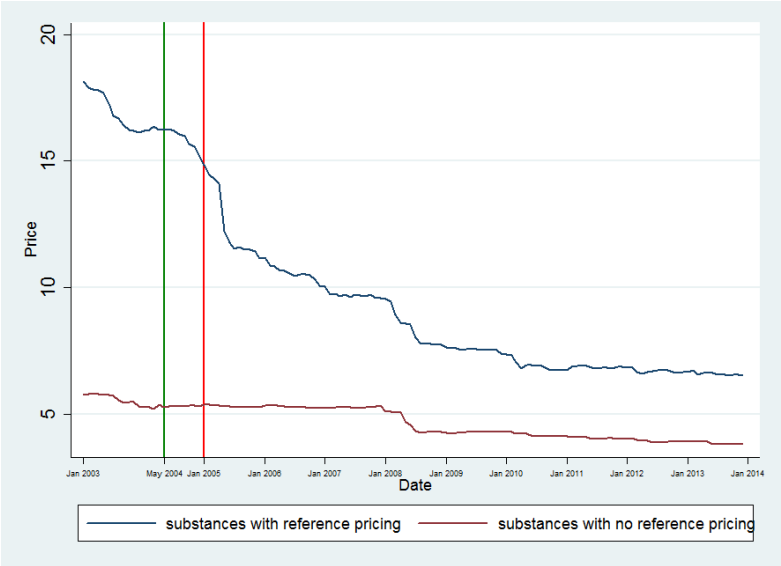

Figure 5: Average originator prices. Trend for substances subject to reference pricing (RP) and not subject to reference pricing (CR)

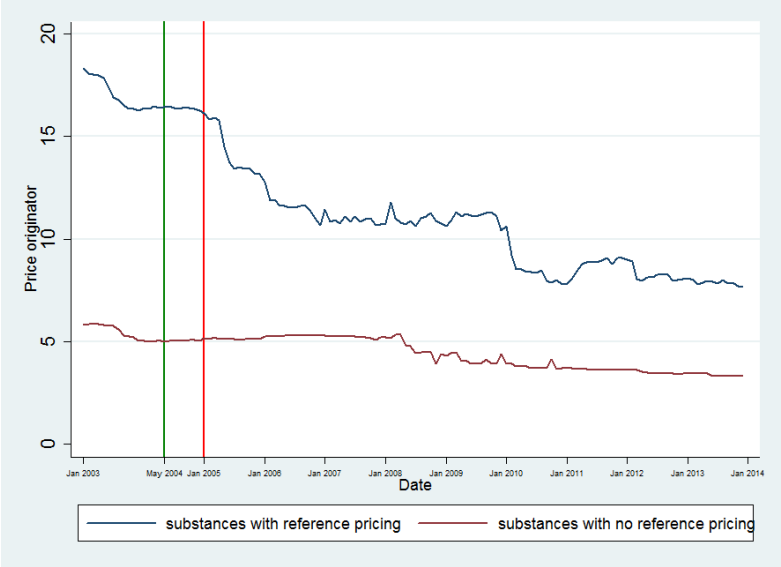

Figure 6: Average generic prices. Trend for substances subject to reference pricing (RP) and not subject to reference pricing (CR)

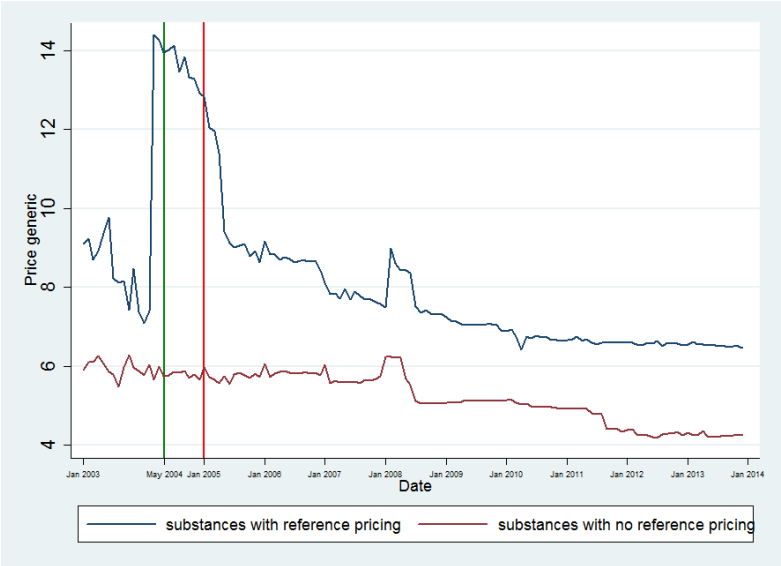

Figure 7: Average revenues. Trend for substances subject to reference pricing (RP) and not subject to reference pricing (CR)

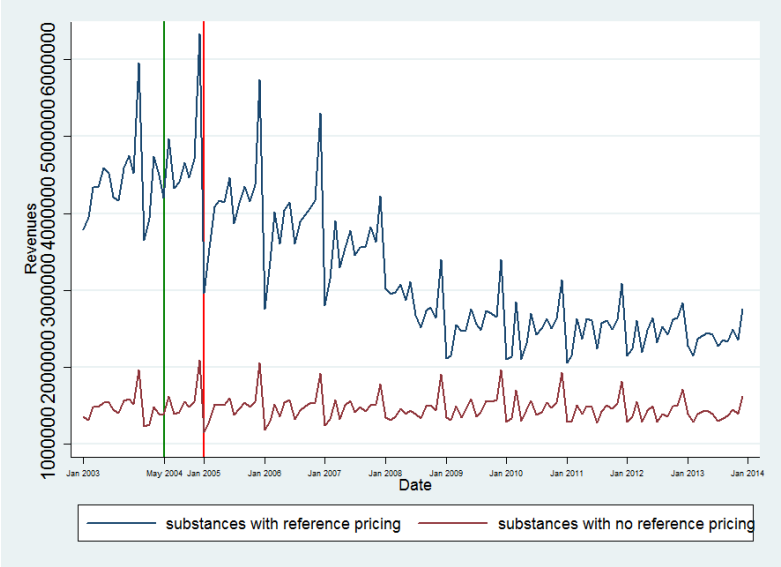

Figure 8: Average volumes, in DDD. Trend for substances subject to reference pricing (RP) and not subject to reference pricing (CR)