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Dissertação apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Economia, realizada sob a orientação científica da Doutora Aida Isabel Pereira Tavares, Professora Auxiliar do Departamento de Economia, Gestão e Engenharia Industrial da Universidade de Aveiro.

Dedico este trabalho à minha família por todo o amor e o apoio que me transmitiram ao longo da minha formação académica.

o júri

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palavras-chave

Indústria farmacêutica, genéricos, risco moral, escalões de comparticipação
Classificação JEL: I11, I18, L13, L65.

resumo

Este trabalho mostra evidência empírica sobre a existência de risco moral na prescrição de medicamentos em Portugal. A questão é abordada numa situação onde os copagamentos de alguns pacientes são muito baixos. Assim, o principal objetivo é testar se os pacientes, que são abrangidos pelo escalão de comparticipação superior, consomem menos genéricos prescritos por médicos do que os pacientes com maior copagamento.
O modelo econométrico estimado pelo Método dos Mínimos Quadrados; métodos dos Efeitos Fixos e Efeitos Aleatórios e pelo método "Equação de Estimação Generalizada" a partir de um painel de vendas dos medicamentos de Sistema Nacional de Saúde e os dados de despesas de Sistema Nacional de Saúde por mês para o período de 2004 a 2009. Os dados abrangem 38 subgrupos farmacêuticos.
Os resultados mostram que quando o nível de comparticipação aumenta (ou a parte do custo que Sistema Nacional de Saúde paga) o rácio do consumo entre medicamentos genéricos e de marca diminui. É encontrada assim evidência empírica da existência de risco moral na prescrição médica. No entanto, quando é considerada a diferença de preço entre medicamentos de marca e genéricos a existência de risco moral é parcial.

keywords Pharmaceutical industry, generic drugs, moral hazard, reimbursement level.
JEL classification: I11, I18, L13, L65.

abstract This work provides evidence on the existence of moral hazard in the prescription of drugs in Portugal. The question is addressed in a setting where co-payments of some patients are very low. So the main aim is to test if patients, who covered by higher reimbursement level, consume fewer generics prescribed by physicians than patients with higher co-payment.
The econometric model is estimated with Pooled Ordinary Least Square Estimation, Fixed and Random Effects, and with Generalized Estimating Equations approach for a panel of monthly National Health System drug sales and reimbursement expenditure data from 2004 to 2009. We use dataset, which covers 38 pharmaceutical subgroups.
The main results show that the greater the reimbursement level that the patient has (or the part of cost that National Health System pays), the lower the proportion of generics prescriptions made by physicians. This confirms the existence of moral hazard. However, when the price difference between branded drugs and generics is considered, only partial existence of moral hazard is found.

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ABBREVIATIONS CONTENTS

DDD	Defined Daily Dose
FE	Fixed Effects estimation
GEE	Generalized Estimation Equation
HG	Homogeneous Group
NHS	National Health System
OLS	Ordinary Least Square estimation
PRP	Pharmacy Retail Price
RE	Random Effects estimation
RP	Reference Price
RPS	Reference Price System
WHO	World Health Organization

“When it comes to health care, higher costs don’t always mean better care.”

Salynn Boyles

1. Introduction

Pharmaceutical expenditure is one of the biggest spending components in medical care expenditure, both public and private. It represents nearly one fifth (19%) of all health expenditure on average in OECD countries and it accounted for more than 700USD billion in 2009. The increase in spending on pharmaceuticals has contributed to the growth of total health expenditure in the last 20 years. In Portugal, between 2000 and 2009, pharmaceutical spending increased on average 1.9% per year in real terms. Pharmaceutical spending represented 2.1% of the Portuguese GDP, in 2009. This is 40% above the OECD average (OECD, 2011).

The rising drug expenditure has been driven by two main factors: the demographic changes (such as the elderly population and the number of individuals with chronic diseases) and the introduction of new high cost drugs. In response to increased expenditure, all countries have introduced different strategies to contain this cost (Mossialos & Barros, 1998). One of these strategies is the promotion of generics competition. In this promotional effort, physicians[1] and patients play an important role. Physician's role is to prescribe drugs for the patients. In some cases patients can influence the physician's choice between two versions of the same drug. The government regulates the prescription procedure. However, it is difficult to control the decision of doctors about prescription, since they can justify it with patient needs. Empirical evidence suggests that physicians and patients prefer branded drugs over generics version. Since generic drugs may present uncertainty about side effects and some therapeutic effects and there are no economic incentives to choose cheaper generics, etc. For instance, high reimbursement level prevents patient from an extra cost, associated with acquisition of branded drugs (Lundin, 2000).

The Portuguese National Health System (NHS) includes a drug reimbursement system that covers the whole population. The cost of drugs is usually shared between the NHS and the patient. The price a patient pays for a prescribed drug, called the co-payment, depends on the patient's disease and the

[1] The pharmacist may substitute branded drugs for generics if the doctor has previously allowed it. However it is difficult to control if the pharmacist substituted the prescribed drug in our statistical data.

patient's social-economic situation. There are four main reimbursement categories in Portugal, which vary from 15% to 90%. In some circumstances, the total drug cost (100%) may be paid by the NHS.

One may wonder if patients who are covered by higher reimbursement rate consume fewer generic drugs. This phenomenon is called moral hazard. It means the high usage of more expensive branded drugs when the patient's marginal costs are low due to insurance (high reimbursement level). Moral hazard is a phenomenon in the pharmaceutical market and it has been subject to several research work both theoretical and empirical (Pauly, 1968; Coscelli, 1998). However, the empirical evidence on moral hazard in pharmaceutical market is not conclusive. Some authors find evidence supporting its existence (Lundin, 2000; Rudholm, 2005); others do not (Hellerstein, 1998).

The main aim of this work is to test the existence of moral hazard in the prescription of drugs in Portugal, that is, to verify if higher reimbursement level motivates doctors to prescribe branded drugs instead of generics.

Our data comprises NHS drugs sales and NHS reimbursement expenditure per month for 38 pharmaceutical subgroups, for which generics exist in the period 2004 to 2009. We use pooled ordinary least squares estimation (OLS), fixed effects approach (FE), random effects approach (RE) and generalized estimating equations (GEE) population-average approach to estimate demand model. For each specification, we test the differences in the coefficients for FE and RE, using a Sargan-Hansen test. We also use the GEE approach and compare results with the RE approach.

The obtained results make it possible to estimate the determinants for the demand of generic drugs. We determine two approaches for testing the existence of moral hazard. The first approach uses reimbursement level and the second one uses the relative expenditure between NHS and patients.

The analysis is done for the set of all pharmaceutical subgroups in the three levels of reimbursement and also for a subset of drugs subgroups in the two lower levels of reimbursement.

The main results confirm the existence of moral hazard in physicians' prescription behavior in the Portuguese pharmaceutical market. However, this effect seems to be stronger in the highest reimbursement category.

This work is organized as follows. The next section is the literature review. In section 3 we describe the hypothesis, estimation method and econometric model. Next we present our data and a descriptive analysis. The results are presented and discussed on section 4. The conclusion and discussion are included in section 5. The references are in the last section. Tables and figures are reported in the appendices.

2. Literature review

2.1 Moral Hazard in pharmaceutical industry

Moral hazard in health care industry is an important problem, which many researchers have studied. Moral hazard in health care was first described by Pauly (1968). Under the presence of uncertainty, people buy insurance. Health insurance leads patients to over consume medical care, not because of "*moral perfidy, but of rational economic behavior*".

Traditional health care plans cover drug prescriptions, hospital stays, physiotherapy, alternative therapy, visits to doctor, diagnostic tests, etc. We will focus on the first one, that is, on medical prescriptions.

Medical insurance can be provided by insurance companies and/or by a third-party payer. In countries with a National Health Service, such as Italy, Portugal, Spain and the United Kingdom, the government implicitly acts as the insurer. A common feature regarding the moral hazard is the price of health care, which is very low or even zero (Zweifel, Breyer & Kifmann, 2009).

Consumption and dispensing of drugs is a complex procedure, in which doctors, the third-party payer (national insurer) and the patients play a role. The physicians are agents both for the patient and for the insurance companies or the national insurer. It may create a "double agency" problem (Blomqvist, 1991). They have to achieve efficiency in performing the tasks for both the patient and the insurance provider. It is impossible to motivate doctors to fulfill their double agency role. Different contract systems influence them to act more in the interest of the patient, while others induce them to act more in the interest of the insurer.

In many countries of Europe the government regulates the prescription procedure. However, it is difficult to control the decision of doctors about prescription and it may be convenient for them to please their patients on prescribing more expensive drugs, certifying the necessity for the prescribed treatment (Arrow, 1963).

2.1.1 Brand name loyalty and agents' preference

Pharmaceutical expenditure is large and increasing in most OECD countries. There are different strategies to reduce this expenditure, for instances the implementation of Generic Substitution Policies. Empirical evidence suggests that these policies have an influence on the increase of generics market share. However, in many countries, branded drugs hold a bigger market share than generics. From the literature we can find different explanations to this fact.

Patients may have preferences for using a branded drug since they were using it for long time, during patent protection. For some patients it may be difficult to accept that a drug with a different name, color and shape can have exactly the same therapeutic qualities (Coscelli, 1998). The doctor as agent may be influenced by the choice of patients (Dalen, Furu, Locatelli & Strom, 2011).

The physicians may prefer the branded drug because of their experience with the product over the period of exclusivity or because there are no incentives to change prescription habits (an example: price of new drugs higher than the reference price) (López-Casanovas & Puig-Junoy, 2000).

In some cases doctors' prescription decision can be influenced by incentives from pharmaceutical companies. There are different forms of incentives: checks (Harris, 2004), food, samples, gifts, trips (Burtka, 2007). These incentives are called detailing.

The role of the physician in the choice between generics and branded drugs was examined by Hellerstein (1998). The author found that physicians are important agents in determining whether patients acquire branded drugs or generics. The author didn't find evidence that patients who are not covered by insurance for prescribed drugs are more likely to get generics. However, Lundin (2000) and Coscelli (1998) remarked that Hellerstein's data set had some limitations. It did not contain relative prices and so one cannot account for the effect of price difference between versions on consumption. Moreover, the information recorded by physicians is related to a two-week period only, so when a

specific patient visited the doctor only once, his preference and habits for a certain version cannot be accounted for.

The importance of doctors' and patients' preferences in the prescription decision was analyzed by Coscelli (1998). The author's detailed dataset contains all the prescriptions in the anti-ulcer drug market during the period 1990-1992. The author found that habits and preferences are very important for both; doctors and patients. The patient may have preferences for consuming branded drugs and may influence the physicians' choice. Doctors' prescribing behavior shows habit persistence. As prices are always the same for different drug versions of the same active ingredient, according to Drug Regulatory System in Italy, there are no economic incentives for either physicians or patients to prefer one version over the other[2].

Coscelli (1998) and Hellerstein's (1998) results are consistent with Caves, Whinston & Hurwitz (1991), who conclude that advantage achieved by branded drugs relatively to later generic entrants is partly due to doctors' habits in using branded drugs.

Thus, on the one hand, lower consumption of generics can be explained by the habit of agents. On the other hand, it can be due to the poor information about cheaper generic drugs. This prevents physicians from prescribing generics, thereby contributing to the dispensation of the branded drugs. Patients, in turn, may trust in their physician and accept what is prescribed.

Some physicians know about price differences. Still, they do not act upon this information. This suggests that they might have other reasons besides the habit for certain version of drug and the lack of information about available alternatives for not always prescribing the cheapest version. On the one hand, it may be associated with the agents' uncertainty in what regards the therapeutic effect of generics - they simply do not know that versions are alike. On the other hand, it also matters who pays the costs. If the government acts as the insurer and reimburse greater part of drugs cost, agents do not have to worry about an extra

[2] During Coscelli's (1998) research, direct advertising to patient for prescription of drugs was not possible. Moreover the pharmacist did not have the right to substitute branded drugs for generics.

cost associated with buying expensive branded drugs. Thus, patients and physicians do not have any real reason to prefer lower-priced generics or do not have incentives to change their habits of using branded drugs (Lundin, 2000). If doctors take into account the patients' interests more than the third-party payer, then the expenditure of third-party payer is not important for them.

In the absence of incentives to keep costs down, prescribing decisions may depend on the experience with branded drug and its reputation; on the absence of confidence to new generics, and on the patients' preferences. Thus, we can expect that amount of generics consumed will decrease with the amount that the government pays.

Therefore, one may wonder if high reimbursement level (and/or low patients' co-payment) can negatively affect the penetration of generics into the market.

2.1.2 Empirical evidence on the existence of moral hazard in consumption of pharmaceuticals

There are some works on the analysis about the effect of insurance co-payment on the pharmaceutical market. It is worth mentioning the study by Leibowitz, Manning & Newhouse (1985). This research is based on data from the Rand Health Insurance Experiment. Results show that a higher rate of reimbursement causes a higher drug acquisition. There is 57% increase in per capita expenditure in the absence of co-payment in respect to the situation in which the coinsurance rate is 95%.

More recently Coulson, Terza, Neslusan & Stuart (1995) found that patients with medical insurance use more prescribed drugs than those with no insurance. Similar results were obtained in the working paper by Coulson & Stuart (1995). Authors concluded that elder patients use less prescription than people, who are covered by employer-sponsored plan.

In the Swedish pharmaceutical market Lundin (2000) examines whether the choice made by physicians to prescribe generics or branded drugs is subject to moral hazard. The author uses a data set with information on exactly what drug was prescribed at a particular patient visit to the physician. The results show that physicians' habits as well as patients' preferences are important. Patients who have to pay more are less likely to have branded drug than patients who pay a small co-payment. This indicates the existence of moral hazard in the Swedish pharmaceutical market.

Rudholm (2005) tested the impact of pharmaceutical insurance on the demand for prescribed pharmaceuticals in Sweden. The data covered all pharmaceutical prescriptions sold in the county of Vasterbotten, Sweden, during 2001. It includes information about patient's gender and age, the number of Defined Daily Doses (DDD)[3], total cost, and the patients' co-payment for the prescription. The main result shows that DDD and price of drugs increase, when pharmaceutical insurer pays part of the cost. There is a large effect between the 10% co-payment level and the 0% level. The author suggests that on introducing a small patient co-payment for all prescriptions can be an effective strategy to reduce pharmaceutical consumption.

Thus, an increase in patients' co-payment leads not only to the reduction of drugs consumption but also to the decrease in the price of drugs. Pharmaceutical producers, in they turn, react to the changes in patients' co-payment. In Germany pharmaceutical producers significantly decreased their prices for drugs after changing patient co-payment (Pavcnik, 2002).

When the reimbursement rate is high, the prices for branded drugs may increase, even after the entrance of cheap generics (Ferrara & Kong, 2008). Authors show in their theoretical model that consumers differ in their insurance coverage and that doctor take these differences into account when prescribing drugs. After patent expiration, when generic drugs become available, doctors

[3] The Defined Daily Dose (DDD) is a statistical measure of drug consumption, defined by the World Health Organization (WHO). It is used to standardize the comparison of drug usage between different drugs or between different health care environments.

continue to prescribe both branded drugs and generics for consumers with low co-payment, but only generics for those with less coverage.

Portela (2009) analyzed the effect of reimbursement level on consumption of generics in Portugal. Panel data set covers drugs, which contributed to the larger proportion of NHS expenditure in Portugal between January and September 2003. By using OLS estimation method, the author finds that the reimbursement level is one of the determinants for generic consumption. Author gets a significant result after controlling for Reference Price System (RPS). This shows that when reimbursement level increases, the consumption of generics relatively to branded also increase. One may conclude that after implementation of the RPS there was no moral hazard effect in Portuguese pharmaceutical market. However, this data includes only drugs covered by reimbursement category C (reimbursement level is 37%) and category B (reimbursement level is 69%), which are the two lower reimbursement categories. Results would probably change if drugs of category A were included.

The insurance co-payment effect on the demand of generics was analyzed by Moreno-Torres (2011). The author uses panel data set of drugs monthly prescribed from 1999 to 2005. It distinguishes between three different levels of insurance, and includes the three most consumed therapeutic subgroups in Spain: statins (anticholesterol), selective serotonin reuptake inhibitors (antidepressants) and proton pump inhibitors (antiulcers). Results confirm the existence of moral hazard effect in the regulated Spanish pharmaceutical market. The greater the reimbursement level the patient has, the lower the proportion of generics prescriptions made by doctors. So, one of the factors which slows down the penetration of generics into the Spanish market is the low level of co-payment.

The importance of price difference and level of national insurance for the probability of choosing generic drugs instead of more expensive original branded version was analyzed by (Dalen, Furu, Locatelli & Strom, 2011). The authors' data set contains all prescriptions dispensed to patients in February 2004 and 2006 for 23 different drugs in Norway. Once again authors confirm importance of both doctors' and patients' characteristics for the choice probabilities. The results show

that the larger the difference in price between branded and generic version, the more likely it is that the generics is purchased, in other words when the patient has to pay more, the probability of choosing generics increase. The patients covered by the national insurance scheme are more likely to use branded drugs. The time after generic entry is a very important issue. The probability of opting for generic prescription increases with time after generic entry.

To sum up, the empirical evidence on moral hazard in pharmaceutical market is not decisive. Some authors find evidence supporting the existence of moral hazard effect (Lundin, 2000; Rudholm, 2005; Moreno-Torres, 2011; Dalen, Furu, Locatelli & Strom, 2011; etc.), other do not (Hellerstein, 1998; Portela, 2009).

In appendix A, it is presented a table 1 that summarizes the literature review.

2.2 Portuguese pharmaceutical market

2.2.1 Reference Price System

In Portugal, the pharmaceutical market is highly regulated. The Portuguese Regulatory Agency for Pharmaceuticals (INFARMED) is a government agency, which subordinates to the Health Ministry. Its objective is the protection of Public Health, by monitoring, assessing and regulating all activities related to drugs and health products.

One of the purposes of the Health Ministry is to control pharmaceutical expenditure, which is large and increased from 2000 to 2009 in 1.9% per year in real terms (OECD, 2011). The government indirectly created incentives to reduce prices of drugs, which supposedly occurred on a voluntary basis, as the case of implementation of the RPS. The RPS in Portugal was introduced in 2002 (Decree-Law No. 270/2002, December 2). The aim was to contain pharmaceutical expenditure by defining a fixed amount to be paid by the NHS, in this way assuring that the patient would have access to an alternative of quality and proven therapeutic equivalence.

The internal Reference Price[4] (RP) is the average price of the five cheapest drugs, which exist in the market and are included in the same homogenous group (Decree-Law nº106-A/2010 of October 1). This homogeneous group (HG) includes drugs with the same active ingredients, pharmaceutical form, strength and route of administration and generics. The same homogeneous group could enclose several sizes of packages, which is denominated as the range size package.

The patient pays the difference between Pharmacy Retail Price (PRP) and Reimburse Price. Reimburse price[5] is RP multiplied by the level of reimbursement.

2.2.2 Reimbursement, prices and advertisement of drugs

Reimbursement system differs between special regime[6] and general regime. Special regime covers pensioners, whose total annual income does not exceed 14 times the minimum wage.

There are four different reimbursement categories. For general regime there are:

- Category A with reimbursement level of 90% (Decree-Law No. 106-A/2010 of October 1);
- Category B with reimbursement level of 69%;
- Category C with reimbursement level of 37%;
- Category D[7] with reimbursement level of 15% (Decree-Law No. 48-A/2010 of May 13).

For special regime there are:

- Category A – 95%;
- Category B – 85%;
- Category C - 52%;

[4] Before 2010, RP corresponded to the generics with the highest public retail price. So, it was closer to brand price. This reduced the incentives to use generics in the higher reimbursement rates.
[5] Reimburse price is PRP multiplied by the level of reimbursement, if particular drug does not have RP.
[6] Our data includes NHS drug sales and reimbursement expenditure for both General and Special regimes
[7] Category D is not observable in the data, because it covers only new drugs, with transitory reimbursement system.

- Category D – 30% (Decree-Law No. 129/2005 of August 11).

Reimbursement level for the beneficiaries of special regime is 95% for "all categories" if PRP of drugs is equal or less than RP (Decree-Law No.106-A/2010 of October 1)[8] .

These reimbursement categories vary according to pharmaceutical groups and subgroups as in Appendix B Table 2 (appendix of Decree No. 924-A/2010 of September 17). To reduce the economic incentives in over consumption of some drugs, some groups and subgroups are included in the various reimbursement categories[9]. It differs according to the indications of the drug, its use, entities that prescribe and even the increased consumption for patients suffering from certain pathologies.

Generic price of drugs must be 35% lower than those of similar branded or 20% in case they cost less than 10 Euros (Decree-law No. 65/2007 of March 14). By the end of 2008 the maximum price of generics, above 5 Euros, was reduced to 30% of the branded drug price (Governmental Decree-law No. 1016 – A/2008 of September 8). The prices of new drugs for which there is HG must be the same or below than the RP of this HG (Governmental Decree No. 914/2003 of September 1)[10]. Prices may be revised annually on rates fixed in a Governmental Decree published jointly by the Minister of the Economy and the Minister of Health, according to the inflation rate. At any time laboratories may apply for a price increase due to new therapeutic indications being discovered or to other changes in the product (pharmaceutical form) (Gouveia & Teixeira, 2002). It must be approved by INFARMED (Governmental Decree No. 1279/2001 of November 14).

Advertisement of drugs in Portugal is highly regulated as well. It is prohibited to advertise to the public, the following drugs:

- Prescribed by physicians;

[8] From 2005 to 2009 reimbursement level for category A was 95% for general regime and 100% for special regime for "all categories". As it was found that reimbursement of 100% induced to the increase of consumption and abuse of special regime, implying a higher expenditure to the NHS, it was changed in 2010, by Decree-Law No. 106 A/2010, to 90% for general regime and 95% for special regime for "all categories".
[9] From our data set, the Antifungals, the Antivirals and the Non-Steroidal Anti-inflammatory Agents may be covered by category B and/or by category C. The Psychodrugs may be included in Categories A,B and C.
[10] Barros & Nunes (2011) reviewed all changes in the legislation about prices and reimbursement system.

- Containing stupefacient and psychotropic substances, under international conventions binding the Portuguese State;
- Reimbursed by National Health System (Decree-Law No. 176/2006 of August 30).

Physicians have to inform the patient about the existence of generic drugs in the market, reimbursed by the NHS and about the drugs with the lowest prices (Decree-Law No. 271/2002 of December 2).

2.2.3 Analyses of pharmaceutical market in Portugal

There are several studies which analyze the pharmaceutical market in Portugal. Portela (2009) concludes that between 2000 and 2005 the RPS did not have much influence on public pharmaceutical expenditure.

Vogler & Leopold (2009) advised the policy makers to continue improving policies to promote generics, accompanied by reduction of generics prices. They concluded that the INFARMED has good publication policies. However, in their opinion the patients do not fully understand the RPS. They suggest the civil society to act as “translators” between regulators and the general public.

Similar conclusions can be found in Gonçalves (2009). The author analyzed 20 countries of the European Union. Portugal is in 11th place in the generic drug market share in value. After questioning physicians, pharmacists and patients the author found that the patients pointed to the lack of information on generic drugs from the government or authorities of pharmaceutical industry; the lack of confidence in generic drugs by doctors and pharmacists.

After survey to the Portuguese population, Cabral & Silva (2009) found that the number of patients who accepted prescriptions of generics increased from 2001 to 2008. However, it is relevant to know if this increase occurs in the same way in different reimbursement categories. And they didn´t provide this analysis.

3. Hypothesis, Methodology and Data Set

In this chapter we start from the definition of the hypotheses and then we explain our methodology. Finally we represent the data set used for the empirical work.

3.1 Hypothesis

The four hypotheses to be tested in this work are presented and explained next.

Hypothesis 1: *The doctors are better agents for the patient than for third party payer*

According to the literature review, some studies find existence of moral hazard effect in the pharmaceutical market. In the presence of this effect physicians are better agents for the patients than for third-party payer, meaning that they prescribe more expensive branded drugs to the patients with higher reimbursement level and for patients with higher co-payment more generics (assuming doctors respond to the patients' demand).

If there is moral hazard effect, then the higher reimbursement level has a negative effect on the relative market share of generics to branded drugs.

We suggest another alternative to test the existence of moral hazard. This is the "relative expenditure between NHS and patients". An increase in this variable may decrease the "relative market share between generics and branded drugs" then it may be deduced that there is evidence of moral hazard.

In order to identify the existence, or not, of moral hazard, the estimated coefficients of these variables, should be negative and statistically significant.

Hypothesis 2: *The generics average price is negatively related with the relative market share of generics to branded drugs*

The generics price should be the more decisive factor in their consumption. So we can expect lower demand for generics in the pharmaceutical subgroups

with the higher average price. The estimated significant negative sign for this coefficient confirms this hypothesis.

Hypothesis 3: *Generic market share depends positively on the life time of generics in the market*

Generic producers require time to distribute their products through markets. Consumers need time to get acquainted with new drugs. Positive statistically significant sign of estimated coefficient confirms third hypothesis.

Hypothesis 4: *Consumption of generics increase with the higher price difference between branded drugs and generics*

When the price of generics is much smaller than the price of branded drugs, patients are more likely to buy generic drugs. Statistically significant estimated positive sign for this coefficient confirms this hypothesis.

3.2 Methodology

3.2.1 Estimation method

There are several studies that find evidence of moral hazard in pharmaceutical market. Usually authors use panel data (longitudinal data) (Moreno-Torres, 2011; Lundin, 2000).

Econometrically we can present panel data in following way:

$$y_{it} = \alpha_{it} + \beta_{it} X_{it} + c_i + \varepsilon_{it}, \qquad [1]$$

where are:

- y_{it} - the dependent variable;
- X_{it} - the independent variables;
- α_{it} - the overall intercept;
- β_{it} - the coefficients for independent variables;

- c_i - the individual effect;
- ε_{it} - the idiosyncratic error;
- i - cross-section observations;
- t - time series observations.

According to econometric literature panel data can be estimated by Pooled OLS; Fixed effects approach (FE) or Random effects approach (RE); and by Method of Generalized Estimation Equation (GEE).

- The Pooled OLS approach ignores the panel structure of the data and simply estimates α_{it} and β_{it} by regressing y_{it} on a constant and on X_{it}. If c_i is correlated with any element of X_{it}, then pooled OLS is biased and inconsistent.
- In the FE approach, the individual-specific effect allowed to be correlated with the explanatory variables $Cov(X_{it}, c_i) \neq 0$.
- In the RE approach, the individual-specific effect uncorrelated with the explanatory variables $Cov(X_{it}, c_i) = 0$.
- The GEE was introduced by Liang & Zeger (1986). The focus of GEE is on estimating the average response over population – "population-averaged effect". Given a mean model, μ_{it} **,** and variance structure V_i, the estimation equation is given by:

$$U(\beta) = \sum_{i=1}^{N} \frac{\partial \mu_{it}}{\partial \beta_k} \times V^{-1} \{Y_i - \mu_i(\beta)\}, U(\beta) = 0 \qquad [2]$$

We use overall F-test to choose between fixed effects approach and pooled OLS. The pooled OLS is the restricted model. Rejection of null hypothesis means that fixed effect is present (Wooldridge, 2002).

For choosing between fixed effects and random effects estimation, it is used Sargan-Hansen test, because it extends straightforwardly to heteroskedasticity and cluster-robust versions, so it is guaranteed generate a nonnegative test statistic. The test is implemented by using the artificial regression approach

described by Arellano (1993) and Wooldridge (2002), in which a random effects equation is re-estimated and augmented with additional variables, consisting of the original regressors transformed into deviations from mean form. The test statistic is a Wald test of the significance of these additional regressors. A large-sample chi-squared test statistic is reported with no degrees-of-freedom corrections.

Ghisletta & Spini (2004) showed that GEE approach for longitudinal data can be applied, when the Random effects approach was chosen. Authors mentioned that the estimators of GEE are unbiased, even with possible misspecification of the longitudinal structure. For these reasons, we estimate the GEE approach and compare results with the random effects approach.

3.2.2 Econometric model and variables

The demand determinants usually considered in the literature are the following: price difference between two drug versions (Dalen, Furu, Locatelli & Strom, 2011), months since generics have been on the market (Moreno-Torres, 2011), average prices of generics and branded drugs, presentations of generic drugs and reimbursement level as determinants for ratio between generics and branded drugs market share (Portela, 2009; Moreno-Torres, 2011).

In our model, prices are calculated from the dataset by dividing values of sales in euros by quantities sold. Patient expenditure is calculated by subtraction NHS[11] drug sales (Pharmacy Retail Price) by NHS reimbursement expenditure (Reimbursed price) per month by pharmaceutical subgroups.

There are different ways to look for evidence of moral hazard. We use two approaches to capture this evidence.

The first approach is based on the correlation between reimbursement level and the relative market share of generics to branded drugs.

[11] NHS drug sales include only sales of reimbursed drugs, which are prescribed by physicians.

The second approach allows for the correlation between the ratio of NHS to patients expenditure for drugs and relative market share of generics to branded drugs.

In both approaches a negative correlation reflects evidence of moral hazard.

Two separate regressions are estimated to avoid multicollinearity that exists between the Reimbursement Level and the Ratio of NHS to patient expenditure for drugs.

The econometric regression for the first approach can be presented in the following way:

$$\ln Rgme_{it} = \alpha_{0_{it}} + \beta_1 \ln APg_{it} + \beta_2 \ln APm_{it} + \beta_3 Eg_{it} + \beta_4 RL_{it} + \beta_5 pres\_g_{it} + c_i + \varepsilon_{it}, \quad [3]$$

where *lnRgme*$_{it}$ means natural logarithm of relative market share between the generics and branded drugs. In other words it is natural logarithm of ratio between generics and branded drugs market shares in packages; *i* is the pharmaceutical subgroup and *t* is the month (more information presented in Appendix B Table 3).

Independent variables are following:

- *lnAPg*$_{it}$ - the natural logarithm of average generics price;
- *lnAPm*$_{it}$ – the natural logarithm of average branded price;
- *Eg*$_{it}$ – the number of months, since the entry of the generic drugs;
- *pres_g*$_{it}$ - the number of generics presentations in the market;
- *RL*$_{it}$ – the Reimbursement Level; it is the ratio between reimbursement expenditure of NHS and NHS drug sales;
- c_{it} - the individual effect;
- ε_{it} – the error term.

Econometric regression for the second approach is following:

$$\ln Rgme_{it} = \alpha_{0_{it}} + \beta_1 \ln APg_{it} + \beta_2 \ln APm_{it} + \beta_3 Eg_{it} + \beta_4 \mathrm{Re}_{it} + \beta_5 pres\_g_{it} + c_i + \varepsilon_{it}, \quad [4]$$

where *Re*$_{it}$ means the relative expenditure between NHS and patients.

We include the price difference between branded drugs and generics to test fourth hypothesis. This minimizes the possible multicollinearity between average prices of generics and branded drugs.

The econometric equation for the first approach is:

$$\ln Rgme_{it} = \alpha_{0_{it}} + \beta_1 \ln Pd_{it} + \beta_2 Eg_{it} + \beta_3 RL_{it} + \beta_4 pres\_g_{it} + c_i + \varepsilon_{it}, \quad [5]$$

For the second approach the econometric equation is:

$$\ln Rgme_{it} = \alpha_{0_{it}} + \beta_1 \ln Pd_{it} + \beta_2 Eg_{it} + \beta_3 \mathrm{Re}_{it} + \beta_4 pres\_g_{it} + c_i + \varepsilon_{it}, \quad [6]$$

where *lnPd*$_{it}$ means natural logarithm of price difference between branded drugs and generics.

3.3 Data Set and descriptive statistic

We use dataset of monthly prescribed drug consumption from 2004 to 2009, provided by INFARMED. Monthly Evolution of NHS Drug Sales by Pharmaceutical Subgroups in value and packages and Monthly Evolution of NHS Reimbursement Expenditure by Pharmaceutical Subgroups available in the official site of INFARMED in medicine statistic publications.

Monthly Evolution of NHS Generics Drug Sales by Pharmaceuticals Subgroup in value and packages; Number of presentations of drugs by pharmaceutical subgroups provided by the Information Centre on Medicines and Health Products in INFARMED.

Data captures the NHS market for the pharmaceutical subgroups for which generics exist in the period 2004 to 2009 in Portugal (Appendix B table 2).

The panel dataset covers 38 pharmaceutical subgroups, for 72 months, in a total number of observations is 2736.

3.3.1 Descriptive statistic

In table 4 in Appendix B, we present some descriptive statistics about prices, reimbursement level and relative market share between generics and branded drugs. It can be seen that the minimum average price of generics is 1.18 euros and the maximum is 78 euros. For the branded drugs 2.66 euros and 76 euros respectively. The maximum average price for generics is higher than for branded drugs because in some pharmaceuticals subgroups, branded drugs have more presentations than the generics counterpart. Since the generics presentations depend on the branded presentations, it may happen that generics presentations mimic the most expensive branded presentations. Thus, in average terms it is possible to find the maximum price of generics higher than the price of branded as shown next:

$$\frac{\sum_{n} Pg}{\sum_{n} pres\_g} > \frac{\sum_{k} Pb}{\sum_{k} pres\_b}, \text{ if } k > n \qquad [7]$$

where *k* – presentations of branded drugs; *n*- presentations of generic drugs; *Pg* – generics prices; *Pb* – branded prices; *pres_g* – generics presentations; *pres_b* – branded presentations.

However, when considering the total sample, the mean value for generics average prices (15.9 euros) is 25% lower than branded average prices (19.4 euros).

The maximum value of relative market share between generics and branded drugs is 2.92 and the minimum is 0, since the entry of generics in the market happens in different times.

Reimbursement level varies from 29% to 100%. In the beginning of 2004 the government reimbursed the total PRP of Anti-Parkinson Drugs.

The number of months was counted from January 2004. In this way, the existence of generics varies from 1 to 72 months. The mean value is 32 months.

It can be seen that the mean value for the presentations of generics is 58. The maximum number of generics presentations is 830. This number corresponds to antihypertensive drugs (Category B).

Figure 1 in Appendix B shows monthly evolution of related market share between generics and branded drugs by reimbursement categories. We divide subgroups according to three categories (A, B and C[12]). There are subgroups, however, which can belong to more than one reimbursement category and these are included in "Mix categories"[13]. Relative market share between generics and branded drugs in category A is much lower than for other categories. Relative expenditure between NHS and patients is much higher in category A (Figure 2 in Appendix B).

From Figure 3 in Appendix B three different level of reimbursement can be observed. It is clear that the reimbursement level for category A is the highest one, followed by category B and in the third place category C. The subgroups that include Mix categories can be observed in the second level. Orange line of Anti-acids and Anti-ulcerous subgroup (Category C) locates in second level of reimbursement (green color). This happens because in our data NHS reimbursement expenditure includes special regime of reimbursement, which can be 95% of reimbursement for all categories if PRP is lower or equal to RP.

In tables 5 – 8 in Appendix B, we present the correlations between the variables considered in the econometric models. A moderate correlation is found between average generics price and average branded price. This is expected because they are both correlated by law in Portugal, which regulates pharmaceutical prices of reimbursed drugs.

[12] Government uses Category D for new drugs (for all pharmaceutical subgroups), with transitory reimbursement system.
[13] "*Mix categories*" basically includes drugs from categories B and C. Only the psychodrugs can be included in categories A, B and C. However, the mean value of reimbursement level in this subgroup is 70%.

4. Empirical results

Table 9 in Appendix C presents the results of the fixed effects estimations for the first and second approaches of testing the existence of moral hazard. We reject the random effects approach, since *p-value* of Sargan-Hansen test is highly significant. F-test shows joint significance for the fixed effects, meaning that individual-specific effect correlated with any explanatory variables and pooled OLS is biased and inconsistent. For the both approaches, the "R-Squared" tells us that 74% of the variation in the variable "Market share ratio" was explained by variations in the independent variables (Knowledge Base, 2012).

The estimated coefficients of the variables, which we use to capture moral hazard, are highly significant and have the expected sign. A 1% increase in the reimbursement level reduces the relative generics market share in 287% and a 1% increase in the ratio between NHS and patients expenditure reduces the market share ratio in 1%.

Therefore, there is evidence of moral hazard. For those patients with greater reimbursement level the consumption of generics is lower than for patients with higher co-payment. In other words, when the government pays more, the consumption of expensive branded drugs increase. This result confirms the first hypothesis that physicians are better agents for the patients than for the NHS and they prescribe more expensive branded products to patients with higher levels of reimbursement. Thus it may be concluded that the low level of co-payment in Portugal has negatively affected the penetration of generics. This result is consistent with those of Moreno-Torres (2011), Dalen, Furu, Locatelli & Strom, 2011), Rudholm (2005) and Lundin (2000).

The estimated coefficient of the variable "Average Generics Price" is significant and it has the negative sign in the both regressions. A 1% increase in the generics price reduces the market share ratio between 1.59% and 1.68%. As expected, prices have a negative effect on the demand for generic drugs. Therefore, the second hypothesis is not rejected. In contrast, the estimated coefficient of the variable "Average branded price" is not significant at the 5% significance level in the presence of reimbursement level. For the second

approach of testing, this coefficient is significant and has negative sign. It means that with the increase of branded price, the consumption of these drugs increase. It is confirmed again the branded loyalty and the fact that the price can be a decisive factor in the consumption of generics.

Concerning the third hypothesis, the estimated coefficients of the variable "Time on the market" are significant and have positive sign. A 1% increase in the number of months of existence of generics leads to the increase of the ratio between generics and branded drugs market share between 0.4% and 0.5%. In other words, the number of generics prescriptions increase as time passes after generics entry. It takes time to increase the consumption of new products in the market, since patients and doctors have to gain confidence in the new generic drugs.

Finally, regarding the number of generics presentations, the estimation shows that a 1% increase of these presentations causes an increase on average and approximately of 0.1% in the relative market share between generics and branded drugs.

We estimate the first and second econometric regressions for the market of Anti-hypertensive, and Anti-ulcer and Anti-acids drugs[14]. Results of these estimations are presented in Appendix C Table 10. Sargan-Hanset test shows that Pooled OLS estimation is appropriate in this case; meaning that effect of individuality is not present. For the both regressions, the "R-Squared" tells us that 99% of the variation in the variable "Market share ratio" was explained by variations in the independent variables. Estimated results show that a 1% increase of generics price expands the generics market share with respect to branded drugs. Generics market share in this case increases for the patients with higher reimbursement level and with the number of months since generics entry to the market. There is no evidence of moral hazard in this case.

[14]These 2 pharmaceutical subgroups belong to reimbursement categories B and C. They present the highest NHS reimbursement expenditure between drugs, which belong to these two reimbursement categories during the period 2004 to 2009 in Portugal.

Table 11 in Appendix C shows the estimation of two regressions with respect to the fourth hypothesis. The random effects estimation cannot be rejected, since *p-value* of Sargan-Hansen test is 0.4319 and 0.3306 respectively. The *p-value* of Wald Chi-Square test is significant, which means that at least one of the regression coefficients in the model is not equal to zero. For the both approaches, the "R-Squared" tells us that 60% of the variation in the variable "Market share ratio" was explained by variations in the independent variables. The results from GLS random effects estimation and GEE population-average model are very similar. The coefficients of price difference are highly significant and have positive sign, as it was expected. A 1% increase in the price difference between branded drugs and generics causes an increase in the ratio between generics and branded drugs market share between 0.156% and 0.165%. This result is consistent with Dalen, Furu, Locatelli & Strom (2011) and it confirms the fourth hypothesis. In other words, the higher the price difference between branded drugs and generics, the more likely doctors are to choose generics.

The estimated coefficient of the variable RL is not significant at the 5% significance level in the first approach. However, there is significant and negative effect of ratio between NHS and patients expenditure on the relative market share. A 1% increase in the variable Re causes a 0.8% decrease in the ratio between generics and branded drugs. This effect is lower than in the estimation of second regression. However, this result reinforces the first hypothesis and indicates existence of moral hazard. Even when information about price difference between branded drugs and generics is available, consumers choose branded drugs when the government pays a bigger part in the drugs cost.

The estimated coefficients of the variable number of months are significant and positive. These results are consistent with those above. The time that generic drugs remain on the market is important because physicians acquire knowledge about therapeutic effect of generics. This result confirms once again the third hypothesis and is coherent with those of Moreno-Torres (2011) and Dalen, Furu, Locatelli & Strom (2011).

Eventually, the number of generics presentations has a positive and significant relation with the relative market share between generics and branded drugs. In this way, the choice between generics and branded drugs depend on the number of generics presentations in the market.

Moreover, we estimate the third and fourth econometric models for the two pharmaceutical subgroups (“Anti-hypertensive drugs” and “Anti-ulcers and anti-acids drugs”). Sargan-Hanset test shows that Pooled OLS estimation is appropriate in this case. In both regressions, the “R-Squared” tells us that 94% of the variation in the variable “Market share ratio” was explained by variations in the independent variables. The estimated result does not show evidence of moral hazard for these subgroups of drugs (Appendix C Table 12). With the increase of government spending consumers prefer generics. No evidence of moral hazard in the markets with reimbursement categories B and C is found.

5. Conclusion and discussion

This work aimed to test the existence of moral hazard in doctors' prescription behavior. To achieve this aim we used two approaches. The first one lies in the estimation of the correlation between the variable Reimbursement level and relative market share between generics and branded drugs as used by Portela (2009). The second approach consists in the estimation of the correlation between the "relative expenditure between NHS and Patients" and market share ratio. Data used for the econometric estimations come from INFARMED for the period 2004 - 2009.

We found that the higher the reimbursement level (or part that the government pays), the lower the proportion of generic drugs prescribed by physicians. In other words, patients with greater insurance coverage consumed more branded drugs than patients with lower coverage. Thus, physicians are better agents for the patients than for the third-party payer. The results here are inconsistent with Hellerstein's (1998); however, they are consistent with the results by Moreno-Torres (2011), Dalen, Furu, Locatelli & Strom (2011), Rudholm (2005) and Lundin (2000).

The price of generics plays an important role in the choice of the version of drugs. For the pharmaceutical subgroups with higher price, the consumption of generics is lower. A higher branded price does not influence patients or doctors' decisions, in some cases even increases the consumption of these drugs. This may be due to the experience with branded drugs, which doctors and patients gained during patent protection. In this way, it may be said that generics need time to gain confidence. This is the reason why the length of time generics have been in the market is so important for the demand.

The higher the number of generics presentations in the market, the greater the number of generics prescriptions made by physicians. On the other hand, laboratories develop more generics presentations, where there is a higher demand. Thus, there is a sort of propagation effect when generics become more prescribed.

When we included the information about price difference between branded drugs and generics, the reimbursement level does not explain consumption of generics while the ratio of NHS expenditure to patients' expenditure does. Thus, partial existence of moral hazard is found. That is to say, the information about price difference between branded drugs and generics influences patients to choose generics.

Finally, we did not find the existence of moral hazard in the pharmaceutical market for Anti-hypertensive, and Anti-ulcer and Anti-acids drugs (Categories B and C). The evidence of moral hazard in patients treated with drugs within category A, seems stronger than in other patients. For policy purpose, we suggest a partial reduction of reimbursement level for category A. For instance, 90% of reimbursement level in category A, when PRP of chosen drug is equal or lower than RP and 85% for the drug with PRP higher than RP. This may not only contribute to the increase in demand for generic drugs, but also to reduce the prices of drugs.

The main conclusion of this work is that the high level of reimbursement in Portugal has negatively affected the penetration of generics. Moreover, it hampers the effort made by the Portuguese government to reduce public expenditure on pharmaceuticals.

This work is a contribution to the empirical studies on the evidence of moral hazard in medical prescription. Two approaches were used to achieve this aim. While the first one (using RL) had been used before, the second approach was proposed by us (using Re). Results show that both approaches are consistent and both show evidence that moral hazard exists.

Our work has relevance for the cost-containment policies in pharmaceutical expenditure. The rational use of generics may contribute to considerable savings. It can be achieved without compromising the quality of medical care and without significant reductions in co-payments of patients, which leads to welfare improvement.

The limitation of this analysis is the lack of information about generics consumption by the beneficiaries of special regime per month[15]. This information could supplement our understanding of generics consumption among different reimbursement levels. This is an issue that may be addressed in future research.

Another limitation is that the data is aggregated for the pharmaceutical subgroups, whereas some drugs have different active ingredients and producers. However, it is difficult to control this heterogeneity.

[15] Data covers NHS drug sales, which include both the special and the general regimes. However, there is no available information about the exact quantity sold per month for the special regime.

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Decree-Law No. 65/2007 of March 14. Decree contain regime of pricing of drugs.

Decree-Law No. 48-A/2010 of May 13. Decree adopts the general scheme of reimbursement of the State in the price of medicines.

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7. Appendices

Appendix A

Table 1: Brief summary of literature review

Authors	Title	Year, Country	Data Set	Estimation Method	Variables	Results
Judith Hellerstein	"The importance of the physician in the generic versus trade-name rescription decision"	USA, 1998	Data from 1989 National Ambulatory Medical Care survey (NAMCS). Datasets consists of patients visits to based physicians. Physicians selected in the survey recorded information of patients that visited their offices over a two-week period. Total number of observation: 8,579.	Random-effects probit model.	Dependent: is 1 when the generic version is prescribed, zero otherwise. Independent: Set of dummies: Age, Gender, White or non-white, Self-pay, Insurance companies, HMO plan, Specialist, Regions.	Results: Physicians are an important agent in determining whether patients receive brand name or generic drugs. Very little can be explained by observable characteristics of individual patients.
Andrea Coscelli	"The importance of Doctors' and Patients' Preferences in the Prescription Decision"	Italy, 2000	Dataset provided by "Istituto Superiore della Sanita". Panel detailed dataset contains all the prescriptions in the anti-ulcer drug market during period 1990-1992. Total number of observations is 75,000.	Fixed effects Probit and Random effects Probit	Dependent: is 1 if the brand prescribed is different from the brand previously prescribed, zero otherwise. Independent: Age; Gender; Total number of prescriptions; Total number of doctors; Total number of molecule, consumed by patient; Month; Quantity, prescribed by doctor; Herfindahl index across brand; Herfindahl index across molecule; Percentage of Old brand; Share of molecules; Dummies if physicians temporary, permanent for patient and if patient returns to previous physician.	Results: habits and tastes are very important for both: doctors and patients. Women prescribe more frequently new brand name drugs, older people are switched to new brand more than young.

(Table 1 cont'd)

Arleen Leibowitz, Willard G. Manning, Joseph P. Newhouse	"The demand for prescription drugs as a function of cost-sharing"	1985. USA	The data for this analysis are derived from the Rand Health Insurance Experiment. HIE Panel data include the expenditure, health, demographic characteristic of enrollees for three or five year period.	Two equation model. Probit. Negative binominal regression. ANOVA, ANOCOVA	Dependent: insurance plan, site, and demographic measures. Independent: Dummies: Insurance plan, Regions, Child, Gender, Per capita expenditure, the number of prescription drugs per capita, the percentage of drugs purchased through physicians and the percentage of generic drugs purchased at pharmacies.	Results: Total expenditure on prescription pharmaceuticals is greater for patients with higher insurance coverage. The patients, who paid nothing, used 60 percent more services than those required to pay price - but the effect on the health of the average person was negligible
Edward Coulson, Joseph Terza, Cheryl Neslusan, and Bruce Stuart	"Estimating the Moral-Hazard Effect of Supplemental Medical Insurance in the Demand for Prescription Drugs by the Elderly"	USA. 1995	Funding for survey design and implementation used in this research was supported by grants from the Pew Charitable Trusts and the Health Care Financing Administration. Data from a mail survey of health insurance and medicine use completed by 4,509 elderly Pennsylvania Medicare beneficiaries in the summer of 1990.	First and second stages multinomial logit	Dependent: Number of prescription Independent: Number of current health problem, Set of dummies: Age, Gender, White or non-white, Marital status, Income, Education, Health, Insurance coverage, Smoker or not.	Results: Patients with medical insurance use more drugs, prescribed by doctors than those without insurance.
Edward Coulson, Bruce Stuart	"Insurance Choice and the Demand for Prescription Drugs"	USA. 1995	Data base from a survey of Health insurance and medicine use in the Commonwealth of Pennsylvania, conducted during the summer of 1990. Panel dataset constructed from survey responses and Medicare claims records for 4,066 elderly Pennsylvanians.	OLS Probit	Dependent: Prescriptions filled in previous 2 weeks, persons with any prescriptions, prescriptions per user. For Probit: 1= report use of prescription drugs; 0 = report no drug use. Independent: Number of current health problem, Set of dummies: Age, Gender, White or non-white, Marital status, Income, Education, Health status and Health habits, Insurance coverage.	Results: Elder peoples use less prescription than people, who covered by PACE, Medicare. This is result of the price subsidy that PACE program beneficiaries enjoy

(Table 1 cont'd)

Douglas Lundin	"Moral hazard in physician prescription behavior"	Stockholm, Sweden. 2000.	Department of Public Health and Caring Sciences, Primary Care Research at Uppsala University. Panel Data: all dispensed drugs by particular physician to patient, from two pharmacies in a small Swedish municipality. Period: 1992-1993. Total number of observations: 6,142.	Random-effects probit model and simple probit.	Dependent: is 1 when the generic version is prescribed, zero otherwise. Independent: Cost difference 1992; Cost difference 1993. Dummies: trade-name prescribed last time; generic prescribed last time; 1993, active ingredient.	Results: Physicians' habits and the tastes acquired by patients are both important. Patients having to pay more are less likely to have brand-name versions prescribed than patients getting most of their costs reimbursed. This indicates moral hazard.
Niklas Rudholm	"Pharmaceutical insurance and the demand for prescription pharmaceuticals in Vasterbotten Sweden"	Sweden. 2005	Data provided by the local county council. It covering all prescription pharmaceuticals sold in the county of Vasterbotten, Sweden during 2001. Total number of observations: 1,977,666	OLS and the instrumental variable method	Dependent: Price and DDD. Independent: Price per DDD, DDD. Dummies: Age, Private clinic, Recommended list, Level of copayment, Gender, District,	Results: show that both, the quantities sold and the price of the drugs consumed, increase when the pharmaceutical insurance system pays part of the total cost of the pharmaceuticals consumed.
Nina Pavcnik	"Do pharmaceutical prices respond to potential patient out-of-pocket expenses?"	Germany. 2002	Data from IMS Health, Datastream International Database Product level panel dataset covering several therapeutic categories before and after the policy change. Period from 1986-1996.	Robust Standard Error Estimate for Cluster Sampling Data	Dependent: Price of Average Daily Dose Independent: Share of Brands, Number of Generics per Active Ingredient, Herfindahl index	Results: In Germany pharmaceutical producers significantly changed prices for drugs after changing in patient copayment.
Ida Ferrara, Ying Kong	"Can health insurance coverage explain the generic competition paradox?"	2008. Canada	Theoretical three-stage model with consumers differing in their health insurance coverage			Paper shows that there are conditions under which the price of brand-name drugs increases following the entry of generic drugs.

(Table 1 cont'd)

Ivan Moreno-Torres	"Generic drugs in Spain: price competition vs. moral hazard"	Spain. 2011	Directorate-General of Pharmacy and Health Products of the Spanish Ministry of Health and Consumer Affairs. Data from the Nomenclator Digitalis of the NHS Health. Base de Datos del ConocimientoSanitario 2005 - BOT PLUS. Panel data set of drugs monthly prescription from 1999 to 2005. Total number of observation: 23,584.	Generalized two-stage least squares random effects and the two-stage generalized method of moments estimations.	Dependent: log of generic drug's market share divided by the brand-names' market share. Independent: Within-generic share; log of generic price per DDD; log of average brand-name price per DDD; Time on the market; Presentations; Number of indications; DDDs per tablet; Units; Dummies: No copayment, Small copayment; RPS1;RPS2; 1st generic entrant; 2nd generic entrant; 3rd generic entrant; 4th generic entrant; 5th generic entrant.	Results: The greater the level of insurance, that the patient has - the lower the proportion of generic prescriptions made by doctors.
Maria Portela	"Reimbursement regimes of government in the drugs price – assessment of Reference Price System´s impact in Portugal"	Portugal. 2005	The Portuguese Regulatory Agency for Pharmaceuticals (INFARMED) Panel Data: of 15 homogenous groups (HG) of drugs analyzed during 72 month. From 2000 to 2005. Total number of observations is 1,080.	OLS estimation.	Dependent: log of generic drug's market share divided by the brand-names' market share and same variable *Dummy RPS. Independent: average price of HG; average price of brand name drugs; presentations of generics and brand name drugs; reimbursement level.	Results: With the presence of Reference Price System consumption of generics increase. Increase of prices and reimbursement level leads to higher consumption of generics relatively to brand name drugs when RPS is considered.
Dag Morten Dalen; Kari Furu; Marilena Locatelli; Steinar Strøm	"Generic substitution: micro evidence from register data in Norway."	Norway. 2011	Norwegian Prescription Database (NorPD) at the Norwegian Institute of Public Health. Dataset contains all prescriptions dispensed to patients in February 2004 and 2006 on 23 different drugs (chemical substances). Total number of observations: 313,078.	Mixed logit maximum likelihood procedure	Dependent: is 1 when the brand name is chosen, zero otherwise. Independent: Price difference, Number of DDD; Dummies: Age, General practitioner, Chains, Drug reimbursed by government; New generics; Index price regime in 2004.	Results: The larger the difference in price between brand and generic version, patient buys more generics. When drugs reimbursed – more brand drugs is purchased. Younger doctors prescribe more generics. The probability of generic prescription increases with time after generic entry.

Appendix B

Table 2: Pharmaceutical subgroups, divided by reimbursement categories

Category A (General regime 90%, Special regime 95%)	Category B (General regime 69%, Special regime 84%)	Category C (General regime 37%, Special regime 52%)	Category D (General regime 15%, Special regime 30%)
Psychodrugs	Anti-hypertensives	Antiacids and Anti-ulcerous	
Anti-Parkinson Drugs	Antibacterial Drugs	Antilipemics	New Drugs:
Insulin, Oral Anti-diabetics and Glucagon	Anticoagulants and antithrombotic	***Non-Steroidal Anti-inflammatory Agents***	with transitory reimbursement system
Antiepileptic and Anticonvulsants	Antiarrhythmic	Antihistamines	
Hormone and Hormone Antagonists	Antiasthmatic and Bronchodilators	***Antivirals***	
Hypothalamus and Pituitary Hormones, Analogues and Antagonists	Sex Hormones	Nasal Preparations	
Immunomodulators	Antigout Agents	Vasodilators	
Treatment of Glaucoma Agents	Drug acting on bone and Calcium Metabolism	Stupefacient´s Analgesics	
	Drugs used in Arthrosis	***Antifungals***	
	Psychodrugs	Drugs for Acne and Rosacea Treatment	
	Antifungals	Drugs Altering Gut Motility	
	Antivirals	Enzymatic Supplements, Lactic Bacillus and Analogues	
	Non-Steroidal Anti-inflammatory Agents	Cough Suppressants and Expectorants	
		Analgesics and antipyretics	
		Topical Anti-infective	
		Antiemetic and Anteverting Drugs	
		Other Central Nervous System Drugs	
		Psychodrugs	
		Corticosteroids	
		Muscle Relaxants	
		Other Genital Disorders agents	
		Antimigraine Agents	

Table 3: Description of variables

Variable	Definition
Market share ratio (Rgme)	Generics market share divided by the branded drugs market share (Monthly prescription NHS drug consumption generics and branded by pharmaceutical subgroups, unit: EUR)
Average generics price (APg)	Average price per pharmaceutical subgroup of the generic drug, unit: EUR (Value of sale in euro/quantities sold)
Average brand price (APm)	Average price per pharmaceutical subgroup of the branded drugs, unit: EUR (Value of sale in euro/quantities sold)
Price difference (Pd)	Average branded price – average generics price, unit: EUR
Number of generics presentations (pres_g)	Monthly evolution of number of generics presentations by pharmaceuticals subgroups in the market
Time on the market (Eg)	Number of months since generics entry to the market. We count number of months from the January 2004.
Reimbursement level (RL)	Ratio between reimbursement expenditure of NHS (Reimbursed price) and NHS drug sales (Pharmacy Retail Price) per month by pharmaceutical subgroups. NHS reimbursement expenditure includes special and general regime.
Patient Copayment (CP)	Ratio between Patient expenditure (Patients' price) and NHS drug sales (Pharmacy Retail Price) per month by pharmaceutical subgroups.
Relative expenditure (Re)	Ratio between NHS reimbursement expenditure and patients copayment (Monthly evolution of NHS and patients expenditure on pharmaceuticals by pharmaceutical subgroups, unit: EUR)

Table 4: Summary statistic

Variable	Obs	Mean	Std. Dev.	Min	Max
Market share ratio (Rgme)	2736	0.1969661	0.258513	0	2.929419
Average generics price (APg)	2736	15.91635	16.07166	1.186615	78.93597
Average brand price (APm)	2736	19.4314	13.81646	2.662459	76.52427
Number of generics presentations (pres_g)	2736	57.6239	124.9876	0	830
Time on the market (Eg)	2736	32.67434	22.01556	1	72
Reimbursement level (RL)	2736	0.6175776	0.1965107	0.2884557	1
Patient Copayment (CP)	2736	0.3824224	0.1965107	0	0.7115443
Relative expenditure (Re)	2736	5.276639	11.31048	0	122.8478

Figure 1: Monthly evolution of related market share between generics and branded drugs by reimbursement categories

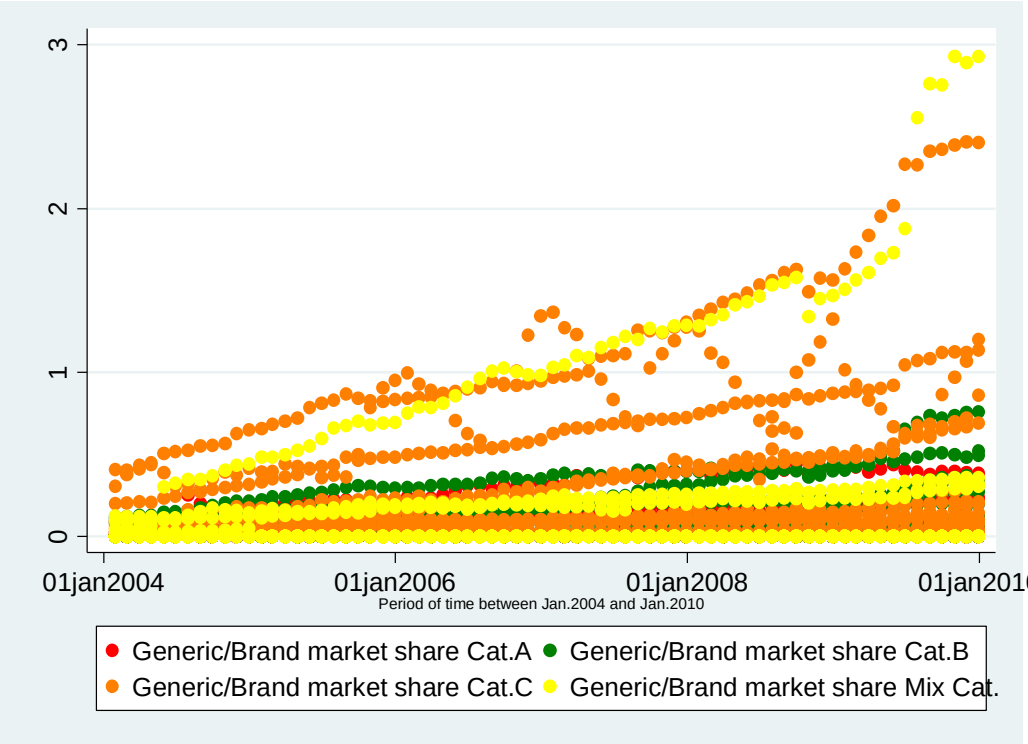

Figure 2: Monthly evolution of related expenditure between NHS and Patients by Reimbursement Categories

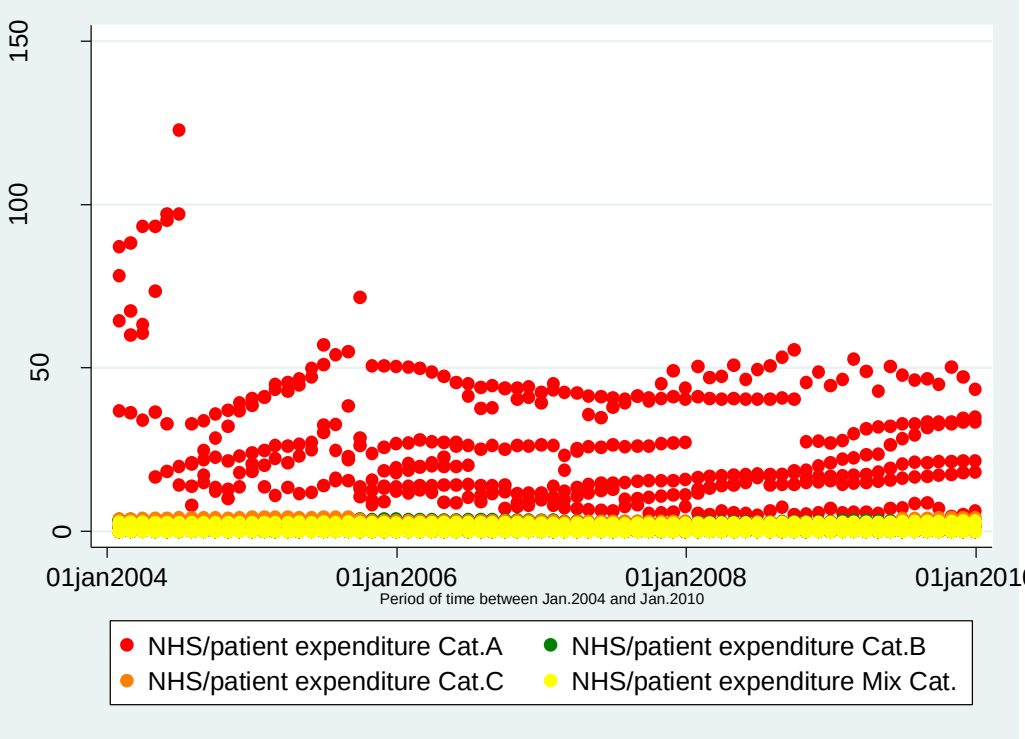

Figure 3: Monthly evolution of reimbursement level by Categories

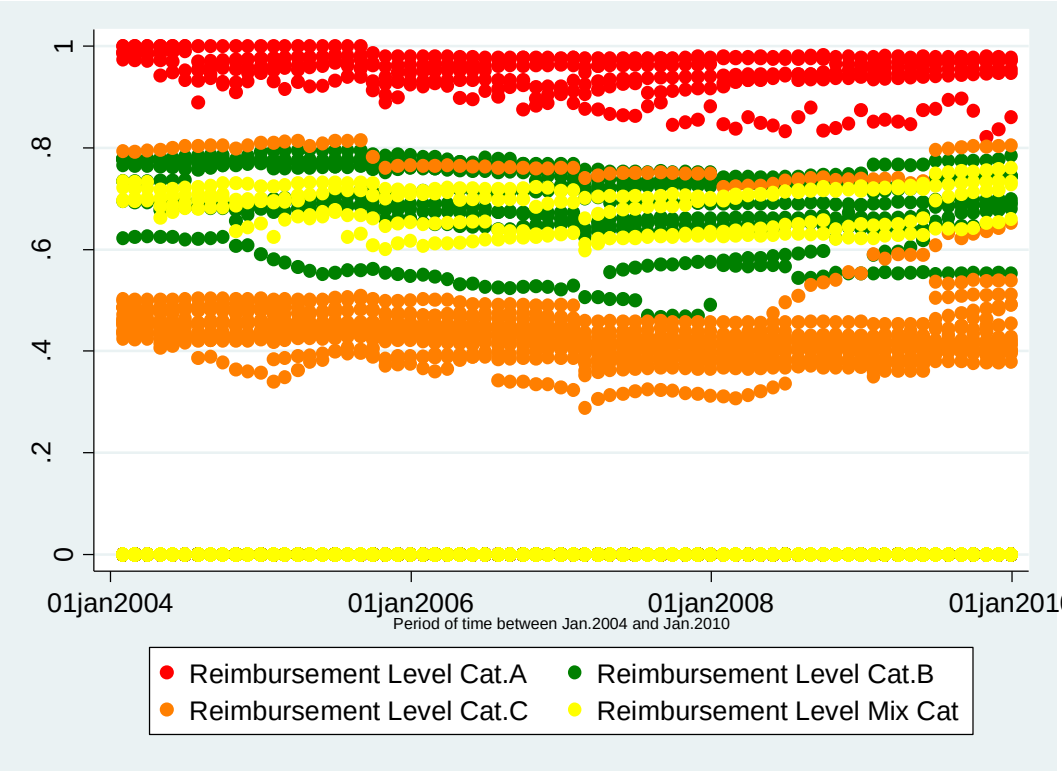

Table 5: Correlation and covariance matrix between variables in the first econometric regression

	lnRgme	lnAP_g	lnAP_m	Qesns	Eg	pres_g
lnRgme	1.0000					
lnAP_g	0.0397	1.0000				
lnAP_m	0.2585	0.6289	1.0000			
RL	0.1421	0.1960	0.3665	1.0000		
Eg	0.0265	0.2535	-0.0004	-0.0142	1.0000	
pres_g	0.2233	0.2201	0.1103	0.1291	0.2455	1.0000

Table 6: Correlation and covariance matrix between variables in the second econometric regression

	lnRgme	lnAP_g	lnAP_m	Re	Eg	pres_g
lnRgme	1.0000					
lnAP_g	0.0397	1.0000				
lnAP_m	0.2585	0.6289	1.0000			
Re	0.0058	0.0786	0.1724	1.0000		
Eg	0.0265	0.2535	-0.0004	-0.0519	1.0000	
pres_g	0.2233	0.2201	0.1103	-0.0715	0.2455	1.0000

Table 7: Correlation and covariance matrix between variables in the third econometric regression

	lnRgme	lnPd	Qesns	Eg	pres_g
lnRgme	1.0000				
lnPd	0.1244	1.0000			
RL	0.1421	0.0404	1.0000		
Eg	0.0265	-0.0758	-0.0142	1.0000	
pres_g	0.2233	-0.2267	0.1291	0.2455	1.0000

Table 8: Correlation and covariance matrix between variables in the fourth econometric regression

	lnRgme	lnPd	Re	Eg	pres_g
lnRgme	1.0000				
lnPd	0.1244	1.0000			
Re	0.0058	0.0268	1.0000		
Eg	0.0265	-0.0758	-0.0519	1.0000	
pres_g	0.2233	-0.2267	-0.0715	0.2455	1.0000

Appendix C

Table 9: Results from the Fixed Effects estimation of the first and second econometric regression

lnRgme	Coef.	P>|t|	Coef.	P>|t|
lnAP_g	-1.678743	0.000	-1.58749	0.000
lnAP_m	-0.2095229	0.078	-.2949521	0.014
RL	-2.866122	0.000	-	-
Re	-	-	-0.0102756	0.000
Eg	0.0039466	0.000	0.0053301	0.000
pres_g	0.0010549	0.000	0.0009538	0.000
cons	2.414414	0.000	0.6723849	0.000
sigma_u	1.4210473		1.1620394	
sigma_e	0.45076008		0.45316304	
rho	0.90858081		0.86799656	
F test that all u_i=0:	F(37, 2693) = 169.12	Prob > F = 0.0000	F(37, 2693) = 166.50	Prob > F = 0.0000
Sargan-Hansen statistic	145.835 Chi-sq(5)	P-value = 0.0000	101.387 Chi-sq(5)	P-value = 0.0000
R-squared	0.7434		0.7406	
Adj. R-squared	0.7394		0.7366	
Overall *F* test	F(5,2693) = 367.94	Prob > F = 0.0000	F(5,2693) = 358.35	Prob > F = 0.0000
Number of observations	2736		2736	

Table 10: Results from the Pooled OLS estimation of the first and second econometric regression for “Anti-hypertensive”, “Anti-ulcers and Anti-acids” subgroups

lnRgme	Coef.	P>|t|	Coef.	P>|t|
lnAP_g	0.4175715	0.000	0.426584	0.000
lnAP_m	1.566213	0.000	1.52242	0.000
RL	1.672822	0.000	-	-
Re	-	-	0.087525	0.000
Eg	0.012456	0.000	0.0124684	0.000
pres_g	-0.000208	0.000	-0.0002293	0.000
cons	-4.980941	0.000	-3.935011	0.000
Sargan-Hansen statistic	Equivalent to pooled OLS		Equivalent to pooled OLS	
R-squared	0.9936		0.9938	
Adj. R-squared	0.9933		0.9935	
F(5,138) Prob > F	4255.77 0.0000		F(5,138) Prob > F	4399.15 0.0000
Number of observations	144		144	

Table 11: Results from the Random Effects GLS and GEE estimations of the third and fourth econometric regressions

lnRgme	Random effects GLS regression				GEE population-average model			
	RL		Re		RL		Re	
	Coef.	P>|z|	Coef.	P>|z|	Coef.	P>|z|	Coef.	P>|z|
lnPd	0.156020	0.000	0.1647191	0.000	0.1559907	0.000	0.1647097	0.000
RL	0.287610	0.348	-	-	0.2896544	0.342	-	-
Re	-	-	-0.007490	0.000	-	-	-0.007486	0.000
Eg	0.0028274	0.000	0.00248	0.000	0.002826	0.000	0.0024792	0.000
pres_g	0.0013276	0.000	0.00128	0.000	0.0013287	0.000	0.0012805	0.000
cons	-1.573897	0.000	-1.35298	0.000	-1.575146	0.000	-1.352986	0.000
R-squared	0.6010		0.6041					
Adj.R-squared	0.5949		0.5981					
Wald chi2(4) Prob > chi2	225.61 0.0000		246.62 0.0000		226.03 0.0000		247.05 0.0000	
Number of observations	2736		2736		2736		2736	
Sargan-Hansen statistic	3.813 Chi-sq(4)	P>Chi-sq(4) 0.4319	4.602 Chi-sq(4)	P>Chi-sq(4) 0.3306				

Table 12: Results from the Pooled OLS estimation of the third and fourth econometric regression for “Anti-hypertensive”, “Anti-ulcers and Anti-acids” subgroups

lnRgme	Coef.	P>|t|	Coef.	P>|t|
lnPd	-0.0971197	0.000	-0.0958493	0.000
Rl	2.140514	0.000	-	-
Re	-	-	0.124959	0.000
Eg	.0199195	0.000	0.0198863	0.000
pres_g	-.0013648	0.000	-0.0013569	0.000
constant	-2.316313	0.000	-1.093948	0.000
Sargan-Hansen statistic	Equivalent to pooled OLS		Equivalent to pooled OLS	
R-squared	0.9365		0.9393	
Adj. R-squared	0.9347		0.9375	
F(4,139) Prob > F	512.38 0.0000		F(4,139) Prob > F	537.40 0.0000
Number of observations	144		144	