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IES Working Paper: 05/2016

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Bibliographic information:
Votapkova J., Zilova P. (2016). " Determinants of Generic Substitution in the Czech Republic" IES Working Paper 05/2016. IES FSV. Charles University.

This paper can be downloaded at: http://ies.fsv.cuni.cz

Determinants of Generic Substitution in the Czech Republic

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February 2016

Abstract:
Using individual level-data, the paper uncovers patient and drug characteristics that determine the probability of using the original patented products despite the presence of generic substitutes in the Czech Republic in the period 2009-2013. Our results reveal different behavioral patterns for drugs against acute and chronic diseases. The results have direct implications for the design of pharmaceutical policies aiming at an increased consumption of generic substitutes.

Keywords: Generic substitution, Drug consumption, Pharmaceutical expenditures
JEL: D19, H51, I18

Acknowledgements: Financial support by GAUK 153 4214 is gratefully acknowledged. We are thankful to Martin Gregor and Lucie Bryndova for their valuable comments and suggestions.

1 Introduction

Pharmaceuticals account for a significant share of the total healthcare expenditures in many countries. An effective strategy to reduce the growing pharmaceutical expenditure without deteriorating the quality of care is generic substitution, as proved by Swedish (Andersson *et al.*, 2007) or British (Kanavos, 2006) experience.

When a drug patent expires, a cheaper generic product (further also 'generics') with the same active chemical substances, therapeutic effect, pharmaceutical form and administration route may enter the market. From the economic point of view, since generics are cheaper, generic substitution should be the optimal decision.[1] However, generics and the original product (further also 'the original') may differ in color, shape etc. and thus patients may not trust it, despite the same therapeutic qualities. Therefore, the original often maintains a strong position in the market and patients remain loyal to it.

Empirical evidence dealing with generic substitution is considerably rich. The studies generally find that demand for certified medication is affected either by patient characteristics (Skipper & Vejlin, 2013; Decollogny *et al.*, 2011; Dalen *et al.*, 2011; Shrank *et al.*, 2007; Federman *et al.*, 2006; Farfan-Portet *et al.*, 2012), physician habits, (Hellerstein, 1998; Granlund, 2009; Shrank *et al.*, 2007) or drug characteristics, (Decollogny *et al.*, 2011; Dalen *et al.*, 2011). The conclusions are area-specific and seem to depend also on country's regulatory conditions and pharmaceutical pricing policies.

A country either prohibits generic substitution or encourages it (indicative generic substitution). In the latter case, the pharmacists can substitute drugs with the therapeutically equivalent effect for the prescribed medication when generic substitution is not explicitly prohibited by the physician on the prescription. In some countries generic substitution is mandatory, i.e. the pharmacists have to dispense the cheapest generics regardless of the doctor's prescription. When patients refuse a generics, they have to pay an additional charge. As for pricing policies, countries can apply external price referencing, internal reference pricing, statutory pricing, pricing based on pharmaco-economic assessment, passive price taking, free pricing or mix of these methods.[2]

In the Czech Republic, generic substitution has been allowed since 2008 when the generic substitution law was enacted. The doctor can prescribe either generics or the original drug. If not explicitly prohibited on a prescription, a pharmacist can substitute the prescribed drug with a cheaper pharmaceutical product with the therapeutically equivalent effect. The demand for drugs in the Czech Republic is still largely physician-driven but we assume that the patients both optimize their budgets, given limited resources, and are interested in their health. They thus search for information about available generic substitutes. Information channels are easily accessible covering the internet, pharmacists and physicians.

The Czech Republic uses external price reference as its pricing policy, i.e. for how much the drug can be sold in the pharmacy. The maximum ex-factory price of a pharmaceutical

[1] The health insurance fund usually reimburses the cheapest drug within a particular therapeutic reference group. If a patient buys a more expensive drug within the group, the consumer bears the additional financial cost of the product.

[2] For details on individual methods see WHO (2015) or OECD (2008).

product is set as the average of three lowest manufacturing prices of the particular drugs in the reference countries.[3] Reimbursement of drugs by health insurance funds is set as a combination of external and internal reference. To set reimbursement through the external reference system, prices of all products classified in the particular reference group in the Czech Republic are compared across all EU member states. The cheapest product in any EU country then determines the reimbursement level. However, the Ministry of Health sets two lists of groups of reimbursed pharmaceuticals. The first list is determined by the "reference reimbursement system" where pharmaceuticals that are therapeutically interchangeable create one reference group. The second list of specific groups of drugs is listed in Annex No. 2 of the Act on Public Health Insurance (Act No. 48/1997 Coll.). It serves for internal reference, according to which one medicament in each group in Annex No. 2 has to be fully covered by the health insurance (in most cases, the cheapest generics from the defined group). The groups in Annex No. 2 are not always the same as the reference groups. Every group in Annex No. 2 is a cluster of drugs which are rather administratively similar than therapeutically bio-equivalent. If, after application of external reference system, there is any group from Annex No. 2 without at least one fully covered pharmaceutical, reference price for this group is not set according to the international price comparison but the amount of reimbursement increases and reimbursement level is set according to the cheapest pharmaceutical in this group.

The current discussion in the literature about demand for certified drugs versus its generics is extensive, but does not include any analysis of the demand in the Czech Republic. This paper will contribute to this stream of missing research. We will estimate the probability of using the original despite the presence of cheaper generics given patient and drug characteristics in the Czech pharmaceutical market. For a robustness check, we employ a fixed effects model, which estimates the probability of using the original drug considering panel data characteristics. Additionally, we will split the sample to uncover the behavioral pattern of patients suffering from chronic and acute illnesses separately. The former will be proxied by medications against high blood pressure. The latter will be proxied by antibiotics.

Using a logistic regression model, we answer the following questions:

- What determines the individual-level choice of the original given the presence of cheaper generics in the market?
- Do the chronically ill and acute patients reveal the same behavior?

The individual-level dataset covers a total of 16,836,334 pharmaceuticals prescribed and dispensed to 4,984,982 adult patients between 18 and 107 years in the period 2009-2013 in the Czech Republic. The records are divided into 11 substitution groups. Each substitution group is identified by the original pharmaceutical and all its corresponding generics with the identical active substance (ATC group), form (tablets, drops, etc.) and administration route (oral, inhalation, nasal, etc.) as the original.

Patients are characterized by socioeconomic variables including sex, age, income of the region where the patient lives respecting one's gender; and treatment complexity proxied by

[3]For details see http://www.mzcr.cz/dokumenty/cenova-regulace-leciv_5886_2516_1.html (in Czech only).

individual public health expenditure and the number of different drugs used per year. Drugs are characterized by their purpose, i.e. whether prescribed against acute or chronic disease the number of years since patent protection of the original expired, the number of generics available, and price differential between the original and its cheapest generics.

The results suggest that occasional drug users, costly patients - be them chronically ill or not - and patients in the productive age prefer the original and thus reveal higher than average willingness to pay. Markets where there are fewer generic substitutes available and markets where the price differential between the original and the generics is higher are also associated with higher preference for the original. The results further show that the willingness to pay for drugs against chronic disease is higher than the willingness to pay for drugs against acute diseases.

Analyses of antibiotics and high blood pressure medications suggest that men are sufficiently price-elastic only when drugs against acute diseases are concerned; in the market for drugs against chronic diseases, they would need further incentives to substitute towards generics. The people living in higher-income regions are sufficiently price elastic only when prescribed pharmaceuticals against chronic diseases. For antibiotics, their transaction costs to search information about generics are too high. In the market for antibiotics, the patients generally opt for the original regardless of how long the market has been opened for competition, whereas in the market for anti-hypertensives, the longer the market is opened for competition, the more the patients are price-elastic, i.e. substitute towards generics.

This paper is organized as follows. Section 2 provides methodological background for pooled and fixed-effects panel data logistic regression model. Section 3 presents the dataset and introduces variables employed. Section 4 reports and comments on the results. Section 5 concludes and discusses practical application of the results.

2 Methodology

When measuring the probability of using the original despite the presence of cheaper generics given patient and drug characteristics in the Czech Republic, we estimate a logistic regression model with a binary outcome variable

The model takes the following form:

$$D_{it} = \alpha + \beta x_{it} + \gamma z_{it} + \varepsilon_{it} \tag{1}$$

where D_{it} is a dummy variable taking the value 1 if the original is sold and dispensed, 0 if a generics is the case; x_{it} is a matrix of patient characteristics, z_{it} is a matrix of drug characteristics; and ε_{it} is the error term. Subscripts $i \in \{1, \ldots, I\}$ and $t \in \{1, \ldots, T\}$ denotes observations of the pooled panel.

Variance of ε is assumed to be equal to $\frac{\Pi^2}{3}$ and a binary logit model is defined as (Long & Freese, 2006):

$$Pr(y = 1|x, z) = \frac{\exp(\alpha + \beta x + \gamma z)}{1 + \exp(\alpha + \beta x + \gamma z)} \tag{2}$$

The model is estimated using the maximum likelihood obtained by iterative methods, where $\hat{\beta}$ is computed by maximization of the log-likelihood function. The function $Q(\beta)$ is the log-likelihood function for N independent observations in time dimension T such that:

$$Q(\beta) = \sum_{i=1}^{N} \sum_{t=1}^{T} \left[y_{it} \ln F(x_{it}^{T} \beta) + (1 - y_{it}) \ln \left\{ 1 - (x_{it}^{T} \beta) \right\} \right] \tag{3}$$

We report coefficients and odds ratio. The value of the odds ratio is the exponential function of the coefficient. Odds ratios are interpreted as the change in the probability of using the original drug as compared to the probability of using a generic for a one-unit change in the independent variable. The odds ratio is defined as:

$$\text{odds}(Y = 1) = \frac{Pr(Y = 1)}{Pr(Y = 0)} = \frac{Pr(Y = 1)}{1 - Pr(Y = 1)} \tag{4}$$

A positive regression coefficient suggests that with increasing value of independent variables, a patient is more likely to use the original than a generics. A negative regression coefficient means that with increasing value of independent variables, a patient is less likely to use the original.

Homoskedasticity of the errors in the logistic regression model is checked using the Wald test.

2.1 Robustness check

We carried out a robustness check employing a fixed effects logistic regression to verify correctness of the results of the main analysis. The fixed effects model estimates within-individual differences with individuals serving as their own controls (Williams, 2013), as opposed to logistic regression of the pooled cross-sectional data where information about differences between individuals was used. Besides patient and drug characteristics, we now control for patient characteristics which are stable and are not captured directly in the dataset. The fixed effects logistic model takes the following form:

$$\log \left(\frac{p_{it}}{1 - p_{it}} \right) = \mu_i + \beta x_{it} + \alpha_i, \qquad t = 1, 2, \ldots, T \tag{5}$$

where p_{it} is the probability that the patients choose the original drug, x_{it} is a vector of time-varying independent variables, and α_i represents the combined effects of all time-invariant unobserved characteristics. (Allison, 2009)

Equations (2) - (4) defined for the pooled panel are used analogically for the fixed effect model.

3 Data

The dataset contains all prescribed and dispensed pharmaceuticals in the Czech Republic during the period 2009-2013. Each record represents a separate prescription. The data includes both patient and drug characteristics as retrieved from the Ministry of Health of the

Czech Republic. Data to identify substitution groups and post-patent markets was obtained from The State Institute for Drug Control (SUKL, 2015).

Each substitution group is identified by the original pharmaceutical and all its corresponding generics with the identical active substance (ATC group), form (tablets, drops, etc.) and administration route (oral, inhalation, nasal, etc.) as the original. Only substitution groups where the original competes with at least one generics enter the analysis. We keep only the substitution groups, in which the original entered earlier than the generics. If generics precede the original, results of the analysis may be biased, because the people might not recognize what the original and what a generics is, and thus may decide under imperfect information. In addition, we exclude substitution groups in which generic substitution is not appropriate (for example when the process of absorption of the active substance into the body is important) and the doctor is likely to discourage or even prohibit generic substitution.[4] Due to technical constrains, we use only substitution groups where the date of entry of the first generics into the market is before 2009.

The final dataset consists of a total of 16,836,334 pharmaceuticals prescribed to 4,984,982 patients aged between 18 and 107 years. The children do not choose drugs themselves and thus were excluded. The records are divided into 11 substitution groups. In the dataset, there are 96 different drugs represented regardless of the amount of active substance included and package size; when distinguishing the amount of active substance included and package size, there are 496 drugs represented.

For the fixed-effects logistic panel data model in the robustness check, we analyze the total of 6,669,363 prescriptions issued to 766,728 patients. Due to technical reasons, we dropped 6 % of the original sample to keep only one record per patient a day. Were there more drugs dispensed in a single day, we randomly selected one prescription. Additionally, as many as 9,087,604 observations were dropped, so that we analyze only patients whose values of the dependent variables changed over time.[5]

3.1 Dependent and independent variables

The dependent variable *original* is a dummy which equals 1 if the original (previously patented) drug was sold, and zero if a generics was sold.

A set of variables influences the drug choice and substitution between the original and its generics. The selection of variables that characterizes patients and pharmaceuticals was guided by empirical studies and data availability.

3.1.1 Patient characteristics

The dummy variable *Pensioner* takes the value 1 if a male is older than 61 years and a female is older than 59 years. This is the average retirement age in the Czech Republic in 2009 as reported by Eurostat.[6] It proxies patients' attitudes towards, or knowledge of the possibility

[4]Charles University, The Faculty of Pharmacy provided us with the necessary information.

[5]The fixed-effects model examines the determinants of within-individual variability. If there is no variability within an individual, the analysis is hampered.

[6]http://apl.czso.cz/ode/tab/tsdde420.htm

of generic substitution. On one hand, the elderly are usually poorer and thus rather price elastic. They therefore prefer generics which are cheaper than the original medication (Shrank *et al.*, 2007; Bertoldi *et al.*, 2005; Nelson Jr & Gagnon, 1975). On the other hand, the elderly tend to remain loyal to the original prescribed by the practitioner whom they fully trust (Decollogny *et al.*, 2011) or they worry that the generics are less effective than the original (Dalen *et al.*, 2011; Koulayev *et al.*, 2013; Figueiras *et al.*, 2008), which makes them opt for the generics less than younger age cohorts. The resulting effect of age depends on which of these influences overweight. Given the circumstances of the Czech pension system and the fact that 17.2% of pensioners live in poverty (Czech Statistical Office, 2012), the negative effect of the variable *Pensioner* is expected in the Czech Republic. Even though time-invariant for some patients, it varies for a sufficiently large number of individuals to be able to capture the influence in the fixed-effects model in the robustness check.

The dummy variable *Expenditures* takes the value 1 if individual health care costs paid from the public funds are above CZK 23,329, which are the average public health care costs per capita in the Czech Republic in 2009 (UZIS, 2013). Higher health care expenditures proxy worse health status (complications, operations, etc.). We expect a positive effect of this variable because people with poor health are often brand-loyal customers. They also worry that different drugs than exactly those prescribed by the physician may worsen their conditions as found by Decollogny *et al.* (2011), Tootelian *et al.* (1988), Ganther & Kreling (1999) or Figueiras *et al.* (2008).

The dummy variable *Sex* takes on the value 1 for males. We expect negative effect of this variable which is consistent with Hellerstein (1994), Lambert *et al.* (1980) or Koulayev *et al.* (2013). Women have more comorbidities than men, which is proved by Roter *et al.* (1991) or van Wijk *et al.* (1992) and therefore they do not want to experiment with alternatives worrying that it may worsen their health conditions. Women are thus expected to remain loyal to the original. The variable *Sex* is time-invariant for all individuals, and thus was dropped for the fixed-effects robustness check.

The variable *Income* denotes average hourly wage at the level of the region where patients live, respecting patients' gender. Average hourly wages are published by the Ministry of Labour and Social Affairs of the Czech Republic (MPSV, 2009-2012). It controls for unobservable regional characteristics similar to Farfan-Portet *et al.* (2012), not real individual income. When individual data or other alternatives are not available, income of the region is commonly used in the healthcare literature as noted by Shrank *et al.* (2007).

We expect a negative influence of this variable as suggested by Shrank *et al.* (2007) who found out that patients living in high-income zip codes are more likely to use generics than patients in low-income regions. Similarly, Muirhead (1994) and Nelson Jr & Gagnon (1975) highlight that lower-income patients are rather negative about generic versions of the medicament believing in their worse quality.

The variable *Drugs* indicates the number of different drugs used per year. It serves as a proxy for treatment complexity and existence of comorbidity. It captures an additional effect not accounted for by the variable *Expenditure* which proxied a poor health status. A person taking a number of different drugs must not necessarily cost the system too much.

At the same time, a costly patient diagnosed with a specific disorder may require technically demanding interventions rather than a number of different drugs.

The patients who take more different pills and try generic substitution once may take advantage of the experience and substitute also with other drugs they are prescribed. However Håkonsen *et al.* (2009) and Decollogny *et al.* (2011) found that the number of different drugs decreases the probability of generic substitution and strengthens brand loyalty. We expect the results of our analysis to be consistent with the empirical literature.

3.1.2 Drug characteristics

The maturity of market competition is measured by the variable *Patent*. It is a difference between the year of observation and the year in which the patent protection expired. It takes time to get used to a new drug which enters the market. We suppose a negative influence of this variable. The longer, the market is opened for competition, the larger probability of substitution towards generics as supported by Dalen *et al.* (2011).

The variable *Chronic* is a dummy taking the value 1 if the drug is used against chronic illnesses and 0 if it treats acute illnesses. It adds to patient characteristics *Expenditure* and *Drugs* and captures another dimension of patient's health status indicating whether the person is chronically or just occasionally ill. Consistent with Tootelian *et al.* (1988), Merino-Castelló (2003), Figueiras *et al.* (2008), Hassali *et al.* (2005) and Himmel *et al.* (2005), we expect a positive effect of this variable because the chronically-ill may worry to take generics which they are not used to, the more so if they are satisfied with the original.

The variable *Market* denotes the number of generics offered in each substitution group. It proxies the level of openness of the particular market. Decollogny *et al.* (2011) confirmed that substitution from the original took place more often in the groups containing many generics. We expect the same effect.

The variable *Price* represents a price difference between the original and the cheapest substitute in each group. To calculate the price difference, maximum possible prices that patients can pay in the pharmacy as of November 2014 were used. However, due to market competition, retail price often differs from the legislatively set maximum possible price. Retail price then also varies across pharmacies.

Price is the main reason for choosing the generic version (Appelt, 2010; Heikkilä *et al.*, 2007; Decollogny *et al.*, 2011). But Lambert *et al.* (1980) assert that the people may be suspicious when a generics is too cheap in comparison with the original. The resulting effect thus depends on to what extent consumers believe that price proxies quality of the product; and consumers' price elasticity.

Descriptive statistics of all variables is provided in Table 1. Correlation matrix in Table A1 reveals that there is no strong correlation between any two independent variables. Only a moderate positive relationship is between the variables *Chronic* and *Market size*.

4 Empirical results

We estimate Equation (1). Results are provided in Table 2.

Table 1. Summary Statistics

Variable	Mean	Std. Deviation	Minimum	Maximum
Age	61.375	15.882	18	107
Original	0.339	0.473	0	1
Pensioner	0.583	0.493	0	1
Sex	0.433	0.496	0	1
Expend.	0.463	0.499	0	1
Chronic	0.572	0.495	0	1
Patent	5.417	1.945	1	12
Market	12.801	8.570	2	23
Drugs	4.219	2.722	1	40
Income	153.432	17.241	54	220
Price	299.116	181.019	66	763

Table 2. Logistic Regression

Original	Coef.	Odds Ratio	P-value	95% Conf.	Interval
Pensioner	-0.1344	0.87426	0.000	-0.13686	-0.13188
Sex	0.0406	1.04147	0.000	0.03819	0.04307
Expend.	0.0832	1.08679	0.000	0.08089	0.08556
Chronic	1.0336	2.81109	0.000	1.03084	1.03631
Patent	-0.0650	0.93705	0.000	-0.06558	-0.06445
Market	-0.1228	0.88444	0.000	-0.12295	-0.12265
Drugs	-0.0151	0.98502	0.000	-0.01554	-0.01464
Income	-0.0005	0.99951	0.000	-0.00056	-0.00042
Price	0.0007	1.00074	0.000	0.00072	0.00074
Intercept	0.4971	1.64389	0.000	0.48628	0.50784

All coefficients are statistically strongly significant even at 0.01 level. The *pensioners* choose the original by 12.6%[7] less likely than other age cohorts, holding all other independent variables constant. The results suggest that the elderly are price elastic and thus often opt for cheaper generics. Price elasticity overweights product loyalty.

Men tend to prefer the original by 4.1 % more than women. The direction of the effect suggests that since women suffer from more comorbidities than men, they may be more experienced in generic substitution. However, other potential explanations are at stake too.

Higher than average expenditure on health care is associated with the increase in odds of using the original pharmaceutical. The coefficient for variable *Expenditures* is 0.083 suggesting that the sick are 8.7% more likely to choose the original than the rest of the population, ceteris paribus. The positive effect suggests that the people with poor health are brand-loyal and

[7]Obtained as $1 - e^{-0.1344}$.

do not want to change what they have been satisfied with. Similar explanation holds for the positive odds of choosing the original in case of the variable *Chronic*. The chronically-ill use the original 181.1 % more likely than the rest of the population.

The results for the variable *patent* suggests that a one-year increase in the length of generic availability is associated with 6.3 % decrease in odds of choosing the original drug, holding all other independent variables constant. It suggests that the people need more time to adjust to new products.

The coefficient for the variable *Market* is -0.125. The probability of using the original thus decreases with an additional substitute in the group by 11.6 %, ceteris paribus. The wider the choice, the more likely the patients are to use generics.

The patients who take more different drugs are 1.5 % less likely to choose the original. These results contradict those of the variables *expenditure* and *chronic*, confirming our hypothesis that neither the costly patients, nor the chronically-ill must necessarily take a number of different drugs. The patients who take different medications throughout the year seem to be either experienced in generic substitution or are price-elastic.

The coefficient -0.0005 for the variable *Income* suggests that the people living in region with a higher average income are less likely to choose the original by 0.05 %, ceteris paribus. The coefficient is the smallest among all the variables considered because the effect is assessed at a CZK 1 (EUR 0.04) change of an hourly wage. Hourly wage is expected to proxy the level of education of the region. The direction of the effect suggests that people living in regions with a higher average income - thus education - have sufficient information about generic substitution and do not worry to use low cost drugs.

The coefficient for variable *Price* is 0.0007. It is the second lowest value because the effect of price differential is assessed at a CZK 1 (EUR 0.04) change. In substitution groups where there is a higher price differential between the original and the cheapest substitute, the odds of using the original increases by 0.07 %, holding all other independent variables constant. It suggests that a larger price gap makes the people suspicious about generics. In the Czech environment, the people often believe that price reflects quality and efficiency of the product.

Table 3 strongly confirms appropriateness of the full logistic regression model. The log-likelihood of the full model is significantly larger than the log likelihood of the intercept-only model which is proved by the likelihood-ratio test with 9 degrees of freedom and χ^2 distribution. McFadden's R^2 which is also based on likelihood ratio of the full and intercept-only models, confirms the above. When penalized for model size, particularly for the variables that do not improve the model enough, the Bayesian and Akaike's information criteria justify the full model.

Additionally, we will uncover the behavioral pattern of patients suffering from chronic and acute illnesses separately. The former will be proxied by medications against high blood pressure. The latter will be proxied by antibiotics.

4.1 Analysis of drugs against chronic diseases

The consumption of high blood pressure medications in the Czech Republic significantly exceeds other EU countries. In our sample, the anti-hypertensives represent the total of

Table 3. Measures of Fit for logit of the Original

Log-Lik Intercept Only:	$-1.078 \cdot 10^7$	**Log-Lik Full Model:**	$-9.333 \cdot 10^6$
D(16836324):	$1.867 \cdot 10^7$	**LR(9):**	2894193.614
		Prob > LR:	0.000
McFadden's R2:	0.134	**McFadden's Adj R2:**	0.134
Maximum Likelihood R2:	1.000	**Cragg & Uhler's R2:**	1.000
McKelvey and Zavoina's R2:	0.203	**Efron's R2:**	0.171
Variance of y*:	4.130	**Variance of error:**	3.290
Count R2:	0.726	**Adj Count R2:**	0.191
AIC:	1.109	**AIC*n:**	$1.867 \cdot 10^7$
BIC:	$-2.615 \cdot 10^8$	**BIC':**	$-2.894 \cdot 10^6$

7,870,753 prescriptions issued to 848,898 patients aged between 18 and 107 years. They form two substitution groups, which contain 199 different drugs.

We estimate the logistic regression Equation 1. Estimation results are provided in Table 4. The variables *Chronic* and *Price* were omitted because of perfect collinearity.

Table 4. Logistic regression of anti-hypertensive medications

Original	Coef.	Odds Ratio	P-value	95% Conf.	Interval
Pensioner	-0.00486	0.99516	0.016	-0.00880	-0.00091
Sex	0.06742	1.06974	0.000	0.06350	0.07134
Expend.	0.07419	1.07701	0.000	0.07058	0.07780
Patent	-0.17665	0.83807	0.000	-0.17815	-0.17514
Market	-0.12684	0.88087	0.000	-0.12707	-0.12661
Income	-0.00122	0.99878	0.000	-0.00135	-0.00108
Intercept	2.45566	11.65408	0.000	2.43395	2.47737

After a preliminary analysis, we also exclude the variable *Drugs* because it proved insignificant. The number of different drugs used per year therefore does not affect generic substitution among patients suffering from high blood pressure. Other results are consistent with the main analysis. All the coefficients proved significant at 0.05 level and their confidence intervals are sufficiently narrow.

The elderly are price elastic and thus prefer cheaper generics to the original. The higher the average income in the region, the more likely the patients are to opt for generics. Preference for generics also increases with the number of generic substitutes available in the market. And the longer the market is opened for competition, the more patients are likely to substitute from the original. On the other hand, men and costly patients are more likely to choose the original drug. Appropriateness of the model was tested. Results are upon request from the authors.

4.2 Analysis of drugs against acute diseases

Medications against acute diseases are proxied by macrolide antibiotics which treat bacterial infections. They are widely prescribed across patient characteristics. The final dataset consist of a total of 1,555,160 prescriptions issued to 1,123,252 patients between 18 and 107 years old. The macrolide antibiotics are represented in one substitution group which contains 23 different drugs.

We estimate Equation (1). Estimation results are provided in Table 5. The variables *Chronic*, *Price* and *Market* are omitted due to perfect collinearity.

Table 5. Logistic regression of antibiotics

Original	Coef.	Odds Ratio	P-value	95% Conf.	Interval
Pensioner	-0.10339	0.90178	0.000	-0.11141	-0.09537
Sex	-0.02825	0.97215	0.000	-0.03520	-0.02130
Expend.	0.20151	1.22324	0.000	0.19446	0.20855
Patent	0.12013	1.12764	0.000	0.11756	0.12270
Drugs	-0.01487	0.98524	0.000	-0.01642	-0.01332
Income	0.00203	1.00204	0.000	0.00188	0.00219
Intercept	- 1.54426	0.21347	0.000	-1.57162	-1.51689

All the variables are significant at 0.05 level. The effects of the variables *Pensioner*, *Expenditures* and *Drugs* are consistent with the main results. The elderly are price-elastic, thus more likely opt for cheaper generics. Costly patients rather prefer the original being brand-loyal. The patients who take more different medications throughout the year seem to be either experienced in generic substitution or are price-elastic.

The effects of the variable *Sex*, *Patent* and *Income* contradict the results of the main analysis and the analysis of demand for drugs against chronic diseases. It suggests that the demand for acute and chronic medications behaves differently and should be analyzed separately.

With antibiotics, men more likely opt for generics than women. The coefficient for the variable *Income* suggests that people living in higher-income regions rather prefer the original version of antibiotics. They seem to face higher opportunity costs and save relatively less when they search for generics which are used only occasionally. High transaction costs thus cause the patients to be satisfied with the original. The coefficient for the variable *Patent* suggests that the people prefer the original regardless of how long the market has been opened for competition supporting once again the transaction cost argument.

In overall, demand for medication against acute diseases is less price elastic than the demand for medication against chronic diseases. For occasionally used drugs, transaction costs likely exceed savings resulting from generic substitution.

4.3 Robustness check

We estimate Equation 5. All results in Table 6 are consistent with those of the logistic regression in the pooled cross-sectional analysis.

Table 6. Fixed Effects Logit Model

Original	**Coef.**	**Odds Ratio**	**P-value**	**95% Conf.**	**Interval**
Pensioner	-0.4011	0.66957	0.000	-0.41789	-0.38434
Expend.	0.0491	1.05036	0.000	0.04222	0.05603
Chronic	1.5767	4.83915	0.000	1.56744	1.58604
Patent	-0.2202	0.80236	0.000	-0.22167	-0.21873
Market	-0.2009	0.81803	0.000	-0.20137	-0.20034
Drugs	-0.0223	0.97795	0.000	-0.02361	-0.02099
Income	-0.0053	0.99468	0.000	-0.00563	-0.00504
Price	0.0009	1.00092	0.000	0.00091	0.00094

The odds ratio for the variable *Pensioner* is 0.66957. It suggests that, if a patient retires, the odds of choosing the original drug decreases by 33 %, holding all other independent variables constant. It confirms that the elderly are price-elastic.

The odds ratio for the variable *Expenditures* is 1.05036, suggesting that if a patient costs the healthcare system more than usual, the odds of choosing the original drug increases by 5 %, holding all other independent variables constant. Higher than average health expenditures proxy poor health status, therefore if patient's conditions worsen, they are more likely to choose the original drugs.

The odds ratio for the variable *Chronic* is 4.83915. This means that, if a patient becomes chronically ill, the odds of choosing the original increase by 384 %, ceteris paribus. The chronically-ill often worry to use cheaper drugs and stick with the original.

The odds ratio for the variable *Patent* is 0.80236. One year increases in the length of generic availability is associated with a 20 % decrease in odds of choosing the original drug, holding all other independent variables constant. The people need more time to adjust to new products.

The odds ratio for the variable *Market* is 0.81803. If a patient takes drugs from the substitution group, which has one more generics available in the market, s/he is less likely to choose the original drug by 18 %, holding all other independent variables constant. When a person has more substitutes to choose from, one is more likely to do so.

The odds ratio for the variable *Drugs* is 0.97795. If a patient uses more medication, the odds of choosing the original decrease by 2 %, ceteris paribus. These people seems to be informed about generic alternatives available, and may even likely have own personal experience with generic substitution.

The odds ratio for the variable *Income* is 0.99468. If personal or regional characteristics determining the level of income change (sex, age, higher-income region) and income increases, a patient is 1 % less likely to choose the original. This could be caused by unobservable regional characteristics (e.g. different practices in pharmacies across regions, etc.) or unobservable characteristics attributable to gender. It suggests that higher income is associated with a higher level of education and thus easier access to information.

The odds ratio for the variable *Price* is 1.00092. If a patient takes drugs from the substitution group where there is a larger price difference between the original and the cheapest substitute, the odds of choosing the original increase by 0.1 %, holding all other independent variables constant. The patients may be suspicious of too cheap generics.

Table 7. Measures of Fit for logit of Original

Log-Lik Intercept Only:	$-2.539 \cdot 10^6$	**Log-Lik Full Model:**	$-2.070 \cdot 10^6$
D(766720):	4139718.181	**LR(8):**	938359.011
		Prob > LR:	0.000
McFadden's R2:	0.185	**McFadden's Adj R2:**	0.185
Maximum Likelihood R2:	1.000	**Cragg & Uhler's R2:**	1.000
Count R2:	0.673		
AIC:	5.399	**AIC*n:**	4139734.181
BIC:	$-6.249 \cdot 10^6$	**BIC':**	-938250.612

Table 7 reports measures of fit of fixed effects model. From the comparison of the log-likelihood of the full model with the log-likelihood of the intercept only model, we conclude that the full model fits the data significantly better than the nested model. The likelihood-ratio statistics equals 938359.011 with 8 degrees of freedom, $McFadden's\ R^2$ is 0.185 and Tjur's coefficient of discrimination (D) reaches $1.867 \cdot 10^7$. Penalizing the model for its size, AIC = 5.399, BIC = $-6.249 \cdot 10^6$ and BIC' = -938250.612, which again confirms that the model is appropriate.

Comparing the pooled panel data model and the fixed effects model using F-test, we reject the null hypothesis that the fixed-effects model is no better than the pooled panel data model. The preference for the fixed-effects panel data model is however caused by the large sample size.

When interpreting the results of the analysis one has to bear in mind that physicians' and pharmacists' recommendations and characteristics may also influence the choice of drugs. The physicians are also bound by prescription limits which sets the maximum total annual costs of drugs, the doctors are allowed to prescribe to all patients in total that the insurance fund reimburses. If the doctors exceed the annual prescription limits, they are penalized. Besides, chains of pharmacies produce "brand drugs", i.e. their own drugs for a specific active substance. No other drug than the brand one is available on store. If the consumer requires a different drug, e.g. the one prescribed or its generics, it is usually available over-night at the earliest. This transaction cost imposed on a patient may also influece the choice. None of this information was however directly observed, but some of it is embedded in other characteristics included in the model.

5 Discussion and Conclusion

The paper assesses the probability of using the original medication despite the presence of cheaper generics in the Czech pharmaceutical market, given patient and drug characteristics. A logistic regression is carried out. In a robustness check, we analyze drugs against acute (proxied by antibiotics) and chronic (proxied by anti-hypertensives) diseases.

The elderly in the Czech Republic seem to be price sensitive and prefer cheaper generics. However, they may also be familiar with the drugs they have long been taking and their substitutes. Costly patients, i.e. those which cost the public healthcare system more than average, tend to prefer the original. They worry that cheaper generics may worsen their yet considerably bad health status. The same effect and explanation holds for patients taking medicine against chronic diseases which captures additional dimension of patient's health conditions in the main analysis - being a costly patient does not necessarily mean that one is chronically ill.

Men more often choose the original drug than women, however when being prescribed antibiotics, they opt for generics more often than women. The people living in higher income regions tend to prefer generics. Income is assumed to proxy the level of education in the analysis. More educated patients thus approach information easier and do not worry to take cheaper generics. However, when being prescribed antibiotics, transaction costs for the more educated are not worth searching information about generics.

A one-year increase in the length of generic availability is associated with a decrease in odds of choosing the original drug, however only in the market for drugs against chronic diseases. It suggests that the chronically-ill need more time to adjust to new products. In case of drugs against acute diseases, the people prefer the original regardless of how long the market has been opened for competition. It again suggests that transaction costs to search for generics are too high for occasional drug users. The more substitutes for the particular original drug there are available in the market, the higher the probability to substitute from the original. Intake of one additional medication decreases the odds of using the original drug. The result suggests that people who use more different drugs are familiar with generic substitution and do not worry to substitute also when they are prescribed additional drugs. In substitution groups where there is a higher price differential between the original and the cheapest substitute, we observe a higher probability of choosing the original. The belief that price proxies quality of the product thus may overweight price elasticity in the Czech pharmaceutical market.

The analysis brings two important sets of conclusions, both of which may help design pharmaceutical policies in the Czech Republic. (1) It uncovered characteristics that determine the probability of using the original medication despite the presence of cheaper generics; and (2) it found out that drugs against acute and chronic deseases are associated with different behavioral patterns. Specifically, our results could help determine the specific drugs to be put on the "Positive list of drugs" that the practitioners are recommended to prescribe.[8]

[8] "Positive Lists" of pharmaceuticals were introduced to help save costs of the healthcare system. Each insurance fund has its own Positive Lists of drugs, the price of which the insurance fund negotiates with individual producers. It is usually 15-30 % cheaper than the price set through the national reimbursement

Should the aim of the state be the increase of generic substitution, the government should be interested in including into the Positive Lists the generics from those substitution groups, where the original is more likely chosen considering drug characteristics and structure of the consumers that prefer the original medication. Positive list should ideally be accompanied by information campaigns about equal quality of the original and its substitutes.

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Appendix

Table A1. Correlation Matrix

	Pensioner	Sex	Expend.	Chronic	Patent	Market	Drugs	Income	Price
Pensioner	1.0000								
Sex	-0.1208	1.0000							
Expend.	0.1453	-0.0809	1.0000						
Chronic	0.2146	0.1378	-0.0398	1.0000					
Patent	-0.1647	0.0079	-0.0591	0.0038	1.0000				
Market	0.1520	0.0905	-0.0308	0.5185	0.0271	1.0000			
Drugs	0.2592	-0.0476	0.2615	0.1722	-0.1561	0.0560	1.0000		
Income	0.1814	0.3354	0.0537	0.1665	-0.0222	0.1350	0.0903	1.0000	
Price	-0.1750	-0.0072	-0.0355	-0.2186	0.2020	-0.0404	-0.1285	-0.1093	1.0000

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