Düsseldorf Institute
for Competition Economics

DISCUSSION PAPER

No 307

Extra Costs of Integrity: Pharmacy Markups and Generic Substitution in Finland

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January 2019

HEINRICH HEINE
UNIVERSITÄT DÜSSELDORF

d|u|p düsseldorf university press

IMPRINT

DICE DISCUSSION PAPER

Published by

düsseldorf university press (dup) on behalf of
Heinrich-Heine-Universität Düsseldorf, Faculty of Economics,
Düsseldorf Institute for Competition Economics (DICE), Universitätsstraße 1,
40225 Düsseldorf, Germany
www.dice.hhu.de

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DICE DISCUSSION PAPER

ISSN 2190-9938 (online) – ISBN 978-3-86304-306-3

Extra Costs of Integrity: Pharmacy Markups and Generic Substitution in Finland (DICE Working Paper)

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Düsseldorf Institute for Competition Economics

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Abstract

I evaluate how the probability of substitution of a prescribed drug in a pharmacy depends on the pharmacists' profits and patients' out of pocket costs. I use Finnish population-wide data covering all prescriptions of three popular antidepressants. I find that one euro increase in the total markup difference between the prescribed drug and its cheapest available substitute is associated with 1.7 percentage points decrease in the probability of substitution. This result is driven by brand-name drugs. An increase in the patients' out of pocket cost differential yields a 0.6 percentage points increase in the probability of accepting the substitution. My findings offer novel evidence that pharmacists' incentives are instrumental for prescription drug cost savings and overall cost effectiveness of the health care system.

JEL: D78, I11, I18, L11, L65
Keywords: Generic substitution, Pharmacies, Prescription drugs

*I thank Otto Toivanen, Annika Herr, Janne Tukiainen, Tanja Saxell, Marko Terviö, Brett Wendling, Michele Crescenzi, Markku Siikanen, Tuomas Takalo, Leena Saastamoinen, Min Zhu and Milla Siikanen for guidance and extremely useful suggestions. I also thank the officers of the Finnish Social Insurance Institution for helping me to obtain the data and Yrjö Jahnsson Foundation for funding the data retrieval fees. I would like to express my gratitude to Emma Hokkala and Jukka Hirvonen, and Jaakko Ritvanen for helping me to understand the Finnish pharmaceutical market in depth. I am grateful to audiences of numerous conferences and seminars for useful comments. Parts of this research have been conducted during my doctoral studies at the University of Helsinki, and visits to Health Care Management Department of Wharton School and the Department of Economics of Boston University, I greatly appreciate their support. All errors are mine. Contact: olena.izhak@hhu.de

1 Introduction

In recent years approximately 20% of all health care costs in developed countries are attributed to medicines (Belloni et al. 2017). Pharmaceutical expenditures and the fraction of drug costs reimbursable by national health insurances also grow.[1] Price caps, reference pricing and generic substitution are the most common policies used for containing prescription drug costs. They stimulate the competition between generic and brand-name drugs and ultimately increase the market share of generics. To the extent generic and brand-name drugs are perfect substitutes, these policies lead to health care cost savings without compromising the quality of treatment.

Pharmaceutical producers, wholesalers and retail pharmacies are the key supply side actors affected by pharmaceutical policies. There exists an ample body of literature analysing the decisions and actions of pharmaceutical producers and regulators, which traces back to seminal papers by Scherer (1993) and Frank and Salkever (1997). Pharmacies (as well as pharmaceutical wholesalers) have largely been overlooked by economists, plausibly due to the lack of reliable data and perceived insignificance of their role. Nonetheless, pharmacies are a special kind of retailers and deserve special attention. Apart from setting drug prices and choosing the assortment, their central task is to help patients to understand how medicines work and how to use them. Generic substitution policy is directly linked to this task, as it requires pharmacists[2] to substitute prescribed drugs with cheaper biologically equivalent products.[3] This policy and the role pharmacists played in its implementation are the subject matter of my study.

Following other Nordic countries[4] Finland introduced generic the substitution policy in April 2003. Before the reform, pharmacists were required to dispense drugs (specific trade names) prescribed by doctors. The new regulation instructs pharmacists to inform customers about the existence of cheaper drug options when doctors prescribe more costly medications (provided such cheaper alternatives exist). Not all medicines were subject to substitution. Upon the implementation of the reform Finnish Social Insurance Institution, also known as KELA,[5] started to publish and regularly update the lists of substitutable drugs.[6] Generic substitution per se required minimal intervention and allowed freedom of choice on the consumer' side: even if a cheaper alternative to the prescribed drug was recommended by the pharmacist, patients still had the right to reject substitution. Even if the patient declined the substitute, the coinsurance and deductible would be the same. This means that the generic substitution regulation in Finland initially was not coupled with reference pricing. The reference pricing policy, which tied coinsurance to the prices of cheaper substitutes was implemented 6 years later.

Another important aspect of the Finnish pharmaceutical regulation is that the markup[7] a pharmacist receives from selling a reimbursable prescription drug is equal to a certain percentage of its wholesale price plus a fixed euro amount.[8] Hence pharmacies earn higher markups on more expensive medicines. A fixed percentage markup and generic substitution together result in conflicting incentives for pharmacists. On the one hand, they are obliged to inform patients about

[1] As an example, the recent dynamics of prescription drug cost in Finland is depicted in Figure A.1 in the Appendix A.

[2] Hereafter "pharmacy" and "pharmacist" are used interchangeably.

[3] Biologically equivalent drugs contain the same amounts of a given active ingredient in the same dosage form and can be delivered to the site of action in the amounts, which are enough for the necessary pharmacologic response (Strom, 1987).

[4] Denmark was the first to introduce generic substitution in 1991, followed by Iceland in 1995, Norway in 2001 and Sweden in 2002.

[5] *Fin.:* Kansaneläkelaitos.

[6] *Fin.:* Luettelot Kelalle ilmoitetuista vaihtokelpoisten valmisteiden hinnoista. See the Institution's web-page: `http://www.kela.fi/luettelot-vaihtokelpoisista-laakkeista`

[7] Pharmacies in Finland are for the most part retailers (they produce negligible amount of drugs), so markup in my context is the absolute markup, i.e., the difference between retail and wholesale prices in euros. For definition see, for example, Vohra and Krishnamurthi (2012).

[8] Finnish Government Decree on the Drug Rates (2001/844) `https://www.finlex.fi/fi/laki/alkup/2001/20010844`

the existence of cheaper substitutes. This implies that they have to exert the effort, e.g., keep the substitutes in stock; check if the prescribed drug is actually substitutable; spend time talking to patients about other options. On the other hand, pharmacists forgo profits each time a patient accepts the substitution, because the markups are strictly higher on more expensive drugs. Generic substitution, which initially was not coupled with the reference pricing, along with strictly higher markups on more expensive drugs make the Finnish setting very peculiar. The conflicting incentives on the pharmacists' side have not been noted and documented previously. Using a unique prescription level data set I analyse the enactment of the generic substitution reform in Finland. The main goal of this paper is to empirically evaluate how the probability of substitution depends on the pharmacists' profits and patients' out of pocket (OOP) costs. I empirically show that the more markup a pharmacist stands to lose due to substitution, the less likely it is to happen. Each additional euro of potentially forgone markups translates in 1.7 percentage points decrease in the likelihood of substitution. This result is driven by the brand-name drugs for which the probability of substitution decreases as much as 5.1 percentage points with each euro of additional markup. Patients' OOP costs have the opposite effect: higher potential savings imply a higher probability of substitution.

To the best of my knowledge, there is no literature identifying the effects of pharmacists' profits and patients' OOP costs on generic substitution in the Finnish context. In addition most of the related literature discussed in detail is the following Section, e.g., Brekke et al. (2013), focuses on the indirect price and drug market shares' responses to the pharmaceutical cost saving policies. Instead I directly analyse the substitution frequency, the key outcome of the policy, in its relation to the incentives of the main agents of the policy.

The rest of this paper is organized as follows: Section 2 is a summary of the existing literature concerning generic substitution policy implementation and pharmacies. Section 3 contains a detailed description of the Finnish pharmaceutical market and its regulations. Section 4 includes the sketch of a theoretical framework and formulates testable hypotheses for the empirical analysis. It also outlines the empirical strategy, measurement and identification. Section 5 describes a unique data set I use for the analysis. Section 6 discusses the main results and robustness checks, and lastly Section 7 concludes.

2 Related Literature

The current study is linked to three strands of economic literature: first, papers analyzing the effects of generic substitution and reference pricing policies on drug prices and consumer welfare in Finland; second, the literature focusing on pharmacy markets and third studies of retailers agency in influencing consumers choices, and more specifically pharmacies' role in promoting generics.

Overall literature on the economic effects of generic substitution traces back to medical and economic evaluations of the policy (initially called drug product selection legislation) in the U.S. Goldberg et al. (1979), one of the earliest works on the topic, find very modest savings from allowing generic substitution in pharmacies during the early years of its adoption in Michigan. They also find that the pharmacists were more likely to substitute when patients did not have drug insurance coverage, which likely promoted adherence. Leibowitz et al. (1985) using data from RAND Health Insurance Experiment observe that less generous insurance coverage does not prompt patients to choose generics over branded drugs. The caveat of their analysis is that the data does not allow them to distinguish if generics were dispensed because they were prescribed or due to the substitution in pharmacy.

Papers focusing on the generic substitution policy in Finland are the closest to this study in terms of the institutional setting. Aalto-Setälä (2008) explores the impact of generic substitution regulation on drug prices within one year of its implementation. He finds that the prices of substitutable drugs decreased by 10% on average post-reform. He also detects sub-

stantial heterogeneity in price responses across products. Hokkanen et al. (2012) attempt to analyse the changes in the Finnish pharmaceutical market structure after generic substitution was implemented. They empirically show that upon the reform Finnish pharmaceutical market became segmented, which led to a decrease in generics' prices and no change in brand-name drug prices. In a more recent follow-up study Hokkanen et al. (2016) conclude that in the long run the generic substitution policy in Finland led to a decrease in prices of both generic and originator drugs, but the decrease in the prices of generics was substantially larger. I also analyse the generic substitution reform in Finland, but in my setting drug prices are to some extent exogenous from the point of view of the pharmacists. I evaluate whether pharmacists acted according to the requirements of the regulation, and if not, what was the driving force of their defiance. Pharmacology survey studies trying to identify the attitudes of Finns towards generic substitution reform and the effectiveness of generic drugs are also related to my work. For example, Heikkilä et al. (2007) and (2011) find that pharmacists' endorsement was an important factor patients considered while accepting substitution.[9]In general, to the best of my knowledge, there is no literature rigorously analysing pharmacies and the role they played in generic substitution in Finland.

Doctors are not always acting in the best interests of their patients while prescribing drugs both in terms of health outcomes and costs (Meeker et al., 2016; Iizuka, 2012). Generic substitution and reference pricing also help to overcome possible agency problems on doctors' side, if they fail to internalize patients' costs. Ample literature analyses doctors' prescription behavior,[10] but the literature analysing pharmacies is scarce. The main reason for this gap is the lack of reliable data at pharmacy level. Sorensen (2000), one of the first contributions in this field, hand collected data from several pharmacies in New York state. He finds that there is a significant price dispersion across pharmacies due to consumer search costs and pharmacy heterogeneity, with the most popular medicines being the cheapest.

Pharmacists' incentives to dispense generic or branded drugs play an important role in the substitution process. Using the U.S. data, Mott and Kline (2002) find that pharmacists' unobservable characteristics account for 44% of the variation in generic substitution incidences. Iizuka (2012) documents that Japanese doctors who simultaneously prescribe and dispense drugs are more likely to prescribe generics as the markups they earn on generics are on average higher than those on brand-name drugs. There is no effect of markups on the likelihood of prescribing generics for doctors who do not sell drugs. Using Norwegian drug registry – Norwegian Prescription Database (NorPD) – Dalen et al. (2011) analyse the factors affecting the likelihood of choosing generics over branded medicines. They find that the likelihood of choosing generics varies greatly across pharmacy chains.

Tesler (1960) noted that retailers are able to affect consumers' choices. This idea is particularly relevant in case of the generic substitution regulation in Finland, as pharmacists are obliged to actively influence consumer choices in order to ensure substitution. Producers in turn could influence pharmacists using the wholesale pricing.[11] Brekke et al. (2013) build a

[9]A survey study from New Zealand find that most pharmacists perceive generic and branded drugs as equally safe and effective, Babar et al. (2011). However, pharmacists cite costly effort needed to persuade customers to switch to generics and inadequate dispensing fees as the major obstacles for implementing generic substitution, which is in line with my findings.

[10]This literature traces back to Hellerstein (1998), who made one of the first attempts to determine which factors play role in doctors' generic prescription decision. Among other things she finds that if doctors have to sign their names twice on the prescription in order to forbid substitution the likelihood of generic prescription increases. Thus even a negligible cost matters for doctors' choice. Lundin (2000) finds that doctors are sensitive to patients' OOP costs while prescribing medicines. Skipper and Vejlin (2015) relying on Danish drug registry find that doctors' socio-economic characteristics (as well as unobservables captured by doctor level fixed effects) explain very little variation in generic drug use.

[11]Interviews I conducted with pharmacists revealed that currently they can receive discounts on over the counter drugs or free products from distributors while placing large orders of prescription drugs. Anecdotal evidence suggests that before 2006 producers could also provide discounts directly on prescription drugs.

theoretical model that incorporates pharmacy profits and efforts while promoting substitution. They explicitly state that if branded drug markups are fixed percentages of their wholesale prices, pharmacists have no incentives to exert effort on substitution, so such a markup rule is "detrimental for stimulating generic competition". Using the aggregation of NorPD Brekke et al. (2013) also empirically confirm that higher pharmacy generic markups are associated with bigger market shares of these drugs. So far, their study offers the most compelling evidence that pharmacists' incentives are critical for generic substitution. Sæthre (2016) suggests that unobservable sales effort can influence demand and failing to account for such effort would result in biased estimates demand elasticity with respect to price. He confirms findings of Brekke et al. (2013) incorporating the unobservable retailers' effort into a structural model: market share of generics is explained by pharmacies' profit margins, which vary across Norwegian pharmacies even though the prices are fixed. Granlund (2015) using prescription level data from Sweden analyses the pharmacists' role in lower likelihood of dispensing cheaper parallel imported medicines[12] after a reform which allowed pharmacies to receive discounts from producers and importers. Although the reform intended to boost the market share of cheaper parallel imported drugs, pharmacists received higher discounts on locally sourced drugs, so the likelihood of dispensing parallel imported drug decreased post-reform, leading to 11% drop in their market share.

My study resonates with theoretical and empirical findings of Brekke et al. (2013), Granlund (2015) and Sæthre (2016). It is clear that pharmacists' incentives are instrumental for stimulating generic market penetration. However, Finnish legislations set these incentives diametric to the main goals of the regulator. Apart from using a different country setting, I am able to offer a more granular look at the substitution policy and the pharmacist's role in its implementation. I observe both the prescribed and dispensed drugs on each purchase instance, so I precisely can tell if the drug was substituted in pharmacy, whereas Brekke et al. (2013) can only approximate the substitution intensity using generic product market shares. I directly calculate the difference in markups between prescribed and dispensed drugs, as well as the markup differences between each prescribed drug and each of its substitutes. This means that I am able to pin-down both the real markup loss pharmacists incurred if substitution was accepted and the potential markup loss if substitution was rejected. I also control for the patient OOP costs and socio-economic characteristics. Hence, I am able to directly disentangle the effects of patients' and pharmacists' monetary incentives. I also control for the unobservable heterogeneity among pharmacies using pharmacy specific fixed effects, as my data covers the entire population of Finnish pharmacies over 4 years.

I next turn to a detailed description of the Finnish pharmaceutical market setting: its main players and policies. I also summarize the mechanics of the generic substitution policy and the role which was assigned to the pharmacists in its implementation.

3 Institutional Background

3.1 Finnish Pharmaceutical Market: Main Players

The Demand Side

The health care is universal in Finland: in 2015 there were approximately 5.5 million people covered by the National Health Insurance.[13] Government and municipalities compensate a substantial part of medical expenses of residents, including prescription medicines costs. Some

[12] Parallel importing firms buy (typically branded) drugs in countries with lower wholesale prices and sell them to pharmacies in countries with higher wholesale prices.

[13] All citizens and permanent residents are eligible for the national insurance (Ministry of Social Affairs, Act on the Application of Residence-Based Social Security Legislation §2 (1993/1573).

proportion of the population is also covered by a supplementary private health insurance, which is either provided by their employer or bought voluntarily. Finnish Social Insurance Institution (henceforth KELA[14]) is the provider of the National Health Insurance and is responsible for the reimbursements of prescription drugs in the outpatient care.[15] Licensed doctors (including dentists and some nurses) are allowed to prescribe drugs for outpatient care. In almost all cases a certain trade name of a drug is prescribed.[16]

Drug expenses are covered by the National Health Insurance provided the producer applied for the reimbursement status, which in turn requires marketing authorization. Moreover, a drug must be used for *a treatment of a disease* in order to be reimbursed.[17]The price each patient pays in a pharmacy already excludes the amount covered by the National Health Insurance. KELA is paying the drug cost reimbursements directly to the pharmacy. The reimbursement percentage (1 - coinsurance) is based on patient's eligibility category determined according to her diagnosis. Eligibility categories and corresponding copays and reimbursement percentages from 2002 to 2013 are summarized in Table 1 below.

Year	*2002 – 2005*		*2006 – 2013*		*2013 – 2016*	
Eligibility Category	Reimb., %	Copay, EUR	Reimb., %	Copay, EUR	Reimb., %	Copay, EUR
Basic	50	10	43	–	35	–
Lower Special (e.g., asthma, hypertension diagnosed)	72	10	75	–	65	–
Higher Special (e.g., cancer, diabetes diagnosed)	100	5	100	3	100%	3

Table 1: Drug Cost Reimbursement Percentages Across Eligibility Categories in Finland in 2002 – 2013

Between 2002 and 2005 patients from basic coinsurance category faced EUR 10 copay[18] times the reimbursement percentage before the insurance started to cover drug costs. The patients from special coinsurance eligibility categories were responsible for EUR 5 copay[19] before the coinsurance kicked in. Special reimbursement eligibility is assigned to patients based on physician's certificate and application with KELA.[20] If patient reaches the yearly medicine deductible limit of about EUR 600[21] her only OOP cost would constitute EUR 1.5 per purchase instance provided she files the corresponding application with KELA. I use this information to calculate the potential OOP costs in my analysis and verify my calculations using the actual amounts of reimbursements I have in my data. An example of the OOP cost calculation is provided in Appendix B. There are also some additional reimbursements and discounts patients may receive. Patients are only eligible for reimbursements of 3 months supply of their medicines at a time.[22]

The Supply Side

Pharmaceutical producers, distributors and retail and hospital pharmacies constitute the supply side of the Finnish pharmaceutical market. There are over 100 pharmaceutical companies operating in Finland, including multinational giants (Pfizer, Merck, Teva) and local producers (Orion Oy, Vitabalance Oy). There are also several parallel importers, for example, Orifarm

[14] *Fin.:* Kansaneläkelaitos

[15] It also collects and analyses the data on drug prescriptions and reimbursements.

[16] Even though generic prescribing, i.e. prescribing a certain active ingredient, is permitted, it is virtually non-existent, Martikainen and Rajaniemi (2002).

[17] For example, if contraceptives are prescribed for pregnancy prevention, their cost are not covered, but if they are prescribed as treatment of polycystic ovarian syndrome they are reimbursable.

[18] *Fin.:* Ostokertakohtainen omavastuu. Copay is charged per transaction.

[19] This copay was also abolished in 2006 for the lower and decreased to EUR 3 for higher special eligibility.

[20] `http://www.kela.fi/laakkeet_erityiskorvaus`

[21] Specifically: 601.15, 604.72, 606.95 and 616.72 EUR in 2003, 2004, 2005 and 2006 respectively.

[22] Finnish Health Insurance Law §9 (*Fin.* Sairausvakuutuslaki.)

Oy and Paranova Oy. There are two major drug wholesalers – Tamro Oy and Oriola Oy (both subsidiaries of multinational drug distributors) which supply almost 100% of all drugs to pharmacies. They work using so-called single channel distribution model: each company is specialised on supplying drugs from certain producers (Valiluoto 2012).

There are about 800 retail pharmacies[23] or about one pharmacy per 6,600 inhabitants in Finland. This implies that Finland has the highest density of pharmacies per inhabitant among Nordic countries. For comparison, there were only 400 pharmacies in Denmark[24] in 2016 (Association of Danish Pharmaconomists, Newsletter). The Finnish Medicines Act does not regulate the number of pharmacies that can operate in Finland, but its §39 says that pharmacies should be located so that the consumers can obtain medicines without difficulties. In order to open a new pharmacy or take over the license of an existing pharmacy, the entrepreneur is required to have a Master degree in Pharmacology, several years of working experience in the industry and be not older than 68. In addition to the main store pharmacy owners are allowed to open up to 3 smaller subsidiary pharmacies So, there is no pharmacy chain stores in Finland and each pharmacy can be considered to be an independent entity. One exception is the University Pharmacy (Yliopiston Apteeki), which is a subsidiary of the University of Helsinki and operates a chain of 16 pharmacies (as of 2016) in 12 counties and employs over 10% of Finnish pharmacy personnel. My data neither allows to identify the chain store, nor distinguish between main and subsidiary pharmacies. There are several official alliances of pharmacies in Finland. The largest ones were Cooperation Pharmacies and Open-Pharmacies,[25] which as of 2018 included over 200 outlets around Finland. Independent pharmacies established these organizations mainly in order to increase profitability through consolidating some enterprise functions, such as inventory planning or product ordering through a centralized information technology systems.[26]

Instead of income tax pharmacies pay a fixed percentage of the turnover, called the pharmacy fee.[27] Pharmacy markups on prescription drugs are determined by the government decree. They consist of a regressive percentage of wholesale prices plus a regressive fixed euro amount. The pharmacy pricing scheme and markups[28] are provided in Table 2.

Wholesale Price, EUR	**Retail Price, EUR Less 8% VAT**
0 – 9.25	1.5 × wholesale price + 0.50
9.26 – 46.25	1.4 × wholesale price + 1.43
46.26 – 100.91	1.3 × wholesale price + 6.05
100.92 – 420.47	1.2 × wholesale price + 16.15
> 420.47	1.125× wholesale price + 47.6

Table 2: Finnish Reimbursable Drugs' Pricing and Pharmacy Markup Scheme – Lääketaksa in 2002-2013

Although the markup percentage is a decreasing function of wholesale prices, the absolute markup is a strictly increasing function of the wholesale price, implying that pharmacists earn more profits from dispensing more expensive medicines. Put differently, selling cheaper drugs is strictly less profitable in absolute terms, which creates monetary disincentive for generic substitution. To illustrate this graphically, I plot markups as a function of wholesale prices in absolute amounts (grey line) and in percentages (black line) on Figure 1. The pharmacist

[23]Figure A.2, panel (a) in Appendix A provides the information on the number of pharmacies in Finland in 2001 – 2016.

[24]Danish pharmacy market regulations are very similar to those in Finland.

[25]*Fin.:* Yhteistyö Apteekit and Avain-Apteekit. The chains merged in May 2018

[26]Information obtained during an interview with a pharmacist.

[27]Pharmacy fee (*Fin.:* apteekimaksu) is regulated by the separate Law of Pharmacy Fee (after 2016 Pharmacy Tax). `https://www.finlex.fi/fi/laki/ajantasa/kumotut/1946/19460148`

[28]Source: Finnish Government Decree on the Drugs Rates (2001/844) `https://www.finlex.fi/fi/laki/alkup/2001/20010844`

also received a fixed dispensing fee[29] of EUR 0.42 per each purchase in order to compensate for the dispensing effort, however this amount is typically negligible compared to markups. The regulator increased the dispensing fee fivefold in 2015.

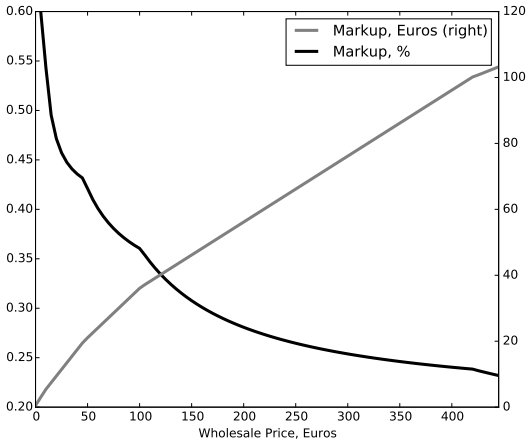

Figure 1: Prescription Drugs' Wholesale Prices and Markups: Graphical Representation.

3.2 Medicine Pricing in Finland

The Pharmaceutical Pricing Board or HILA[30] is an authority that decides on wholesale prices of reimbursable drug and reimbursements covered by the National Health Insurance. HILA consists of 7 people (the representatives come from KELA, Ministry of Finance, Ministry of Social Affairs, Finnish Medicines Agency – FIMEA) appointed for 3 years by the Ministry of Social Affairs.[31] According to the Health Insurance law §5 and 6, prices of reimbursable medications are set by HILA mostly based on prices of comparable products in Finland if similar drugs are already available on the market, and/or prices of the product in other states of the European Union, and also taking into drug benefits and availability of public funds.

In order to start selling a new drug on the Finnish market a pharmaceutical company applies for marketing authorisation to the Finnish Medicines Agency (FIMEA).[32] If the company wants the drug to be reimbursed by the National Health Insurance, it applies to the Pricing Board. HILA decides on the reimbursement category and approves the drug price. Initially all new drugs are assigned to the basic reimbursement eligibility category and can only be added to the special reimbursement category after two years on the market. Drug producers are required to submit health economic evaluations of drugs' costs and benefits to HILA. In practice, the final price is determined by negotiation between HILA's experts in pharmacology and health economics (secretariat) and drug producers. If a reimbursable drug is a new active ingredient on the market, then its initial wholesale price approved by HILA essentially becomes the price cap (known as *reasonable wholesale price*[33]) for the other drugs made with the same active ingredient, which subsequently enter the market. The price caps of new active ingredients may be revised after 3 years. The price caps of older drugs can be updated every 5 years.

Before January 1, 2006 wholesale prices of the reimbursable drugs below the price cap could vary across pharmacies, as drug producers were allowed to give pharmacies discounts. These discounts on prescription drugs are neither observable to the regulator nor captured in my data. Anecdotal evidence and the data suggest that, in this period, retail prices of reimbursable drugs

[29] *Fin.:* toimitus maksu.
[30] *Fin.:* Hintalautakunta.
[31] `http://www.hila.fi/en/operations-and-organisation/pharmaceuticals-pricing-board`
[32] The role of FIMEA resembles that of Food and Drug Administration (FDA) in the US.
[33] *Fin.:* kohtuullinen tukkuhinta.

were virtually identical in every pharmacy throughout the country, so pharmacists did not pass on cost savings to consumers. The actual prices charged from the customers are typically equal to the prices reported in KELA substitutable drug lists with some minor adjustments. Hence, it is likely that I observe the lower bound of pharmacists' profits in the first 2.5 years of my observation period. The Medicines Act was amended in 2006, so that all wholesale prices of prescription drugs (both reimbursable and non-reimbursable) *including all discounts* provided by the wholesalers were bound to be the same for every pharmacy throughout the country.[34]

Producers have to report any medicine price updates (even if they do not change the price cap level) with corresponding expiration and starting dates to HILA, which then shares this information with KELA. The prices can be updated at the beginning of each two week period, typically on the first and on the fifteenth day of the month. In addition, producers also have to report the drug prices to KELA separately four times a year. The wholesale prices of the drugs, which are not covered by the National Health Insurance are set freely. Overall Finnish pharmaceutical market is tightly regulated, policy changes are frequent and reactive to the market dynamics. Striking examples of such policy changes are two amendments to the Health Insurance Act, which slashed wholesale prices of all reimbursable drugs by 5% in 2006 and 2013.[35]

3.3 Finnish Generic Substitution Reform

The generic substitution policy in Finland was announced on September 27, 2002 and came into force on April 1, 2003. It requires retail pharmacies to offer patients cheaper alternatives to the prescribed drug provided such alternatives exist, the substitution yields substantial cost savings and the physician does not forbid the substitution.[36] Before the reform, it was prohibited to fill prescriptions with anything other than what had been prescribed.[37] The patient can accept or reject the substitute offered by the pharmacist. The National Health Insurance covered the drug cost according to her eligibility category. Implying that the generic substitution in Finland was not coupled with the reference pricing policy as it was typically done in other countries (e.g., Norway). The reference pricing, which tied the drug reimbursements to the prices of their cheaper alternatives, was introduced in Finland in April 2009.

In order to facilitate the substitution KELA started to publish quarterly lists of substitutable products in October 2003. The lists arrange drugs into the substitution groups according to their active ingredient, package size, dosage and form. They also include information about each drug's producer and retail price. It is also possible to identify possible substitutes using these lists: cheap alternatives within each substitution group are marked by asterisks. A drug cheaper than EUR 40 is marked by the asterisk if its price does not exceed the price of the cheapest drug within its group by EUR 1.5 or less. A drug more expensive than EUR 40 is marked if its price exceeds the price of its cheapest alternative by EUR 2 or less. The marked drugs in the lists are commonly known as the drugs "from the price corridor"[38]. The lowest price within each substitution group is provided separately in bold at the end of each group roster. An excerpt from a substitutable drug list is presented in the Table 7, Appendix A. Certain drugs, which have generic substitutes, are not included in the set of substitutable drugs for clinical or pharmacological reasons (e.g., insulins or their analogues).[39] Heikkilä (2013) reports that during the early days of the reform only about 66% of drugs sold in Finland were substitutable.

[34] Finnish Medicines Act §37a.

[35] The Law Amending or Temporarily Amending the Finnish Health Insurance Act, §19 `https://www.finlex.fi/fi/laki/alkup/2005/20050885`

[36] Finnish Medicines Act (Translation), Section 57b (22/2006) `https://www.fimea.fi/documents/160140/765540/18580_Laakelaki_englanniksi_paivitetty_5_2011.pdf`

[37] As mentioned above in Finland starting from 2002 doctors have been allowed to write generic prescriptions, but in practice, also observed in my sample, it has been an extremely rare event.

[38] *Fin.:* hintaputki

[39] `http://www.kela.fi/laakkeet-laakevaihto-ja-viitehinta`

Finnish Medical Association, pharmaceutical producers and some pharmacy owners opposed the policy (Heikkilä et al., 2007). Based on a survey made by the Finnish Pharmacist Association in mid-2003, it was estimated that generic substitution increased pharmacists' total workload by a labor equivalent of over 200 full time employees. This estimate is comparatively large, as the total number of employees in the pharmacy sector in 2003 was 7999.[40] Panel (b) of Figure A.2 in Appendix A implies that the pharmacists underestimated the increase in their workload: the total headcount of pharmacists and technical personnel increased by almost 10% between 2002 and 2004. There has also been a slight increase in the number of MPharms,[41] whereas the number of pharmacy owners and pharmacy shops (panel (a) of Figure A.2) did not change significantly.

4 Empirical Strategy

4.1 Conceptual Framework

Offering a substitute to a patient clearly is a costly action on the pharmacist side. Higher markups on generics relative to brand-name drugs should encourage pharmacists to recommend substitution because the higher profits offset the cost of substitution effort. It is plausible that pharmacists would exert the biggest effort promoting the most profitable generics, which in turn would increase their market penetration. If the markup is a fixed percentage of the wholesale price it is strictly more profitable for pharmacists to dispense more expensive drugs. If the wholesale prices of brand-name drugs are higher than those of generics the pharmacists forgo the difference in profits between the prescribed drug and its substitute (provided patient accepts substitution), in addition to bearing the cost of substitution effort. In this case in equilibrium rational pharmacists never exert any substitution effort (in absence of sanctions for not informing the patients). The substitution would take place only if the patient is informed herself and asks for a substitute.

Brekke et al. (2013) were the first to formally model the relation between substitution effort and pharmacists' profits. They find that the optimal substitution effort is increasing in the difference between the profits on branded and generic drugs. Under certain assumptions the difference in copays between brand-name and generic drugs also increases substitution effort, reinforcing the effect of the profits on substitution. As described in Section 3 pharmacy markups are legally set as fixed percentages of drugs' wholesale prices in Finland. The wholesale prices of brand-name drugs are typically higher than those of generics.[42]Therefore, pharmacists earn strictly higher profits on more expensive brand-name drugs in Finnish context. This implies, that even though pharmacists are legally obliged to offer substitutes, they do not have any direct monetary incentives to do it. However, possible sanctions might incentivise substitution. According to the interviews I conducted with Finnish pharmacists, the regulator (KELA) does not explicitly check if the substitution takes place, instead it monitors the reimbursable medicine stock and imposes fines if cheaper "price corridor" drugs are not available. Thus, the legal penalties might be considered as negligible. Nevertheless, pharmacists might be inclined to substitute because they have innate preference for law abiding behaviour or value their reputation.[43] It is plausible that Finnish pharmacists exert the minimal substitution effort in order to avoid

[40] Annual Review of Finnish Pharmacies Association (2003).

[41] *Fin.:* Proviisorit or *eng.* Masters of Pharmacology.

[42] This is not the case in other settings, for example in UK or Japan (see for example Iizuka, 2012). Anecdotal evidence suggests that in Finland generic companies were offering discounts to pharmacies, which were outlawed in 2006.

[43] More formally, pharmacist's objective function is: $U = mpq(p) - \gamma(e, s) - f(q(p))$, where m is the markup percentage, p – wholesale price, $q(p)$ – quantity, $\gamma(e, s)$ – substitution cost function, increasing in effort e and decreasing in customer satisfaction s, $f(q(p))$ – penalty for misbehaving (e.g., fine for not keeping generics in stock or guilt of breaking the law or loss of reputation).

sanctions or ruminating on breaking the law. The substitution should be more likely in cases where potentially lost profits and expected substitution efforts are relatively lower, for example, when a branded drug might be switched to an authorized generic.[44] Pharmacist would also likely keep the most expensive generics in stock. If due to the monetary incentives' pharmacists are mostly substituting among generics in order to technically fill the legal requirement, this might increase price competition among generics, leaving branded prices intact or even leading to their increase, which might explain the "generic competition paradox" (Schrerer, 1993).

Given the theoretical argument above I expect that the more profits pharmacists stand to lose from offering substitutes, the less likely is the substitution. It is not feasible to directly observe the amount and cost of the extra effort needed to convince a given consumer to accept substitution. Markups made on each sale and possibly lost due to substitution, however, give a clear measure of real monetary costs of the substitution, which in turn affect its probability. I expect that the probability of observing generic substitution is *negatively related* to the difference in markups between the prescribed drug and its cheapest available substitute. It is also plausible that the substitution is more elastic with respect to the forgone profits in case of brand-name drug prescriptions: marginal changes of markup differences for branded drugs will have higher effect on likelihood of substitution compared to those of generics. In contrast, the more patients stand to gain from the substitution, the more likely they are to accept it. Therefore, I hypothesise that the probability of observing generic substitution is *positively related* to the difference in OOP costs between the prescribed drug and its cheapest alternative (other things being equal).

4.2 Measurement and Variable Construction

The data allows me to directly observe if generic substitution took place for each transaction. The main dependent variable in the empirical analysis is a dummy, which equals to one if generic substitution took place, and zero otherwise, i.e., it equals to one if the prescribed and dispensed drugs do not match. Even if a drug is mentioned in KELA lists, *de facto* it is not substitutable if it is the only drug within its substitution category (for an example see the last entry in Table 7 of Appendix A). So, I focus on non-singleton drugs within their substitution groups. Substitution is also not possible if a doctor explicitly forbids it on the prescription. The data allows me to identify and exclude such observations from the sample.

The law requires pharmacists to substitute drugs marked by asterisks ("price corridor drug") for the prescribed drugs, in case the prescribed drugs are not marked. In practice, I observe the drugs from the "price corridor" being substituted for each other, or cheaper drugs which do not belong to the "corridor" substituted for more expensive drugs.[45] Hence, any prescribed drug is substitutable provided it belongs to a non-singleton substitution group and substitution is not prohibited by the physician, regardless of its "corridor" status. A pharmacist makes an active decision to substitute only provided it is possible, therefore my final outcome variable is a conditional probability of substitution: $\mathbb{P}[Substituted = 1|Possible]$.

To approximate monetary (dis)incentive for substitution, using the markup scheme from Table 2, prices and total per purchase cost information, I back engineer the real and potential markups made by pharmacist on each purchase instance. I provide an example of the calculation in Appendix B. I can make a similar calculation for the cheapest alternative of the prescribed drug, using its retail price and real number of packages bought. The prices can be updated every two weeks and pharmacists observe the most recent prices, so I calculate the price of the cheapest alternative within each substitution group during each biweekly period directly from the data.[46] Likewise, I approximate patients' monetary incentives to accept substitution by the

[44] Authorized generics are generics produced by the drug patent holding companies prior to its expiration. They are also called pseudo generics (Appelt, 2015).

[45] Drugs are substituted across different substitution groups in 216 cases within my sample.

[46] The correlation between the lowest drug price calculated from the data and the quarterly price from KELA lists is 0.982.

OOP cost differential between the prescribed drug and its cheapest substitute in a given biweekly period.[47] If a patient has reached her yearly deductible or if she belongs to the higher special reimbursement category the OOP cost differential is zero. I also create a dummy variable, which equals one if the branded (e.g., patent holding) drug had been prescribed.[48]To control for generic drug habit formation, I calculate the share of generics in all patient's purchases up until a given purchase instance. In order to control for more rigid "long term" tastes for generics, which might stem from pre-substitution era, I calculate the total percentage of non-originator drug prescriptions each patient received prior to implementation of the generic substitution policy.

4.3 Identification

I am interested in evaluating how the monetary incentives, namely the markup difference between the prescribed drug and the cheapest generic drug within its substitution group affect the likelihood of the substitution. I also check how patient's OOP costs and other characteristics affect the probability of substitution in the pharmacy.

Patients might have inherent preferences for the prescribed drug, for example, if they are concerned about adverse effects. For some patients monetary savings from substitution will not outweigh the real or perceived benefits of more expensive prescribed medication. In such cases even if the pharmacist informs about the existence of a cheaper option, the patient might still stick with the original prescription. Inherent preferences for the prescribed (or branded) drug might be related to patients' observable characteristics. So, I control for the preference for the prescribed drug using patients' observable characteristics, such as demographics, cumulative percentage of generic purchases a patient made thus far or percentage of generic prescriptions one filled prior to the reform.

In order to capture marketwise idiosyncracies, which might affect the probability of substitution, I include the bi-weekly period fixed effects in the model. Such shocks encompass aggregate market level demand fluctuations, price updates and inflation. I also include substitution group dummies to capture the product specific unobservable characteristics, which might affect substitutability. I add pharmacy specific fixed effects in order to control for the time invariant unobserved characteristics of pharmacies, which might potentially influence the probability of substitution. The unobserved heterogeneity captured by these fixed effects includes, among other things, pharmacy size, clientele, market power, preferences and expertise of the employers. So, I estimate the following regression equation:

$$\begin{aligned}\mathbb{P}[Subsituted &= 1|Possible]_{ijkpt} = \alpha\Delta\pi_{ijt} + \beta\Delta\omega_{ijt} + \\ &+ \gamma\text{Orig}_{ijt} + \delta\text{Orig}_{ijt} \times \Delta\pi_{ijt} + \kappa\mathbf{X} + \Omega_{jkpt} + \varepsilon_{ijkpt}\end{aligned}$$

where $\mathbb{P}[Substituted = 1|Possible]_{ijkpt}$ is a binary variable, which equals one if on a purchase instance i a drug from a substitution group j prescribed by a physician p made in a pharmacy k, on a date within the biweekly period t was substituted for another equivalent drug provided the substitution is possible. $\Delta\pi_{ijt} = \pi_{Rx,it} - \pi_{\min,jt}$ – the main explanatory variable, corresponds to the difference in total per purchase markups between the prescribed drug and the cheapest available alternative within its substitution group; $\Delta\omega_{ijt} = \omega_{Rx,it} - \omega_{\min,jt}$ is the difference in total per purchase OOP costs between the prescribed drug and its cheapest alternative; Orig_{ijt} is a binary variable, which equals one if the prescribed drug is an originator brand-name (e.g., Cipramil, Fontex or Remeron); $\mathbf{X}$ is a matrix of a purchase instance specific covariates described above, including a dummy variable if the purchase was made by a female, the natural logarithm of patient's age and its square, the cumulative average percentage of the non-originator drug purchases a patient made so far or, in an alternative specification, the patient's percentage of

[47]Using the markup and OOP cost differentials calculated based on the quarterly minimal prices from KELA lists instead of biweekly minimal prices in the estimations does not significantly change the results.

[48]The branded drugs in my sample are: Fontex (fluoxetine), Cipramil (citalopram) and Remeron (mirtazapine).

total pre-reform prescriptions filled with generics, a binary variable with equals one if the patient filled all prescriptions in the same pharmacy during the sample period; Ω_{jkpt} is a matrix of fixed effects, which include the substitution group, biweekly period, pharmacy fixed effects and the interaction of the biweekly and substitution group fixed effects; ε_{ijkpt} is the i.i.d. mean zero error term.

4.4 Threats to Validity and Assumptions

There are several potential threats to the internal validity of my empirical approach. First, a measurement error in the main explanatory variable is likely. Moreover, this variable might be jointly determined with the outcome variable. I discuss these threats and the ways I address them in detail below.

As mentioned in Section 3, regulation prohibiting suppliers' discounts to pharmacies was enacted in 2006. Although it is not clear if the discounts actually existed, anecdotal evidence suggests that drug producers did provide discounts, which I cannot observe. The presence of discounts implies that the markup differential that I calculate using the drug prices and the markup schedule is the upper bound for the actual markup differential under the assumption that generic companies were more motivated to provide the discounts.[49] I assume that the measurement error due to discounts is cancelled out by the substitution group $\times$ weekly fixed effects and pharmacy fixed effects, so they wipe out the error. In addition, I run separate regressions only for the 2006 subsample, i.e., in a period when discounts became illegal.

The main threat to the validity of my analysis is simultaneity: the markups and the substitution probability are likely jointly determined. Pharmaceutical producers did respond to substitution by changing the drug prices (as showed in Figure A.4), which in turn likely translated into changes in both real and potential profits for pharmacist and eventually changed their substitution behaviour. I also observe entry of generics shortly before and after the reform, which also shifted down the lowest price in some of substitution groups. Lastly, in the post-reform period, I observe that generic producers also started to frequently update their prices due to substitution, reducing the lowest price even further. Ideally, I should instrument the markups, for example, using drug prices in similar markets such as Sweden or Denmark. In absence of such data, I tackle this endogeneity by estimating the regressions on the data from time periods when the drug prices were not updated. As mentioned in Section 3, the drug producers can update their prices at the beginning of every two weeks. So, if there was a price update in a substitution group, I exclude all observations from this substitution group within a given bi-weekly period from my sample.

I make an implicit assumption that there is no difference in health outcomes between a prescribed drug and all its substitutes.[50] It is plausible that this is true in my context. Doctors are informed about the substitution. They can forbid it if they are concerned about the lack of efficacy or side effects of substitutes. I exclude observations where the substitution was forbidden by the physician from my analysis.

Another assumption implicitly inbuilt in my study is that Finnish doctors have not drastically changed their prescription behavior after the reform. Namely, they did not start to prescribe more (or less) brand-name drugs after the reform. The estimates on markup differential would be positively biased if this is not the case.[51] This is not completely feasible as doctors might receive perks from the pharmaceutical companies for prescribing certain drugs.[52]

[49] I assume that brand-name producers have been aware that pharmacists earn more on selling their drugs and that law obliges pharmacists to substitute. Therefore, it is unlikely that brand-name companies provided discounts.

[50] This might be not an innocuous assumption from the pharmacologic point of view, for example, due to differences in excipients (Strom, 1987).

[51] For example, if doctors started to prescribe more branded-drugs in response to substitution, the average markup differential would increase and pharmacists on average might be more likely to substitute.

[52] Such practice is commonly known as *detailing*.

However, since doctors are allowed to forbid substitution, I expect physicians who were to lose most perks due to the substitution actively forbade it. My data allows me to observe if a doctor forbade substitution[53] and excluding such observations tackles this issue too. Moreover, the results do not drastically change if I include doctor level fixed effects to the regressions.[54]

Finally, note that I cannot perfectly observe actions on the side of pharmacists, i.e., whether they recommended the substitution or not. Hence, my main outcome variable is the unconditional probability of substitution. In my setting the ideal outcome variables would be two of its constituents: the actual probability of pharmacists to recommend the substitution and patients' probability of accepting substitution conditional on receiving a recommendation. Telling apart these probabilities, given my dataset, might be possible using a bivariate probit model, which is on my future research agenda.

5 Data

5.1 Data Sources and Main Variables

I use three data sets in my empirical analysis. The main data comes from a proprietary prescription registry collected by KELA. I supplement the prescription registry with two publicly available datasets: the aforementioned lists of substitutable drugs from KELA and the lists of approved and potentially substitutable drugs prepared by FIMEA.[55] My sample period is from April 1, 2003 to December 31, 2006, that is, about 3.5 years immediately following the reform implementation. I also use the data from the period preceding the reform, starting from January 1, 2002, in order to construct some control variables. The full data at my disposal contains 59 different molecules and covers the period until December 31, 2013. However, I decided to focus on the popular[56] antidepressant drugs (see Figure A.3 in Appendix A for the consumption dynamics of these medicines). There are 2 selective serotonine reuptake inhibitor (SSRI) molecules in my sample: fluoxetine and citalopram and one atypical antidepressant – mirtazapine. I chose these drugs for several reasons: first, there is steadily growing demand in terms of daily doses throughout my sample period (see Panel (b) of Figure A.3 in Appendix A.1) which leads to a large number of observations; second, the presence of both substitutable and non-substitutable drugs among these drugs; third, active entry and exit of companies in these markets. Antidepressants are also a creative and unconventional choice as compared to other studies analysing prescription drugs. [57]

The main variables from the KELA registry could be divided into several main categories listed below.

Drug Specific: drug identifier (VNR code);[58] active ingredient identifier (Anatomical Therapeutic Chemical – ATC code);[59] retail prices of prescribed and dispensed drugs and the dates these prices went into force; producer; pharmacy identification number; dates of purchase and prescription: the number of packages; the number of defined daily doses; the total cost of the purchase; reimbursement and extra reimbursement amounts covered by KELA in cents.

[53]This information is recorded in the "reason for declining substitution" variable.

[54]These results are available upon a request.

[55]FIMEA lists are available here: `http://www.fimea.fi/laakehaut_ja_luettelot/laakevaihto/keskenaan-vaihtokelpoisten-valmisteiden-luettelo`

[56]For instance, one of the drugs from my sample, namely, Cipramil was the most popular drug sold in Finland in 2001 `https://yle.fi/uutiset/3-5101671`

[57]Typically antiulcer, anticholesterol and antihypertension drugs are analysed in the literature, see, for example, Coscelli (2000), Saxell (2014), Sæthre (2016). Dickstein (2018) is one of the rare works focusing on antidepressants.

[58]Nordic article number or *(Pohjoismainen tuotenumero - VNR)*, 6 digit unique identifier for each drug package - Nordic equivalent of U.S. national drug code – NDC (`http://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm`).

[59]The World Health Organization definition of the ATC nomenclature can be found here: `https://www.whocc.no/atc/structure_and_principles/`

Patient Specific: patient ID; dates of birth and death; gender; hospital district identification code; reimbursement eligibility category; in some cases, when the substitution did not take place – the reason why it was declined; diagnosis in cases when the patient belongs to the special reimbursement eligibility category.

Doctor Specific: prescribing doctor ID;[60] specializations and years of practice between the date of prescription and the date of receiving specialization.

I collect some additional *drug specific information* from KELA and FIMEA lists, namely: prescribed and dispensed drugs' strength, form, package size and trade name; substitution group ID; the "price corridor" status (i.e., if the drug is marked by the asterisk in a given quarter); drug price as listed by KELA and the minimal drug price in each substitution group.

5.2 Descriptive Statistics

The main variables are summarized in Table 3 below. In the first two panels of Table 3 the key variables are tabulated according to the prescribed drug type: the originator brand-name drugs and the generics. 29.8% of the prescriptions in my sample were made for branded drugs and 60% of them were successfully substituted. The average markup difference between the prescribed drug and its cheapest substitute in this group is about EUR 13.42, with a standard deviation of EUR 10, ranging from 15 cents to almost EUR 130. The OOP difference for branded drugs in my sample is even larger, EUR 19.44 on average. The mean rate of substitution of generics was 12.8%. The markup difference in this group is over 10 times lower than that for branded drugs (EUR 1.24, with a standard deviation of EUR 1.68.) The OOP cost difference is also considerably lower (EUR 1.55).

Table 3: Summary statistics of the antidepressant sample

Variable	Mean	Std. Dev.	Min	Max	N
Only Originator brand-name Drug Prescription Purchases					
Substituted	0.600	0.490	0.000	1.000	439538
ΔMarkup: Rx and Cheapest Drug	13.416	10.000	0.154	129.786	439538
Δ OOP: Prescr. and Cheapest Drug	19.435	20.642	0.000	197.800	439538
Only Generic Prescription Purchases					
Substituted	0.128	0.334	0.000	1.000	1034615
ΔMarkup: Rx and Cheapest Drug	1.242	1.683	0.154	55.44	1034615
Δ OOP: Prescr. and Cheapest Drug	1.550	3.162	0.000	87.320	1034615
All Purchases					
Substituted	0.269	0.443	0.000	1.000	1474153
Δ Markup: Prescr. and Cheapest Drug	4.872	7.926	0.154	129.786	1474153
Δ OOP: Prescr. and Cheapest Drug	6.883	14.177	0.000	197.800	1474153
Orig. Brand Prescr.	0.298	0.457	0.000	1.000	1474153
Orig. Brand Prescr. × Δ Mark-Up	4.000	8.215	0.000	129.786	1474153
Orig. Brand Prescr. × Δ OOP	5.795	14.356	0.000	197.800	1474153
Age	53.555	18.515	0.167	104.912	1474153
$\log Age$	3.912	0.389	-1.790	4.653	1474153
$(\log Age)^2$	15.454	2.940	0.781	21.652	1474153
Female	0.652	0.476	0.000	1.000	1474153
Specialized Doctor's Prescription	0.681	0.466	0.000	1.000	1474153
Always Same Pharmacy	0.360	0.480	0.000	1.000	1474153
Cumulative % of Non Brand Purchases	0.578	0.411	0.000	1.000	1474152
% of Non-Orig. Prescr. Before Reform	0.306	0.438	0.000	1.000	849173

[1] *Notes:* Table reports summary statistics for the sample obtained from KELA prescription registry. It covers fluoxetine, citalopram and mirtazapine purchases made in Finland in years 2003 – 2006.

The average probability of substitution is 26.9% for both groups of drugs together. The

[60] Doctor licence number – *Fin.* SV-numero.

markup difference between the prescribed drug and its cheapest substitute is EUR 4.87, and the OOP cost differential is over EUR 6.88. The average age of a patient is over 53.5 years old with a standard deviation 18.52. Over 65% of purchases in my sample are made by women. Specialized doctors wrote 68.1% of prescriptions in the sample (mostly specialized in general medicine and psychiatry). Notably, 36% of purchases were made by patients who filled all their prescriptions in the same pharmacy during sample period.

The total number of substitution groups (i.e., active ingredients in a certain form and strength packed in a certain package size) included in my sample varies from 11 in 2003 to 18 in 2006. Some substitution groups were added and some removed, resulting in the net increase in the number of substitution groups during 3.5 years. Citalopram 20 mg in 100 tablet packages was the most popular medicine throughout the observation period. I plot its price dynamics in Figure A.4 in Appendix A. The most instances of substitution occurred in case of citalopram 10 mg, 100 tablets in 2003 and 2004, citalopram 30 mg 100 tablets in 2005 and mirtazapine 30 mg 30 tablets in 2006. Overall, the probability of substitution markedly decreases in 2006. It was well below 20% in most substitution groups in this year. This might be explained by the exit of Cipramil – the branded version of citalopram. Most of the substitution instances – around 50% of all cases in my sample – are taking place between Cipramil and its authorized generic Sepram. Cipramil was withdrawn from Finnish market in mid-2006. Its producer, Lunbeck, subsequently introduced escitalopram, marketed in Finland under the brand-name Cipralex in mid-2004.

Figure A.5 in the Appendix presents some dynamics of the total costs of generic and brand-name drugs from the sample, as well as the real and potential savings from substitution. It is evident from the figure that the total cost of branded drugs dramatically decreased from over 8 millions euros per year in 2003 to 4 millions in 2005, while total costs of generics were increasing. The real savings on the plot are calculated as the difference between the total costs of prescribed and dispensed drugs. Potential savings are defined as the difference between the costs of prescribed drugs and their cheapest available alternatives. The potential savings from substitution among generics are growing, whereas the real savings remain flat. Combined with an increasing share of generics in prescriptions, this suggests that more expensive generics are being prescribed and dispensed. The real and potential savings from branded drug substitution are decreasing as their share in prescription and prices decrease.

6 Results

6.1 Main Results

My main goal is to disentangle how pharmacists' monetary incentives affect the probability of successful substitution. The results of the full model including control variables and fixed effects are presented in Table 4. The first column contains the results with the full set of control variables but no fixed effects. I add biweekly fixed effects in the next column, followed by the model including biweekly-substitution group level fixed effects. Column 4 contains the results of a regression including also pharmacy fixed effects and column 5 presents the results of the main model from equation (1) with the full set of controls, as well as the pharmacy and biweekly $\times$ substitution group level fixed effects.

Consistent with results from the basic specifications (Table 8 in Appendix B) the substitution probability is positively related to the markup difference for the generic and negatively for the brand-name drugs. The magnitude of coefficients on the main explanatory variables increases upon introducing controls. Estimates from column 5, the full model, suggest that each additional euro of the markup differential for the originator drugs decreases the probability of substitution by over 5 percentage points. The effect for the non-originator drug is reverse: each additional euro of markup difference increases the chances of substitution by 3.4 percentage

points. One standard deviation or a 10 euros increase in the markup differential for branded drugs decreases the probability of substitution by over 1 standard deviation or 51 percentage points. If these estimates are taken at face value they imply that should the average markup differential on branded drugs increase by slightly less than 10 euros the chance of substitution is zero. The positive effect of the generic drug markup differential on substitution is smaller, translating into 17 percentage points increase in the likelihood of substitution for every standard deviation or about 1.7 euro increase in the generic markup differential. This is also a sizeable effect, considering that the baseline probability of substitution for generics is 12.8%. Two point estimates on the markup differential and the interaction term together imply that for each euro increase in the markup differential the probability of substitution decreases by 1.7 percentage points. I also report the *p-value* from the *t-test* of the sum of the coefficients on the markup differential and its interaction term confirming that their sum is significantly different from zero.

Table 4: Pharmacy Markups and Probability of Successful Generic Substitution: Linear Probability Model Estimates With Fixed Effects

	(1)	(2)	(3)	(4)	(5)	(6)
Δ Markup: Prescr. and Cheapest Drug	0.019***	0.021***	0.020***	0.020***	0.034***	0.036***
	(0.001)	(0.000)	(0.000)	(0.000)	(0.005)	(0.005)
Orig. Brand Prescr. $\times$ Δ Markup	-0.031***	-0.034***	-0.036***	-0.036***	-0.051***	-0.053***
	(0.001)	(0.001)	(0.001)	(0.000)	(0.005)	(0.005)
Δ OOP: Prescr. and Cheapest Drug	0.006***	0.006***	0.006***	0.006***	0.006***	0.005***
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Orig. Brand Prescr.	0.598***	0.589***	0.669***	0.666***	0.707***	0.732***
	(0.004)	(0.004)	(0.004)	(0.004)	(0.018)	(0.014)
log *Age*	0.362***	0.336***	0.305***	0.265***	0.267***	0.240***
	(0.029)	(0.028)	(0.027)	(0.024)	(0.020)	(0.024)
$(\log Age)^2$	-0.052***	-0.049***	-0.045***	-0.038***	-0.039***	-0.034***
	(0.004)	(0.004)	(0.004)	(0.003)	(0.003)	(0.003)
Female	-0.004***	-0.008***	-0.009***	-0.011***	-0.010***	-0.011***
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)
Specialized Doctor's Prescription	-0.013***	-0.014***	-0.013***	-0.015***	-0.015***	-0.016***
	(0.002)	(0.002)	(0.002)	(0.001)	(0.001)	(0.001)
Always Same Pharmacy	-0.007***	-0.007***	-0.004**	0.003*	0.002*	-0.011***
	(0.002)	(0.002)	(0.002)	(0.001)	(0.001)	(0.001)
Cumulative % of Non-Orig. Purchases	0.072***	0.064***	0.062***	0.063***	0.062***	
	(0.002)	(0.002)	(0.002)	(0.002)	(0.003)	
Patient % of Non-Orig. Prescr. Before Reform						0.056***
						(0.003)
Constant	-0.551***	-0.484***	-0.546***			
	(0.052)	(0.050)	(0.050)			
Subst. Group FE			×	×	×	×
Biweekly FE		×	×	×	×	×
Biweekly FE $\times$ Subst. Group FE					×	×
Pharmacy FE				×	×	×
Mean dep. variable	0.269	0.269	0.269	0.269	0.269	0.294
Observations	1474152	1474152	1474152	1474152	1474150	849169
R-squared	0.274	0.290	0.308	0.320	0.338	0.365

[1] *Notes:* This table reports the OLS regression estimates of f the effect of markup and OOP cost differentials between the prescribed drug and its cheapest available substitute on the probability of successful generic substitution in a pharmacy – $\mathbb{P}[Subst. = 1|Possible]$. Each specification includes a full set of controls and multiple fixed effects. The sample includes fluoxetine, citalopram and mirtazapine purchases made in Finland in years 2003 – 2006. Standard errors clustered at the pharmacy level are reported in parentheses. $^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$.

The coefficient on the OOP cost differential is positive, which means that the increase in the difference in out of pocket costs between the prescribed and the cheapest available drug option increases the likelihood of accepting the substitution. The point estimates suggest that each euro in potential copay difference between prescribed drug and its cheapest substitute increases the chances of accepting the substitution by 0.6 percentage points.[61] The results imply that increasing the OOP cost savings by one standard deviation or about 14 euros would increase

[61] The interaction term of OOP cost with the branded drug dummy is not included in the estimation, due to

the probability of substitution by 19 percentage points. Consistent with my initial hypotheses, branded drugs are more likely to be substituted. The positive effect of the markup differential on substitution among generics might potentially be explained by the negative correlation between markups on these drugs and discounts. I explore this idea further in a robustness check, where I exclude from the sample the periods, when discounts were allowed.

Regarding other explanatory variables that influence the probability of substitution, females are less likely to accept the substitution, which is implied by -0.010 coefficient on the female dummy variable reported in column 5 of Table 4. The relation between the age and the probability of substitution is an inverted-U, meaning that the probability of substitution increases with age until about 33 years, implying each year of age increases the probability of substitution by about 3 pp. Thereafter the chances of substitution decrease. However the magnitude of the coefficient is relatively small – 0.038. I conclude that there is no clear relationship between age and probability of substitution for people over 33. If a drug was prescribed by a specialized doctor it is 1.5 percentage points less likely to be substituted and the relationship is robust across specifications.

It might be plausible that patients who do not shop around and change their pharmacy might also be conservative in their drug choices. However, there is no clear evidence that patients who fill all their prescriptions in the same pharmacy are less likely to substitute. The magnitudes of coefficients on this variable are relatively low and change signs across specifications, varying from -0.011 to 0.002. To control for the habit formation, I introduce the cumulative percentage of non-branded purchases made by a given patient until the current purchase instance i. The effect of this variable is modest but very robust – almost constant in every specification. The results imply that one percent increase in non-branded purchase counts increases the probability of substitution by 0.063%. In language of standardized coefficients, a standard deviation increase in cumulative generic purchases increases the likelihood of substitution by 0.05 standard deviations. In the last column of Table 4, instead of the cumulative sum of generic purchases, I include the total percentage of generic prescriptions received by a given patient in my sample in the period before generic substitution was enacted. The point estimate of 0.056 suggests that pre-reform exposure to generics increases the probability of substitution. To be able to calculate this variable I only include the patients which both had a sufficient number of purchases in the pre-reform period and also continued to get antidepressants in the period after. I have about 850,000 observations in this subsample. The point estimates on the main explanatory variables are similar but somewhat larger for this group. However, the baseline relationship of 1.7 percentage points lower probability of substitution with each euro increase in markups is unchanged. It is also noteworthy that in this subsample the likelihood of substitution of branded drugs is markedly higher – 0.732 as opposed to 0.707.

6.2 Robustness Checks

The main results are very robust to addition of controls and fixed effects. In Table 8 of Appendix B I report the results where I add the main explanatory variables one at a time to each consecutive specification without adding control variables and fixed effects. The results of the model, which includes all variables of interest, are reported in column 5 of Table 8. They suggests that the probability of substitution decreases by 1.3 percentage points with every euro increase in markup differential. Higher OOP costs are associated with a higher likelihood of substitution, translating into 0.6 percentage points increase in substitution with each euro of increase in savings. This point estimate is identical to those reported in Table 4.

As discussed in detail in Subsection 4.4, substitution and markups are likely jointly determined. To account for the possible price adjustments induced by the substitution, I focus on

the multicollinearity with the markup interaction term. I report the results of fully interacted models in Table 9, Appendix B instead.

a subsample of the data, which includes only observations from the periods and substitution groups, where prices were not updated. I report the results of regressions based on this subsample in Table 5. Although this approach does not eliminate the bias in estimates stemming from endogeneity, it removes the variation in substitution due to the immediate reaction of pharmacists to price shifts within certain substitution groups.

Table 5: Pharmacy Markups and Probability of Successful Generic Substitution: Sample Excluding the Substitution Groups in Periods When Any Price Changed

	(1)	(2)	(3)	(4)	(5)	(6)
Δ Markup: Prescr. and Cheapest Drug	0.010***	0.013***	0.012***	0.012***	0.029***	0.033***
	(0.000)	(0.000)	(0.000)	(0.000)	(0.007)	(0.008)
Orig. Brand Prescr. × Δ Markup	-0.022***	-0.026***	-0.027***	-0.027***	-0.046***	-0.051***
	(0.000)	(0.000)	(0.000)	(0.000)	(0.008)	(0.008)
Δ OOP: Prescr. and Cheapest Drug	0.006***	0.006***	0.006***	0.006***	0.006***	0.005***
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Orig. Brand Prescr.	0.588***	0.588***	0.676***	0.672***	0.714***	0.745***
	(0.004)	(0.004)	(0.004)	(0.004)	(0.022)	(0.016)
$\log Age$	0.367***	0.330***	0.300***	0.266***	0.266***	0.215***
	(0.027)	(0.026)	(0.025)	(0.023)	(0.023)	(0.030)
$(\log Age)^2$	-0.053***	-0.048***	-0.043***	-0.038***	-0.038***	-0.031***
	(0.004)	(0.004)	(0.004)	(0.003)	(0.003)	(0.004)
Female	-0.004***	-0.006***	-0.009***	-0.010***	-0.009***	-0.011***
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)
Specialized Doctor's Prescription	-0.014***	-0.015***	-0.014***	-0.016***	-0.016***	-0.017***
	(0.002)	(0.002)	(0.002)	(0.001)	(0.001)	(0.001)
Always Same Pharmacy	-0.006***	-0.006***	-0.002	0.004**	0.003**	-0.009***
	(0.002)	(0.002)	(0.002)	(0.001)	(0.002)	(0.001)
Cumulative % of Non-Orig. Purchases	0.069***	0.063***	0.059***	0.060***	0.059***	
	(0.002)	(0.002)	(0.002)	(0.002)	(0.003)	
Patient % of Non-Orig. Prescr. Before Reform						0.053***
						(0.004)
Constant	-0.568***	-0.496***	-0.566***			
	(0.048)	(0.047)	(0.047)			
Subst. Group FE			×	×	×	×
Biweekly FE		×	×	×	×	×
Biweekly FE × Subst. Group FE					×	×
Pharmacy FE				×	×	×
Mean dep. variable	0.256	0.256	0.256	0.256	0.256	0.280
Observations	967198	967198	967198	967198	967183	547189
R-squared	0.298	0.316	0.337	0.348	0.365	0.395

[1] *Notes:* This table reports the OLS regression estimates of the effect of markup and OOP cost differentials between the prescribed drug and its cheapest available substitute on the probability of successful generic substitution in a pharmacy – $\mathbb{P}[Subst. = 1|Possible]$. Each specification includes a full set of controls and multiple fixed effects. The sample includes purchases of antidepressant drugs in Finland from substitution groups, in which there was no price update within any biweekly period between 2003 and 2006. Standard errors clustered at the pharmacy level are reported in parentheses. $^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$.

The results are comparable to those obtained using the entire sample, although the magnitude of the markup differential coefficients are somewhat lower in the first four specifications. However, here I also find 1.5 – 1.7 percentage points decreases in the probability of substitution for every euro increase of markup differential between the prescribed drug and its cheapest substitute. The coefficients on OOP costs do no vary across specifications and are identical to those reported in Table 4, translating in 0.6 percentage points of increase in substitution for every euro saved. Remarkably, all other coefficients, including those on age and the female dummy, are also virtually identical to those estimated from the full sample (note, that the magnitude of the coefficients on cumulative generic drug purchases is consistently lower in this subsample).

These results imply that pharmacists might not be very responsive in their substitution decisions to the immediate fluctuations in prices. This approach allows, at least somehow, to account for the simultaneous shifts in markups and substitution. Instrumenting markup differentials with price differentials of same drugs from Germany and/or Sweden (Hausman type

instruments) is on my future research agenda.

Another threat to the internal validity of my analysis is possible measurement error in the markup differentials between the prescribed drug and its cheapest available substitute. Before 2006, pharmaceutical producers (via wholesalers) were allowed to give pharmacies discounts, which I do not observe. In 2006 it became illegal to provide discounts on prescription drugs to pharmacies. Therefore, as a robustness check, I estimate my regression model using only observations from 2006. The results from these regressions differ from those from the full sample and are reported in Table 6.

Table 6: Pharmacy Markups and Probability of Successful Generic Substitution: No Discounts

	(1)	(2)	(3)	(4)	(5)	(6)
Δ Markup: Prescr. and Cheapest Drug	-0.001***	0.000	-0.004***	-0.004***	-0.002	0.002
	(0.001)	(0.001)	(0.001)	(0.001)	(0.006)	(0.004)
Orig. Brand Prescr. $\times$ Δ Markup	-0.005***	-0.007***	-0.005***	-0.005***	-0.008	-0.012***
	(0.001)	(0.001)	(0.001)	(0.001)	(0.006)	(0.004)
Δ OOP: Prescr. and Cheapest Drug	0.006***	0.006***	0.005***	0.005***	0.005***	0.004***
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Orig. Brand Prescr.	0.182***	0.193***	0.169***	0.175***	0.209***	0.208***
	(0.004)	(0.005)	(0.007)	(0.007)	(0.032)	(0.025)
$\log Age$	0.531***	0.538***	0.475***	0.425***	0.427***	0.283***
	(0.031)	(0.031)	(0.030)	(0.027)	(0.028)	(0.051)
$(\log Age)^2$	-0.076***	-0.077***	-0.069***	-0.061***	-0.062***	-0.043***
	(0.004)	(0.004)	(0.004)	(0.004)	(0.004)	(0.007)
Female	-0.017***	-0.017***	-0.006***	-0.008***	-0.008***	-0.007***
	(0.002)	(0.002)	(0.002)	(0.002)	(0.001)	(0.002)
Specialized Doctor's Prescription	-0.009***	-0.008***	-0.009***	-0.012***	-0.012***	-0.014***
	(0.002)	(0.002)	(0.002)	(0.002)	(0.001)	(0.002)
Always Same Pharmacy	0.002	0.001	-0.004*	0.003*	0.003**	-0.006***
	(0.002)	(0.002)	(0.002)	(0.002)	(0.001)	(0.002)
Cumulative % of Non-Orig. Purchases	0.020***	0.022***	0.029***	0.029***	0.030***	
	(0.002)	(0.002)	(0.002)	(0.002)	(0.003)	
Patient % of Non-Orig. Prescr. Before Reform						0.029***
						(0.003)
Constant	-0.783***	-0.828***	-0.687			
Only year 2006	$\times$	$\times$	$\times$	$\times$	$\times$	$\times$
Subst. Group FE			$\times$	$\times$	$\times$	$\times$
Biweekly FE		$\times$	$\times$	$\times$	$\times$	$\times$
Biweekly FE $\times$ Subst. Group FE					$\times$	$\times$
Pharmacy FE				$\times$	$\times$	$\times$
Mean dep. variable	0.162	0.162	0.162	0.162	0.162	0.144
Observations	519566	519566	519566	519566	519566	232562
R-squared	0.055	0.060	0.085	0.104	0.113	0.117

[1] *Notes:* This table reports the OLS regression estimates of the f the effect of markup and OOP cost differentials between the prescribed drug and its cheapest available substitute on the probability of successful generic substitution in a pharmacy – $\mathbb{P}[Subst. = 1|Possible]$. Each specification includes a full set of controls and multiple fixed effects. The sample includes fluoxetine, citalopram and mirtazapine purchases in Finland, made in year 2006, when discounts offered by wholesalers to pharmacists became prohibited by law. Standard errors clustered at the pharmacy level are reported in parentheses. $^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$.

The probability of substitution is over 10% lower in 2006: 16.2% compared to 26.9% in the full sample. The fraction of brand-name drug prescriptions decreased drastically in 2006 compared to the overall sample (see column 4 of Table 9). This implies that doctors did change their behaviour in response to substitution. The coefficient on the branded prescription dummy variable changes from about 0.7 as reported in columns (3) to (6) of Table 4 to 0.2 in the identical columns of Table 6. Notably, the coefficient on the markup differential for generic drugs becomes negative (or zero) in all specifications. I interpret this as an evidence that generic companies indeed were giving pharmacies discounts in order to boost their sales. Once discounts became illegal pharmacies also started to substitute cheaper generics for pricier ones. The coefficient on the branded drug markup differential remains negative and significant in this subsample. However, its magnitude decreases, implying 0.5 percentage points decrease in the probability of

substitution for every euro of forgone markups. I conclude that the markup differential decreases the probability of substitution for branded drugs even if the confounding effect of discounts is ruled out. The OOP cost differential is significant, almost constant throughout all specifications reported in Table 6 and virtually identical to the overall effect reported Table 4. Thus, patients' cost savings have a small but very robust effect on substitution.

As for the controls, the inverted U-relationship between age and the probability of substitution remains. In 2006 it increases with age only up to 30 years and henceforth begins to decrease. As in the overall sample, females are less likely to substitute. This effect is more pronounced in the first two specifications reported in Table 6. Prescriptions from specialized doctors are less likely to be substituted in 2006, but the effect is lower in magnitude. There is still no clear relationship between consistently buying drugs in the same pharmacy and substitution, and exposure to generics over time increases the chance of substitution.

More work needs to be done to pin down the role of producer discounts in generic substitution implementation in Finland; my analysis is only the first step in this direction.

7 Conclusion

I contribute to the scarce body of economic literature analysing pharmacies. I evaluate the role pharmacists' profits played in the implementation of the generic substitution policy in Finland. The policy was introduced in a way that created conflicting incentives for Finnish pharmacists. On the one hand, they are legally obliged to offer cheaper substitutes to patients in cases doctors prescribe expensive medications. On the other hand, they forgo profits when patients accept cheaper substitutes, as the fixed percentage markup schedule set by another regulation implies strictly higher markups on more expensive drugs. Offering cheaper alternatives to the prescribed drugs is costly for pharmacists because they need to spend time and effort to talk patients into switching between the medicines. Pharmacists also have to keep larger drug assortments in stock. Plausibly, the more effort pharmacists spend recommending substitution the more likely it is to take place. At the same time, a high rate of substitution implies that more profits are lost, as more expensive drugs are more profitable for pharmacists. Essentially, the features of the pharmaceutical regulations imply that integrity comes to Finnish pharmacists with extra costs. I test how the extra costs of substitution borne by Finnish pharmacists affect its probability using a unique large prescription level data set collected by the Finnish National Insurance Institution. The data allows me to directly observe substitution and reverse engineer pharmacy markups as well as patients' OOP costs at the transaction level. I approximate the financial disincentive for substitution on the pharmacists' side by the difference in markups between the prescribed drug and its cheapest available substitute. I include the OOP cost differential in the same linear probability model to account for patients monetary incentives to accept substitution.

I find that every additional euro of the markup differential decreases the likelihood of substitution by 1.7 percentage points. As expected, the main effect is coming from more expensive originator brand-name drugs. Specifically, in case of the brand-name drug prescription, each additional euro of lost markups is translated into over 5 percentage points decrease in substitution. Markups on generic drugs seem to have the opposite effect on the probability of substitution, which increases by 3.5 percentage points with every euro of markup differential. This positive effect might be driven by the unobservable discounts, which pharmacists received from producers. I also find that the patients OOP costs are positively related to the probability of substitution. Each euro savings in out of pocket costs arising from substitution increases its probability by 0.6 percentage points. Markups and substitution are endogenously related. However, my results survive multiple robustness checks, which might imply that I am capturing a causal effect. Addressing the simultaneity of markups and substitution more rigorously using instrumental variable approach is on my research agenda.

Brekke et al. (2013) were the first to note that having a fixed percentage markup schedule

would hurt generic substitution and more broadly decrease the market share of generics. My analysis provides solid empirical evidence in favour of their argument. The goal of generic substitution policy is to trickle into the pool of patients who are valuing branded drugs highly, are less price sensitive or are not used to generics and induce the change in their preferences. If pharmacists manage to persuade such patients to accept the substitution and patients verify that generic drugs work as well as branded, they are likely to continue to use generics. Ideally, this would secure long term cost savings both to patients and national health insurance. I find evidence that Finnish pharmaceutical market regulations per se might have failed to accomplish the main goal of the substitution policy. Pharmacists have a clear disincentive to convince patients to opt for generics in Finland. In many cases generics were substituted for generics and overall pharmacists tend to substitute prescribed drugs when the forgone profits are lower. It is evident that the policy makers should take the incentives of the main agents of the reforms into account while drafting them. In 2009 reference the pricing regulation[62] has been introduced in Finland tying the patient copays to prices of generics. In the future, I plan to test if reference pricing exacerbated the negative effect of branded markup differential on substitution.

[62]Law Amending the National Health Insurance Act: `https://www.finlex.fi/fi/laki/alkup/2008/20080802`

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Appendices

Appendix A: Finnish Pharmaceutical Market Statistics and Regulations

I collect the drug related expenditure data from Finnish Statistics on Medicines almanacs,[63] Annual reviews of Finnish Pharmacies Association and data provided by National Institute for Health and Welfare[64] in years 2002 – 2016. The expenditures figures are based on the total wholesale values of supplied (not necessarily dispensed) medicines, including the medicines dispensed in hospitals. Finnish pharmacy personnel statistics is collected from the Annual reviews of Finnish Pharmacies Association, 2002 – 2016 editions.[65]

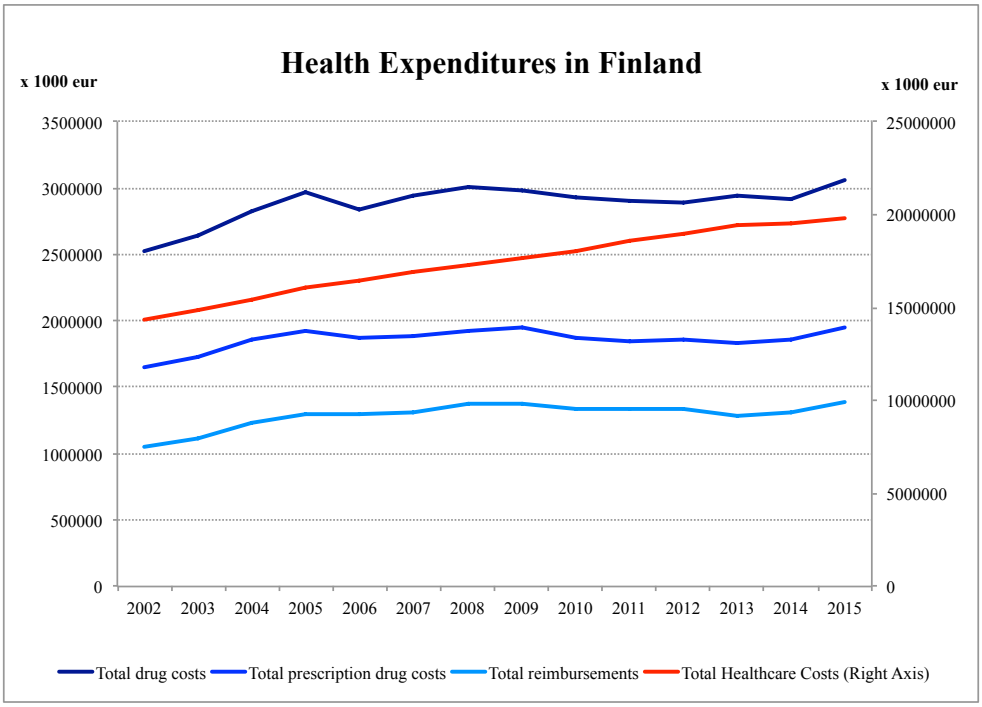
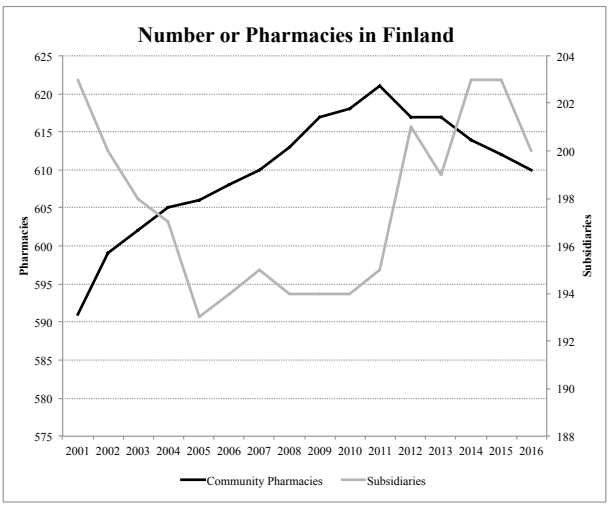
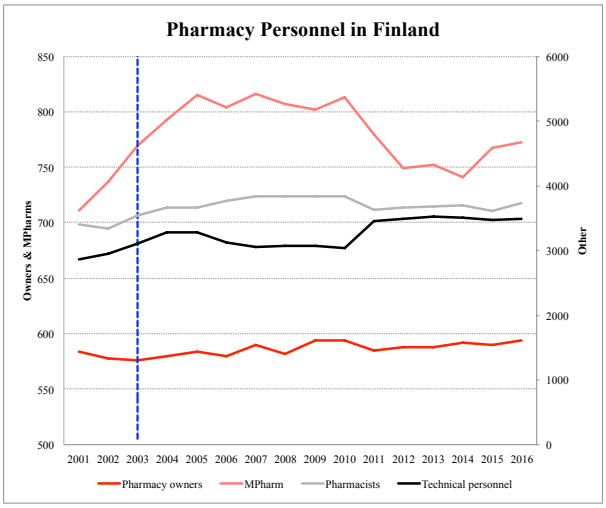


Figure A.1: Pharmaceutical Expenditures in Finland in 2002 – 2015 (in 2016 euros)

[63] *Fin.:* Suomen Lääketilasto (SLT): `https://www.kela.fi/tilastojulkaisut_suomen-laaketilasto.`
[64] `https://thl.fi/en/web/thlfi-en/statisticshttps://thl.fi/en/web/thlfi-en/statistics`
[65] `http://www.apteekkariliitto.fi/liitto/vuosikatsaukset.html`

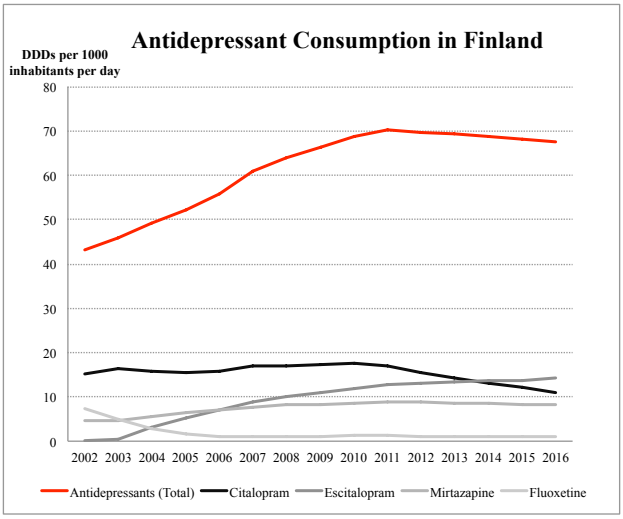


(a) Numbers of Pharmacies in 2001 – 2016

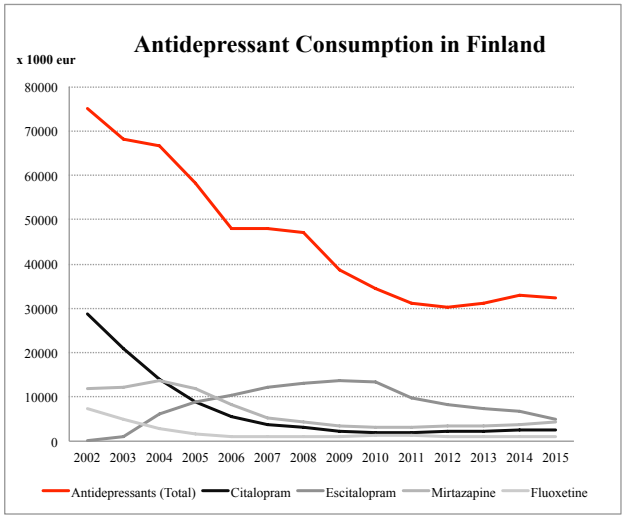


(b) Pharmacy Personnel in 2001 – 2016

Figure A.2: Finnish Pharmacy Market Dynamics



(a) Consumption in 2002 – 2016



(b) Expenditures in 2002 – 2016 (in 2016 euros)

Figure A.3: Antidepressant Consumption and Expenditures in Finland in 2002 – 2016

Sub. group	VNR	Sub. group code	Retail price + VAT, EUR	Drug name	Strength	Pack. size	Form	Producer	Active ingredient
000384	012342	0003840030	10.16	*CITALOPRAM GENERICS	20 mg	30	tablet, film coated	NM Pharma AB	Citalopram
000384	009419	0003840030	10.61	*CITALOPRAM-RATIOPHARM	20 mg	30	tablet, film coated	Ratiopharm GmbH	Citalopram
000384	008098	0003840030	11.19	*CITALOPRAM ALPHARMA	20 mg	28	tablet, film coated	Alpharma A/S	Citalopram
000384	011501	0003840030	11.25	*EMOCAL	20 mg	28	tablet, film coated	Hexal A/S	Citalopram
000384	010298	0003840030	12.19	SEPRAM	20 mg	28	tablet, film coated	H. Lundbeck A/S	Citalopram
000384	008964	0003840030	13.01	CITALOPRAM SANDOZ	20 mg	30	tablet, film coated	Sandoz GmbH	Citalopram
000384	159632	0003840030	40.22	CIPRAMIL	20 mg	28	tablet, film coated	H. Lundbeck A/S	Citalopram
		0003840030 Min	10.16						
000384	010439	0003840056	20.06	*SEPRAM	20 mg	56	tablet, film coated	H. Lundbeck A/S	Citalopram
000384	159517	0003840056	75.48	CIPRAMIL	20 mg	56	tablet, film coated	H. Lundbeck A/S	Citalopram
		0003840056 Min	20.06						
000384	012353	0003840100	23.99	*CITALOPRAM GENERICS	20 mg	100	tablet, film coated	NM Pharma AB	Citalopram
000384	009395	0003840100	24.89	*CITALOPRAM-RATIOPHARM	20 mg	100	tablet, film coated	Ratiopharm GmbH	Citalopram
000384	008072	0003840100	26.20	CITALOPRAM ALPHARMA	20 mg	98	tablet, film coated	Alpharma A/S	Citalopram
000384	008942	0003840100	26.49	CITALOPRAM SANDOZ	20 mg	100 × 1	tablet, film coated	Sandoz GmbH	Citalopram
000384	011523	0003840100	26.49	EMOCAL	20 mg	98	tablet, film coated	Hexal A/S	Citalopram
000384	010603	0003840100	28.47	SEPRAM	20 mg	98	tablet, film coated	H. Lundbeck A/S	Citalopram
000384	159194	0003840100	122.00	CIPRAMIL	20 mg	98	tablet, film coated	H. Lundbeck A/S	Citalopram
000384	468124	0003840100	122.00	CIPRAMIL	20 mg	100	tablet, film coated	H. Lundbeck A/S	Citalopram
		0003840100 Min	23.99						
000384	008962	0003840250	70.34	*CITALOPRAM SANDOZ	20 mg	250	tablet, film coated	Sandoz GmbH	Citalopram
		0003840250 Min	70.34						

Table 7: Excerpt from the KELA List of Substitutable Drugs, Quarterly Edition 1.07.2005–30.09.2005

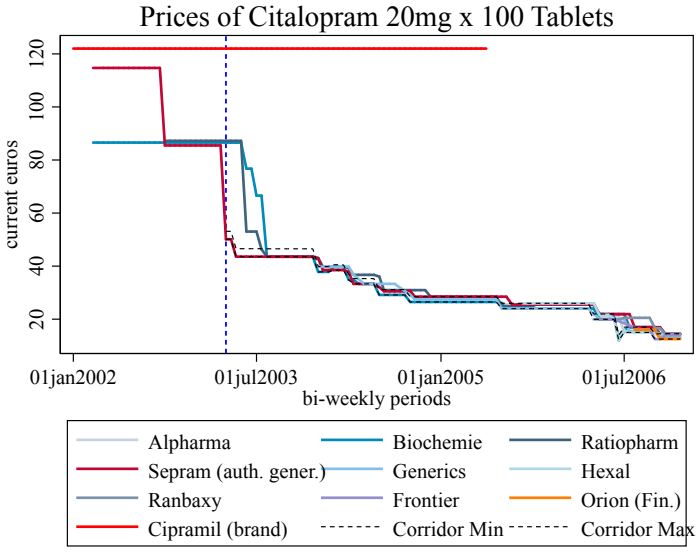


Figure A.4: Price Dynamics of Citalopram in 2003 – 2006

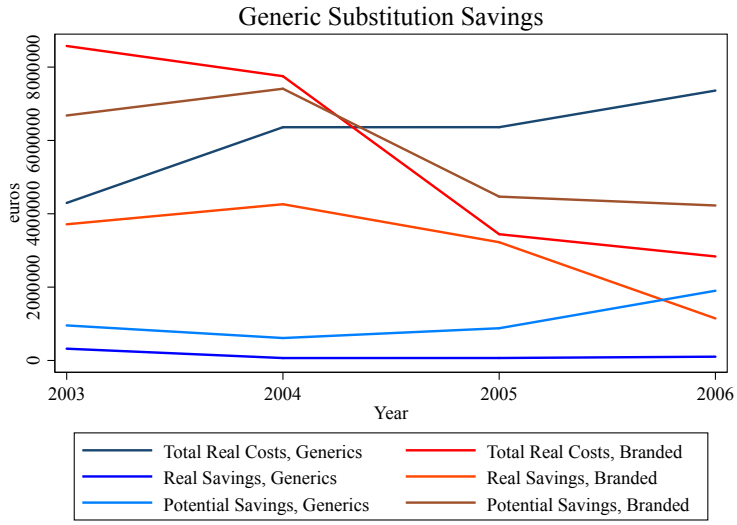


Figure A.5: Real and Potential Costs Savings from Substitution of citalopram, fluoxetine and mirtazapine in Finland in 2003 – 2006 (in current euros)

Appendix B: OOP Cost and Markup Calculation Examples

OOP Cost Calculation

Here is an example of the calculation of reimbursements and OOP costs of prescription drugs in Finnish context in period between 2003 and 2006. If the cost of a prescription (including 8% VAT and the flat pharmacy service fee EUR 0.42) was EUR 15 the patient from the basic eligibility category first had to cover EUR 5 copay (EUR 10 $\times$ 50%). In addition she pays 50% of the full cost of the prescription (according to her coinsurance), that is EUR 7.5 (EUR 15 $\times$ 50%). In sum, the total out of pocket cost is EUR 7.5 + 5 = 12.5 and the reimbursement then constitutes EUR 2.5.

Markup Calculation

As mentioned in Subsection 4.2 using the markup scheme from Table 2, prices and total per purchase cost information I back engineer the real and potential markups made by pharmacist on each purchase instance. For example, if the prescribed drug price is EUR 15 EUR, I first calculate its price excluding VAT $\frac{15}{1.08} = 13.89$, then I calculate the wholesale price as: $\frac{13.89-1.43}{1.4} = 8.90$ EUR. The markup pharmacist earns in this case is $\sim$ EUR 4.99. I then multiply the estimated markup by the number of packages acquired. Similar procedure can be applied to the any drug within each substitution group (including the cheapest).

Appendix C: Additional Regressions

Table 8: Pharmacy Markups and Probability of Successful Generic Substitution: Basic Linear Probability Model Estimates

	(1)	(2)	(3)	(4)	(5)
Δ Markup: Prescr. and Cheapest Drug	0.017***	0.006***	-0.004***	-0.011***	0.018***
	(0.000)	(0.000)	(0.000)	(0.000)	(0.001)
Δ OOP: Prescr. and Cheapest Drug		0.009***		0.007***	0.006***
		(0.000)		(0.000)	(0.000)
Orig. Brand Prescr.			0.519***	0.494***	0.557***
			(0.004)	(0.004)	(0.004)
Orig. Brand Prescr. $\times$ Δ Mark-Up					-0.031***
					(0.001)
Constant	0.185***	0.180***	0.133***	0.132***	0.096***
	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)
Mean dep. variable	0.269	0.269	0.269	0.269	0.269
Observations	1474153	1474153	1474153	1474153	1474153
R-squared	0.094	0.130	0.240	0.260	0.269
H_0: Δ Markup+Orig. Brand$\times$ Δ Markup=0					
Wald test, *p-value*					0.000

[1] *Notes:* Table reports OLS regression estimates of the effect of markup and OOP cost differentials between the prescribed drug and its cheapest available substitute on $\mathbb{P}[Subst. = 1|Possible]$ – the probability of successful generic substitution in pharmacy. No control variables or fixed effects are added to the regressions. The sample includes fluoxetine, citalopram and mirtazapine purchases made in Finland in years 2003 – 2006. Standard errors clustered at the pharmacy level are reported in parentheses. $^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$.

Table 9: Substitution of Antidepressants in 2003 – 2006: Fully Interacted Models

	(1)	(2)	(3)	(4)
	Original Brand Prescriptions			
Δ Markup: Prescr. and Cheapest Drug	-0.013***	-0.018***	-0.018***	-0.013***
	(0.000)	(0.001)	(0.001)	(0.000)
Δ OOP: Prescr. and Cheapest Drug	0.006***	0.005***	0.005***	0.004***
	(0.000)	(0.000)	(0.000)	(0.000)
Mean dep. variable	0.650	0.681	0.776	0.302
N	439538	439523	289541	101912
R-squared	0.062	0.315	0.328	0.201
	Generic Prescriptions			
Δ Markup: Prescr. and Cheapest Drug	0.010***	0.024***	0.031***	0.002
	(0.001)	(0.003)	(0.003)	(0.004)
Δ OOP: Prescr. and Cheapest Drug	0.011***	0.012***	0.008***	0.006***
	(0.000)	(0.002)	(0.002)	(0.002)
Mean dep. variable	0.128	0.128	0.109	0.128
N	1034615	1034610	677627	417650
R-squared	0.022	0.089	0.078	0.076
Controls	×	×	×	×
Pharmacy FE	×	×	×	×
Biweekly FE × Subst. Group FE	×	×	×	×

[1] *Notes:* Table reports fully interacted OLS regressions' estimates of the effect of markup and OOP cost differentials between the prescribed drug and its cheapest available substitute on $\mathbb{P}[Subst. = 1|Possible]$ – the probability of successful generic substitution in pharmacy. The sample includes fluoxetine, citalopram and mirtazapine purchases made in Finland in years 2003 – 2006 in columns (1) – (3) and in year 2006 only in column (4). Standard errors clustered at the pharmacy level are reported in parentheses. $^{*}\ p < 0.10$, $^{**}\ p < 0.05$, $^{***}\ p < 0.01$.

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ISSN 2190-9938 (online)
ISBN 978-3-86304-306-3