# MANDATORY RESERVES SYSTEM AND THE PRICING OF PHARMACEUTICAL PRODUCTS IN FINLAND

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**Author: Youssef Zad**
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**Supervisors: Mika Haapanen & Petri Böckerman**

**ABSTRACT**

Author
Youssef Zad

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Abstract

The purpose of this thesis is to shed light on the mandatory reserves system of pharmaceutical products in the Finnish markets and to estimate its possible effects on pricing using microdata on pharmaceutical prices.

Mandatory reserves system was implemented to enforce pharmaceutical companies to store certain essential products in amounts that would ensure the availability of pharmaceutical products even if supply disruptions would occur. The initial legislation for mandatory reserves was enacted in 1984, but it has been adjusted multiple times since.

In 2009 new pharmaceutical products were introduced to the mandatory reserves system. Furthermore, in 2009 a reference pricing system was implemented almost simultaneously with the policy change of mandatory reserves system, which makes the estimation of the effects of mandatory reserves difficult.

The difference-in-differences estimation method is used to exploit the fact that some pharmaceutical products were introduced to the list of mandatory reserves, while others were not. Statistically significant results are found indicating that the prices of pharmaceutical products fell by approximately 2.6 percent when they were assigned to the system. The effects are significant only for products not assigned to the reference pricing system.

Key words
Pharmaceutical markets, Pricing, Mandatory Reserves System

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**TIIVISTELMÄ**

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Lääkkeiden velvoitevarastointijärjestelmä ja lääkkeiden hinnoittelu Suomessa

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Tiivistelmä

Tämän pro gradu -tutkielman tarkoituksena on valottaa lääkkeiden velvoitevarastointijärjestelmää ja estimoida sen mahdollisia vaikutuksia lääkkeiden hinnoitteluun.

Lääkkeiden velvoitevarastointijärjestelmän avulla lääkeyritykset velvoitetaan varastoimaan tiettyjä kansallisesti tärkeitä lääkeaineita sellaisina määrinä, ettei niiden saatavuus vaarantuisi toimitushäiriöiden aikana. Lääkkeiden velvoitevarastointijärjestelmä otettiin käyttöön vuonna 1984, mutta lainsäädäntöä on muutettu useaan otteeseen sen käyttöönoton jälkeen.

Vuonna 2009 velvoitevarastointijärjestelmän uudistuksen myötä lukuisia uusia lääkkeitä päätyi järjestelmän piiriin. Lisäksi vuoden 2009 aikana otettiin käyttöön lääkkeiden viitehintajärjestelmä melkein samanaikaisesti velvoitevarastointijärjestelmän muutosten kanssa, mikä tekee hintavaikutusten arvioinnista hankalaa.

Muutosten ero -mallin avulla hyödynnetään sitä, että vuoden 2009 lakimuutoksen aikana velvoitevarastointijärjestelmään päätyi useita uusia lääkkeitä ja useita lääkkeitä jäi järjestelmän ulkopuolelle. Velvoitevarastointiin päätyminen vaikuttaisi laskeneen lääkkeiden hintoja keskimäärin 2,6 prosenttia tilastollisesti merkitsevästi. Hintavaikutuksia havaitaan kuitenkin vain lääkkeillä, jotka eivät päätyneet viitehintajärjestelmään.

Asiasanat
Lääkemarkkinat, Hinnoittelu, Velvoitevarastointi

Säilytyspaikka
Jyväskylän yliopiston kirjasto

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# 1 INTRODUCTION

Having good health is in the very base of the Maslows' hierarchy of needs, which hypothesizes that people value health almost more than anything else. However, good health sometimes comes with a price, meaning we have to invest in ourselves to maintain health. Sometimes we face conditions, where we must seek medical aid to stay functional. Most commonly, there exist two ways to seek help; inpatient or outpatient care, and regularly both options include consuming pharmaceutical products. Having the option to consume pharmaceutical products, when needed, is regarded as one of the basic human needs in our modern western society.

Modern welfare societies have reached a consensus that everyone should have access to properly functioning primary healthcare, which requires support from the public sector. Organisation for Economic Co-operation and Development (OECD) countries spent USD 569 billion on pharmaceutical products in outpatient care in 2005. The spending on pharmaceuticals accounts for a significant share of total healthcare expenditures. The average spending on pharmaceutical products from the total health expenditures in the high-income countries was 19.7% in 2006 (Acosta, Ciapponi, Aaserud, Vietto, Austvoll-Dahlgren, Kösters, & Oxman, 2014). In Finland, the total spending on retail pharmaceutical products per capita in 2019 was USD 508, which is a little less than the OECD average of USD 564. (OECD, 2019.)

Although pharmaceutical usage might be costly to the public sector, it is still a favourable option to invest in pharmaceutical consumption for outpatient care than delaying treatments to inpatient care. Inpatient care is usually a much more expensive option compared to outpatient care.

The availability of drugs is a crucial part of a functioning healthcare system. Due to complicated supply chains and concentrated raw-material production, there have been increasing problems with the availability of drugs throughout the years. Drug shortages have been in the news lately, and multiple organizations around the world have recognized the phenomenon. The risks of significant supply problems and their severe costs are apparent, but there exist no easy solutions to mitigate these risks.

The mandatory reserves system (MRS) is one of the policies implemented to mitigate the risks of drug shortages. However, pharmaceutical companies in Finland have criticized the system of being inflexible and not helping on reducing the chances of supply disruptions. Moreover, pharmaceutical companies have stated that the system is expensive to maintain and makes Finland a relatively unattractive marketplace and could even decrease the total supply due to market exits. National Emergency Supply Agency (NESA) reimburses pharmaceutical companies for the expenses of the mandatory reserves system. Still, according to pharmaceutical companies, even after accounted for the reimbursements, the costs are substantially higher.

The initial hypothesis of this thesis is that if the reimbursements paid by NESA do not cover the total costs of MRS, products assigned to the system should exhibit price increases. Since the Finnish healthcare system heavily subsidizes pharmaceutical consumption, there are possible hidden costs for the public sector inflicted by the MRS that should be understood when analysing the net benefits of the system.

To estimate the effects of MRS on the pricing of pharmaceuticals, a change in legislation from 2009 is used as quasi-experimental study design. In 2009 several new pharmaceutical products were added to the mandatory reserves system, which forced pharmaceutical companies to increase the storage amounts for these products. Increasing the storage increases the total costs of the supply chain, and thus we should observe changes in pricing.

To the best of my knowledge, no prior studies have studied the effects of the mandatory reserves system on the pricing of pharmaceutical products. Moreover, I am not aware of any other country aside from Finland having a similar system that controls pharmaceutical products' minimum storage amounts.

This thesis is structured as follows: Chapter 2 describes the institutions, legislative environment, and overall pharmaceutical markets in Finland. The nature of pharmaceutical markets is discussed, focusing on price control schemes and other policies implemented to regulate pharmaceutical markets around the world. Moreover, the existing literature on price-control policies regarding pharmaceutical markets is discussed in depth. The literature review focuses mainly on empirical research that provides ideas on how pharmaceutical prices can be analysed in this thesis.

Chapter 3 explains the legislative process behind the mandatory reserves system in detail and discusses the past literature on drug shortages and their effects. Most importantly, the policy change used to estimate the effects of the MRS is discussed thoroughly.

In chapter 4, the data, along with the empirical approach, is presented. The preparation of the final dataset and its possible caveats are explained. Chapter 5 presents the results of the analysis, and they are discussed in chapter 6. Finally, chapter 7 concludes the thesis.

# 2 INSTITUTIONAL SETUP, PRICING AND PHARMACEUTICAL MARKETS IN FINLAND

The pharmaceutical markets are highly unusual by many standards. The price elasticity, the importance of pharmaceutical products for the society, the asymmetry of information, and the heavy regulation sets a stage for a unique market to study.

A substantial number of drugs sold in Finland are imported from other countries, mostly from Europe (Heiskanen, Ahonen, Karttunen, Kanerva & Timonen, 2014). Figure 1 illustrates the pharmaceutical production levels in European countries. Finnish pharmaceutical production is rather small when compared to other countries. For example, Sweden and Denmark have much larger domestic production even when adjusted for population.

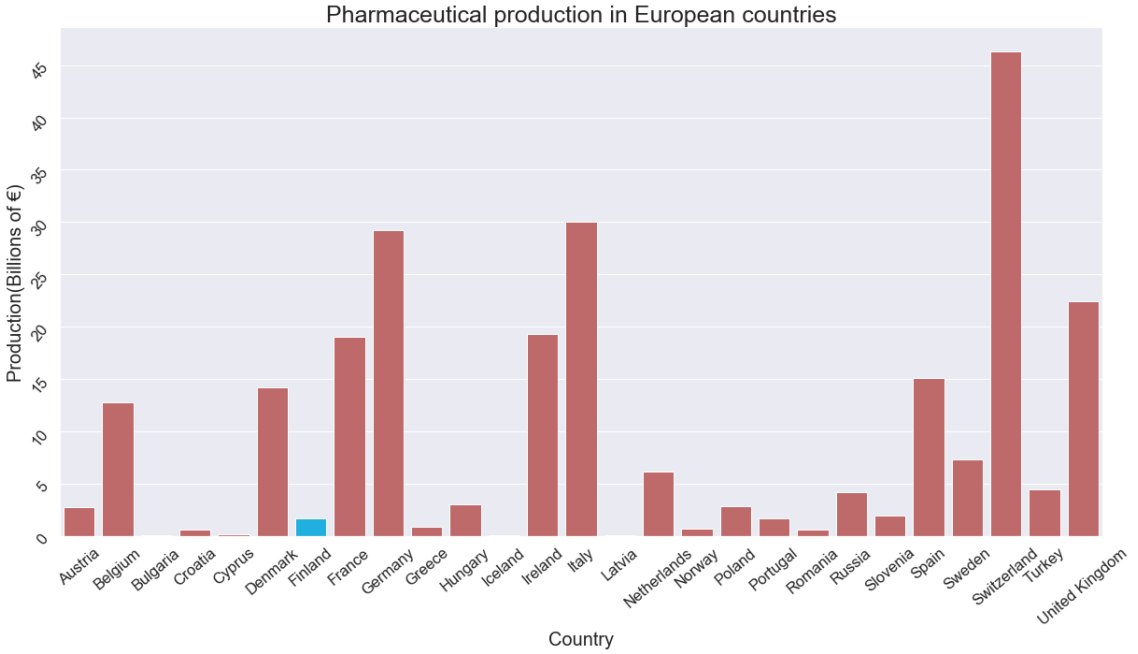


FIGURE 1: Value of pharmaceutical production in European countries in 2016. (EFPIA, 2018)

The fact that Finland does not have much domestic production leaves Finnish pharmaceutical markets dependant on imports. Moreover, Finland being a small market and located in a logistically tricky area and not belonging to the North Atlantic Treaty Organization (NATO), which has a pharmaceutical supply agreement between its countries, possibly leaves Finnish markets more exposed to outer risks.

## 2.1 Supply chain of pharmaceuticals and legislation in Finland

Policy guidelines for the Finnish pharmaceutical sector are outlined mainly in separate legislative texts. The Finnish Medicines Act (395/1987 and 904/2013) governs the overall safety, proper use, manufacturing processes, and availability requirements of pharmaceuticals. The Finnish Medicines Decree (693/1987) governs the importing, manufacturing, and wholesale business and its requirements. The Finnish Health Insurance Act (1224/2004) directs the health insurance system and the reimbursement practices for pharmaceutical products.

For this thesis, most importantly, the mandatory reserves system is provided by the Mandatory reserves act of pharmaceuticals (402/1984) and (1114/2008). Finally, the Council of State Decree on the price list for drugs (713/2013) determines the pharmacies' profit-margin; hence they fix the retail prices. Furthermore, the Council of State Decrees maintains the lists of active ingredients assigned to the mandatory reserves system. (OECD, 2014.)

The supply chains of pharmaceuticals are lengthy and complicated from the production phase to the consumer. They typically consist of four parts: chemical plants for raw materials production, pharmaceutical companies for the production of the actual products, distribution affiliates or wholesalers, and lastly, the healthcare facilities or pharmacies. (Saedi, Kundakcioglu & Henry, 2016.) In the context of this thesis, the focus is on the prices in the wholesale and retail level and how they are affected by the possible storage costs of mandatory reserves.

According to the Finnish Medicines Act (395/1987), pharmacies are tasked with the retailing, distribution, and manufacturing of pharmaceutical products. Additionally, pharmacies are responsible for advising customers and services regarding pharmaceutical products (Finnish Medicines Agency, 2019).

In Finland, pharmacies can be owned only by certified pharmacists, and the number of pharmacies is strictly controlled by the Finnish Medicines Agency (Fimea). Fimea sets the number of pharmacies based on their assessment of the need for pharmacy-services in each area. If Fimea decides a pharmacy to be opened, they proceed with giving rights to new pharmacists, who runs the pharmacy as a personal business (Finnish Medicines Act, 1987/693).

Pharmacies are usually the final link between patients and the markets. In addition to pharmacies, hospitals dispense pharmaceutical products, but unfortunately, hospital markets are out of the scope of my thesis. The hospital markets operate mainly with tendering processes, which differ considerably from pharmacy markets.

Pharmaceutical wholesalers act as a link between pharmacies and pharmaceutical companies. The wholesale business in Finland is dominated by two large companies, Oriola and Tamro, and together they deliver most of the pharmaceutical products to the retail and hospital markets.

The distribution of Pharmaceuticals in Finland works as a single-channel system, where one wholesaler distributes all pharmaceutical products of a single producer (Heiskanen, Ahonen, Kanerva, Karttunen & Timonen, 2017). The

single-channel distribution could mean drastic changes in market shares if one sizeable pharmaceutical company decides to change wholesaler it wants to do business. However, changing the wholesaler might inflict high costs in the initial phase, which could lead to a status quo, and pharmaceutical companies tied to use only one business partner continuously. Only an average of 2-4 pharmaceutical companies change wholesalers each year, and some new market entries happen yearly. According to the Finnish Competition and Consumer Authority (FCCA), the single-channel system is not statutory but rather a well-established practice in the Finnish pharmaceutical industry (FCCA, 2012).

The single-channel system has potential shortcomings if one of the wholesalers has distribution problems. In 2017 the risks realized when Oriola had problems implementing its new ERP system, resulting in several products not being distributed to pharmacies (Fimea, 2017). In such a situation, the mandatory reserves system does not help since the wholesalers are usually maintaining the safety stocks of an entire company due to the single-channel system.

The pharmaceutical industry is international and not very concentrated, and more than 200 pharmaceutic industrial manufacturers participate in the Finnish markets (FCCA, 2012). Pharmaceutical companies can sell their products by applying market authorization by four distinct procedures. In the national procedure, Fimea evaluates the safety of the product with the information provided by the applicant. In the so-called Mutual Recognition Procedure (MRP), Fimea honours decision where a product is already authorized in another EU-member state, Norway, or Iceland. The decentralized procedure means that a pharmaceutical company simultaneously applies for authorization in several or all EU Member States, and the authorities of one Member State act as lead assessors while others are responsible for supporting tasks. Finally, in the centralized procedure, the authorization is evaluated by the European Medicines Agency (EMA) and shall be valid in all member states after the decision. (Fimea, 2019.)

## 2.2 Costs, prices, and governing institutions

In addition to having heavy regulation, the Finnish pharmaceutical markets are overseen by several powerful institutions. The Ministry of Social Affairs and Health is in charge of guiding, planning, and implementing the general social and health policies in Finland.

Fimea, a subordinate to the Ministry of Social Affairs and Health, is responsible for the market authorizations and monitoring of the safety regulations. The pharmaceutical Pricing Board (Hila) is responsible for reviewing which pharmaceutical products are covered by the reimbursement system, as well as their maximum wholesale prices, essentially deciding price caps for reimbursed drugs. The pricing of pharmaceuticals in the wholesale level is only capped when

the manufacturer applies the drug to be reimbursed by the social insurance system.

Moreover, after the implementation of the reference pricing system (RPS) in 2009, Hila is responsible for confirming the reference price groups and their reference prices. The Finnish Social Insurance Institution (Kela) is, in turn, responsible for executing the National Health Insurance scheme and using the pricing and reimbursement information provided by Hila to reimburse appropriate amounts for pharmacies automatically. Figure 2 illustrates the governing institutions and their objectives. Patients are the most crucial part of the system, and all the institutions are there to ensure safe and adequately working pharmaceutical markets.

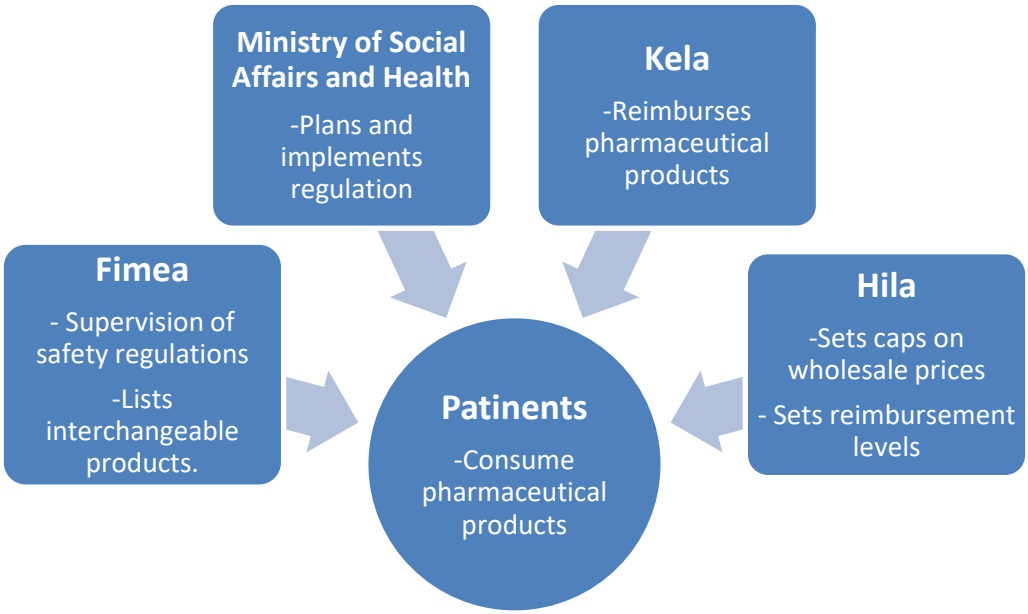


FIGURE 2: Institutions governing the pharmaceutical markets.

Finnish government provides universal healthcare for its citizens, and a portion of the medical expenses are covered by the Social Insurance System run by Kela, for which the participation is mandatory, and funding is arranged from payments collected in the form of taxes. The amount of reimbursed pharmaceutical expenditures depends on the product in question and previous medical expenses faced by the consumer each year.

The amounts reimbursed by the Social Insurance System are substantial; as much as 45 percent of the total pharmaceutical costs were covered in 2017. Reimbursement of drugs starts to affect consumption after a 50 euros deductible part that resets at the beginning of each year. The deductible part leaves consumers accountable for the first 50 euros spent on pharmaceuticals each year, but concerns only customers older than 19 years.

The reimbursement scheme, presented in table 1, is divided into different categories varying on the amounts reimbursed. The Insurance scheme covers 40% of the retail price of drugs included in the basic refund category, 65% in the lower special refund category, and 100% in the upper special refund category except that the consumer has to pay 4.5 euros for each purchase. After the consumer has reached a threshold of 577.66 euros, they are eligible for the full refund category, where only 2.5 euros is charged for each refundable product regardless of its price. (Kela, 2020.)

TABLE 1 Reimbursement in Finland (Kela, 2020).

| **Policy name** | **Parameters** | **Effects on consumers** |
|---|---|---|
| Deductible part | 50€ | After 50 euros of total spending the, reimbursement system kicks in |
| Basic Refund Category | -40% | Payment -40% of the initial price |
| Lower Special Refund | -65% | Payment -65% of the initial price |
| Upper Special Refund | -100% +4.5€ | 4.5 € paid for each product |
| Expenses ceiling | 577.66€ | Consumption above is reimbursed with the full refund category |
| Full refund | 2.5€ | 2.5 € paid for each product |

Pharmaceutical expenditures have been increasing in the 21st century in several developed countries, including Finland. In 2018 the total size of pharmaceutical sales in Finland was just above 3.2 billion euros (+6.8% from 2017), and reimbursements by the government reached almost 1.4 billion euros (+5.3% from 2017) (Finnish Statistics on Medicines, 2018).

Tables 2 and 3 provide more specific information about pharmaceutical expenditures in Finland. In table 2, we can see that total expenditure consists mainly (66.6%) on prescription drugs of outpatient care, but the size of hospital markets has grown significantly, increasing their relative size (22.6%). Moreover, the OTC-market only accounts for a modest (10.8%) share of the total markets.

In table 3, most of the reimbursements are paid in special refund categories (65.6%), but a substantial amount of refunds is also paid in the full refund category (11.4%), implying a significant number of consumers reaching the expenses ceiling each year. The basic refund category accounts for 22.8% of the total refunds.

TABLE 2 Size of Finnish pharmaceutical markets (Finnish Statistics on Medicines, 2018).

| **Description** | **Amount, millions of €** | **Share, %** |
|---|---|---|
| Prescription drugs in outpatient care (retail prices incl. VAT) | 2.188 (+3.9%) | 66.6% |
| OTC medicines in outpatient care (retail prices incl. VAT) | 355 (+1.2%) | 10.8% |
| Hospital markets (wholesale prices) | 745 (+19.8%) | 22.6% |
| Total pharmaceutical market | 3.287 (+6.8%) | 100% |

TABLE 3 Reimbursements of pharmaceuticals in Finland (Finnish Statistics on Medicines, 2018).

| **Refund category** | **Amount, millions of €** | **Share, %** |
|---|---|---|
| Basic Refunds | 307 (-3.5 %) | 22.8% |
| Special Refunds | 979 (+7.5%) | 65.6% |
| Full Refunds | 174 (+10.2%) | 11.4% |
| Total reimbursement | 1.460 (+5.3%) | 100% |

Due to rapidly increasing healthcare spending, several countries have imposed price-controlling mechanisms on pharmaceutical markets. Countries imposing price control usually have relatively low wholesale prices, but the lower wholesale prices do not necessarily lead to low prices in retail markets, due to different tax-policies and profit margins of pharmacies. In Finland, the wholesale prices of drugs were below the European average, but the retail prices (incl. taxes) were above the average (Martikainen, 2012).

When pharmaceutical prices increase rapidly, so do the reimbursement expenditures. In figure 4, we can see that reimbursement expenditures have been increasing rapidly since 2008 in Finland. Between 2008 and 2011, the expenditures were increasing slower than they are currently, due to the implementation of a price control system, which is discussed in later subchapters.

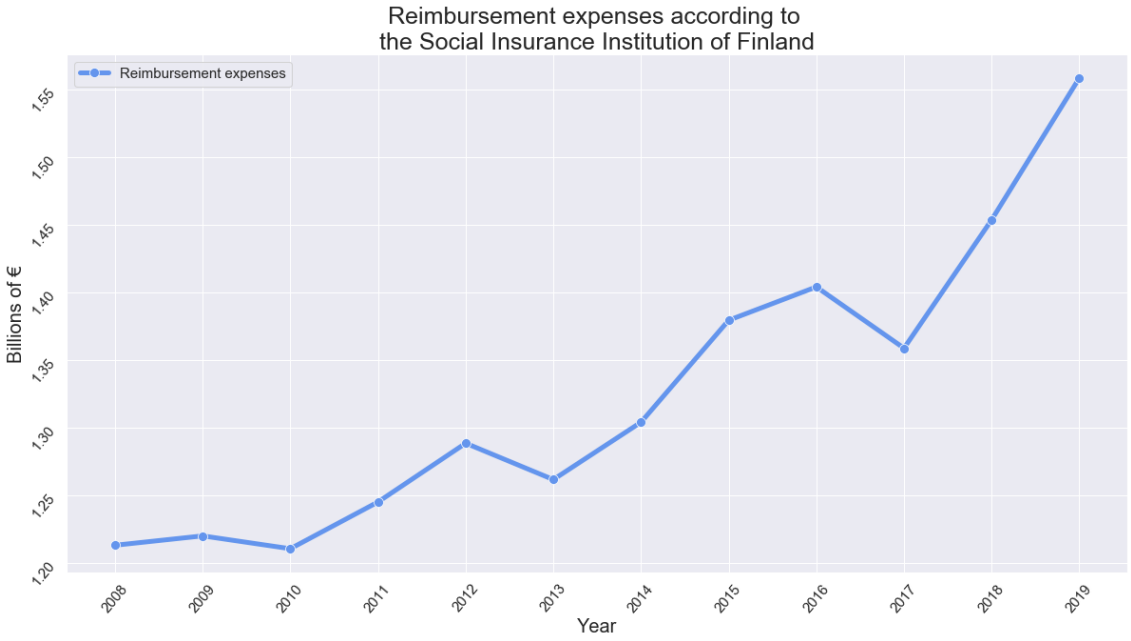


FIGURE 3: Reimbursement expenditures in Finland in 2008-2019. (Kela, 2020)

Due to increasing reimbursement expenses, the governments have strong incentives to control the prices. However, Finnish pharmaceutical companies have voiced concerns that strict price control possibly leads to decreased availability of pharmaceutical products. Pharmaceutical companies argue that decreasing the prices of pharmaceutical products puts pressure on supply chains to operate more cost-efficiently and ultimately leads to increases in supply disruptions. There exists theoretical and empirical evidence that lower market prices could decrease the optimal amounts of storage, which could lead to an increase in severe supply disruptions.

In Finland, the reimbursed pharmaceuticals' prices are controlled at the wholesale level by Hila and indirectly at the retail level, since the Council of State determines the profit margins of pharmacies[1]. (Finnish Pharmacy Mark-up Decree, 713/2013.)

The price control for pharmaceutical products is supported by the idea of a moral hazard problem in prescribing since physicians might not internalize the costs of their prescriptions to the patient or the corresponding provider of insurance. Patients and physicians might become insensitive to changes in prices, leaving the decision-making processes of consumption suboptimal. In other words, there are severe market failures in the pharmaceutical sector. (Pavcnik, 2002.)

The next subchapters explain in detail why we have price controlling schemes, how they have affected the pharmaceutical markets and what does the existing literature says about them.

[1] See appendix 5 for more detailed information about pharmacy price mark-ups

One of the most impactful price control mechanism was enacted simultaneously with the policy change in mandatory reserves system. Since the empirical section of this thesis estimates the impact of mandatory reserves system on the prices and other price-affecting policies are enacted simultaneously, it is crucial to control and understand the effects of these policies that possibly confound the results. Moreover, since the existing empirical literature focuses on the price controlling mechanisms and their effects, the methods and findings of these studies are summarized in the next sub-chapters. Some empirical approaches used in the existing literature on the pricing of pharmaceuticals are incorporated into this thesis.

## 2.3 Pharmaceutical markets and price control

An efficient market economy is a system where the supply and demand determine the price of a product, and buyers and sellers should be left to interact to find the optimal solution for their transactions. Governments tend to regulate pharmaceutical markets since the conditions of perfect markets are rarely met in this sector. (WHO, 1997).

Perfectly competitive markets should satisfy the following conditions:

- Suppliers participating cannot affect market prices.
- Firms and products must be substitutable: Homogenous products with the same quality.
- Each consumer participating cannot affect market prices.
- No imperfect information
- Suppliers and producers have free entry and exit from the markets.
- No large externalities.
- Zero transaction costs.

In the pharmaceutical sector, consumers of OTC-drugs rely heavily on physicians and pharmacists for the information required for the purchasing decisions. In the case of prescription drugs, physicians usually decide which product the consumers buy, thus acting as a decision-maker between the consumer and supplier but does not face any costs of his decision.

Moreover, pharmaceutical companies face high market entry costs due to time-consuming and expensive R&D procedures and licensing costs for their products (market entry problems). Market entry requires a lot of regulatory inspections and bureaucratic procedures before any sales.

Additionally, there are substantial externalities in consuming pharmaceutical products, e.g., immunization with vaccines. Finally, the consumer does not face the full economic consequences of their decisions since pharmaceutical consumption is heavily subsidized. (WHO, 1997 & WHO, 2015.)

Market power is usually observed in monopsony and monopoly competition settings, but pharmaceutical companies exert market power usually through long patent protection, market segmentation, and brand loyalty of consumers (WHO, 1997). An excellent example of brand loyalty market power is the treatment for high cholesterol, where a drug called Lipitor is the original branded product. After its patent expired in 2011, a generic product entered the market named Atorvastatin. The products are identical, but Lipitor costs USD 184, while Atorvastatin costs USD 36. Simvastatin is a product therapeutically equivalent to Lipitor and Atorvastatin but costs only USD 7. Substantial price differences persist between these similar products implicating that even though the consumers could use either one product, the consumption habits persist for some reason.

Moreover, since the consumers do not face the full economic consequences of their activities in the pharmaceutical markets due to public reimbursement schemes, the consumption decision might become distorted. Shifting from one drug to another, when we have already established the effectiveness of the original drug, is something that not everyone is willing to do, which implies high switching costs between products in pharmaceutical markets. (Henka, 2018.)

In a monopsony setting, the buyer or consumer can negotiate lower prices, being the only buyer and thus putting pressure on the supplier to offer a reasonable deal, which happens in Finland, when Hila is negotiating maximum wholesale prices for pharmaceutical products.

When suppliers or consumers have market power, they can affect the market pricing mechanism with their decisions. An absolute monopoly market is quite usual when new treatments enter the markets. New treatments have long market exclusivity periods, and the consumers do not usually have other options available in the markets. These kinds of absolute monopoly situations greatly affect the prices of pharmaceuticals. (WHO, 2015.)

The pricing of pharmaceuticals and medical care also suffers from the dilemma of a public good, since the evaluation of the safety of a pharmaceutical product is something that a single consumer cannot evaluate it is tasked to a publicly funded body. After the evaluation is finished, the use of information by a single consumer does not affect the ability of other consumers' usage. (WHO, 2015.)

Important distinctions of pharmaceutical markets that separates them from other goods in Finland:

1) Pharmaceutical prices have inelastic demand because sometimes product unavailability leads to death or permanent disability.
2) Pharmaceuticals have substantial R&D costs before market entry.

3) Patents are implemented to cover huge R&D costs, and they usually last relatively long.
4) Buying pharmaceutical products require expert advice and sometimes prescription from a physician. (asymmetric information).
5) Sometimes consuming pharmaceutical products yield significant positive externalities, e.g., in the case of vaccinations and treatments to diseases that could infect others (externalities).
6) Pharmaceutical markets are heavily regulated.
7) The consumer does not face the full costs of his consumption.
8) Prices controlled by the government.

In general, pharmaceutical products' price elasticity of demand (PED) is found to be inelastic. As consumption of pharmaceuticals happens mostly when we already have a condition and sometimes leaving the condition untreated has severe consequences, even death, it should be evident that we would likely consume pharmaceutical products even if their prices increased significantly. The PED for pharmaceutical products most likely varies substantially between groups, with the severity of the condition treated.

The PED of pharmaceutical products has been estimated by several studies. For example, Yeung (2016) estimated the PEDs of pharmaceuticals in the United States ranges between -0.09 to -0.87 with an average of -0.16, exploiting a natural experiment study design, where cost-based formulary (CBF)2 was substituted by value-based formulary (VBF)3. The policy change was implemented for certain product groups giving the study an ideal design for estimation. Yeung (2016) argue that individual pharmaceutical products have more substitutes than complements, which is most likely true within a certain product group, but unrealistic in the context of all pharmaceutical products.

If we assume a patient is having a national chronic disease such as diabetes, the treatment plans would include only drugs for diabetes and certainly not antihistamines; thus, the cross-price elasticity between different groups of pharmaceuticals is most likely low. However, there are multiple products to treat diabetes from multiple manufacturers, making it an important factor to control when analyzing the PEDs of pharmaceuticals products. Pharmaceutical demand can be elastic at the product level but inelastic at the group level. (Yeung, 2016.)

Landsman, Winnie, Xiaofeng, Teutsch & Berger (2005) found that drugs treating asymptomatic conditions (-0.1 to -0.16) have lower elasticities than drugs treating symptomatic conditions (-0.24 to -0.6). Moreover, Manning, Newhouse,

[2] Typically, the pharmaceutical products are grouped into tiers based on their prices, thus incentivizing consumers to buy cheaper products (Yeung, 2016).
[3] VBF, a value-based formulary, is a policy tool to adjust amounts of copayments according to the price and effectiveness of a pharmaceutical product. Basically, if a pharmaceutical product is expensive but effective, the copayment can be lower. In contrast, cheap products with minor effects can have relatively high copayment levels. VBF makes consumers more susceptible to their consumption decisions, even within product groups containing similar drugs.

Duan, Keeler, Leibowitz & Marquis (1987) had access to a randomized trial[4], where participating families were assigned 14 different fee-for-service insurance groups or to a prepaid group. The groups varied in coinsurance rates and upper annual limits for out-of-pocket expenses. The price elasticity of health services was estimated to be around -0.2.

There are four major determinants of the price elasticity of demand for a good; substitutability, the proportion of income committed to the purchase, whether it is a luxury or a necessity, and market timing (WHO, 2015). Based on the existing literature, there is a strong argument for an inelastic demand for pharmaceutical products in general, but the possibility of an elastic demand for products with similar substitutes.

The market-entry for new treatments comes with high sunk R&D and regulatory costs. However, market power is granted by enabling relatively long patents for pharmaceuticals to promote innovation. As a result, when market power and price inelastic demand are coupled, there are possibilities for monopolistic profits[5]. Furthermore, since the medical expenditures are subsidized from governmental budgets, and several other market failures exist simultaneously, national governments have implemented various means to curb medical expenditures. (Brekke, Königbauer & Straume, 2007.)

In the next subchapters we will rigorously analyse the price control schemes implemented by multiple countries, and their implications on the pharmaceutical markets. Since price controlling and competition boosting regulations are an important control for the econometric analysis presented later, the existing literature on competition and pricing mechanisms of pharmaceutical products is important to analyse. The existing literature on pharmaceutical prices gives us good implications on how to proceed with our empirical analyses.

### 2.3.1 Generic substitution

In Finland, Fimea keeps a list of drugs that are substitutable with each other. Due to generic substitution laws, physicians prescribe products by name or by the active ingredient, and pharmacies are required to offer the cheapest option from the substitution group unless the physician explicitly prohibits it due to medical reasons. Patients are also entitled to decline from the generic substitution.

The generic substitution was implemented in April 2003 by the Ministry of Social Affairs and Health. The policy required the pharmaceutical companies to report the prices of their products directly to the Association of Finnish

[4] The Random Health Insurance Experiment (RAND HIE) was introduced by the U.S government to study how the demand for health services reacted to insurance-induced changes in the price.
[5] Appendix 2 gives a real-life example of the effects of strong market power in pharmaceutical markets.

Pharmacies, the Social Insurance Institution, and to the University Pharmacies 21 days before the beginning of each quarter (Ministry of Social Affairs and Health 2003/210). The system obligated the pharmacists to substitute the prescribed products to any cheaper product within a specific range from the cheapest product of the substitution group (Timonen, Karttunen, Bengtström & Ahonen, 2009).

The accepted price range for generic substitutes is called the price corridor, which is determined at the beginning of each quarter using the price of the cheapest product within the substitution group added with a premium, giving pharmaceutical companies some room to manoeuvre with product pricing. The price corridors and changes to them are presented in table 4.

TABLE 4 Price corridors in the generic substitution policy.

| **Price of the product** | **Price corridor 2003** | **Price corridor 2008** | **Price corridor 2017** |
|---|---|---|---|
| Price < EUR 40 | Cheapest + 2€ | Cheapest + 1.5€ | Cheapest + 0.5€ |
| Price ≥ EUR 40 | Cheapest + 3€ | Cheapest + 2€ | Cheapest + 0.5€ |

Timonen et al. (2009) found that after the implementation of generic substitution in Finland, the turnovers were decreasing for companies selling branded products while increasing for companies selling generic competitors between the years 2004 and 2009. Moreover, the gross margin per cent decreased for both branded and generic companies implicating an overall price decreases in generic and branded categories. The research done be Timonen et al. (2009) was descriptive, so the causal interpretations remain uncertain, in my opinion.

Generic substitution and competition policies are aimed towards lowering the prices of pharmaceuticals by increasing the level of competition between pharmaceutical products. In addition to Finland, the generic substitution has been implemented in several countries and has been linked to substantial cost savings by multiple pieces of research and statistical analyses. According to the Congress of the United States' Congressional Budget Office (CBO), purchasers saved USD 8-10 billion just in 1994 due to generic competition.

Generic medicines are drugs not protected by patents and can be produced from the same chemical compounds, using identical or different production techniques, than the original drug. Multisource pharmaceutical products are pharmaceutically equivalent but are not necessarily therapeutically equivalent. The reason for therapeutic differences in multisource pharmaceuticals come from differences in production techniques affecting the product performances. (WHO, 2015.)

The expiration of patents drastically lowers the barriers of market entry for generic products. Producers of generic pharmaceutical products are not

obliged to go through rigorous clinical trials and safety inspections to prove the effectiveness of the drug since they are essentially producing an already approved product that has already established all the requirements. Generic competitors can skip many expensive phases of product development, lowering their R&D costs and thus giving them an option to compete mainly by lower prices. Usually, multiple companies enter the market to compete with generic products, and the prices fall dramatically after patent expirations. (WHO, 2015).

In general, it is believed that the presence of generic competition lowers the prices of pharmaceuticals, but this might not be the case in all product groups and institutional setups. Babar (2006) studied the effects of pharmaceutical distribution privatization on drug prices in Malaysia. They found extraordinary price hikes in some drug categories that could not be explained by general inflation rate or international price hikes. Significant price increases were recorded in life-saving and arrhythmic drugs such as adrenaline, lignocaine and dopamine. Interestingly the prices were increasing especially in product categories, where the patents had already expired, and generic competitors were available. Researchers argue that the reason for price hikes despite generic competition comes from the fact that Malaysia does not exercise price control for pharmaceutical products (Babar, 2006).

The absence of other institutions such as price controls, reference pricing and price negotiations between governments and pharmaceutical industry might hinder the price lowering effect of generic competition, making it conditional on the presence of supporting institutions (Babar, 2006).

Saha, Grabowski, Birnbaum, Greenberg & Bizan (2006) analyses a sample of drugs experiencing generic competition between 1992 and 1998 in the United States. The researchers report, that amount of generic competition (Number of generics in the market) is influenced by three key variables: generic price-to-brand ratios, generic market shares and generic entries each year. Generic entries are exogenously pre-determined, and generic-to-brand price ratio and share of the market of all generics are jointly determined making them endogenous variables when analyzing the system of competition between generics and branded products. Share of the market captured by generic competitors is a significant determinant of the market prices and prices, in turn, are an important determinant of the market share. Moreover, the number of generic entrants and the size of the markets affect both generic-to-brand price ratio and the shares of generic products in the markets. (Saha et al., 2006.)

Generic competition is more intense with so-called blockbuster drugs, which are defined as drugs with annual sales larger than USD 500 million before generic competition sales. Blockbuster drugs face, on average, two more generic competitor entrants each year, compared to non-blockbuster drugs. Moreover, the number of generic entrants affects the price level and share of generic drugs, meaning that blockbuster drugs experience larger erosion in prices due to more intense generic competition. Also, drugs treating chronic conditions are faced with more aggressive generic competition. Each new generic entrant reduces the average deflated brand prices by 0.2 percent, which means that prices are

negatively affected by the generic competition and also by the number of competitors in the markets. (Saha et al., 2006.)

In 2017, 90 percent of the prescriptions filled in the United States were for generic drugs, yet only 23 percent of the total drug costs were generated from these drugs. The majority of drugs sold in the United States are drugs with generic competition, but the majority of the turnover comes from patented drugs with no competition. The U.S Food and Drug Administration (FDA) has taken new steps to encourage competition and to disable so-called gaming strategies, where incumbent companies try to delay the market entry for generic drug competitors. Such gaming strategies include for example "pay-for-delay", where incumbents compensate generic competition for forestalling their market entry. Other commonly recognized gaming strategies include increasing the unavailability of certain branded products for comparative testing, by blocking generic drug company's access to testing samples with legal measures. Furthermore, the FDA is working to increase competition by shortening the processing times for testing and reviewing the safety and of a generic drug entering the markets. (Hemphill, 2019.)

Between 2008 and 2016 in the United States, the prices of patented drugs hiked almost 210 percent, while the generic drugs saw an average price drop of almost 23 percent in the same period (Hemphill, 2019). Furthermore, the Government Accountability Office (GAO) found out that some 300 generic drugs saw price increases of 100 percent or more, which essentially means that significant price increases were mitigated by the overall price declines of generic drugs (Hemphill, 2019).

GAO (2016) examined the price trends of 2,378 generic products[6] and surveyed the factors affecting the prices of generic drugs during the years 2010-2015. GAO found that on average, the generic products saw price declines, but there were some generic products with extraordinary price hikes of 100 percent or more.

Generic products that entered and/or exited during the timeframe of the study had very different price trends compared to products that were presented during the whole time of the survey (no exits or entries). From the 1st quarter of 2010 through the 2nd quarter of 2015, the prices of all generic products fell 59 percent on average. The drugs that stayed in markets the whole time of the study[7] saw an average price drop of only 14 percent, and from these drugs, more than 300 saw price increases of 100 percent or more and these drugs moderated the average price declines of all products. The products that experienced substantial price hikes pushed the whole price index up by 25 percentage points. However, the majority of the drugs that saw large price increases were not amongst the most used drugs. (GAO, 2016.)

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[6] The generic products studied were part of Medicare Part D. program; thus, the results might not apply other products.

[7] The number of drugs that stayed in the markets for the whole time was 1,441.

The fact that exiting products and new entrants exhibit different price behavior compared to incumbents is vital to take note. For the empirical section of this thesis, the final regression models are run after excluding products that entered or exited the markets to prevent biases of potential exit strategies or market entries.

According to manufacturers, the competition, determined by the price and availability of the same drug from other manufacturers, is the most important factor of generic drug prices. The manufacturers also reported that the level of competition is strongly affected by multiple factors such as material shortages, production difficulties, consolidation among manufacturers and backlogs of new generic drug applications[8]. Furthermore, according to stakeholders, certain drugs are challenging to manufacture and require intensive measures to fulfil all safety, and quality requirements and for this reason, there might be only a few manufacturers producing the active ingredients or the specific product. As a result, production difficulties with one manufacturer could lead to substantial price changes due to insufficient supply in the markets. (GAO, 2016.)

In the research done by the U.S governmental accountability office, has interesting discussion about supply disruptions and the possibility of price changes. If the risk of severe supply disruptions exists in the pharmaceutical industry, there might be a possibility to mitigate these risks for example by optimizing storages, which is discussed briefly in the section about mandatory reserves system later in this thesis.

The Hatch Waxman Act in the United States has facilitated the generic competition entries since the bill was passed in 1984. The new legislation gave generic competitors easier access to markets through the Abbreviated New Drug Application process (ANDA). Under the new process, the generic manufacturers can participate in the pharmaceutical markets by only demonstrating bioequivalence of their product compared to the branded version. Before the ANDA process, the prospects of generic competitors had to go through similar clinical trials as their branded counterparts, which often required millions of dollars and several years of rigorous testing. Due to these market entry barriers, only 35 percent of the best-selling off-patent drugs were estimated to have generic competition in 1983. (Grabowski & Kyle, 2007.)

Furthermore, the Hatch Waxman act gave generic competitors research exemption for bioequivalence studies, which made it possible to research bioequivalence before patent expiration of the branded product. This process speeded up the possible market entries and created incentives for generic manufacturers to challenge patents of the branded products before their expiration. (Grabowski & Kyle, 2007.)

Olson & Wendling (2018) estimate the causal effects of generic entries to the market price of drugs using a regression model. The researchers use the fact

[8] The backlogs happen due to rigorous reviews that the FDA must make before accepting new entrants to markets. FDA has invested money to shorten the review times as discussed in Hempfield (2019).

that Hatch-Waxman acts' paragraph four in the United States gave generic competitors 180 days of market exclusivity if the generic manufacturer successfully challenges the existing patent and wins the case in court. The exclusivity of the generic competitor means that no other generic competitors could enter the markets during these 180 days.

The effects of market entries to the prices could be misinterpreted if endogenous selection bias exists due to the sizes of the markets of the drugs in question. Olson & Wendling (2018) study, if endogenous selection bias could explain the correlation between generic drug prices and the number of generic competitors and if so, how much. The identification relies on a difference-in-differences estimation method, where the first difference compares prices against drugs of the same molecule with a different number of competitors and the second difference compares the price differences attributed to the number of competitors during the Paragraph Four exclusivity period to the price difference attributed to the number of competitors outside of the paragraph four exclusivity period.

The effects of competition are reported when small- and large markets are pooled together for each control group. Prices tend to decline for each control group samples when the number of competitors increases. The results are similar during the generic exclusivity period and outside of the exclusivity period. When two competitors are introduced to the markets, the prices tend to decrease by 10.1 – 14.0 percent, relative to a single competitor. However, these results are statistically significant only at the 10%-level for the full sample control group outside of the exclusivity period. As the third competitor enters the markets, prices decrease by 24 to 39.7 percent compared to a single competitor and the effect is statistically significant at the 5% level for all control groups inside and outside of the exclusivity period. (Olson & Wendling, 2018.)

For small-market drugs, three competitors or more result in lower prices of average 26.2 to 33.5 percent and the effects are similar outside and inside of the exclusivity period, meaning that selection bias is not a problem, but for large market drugs, the effects are not so straightforward. The results during the exclusivity period are statistically significant for three or more competitors, but outside of the exclusivity period, the results are statistically insignificant in two of the three control group samples. The difference-in-difference estimation for the effects of two competitors is -53.8 percent at the 10% confidence level, and the same estimate for three competitors is -73.8 percent at the 5% confidence level. Large difference-in-differences estimates signal that the sample selection is important in large drug markets when considering full sample control group. Large markets attract more competition in general, but those large markets not facing much competition after the exclusivity period may have such cost structure or demand conditions that do not attract competition. (Olson & Wendling, 2018.)

As stated before, the endogenous selection might be a problem for causal interpretation for generic entrants and market prices, and market size could be a significant driver of the results. Research done by Olson & Wendling (2018) tackles this problem by analyzing small markets and large markets separately within and outside of the 180 exclusivity period granted by the Hatch-Waxman act.

Selection bias does not seem to be a problem within small markets, but for large markets it is. Two to three competitors reduce prices more during the exclusivity period of 180 days than outside of it. Inside the 180-days exclusivity period, the market entries are controlled, and thus selection bias is unlikely. Outside of the 180 days exclusivity where the market entry is free, makes it possible to identify the effects of selection biases. These results advocate for the presence of endogenous selection bias. Due to said bias, the effects of early market entries are most likely underestimated, while the effects of later entries are overestimated. Among small markets, the selection bias is not present, but in large markets, the selection bias exists. For large market drugs, two to three competitors reduce more within the exclusivity period than outside of the period. This effect is most likely caused by selection bias in large markets and is significant. (Olson & Wendling, 2018.)

Grabowski & Kyle (2007) analyze how the market shares of branded products evolved after generic entries, how the number of generic entries changed and what happened to the length of market exclusivity of new patented drugs in the United States after the implementation Hatch Waxman Act. The study incorporates data on market exclusivity from 332 drugs experiencing new generic competition between January 1995 and December 2008, where 200 of these products are entirely new, and 132 are new formulations of older drugs and the results are consistent between new formularies and new products. The data was supplemented by detailed records of Paragraph IV filings from multiple sources to identify drugs that experienced Paragraph IV challenges. (Grabowski & Kyle, 2007).

The average market exclusivity periods for branded and patented products have been declining steadily after the Hatch Waxman Act, and the patent challenges increased during the same period. The size of the markets for specific drugs was identified as an essential factor for the amount of generic competition and larger markets attract more generic competition.

The number of generic entries increased in all market sizes during the time of the research, meaning that the competition has become more intense during 1995-2008. The average lengths of market exclusivities for the branded products have also been declining from an average of 13.5 years to 12.4 years during the timeframe of the data. Furthermore, the market share erosion for branded products seems to happen much faster and to lower levels after the first generic entry in 2008, than 1995. In the first year of the new generic entrant, the market share of branded products declined on average to 44 percent in 1995, but in 2008 the market shares declined first rapidly to 37 percent during the first month and to 19 percent in six months and finally towards 15 percent in the first 12 months. (Grabowksi & Kyle, 2007.)

The generic competition under the Hatch Waxman act has become a major reform that has led to declining prices in pharmaceutical products in the United States. However, the research and development costs for new pharmaceutical products are huge and requires a lengthy period for sales to earn positive risk-adjusted returns to satisfy investors. More intense competition might lead to lower investments in pharmaceutical research in the near future, which could be a problem for the health sector. (Grabowksi & Kyle, 2007.)

Aronsson, Bergman & Rudholm, (2001) utilize Swedish quarterly sales and price data of 12 different pharmaceutical molecules from the years between 1972 and 1996 to estimate the effects of generic competition and reference pricing system (RPS) to the market shares and relative prices of these products. The basic regression model captures the change of the market shares of branded products when relative prices ($P^B_{it}/P^G_{it}$)[9] changes. They find lower market shares when relative prices of branded products increase for five of the twelve molecules. Moreover, Aronsson et al. (2001) extend their model to estimate the effects of RPS since it could affect the pricing of original branded products relative to their generic counterparts. The reference pricing system in Sweden[10] was implemented in 1993, and Aronsson et al. (2001) reports lowering market shares for branded products due to RPS, but only for three of the twelve molecules.

Final estimation models of Aronsson et al. (2001) sets relative prices of branded drugs and generic competitors as a response variable and uses the number of generic competitors and dummy for the reference pricing system as the explanatory variables of interest. According to the model, the prices of original products tend to decrease compared to the generic competitors after the implementation of the reference pricing system. However, the study design of Aronsson et al. (2001) uses a before-and-after study design without a control group and thus, the estimates for the reference pricing system are quite possibly biased.

Strøm & Locatelli (2015) used Norwegian longitudinal data between May 2004 and June 2007 to estimate consumption shifts between branded and generic drugs for treating high cholesterol. Results indicate that the average elasticities of the probabilities for shifting from branded to generics were -0.27 over patients and -0.46 over periods meaning that increases in the prices of branded products shifts consumption towards generics. Moreover, intriguing results were drawn from the data that older male doctors more likely keep on prescribing branded products regardless of price, and also the decisions of consumers show autocorrelation across time implying a persistence in habits playing an important role. (Strøm & Locatelli, 2015.)

In my opinion, the prescribing habits of doctors is an important, often overlooked factor in policy reforms. The prescription incentives of doctors might affect pharmaceutical markets even in perverse ways if they are not understood well. Norwegian healthcare system resembles its Finnish counterpart, making the results comparable.

According to several studies, generic competition affects the dynamics in pharmaceutical markets. Generic competition on average seems to shift market shares towards generic products, and prices seem to adjust accordingly. It is important to note that the entry barriers for pharmaceutical markets play a significant role in the level of generic competition. The institutions enabling the

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[9] $P^B_{it}$ = price of the branded product, $P^G_{it}$ = price of the generic competitor.

[10] The Swedish reference pricing system set the maximum reimbursement level of drugs to 110 % percent of the price of the cheapest alternative in the reference group, which means that the customers most likely became more sensitive to pricing.

competition between generic and branded products are important when analyzing the competition of pharmaceutical markets. Moreover, it is crucial to understand the dynamics of competition when we discuss later on the effects of mandatory reserves since they clearly have price effects and the reference pricing scheme was enacted simultaneously with the amendments to mandatory reserves act. It is possible that the strict competition forces pharmaceutical companies to cut costs even by the expense of the supply reliability.

### 2.3.2 Reference pricing system

As noted before, in several studies, the generic competition's price-reducing effects in pharmaceutical markets have been found conditional on other policies. One of the most used policies supplementing generic competition is the reference pricing system (from here on RPS or RP system).

In Finland, the RPS was implemented in 2009 by including some pharmaceutical products from the generic substitution system also to reference pricing system. The RPS supplemented the generic substitution policy by incentivizing consumers not to decline of the substitutable product. If consumers declined the generic substitution, they were fully accountable for any price difference of the product and the upper limit of the price corridor. The RPS was implemented almost simultaneously with the mandatory reserves systems' reform, and thus it is imperative to understand its effects profoundly in the context of my thesis.

In this subchapter, the existing literature done from the pricing of pharmaceutical products focusing on reference pricing system is reviewed. According to existing literature, it seems that RPS has lowered the pharmaceutical prices.

Puig-Junoy (2010) conducted an extensive literature review about European pharmaceutical markets and their price regulation characteristics and their effects on pricing and competition. His findings indicate that market regulations implemented in Europe lead to lower prices, but not all of the potential benefits find their way to lower consumer prices. My takeaway from the review is that European countries have implemented somewhat similar price regulations with most countries setting maximum reimbursement rates using the RPS and direct price caps for generic entrants so that their maximum price ranges between -30 to -50 percent compared to the original branded product. I have replicated the table collected by Puig-Junoy (2010) in appendix 2, where the market regulation characteristics are structurally presented.

Reference pricing system can be implemented in different ways, which affects who is going to bear the costs from the consumption decisions and how the maximum reimbursement amounts are determined. Internal reference pricing (IRP), which is also in use in Finland, bundles pharmaceutical products into clusters of similar interchangeable products and uses the lowest domestic price from that group as reference for the reimbursement level for all of the products in that group. Consumers get their product reimbursed to the level of the cheapest similar product within the reference pricing group, and if they choose to consume a

more expensive product within the group, they have to pay the price difference themselves. External Reference Pricing (ERP) is similar to IRP, except the reference price is determined using foreign and domestic prices.

RP groups can be constructed in multiple ways giving the institutions the power to dictate the level of competition they want to promote. Brekke et al. (2007) presented the clustering of pharmaceutical products in three different mechanisms. I) In generic reference pricing (GRP), only products with identical chemical ingredients belong to the same RP group, and thus the RPS promotes competition between generic substitutes. Said RP system only promotes generic competition between products that do not have existing patents. II) Therapeutic reference pricing (TRP) can be divided into two different subtypes. The first type of TRP clusters drugs that have chemically related active ingredients that are pharmacologically equivalent. The second type of TRP clusters products that have neither chemical nor pharmacological equivalence, but similar therapeutic effects. (Brekke et al., 2007.)

The system of categorizing pharmaceutical products into the reference pricing system works inherently similar to the generic substitution policy. Most European countries have implemented RPS for therapeutically equivalent (branded vs generics) products. However, for example, Germany and the Netherlands use clusters of therapeutically related drugs, promoting competition potentially between different substances and competition even for patented products (Brekke, Canta, & Straume, 2016).

In figure 4, I have illustrated the different levels of RP competition; moving down towards the bottom of the figure, the level of competition increases. In the first level, the RP system can be divided into external or internal RP, varying on the scope of the markets considered for the reference price. The level of competition of ERP is ambiguous, and it depends on the initial level of domestic prices relative to foreign prices. Therapeutic reference pricing implies a much tighter competition than generic reference pricing. Moreover, therapeutic reference pricing can be divided into a more competitive form of therapeutic equivalence and a less competitive form of chemical or pharmacological equivalence.

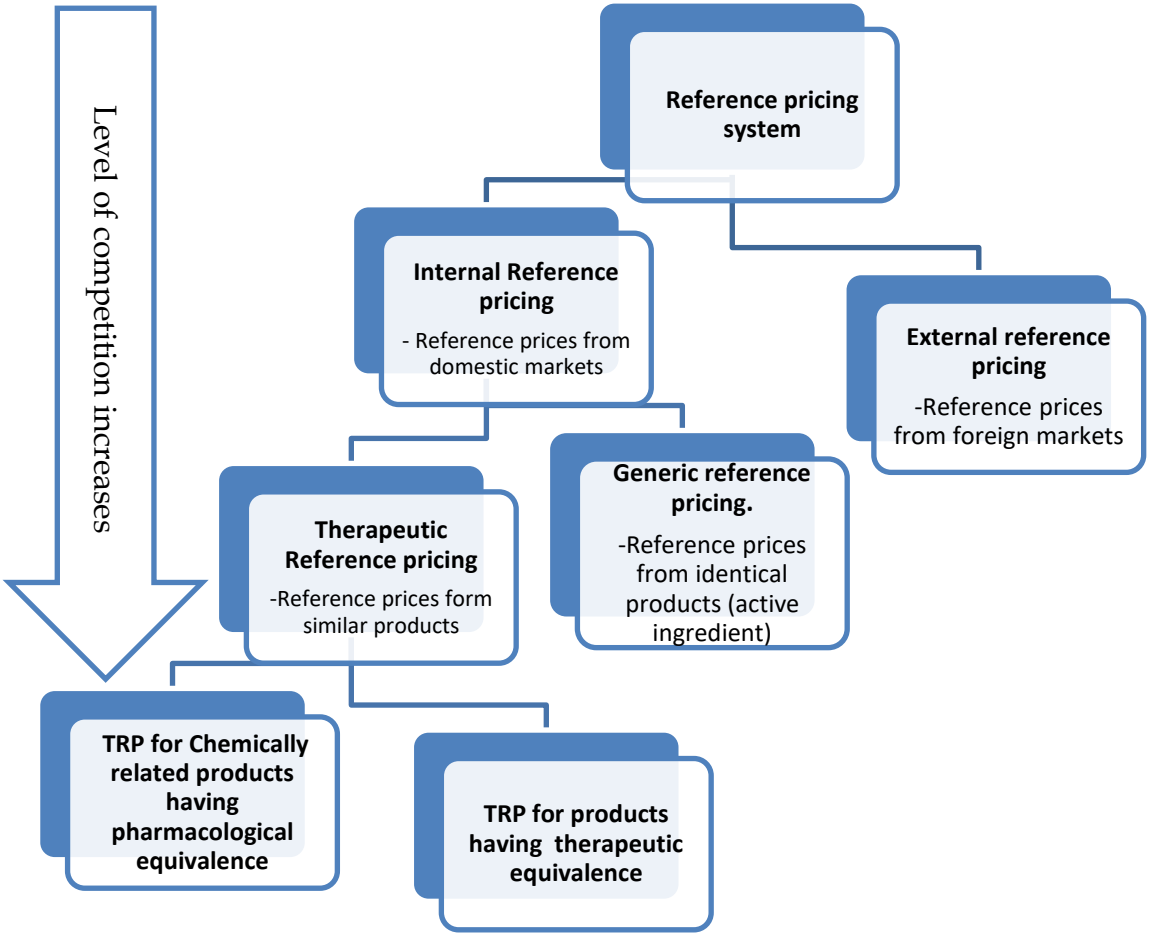


FIGURE 4: Different levels of RPS presented hierarchically.

When moving towards TPR, the level of competition intensifies, putting more pressure for pharmaceutical companies to lower their prices. However, TRP also has a profit-lowering effect for market entries making the innovation incentives lower for new treatments, meaning that theoretically, TRP decreases the number of market entries. If the barriers for entry are substantial, then GRP or even no reference pricing might be socially optimal. TRP can also be seen as a form of patent erosion for new treatments since they can be subjected to intense competition even with existing patents. (Brekke et al., 2007.)

Multiple empirical studies on the effects of RPS ignore market entries by taking the number of generics competing in markets as given. Since the RPS is likely to affect market entries, there might exist indirect price effects which are left unanswered. Brekke et al. (2016) study this question by showing with a theoretical model that reference pricing always discourages generic entry and thus drives up the average prices. However, these results are mitigated if other institutional regulations are in place, such as price caps. According to Brekke et al. (2016), the price response of branded products is relatively low, when reference pricing is implemented with already existing price caps. Due to these results, the implications of reference pricing to overall pharmaceutical prices is ambiguous, making it an empirical question.

Empirical results by Danzon & Chao (2000) seem to corroborate the proposition of Brekke et al. (2016) by showing that generic competition has substantial price lowering effect in countries with free or moderately constraining pricing legislation, e.g. in the United States, United Kingdom, Germany and Canada. For countries with stricter price regulation such as Italy, Japan and France, the generic competition seems to be less effective or even counterproductive. The explanation for cross-country differences in the effects of generic competition might be that in a free pricing environment, the generic competitors have to compete mostly with discounted prices.

Kaiser, Mendez, Rønde & Ullrich (2014) study Denmark's RPS regime change in 2005. Denmark switched from ERP[11] to IRP[12], meaning that reference prices were no longer affected by foreign prices. The study follows the prices of branded, generic and parallel imported statins[13] before and after the reform. Key findings of the study indicate an average drop of 19.6% in list prices, 22.4% in reference prices and 15.6% in patients' co-payments. However, the results varied between product groups so that the highest drop was in generics (-45%), then parallel imports (-33%) and lastly in branded products (-2%). The drop for parallel imports was not statistically significant. A situation where branded products respond to the implementation of RPS by decreasing less or even raising prices compared to generics is known as the generic competition paradox.

As the prices of generics decreased substantially more compared to branded products, the co-payments for brands increased by as much as 24.1 percent. The increase of co-payment levels for branded products leads to net welfare loss for price-insensitive consumers. However, the overall consumption shifted sharply in favour of generics and parallel imports. The results of Kaiser et al. (2014) show that the devil lies in the details when it comes to designing a reference pricing system since price effects depend heavily on the design elements. It is also important to note that branded products might react very differently to RPS compared to generics. (Kaiser et al., 2014.)

Norway introduced an RPS called index pricing[14] for several pharmaceutical products with no existing patents in 2003, replacing previous price cap regulation[15]. Since the index pricing was introduced only to some products, while others were left under the previous price cap policy, a natural experiment setting gave an ideal opportunity to estimate the pricing effects. Using product-level panel dataset Brekke, Grasdal & Holmås, (2009) estimated the effects of RPS on drug prices to be negative both on brand-named (-18% to -19%) and generic drugs (-7 to -8%). Moreover, the results indicated that pharmaceutical products

[11] External Reference Pricing: Reference prices determined by average foreign prices.
[12] Internal Reference Pricing: Reference prices determined by average domestic prices.
[13] Drugs to treat high cholesterol. Highest selling product group in Denmark (Kaiser et al., 2014)
[14] Maximum reimbursement price is calculated using sales-weighted average prices of branded and generic products.
[15] In Norway, the price cap regulation was based on international price comparison of West-European countries.

left under the price cap regulation also saw negative price effects (-2.2%), implying a negative cross-price effect on therapeutic substitutes.

The negative cross-price effect implies that even if RPS promotes only generic competition, the presence of therapeutic competition can still put downward pressure on the prices of related products. The effect of negative cross-price was weaker than the direct price effect supporting an idea that generics are closer substitutes than branded products having only therapeutic equivalence [16]. (Brekke et al., 2009).

The fact that pharmaceutical products exhibit negative cross-price effects is important in the context of my thesis since we have to analyse products that are affected by the Finnish RPS and mandatory reserves system simultaneously. There might be price correlations between therapeutic substitutes that should be accounted for if possible in the empirical analysis.

Concalves & Rodriguez (2018) argue that under the RPS, the prices of pharmaceuticals increase with the copayment rate and they converge to fixed percentage reimbursement (FPR)[17] prices, as the co-payment level approaches one. In contrast, Brekke et al., 2007 find that prices are independent of the co-payment rate. Concalves & Rodriguez (2018) also find that while social welfare is always higher in the RPS when comparing to FPR, it decreases with the co-payment rate. The elasticity of demand assumption explains the results found in the research. If the copayment rate increases in FPR, the relative prices of pharmaceuticals faced by the consumer do not change, but in the RPS the relative prices change in favor to the more expensive, usually branded products. These findings imply that higher copayment rates lead to higher market prices in pharmaceutical products. From the social welfare standpoint, the higher co-payment rates lead to lower consumption and higher pharmaceutical expenditures, lowering social welfare. (Concalves & Rodriguez, 2018).

The reference pricing system emerges as a preferable reimbursement scheme. However, the interaction of demand elasticities and co-payment rate is complex, which leads to the possibility that higher co-payment rate (lower reimbursement rate) results in higher government expenditures (Concalves & Rodriguez, 2018).

The effects of RPS and extension of generic substitution[18] has been studied in Finland by Koskinen, Ahola, Saastamoinen, Mikkola & Martikainen (2014), by analysing the prices of antipsychotic drugs between 2006 and 2010, with a segmented linear regression model of interrupted time series[19].

Major decreases of -22.9 to -66.3 percent in prices were observed one year after the RPS was implemented. However, the price decreases were mostly due to generic substitution, and the additional cost savings achieved with RPS were

[16] Different chemical compounds, but similar therapeutic properties.
[17] In FRP government reimburses a fixed percentage on all pharmaceutical purchases.
[18]New products added to generic substitution system.
[19] Segmented regression model estimates separate regression equations with different intercepts (levels) and coefficients (trends). Koskinen et al. (2014) estimated the equations for the time before the policy change and the time after for each product group.

comparatively low. The study followed the prices of drugs that I) were already assigned to generic substitution program before 2006 II) were assigned to generic substitution in 2008 III) were introduced to generic substitution and RPS simultaneously in 2009. The lack of control groups in the analysis of Koskinen et al. (2014) yield possible biases and might leave the causal interpretation debatable. However, the results seem to corroborate several other studies combined with substantially large point estimates with clear graphical presentations makes the results convincing.

In 1989 Germany implemented a policy reform exposing the consumers to pharmaceutical prices by substituting a flat prescription fee with a maximum reimbursement rate, making it a classic RP-system[20]. Pavcnik (2002) analyses a panel dataset from Germany as a before-and-after study of the reform using the markets for two separate therapeutic groups (oral antidiabetics and antiulcerants). The data indicated that producers decreased prices significantly (10% to 26%) after the potential costs faced by the customer changed. The effects were more visible with branded products and even more so in product categories facing generic competition. The price drops were more significant for generic competition within the active ingredient than therapeutic substitutes. (Pavcnik, 2002). To be precise, the estimates of Pavcnik (2002) might include biases due to cross-price effects between control and treatment groups.

In Finland, pharmaceutical companies must report prices of their reference priced products, to Hila before each quarter. The information received from pharmaceutical companies is used to set the reference price and corresponding corridor for each group just like in the generic substitution policy.

The reference price is set for three months at the time, but the pharmaceutical companies can change their prices every two weeks. Changing the prices two times a month gives the companies some flexibility to respond to the changes in the markets. If pharmaceutical companies want their products to be reimbursed, they have strong incentives adjust their prices according to the reference price each quarter, since pharmacies are required to change prescribed products to cheaper alternatives if their price is above the price corridor.

Figure 5 illustrates the possible pricing behaviour of drugs competing at the beginning of a quarter (T) and two weeks after (T+1). First, the reference price is set according to the cheapest product within the reference group and in this case, product E, at 25 euros. Moreover, the price corridor is set to 25.5 euros illustrated by the two dashed blue lines.

Pharmaceutical companies have strong incentives to adjust their prices at the upper bound of the price corridor since the reimbursed amount is the same regardless of the price of the product within the price corridor. Some, usually

[20] The governing institutions set reference prices by first determining the therapeutic groups under the RPS and after that the reference prices, which were usually set below the most expensive brand, but above the generic prices. Between 1989 and 1996 the RPS slowly encompassed a larger portion of the pharmaceutical markets, reaching 75 percent by 1996. (Pavcnik, 2002.)

branded products, might not react to reference pricing easily due to a strong market position. In figure 5, product B represents a branded drug.

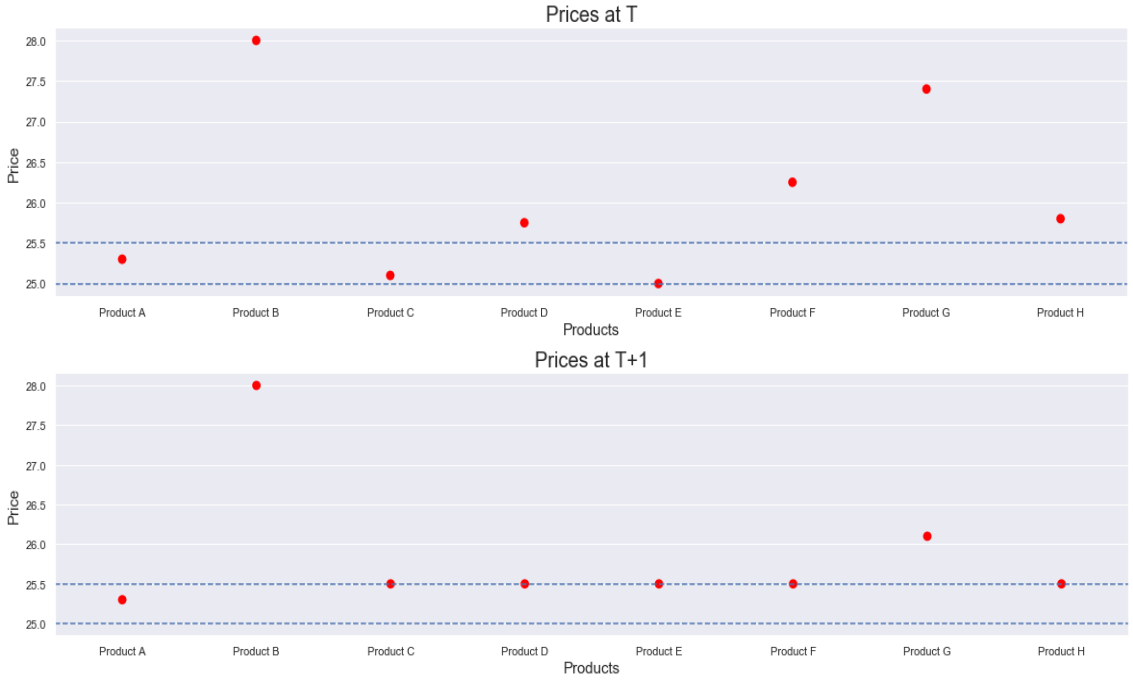


FIGURE 5: Pricing behaviour of pharmaceutical companies at the beginning of RP-period and two weeks afterwards.

# 3 MANDATORY RESERVES AND PRICING

In this chapter, the supply disruptions in pharmaceutical markets and their effects are explored. Furthermore, the legislation regarding the mandatory reserves system in Finland and how it seeks to prevent the supply disruptions from affecting consumers is analysed. To the best of my knowledge, Finland is the only country having enacted such legislation on pharmaceutical markets. Moreover, its effects on pricing the pricing of pharmaceuticals have not been studied in the field of economics.

Apart from Finland, several other national governments have recognized potential risks of supply disruptions in pharmaceutical markets and have implemented other measures to improve the resilience of drug supply.

## 3.1 Drug shortages and mitigation

Saedi et al. (2016) define drug shortage as a situation where the product is not available for consumption at all or in insufficient quantities to meet the demand. Even though pharmaceutical products' availability is considered excellent in Finland, the amount of supply shortages has skyrocketed in the past years. The implications of drugs not being available for customers in hospital or pharmacies are severe. The worst-case scenario could lead to a patient's death.

Human life has intrinsic value, and losing or incapacitating a patient due to inadequate pharmaceutical supply, inflicts substantial pecuniary costs for the whole society. Unavailability of pharmaceutical products can lead to prolonged patient treatment times and even some critical procedures being cancelled, such as surgeries (Landis, 2002).

In Finland, a drug shortage usually does not pose a critical danger to patients, since replacement products can be found easily. However, replacing an existing product with substitute takes time from medical professionals since they must devote time to research for alternatives (Saedi et al., 2016). The time spent on researching alternative treatments due to drug shortages is an indirect cost coming from supply problems. There are several cases in outpatient care, where finding an alternative drug takes time from medical experts. These isolated cases are easily brought up in the news, so it is hard to pinpoint exact costs from time lost by medical experts. One example can be found from YLE-news, where the process of finding a replacement drug is illustrated clearly (Toivonen & Tolkki, 2019).

In Belgium, hospital pharmacists spent a median of 65 [21] minutes each week solving problems related to drug supply. About 33% of the time was dedicated to information gathering regarding the supply problems and 66% of the supply problems caused by drug shortages. Drug shortages lead to pharmacists having to use their time to switch the initial drug used in the treatment to a therapeutic alternative. For most of the cases in Belgium, a replacement drug could be found, but the process takes time from other productive work. (De Weerdt, De Rijdt, Simoens, Casteels & Huys, 2017.)

Drug shortages are causing problems globally, and results from multiple surveys indicate substantial effects for the health care sector. Results from Europe, in general, show that around 1 to 15 hours per week is spent finding solutions to supply disruptions. Furthermore, in the United States, the pharmacists spent approximately 9 hours per week solving problems related to drug shortages (De Weerdt et al., 2017).

In Finland, the amounts of drug shortages have been increasing despite the implementation of the mandatory reserves system. Figure 6 illustrates the development of drug shortage notifications received by Fimea between 2010 and 2019. The shortage notifications went from about 100 per year in 2010 to more than 1200 per year in 2018. The data presented in figure 6 is collected until mid-2019, meaning that the total amount of drug shortage notifications most likely increase between 2018 and 2019.

It seems that even with the mandatory reserves system, the shortage-notifications have increased significantly. There could be multiple explanations for the increases in the drug shortages; the vigilance of pharmaceutical companies might have increased, explaining some of the increases in notifications. However, other countries have reported similar observations about increases in shortages that corroborate with the data received by Fimea. In an example, the United States reported that shortages tripled from 2010 to 2015 reaching a yearly level of 300 (Bocquet, Degrassat-Théas, Peigné, Paubel, 2017).

[21] Totally a median of 109 minutes were spent, but pharmacy technicians and logistic personnel handled some of the work.

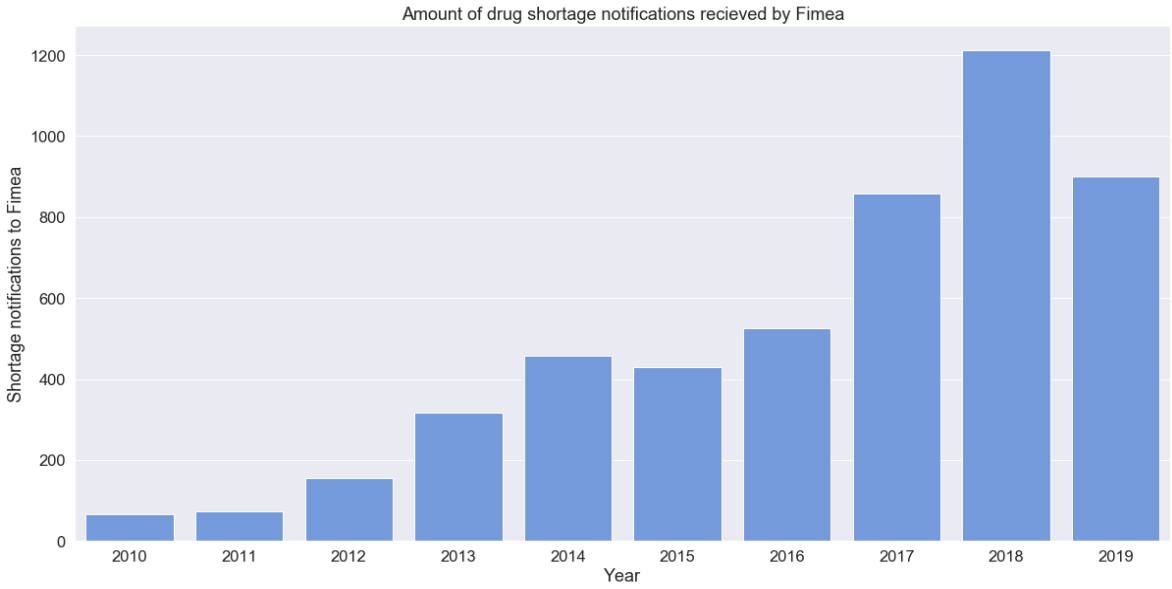


FIGURE 6: The amount of drug shortages seems to be increasing. The amount for 2019 is based on reported shortages from January to July. (Fimea, 2019)

Heiskanen et al. (2017) study the underlying reasons behind drug shortages from the perspective of pharmaceutical companies and wholesalers in Finland. Their study included a semi-structured interview for 41 companies and wholesalers in 2016. The interviewees were asked about the pharmaceutical markets in Finland and how do they differ from other countries. Moreover, the interviewees were asked if there are some market characteristics specific to Finland that might affect the availability of drugs. The final topics of the interviews were centred around the availability of pharmaceutical products in Finland and the reasons behind shortages (Heiskanen et al., 2017).

Thematic analysis of the interviews revealed that the reasons for drug shortages in Finland are due to:

1. Small market size (29 of the 30 interviewees)
    - The volumes marketed in Finland were considered small and thus leaving Finland more open to shortages.

2. Stochastic and fluctuating demand (28/30)
    - Supply shortages faced by competitors can suddenly increase demand for other companies.
    - Seasonal fluctuations were also identified as a challenge.

3. Small stock size in all parts of the supply chain (25/30)
    - A quote from the interview suggests that pharmaceutical companies do not want to tie up their capital in stocks and inventories, but to invest it in other more profitable endeavours.
    - Warehousing costs in Finland were regarded as higher than in some European countries.

4. Long delivery times from headquarters (23/30)
    - Long and varying delivery times leaves wholesalers to forecast the demand further into the future.

5. Dependence of foreign manufacturing (22/30)
    - Domestic manufacturing reduces risks when facing global supply disruptions.
    - Foreign supply was also considered one reason for long and complex supply chains.

6. Mandatory reserves supply (13/30)
    - Mandatory reserves supplies were mentioned by 13 of the 30 interviewees, which meant 16th place on the list of most mentioned causes for drug shortages.
    - Mandatory reserves supply was identified as a problem, especially in hospital trade markets.

(Heiskanen et al., 2017).

Mostly the drug shortages are due to problems in the supply side than the demand[22]. The underlying reasons for the shortages were complex, and more than one cause was usually identified simultaneously. (Heiskanen et al., 2017.)

It seems unlikely that pharmaceutical companies are incapable of predicting seasonal fluctuations in the long run. Still, it seems reasonable that supply disruptions for other companies are not possible to predict, which eventually could result in stochastic demand when some companies face increasing demand due to supply problems of other companies.

Intriguingly, small stock sizes were identified as a significant problem, yet mandatory reserves system was also mentioned as one cause of supply disruptions. The mandatory reserves system was identified as a problem specifically in the hospital markets (Heiskanen et al., 2017). The mechanism between drug shortages and mandatory reserves system might only exist in hospital markets, which, unfortunately, is left out of the context of this thesis. Hospital markets and pharmacy markets operate very differently, so it is not possible to draw definite conclusions from hospital markets to pharmacy markets or the other way around.

[22] Demand problems, in this case, mean substantial unpredictable fluctuations in demand

Hospital markets have a tendering process between the supplier and several hospitals belonging to the same hospital districts. Winning the tender means supplying drugs to multiple hospitals suddenly and covering the mandatory reserve requirements simultaneously. The sudden increase in demand is seen as problematic in the case of hospital markets. (Heiskanen et al., 2017.)

In my opinion, pharmaceutical companies most likely optimize their stocks in order to maximize profits and therefore find lost sales and dents to their reputation a smaller price to pay, than the possibility of larger safety stocks, at least in Finland. Also, it would seem reasonable that small stock sizes are something that could be solved by regulatory processes or by incentivizing pharmaceutical companies to operate more efficiently from the perspective of the whole society by internalizing the benefits of robust supply to the profits received by pharmaceutical companies.

Heiskanen et al. (2014) study the drug shortages in the context of community pharmacies in Finland during the year 2013. Researchers examine randomly selected pharmacies during 27 days period and find that almost 79.8% of the pharmacies experienced drug shortages almost daily. Moreover, the drugs showing shortages in supply were medicines for the nervous system (30.8%) and cardiovascular system (17.5%). Only in 11.2% of the cases, the reason behind the supply shortage was reported to the pharmacies, and the shortages caused problems to pharmacies in 33% of the cases, because usually, a therapeutic substitute was available. The medicines facing supply shortages are drugs used commonly in outpatient care (Heiskanen et al., 2014).

Since drug shortages are a global phenomenon, governments have implemented several policies to avoid them. The French government, for example, implemented coercive measures to prevent shortages of drugs with major therapeutic interest in 2016. The policy included strict information-sharing requirements and exporting restrictions for drugs undergoing shortages. Furthermore, the community and hospital pharmacies are able to adjust their supply chains until the supply returns to normal. Moreover, financial sanctions could be imposed for companies not following the statutory instructions after 2016. (Bocquet, et al., 2017.)

## 3.2 Mandatory reserves legislation

The mandatory reserves system was originally implemented in Finland in 1984. The legislation was adjusted six times before it faced a larger overhaul and was replaced by a new law in 2009. (Mandatory reserves act of pharmaceuticals, 402/1984).

The legislation was implemented to protect the Finnish pharmaceutical services from supply disruptions and to increase the resilience of the domestic pharmaceutical markets. All pharmaceutical producers and importers, who are

producing or importing drugs specified by the legislation, are subjected to mandatory reserves system. The amounts of mandatory reserves are determined by the demand of the previous year of a pharmaceutical product. (Law for the mandatory reserves of pharmaceutical products, 2008/976).

Figure 7 illustrates the process of assigning the pharmaceutical products to the mandatory reserves system. First, the legislation is passed by the Finnish parliament and the pharmaceutical product groups are outlined in legislative texts with the corresponding sizes of safety storages. Afterwards, the Council of State determines the active ingredients according to the legislation. Finally, Fimea publishes a list of individual products required to have mandatory reserves. (Law for the mandatory reserves of pharmaceutical products, 2008/976.)

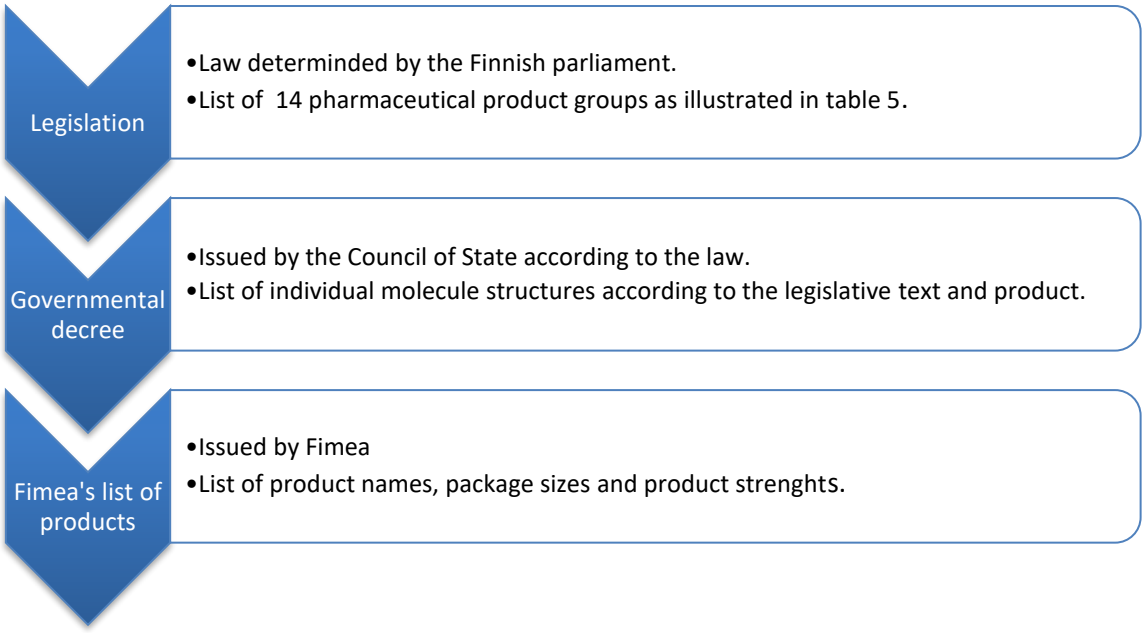


FIGURE 7: The hierarchical decision-making setting individual products to the mandatory reserves system.

Pharmaceutical products assigned to the mandatory reserves system are determined by several crucial characteristics that might have an effect on their supply and demand, or due to their importance to the Finnish health care system. The relevant features of the products are listed as follows:

- Critical products necessary in life-saving treatments
- Crisis-specific products, whose demand drastically increase in a crisis.
- Products having only one or a few producers
- Irreplaceable products, which cannot be replaced by another active substance or manufacturer or by a change in method of treatment
- Import-dependent products, especially those manufactured outside of EU

- Rare products, which are needed in biological, chemical or radiation emergencies, and are not stored through normal sales or consumption.
- Products needed in global crises situations, for which the global supply cannot react.
- Strategic products that national states would stockpile, when a serious disruption is imminent, e.g. field medicals.

Pharmaceutical products assigned to MRS are divided into 14 groups based on the conditions they are designed to treat. Each group contains several active substances designed to treat specific conditions. The groups specified in the legislative text of 2009 are presented in Table 5.

TABLE 5 The 14 different mandatory reserves groups.

| | |
|---|---|
| 1) | Antimicrobials, antibiotics, sulfoamides and other synthetic antimicrobials |
| 2) | Medicinal products for electrolyte, fluid imbalance and parenteral nutrition solutions, nutritional solutions and albumin solutions |
| 3) | Medicines for cardiovascular disease and diuretics medicines for angina pectoris, medicines for heart failure and arrythmias, medicines for hypertension and diuretics |
| 4) | Medicinal products for the treatment of metabolic and endocrine disorders, antidiabetic and thyroid drugs, and corticosteroids |
| 5) | Antirheumatic and antipyretic drugs: Morphine derivatives and antipyretic analgesics. |
| 6) | Medicines for local anaesthesia and general anaesthesia |
| 7) | Medicines for poisoning, vaccines, immunosera and immunoglobulins essential for the treatment and prevention of hepatitis A and B, rheumatoid arthritis and tetanus, and human normal immunoglobulin. |
| 8) | Asthma medications for respiratory diseases |
| 9) | Medications for the treatment of gastrointestinal ulcers. |
| 10) | Medications for the human psyche: Antipsychotics, neuroses and depression |
| 11) | Anti-epileptics and antiparkinsonian drugs |
| 12) | Ophthalmic drugs for glaucoma and ocular antimicrobial agents |
| 13) | Anticancer drugs and drugs for the treatment of their side effects, immunostimulants, immunosuppressants, antithrombotic drugs and hemostats |
| 14) | Veterinary medicinal products such as rabies vaccines and medicinal products for the treatment of food-producing animals and for the treatment or prevention of disease. |

The 14 storage groups presented in table 5 require different amounts of safety stocks to satisfy the obligation for mandatory reserves. According to current legislation, the pharmaceutical products in groups 1 and 2 require storages equal to the average consumption of 10 months. Groups 3-6 must satisfy the

demand for 6 months, and groups 7-14 must satisfy the average demand of three months.

The average monthly consumption levels are calculated using the consumption information from March and April of the previous year. Each stockholding obligation period lasts for a calendar year, but if the demand of a pharmaceutical product increases or decreases 30 percent the subject is obliged to adjust his stocks accordingly (Law for the mandatory reserves of pharmaceutical products, 2008/976).

Table 6 illustrates the required amount of storages from each storage group in the mandatory reserves system before and after the policy change of January 2009. For groups 1 and 2, the storage amounts did not change. However, for groups 3 and 4, the storage obligations increased 20 percent, for groups 7 to 10 and 13 the storage obligation decreased for 70 percent and finally for groups 11, 12 and 14, the storage amounts decreased for 40 percent. Several pharmaceutical products were added to each group during the policy change. However, some products were excluded from the system.

TABLE 6 Storage obligation amounts for individual product groups

| **Product Group** | **Before January 2009 Average consumption in months in storages** | **After January 2009 Average consumption in months in storages** |
|---|---|---|
| 1 | 10 | 10 |
| 2 | 10 | 10 |
| 3 | 5 | 6 |
| 4 | 5 | 6 |
| 5 | 5 | 6 |
| 6 | 5 | 6 |
| 7 | 10 | 3 |
| 8 | 10 | 3 |
| 9 | 10 | 3 |
| 10 | 10 | 3 |
| 11 | 5 | 3 |
| 12 | 5 | 3 |
| 13 | 10 | 3 |
| 14 | 5 | 3 |

The storage obligation is in effect only when the product has a trading license in the Finnish markets. Furthermore, if the product license is going to expire, the owner of the license is allowed to start emptying the stocks for 10 months before the expiration date.

Pharmaceutical companies subjected to the mandatory reserves system are entitled to pecuniary compensation from the National Emergency Supply Agency of Finland (NESA). The compensation is paid each year, and

pharmaceutical companies must apply for the compensation by sending an application to NESA. The amount of compensation is calculated using the committed capital in the mandatory reserves augmented with the interest rate of the Bank of Finland (BoF) plus two or four percent depending on the product in question (National Emergency Supply Agency, 2019).

$$Compensation = \begin{cases} Committed\ capital * (BoF + 2\%), for\ all\ products\ except\ infusions \\ Committed\ capital * (BoF + 4\%), for\ infusions \end{cases} \quad (1)$$

In the context of this thesis, there could exist a mechanism on how the mandatory reserves system affects the pricing of pharmaceutical products through cost structure. Firstly, the sizes of storages required[23]; larger storages increase the overall costs of the supply chain, and pharmaceutical companies might internalize those costs by increasing the wholesale prices they would be willing to participate the Finnish markets. Secondly, the interest rate of BoF and the amount of compensation paid by NESA. Large compensations could mean that pharmaceutical companies' net costs of keeping safety stocks are close to zero or even negative. If the compensations paid by NESA would be larger than the total costs of keeping safety stocks, in theory, prices may even decrease.

According to NESA, the total value of yearly mandatory reserves is about EUR 200 million, and pharmaceutical companies are reimbursed from 3 to 6 million each year for the costs of managing larger stockpiles (Pihlava, 2017).

The policy change in January 2009 gives an interesting study design since several changes were made at the same time. The sizes of storages were changed between several groups and new products, and new active ingredients were included in the governmental decree. In the empirical section in the next chapter, the effects of MRS are estimated using the price information of pharmaceutical products newly introduced to the system.

[23] Sizes of storages are measured by months-worth of consumption the safety stocks have to suffice without any supply.

# 4 DATA AND METHODOLOGY

The dataset used in this thesis is compiled from several different sources in order to acquire adequate information about mandatory reserve statuses and pricing information for each pharmaceutical product. Some parts of the data were in pdf-form, which lead to manual work before statistical analysis was possible.

To estimate the effects of mandatory reserves system on prices, the difference-in-differences (DD) estimation method is used. This chapter will discuss the methods used to link information between the available datasets and possible caveats of the data that potentially bias the results. Moreover, the theory behind the DD-estimation method is discussed with other methodologically relevant approaches for this thesis.

## 4.1 Sources of data

The main dataset for this thesis was acquired from the Association of Finnish Pharmacies (price data), which includes wholesale and retail prices of all pharmaceutical products sold in Finnish pharmacies between 2004 and 2018. Price observations are reported two times a month for each product. The price data also includes information about which products are assigned to the reference pricing system and generic substitution programs, making it possible to control their effects.

For each product, the price data includes a unique product code called the Nordic Article Number (vnr-number[24]), identifying each product all the way to the package size information. Any changes in the pharmaceutical product require a new vnr-number, and therefore any price-affecting changes in product level can be controlled.

The second dataset was constructed from Fimea's lists of pharmaceutical products assigned to MRS (storage data), which is published usually once a year. The storage data is compiled according to the mandatory reserves act and Council of State Decrees for pharmaceutical companies and stakeholders. According to Fimea, the storage data is only indicative, but not exhaustive, meaning that products can be in the mandatory reserves system, but not mentioned by Fimea's list. Depending on the year, there are about 900-1500 products listed as having a storage obligation.

Lists of products assigned to MRS are available in machine-readable form after January 2009 and in pdf-form the years before. Storage data include variables for the storage group, ATC-code (after 2009), active ingredient, product name, products strength, dosage form, and the marketing authorization holder.

[24] An identification code including six digits (000001-199999 and 370000-599999).

Unfortunately, the storage data do not include VNR-codes making the linking of datasets cumbersome.

Since the storage data might be defective, the Council of State Decrees are used as a secondary method to identify products required to have mandatory reserves. The Council of State Decrees contain lists of active ingredients assigned to the mandatory reserves system. By comparing the lists before and after the policy change, it is possible to identify novel compounds assigned to MRS. Appendix 3 presents the list of active ingredients collected from the Council of State Decrees before and after the policy change.

## 4.2 Data preparation

Several different methods can be used to identify drugs belonging to MRS from the price data. First, the active ingredients from the storage data are used as a link between the datasets. This method is rather fast since the data after January 2009 is in machine-readable form and manual work is only needed to match active ingredients from the periods before the policy change. However, several combinations of active ingredients cannot be matched; e.g., ibuprofen is used separately and as a combination-ingredient with codeine in the price data, but the storage data only displays the active ingredients as either ibuprofen or codeine. The inclusion of ATC-codes[25] would have solved the problem, but unfortunately, variable for ATC-codes is not available in storage data before January 2009.

As a second method, product names are used from the storage data, and relevant matches for each product are linked to the price data. This method is more reliable but time-consuming since each product has to be confirmed separately.

Finally, the Council of State Decrees are used to compile information about the active ingredients assigned to the mandatory reserves system. With the lists of active ingredients, it is possible to find matches from the pricing data and assign products to the proper storage groups.

With all of the methods used, more drugs are classified to MRS, than the original storage data of Fimea explicitly mentions, which indicates a possible bias in the regression results. However, as mentioned earlier, Fimea's dataset might not include all the products assigned to the MRS. Other possible explanations for the mismatch could be that some products are priced without any actual sales in Finland. Furthermore, some products could represent such an insignificant part of the total pharmaceutical sales that they get an exemption from the mandatory reserves system. Moreover, pharmaceutical companies can also store the raw materials needed to produce the drug specified in the Council of State decrees. In

[25] Appendix 1 provides more detailed information about the ATC-system.

this case, the raw materials must be stored inside the borders of Finland, and there needs to be proof that the Finnish medical industry would be able to produce the drug if its availability is otherwise compromised. It is unclear how many drugs get an exemption from Fimea due to special circumstances mentioned here.

All the methods used to link information between the datasets seem to produce similar results when applied to the regression model. This could indicate that the bias cannot be removed with the datasets available for this thesis or that there is no significant bias in the first place.

After the datasets are linked, dummy-coding is used to express each product's mandatory reserves status in a given time. A value of one is assigned for products in the mandatory reserves system and a value of zero for other products. Moreover, for the DD estimation, a variable indicating treatment is created by assigning a value of one for new products added to the MRS after the policy change in 2009. By adding the treatment variable, the control groups can be separated from the treatment groups. Finally, dummy-coding is used to separate the periods before and after the policy change, by assigning a value of one indicating periods after the policy change and a value of zero indicating periods before the policy change.

Since the reference pricing system was implemented almost simultaneously with the mandatory reserves policy change, the effects of MRS are estimated separately for products in the reference pricing system and outside of the reference pricing system. Dummy-coding is used to express the reference pricing status for each product, by assigning a value of one for products introduced to the reference pricing system and zero otherwise.

The wholesale prices will be set as the dependent variable since Finnish legislation fully controls the retail prices[26]. For each price observation, a natural logarithm is taken to account for the fact that prices are not normally distributed and to increase the interpretability of the regression coefficients. Finally, any veterinary medicines are excluded by deleting observations having an ATC-code indicating treatment for animals.

Each regression model is run with a balanced panel data meaning that products entering or exiting the markets are excluded from the analysis during. Exiting or entering products might have different pricing strategies than incumbent products, which might affect the results. In practice, each vnr-number must have a price observation in every pricing period in the dataset used for analysis.

Table 7 presents descriptive statistics in the treatment and control group for products that were assigned to the reference pricing system. The treatment group consists of 335 individual products, while the control group consists of 1073 individual products with different vnr-numbers. Comparison of mean prices between the treatment and control group indicates that products between the two groups are fairly similar, making the comparison between groups reasonable. However, the control group has substantially higher variation in prices

[26] Appendix 5 includes details about the pharmacy price control.

compared to the treatment group, indicating that the control group might consist of a very homogeneous set of products.

TABLE 7 Descriptive statistics of products assigned to reference pricing system

| | Control Group 1<br>Mean (SD) | Treatment group 1<br>Mean (SD) |
|---|---|---|
| Wholesale price | 16.47<br>(31.98) | 14.79<br>(18.57) |
| Log of wholesale price | 2.97<br>(1.29) | 2.21<br>(0.95) |
| Min wholesale price | 0.53 | 0.62 |
| Max wholesale price | 372.78 | 191.74 |
| ATC-4 groups | 75 | 15 |
| Number of products | 1074 | 335 |
| T (Number of time periods) | 50 | 50 |
| N (Number of observations) | 53 700 | 16 750 |

Table 8 in turn presents descriptive statistics for the treatment and control groups outside of the reference pricing system. The prices are higher in the control group, which can be explained by the fact that the products not assigned to reference pricing have existing patents, meaning higher market power and higher prices. Moreover, the control group possibly includes some special products sold for rare condition, which can be seen from the large difference in maximum prices in the descriptive statistics between the two groups.

TABLE 8: Descriptive statistics of products not assigned to reference pricing system

| | Control Group 2<br>Mean (SD) | Treatment group 2<br>Mean (SD) |
|---|---|---|
| Wholesale price | 139.93<br>(465.95) | 68.48<br>(126.61) |
| Log of wholesale price | 3.29<br>(1.68) | 3.37<br>(1.28) |
| Min wholesale price | 0.5 | 1.24 |
| Max wholesale price | 10 336 | 1 134 |
| ATC-4 groups | 459 | 51 |
| Number of products | 3 748 | 558 |
| T (Number of time periods) | 50 | 50 |
| N (Number of observations) | 187 400 | 27 900 |

## 4.3 Identification strategy

Prices of pharmaceutical products in treatment groups are compared to the prices of pharmaceutical products in control groups before and after the policy change to estimate the causal effects of MRS. More specifically, the average changes in the mean of the log prices between the groups before and after the policy change are compared by using the difference-in-differences estimation method.

The treatment group consists of pharmaceutical products newly included in the MRS after January 2009, while the control group consists of pharmaceutical products not assigned to MRS. Identification relies on the assumption that the prices of pharmaceutical products in the treatment group would have developed similarly compared to the control group in the absence of the treatment. In other words, the prices of the pharmaceutical products in the control group are used as a counterfactual for the treatment group's prices in the imaginary situation, where the treatment was never implemented. Because the reference pricing system was implemented almost simultaneously with the MRS, the analysis is performed by estimating the effects of MRS separately for products assigned and not assigned to the reference pricing system.

The assignment of new pharmaceutical products to the MRS should be random to draw a strong causal relationship between prices and mandatory reserves system. In this case, however, the treatment is weakly exogenous, since the products in the treatment group have a higher risk for supply disruption and are seen as more critical for the healthcare system than products in the treatment group. In other words, the characteristics of the products are determining treatment statuses, and the characteristics posed by the pharmaceuticals assigned to the MRS may affect the pricing in a way that cannot be controlled.

The fact that pharmaceuticals are systematically assigned to the treatment group implies that study design is not very reliable, and the results presented should be interpreted with caution. Nevertheless, the primary identifying assumption for the DD estimation is the parallel trends of the dependent variable in the pre-treatment period, which holds up in this study's context. Visual evidence of parallel price trends can be confirmed from figures 8 and 9.

In figure 8, the orange line represents the mean log prices of pharmaceutical products not assigned to the MRS nor to the reference pricing system (control group). The blue line represents the mean log prices of products assigned to the MRS, but not to the reference pricing system (treatment group). The prices of treatment and control groups had identical trends in the pre-treatment period, and shortly after the policy change, the prices of the treatment group started to decrease, while the prices in the control group continued similarly compared to the pre-treatment period.

In figure 9, the orange line represents the mean log prices of pharmaceutical products assigned to the reference pricing system, but not to MRS (control group). The blue line represents the mean log prices of pharmaceutical products assigned to both the reference pricing system and MRS (treatment group). Once

again, the price trends are identical before the policy change, and immediately after the treatment, the treatment group's price trend deviates from the control group. To both figures, red dashed lines are added to represent time, when the reference pricing system reached the Finnish parliament for discussion and when it was finally implemented. Furthermore, blue dashed lines are added to represent the same for mandatory reserves system's policy change.

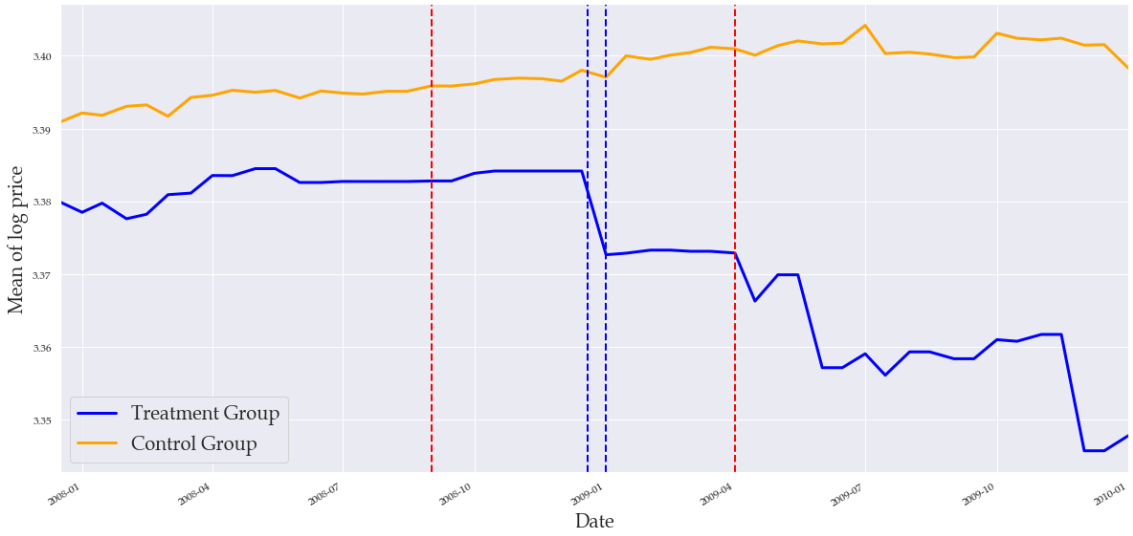


FIGURE 8: Mean log prices of non-reference-priced products in the treatment and control group

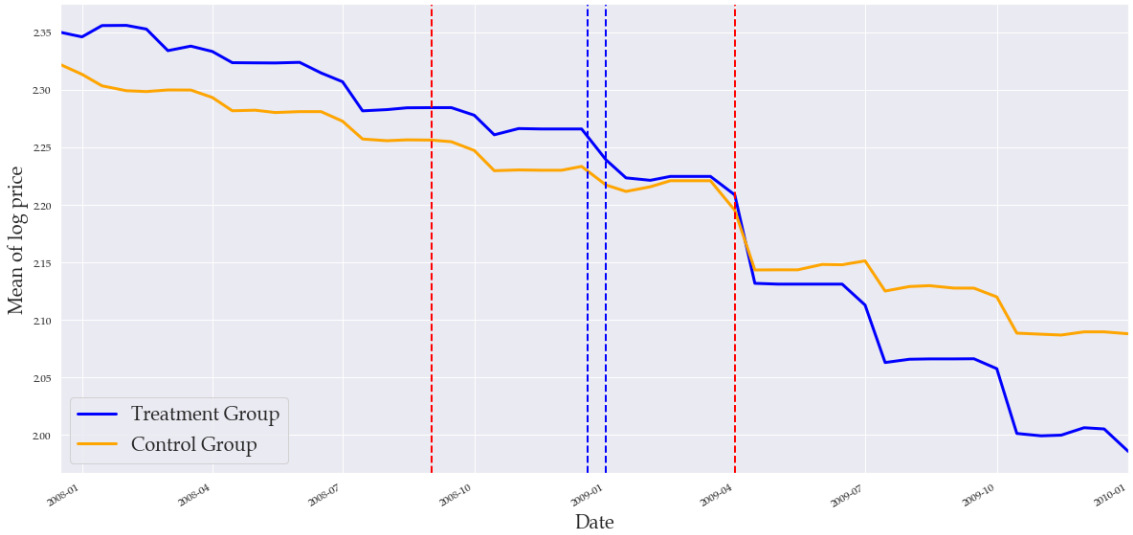


FIGURE 9: Mean log prices of reference priced products in the treatment and control group

I assume that even though the pharmaceutical products are inherently different between the treatment and control groups, their similar price trends of the pre-treatment period would have continued in the absence of the treatment during the post-treatment period. The common price trend in the absence of treatment is the primary identifying assumption in the DD model. Furthermore, I assume that the treatment did not affect the control group in the post-treatment period.

As mentioned before, the reference pricing system was implemented right after the mandatory reserves system and thus potentially mixes up the results. However, the effects of RPS can be controlled by comparing drugs assigned to the RPS and drugs that were not. With the dataset acquired for this thesis, it is possible to reliably identify the drugs assigned to the RPS and thus control its effects in the regression analysis.

## 4.4 Difference-in-differences

The difference-in-differences method has become a widely accepted method for estimating causal relationships in social sciences. In essence, the DD estimation compares the outcome variable between a group that is affected by treatment (treatment group) and a group that is not affected by the treatment (control group) at periods before and after the treatment is implemented. By comparing the treatment and control groups' differences in the outcome variable before and after the treatment, it is possible to extract the causal effects of a policy change of interest. (Bertrand, Duflo, & Mullainathan, 2004.)

The DD-method has been previously used, e.g. by Brekke, Holmas & Straume (2011) and Ghislandi, Armeni & Jommi (2013) to estimate the effects of reference pricing and generic substitution policies, meaning that the method has been validated in peer-reviewed academic studies that estimate the price effects of policies in pharmaceutical markets.

However, the DD model has limitations, and if not used properly, the results could be biased. Firstly, if the assignment to treatment is not random, the model might suffer from endogeneity bias which is the most common problem in DD models. In this thesis, the endogeneity of the treatment potentially biases the results because the assignment to the MRS is not random even though it is decided by the Finnish government and not by pharmaceutical companies. In other words, the characteristics of a pharmaceutical product determine the assignment to the treatment, as is mentioned in chapter 3.

The DD estimation method also requires that the policy studied should not affect the control group in any way, but in the context of this thesis, it might not be the case. As mentioned by Brekke et al. (2009) and Brekke et al. (2011), pharmaceutical products might exhibit cross-price elasticity, meaning that prices

could be correlated across therapeutic competitors. Primarily due to the implementation of the reference pricing system almost simultaneously with the MRS, we could see the reference pricing system affecting the prices of other products in a way that cannot be controlled.

Furthermore, the pharmaceutical prices exhibit serial correlation, which also could bias the results if not accounted for properly. Clustered standard errors are used at ATC-4 level, meaning that the model presented in this thesis accounts for the possibility of similar products having price correlation and the serial correlation between time periods. The correlation of prices for different products is possible between substitutable products, and ATC level is a good indicator of the substitutability between products.

## 4.5 Clustered standard errors and fixed effects

As mentioned by Brekke et al. (2009), pharmaceutical prices are possibly correlated between product groups. In the context of this thesis, the products assigned to control and treatment groups might not exist in separated markets, and thus prices of products in mandatory reserves system might be affected by the prices of products outside of the mandatory reserves system and vice versa. Moreover, the prices of pharmaceuticals exhibit serial correlation, meaning that pricing at time T affects the pricing at T+n. Especially due to implementation of RPS the effects of price correlation could affect the results of my analysis.

Bertrand et al. (2004) note that serial correlation is a well-understood phenomenon, but often ignored in empirical studies using DD estimation method. If standard errors are not adjusted to account for serial correlation, the null hypothesis[27] might get rejected too easily. By generating datasets using Monte Carlo methods and implementing DD estimation to randomly created policy-changes (which do not have any real effects), Bertrand et al. (2004) find that if standard errors are not adjusted accordingly, statistically significant effects can be found, for policy changes that did not even exist. Fortunately, serial correlation can be accounted for by estimating clustered standard errors and thus adjusting the confidence intervals of the model.

Abadie, Athey, Imbens & Wooldridge (2017) point out that the clustering should not be done in an unnecessary aggregated level so that the confidence intervals would not be over-inflated and lead to exceedingly conservative standard errors. Furthermore, Abadie et al. (2017) argue that if the assignment mechanism to treatment is clustered, the clustering of standard errors should be appropriate. However, even if clustering of standard errors has an impact on the confidence intervals, which it usually does, the clustering should be carefully justified by substantive knowledge of the topic under study.

[27] The null hypothesis in this thesis is that the mandatory reserves system had no effect on prices.

Abadie et al. (2017) also mention that heterogeneity of treatment effects is another possible reason to cluster standard errors. In this thesis, the pharmaceutical products are exposed to different storage groups with different amounts of minimum storage size obligations, meaning that the intensity of treatment varies between groups.

In the context of this thesis, the Council of State Decrees assign pharmaceutical products to mandatory reserves system using the active ingredients meaning that the treatments statuses for each product is determined simultaneously for a cluster of pharmaceuticals making the assignment to treatment process for a pharmaceutical product conditional on belonging to a certain cluster of products. The regression models in this thesis are run with clustered standard errors at ATC-4 level to account for the serial correlation in prices across time and price correlation between generic and therapeutic competitors.

Each pharmaceutical product has unique characteristics that possibly affects the pricing decisions of pharmaceutical companies, which might leave the regression model to suffer from omitted variable bias. For the regression analysis in this thesis, the omitted variables are assumed to be constant over time for each product and thus could be controlled by using product-level fixed effects. Assuming product level omitted variables to be constant over time, but varying between products is realistic since each product requires a new vnr-number when changes to the product are made. Any relevant changes made to the products would be captured by the change in vnr-number. By running regression models with product-level[28] fixed effects, all the time-invariant omitted variables are eliminated at the product level.

Moreover, the prices of pharmaceuticals might be affected by time-varying phenomena that affect all products similarly. For example, in 2006 and 2013 the wholesale prices of pharmaceuticals sold in Finland were cut by five percent. These time-varying and product-invariant changes could have substantial effects on the results. Fortunately, these effects can be controlled by using time fixed effects, in essential by estimating a coefficient for time dummies for each pricing period in the dataset.

To implement fixed effects to the regression model, let us write the following equation:

$$E\ (Y_{0it}|A_i\ , X_{it}, t, D_{it}) = E(Y_{0it}|A_i\ , X_{it}\ , t), \qquad (1)$$

in which $X_{it}$ represents a vector of observed time-varying covariates, $Y_{it}$ is a variable representing the outcome for the price of pharmaceutical product *i* on time *t* and $A_i$ represents a vector of unobserved, but fixed confounders for product *i*. $D_{it}$, in turn denotes, if the pharmaceutical product *i* belongs to mandatory reserves system at time *t*. As mentioned before, in fixed effects model, the

[28] Each vnr-number represents a unique product, so product-level fixed effects are also vnr-number fixed effects.

unobserved confounders are assumed to be time-invariant and hence $A_i$ presented without time subscript *t*. Following (1), we get

$$E(Y_{0it}|A_i, X_{it}, t) = \alpha + \lambda_t + A'_i\gamma + X'_{it}\mu, \quad (2)$$

Assuming, that the causal effect of mandatory reserves system is additive and constant, we can estimate the following model:

$$E(Y_{1it}|A_i, X_{it}, t,) = E(Y_{0it}|A_i, X_{it}, t) + \rho D_{it} \quad (3)$$

Combining (2) and (3) together we get:

$$E(Y_{it}|A_i, X_{it}, t, D_{it}) = \alpha + \lambda_t + \rho D_{it} + A'_i\gamma + X'_{it}\mu \quad (4)$$

In equation (4), $\rho$ represents the causal effects of mandatory reserves system, which is also the variable of interest in this thesis. Equation (4) can also be presented in different form:

$$Y_{it} = \alpha_i + \lambda_t + \rho D_{it} + X_{it}\mu + \varepsilon_{it}, \text{ where} \quad (5)$$

$$\varepsilon_{it} \equiv Y_{it} - E(Y_{0it}|A_i, X_{it}, t) \text{ and} \quad (6)$$

$$\alpha_i \equiv \alpha + A'_i\gamma \quad (7)$$

In equation (5), we have the basic fixed effects model, where product level fixed effect term, $\alpha_i$ and the time effect[29] ($\lambda_t$) are treated as parameters to be estimated. The product level unobserved, but fixed characteristics are treated as coefficients for product dummies and time effects are treated as coefficients for time dummies. (Angrist & Pischke, 2008.)

Dummy-coding for each product and time period would lead to a computationally expensive model, where the number of estimated parameters would be too large to handle. Fortunately, there exists an algebraically equivalent method called demeaning, where each product's price observations through time are compared to its mean. (Angrist & Pischke, 2008.)

Firstly, individual means for each product is calculated:

$$\bar{Y}_i = \alpha_i + \bar{\lambda} + \rho \bar{D}_i + \bar{X}_i\mu + \bar{\varepsilon}_i \quad (8)$$

If equation (8) is subtracted from (5) the following form is established:

$$Y_{it} - \bar{Y}_i = \lambda_t - \bar{\lambda} + \rho(D_{it} - \bar{D}_i) + \mu(X_{it} - \bar{X}_i) + (\varepsilon_{it} - \bar{\varepsilon}_i) \quad (9)$$

[29] Time effects, in this case are estimated for each pricing period (two times a month).

By using demeaning, the individual unobserved effects ($\alpha_i$) are eliminated or in other words, absorbed, and the model can be estimated without coefficients for each product dummy (Angrist & Pischke, 2008).

To sum up, the regression models presented in the next subchapter include unit fixed effects to control for unobserved product-specific, but time-invariant confounders and time fixed effects to control for time-specific, but unit-invariant confounders[30].

## 4.6 The model for estimation

Let $Y_{ist}$ be the log of price of a pharmaceutical product *i* in group *s* and time *t*, where *s* specifies if a product belongs to treatment or control group. Moreover, let $D_{st}$ be a dummy-variable getting a value of 1 if product *i* belongs to the mandatory reserves system at time *t* and otherwise a value of 0. $Y_{ist}$ is either observed as $Y_{i0t}$ or $Y_{i1t}$ , meaning a product will be either assigned to mandatory reserves system or not.

$Y_{i0t}$ = Log of price of a pharmaceutical product at time *t* if product *i* is not assigned to mandatory reserves system (*s*=0).
$Y_{i1t}$ = Log of price of a pharmaceutical product at time *t* if product *i* is assigned to mandatory reserves system (s=1).

Only one of the potential outcomes can be observed for a given product since it is impossible to observe a product both being assigned and not assigned to mandatory reserves system simultaneously. If a product is not assigned to mandatory reserves system, we can assume the following in a DD setup due to additive structure:

$$E(Y_{ist}|s = 0, t) = \gamma_s + \lambda_t \quad (10)$$

Equation (10) establishes that the log of price of a pharmaceutical product in the absence of mandatory reserves system is the sum of a time-invariant product group effect ($\gamma_s$) and a common time period effect across products ($\lambda_t$). (Angrist & Pischke, 2008).

Next, let us introduce the dummy variable $D_{st}$ for products assigned to mandatory reserves system. By assuming that the effect of mandator reserves system ($E[Y_{1it} - Y_{0it}|t]$) can be denoted with a constant $\beta$, the following equation can be derived:

$$Y_{ist} = \gamma_s + \lambda_t + \beta D_{st} + \varepsilon_{ist}, \quad (11)$$

[30] This method is also known as two-way fixed effects or 2FE.

where $E(\varepsilon_{ist}|s,t)$=0. In equation (11) the log of the price of a pharmaceutical product depends on the group effect ($\gamma_s$), time effect ($\lambda_t$) and on the treatment effect ($\beta D_{st}$). Next, let us present the following:

$$E(Y_{ist}|s = NoMrs, t = After) - E(Y_{ist}|s = NoMrs, t = Before) = \lambda_{after} - \lambda_{before} \quad (12)$$

and

$$E(Y_{ist}|s = Mrs\,, t = After) - E(Y_{ist}|s = Mrs\,, t = Before) = \lambda_{after} - \lambda_{before} + \beta \quad (13)$$

The difference-in-differences between products assigned to mandatory reserves system can be estimated by subtracting (12) from (13).

$$[E(Y_{ist}|s = NoMrs\,, t = Before) - E(Y_{ist}|s = NoMrs, t = After)]$$

$$-[E(Y_{ist}|s = Mrs\,, t = Before) - E(Y_{ist}|s = Mrs\,, t = After)] = \beta, \quad (14)$$

where $\beta$ represents the effect of mandatory reserves system. As mentioned before, the common price trends between the treatment and control groups and that the they would have continued in the absence of the treatment is the key assumption in DD models. The treatment is assumed to induce a deviation between the price trends, which can clearly be confirmed form figures 8 and 9. Furthermore, when fixed effects are added to the model, we account for the fact that individual products in treatment and control groups can differ.

To estimate the effects of mandatory reserves system, a regression model can be implemented to the panel dataset. Let us introduce the basic model for estimation:

$$Y_{it} = \alpha + \gamma(Mrs) + \lambda(Post) + \beta_1(MRS * Post) + \varepsilon_{\mathrm{it}}\,, \quad (15)$$

where $\gamma$ represents the difference between the control and treatment groups before the treatment, $\lambda$ the overall change between pricing periods of before and after the implementation of the policy change of interest and $\beta_1$ represents coefficient of the effects of the interaction of post treatment periods and mandatory reserves system. Error term is represented by $\varepsilon_{it}$.

The regression models are run with product level and time fixed effects resulting in the following equation, where the coefficients for the *Post* and *Mrs* terms are dropped since they do not have any variation in the data after adding the fixed effects to the model:

$$Y_{it} = \alpha + \beta_1(Mrs * Post) + ProductFE + TimeFe + \varepsilon_{\mathrm{it}} \quad (16)$$

Since reference pricing was implemented almost simultaneously with the mandatory reserves system, it is likely that results would be biased without taking it

into account. Furthermore, the effects of mandatory reserves system could be different for reference priced products compared to products not assigned to RPS. Two more coefficients are estimated; one for the interaction of reference pricing system and post treatment period capturing the overall effect of the reference pricing system and one term for the interaction of reference pricing, mandatory reserves system and post-treatment period representing the effects of mandatory reserves system on products that are also assigned to reference pricing system.

Final regression equation takes the following form:

$$Y_{it} = \alpha + \beta_1(Mrs * Post) + \beta_2(Rps * Post) + \beta_3(Rps * Mrs * Post) + TimeFe + ProductFe + \varepsilon_{it} \quad (17)$$

According to the model presented in equation (17), the log of the price of product *i* in time-period *t* depend if the product belongs to the reference pricing system (*Rps*), to the mandatory reserve system (*Mrs*), to both or to neither one of the systems. The term *Rps* is dummy variable assigned a value of zero if the product was assigned to the reference pricing system and zero otherwise, capturing the average effect of reference pricing. The term *Mrs* is also a dummy-variable getting the value of one if the product was assigned to the mandatory reserves system and otherwise a value of zero capturing the average effect of mandatory reserve system on the prices of drugs. The *Post*-term gets a value of one after the 1st of January 2009 and a value of 0 before the 1st of January. The post-treatment term is only utilized in the interaction term with *Mrs* and *Rps* since the model uses two-way[31] fixed effects.

The regression models will be implemented hierarchically by adding first the term for mandatory reserves and then adding the effect of reference pricing and finally the interaction of mandatory reserves system and reference pricing. Moreover, all the regression models include the fixed effects and standard errors are clustered at ATC-4 level. The regression models are run with two different time frames to see if the effects change over time.

[31] Unit fixed effects and time fixed effects.

# 5 RESULTS

This chapter presents the results on how mandatory reserves system affected the pharmaceutical prices in Finland. First subchapter estimates the effects of mandatory reserves system using difference-in-differences regression model. The second subchapter presents robustness checks of this model.

## 5.1 Price effects of mandatory reserves system

The results indicate approximately a 2.5 to 2.7 percent decrease in the prices of pharmaceuticals assigned to mandatory reserves system. However, the results are statistically significant at the 5% level only for products that were not assigned to the reference pricing system.

The results of the regression models are presented in table 9 for a time frame of 12 months (6 months before the policy change and 6 months after). The model is built hierarchically by adding a variable, while moving to a more complex model. Model 1 estimates the overall effect of mandatory reserves system without accounting for the introduction of reference pricing system. The interaction term of mandatory reserves system and periods after the policy change (*Mandatory*Post*) captures the overall effect of mandatory reserves system for all pharmaceutical products in the prepared dataset. According to model 1, the mandatory reserves system lowered the prices of pharmaceutical products by 4.2 percent with statistical significance at the 5% level.

Model 2 separates the effects of mandatory reserves system from the effects of reference pricing system by estimating coefficients for the interaction terms *Mandatory*Post* and *Reference*Post*. According to model 2, the assignment to mandatory reserves system resulted in 3.2 percent lower prices for pharmaceuticals, whereas the reference pricing system resulted in approximately 6.8 percent lower prices. However, the interaction term of *Reference*Post* should not be interpreted as the causal effect of the reference pricing system, since no proper control group is determined for these products.

Moreover, the pre-treatment price trends of products assigned to the reference pricing system are not similar with products that were not assigned to the reference pricing system, which can be confirmed visually by comparing the price trends of the two groups from figure 8 to the price trends of the two groups from figure 9. In fact, the price trends of the two groups in figure 8 exhibit a downward trend before the actual treatments. The interaction term of *Reference*Post* is used to separate the effects between reference priced products assigned to the MRS and non-reference priced products assigned to the MRS.

Finally, in model 3, the mandatory reserves system is estimated to decrease pharmaceutical prices for products outside of the reference pricing system by 2.5 percent with statistical significance. The interaction term *Mandatory*Post* estimates the effects of mandatory reserves system for products not assigned to the reference pricing system and the interaction term of *Reference*Post* estimates the effects of reference pricing system for products not assigned to mandatory reserves system. Furthermore, the interaction term *Mandatory*Reference*Post* estimates how the effect of mandatory reserves system changes, when a pharmaceutical product is also assigned to the reference pricing system.

According to model 3, the price decreasing effect of reference pricing system is 6.3 percent and the result is statistically significant. Moreover, the effect of mandatory reserves system for reference priced products is -2.2 but without statistical significance. Again, the effects of reference pricing (*Reference*Post*) should not be interpreted as causal effects.

In table 10, the regression results are reported similarly compared to table 9, but for a timeframe of 24 months. Model 4 in table 10 reports the overall estimated effect for mandatory reserves system (*Mandatory*Post*) to be -4.2 percent, and the estimated coefficient is statistically significant at the 5% level. Model 5 estimates the overall effects of mandatory reserves system (*Mandatory*Post*) to be -4.8 percent and the overall effect of reference pricing system (*Reference*Post*) to be -12.9 percent, both with statistical significance.

Finally, model 6 reports the overall effect of mandatory reserves system for pharmaceutical products not assigned to reference pricing system (*Mandatory*Post*), the overall effect of reference pricing system for pharmaceutical products not assigned to mandatory reserves system (*Reference*Post*) and the effect of mandatory reserves system for products assigned to reference pricing system (*Mandatory*Reference*Post*). The effect of mandatory reserves system was -2.7 percent for products not assigned to RPS with statistical significance at the 5% level. The effect of mandatory reserves system on products assigned also to reference pricing system was -2.2 but not statistically significant.

The average effect of mandatory reserves system is statistically significant in all regression models. However, it seems that the effects are only present in pharmaceutical products outside of reference pricing system. The interaction term of *Mandatory*Reference*Post* is not statistically significant, meaning we do not observe meaningful price effects for products assigned to mandatory reserves system and to the reference pricing system.

TABLE 9 Regression results for a timeframe of 12 months (6 months before and after)

| | Model 1 | Model 2 | Model 3 |
|---|---|---|---|
| Mandatory * Post | -0.0422*<br>(0.0196) | -0.0323*<br>(0.0157) | -0.0248*<br>(0.0101) |
| Reference * Post | - | -0.0675***<br>(0.0123) | -0.0631***<br>(0.0137) |
| Mandatory * Reference * Post | - | - | -0.0217<br>(0.0297) |
| Time Fixed Effects | Yes | Yes | Yes |
| Entity Fixed Effects | Yes | Yes | Yes |
| R2 | 0.0102 | 0.0465 | 0.0471 |
| Clustered | ATC-4 | ATC-4 | ATC-4 |
| N | 6372 | 6372 | 6372 |
| Clusters | 491 | 491 | 491 |
| T | 12months (26periods) | 12months (26periods) | 12months (26periods) |

Note: *= p<0.05, **= p<0.01, ***=p<0.001. Cluster robust standard errors in parenthesis.

TABLE 10 Regression results for a timeframe of 24 months (12 months before and after)

| | Model 4 | Model 5 | Model 6 |
|---|---|---|---|
| Mandatory * Post | -0.0681*<br>(0.0317) | -0.0484*<br>(0.0232) | -0.0266*<br>(0.0116) |
| Reference * Post | - | -0.1290***<br>(0.0220) | -0.1163***<br>(0.0239) |
| Mandatory * Reference * Post | - | - | -0.0634<br>(0.524) |
| Time Fixed Effects | Yes | Yes | Yes |
| Entity Fixed Effects | Yes | Yes | Yes |
| $R^2$ | 0.0138 | 0.0827 | 0.0854 |
| Clustered | ATC-4 | ATC-4 | ATC-4 |
| N | 5715 | 5715 | 5715 |
| Clusters | 475 | 475 | 475 |
| T | 24months (50periods) | 24months (50periods) | 24months (50periods) |

Note: *= p<0.05, **= p<0.01, ***=p<0.001. Cluster robust standard errors in parenthesis.

## 5.2 Robustness checks

Robustness checks are performed by estimating additional models that include placebo treatment for reference pricing system and mandatory reserves system in two different pre-treatment periods. The first placebo treatment gets a value of one for periods after June 2008, thus estimating the placebo effect for periods before the reference pricing system or mandatory reserves system entered the discussion in the Finnish parliament. The second placebo treatment gets a value of one just after the reference pricing system entered the Finnish parliament for discussion. Results for the placebo-DD models are presented in tables 11 and 12. The robustness checks performed here are more formal approaches to test the parallel trends assumptions, required for the causal relationship estimation (Fredriksson & Oliveira, 2019).

In table 11, the estimation is performed by using a placebo treatment that gets a value of one after June 2008. The results indicate statistically insignificant effects for the mandatory reserves system both, for products that were not assigned to the reference pricing system and for products that were assigned to the reference pricing system in the pre-treatment periods. Statistically insignificant results for the placebo suggests that the real treatment effects are not over-estimated for mandatory reserves system, and the parallel trends assumption seems to hold.

However, the placebo treatment effects are large and statistically significant for the reference pricing system. These results corroborate with visual observations in figures 8 and 9 presented earlier, where the price trends in the pre-treatment periods are not similar when comparing the products that were assigned to reference pricing system to products that were not, which in turn indicates that the interaction term estimating the effects of reference pricing should not be interpreted as the causal effect of the reference pricing system.

In table 12, model 8 estimates the effects of placebo treatment and real treatment effects, but the pre-treatment term is given a value of one just after the reference pricing system entered the Finnish parliament for discussion. The results presented in table 12 yields statistically insignificant results for placebo treatment for the mandatory reserves system supporting the parallel trends assumption when comparing products assigned to mandatory reserves system to the products not assigned to the mandatory reserves system. Furthermore, the placebo treatment for the reference pricing system yields statistically significant results, meaning that the effects of reference pricing system should not be interpreted causally.

TABLE 11 Difference-in-differences estimation with placebo treatment at June 2008

| | Model 7 |
|---|---|
| Mandatory * Pre-treatment | 0.0029 |
| | (0.0037) |
| Reference * Pre-treatment | -0.0489*** |
| | (0.0111) |
| Mandatory * Reference * Pre-treatment | -0.0149 |
| | (0.0209) |
| Mandatory * Post | -0.0254* |
| | (0.0108) |
| Reference * Post | -0.0972*** |
| | (0.0229) |
| Mandatory * Reference * Post | -0.0614 |
| | (0.0483) |
| Time Fixed Effects | Yes |
| Entity Fixed Effects | Yes |
| R2 | 0.0938 |
| Clustered | ATC-4 |
| N | 5715 |
| Clusters | 475 |
| T | 24months (50periods) |

Note: *= p<0.05, **= p<0.01, ***=p<0.001. Cluster robust standard errors in parenthesis.

TABLE 12 Difference-in-differences estimation with placebo treatment at October 2008

| | Model 8 |
|---|---|
| Mandatory * Pre-treatment | -0.0004 |
| | (0.0045) |
| Reference * Pre-treatment | -0.0537*** |
| | (0.0109) |
| Mandatory * Reference * Pre-treatment | -0.0086 |
| | (0.0188) |
| Mandatory * Post | -0.0234* |
| | (0.0099) |
| Reference * Post | -0.0792*** |
| | (0.0190) |
| Mandatory * Reference * Post | -0.0614 |
| | (0.0446) |
| Time Fixed Effects | Yes |
| Entity Fixed Effects | Yes |
| R2 | 0.0937 |
| Clustered | ATC-4 |
| N | 5715 |
| Clusters | 475 |
| T | 24months (50periods) |

Note: *= p<0.05, **= p<0.01, ***=p<0.001. Cluster robust standard errors in parenthesis.

# 6 DISCUSSION

Results of the regression analysis presented in this thesis are counterintuitive; if pharmaceutical markets are working efficiently and the pharmaceutical companies' storages were optimized before mandatory reserves system was implemented, we should not observe decreasing pharmaceutical prices caused by the policy change. Since the mandatory reserves system allegedly increases the operating costs, we should observe price increases. Moreover, because pharmaceutical companies have strong incentives to maximize profits and cost optimization is a crucial part of profit-maximizing behaviour, it is reasonable to assume that storages would already be optimized to minimize the total costs.

However, the pharmaceutical companies receive reimbursements from NESA for holding excess storages required by mandatory reserves system, so hypothetically if the amounts reimbursed are larger than the costs of holding larger storages, total costs could decline and thus decrease the market prices through competition.

Moreover, according to the theories of storage optimization, there exists a possibility for cost-savings if supply disruptions would be taken into account more effectively when deciding the sizes of storages. Encouraging results are provided by using e.g. the newsvendor model and mathematical simulations of optimal storage amounts.

The mandatory reserves system could, in theory, lower the costs for pharmaceutical companies, if the Finnish government would be capable of recognizing which products would benefit from larger storages. There exist a plethora of studies stating that storage optimization and preparedness for supply disruptions could increase profits. However, it would be highly doubtful to argue that the effects of mandatory reserves system are visible immediately after its implementation due to optimized storages. Moreover, it is unlikely that pharmaceutical companies had not realized cost-saving potential of supply disruption mitigation by increasing storages, especially since the legislation for mandatory reserves has been active since 1984. The pharmaceutical companies would have had time to learn and adjust their storage policies accordingly many years before the legislation was adjusted in January 2009.

There might be other factors driving the results that could not be controlled with the models presented in this thesis. The most likely suspect is the reference pricing system that was implemented soon after the mandatory reserves system. It is entirely possible that the pharmaceutical companies started anticipating the tightening competition due to reference pricing system by lowering their prices before the actual implementation of the system and the model presented in this thesis captures first, the anticipatory effects of the reference pricing system and then the real effects of reference pricing system due to cross-price elasticities.

This thesis provides excellent roadmaps for future studies on the effects of mandatory reserves system on pharmaceutical prices. Even though, the results presented should not be interpreted causally partially due to unreliable data and other confounding policy changes affecting the pharmaceutical prices at the same time, the results and methods presented in this thesis can be used as a reference point in future studies.

There are multiple ways to extend the analysis or increase the accuracy of the results that could be implemented in future research. One possibility is to use weighted regression models by using the quantities sold in each period as a weight. Through weighted data, more realistic results could be achieved since some price changes affecting the data could have been from products having no real impact on the total market prices due to insignificant sales.

An interesting question not studied in this thesis is the changes between the storage groups in the intensities of the storage obligations before and after the policy reform. Storage groups 7 to 10 and 13 experienced a substantial decrease in required sizes of mandatory reserves; before the policy reform of 2009, the minimum storage sizes had to cover up to 10 months of average demand, but after the policy change, the minimum storages had to cover only up to 3 months of demand. The effect of the policy reform meant a 70% drop in the intensity of mandatory reserve requirements for storage groups 7 to 10 and 13. Treatment group could be formed by using the products that were covered by the mandatory reserves system before and after policy reform in 2009 in groups 7 to 10 and 13. Furthermore, storage groups 3 to 6 were affected by a 20% increase in storage sizes. This kind of variation in storage obligation intensities could provide a good study design for future research.

Another interesting approach could be to use prices from other Nordic countries as a control for domestic prices. Price data for pharmaceutical products sold in other countries are available, but potential problems could occur when trying to identify comparable products. One option is to search for products having the same vnr-number and construct a control group for the prices in Finland that include the same products from other countries.

Finally, perhaps the most viable option is to identify a better subset of pharmaceutical products more comparable against each other. Since the estimation technique in this thesis relies heavily on properly defined treatment and control groups, more reliable estimates could be achieved by using a more carefully picked subsample of products.

Since mandatory reserves system makes Finnish pharmaceutical markets more regulated and possibly less attractive combined with intense generic competition and reference pricing, it might be possible that we see fewer market entries and more market exits in the future and thus have less competitive markets. Less competition could lead to higher prices and increase the adverse effects supply disruptions if smaller amounts of producers are participating in Finnish markets. The market exits and entries could be analyzed with the data used for this thesis.

The general topic regarding crisis readiness is vital, and the COVID-19 pandemic has shown the importance of resilient supply chains and availability of medical products. Struggling with the availability of protective gear for hospital and healthcare usage might lead to discussions about the ability to withstand supply disruptions or sudden changes in demand. To be prepared for a crisis includes sound policies and clear procedures on how to mitigate the adverse effects. One important way for mitigation is to have adequate amounts of materials ready for usage.

The mandatory reserves system in general is not a popularly used policy but the current pandemic caused by the COVID-19 possibly shows some weaknesses on global supply chains and opens new debates of risk preparedness. The supply chain resilience should also be studied as a cost-benefit analysis and this thesis could give some roadmaps on how to estimate the possible costs of one possible risk-mitigation policy.

To the best of my knowledge, this thesis is currently the only empirical study trying to achieve causal inferences between the pricing of pharmaceutical products and mandatory reserves system. Furthermore, this thesis contributes to the existing literature of pricing of pharmaceuticals by presenting ideas on how to estimate effects policies forcing pharmaceutical companies to mitigate risks so that the society would be better off. In the future, it is imperative that the effects of pharmaceutical market regulation policies are analyzed carefully.

# 7 CONCLUSION

The main goal of this thesis is to analyse the effects of mandatory reserves system on the pricing of pharmaceutical products and provide ideas on how the topic could be studied in future researches. Furthermore, this thesis provides an extensive literature review on the Finnish pharmaceutical markets in general and its market regulation. Finally, this thesis explores the existing price regulation in pharmaceutical markets in Finland and other countries. The empirical section focuses on providing robust evidence on how mandatory reserves system possibly affects the prices of pharmaceuticals.

In order to generate convincing results, product-level price data is combined with information on which pharmaceutical products are covered by the mandatory reserves system and reference pricing system. A policy change in 2009 that assigned several new products to the mandatory reserves system is used as a quasi-natural experiment to estimate price effects. Unfortunately, the reference pricing system was implemented almost simultaneously with the mandatory reserves system leading to the possibility of biased results due to cross-price elasticity effects.

The effects of mandatory reserves system are estimated for products assigned to the reference pricing system and those products that were not assigned to the reference pricing system using the difference-in-differences regression model with two-way fixed effects and clustered standard errors.

Results indicate that the effect of mandatory reserves system for products assigned to reference pricing system is not statistically significant, but for products not assigned to reference pricing system, the effect of mandatory reserves system is approximately -2.5 to -2.6 percent. The regression results display beta-coefficients also for the reference pricing system, which should not be interpreted as the causal effect due to violation of parallel trends assumption.

Robustness check is performed by estimating a placebo treatment in the pre-treatment period. The placebo estimation indicates no statistical significance for the beta-coefficients of the mandatory reserves system, but statistically significant results are found for the reference pricing system, supporting the idea of parallel trends violation regarding the effects of the reference pricing system. However, the placebo estimation supports the idea that the main regression model presented in this thesis works well when estimating the effects of mandatory reserves system on non-reference priced products.

This thesis presents new and exciting results about a topic that has not yet been studied empirically in the field of economics. The effects of mandatory reserves system should be studied more thoroughly and with other empirical approaches before conclusions should be drawn. In other words, the results presented in this thesis should be used with caution and possibly as a reference for future studies.

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## APPENDIX 1 – The ATC-System

ATC-system is a standard classification system for pharmaceuticals managed by the World Health Organization Collaborating Centre for Drug Statistics Methodology (WHOCC). The active substances of pharmaceuticals are classified in a hierarchical system with five different levels. At the first level, all of the available drugs are divided into 14 groups, representing the anatomical classification of the human body (1st level). Each of the 14 groups is divided into different subgroups representing either pharmacological or therapeutic groups (2nd level). After this comes the 3rd and 4th sublevels, which represent either chemical, pharmacological, or therapeutic subgroups. Finally, the 5th level in the ATC-classification system represents the active chemical substance in a drug. (WHOCC, 2018.)

Let's take an example of a drug called Metformin Actavis, which is used to treat diabetes with the active ingredient called metformin hydrochloride. The ATC-code for metformin is A10BA02, and the complete decomposition of the classification is presented in table 10.

TABLE 13 Example of ATC-system classification

| | | |
|---|---|---|
| 1st level | A | Alimentary tract and metabolism<br>(Anatomical main group) |
| 2nd level | A10 | Drugs used to treat diabetes<br>(Therapeutic subgroup) |
| 3rd level | A10B | Blood glucose lowering drugs, excluding insulins<br>(Pharmacological subgroup) |
| 4th level | A10BA | Biguanides<br>(Chemical subgroup) |
| 5th level | A10BA02 | Metformin<br>(Chemical substance) |

## APPENDIX 2 – The Market Power of Innovative Drugs

The demand for single-source medicines is likely to be very inelastic. If the producer sells essential products protected by patent, they are in a strong market position and can affect the pricing easily without suffering from decreased demand. (WHO, 2015.)

There are examples of patented drugs having astronomical prices when used to treat rare diseases. A drug called Nusinersen (Spinraza) was approved by the U.S Food and Drug Administration (FDA) in December 2016. The drug was developed to treat a rare SMA-muscular disease, which means the potential customer base is relatively small. The treatment costs approximately 500.000 euros for the first year and 250.000 euros for the continuing years. The production costs of the drug affecting the price are insignificant. However, the R&D costs are enormous in this case, and they must be divided between the consumers, and since the pharmaceutical companies act as profit-maximizing units, they extract the highest price possible compared to the economic-health benefits.

According to Professor Lasse Lehtonen from the University of Helsinki, the R&D costs in the case of this particular drug would be approximately USD 30 Million, and current sales quarterly sales in the U.S are USD 200 Million. The patent for this particular drug is for 15 years, which implies significant market power for patented pharmaceuticals having no direct therapeutic competitors (Lehtonen, 2018).

The governments can limit the monopolistic powers of pharmaceutical companies by establishing price regulations or by controlling the profits from sales. The markets can also incentivize other companies to produce therapeutic competitors by offering patents only for chemical compounds, but not for the therapeutic indications (WHO, 2015).

## APPENDIX 3 – List of Active Ingredients in Mandatory Reserves System

New active ingredients added to the mandatory reserves system are identified with (**), and active ingredients dropped out of the mandatory reserves system after the policy change in 2009 with (*).

TABLE 14 Active ingredients in mandatory reserves system according to Council of State Decrees.

| Storage group | Before January 2009 | After January 2009 |
|---|---|---|
| 1) Antimicrobial drugs | 1) amoxicillin<br>2) benzylpenicillin<br>3) doxycycline<br>4) erythromycin *<br>5) phenoxymethylpenicillin<br>6) isoniazid<br>7) chloramphenicol *<br>8) metronidazole<br>9) miconazole *<br>10) rifampicin<br>11) ciprofloxacin<br>12) tobramycin<br>13) trimethoprim | 1) amoxicillin<br>2) amoxicillin + clavulanic acid **<br>3) benzylpenicillin<br>4) doxycycline<br>5) clarithromycin **<br>6) phenoxymethylpenicillin<br>7) isoniazid<br>8) metronidazole<br>9) fluconazole **<br>10) rifampicin<br>11) ciprofloxacin<br>12) levofloxacin **<br>13) tobramycin<br>14) trimethoprim<br>15) acyclovir **<br>16) oseltamivir **<br>17) cephalexin **<br>18) ceftriaxone **<br>19) ceftriaxone + lidocaine **<br>20) cefuroxime **<br>21) clindamycin **<br>22) meropenem **<br>23) pyrazinamide **<br>24) vancomycin **<br>25) cloxacillin ** |
| 3) Medicines and diuretics for cardiovascular disease | 1) digoxin,<br>2) diltiazem<br>3) enalapril *<br>4) furosemide<br>5) glyceryl trinitrate<br>6) hydrochlorothiazide<br>7) lidocaine *<br>8) metoprolol | 1) digoxin<br>2) diltiazem<br>3) ramipril**<br>4) furosemide<br>5) hydrochlorothiazide<br>6) glyceryl trinitrate<br>8) metoprolol<br>9) reteplase **<br>10) tenecteplase **<br>11) dobutamine **<br>12) isosorbide mononitrate ** |

| | | |
|---|---|---|
| | | 13) obidoxime ** |
| 8) Medicines for respiratory diseases | 1) adrenaline<br>2) beclomethasone*<br>3) budesonide<br>4) salbutamol<br>5) salmeterol<br>6) theophylline | 1) adrenaline<br>2) fluticasone**<br>3) budesonide<br>4) salbutamol<br>5) salmeterol<br>6) theophylline |
| 9) Gastrointestinal Diseases | 1) aluminium hydroxide*<br>2) ranitidine* | 1) omeprazole**<br>2) esomeprazole**<br>3) pantoprazole**<br>4) lansoprazole **<br>5) rabeprazole** |
| 10) Psyche drugs | 1) diazepam<br>2) doxepin*<br>3) fluoxetine*<br>4) chlorpromazine*<br>5) temazepam | 1) diazepam,<br>2) amitriptyline**<br>3) citalopram**<br>4) clozapine**<br>5) olanzapine**<br>6) temazepam<br>7) haloperidol** |
| 11) Neurological drugs | 1) phenytoin,<br>2) carbamazepine<br>3) levodopa | 1) phosphenytoin **<br>2) valproic acid **<br>3) carbamazepine<br>4) levodopa<br>5) oral levodopa+carbidopa preparations **<br>6) levodopa+benseratsidi ** |
| 4) Medicinal products for metabolic and endocrine disorders | 1) glipalamide *<br>2) insulin<br>3) levothyroxine<br>4) prednisolone | 1) glimepiride **<br>2) short and long-acting insulins<br>3) levothyroxine<br>4) prednisolone<br>5) methylprednisolone **<br>6) metformin ** |
| 5) Pain, antirheumatic and antipyretic | 1) acetylsalicylic acid<br>2) ibuprofen<br>3) morphine<br>4) paracetamol<br>5) pethidine * | 1) acetylsalicylic acid<br>2) ibuprofen<br>3) morphine<br>4) paracetamol<br>5) oxycodone + paracetamol **<br>6) oxycodone + ibuprofen **<br>7) codeine + paracetamol **<br>8) codeine + ibuprofen ** |

| | | |
|---|---|---|
| 6) Medicines used for local anaesthesia and general anaesthesia | 1) atropine<br>2) enflurane *<br>3) ketamine<br>4) lidocaine<br>5) neostigmine<br>6) pancuronium *<br>7) suxamethonium<br>8) thiopental * | 1) atropine<br>2) sevoflurane**<br>3) propofol **<br>4) lidocaine<br>5) neostigmine<br>6) neostigmine +glycopyrroniumbromide **<br>7) suxamethonium<br>8) ketamine<br>9) bupivacaine **<br>10) fentanyl **<br>11) rocuronium ** |
| 2) Medicines for electrolyte and fluid imbalance and for paternal nutrition | 1) albumin<br>2) dextran<br>3) glucose<br>4) potassium phosphate<br>5) sodium bicarbonate<br>6) sodium chloride | 1) albumin<br>2) hydroxyethyl starch glucose **<br>3) glucose<br>4) potassium phosphate<br>5) sodium bicarbonate<br>6) sodium chloride<br>7) calcium chloride **<br>8) amino acid solution **<br>9) calcium gluconate **<br>10) calcium glubionate **<br>11) all combinations of the aforementioned ingredients ** |
| 12) Ophthalmogolists medicinal products | 1) pilocarpine<br>2) timolol | 1) pilocarpine<br>2) timolol<br>3) chloramphenicol** |
| 13) Hematologists medicinal products | 1) heparin<br>2) coagulation factor VIII<br>3) coagulation factor IX<br>4) warfarin | 1) heparin<br>2) coagulation factor VIII<br>3) coagulation factor IX<br>4) warfarin<br>5) dalteparin **<br>6) enoxaparin **<br>7) anticancer medicinal products listed separately. |
| 7) Poisoning drugs and vaccines | 1) activated charcoal<br>2) tetanus vaccines<br>3) hepatitis B vaccines<br>4) whooping cough vaccines *<br>5) diphtheria vaccines *<br>6) polio vaccines *<br>7) meningococcus vaccines *<br>8) rabies vaccines<br>9) tuberculosis vaccines *<br>10) gamma globulins for intravenous and intramuscular use<br>11) Immunoglobulins for the treatment of tetanus, rabies and hepatitis B<br>12) botulinum, diphteria, Snake serum * | 1) activated charcoal<br>2) obidoxime **<br>3) hepatitis B vaccines<br>4) hepatitis A vaccines **<br>5) rabies vaccines<br>6) gamma globulins for intravenous and intramuscular use<br>7) Immunoglobulins for the treatment of tetanus, rabies and hepatitis B<br>8) Vaccines included in the national vaccination program imported or procured by the National Institute for Health and Welfare (THL), with the exception of influenza vaccines |

Note: *= dropped out of the MRS, **= added to MRS

# APPENDIX 4 – Price Regulation Schemes in Europe

TABLE 15 Pharmaceutical market regulation in European countries (Puig-Junoy, 2010).

| Country (year reference pricing started) | Level of equivalence | Maximum reimbursement rate | Price regulation of generic medicines |
|---|---|---|---|
| Austria | N/A | As of third generic, 60% below the price of the original product | 1st generic -48% compared to original<br>2nd generic -15% compared to 1st generic<br>3rd generic -10% compared to 2nd generic<br>4th and rest -10% compared to 3rd generic |
| Belgium (2001) | Chemical | -30% compared to original product | Generic -30% compared to the original product |
| Czech Republic (1995) | Chemical, Pharmacological and therapeutic | Lowest price in group | -55% compared to original product |
| Denmark (1993) | Chemical | Lowest price in reimbursement or substitution group | Generic must be priced lower than to branded original product. Pirce difference not specified |
| Estonia (2003) | Chemical | 2nd lowest price in the group | N/A |
| Finland (2009) | Chemical | Lowest price plus € 1.5 and + € 2, if product price is more than 40 euros (later changed to 0.5 and 0.5 euros) | N/A |
| France (2003) | Chemical | Average of generics with one active ingredient | -55% of the price of the original product. |
| Germany (1989) | Chemical, Pharmacological and therapeutic | 30% of the lowest price in the reference group, which has chemical equivalence | N/A |
| Greece (2006) | Pharmacological | Lowest price of the reference group | -80% of the price of the original product. |
| Hungary (1997) | Chemical | Lowest price of the reference group | -30% compared to the original product, but now higher than the reference price. |
| Ireland | N/A | N/A | -30% compared to the original product |
| Italy (2001) | Chemical | Lowest price of the reference group | -20% compared to the original product |
| Latvia (2005) | Therapeutic | Lowest price of the reference group | N/A |
| Lithuania (2005) | Chemical | Lowest price of the reference group | -30% compared to the original product |
| Malta | N/A | N/A | No regulation |
| Netherlands (1991) | Chemical, pharmacological and therapeutic | Lowest price of the reference group | Price cap based on the average of four EU countries |
| Poland (1998) | Chemical and pharmacological | Lowest price of the reference group | N/A |
| Portugal (2003) | Chemical | Price of the most expensive generic | -35% lower than the original product |
| Romania (1997) | Chemical | Lowest price of the reference group | N/A |
| Slovakia (1995) | Chemical and Pharmacological | Lowest price (per defined daily dosage) in group | N/A |
| Slovenia (2003) | Chemical | Lowest price of the reference group | N/A |
| Spain (2000) | Chemical | Average price of the three cheapest products | N/A |
| Sweden (discontinued in 2002) | N/A | Compulsory substitution with the lowest priced product from the reference group | Free pricing. but purchase agreements are negotiated. |
| UK (2005) | Chemical | Weighted average price | N/A |

## APPENDIX 5 – Pharmacy Mark-up System in Finland

The prices of pharmaceutical products are the same nationwide since price discounts at the wholesale level are prohibited, and negotiated by Hila. The price mark-ups for pharmacies are decreasing in nature, meaning that more expensive products yield lover mark-ups for pharmacies. Moreover, price mark-ups are different for prescription drugs and OTC-drugs. (Finnish Pharmacy Mark-up Decree, 713/2013).

TABLE 16 Pharmacy mark-ups for prescription drugs (Finnish Pharmacy Mark-up Decree, 713/2013)

| Purchase price for pharmacy | Retail price |
|---|---|
| 0 – 9.25 € | 1.45 x Purchase |
| 9.26 – 46.25 € | 1.35 x Purchase + 0.92 € |
| 46.26 – 100.91 € | 1.25 x Purchase + 5.54 € |
| 100.92 – 420.47 € | 1.15 x Purchase + 15.63 € |
| >420.47 € | 1.1 x Purchase + 36.65 € |

TABLE 17 Pharmacy mark-ups for OTC-drugs. (Finnish Pharmacy Mark-up Decree, 713/2013).

| Purchase price for pharmacy | Retail price |
|---|---|
| 0 – 9,25 € | 1.5 x Purchase + 0.50 € |
| 9,26 – 46,25 € | 1.4 x Purchase + 1.43 € |
| 46,26 – 100,91 € | 1.3 x Purchase + 6.05 € |
| 100,92 – 420,47 € | 1.2 x Purchase + 16.15 € |
| > 420,47 € | 1.125 x Purchase + 47.68 € |