The effects of regulative instruments on stakeholders in the German pharmaceutical market

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Meinen Eltern gewidmet

To absent friends, lost loves, old gods, and the seasons of the mist.
May each and everyone of us always give the devil his due.

(Neil Gaiman, The Sandman #22: Seasons of the mist)

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I. Abstract

The German Statutory Health Insurance (SHI) system provides medical services for the majority of the German population. Thereby the treatment with prescription drugs does play a major role for the health of insurants. However, with the increasing possibility for the treatment of illnesses with prescription drugs, also the expenditures for such drugs have increased in the past decade. While in 2000, expenditures for prescription drugs amounted to 19.4 billion euro, in 2010, these expenditures have increased to 30.2 billion euro. Therefore, prescription drugs are a large cost driver of the SHI system. In reaction to this development, various regulative instruments were implemented to reduce the drug expenditures.

The thesis analyzes, both theoretically and empirically, the impact of reference pricing, the possibility to exempt drugs from patient related co-payments, and rebate contracts on the pricing behavior and the demand reaction of different kinds of pharmaceutical producers, the prescription behavior of physicians and the negotiation strategies of sickness funds.

The presented papers add to the existing literature in various ways. For the first time, the price setting reactions of patent, original, and generic producers, following the implementation of a joint reference price are evaluated. Also, for the first time, the effects of the implementation of reference pricing, exemption from patient related co-payments, and rebate contracts on the demand of branded and non-branded generic drugs are estimated. Shifting the perspective towards the physician, the effects of the implementation of the previously mentioned regulative instruments on the prescription behavior of SHI physicians is shown for the first time. Lastly, the thesis includes a new theoretical approach to explain the strategic behavior of different types of sickness funds and generic drug producers in the negotiation process of rebate contracts.

First, the effects of the implementation of reference prices, a maximum reimbursement limit for prescription drugs, on the prices of patent drugs, off-patent original drugs and generic drugs are analyzed. Using the simultaneous introduction of patent, original and generic statins and proton pump inhibitors to the reference price system in 2005, the price reactions of the different types of producers to reference price policy changes were examined. As expected in the theoretical framework, patent drugs producers lower their prices to a lesser account than producers of original drugs. Also, increasing competition, measured by the number of competitors within an active ingredient, has an overall negative effect on prices, where the impact is stronger for generic products than for patent or originals. At last, the role of competition increases after the reference price implementation.

Following this, the next part of the thesis analyzes the impact of the introduction of reference pricing, the possibility to exempt drugs from patient related co-payment, rebate contracts and price freezes on the market shares of generic and the corresponding original drugs. Also, in an extended model, the effects of the considered regulative instruments on the market shares of brand name and non-branded generic drugs were shown. Both analyses included data of 93 drugs of six different active ingredients between the years 2004-2007. The strongest increase of demand is found for generic drugs that were participating in rebate contracts with sickness funds. The observed effect is weaker for branded than for non-branded generics. The demand for generic drugs, that have been exempted from patient related co-payments also increases. The effect is smaller than in the case of rebate contracts and not significantly different for branded and non-branded generic producers. The weakest market share increase for a generic drug is found after the introduction of reference pricing. In this case, the demand reaction is stronger for branded than for non-branded generic drugs. At last, the demand for generic drugs is lower in time periods with price freezes.

The next chapter the focus of analysis is shifted from the pharmaceutical producer towards the prescribing physician. It analyses the effects of physician, patient, and drug characteristics as well as the implementation of regulatory schemes on the prescription behavior. In detail, the probability of a change of the dispensed drug

for a patient was estimated as a function of physician, patient and drug related characteristics and habits. Thereby, a particular emphasis was given on the effects of the implementation of various regulatory instruments. The analysis used routine data of a large German sickness fund, that included prescription data on patient level for three major indication areas. Our results show the significance of both patient and physician habits al well as drug related characteristics on the probability for a change in the dispended drug. These results give evidence for the existence of persistence in drug choices by both the physician and the patient. In addition, we find evidence for a significant impact of regulatory regimes on the probability of a drug switch for the patient. The strongest effect on a change of the dispended drug was found for rebate contracts, followed by reference pricing and exemption from patient related co-payments.

The last part of the thesis analyses the interaction between generic drug producers and sickness funds concerning the introduction of rebate contracts, which guaranteed market exclusivity in the market of the sickness fund. Using a theoretical model, the paper answers the question if rebate contracts are a way to safe costs, without reducing the level of medical care, or if they lead to (collusive) oligopolistic structures with a higher price level in the long term. We model the effects of the introduction of two different types of rebate contracts, contracts only considering a specific active ingredient (API contracts) and contracts including the whole product portfolio of a producer (portfolio contracts). There are two generic producers, but only one can offer a portfolio contract and two types of sickness funds representing different groups of insurants. For one group, products, offered by both producers, are seen as homogenous, while the other group has a preferred producer. We find that the preferred producer has an advantage in three out four possible scenarios. It can outrival the other firm, due to its monopolistic power and its portfolio. Following these results, competition seems to diminish. However, sickness funds can still save money as producers cannot only threaten to enter a rebate contract. Therefore, as long as mismatch and access cost are low and portfolio contracts are not allowed, competitors will not be able to use their (potential) monopolistic power in the market to diminish competition.

II. Introduction

In 2010, over 90 % of the German citizens were insured in the German Statutory Health Insurance (SHI) system.[1] These insurants received both outpatient (ambulant care) and inpatient (hospital care) services in various forms.

Thereby, the supply with drugs plays an important role in the German Statutory Health Insurance (SHI) system. On their own or in combination with treatments of illnesses in hospitals or by resident physicians, drugs help to cure diseases or ease pain and suffering. While drugs can be classified in various ways, for example by their effectiveness for diseases or their patent protection status, it is also possible to focus on the expenditure side, and differentiate between over-the-counter (OTC) drugs and pharmaceutical products requiring a prescription by a physician. While the former drug type is usually not fully reimbursed by the SHI, and thus financed out-of-pocket by the patient, prescription drugs are usually fully reimbursed, leading to expenditures within the SHI system. In 2010, these expenditures amounted to 30.2 billion euro.[2] Therefore, prescription drugs were the second largest cost driver of the SHI system in 2010. The other two areas that cause the majority of expenditures are medical services in ambulant care (29.1 billion euro in 2010) and hospital treatments (58.1 billion euro in 2010).[3]

However, as Figure 1 shows, prescription drugs show the strongest increase of all three sectors between 2000 and 2010. The annual average growth rate of the expenditures for prescription drugs was 4.5 %. The rate is substantially higher than for medical services in ambulant care (2.1 %) and hospital treatments (2.8 %).

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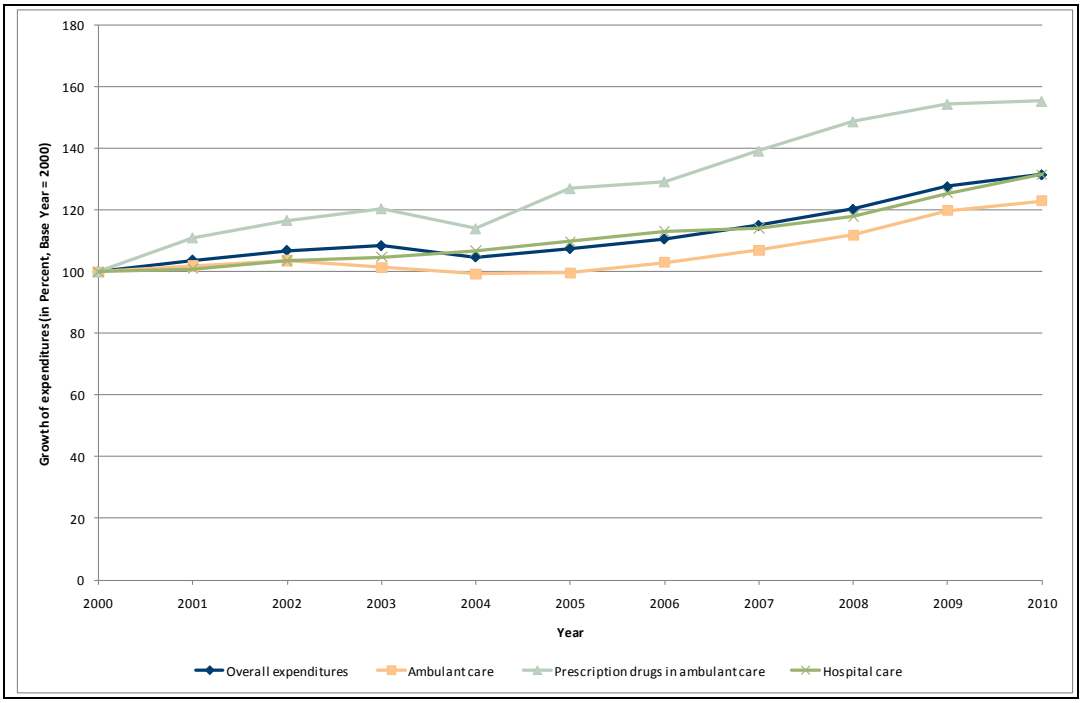
1 See Bundesministerium für Gesundheit (2011b) and Statistisches Bundesamt (2010)

2 See Bundesministerium für Gesundheit (2011b)

3 See Bundesministerium für Gesundheit (2011b)

Figure 1: Development of expenditures in the SHI system in billion euro, 2000-2010



Source: Bundesministerium für Gesundheit (2011b)

In addition, per annum, the expenditures for prescription drugs increased even more than the overall expenditures of the SHI system (2.8 %).

In response to the rising drug expenditures in the last decade, the German Federal Ministry of Health, responsible for the regulation of the drug market, implemented various cost control instruments.

The instruments were part of several health care reforms, implemented by the legislator. As there are several stakeholders like sickness funds, physicians, pharmacies and pharmaceutical producers involved in the process of supplying patients with prescription drugs, the regulative instruments targeted one or several of these parties.[4]

The aim of this thesis is to analyze the effects of a selection of the most important regulative instruments on key stakeholders within the SHI system between 2004 and 2007. The papers, presented in the next chapters, display the effects of the

[4] See Busse et al. (2004) and Denda (2010)

instruments on pricing decisions and the development of market shares various pharmaceutical producers, the impact of on the prescription behavior of physicians as well as the strategic behavior in negotiations between pharmaceutical companies and sickness funds. The majority of the presented papers are of econometric nature, using three different dataset which will be explained in detail later.

Following the abstract (Part I), the first part of the thesis (Part II) describes the system of ambulant care in the SHI system and also introduced the most import stakeholders of the SHI system involved in the supply with prescription drugs. Also, the major regulative instruments of drug market will be discussed in detail. Special attention will be paid to the regulative schemes analyzed in following parts of the thesis. At last, Part II gives an overview about the various datasets and statistic and mathematical software tools used in the following chapters.

Part III describes the effects of the introduction of reference prices (RP), a maximum reimbursement limit for prescription drugs, on the pricing strategies of various kinds of pharmaceutical producers competing with each other. The simultaneous inclusion of patent, original, and generic drugs in a shared reference price group in 2005 was used to examine the price setting behavior of the different producers in reaction to the reference price policy implementation.

Part IV uses an econometric model to estimate the effects of the introduction of reference pricing, exemption from patient related co-payment, rebate contracts, and price freezes on the demand of generic and corresponding original drugs. The overall dataset included 93 drugs, distributed over six different active ingredients. In addition, the different demand reactions of non-branded and brand name generic drugs following the implementation of the selected regulatory instruments are analyzed.

Part V examines the effects of physician, patient and drug characteristics on the probability for a change in the dispended drug of a patient.[5] Using a patient-level panel dataset from a large SHI sickness fund covering three major therapeutic groups, the probability for a switch of the dispended drug for a patient is estimated as a function of physician, patient and drug related characteristics and habits. Following the overall goal of the thesis, the effects of the introduction of regulatory instruments, in particular reference pricing, the possibility to exempt drugs from patient related co-payments, the lead compound rule, and rebate contracts are emphasized in the paper.

The last part of the thesis (Part VI)[6] analyses the concept of two different kinds of direct rebate contracts between sickness funds and pharmaceutical companies for generic drugs on a theoretical base. In detail, the goal of the analysis is to show if rebate contract are a way to save drug expenses or if they lead to oligopolistic drug supply structures, followed by an long-term increase of drug expenses. Therefore, the provided model examines the strategic interaction between two types of generic producers and two kinds of consumers/sickness funds. The considered generic producers differ only in the range of their product portfolio, as one of them provides a larger variety of active ingredients while the other only offers one active ingredient. The demand side is represented by consumers/sickness funds of a first type, for whom the two offered generic products are homogenous, and consumers/sickness funds of a second type, holding a preference for a specific generic producer. Considering the differences in the consumer preferences using a Hotelling approach, the possibility of Nash equilibra in pure strategies for the resulting strategic interactions in the negotiation process of rebate contracts between the firms and consumers/sickness funds are shown. Thereby two types of rebate contracts, single active pharmaceutical ingredient contracts and portfolio rebate contracts are analyzed.

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[5] This part of the thesis is a joint work with Christoph de Millas

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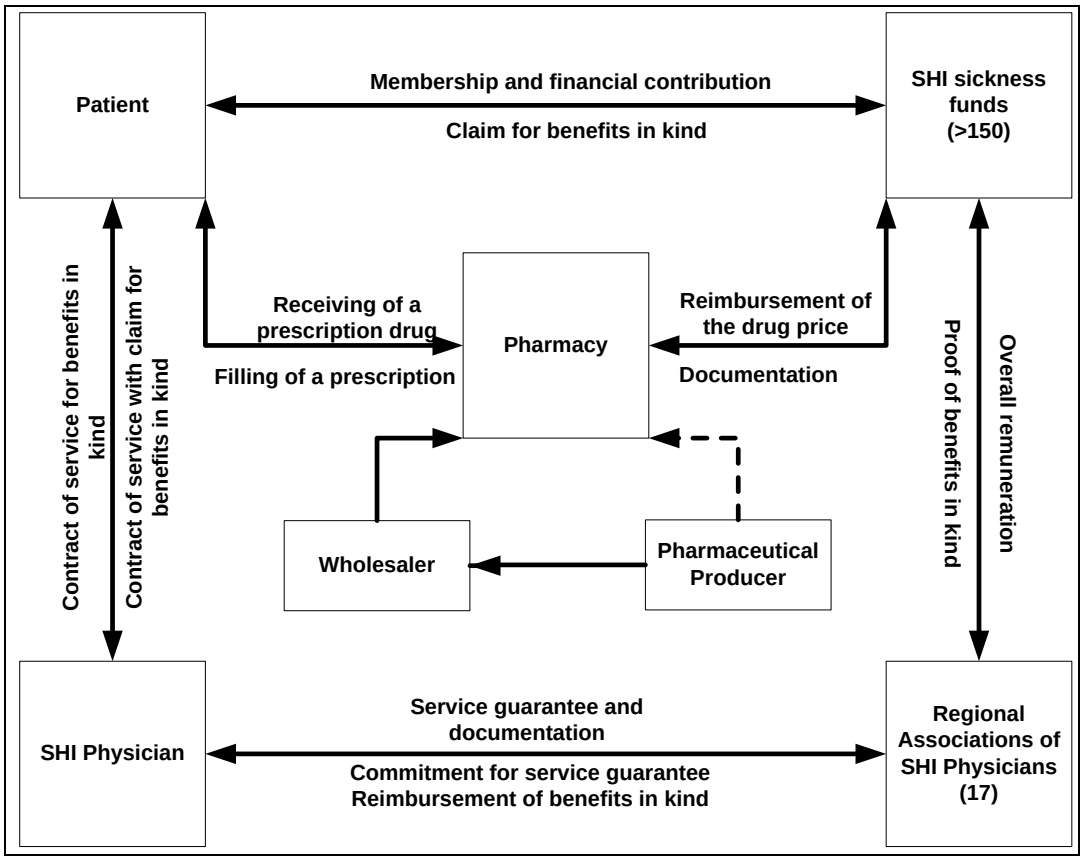
II.1 The supply of prescription drug in the Statutory Health Insurance

II.1.1 The system of ambulant care in the SHI and its major stakeholders

Figure 2 gives an overview about the ambulant care system in the Statutory Health Insurance. It shows the various stakeholders, their relationship (with each other), and the organization of the supply of prescription drugs in the SHI system.

Figure 2: The SHI system of ambulant care



Source: Illustration by the author based on Fünftes Buch Sozialgesetzbuch (SGB V)

The central position in the SHI system is inherited by the patient who is insured by a SHI sickness fund. In return for the membership and the associated financial contributions the patient has a claim for benefits in kind. The patient receives these benefits in kind from SHI physicians who are in charge of the ambulant care

treatment for the patient.[7] At the end of 2009 over 137.000 physicians treated patients in ambulant care. About 43.9 % of them were general practitioners, while 56.1 % of the SHI physicians were specialists.[8]

SHI physicians are also responsible for the prescription of drugs.[9] The patient submits these prescriptions in pharmacies to receive the drugs. Thereby, the patient only has to pay a maximal co-payment of ten euro, depending on the retail price of the drug. Beside these co-payments, prescription drugs are fully reimbursed in the SHI system by the sickness funds.[10] The pharmacies are supplied with products by wholesalers or directly by pharmaceutical producers. They receive payments for the dispended drugs by the sickness funds following the exact documentation about which drugs were dispended to the patients of each sickness fund. In this way, sickness funds can also monitor the observance of several regulations that target the pharmacies.[11]

In contrast to pharmacies, SHI physicians are reimbursed for the provision of the benefits in kind by the Regional Association of Statutory Health Insurance Physicians (RASHIP).[12]

Each RASHIP is responsible for the medical supply of compulsorily insured persons in a specific geographic region of Germany. Currently there are 17 of such regions which are mostly identical to the federal states (Bundesländer).[13] Physi-

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7 See § 73 (2) SGB V for an overview of services in ambulant medical care of the SHI system.

8 See Kassenärztliche Bundesvereinigung (2010)

9 See § 73 (2) SGB V

10 See § 61 SGB V

11 See § 129 (6) SGB V

12 See § 72 (2) SGB V

13 See § 77 (1) SGB V

cians who want to treat persons insured by a SHI sickness fund have to be members of the responsible RASHIP.[14]

Therefore the RASHIP acts as an intermediary body between sickness funds and SHI physicians, distributing the budget for ambulant care services between their members that provide ambulant medical services for compulsorily insured patients.

The SHI sickness funds are responsible for the reimbursement of the benefits in kind that are provided by the SHI physicians. The sickness funds transfer an annually adjusted overall remuneration to RASHIPs. It includes all benefits in kind for all insured persons that are provided by SHI physicians within a year for the specific region.[15] The payment of the remuneration has liberating effects for the SHI sickness funds, as the responsibility for the provision of ambulant medical services for their insurants is transferred to the RASHIPs.[16]

As the relationships between the different stakeholders in the SHI system, shown in Figure 2, indicate that the German Statutory Health Insurance is organized as a system of the joint self-government. Therefore the stakeholders of the systems, especially physicians and sickness funds, define the range of services the system provides for the insurants, while the Federal Ministry of Health is not directly involved in the organization of the healthcare system. However, the Federal Ministry of Health is, among other duties,[17] responsible for the formulation of bills, ordinances and administrative regulations to improve the effectiveness of the SHI system.

The highest decision making body of the joint self-government is the Federal Joint Committee. It consists of representatives of ambulant care SHI physicians, ambu-

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14 See § 73 (1a) SGB V

15 See § 85 (1) SGB V

16 See § 85 (2) SGB V

17 See Bundesministerium für Gesundheit (2011a) for an overview of the duties of the Federal Ministry of Health.

lant care SHI dentists, hospitals, and sickness funds in Germany.[18] It issues directives for the benefit catalogue of the SHI system and specifies which medical services are reimbursed by the SHI.[19]

The National Association of Statutory Health Insurance Physicians (NASHIP) represents the SHI physicians working in ambulant care on the national level. It is the head organization of the Regional Associations of SHI Physicians, representing the interests of all SHI physicians in ambulant care on the political stage. The NASHIP also keeps the federal registry of physicians, advocates the physician related positions in legislative processes, and concludes contracts with the umbrella organization of the SHI sickness funds. In addition, representatives of the NASHIP are members of the Federal Joint Committee.[20]

The umbrella organization of the SHI sickness funds is the National Association of Statutory Health Insurance Funds. It represents the interests and political ambitions of SHI sickness funds on the national level. It is also responsible for compliance and the enforcement of several regulative instruments. Similar to the NASHIP, it sends representatives to the Federal Joint Committee.[21]

Following the short presentation of the key stakeholders in ambulant care of the SHI system, the question arises, which of them are primary targeted with regulative instruments to contain the expenditures for prescription drugs. As indicated, especially pharmacies, pharmaceutical producers, physicians, and patients are the objective of various regulations. The next section gives an overview about the regulative instruments aiming at these key players on different levels.

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18 See § 91 (1) SGB V

19 See § 92 (1) SGB V

20 See § 77 (1) SGB V

21 See § 217a SGB V

II.1.2 Instruments of drug regulation in the German SHI system

The instruments to contain the growth of drug expenditure for can be classified in various ways. Following Schreyögg and Stargardt (2006), regulation schemes can be separated into three groups of instruments. While the first type of instruments affects the price of prescription drugs, the second type of regulatory instruments targets the drug volume dispended in the SHI system. The third category of regulatory instruments restricts total expenditures for prescription drugs.

In addition, it is also possible to classify regulatory instruments as regulative schemes targeting the supply side (pharmaceutical producers, pharmacies or the wholesalers), and instruments aiming at the demand side (patients, physicians).[22] The approach in Figure 3 distinguishes the regulative schemes by the effect level of the regulation (macro-, meso-, and micro- level) and the targeted parties of the SHI drug market.[23] Most of the regulative instruments are included in the "Fünftes Buch Sozialgesetzbuch" (SGB V), which defines the content and the legal requirements of the Statutory Health Insurance system.

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22 See Busse et al. (2005)

23 Figure 3 does not include the possible changes from reforms after December 2007. However all amendments to the cited laws and regulative instruments were included until the end of 2010.

Figure 3: Instruments of drug expense restriction between 2004 and 2007

Effect level	Pharmaceutical producer	Physician	Patient	Pharmacy
Macro level (overall SHI drug market; all pharmaceutical producers; physicians; patients or pharmacies)	• Manufacturer discount • Price moratorium	• Framework agreement	• Co-payments for prescription drugs	• Pharmacy specific discounts • Predetermined price margin for prescription drugs • Import quota • Prohibition of natural discounts • Aut-Idem rule
Meso level (Groups of pharmaceutical producers or drugs; physicians; patients or pharmacies)	• Reference price • Exemption of OTC drugs from reimbursement • Exemption of Lifestyle drugs from reimbursement	• Medical specialist group specific prescription limits • Regional drug agreements • Bonus malus rule	• Additional co-payments for drugs in reference price groups	
Micro level (singular pharmaceutical producers or drugs; physicians; patients or pharmacies)	• Exemption or limitation from reimbursement following cost - effectiveness analysis • Off-Label use • Exemption from co-payments • Rebate contracts • Price ceilings • Second opinion procedure	• Physician specific prescription limit	• Exemption from co-payments for prescription drugs	

Source: SGB V

Macro level regulations

Following Figure 3, several regulative instruments affect the SHI drug market at macro level. They are described in detail in the following for each stakeholder group.

For every prescription drug sold within the SHI system, the corresponding pharmaceutical producer has to a pay manufacturer's discount to the sickness funds[24]. The percentage of discount differs for drugs with and without patent protection. Both discounts are regulated in SGB V.[25]

Unlike in other European countries (e.g. Great Britain[26]), one of the most restrictive form of regulation on the macro level, direct drug price setting by a governmental institution, is not applied in the German SHI system. While statutory charges for whole sellers and pharmacies do exist, pharmaceutical producers are

24 In reality, the process is slightly more difficult. In the first step, the pharmacies have to pay the discount to the sickness funds. Following this, the pharmaceutical producers have to reimburse this discount to the pharmacies.

25 See § 130a (1) and (3b) SGB V for pharmaceutical producer related discounts.

26 See Mossialos et al. (2004)

allowed to set their manufacturer's price freely. Following this, the retail price for each drug dispensed at the expense of the SHI system is identical in every pharmacy.

While direct price regulation is not applied in the SHI drug market, drug prices and therefore pharmaceutical producers are targeted indirectly. One way of doing this are temporary price moratoria, freezing drug prices on a specific level for a limited time period. The instrument has been frequently used in the past, for example between May 1992 and December 1994, October 2002 and December 2004, November 2005 and March 2008. The latest price freeze comes into effect in August 2010 and is planned to last until December 2013.[27] During the price freezes pharmaceutical companies are still able to set their prices freely. However, they are obliged to render any additional profits resulting from price increases above the pre-determined price level, to the sickness funds of the SHI system as an additional rebate.[28]

Physicians hold a central role within the SHI system, ultimately deciding about the drug a patient receives. Although therapeutic freedom when choosing medication is existent in theory, various regulative instruments affect the decision of the physician. As most of physician related regulations are established on the regional (meso) or individual (micro) layer, only the framework agreement[29] between SHI sickness funds and the National Association of Statutory Health Insurance Physicians affects physicians on the macro level. The agreement includes the agreed growth rate for outpatient drug expenditures for the following year as well as supply and efficiency goals for the SHI system. An example for the second goal are suggestions about possible lead compounds for selected therapeutic areas. It has to be noted, that these goals and suggestions are refined on the regional level, lead-

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27 See § 130a (3a) SGB V

28 See Busse et al. (2005)

29 See § 84 (1) SGB V

ing to regional drug agreements between the local sickness funds and the RASHIPs.

One of the few regulative instruments which target insurants of the sickness funds within German SHI system as a whole, are prescription charges. Following the latest change of patients co-payments,[30] implemented in 2004, patients are forced to make a prescription related co-payment – currently between five and ten euro, depending on the price of the drug prescribed. Drugs priced lower than five euro have to be paid completely by the patient. Consequently, the price sensitivity of patients is assumed to be weak, especially in regard to other European countries[31] as patients receive any drugs for a maximal co-payment of ten euro – independent of the actual price of the drug. However, co-payments are regarded as a mode of limiting the Moral Hazard problem – related with the consumption of drugs.[32] Also, the co-payments are a considerable source of funding amounting to 1.650 million euro in 2009 and 1.701 million euro in 2010.[33]

There are several exemptions from the co-payment rule. Patients suffering from a chronic disease, minors and patients with a low income are or can be excluded from co-payments. Also, the implementation of certain regulative instruments on the micro level can result in the exemption from patient related co-payments.[34]

Pharmacies inherit the role of a intermediary between pharmaceutical companies and patients. Following their importance as the distributer of drugs, they are faced with a set of regulations. In addition to the pharmacy specific discounts and the predetermined price margins,[35] pharmacies have to follow guidelines that urge the

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30 See "Gesetz zur Modernisierung des Gesundheitssystems" (2003)

31 See Merino-Castelló (2003)

32 See Thomson et al. (2004)

33 See Häussler et al. (2011)

34 See § 43 (1) SGB V

35 See § 130 (1) SGB V

dispense of cheaper imported drugs.[36] These so-called parallel imports differ by the prices set within the different markets / countries. Following this, parallel importers buy drugs on the cheaper market (Market 1), import them to the more expensive market (Market 2), switch the packaging and patient information sheet, and sell the drug for a lower price than of the domestic drug in Market 2.[37] Also, pharmacies are able to utilize specific wholesale rebates, which include the supply of additional drugs free of charge ("buy two get one for free"). This "habit" was stopped through a legal change in May 2006,[38] which prohibited the so-called "natural rebates" to pharmacies.

At last, the Aut-idem rule[39] mandates pharmacies to exchange expensive with cheaper drugs of the same active ingredient if these are available in the same strength and package size. Following the legal requirements that were implemented in 1989,[40] the pharmacist has to choose between the three drugs with the lowest price. For the case that the physician writes a specific drug name on the patient's prescription instead of the name of the chemical substance, the pharmacist is allowed to choose between the three cheapest drugs and the named drug instead. However, physicians can suspend this procedure by adding a reservation to the prescription. If a physician opts for this, pharmacies are prohibited to substitute the prescribed drug with another, possible cheaper, drug.

While the already presented regulative schemes aim at stakeholder groups as a whole, the instruments depicted on the meso level in Figure 3 target specific subgroups of drug manufacturers, physicians, patients, and pharmacies.

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36 See § 129 (2) SGB V

37 See Hancher (2004)

38 See "Gesetz zur Verbesserung der Wirtschaftlichkeit in der Arzneimittelversorgung" (2006)

39 See § 129 (1) SGB V

40 See "Gesetz zur Strukturreform im Gesundheitswesen" (1988)

Meso level regulations

Groups of pharmaceutical producers are affected by several regulative instruments on the meso level. An instrument which has a strong impact on the pricing of prescription drugs is reference pricing – an indirect price regulation mechanism, implemented in 1989.[41] It sets a uniform reimbursement limit – the reference price (RP) – for one or several active ingredients. Therefore all producers providing drugs containing the included active ingredient are affected by the regulative instrument, and in addition physicians and patients. If the price of a product exceeds the reimbursement level, patients have to pay the difference between the RP and the retail price by themselves.[42] Originally, only original drugs and their generic versions were included in the RP system.[43] Since 2004, patent protected drugs can also be set into reference price groups. In this case, the reference price groups consist either of various patent protected drugs or of a mixture of patented originals, off-patent original drugs and their generic versions.[44] Therefore reference pricing can affect multiple active ingredients at once. The level of the specific reference prices are set by the Association of Sickness Funds in agreement with the Federal Ministry of Health and revised annually. While the reference price differs from group to group, it is always set below the price of original brand name drugs.

In addition, specific sub-groups of pharmaceutical producers were affected by changes in the reimbursement system. Especially producers of Over-the-counter drugs are confronted with a changed market environment, as OTC drugs have generally been excluded from reimbursement since 2004.[45] Also, unlike in the case of prescription drugs, price setting is unrestricted on every step of the distri-

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41 See "Gesetz zur Strukturreform im Gesundheitswesen" (1988)

42 See Giuliani et al. (1998)

43 See "Gesetz zur Modernsierung des Gesundheitssystems" (2003)

44 See Stargardt et al. (2005)

45 See § 34 (1) SGB V

bution chain for OTC drugs.[46] Therefore, it is possible for pharmacies to set different prices for the same OTC drug, leading to a possible price competition between pharmacies. At last, producers are faced with the risk that their products are declared to be lifestyle drugs[47] and thus to be excluded from SHI reimbursement.

As mentioned before, the majority of regulative instruments affecting physicians are located on the meso level. A regulative instrument which targets physicians of different medical specialties is the physician specific prescription drug budget. The limit, in its current form, was implemented in 2001.[48] It restricts the drug expenditures per patient, depending on socioeconomic variables like age and gender of the patient, but also on the speciality of the physician. It also differs between the federal states. The actual, physician specific drug budget is calculated on the individual level, concerning the described variables as well as the number of patients treated in the past year. The effects of overstepping this budget for the singular physician (micro level) will be discussed later.

Other regulative instruments target physicians at regional level, such as the mentioned regional drug agreements between sickness funds and the Regional Association of Statutory Health Insurance Physicians. These regional agreements can include specific rules concerning efficiency goals. One of the most important regulative instruments in this context is the lead compound rule, implemented in 2007.[49] Following this regulative scheme, the prescription of preferred active ingredients for certain indication areas is promoted. Therefore, regional drug agreements include quotes, determining that a certain percentage of dispended drugs in the indication area should belong to the chosen active ingredient (lead

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46 See Schreyögg et al. (2006)

47 Lifestyle drugs are defined as drugs primarily used to increase the quality of life. This includes drugs used against erectile dysfunction, regulation of body weight and smoking cessation. See § 34 (1) (7) SGB V.

48 See "Gesetz zur Ablösung des Arznei- und Heilmittelbudgets" (2001)

49 See "Gesetz zur Verbesserung der Wirtschaftlichkeit in der Arzneimittelversorgung" (2006)

compound). The foremost intention of this regulation is to increase the market share of cheaper molecules in relation to therapeutic comparable active ingredients that are more expensive.

Another regulative instrument, that is part of the regional drug agreements, is the bonus-malus rule. Implemented following a legal change in 2007,[50] the bonus-malus regulation forces payments by physicians in case they overstep fixed daily therapy costs for certain illnesses (malus).[51] If physicians stay below the fixed average daily therapy costs, a bonus will be paid to all physicians by the Regional Association of Statutory Health Insurance Physicians. While the regulation was implemented in 2007, it has already been discharged in 2008, conflicting with other regulatory instruments making the calculation of the actual daily therapy costs difficult.[52]

On the meso level, as Figure 3 shows, certain groups of patients were affected by the implementation of reference pricing. This is the case when patients receive drugs priced above the reference price, as they have to pay the difference between the reference price and the more expensive drug on their own. While such cases are rather uncommon,[53] as pharmaceutical manufactures normally decrease their prices at least to reference price level, the case of additional, patient related payment is only mentioned for the sake of completeness.

Micro level regulations

The last row (micro level) of Figure 3 shows that also the singular pharmaceutical manufacturer can be affected by a variety of regulative instruments.

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50 See "Gesetz zur Verbesserung der Wirtschaftlichkeit in der Arzneimittelversorgung" (2006)

51 See § 84 (3) SGB V

52 See Rieser (2007)

53 An example is the case of atorvastatine (brand name Sortis®), whose producer Pfizer® did not reduce the price onto the reference price or below after the inclusion of the active ingredient in a reference price group.

Especially producers of high priced patent drugs are possible targets of cost-effectiveness analysis, conducted by the Institute for Quality and Economic Efficiency (IQWiG) on behalf of the Federal Joint Committee.[54] Following a cost-effectiveness analysis, active ingredients and therefore the corresponding drugs, can be excluded from reimbursement or limited to certain patient groups.

The Federal Joint Committee can also allow or deny the so-called off-label use of prescription drugs.[55] In the case of a positive decision of the committee, testifying an additional utility for patients, the corresponding drugs can be prescribed in medical indication areas without being accredited for the specific indication. This practice is mostly utilized for serious illnesses such as various forms of cancer or HIV.

Another important regulative instrument, targeting the singular manufacturer is to exempt the manufacturer's drugs from patient related co-payments. This can lead to demand increases, since patients, as well as physician, usually prefer drugs without co-payments. The exemption can result from two regulative instruments:[56] The first option is based on the reference price system. Following a health care reform in 2006,[57] the Federal Association of the Health Insurance Funds,[58] is able to exempt drugs in certain reference price groups from the patient prescription charge. To be able to utilize this exemption, producers have to lower their prices to a certain level below the reference price.[59]

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54 See § 35b (1) SGB V

55 See § 35b (3) and § 35c SGB V

56 Beside these two options, patients can be exempted from drug related co-payments if the sum of their yearly co-payments exceeds a certain yearly level, the so-called “Belastungsgrenze”. The various regulations and special cases for chronically ill patients can be found in § 62 (1) (2) SGB V

57 See "Gesetz zur Verbesserung der Wirtschaftlichkeit in der Arzneimittelversorgung" (2006)

58 See § 213 (2) SGB V

59 See § 31 (3) SGB V

The second option for manufactures to exempt their drugs form the patient prescription charge follows the conclusion of a rebate contract with a sickness fund. Rebate contracts, comprise of agreements on additional discounts between producers and sickness funds and usually cover a specific active ingredient or the whole product portfolio of the producer. Introduced in 2003, rebate contracts were not common until 2007. Following legal changes in that year,[60] rebate contracts now overwrite the previously stated Aut-idem rule. Therefore pharmacists are forced by law to dispense the drugs which are part of the rebate contract unless the physician has not prevailed substitution. Following the conclusion of a rebate contract, sickness funds can exempt the rebated drugs half or fully from patient prescription charges.[61]

Another regulation that was implemented following another health care reform in 2007,[62] are price ceilings for drugs which are not included in the reference price system.[63] The price ceilings are either negotiated between the pharmaceutical companies and the Federal Association of the Health Insurance Funds on a voluntary base or are set after cost-effectiveness analysis has been conducted. However, until December 2010, the instrument has not been used in the SHI system.

At last, drugs of singular producers that are associated with huge yearly therapy costs or a strong risk potential can be targeted by the second-opinion procedure.[64] In this case, the drug treatment can only be performed by the attending physician after the consultation of an specialist for pharmacotherapy. Until now (December 2010), only drugs containing specific active ingredients for the treatment of pulmonary hypertension are affected by this regulation.

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60 See "Gesetz zur Stärkung des Wettbewerbs in der gesetzlichen Krankenversicherung" (2007)

61 See § 31 (3) SGB V

62 See "Gesetz zur Stärkung des Wettbewerbs in der gesetzlichen Krankenversicherung" (2007)

63 See § 31 (2a) SGB V

64 See § 73d SGB V

The most important regulative scheme, targeting the singular physicians, is a consequence of the individual prescription limit that was explained on the meso level section. In case of overstepping the individual prescription budget the physician can be forced to undergo a verification process, determining the reasons for the budget excess. This procedure, enforced by the responsible RASHIP, can lead to various results. In the worst case, the physician can be made liable for excess prescriptions. Fearing the negative financial consequences, physicians usually try to avoid the verification process by prescribing less expensive drugs, e.g. generic drugs to relieve their prescription budget.

II.2 Datasets and econometric software

The empirical analyses conducted in this thesis are based on three different datasets.

The first dataset, provided by the German market research company INSIGHT Health, contains approximately 99 % of the drug prescriptions in the German SHI market, covering the time span from January 2004 to December 2007 on a monthly basis. For each manifestation, in terms of strength, package size and dosage form, of every drug prescribed in the SHI system the data includes information on sales volume and the amount of dispensed Defined Daily Doses (DDD).[65] The dataset also contains information on the producer and the status of the drug as a generic or original drug with or without patent protection. For the analysis conducted in this thesis, several active ingredients were chosen from the dataset.

The use of the INSIGHT Health data has some advantages. First of all, as 99 % of the SHI prescription drug market is covered, the risk for misleading results, following a possible bias of the database is small. Secondly, as the dataset is not limited on certain active ingredients, the SHI drug market can be analyzed in more detail.

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[65] Defined Daily Doses (DDDs) are a WHO statistical measure of drug consumption used to standardize the comparative usage of various drugs between themselves or between different health care environments.

The second dataset, provided by a large German sickness fund, includes information on the complete prescription history of patients and their physicians between January 2004 and December 2007 on a monthly basis for three different indications. The identity of patients and physician was made anonymous. The dataset also includes socio economic variables like age, gender and the employment status of patients, as well as information on the nature and the dispatch date of the drug. In opposition to the first dataset, these so-called routine data represent only a share of the SHI market. Since only the dataset of a singular sickness fund was available – even though it comprises of a large number of members (>1.5 million insured persons) – the results could be biased. This is due to the historically determined differences in the sickness funds risk profiles, as before 1993, each sickness fund contracted specific population subgroups.[66] Therefore, the dataset collected from a singular sickness fund cannot be regarded as representative for the overall German population.[67] Thus, the results of the analysis in Part IV should to be interpreted considering this limitation.

The third dataset was created from different sources. As a main focus of the thesis are regulative instruments, a dataset was constructed containing information on the inclusion of drugs in rebate contracts,[68] reference price groups[69] and the corresponding possible exemption from patient related co-payments.[70] Also drugs with active ingredients which were part of the lead compound regulation were identified through the framework agreement between sickness funds and the National Association of Statutory Health Insurance. The third dataset is connected to the

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66 For example, the TK (Techniker Krankenkasse) contracted only individuals with technical professions like engineers or master craftsmen.

67 See Holle et al. (2005)

68 Information provided by INSIGHT Health

69 Information provided by the Federal Joint Committee and the German Institute of Medical Documentation and Information

70 Information provided by the National Association of Statutory Health Insurance Funds

first and the second one through the central pharmaceutical number (PZN) that identify a drug uniquely within the SHI system.

All econometric analysis in part III - V were conducted using the STATA 10.1® software package (StataCorp LP). In some parts of the thesis user-written commands for the STATA software were used. These commands were in detail "xtivreg2" in Part IV[71] and "margeff." in Part V.[72] For the theoretical analysis of the rebate contracts, conducted in Part VI, Mathematica 5.0® was applied.

II.3 References

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71 See Schaeffer (2008)

72 See Bartus (2005)

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III. The influence of reference price policy changes on the pricing of patent, original and generic pharmaceuticals

III.1 Introduction

The increase in drug expenditures is one of the biggest challenges for the German healthcare system. In 2010, the expenditures for prescription drugs (also called Rx drugs) amounted to 30.2 billion euro.[1] In comparison with the expenditures for Rx drugs in 2010 (19.4 billion euro), the expenditures increased strongly in the last decade. While the overall expenditures in the SHI system also have increased between 2000 and 2010 from 133.7 billion euro to 176.0 billion euro, the share of the expenditures for Rx drugs has increased over time.[2] In 2000, 14.5 % of the overall expenditures in the SHI system were drug related. In 2010 the share had increased to 17.1 %.

Rx drugs can be divided into three different groups, depending on their patent status. The first group are drugs under patent protection, called patent drugs. It is not allowed to produce and sell drugs with the same active ingredient without the permission of the patent holder. The second type of drugs consists of active ingredients whose patent protection has expired. These drugs, called original (off-patent) drugs,[3] can be produced by other companies without legal issues. The pharmacological identical versions of these original (off-patent) products are called generic drugs. They form the third kind of drugs.

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1 See Bundesministerium für Gesundheit (2011)

2 See Bundesministerium für Gesundheit (2011)

3 In the following, the terms original drugs and original (off-patent) drugs are used synonymously.

The German government introduced different instruments to control the rising cost for prescription drugs. One of the most important instruments, implemented in 1989, are reference prices.

The reference price system is an indirect method for controlling prices of prescription drugs. Unlike for other prescription drugs, the reimbursement of drugs belonging to a reference price group through the Statutory Health Insurance is limited. This ceiling price is called reference price. If the price of the reference drug is above that amount, the consumer has to pay the difference.

Until 2004 drugs under patent protection were excluded from the reference price system. As a consequence only original (off-patent) drugs and their generic competitors were included in reference price groups. The approach was changed in 2005. Since then it is possible to establish reference price groups which include therapeutically and pharmacologically comparable patent, original, and generic drugs. The reference price, which is set below the prices of original and patent drugs,[4] let producers choose to either decrease their prices at least to the reference price level or, by denying this, forcing patients to pay the difference between the retail price and the reference price.

Market data from various European countries shows that most producers choose to decrease their prices to be competitive as the results of the studies of Schneeweiss et al. (1998), Aronsson et al. (2001), Lexchin (2004), Puig-Junoy (2007) and Kaló et al. (2007) show. However, these studies do not determine, which share of price reduction was caused by reference pricing and not due to the competitive situation in the various European markets.

Pavcnik (2002) was the first author who compared the price development of therapeutic groups after the introduction of a reference price system, distinguishing between original (off-patent) drugs and their generic competitors while controlling for the degree of competition in the observed markets. Her results for two

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[4] The reference price is located above the price level of the generic competitors, which are cheaper than their original counterpart.

indication areas in the German SHI market indicate a larger price decrease for original drugs with increasing competition through additional generic drugs.

Brekke et al. (2009) used the introduction of the reference price system in Norway in 2003 to estimate the effects of the policy change on the pricing strategies of pharmaceutical firms. The results show that the prices of generics and original (off-patent) drugs decrease significantly. The effect is stronger on the prices of original (off-patent) drugs.

The theoretical framework of Pavcnik (2002) and Brekke et al. (2009) can be found in Danzon and Lui (1996), and Zweifel and Crivelli (1996). The first authors argue that all prices within a reference price cluster converge towards the determined reference price. They conclude that the prices of original drugs decrease to the level of the reference price, while the prices of generic drugs increase.

Zweifel and Crivelli (1996) developed a theoretical model that suggests that the reference price system has a primary effect on the prices of original products while the prices of generics remain stable. Both motivations are not completely in line with the recent results of Pavcnik (2002) and Brekke et al. (2009). While both studies find that the prices of original drugs decline after the implementation of reference prices, the prices of generics did not remain stable but also decreased.

At last, Augurzky et al. (2009) showed the effects of the German reference price system on ex-factory prices. The results indicate that ex-factory prices do not adjust fully to changes of reference prices, as a change of reference prices of 1 % leads to a 0.3 % change of market prices. In addition, the authors found that the introduction of reference prices leads to a 7 % reduction of market prices for affected drugs.

All presented empirical studies suggest that the reference price system has an impact on the prices of original and generic products. However, while these studies analyze the effects of reference pricing on original products, none of the works distinguishes between on-patent drugs and original drugs with an expired patent protection. Yet, the differentiation between these types of original drugs seems

crucial for the explanation of differences in price reactions on the introduction of reference pricing.

As the research of Ellison et al. (1997) and Morton (1997) showed, the main competition occurs between original and generic products with the same active ingredient and not between products with different but comparable active ingredients. Consequently, it seems reasonable that the producers of on-patent drugs have a lower price elasticity than producers of original drugs. Thus, the price response of patent drugs on the introduction of reference pricing should be weaker than price reactions of original drugs.

Since none of the existing studies[5] considered this aspect, the main contribution of this paper is the analysis of differences in the price reactions of patent, original and generic drugs following the implementation of a joint reference price.

Thereby, the inclusion of two major therapeutic groups in the reference price system is used to investigate, for the first time, the effects of a joint reference price on the pricing of patent, original, and generic drugs. The included therapeutic groups, HMG-CoA reductase inhibitors (statins) and proton pump inhibitors (PPI) were chosen for various reasons. Most important, both therapeutic groups include patent, original, and generic drugs. In addition, they provide treatment for major diseases in civilized countries and are widely prescribed.

Statins are used in the therapy of high cholesterol levels to reduce the risk of cardiovascular diseases. PPIs are applied to treat dyspepsia, peptic ulcer disease, and the laryngopharyngeal reflux disease.

The results indicate that prices of patent, original, and generic drugs decreased after the reference price implementation. The price decrease for original (off-patent) drugs was stronger than for patent drugs although patent drug prices were higher than original drug prices before the introduction of the reference price system. The results also indicate that competition reduces the prices of drugs. The

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[5] See López-Casasnovas and Puig-Junoy (2000) for an overview on additional studies concerning reference pricing.

effect is weaker for branded (patent or original) drugs than for generics. Moreover, the impact of competition on prices is stronger after the introduction of reference prices. Again, branded drugs are less affected by additional competitors.

The paper is structured as follows: The next section gives information about the German SHI market for Rx drugs mainly focusing on the systematic of the reference price system. Section III.3 shows the theoretical motivation behind the different price reactions of the three drug types. The description of the database and the descriptive statistics for both therapeutic groups are provided in Section III.4 and III.5. The econometric model and the discussion of the empirical results are presented in Section III.6. The article concludes with a résumé of the results and possible explanations of the pricing strategies for the different types of drugs.

III.2 Reference Pricing in the German market for pharmaceuticals

The German Health System features a statutory health insurance (SHI) which covers most of the German population (about 90 %).[6] The insurance system reimburses the costs for the majority of consumed drugs. Only over-the-counter drugs (OTC-Drugs) and certain specific drugs are excluded from general reimbursement.

The German market for Rx pharmaceuticals is highly regulated.[7] The legal framework regulates the market entry and distribution of drugs. Also, several statutory regulations concerning the restriction of drug expenditures in the SHI market exist. The regulation authority of the German SHI market, the Federal Ministry of Health, uses several of such instruments to contain the drug expenditures.[8] The regulations include mandatory discounts for drugs to the Statutory Health Insur-

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6 See Bundesministerium für Gesundheit (2011) and Statistisches Bundesamt (2010a)

7 This analysis is focused on the Statutory Health Insurance Market. The private health insurance market is not part of the analysis.

8 For an overview of these instruments, see Busse et al. (2005), Greß et al. (2007), and Denda (2010)

ance, restricting the retail pharmacist to dispense one of the cheapest comparable drug to the customer (aut-idem), and affecting the prescription behavior of physicians through physician specific drug budgets. Especially the drug budget[9] encourages physicians to prescribe cheaper drugs as overstepping of the budget leads to discussions with sickness funds and the Regional Association of Statutory Health Insurance Physicians.[10] Following this discussion, the physician can be made financially responsible for the difference between his drug budget and his overall amount of prescribed drugs in the quarter.

Another important regulative instrument is the reference price scheme, implemented in 1989. It represents a maximal reimbursement schema for Rx pharmaceuticals. If the price of a drug which is included in a reference price group exceeds the stipulated reference price, the patient is forced to make out-of-pocket payments, covering the difference between the retail price and the reference price.[11]

The Federal Joint Committee[12] decides which drugs are covered by the reference price system. The implementation of the reference prices is left to the National

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9 The drug budget that restricts the drug expenditures per patient and quarter, depends on socioeconomic variables like age and gender of the patients, but also on the specialty of the physician. It also differs between the federal states. The actual, physician specific drug budget is calculated based on the described variables as well as the number of patients treated in the previous year.

10 The Regional Associations of Statutory Health Insurance Physicians (RASHIP) are responsible for the medical supply of compulsorily insured people. Each physician who wants to treat compulsorily insured persons has to be a member of the competent RASHIP.

11 See Stargardt et al. (2005)

12 The Federal Joint Committee is the highest decision -making body of the joint self-government of physicians, dentists, hospitals, and health insurance funds in Germany. It issues directives for the benefit catalogue of the SHI system and specifics which services in medical care are reimbursed by the SHI.

Association of Statutory Health Insurance Funds[13] that also decides on the level of the reference price in agreement with the Federal Ministry of Health. The reference price levels are determined in different steps.[14]

First, the reference price for a standard package/strength is set within a corridor between the manufacturer prices and a price level set by the Federal Joint Committee based on legal requirements of the Book V of the Social Code. Following this, a quasi-hedonic regression equation (Cobb Douglas form) is used to estimate coefficients that are applied to determine the relative reference prices for different package sizes and strengths. After the implementation of the reference prices, they are revised annually and adjusted, if necessary.

In contrast to other countries the German SHI system includes both generic and therapeutic reference pricing.[15] This fact is reflected in the different types of reference price groups. A drug which is proposed to be covered by the reference price system can be sorted into one of three different types of reference price groups:

- Phase 1: Drugs with the same active ingredient (generic reference pricing)
- Phase 2: Drugs with therapeutically and pharmacologically similar active ingredients (therapeutic reference pricing)
- Phase 3: Drugs with comparable therapeutic effect, especially combinations (therapeutic reference pricing)

Until 2004 patent protected drugs were excluded from reference pricing. The special status of patent drugs ended with the introduction of the SHI Modernization

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13 The National Association of Statutory Health Insurance Funds is the central lobby of the statutory health insurance and long-term care insurance funds. It shapes the outline conditions for healthcare in Germany and represents the interests of the SHI sickness funds in the Federal Joint Committee.

14 For a more detailed explanation, see Stargardt et al. (2005)

15 Generic reference pricing allows only the inclusion of drugs with the same active ingredient in a joint reference price group. In therapeutic reference pricing, it is possible to assemble drugs of different active ingredients that are therapeutically or pharmacologically similar in a joint reference price group.

Act[16] in 2005. Following the legal change, it is possible to create joint Phase 2 reference price groups that include patent drugs as well as original drugs and their generics consisting of similar active ingredients. Examples for such joint reference price group are the therapeutic groups of statins and proton pump inhibitors. The various active ingredients belonging to this group became subject to reference pricing in January 2005. The established reference price group includes patent protected active ingredients like atorvastatin but also active ingredients like simvastatin whose patent status is already expired.

Following the policy change, pharmaceutical manufacturers of patent drugs were facing a new market situation. Instead of having the security of a full reimbursement and a monopolistic position during the patent protection period, patent drugs are forced to compete with possible considerable cheaper drugs.

The next chapter shows a theoretical motivation, how the producers of patent drugs (*P*), original drugs (*O*), and generic drugs (*G*) react to the implementation of a joint reference price.

III.3 Theoretical Motivation

Motivating the empirical approach, the following section presents a simple theoretical model which explains the impact of reference price policy changes on the pricing of patent, original and generic drugs. The model is inspired by Brekke et al. (2009).

We assume a therapeutic market with a patent drug (drug *P*), an off-patent original (drug *O*) and a generic drug (drug *G*).

Patients are assumed to be fully insured and only have to make a co-payment of c_i where $i = P,O,G$ with $\frac{\partial c_i}{\partial p_i} > 0$ where p_i is the price of drug *i*.

[16] See "Gesetz zur Modernisierung der gesetzlichen Krankenversicherung" (2003)

The parameter c_j describes the co-payment for a substitute drug with $j = P,O,G$ with $\frac{\partial c_j}{\partial p_j} > 0$ where p_j is the price of drug *j*.

The demand for drug i is $D_i(c_p,c_O,c_G)$, where $\frac{\partial D_i}{\partial c_i} < 0$ and $\frac{\partial D_i}{\partial c_j} > 0$. The revenue of company *i* is given by $\pi_i = p_i D_i(c_p,c_O,c_G)$.

The demand response on rising drug prices is assumed to be different for patent, original, and generic drugs.

In the German Health System the prescribing physician can choose the drug that will be dispensed by the pharmacies. In the case of bioequivalence the choice between original and generic product should not be difficult for the physician. The prescription of the cheaper generic product should be the rational choice for the physician, as both patients (lower co-payment) and physicians (lower burden for the drug budget) benefit from the dispense of generic drugs.

Still, original drugs are normally higher-priced than generics without losing their complete market share.[17] This suggests that original drugs have an additional subjective utility for physicians and/or patients.[18] Such potential additional benefits of original drugs could be the reduction of side effects for patients or the long term experiences of the physicians with the original drug.

Consequently it seems reasonable to assume that an original drug can have a higher price without a complete loss of demand, suggesting that $\frac{\partial D_O}{\partial c_O} > \frac{\partial D_G}{\partial c_G}$.

This coherence should be even more distinctive for patent drugs. Since patent drugs contain a unique active ingredient it is possible that the effectiveness or the

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[17] See Aronsson et al. (2001). The argument is also supported by the results in Section III.5.2III.5.2.

[18] See Hellerstein (1998) and Coscelli (2000) for results on physician's persistence for prescribing brand-named drugs.

range of side effects is better than of any comparable original or generic drug. This aspect can be used by the pharmaceutical companies to apply higher prices than original and generic drugs without losing demand completely. This leads to the following assumption concerning the demand reactions of all three drug types: $\frac{\partial D_G}{\partial c_G} < \frac{\partial D_O}{\partial c_O} < \frac{\partial D_P}{\partial c_P} < 0$.

Even though patent, original and generic drugs are considered therapeutic similar due to the inclusion in a joint reference price group, they are no perfect substitutes. The price reaction on the implementation of a reference price should be different for the three types of drugs.

Let the reference price (p_{RP}) be set below the price of the original and patent drug but above the price of the generic drug:

$$p_G < p_{RP} < p_O < p_P \tag{1}$$

If the price of a drug exceeds the reference price, the difference between p_i and p_{RP} has to be paid by the patient. This type of co-payments[19] has to be differentiated from regular co-payments per drug, which are independent of the reference price. The regular co-payments per drug are defined as a rate $0 < \alpha < 1$ of the retail price (p_i). Thus, patient related costs can be expressed as:

$$c_i = \begin{cases} \alpha p_i & \text{if } p_i \le p_{RP} \\ \alpha p_{RP} + (p_i - p_{RP}) & \text{if } p_i > p_{RP} \end{cases} \tag{2}$$

where α is considered to be equal for all drugs.

The introduction of reference pricing leads to higher co-payments for patent and original drugs. Prior the introduction of reference pricing, patients only had to pay the co-payment rate α independent of the drug type. After the implementation of

[19] The German expression for this type of co-payment is "Aufzahlung".

the regime, the situation changes for patent and original drugs. Patients have to make additional co-payment of (p_i - p_{RP}), given constant prices.

Following this, the first order conditions for the patent, original and generic drugs are:

$$\frac{\partial \pi_P}{\partial p_P} = D_P(c_P, c_O, c_G) + p_P \frac{\partial D_P[\cdot]}{\partial c_P} \tag{3}$$

$$\frac{\partial \pi_O}{\partial p_O} = D_O(c_P, c_O, c_G) + p_O \frac{\partial D_O[\cdot]}{\partial c_O} \tag{4}$$

$$\frac{\partial \pi_G}{\partial p_G} = D_G(c_P, c_O, c_G) + p_G \frac{\partial D_G[\cdot]}{\partial c_G} \alpha \tag{5}$$

The demand for patent and original drugs should therefore be lower for given prices. Since it is assumed that $\frac{\partial D_P}{\partial c_P} > \frac{\partial D_O}{\partial c_O}$, the demand reaction for patent drugs should be weaker than for original drugs.

The situation of generic drugs is more ambiguous. Since the reference pricing leads to higher co-payments for patent and original drugs for given prices, the demand for generic drugs should increase. Consequently, generic producers should increase their prices in reaction. However, if patent and original producers decrease their prices following the reference price implementation to reduce the additional patient related co-payments, generic producers also should respond with a price reduction. Also, it should be noted that cheaper generic prices are preferred by physicians because of their prescription restrictions due to the physician specific drug budget.

Finally, the following hypotheses can be derived from the model:

H 1. Producers of patent drugs as well as producers of original drugs are stimulated to reduce their prices after the introduction of reference prices.

H 2. The price reduction should be stronger for original drugs than for patent drugs.

H 3. The price reaction of generic drug producers is assumed to be weaker and potentially ambiguous.

III.4 Data set

The empirical analysis is based on data of the SHI market for prescription drugs. The dataset, provided by the German market research company INSIGHT Health, contains approximately 99 % of the drug prescriptions in the German SHI market. It covers the relevant market from January 2004 to June 2006 on a monthly base.

The study uses the data for two therapeutic groups, HMG-CoA reductase inhibitors (statins) and proton pump inhibitors (PPIs). Both groups were included in reference price system in January 2005. For that, all drugs containing the active ingredients with the ATC-Code[20] C10AA* (for statins) and A02BC* (for PPIs) became part of the respective reference price group.

Important for this study, both therapeutic groups contain patent, original, and generic drugs. Therefore, the established reference price groups are Phase 2 reference price groups, containing drugs with therapeutically and pharmacologically similar active ingredients.

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[20] In the Anatomical Therapeutic Chemical (ATC) classification system, the drugs are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. Drugs are classified in groups at five different levels. The drugs are divided into fourteen main groups (1st level), with one pharmacological/therapeutic subgroup (2nd level). The 3rd and 4th levels are chemical/pharmacological/therapeutic subgroups and the 5th level is the chemical substance.

The first group, statins, are applied to reduce cholesterol levels and therefore to reduce the risk of cardiovascular diseases. The prescriptions of statins in the SHI system lead to expenditures of 583 million euro in 2006, ranked under the 20 therapeutic groups with the most revenues in 2006. Overall, 1.7 billion Defined Daily Doses (DDD)[21] of statins were dispensed in 2006, making them one of the most dispensed therapeutic groups in 2006.[22]

Table 1: Summary statistics statins

Active ingredient	Total N	Patent	Original	Generics
Simvastatin	33	-	5	28
Lovastatin	19	-	5	14
Pravastatin	2	-	2	-
Fluvastatin	2	2	-	-
Atorvastatin	1	1	-	-

N is the number of products for the active ingredient in the balanced panel. In case of columns (2) - (4), N is the number of patent, original, and generic products for the active ingredient (including re-imports). Source: INSIGHT Health

The second therapeutic group, proton pump inhibitors (PPI), is used in the treatment of acid secretion. In 2006, 996 million DDD of PPIs were dispensed in the German Statutory Health Insurance (SHI) market, leading to drug expenditures of 993 million euro. Therefore PPIs were the therapeutic group with the highest revenues in the German SHI market in 2006.

[21] Defined Daily Doses (DDD) are a WHO statistical measure of drug consumption that are used to standardize the comparative usage of various drugs between themselves or between different health care environments.

[22] Based on NVI Dataset, provided by the German market research company INSIGHT Health, which contains approximately 99 % of the drugs prescriptions in the German SHI market.

Table 2: Summary statistics PPIs

Active ingredient	Total N	Patent	Original	Generics
Omeprazole	19	-	1	18
Pantoprazole	6	6	-	-
Lansoprazole	6	-	6	-
Raboprazole	7	7	-	-
Esomeprazole	1	1	-	-

N is the number of products for the active ingredient in the balanced panel. In case of columns (2) - (4), N is the number of patent, original, and generic products for the active ingredient (including re-imports). Source: INSIGHT Health

The dataset contains the sales volume and the quantity of dispensed drugs for both therapeutic groups. For each version[23] of a drug, the sales volume was expressed in euro. The quantity was delivered in the number of dispensed prescriptions per drug. The quantity then was transformed to the amount of dispensed Defined Daily Doses (DDD) using the official measured value of DDD per package of the drug from WiDO.[24] Following this procedure the sold quantities of all versions of a drug with a specific active ingredient were added up for each producer. This standardization enables a price and volume comparison between different package sizes, strengths, and also across different active ingredients.[25]

[23] Most drugs are sold in different versions, which differ in package size and/or strength.

[24] The "Wissenschaftliches Institut der Ortskrankenkassen" (WIdO) is the scientific institute of the Local Health Care Fund (AOK), Germany's largest health insurance fund. One of its task is the adjustment of the international DDD levels, issued by the WHO on a yearly base, for the German health care market.

[25] For example, a product x of a specific manufacturer has a DDD of 6 g. This is equivalent to 12 standard (500mg) tablets. If a patient consumes 48 (500mg) tablets (i.e. 24g of the drug in total) over six days, this equals a consumption of 4 DDDs of the drug. For more information see Häussler et al. (2007).

Following the suggestions of Stern (1995), Ellison et al. (1997), Pavcnik (2002) and Augurzky et al. (2009), the prices per period were derived in the following way:

$$\text{Price} = \frac{\textit{Cumulated sales of all versions of a drug per producer}}{\textit{Cumulated dispended DDD of all versions of a drug per producer}}$$

In the following, the calculated average price per DDD will be referred to as price. Taking inflation into account a price deflator from the German Federal Statistical Office was used to express the prizes in 2005 euro prices.[26]

The dataset contains additional information about the name of the manufacturer and drug status (patent, original, or generic drug).

In the estimation process a balanced panel data set was used. It only includes products that were available during the whole time period. Following this, the number of observations is identical for every year. The influence of newly launched products on the results is considered by controlling the degree of competition in the estimation.

III.5 Descriptive Results

III.5.1 Average weighted prices

It seems useful to start with an overview on the summarized statistics of the two different therapeutic groups which are covered in this research. Since the dataset is constricted, outliers could strongly bias the descriptive results when using non weighted prices. To solve this problem the prices were weighted with their monthly market share in the corresponding ATC7 group. Table 3 shows the average weighted prices for the different types of statins.

[26] See Statistisches Bundesamt (2010b)

Table 3: Prices of statins

Variable	Mean	S.D.	Minimum	Maximum
Overall drug price	0.089	0.013	0.074	0.107
Price patent drugs	0.473	0.044	0.41	0.532
Price original drugs	0.242	0.05	0.188	0.304
Price generic drugs	0.021	0.001	0.018	0.022

Average weighted prices per DDD (in 2005 euro), Observation period January 2004 - June 2006, Source: NVI, Price Deflator from Federal Statistical Office

The results in Table 3 indicate that patent drugs have the highest average weighted price of all three drug types. As assumed in Section III.3, the average price of original drugs is lower. At last, the average price of generic drugs is located far below the prices of the patent and original drugs.

Table 4 shows the summarized statistics for proton pump inhibitors.

Table 4: Prices of PPIs

Variable	Mean	S.D.	Minimum	Maximum
Overall drug price	0.249	0.031	0.201	0.292
Price patent drugs	0.412	0.048	0.341	0.486
Price original drugs	0.410	0.064	0.321	0.481
Price generic drugs	0.257	0.032	0.207	0.302

Average weighted prices per DDD (in 2005 euro), Observation period January 2004 - June 2006, Source: NVI, Price Deflator from Federal Statistical Office

The mean average weighted price in the therapeutic group of proton pump inhibitors is higher than in the group of statins. Thus, PPIs can be denoted as the more expensive therapeutic group. Still, the price pattern observed for the group of statins is valid for PPIs, as patent drugs are the most expensive drug type, followed by original and generic drugs. However it should be noted, that the average price of patent drugs is only slightly higher than the average price of original drugs.

This is different for the therapeutic group of statins, where the average price difference between patent and original drugs is much larger.

The summarized statistics support the theoretical motivation of Section III.3. For both statins and PPIs the average weighted price of patent drugs is higher than the average weighted prices of their therapeutic competitors. The average weighted price of original drugs is lower than that of patent drugs but above the average weighted price of generic compeitors.

III.5.2 Price development of statins and PPIs

Following the implications in Section III.3, prices of patent drugs should decrease less than the prices of original or generic drugs after the implementation of reference price groups.

Figure 4 shows the development of the average weighted prices[27] during the observation period for the therapeutic group of statins. Figure 5 does the same for the therapeutic group of PPIs. In both figures, the vertical line at month 13 (January 2005) indicates the inclusion of the observed therapeutic groups in the reference price system.

[27] Denoted as average weighted sales per DDD in the figure.

Figure 4: Average weighted prices of patent, original and generic statins

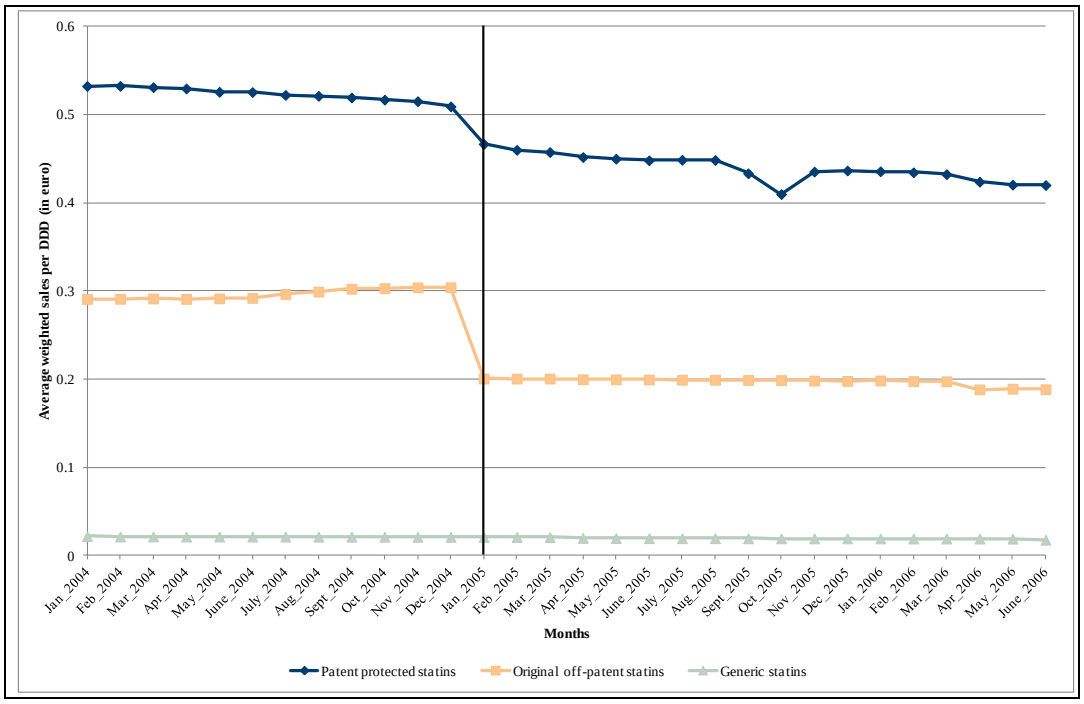
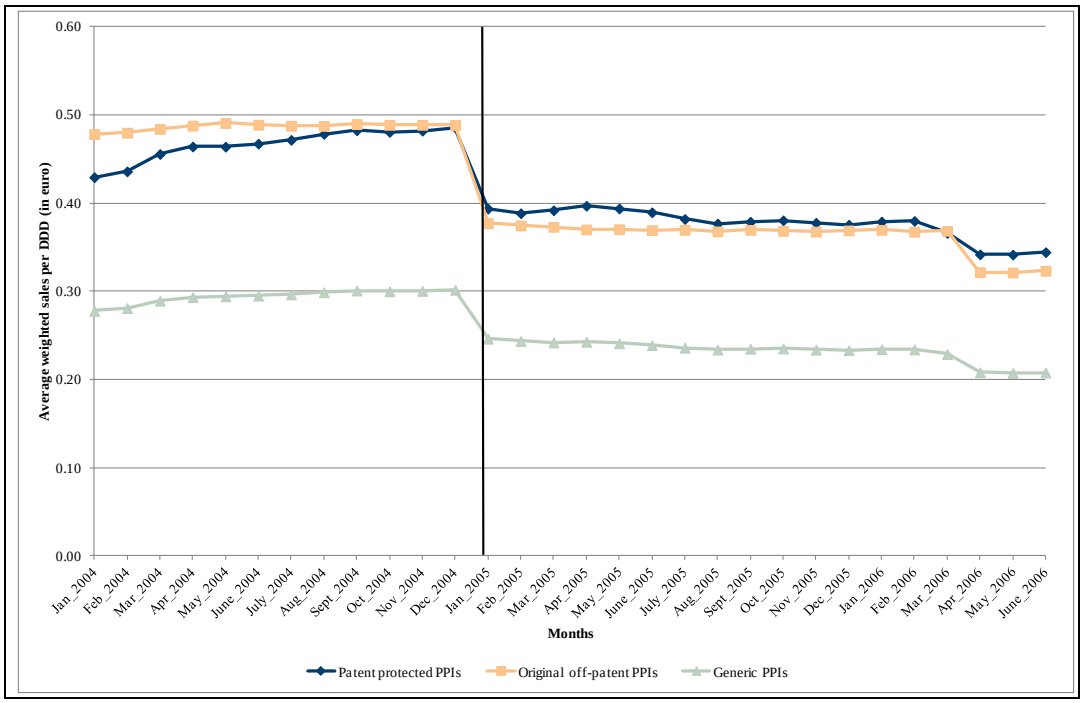


Figure 5: Average weighted prices of patent, original and generic PPIs



The price development for the therapeutic group of statins indicates that the average weighted price of patented drugs is always located above the average weighted price of original drugs, while the average weighted price of generic drugs is located below the level of branded (patent or original) drugs.

The situation is different for the therapeutic groups of PPIs. Before the introduction of reference prices in January 2005, the average price of patent drugs was slightly below the average price of original drugs. The reason for this was the large number of re-imported patent drugs, which were sold on a lower price level than the original drug. Since the line represents the average weighted price of all patent drugs, the existence of these re-imports lowers the average prices for patent drugs in Figure 5. However the price difference diminishes within the observation period before the reference price implementation.

The results in Figure 4 and Figure 5 also confirm the hypotheses, formulated in Section III.3. Both, the weighted prices of patent and original drugs decreased sharply after the introduction of the reference price system. Also, as expected in the theoretical motivation, the price drop was stronger for original drugs than for patent drugs. At last, in line with the third hypothesis, the changes in the average price level for generic drugs were rather small, compared to the price changes of patent and original drugs.

Additional conformation of the hypotheses for the group of statins can be found in Table 5. It shows the average weighted prices for statins before and after the introduction of reference prices in January 2005.

Table 5: Average weighted prices for statins before and after reference price introduction

	Prices before RP introduction	**Prices after RP introduction**	**% price change**
Overall	0.106	0.079	-25.3
	(0.001)	(0.008)	
Patent drugs	0.523	0.439	-16.0

	(0.007)	(0.015)	
Original drugs	0.296	0.197	-33.4
	(0.006)	(0.004)	
Generic drugs	0.021	0.019	-8.6
	(0.001)	(0.001)	

Standard errors are in parentheses.

As indicated in Table 5, the overall average weighted price for statins decreased by 25.3 % following the establishment of a reference price group for statins. The decrease is strongest for original drugs (33.4 %), followed by patent protected statins (16.0 %). The lowest price decrease can be found for generic drugs (8.6 %), which seems reasonable as generic statins were already on a very low price level before the reference price introduction.

The results are similar for the therapeutic group of the proton pump inhibitors, as shown in Table 6.

Table 6: Average weighted prices for PPI before and after reference price introduction

	Prices before RP introduction	**Prices after RP introduction**	**% price change**
Overall	0.258	0.232	-20.9
	(0.008)	(0.012)	
Patent drug	0.466	0.376	-19.2
	(0.018)	(0.017)	
Original drug	0.486	0.362	-25.6
	(0.004)	(0.019)	
Generic drug	0.294	0.232	-21.0
	(0.007)	(0.012)	

Standard errors are in parentheses.

Following the introduction of the reference price system for PPIs in 2005 the overall average weighted price decreased by 20.9 %. The strongest decrease can

be found for original PPIs (25.6 %), followed by generic (21.0 %) and patent protected drugs (19.2 %). As in the case of statins, the price drop of original drugs is stronger than for patent drugs. The results support the first and second of the hypotheses, formulated in Section 3.

Interestingly, the average price decrease for generic PPIs is much stronger than in the case of generic statins (21.0 % for PPI, 8.6 % for statins). A possible explanation for the different price reactions is the diverse competitive environment of both therapeutic groups.

While the number of generics was large in the market of statins from the outset of the observation period, only a few generic proton pump inhibitors were available during the observation period. Thus, the stronger competition between generic producers leads to lower prices of generic statins even before the introduction of the reference price system. As a consequence, the price drop was smaller for generic statins than for generic PPI, which faced less generic competition. These results are in line with hypothesis 3, as the price reaction of generic drugs seems to be ambiguous.

III.5.3 Sales volume development for statins and PPIs

Figure 6 and Figure 7 show the sales development of prescribed DDD for both therapeutic groups. Since physicians are motivated to use generic drugs,[28] it is comprehensive that generic drugs were sold most in both therapeutic groups. The results also indicate that the number of patent drugs DDD sold exceeds the number of original drugs DDD in both therapeutic groups, although the average price of patent drugs is higher than that of original drugs. This could be due to the fact that patent drugs possibly have an additional utility that is acknowledged by both patients and prescribing physicians. In the case of original drugs, physicians and

[28] There are various incentives for physicians to prescribe generics, for example the already mentioned physician drug budget. See Hellerstein (1998), Coscelli (2000), and Zweifel and Crivelli (1996).

patients have the alternative to choose the cheaper generic version. While there could be utility differences in the subjective perception of generic drugs, a medical benefit of the corresponding original drugs should not exist.

Figure 6: DDD sales of statins

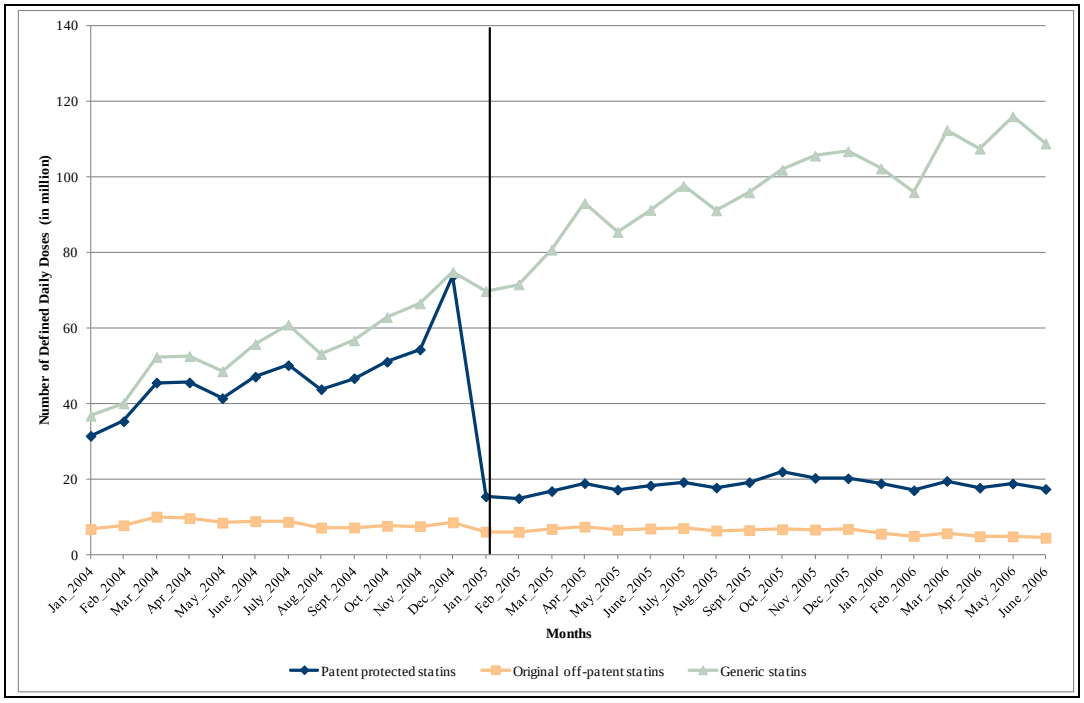
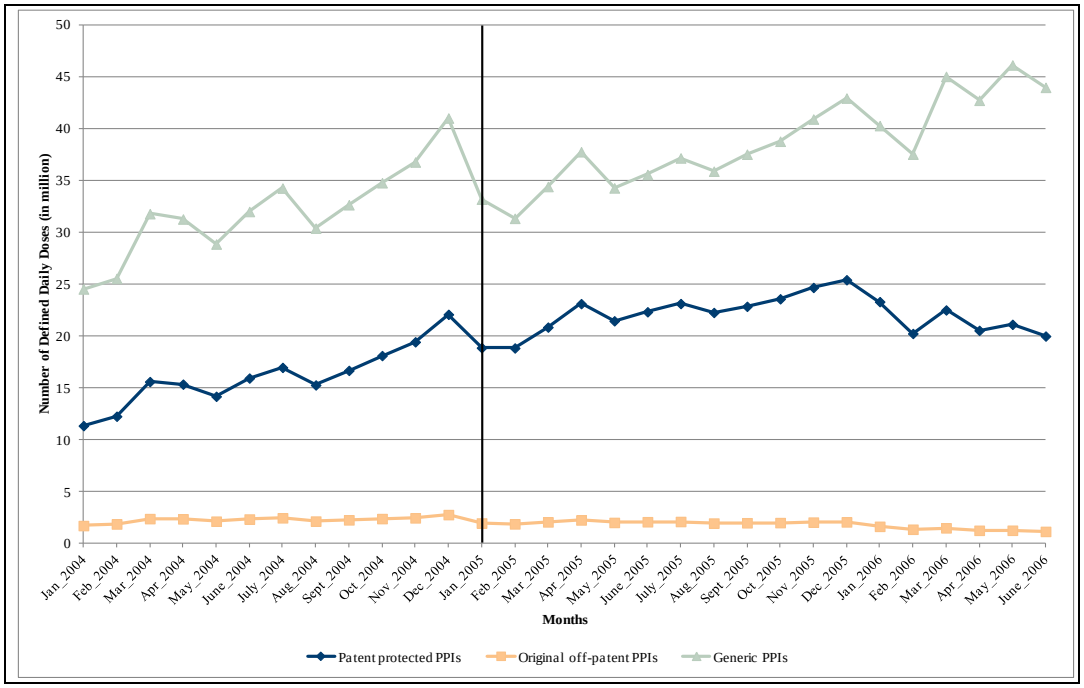


Figure 7: DDD sales of PPIs



The impact of reference pricing on the sales of generic, patent and original drugs was different for the two observed indication areas.

The sales of original drugs were not affected strongly due to the reference price implementation. In both indication areas they remained the group of drugs with the lowest number of sales compared to patent and generic drugs.

The demand for generic drugs continued to increase for both statins and proton pump inhibitors even after the reference price implementation. However, the sales increase was stronger for statins than for PPIs during the observation period.

Similar to the case of original products, the sales figures of patent PPIs remained on the same level throughout the remaining observation period In contrast, the sales of patent statins decreased permanently to a lower level. This development was primary caused by the active ingredient atorvastatin. It lost over 80 % of its sales after the introduction of reference prices due to the refusal of the manufacturer of atorvastatin to reduce the retail price to the reference price level.

III.6 Empirical Analysis

III.6.1 The econometric model

The descriptive statistics in Section III.5 indicate different price reactions of patent and original drugs which are exposed to reference pricing. Following this, the price decrease should be stronger for original drugs than for patent drugs. These effects are analyzed more carefully with the help of an econometric approach that based on the models of Lavy (2002), Pavcnik (2002), and Brekke et al. (2009).

Since all statins and PPIs were included into the reference price system at the same time period, a control group of therapeutic competitor drugs that are not part of the reference price system, does not exist. Therefore the relationship of reference pricing and price setting behavior of pharmaceutical producers is considered by analyzing the variation in prices before and after the implementation of reference prices.

For this purpose a semi logarithmic approach[29] of the following form is used:

$$\ln(p_{it}) = \alpha + \beta_1 RP_{it} + \beta_2 (RP_{it} * P_i) + \beta_3 (RP_{it} * O_i) + FE_i + \delta_t + \varepsilon_{it} \quad (6)$$

where p_{it} is the retail price of product *i*, as defined before, in month *t*.

RP_{it} is a dummy variable taking the value 1 if drug *i* in month *t* is included in a reference price group, and 0 otherwise[30].

The dummy variable P_i takes the value of 1 if drug *i* is a patent protected drug and 0 otherwise. The variable O_i takes the value of 1 if drug *i* is an off-patent original drug, and 0 otherwise. If both variables posse the value of 0, drug *i* is a generic drug.

Since a two way fixed effect panel regression model[31] is estimated, the variable FE_i captures product specific attributes of drug *i* that are not observable.[32] These attributes could be product brand name effects due to yearlong marketing efforts, a special appreciation of the product by the physicians or subjective drug attributes like the form or color of the pills.

The variable δ_t controls for possible unobserved time-variant shocks. It takes the form of a month indicator with the value 1,..,30 for t = 1,...,30. I also calculated

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29 The reason for using a semi logarithmic approach lies in the interpretation of the coefficient β_i. Through the use of a logarithmic depending variable, β_i can be interpreted as the change of the depending variable in percent, when changing an independent variable *i* about one unit.

30 As all products of every observed active ingredient entered the reference price at the same time, RP_{it} is 0 for *t* = 1,..,24 and 1 for *t* = 25,..,48 for each product *i*.

31 The applicability of the fixed effect model was tested, using the Hausman-test. The test results indicate that the Null Hypotheses can be rejected on the 1 % significance level. Therefore the use of fixed effects instead of random effects is suggested.

32 Fixed effects were captured by using dummy variables for each product, following Wooldridge (2002) p.422-433.

the models using year indicators and quarter-year indicators instead.[33] The results do not differ much and can be found in Appendix 1. Therefore I use the month indicator in the following estimation process.

The effect of the reference price introduction is therefore identified by the variation in prices of the year before the reference price introduction and the prices of the first year following the implementation. Using (6), it is possible to explore the total effect of the introduction of reference pricing on generics, patent drugs and original drugs.

The variable β_1 estimates the total effect of the reference price introduction on the prices of generic drug.

The interaction term between RP_{it} and P_i, β_2 captures the additional effect of reference pricing for patent drugs. Thus, the complete effect of the reference price introduction on the price of a patent drug is $\beta_1 + \beta_2$.[34]

The coefficient β_3 prescribes the additional effect of a reference price policy change on prices, if the drug is an off-patent original drug (O_i). Similar to the case of patent drugs, the total effect of the reference price introduction for original drugs is $\beta_1 + \beta_3$.

At last, ε_{it} represents unobserved effects that affect prices. The error term ε_{it} is assumed to be independent and identically distributed (i.i.d). Also, it is assumed that the error term is normal distributed.

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[33] See Pavcnik (2000) for a similar approach.

[34] For example, if the coefficient of the interaction between RP_{it} and P_i, β_2, is negative and β_1 is also negative, the price of an on-patent drug would decrease more than the price of a generic drug.

III.6.2 The effect of price moratoria

While the focus of this research is the effect of the introduction of reference pricing on the pricing of patent, original, and generic drugs, there are other changes in regulations that could influence the price development. These factors have to be controlled in the estimation. During the observation period, especially a regulation scheme called price moratorium falls into this category. This instrument freezes the prices of prescription drugs on a certain price level of an earlier time period that is determined by the Federal Ministry of Health.

It has to be noted, that price moratoria do not eliminate the free pricing mechanism in the SHI prescription drug market. Drug manufacturers are still allowed to set their prices freely during the price moratorium. However, they have to give any additional profits through a price increase above the pre-determined price level to the sickness funds in form of an additional rebate. Therefore manufacturers generally would not increase their prices during a price moratorium, as it would not lead to additional revenues in the SHI market.[35] During the study period, two price moratoria occurred. The first price freeze ended in December 2004, while the second one started in April 2006. To control the possible effects, the dummy variable PF_t is included.[36] It takes the value of 1 if a price moratorium is in effect in month *t*, and 0 otherwise.

III.6.3 The effect of competition

Since competition could possible affect the prices of patent, original drugs and generics,[37] the degree of competition is controlled in the estimation. Following Morton (1997) and Pavcnik (2002) the level of competition is measured by the

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35 See Busse et al. (2005)

36 The variable lacks the index *i*, as all drugs are covered by a potential price moratorium.

37 Patent drugs per definition normally do not have competition through other products with the same active ingredient. Still they face competition through re-importers.

number of competitors NC_{it} in the active ingredient group for each product *i* in month *t*.[38] Also, the differences in the effects of competition on prices of patent and original drugs, summarized under the term branded drugs in the following, and generic drugs are captured by interaction terms.

In addition, several interaction dummies, capturing the effects of competition before and after the reference price introduction, are included in the model. All variables capturing the effects of competition on the reference price introduction are found in the competition control vector CC'_{it}.

The use of the number of competitors to capture the impact of competition on the price development of drugs can cause problems. The most common objection is the possibility of endogeneity, as the number of competitors within an active ingredient could be a function of the price. This would be the case, if a high price level on the market influenced the probability of a market entry. While this factor should be considered, the problem can be toned down in this analysis, as a producer cannot enter a market immediately.[39] Thus, the entry of competitors is not necessarily connected to present prices but to prices in past periods or patent expirations.

Another possibility to control for the level of competition is the use of the Herfindahl index, as proposed by Pavcnik (2002). However, the number of competitors within an active ingredient is chosen to measure the degree of competition due to

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[38] Instead of using the number of competitors within an active ingredient, the degree of competition can also be measured by taking into account the competition between different active ingredients. In this case, every drug *i* is facing the same number of competitors in month *t*, independent of the active ingredient the drugs belong to. However as Morton (1997) and Pavcnik (2002) proclaim, the primary competition occurs between drugs consisting of the same active ingredient. Following their advice, the number of competitors within an active ingredient is used as the measurement of the degree of competition.

[39] See Pavcnik (2002)

the better interpretability of the results. Also, as noted in the latest literature[40], the use of the Herfindahl index as a measurement of the degree in competition in combination with a depending price variable can cause endogeneity problems.

Including the additional variables in (6), the estimation equation takes the following form:

$$\ln(p_{it}) = \alpha + \beta_1 RP_{it} + \beta_2 (RP_{it} * P_i) + \beta_3 (RP_{it} * O_i) + \beta_4 PF_t + \chi CC'_{it} + FE_i + \delta_t + \varepsilon_{it} \quad (7)$$

Since the database used in the study is a product level panel, the data was checked for first-order serial correlation in errors, as Woodridge (2002) proposes. The test rejected the Null-hypothesis that there is no first-order serial correlation ($p<0.01$). In addition, the data was tested for heteroskedasticity of the residuals, using a modified Wald-Test. The results indicate group wise heteroskedasticity ($p<0.01$). For controlling both problems, product-clustered robust standard errors are estimated. These standard errors are robust to heteroskedasticity, as well as to any form of autocorrelation.[41]

III.7 Estimation results

A similar set of models is estimated for both therapeutic groups. Model (1) only measures the effects of reference pricing on patent, original and generic drugs. Model (2) includes the possible effects of a price moratorium. The models (3) - (6) include additional sets of interaction variables, estimating the impact of competition on the pricing of generic and branded (patent and original) drugs.

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[40] See Brekke et al. (2009)

[41] See Kezdi (2005) for additional information about cluster robust standard errors in fixed effect models

III.7.1 HMG-CoA reductase inhibitors (statins)

The first empirical results describe the effects of reference pricing for the therapeutic group of statins. Since the introduction of statins in 1987,[42] the number of different active ingredients, belonging to the therapeutic group has increased.[43] The market is characterized by a large number of generic drugs, whose numbers increased after 2005, and nearly no re-imports. The effects of increasing competition are captured, using the methods presented in Section III.6.1.

Table 7 shows the results of the panel data regression for the price effects of the introduction of reference prices for statins in 2005, using data from January 2004 to June 2006.

Table 7: Effects of the introduction of reference prices on prices of statins, Fixed effect estimation with data from January 2004 - June 2006

	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Coefficient[44]						
RP	-0.021***	-0.059***	-0.043***	0.028	-0.036***	0.096***
	(0.008)	(0.012)	(0.015)	(0.045)	(0.013)	(0.022)
RP*O	-0.273***	-0.273***	-0.265***	-0.282***	-0.280***	-0.466***
	(0.047)	(0.048)	(0.043)	(0.051)	(0.039)	(0.078)
RP*P	-0.074***	-0.074***	-0.093***	-0.161***	-0.099***	-0.233***
	(0.02)	(0.02)	(0.018)	(0.038)	(0.017)	(0.02)
Price Moratorium		-0.022***	-0.023***	-0.023***	-0.023***	-0.023***
		(0.006)	(0.007)	(0.007)	(0.007)	(0.006)

[42] The statin Lovastatin was approved by the FDA in August 1987.

[43] In 2006, the group consisted of 5 different active ingredients.

[44] Avoiding confusion and increasing the clarity of the results, the estimated coefficient for generic drugs are named RP instead of β_1. The same applies for the estimated coefficients of the additional effects for patent (RP*P) and original (RP*O) drugs.

NC			-0.01***	-0.005**	-0.013***	0.003
			(0.002)	(0.002)	(0.002)	(0.002)
NC*RP				-0.002*		-0.005***
				(0.001)		(0.001)
NC*B					0.006*	-0.001***
					(0.003)	(0.002)
NC*RP*B						0.007*
						(0.004)
Month Indicators	Yes	Yes	Yes	Yes	Yes	Yes
Constant	-0.544***	-0.527***	-0.250***	-0.385***	-0.206***	-0.546***
	(0.012)	(0.014)	(0.05)	(0.069)	(0.049)	(0.038)
Observations	1,710	1,710	1,710	1,710	1,710	1,710
Number of products	57	57	57	57	57	57
R-squared	0.71	0.71	0.72	0.73	0.73	0.74

Columns 1 - 3 show the results of the Models (1) - (3), Columns 4 - 5 the results of the Models (4) and (5). Cluster robust standard errors are in parentheses. *** indicates significance at the 1 % - Level; ** indicates significance at 5 % - Level; * indicates significance at the 10 % -Level. Cluster robust standard errors in parentheses.

The results of the regression models are in line with the hypotheses set out in Section III.3.

As predicted, the prices of generics decrease only to a small amount after the introduction of the reference price system (RC) in 5 of the 6 model specifications. The generic prices decrease between -5.9 % (Model (2)) and -9.6 % (Model (6)).

Confirming the first hypothesis, both patent and off-patent original drug producers lowered their prices significantly after the reference price introduction. Also, in line with hypothesis 2, patent producers lowered the prices of their products less (RP*P) than producers of off-patent originals (RP*O).

The price decrease of patent drugs is similar in all estimated models. The full effect[45] is between -10.2 % (Model (1)) and -13.7 % (Model (6)). A stronger price reduction through reference pricing was estimated for off-patent original drugs. Depending on the model, the full effect ranges between -25.4 % (Model (4)) and -36.9 % (Model (6)).

The effect of price moratorium is, as expected, negative and comparable in all estimated models. Therefore prices were about -2.3 % lower in months with an active price moratorium.

The impact of competition was measured by the number of competitors (NC) within an active ingredient. The results show that the number of competitors per active ingredient has a negative impact on prices. For each additional competitor, the prices are decreasing about 1 % (Model (3)).

The effect of additional competition after the introduction of reference prices, estimated by NC*RP in Model (4), is negative. Therefore the effect of competition on prices is stronger, compared to the situation before the reference price introduction, estimated by NC in Model (4).

The interaction term between branded drugs and the number of competitors (NC*B) states, as shown in Model (5), that patent and original drugs are less effected by additional competition than generic drug producer.

This pattern prevails even after the introduction of reference prices. The prices of patent and original drugs are less effected by competition following the reference price introduction as the estimated coefficient in Model (6) (NC*RP*B) indicates.

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[45] Just to remind the reader, the total price effect of the introduction of reference pricing for patent drugs is RP + RP*P, as shown in Section III.6.1. Likewise, the total price effect for original drugs is RP + RP*O.

III.7.2 Proton Pump Inhibitors

The market of PPIs differs from that of statins in various ways. One important difference is the far lower the number of generic on the market of PPIs. Only the active ingredient omeprazole faced continuous generic competition in the complete observation period.[46] In addition, contrary to market environment of statins, the market of PPIs is characterized by a large number of re-importers. Both facts could lead to differences in the results between the two therapeutic groups, especially in concern to the impact of competition on prices.

Table 8 shows the impact of the introduction of the reference price system for PPIs on the prices of patent, original and generic drugs in January 2005.

Table 8: Effects of the introduction of reference prices on prices of PPIs, Fixed effect estimation with data from January 2004 - June 2006

	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Coefficient[47]						
RP	-0.062***	-0.193***	-0.191***	-0.051	-0.125***	0.912***
	(0.015)	(0.02)	(0.02)	(0.15)	(0.012)	(0.078)
RP*O	0.036	0.036	0.035	-0.027	-0.09***	-1.055***
	(0.041)	(0.041)	(0.041)	(0.085)	(0.042)	(0.108)
RP*P	0.056*	0.056*	0.051	-0.033	-0.058***	-1.052***
	(0.033)	(0.033)	(0.032)	(0.095)	(0.022)	(0.088)
Price Moratorium		-0.096***	-0.096***	-0.093***	-0.104***	-0.091***
		(0.008)	(0.008)	(0.008)	(0.008)	(0.008)
NC			-0.001	0.006	-0.038***	0.001

[46] It was only in 2006 generics of another active ingredient, Lansoprazol, entered the market of PPIs.

[47] Avoiding confusion and increasing the clarity of the results, the estimated coefficient for generic drugs are named RP instead of β_1. The same applies for the estimated coefficients of the additional effects for patent (RP*P) and original (RP*O) drugs.

			(0.002)	(0.008)	(0.007)	(0.002)
NC*RP				-0.008		-0.057***
				(0.002)		(0.005)
NC*B					0.039***	0.006
					(0.006)	(0.003)
NC*RP*B						0.051***
						(0.005)
Month Indicators	Yes	Yes	Yes	Yes	Yes	Yes
Constant	0.594***	0.667***	0.683***	0.592***	0.952***	0.610***
	(0.013)	(0.013)	(0.025)	(0.097)	(0.048)	(0.053)
Observations	1,140	1,140	1,140	1,140	1,140	1,140
Number of products	38	38	38	38	38	38
R-squared	0.69	0.69	0.69	0.71	0.71	0.73

Columns 1 - 3 show the results of the Models (1) - (3), Columns 4 - 5 the results of the Models (4) and (5). Cluster robust standard errors are in parentheses. *** indicates significance at the 1 % - Level; ** indicates significance at 5 % - Level; * indicates significance at the 10 % -Level. Cluster robust standard errors in parentheses.

Analog to the case of statins, the introduction of the reference price system lead to a price decrease for generic drugs (RC) in the majority of the estimated models. The prices decreased, depending on the model, between -6.2 % (Model (1)) and -19.3 % (Model (2)).

Both original and patent proton pump inhibitors producers lowered their prices after the reference price introduction, as the coefficients in Model (5) and (6) indicate. Consequently also for the therapeutic group of PPIs, hypothesis 1 can be confirmed. Interestingly, the effects for both types of branded products, however not significant, are weaker than for generic PPIs, when not controlling for the degree of competition (Model (1) and Model (2)).

The use of the more extensive set of variables capturing the degree of competition changes this result. The estimated coefficients in Model (5) and Model (6) indi-

cate the prices for both patent and original drugs decrease more than the prices of generics.

The coefficients show that the price decrease pattern of original and patent drugs supports hypothesis 2. As expected, the effect on prices of patent protected proton pump inhibitors (RP*P) is weaker than the effect on the prices of original PPIs (RP*O). However, it has to be noted, that while hypothesis 2 can be supported, the differences in the price reduction between patent and original drugs are far smaller than in the case of statins.

The results in Table 8 show, that the significant full[48] price reductions of patent drugs after reference price introductions ranges from -14.0 % (Model (6)) to -18.3 % (Model (5)), depending on the model. In comparison, prices of original drugs decrease significantly between -14.3 % (Model (6)) and -21.5 % (Model (5)).

The effect of price moratorium is, as expected, negative. The prices are lower, between -9.1 % (Model (6)) and -10.4 % (Model (4)), during months with a price moratorium.

The significant results concerning the number of competitors indicate that the number of competitors (NC) has a negative influence on the prices of generic drugs as Model (4) shows. The effect diminishes for branded products as indicated by the positive coefficient NC*B. Therefore brand name products seem to be much less effected by competition than generics. As the total effect for brand name products (NC+NC*B) is slightly positive.

The negative effect of additional competition on generic drug prices increases after the reference price introduction for generic drugs as the coefficient NC*RP in Model (6) indicates. Similar to situation in Model (4), the effect of competition

[48] Just to remind the reader, the total price effect of the introduction of reference pricing for patent drugs is RP + RP*P, as shown in the Section III.6.1. Likewise, the total price effect for original drugs is RP + RP*O.

after the introduction of reference pricing is weaker for branded (patent or original) products (NC*RP*B) than for generic drugs (NC*RP).

III.8 Conclusion

This paper estimates the effects of the introduction of a reference pricing in Germany on the price setting behavior of producers of generic, original and patent drugs. To analyze the impact of reference pricing on these drug types, the implementation of joint reference price groups for the two therapeutic groups of statins and proton pump inhibitors in January 2005, was used. Both groups included patent, original, and generic drugs.

The results show that for both of these two major therapeutic groups of drugs, the prices of patent, original, and generic drugs decreased after the reference price introduction. Moreover, the producers of original drugs that were facing generic competition lowered the prices for their products to a greater extent than the producers of patent drugs, whose only direct (same active ingredient) competition are re-imports.

The results also indicate that the competition situation plays an important role for the price setting behavior. In the analysis the number of competitors per active ingredient was used as a measurement for competition.

The results show that an increase in the degree of competition leads to lower generic drug prices. The effect is stronger for generic PPIs in comparison to statins. In opposite, additional competition does not strongly affect the prices of patent and original drugs in both therapeutic groups. At last, the effect of increasing number of competitors is stronger after the introduction of reference prices. This effect is again weaker for original and patented drugs compared to generics.

Overall, the results of the analysis are similar to the findings of Ellison et al. (1997), Pavcnik (2002), and Brekke et al. (2009). All studies ascertain that reference prices trigger different price reductions for off-patent original and generic drugs. Also, the important role of the degree of competition in the therapeutic market for the price reactions of producers is shown. In line with my results,

Pavcnik (2002) finds that the impact of competition is smaller for off-patent drugs than for generic drugs.

However, unlike previous studies, the results of this paper indicate that differences exist in the price reaction of patent and off-patent original drug producers when facing reference prices. The results show that the price decrease is lower for patent protected drugs than for off-patent original drugs, given further evidence for the existence of an additional benefit for patent drugs. Due to this benefit, patent drugs have a competitive advantage that allows them to obtain higher prices even after being included in reference price group with cheaper competitors.

Different potential reasons for this additional benefit can be given. One important argument for the acceptance of the higher prices for patent and, to a lesser extend, for original drugs could be their good reputation among patients and physicians. Studies by Hellerstein (1998), Lundlin (2000), and Coscelli (2000) that physicians and patients develop consistent choice habits. Their results imply that both parties exhibit strong state dependence and are far from being indifferent between branded (patent or original) and generic drugs.

Another explanation is, that both physicians and patients expect better treatment results through the use of a patent drug and/or less side effects, leading to the acceptance of a higher price. Patent producers could build on this reputation and the quasi monopolistic market situation for the specific active ingredient to demand higher prices. Unlike patent drug producers, the manufacturers of original drugs do not have this unique market position. Due to the generic competition they have to decrease their prizes strongly after the reference price policy change to remain competitive.

In addition, the smaller price decrease of patent drugs could be the result of the high research and development cost for the new drug. DiMasi et al. (2003) estimate the costs of developing a new drug at 802 million USD, while other stud-

ies[49] assess the costs between 500 to 2.000 million USD. Even with the huge difference between the two numbers, it becomes obvious that the development of a new drug is very expensive. To refund these expenditures, producers of patent drugs have to demand higher prices than the manufacturers of off-patent originals, that were able to refinance their investments during the time period their products were under patent protection.

Finally, the results strongly suggest that the introduction of reference pricing as well as important reference price policy changes affect generic, original and patent drugs differently. It has to be noted, that the role of the demand side, represented by the physicians and their patients, for the pricing of branded especially patent drugs, needs further research. Also, the possible negative effects of the reduced price level, due to reference pricing, on the market entry decision of future competitors should be investigated more closely.

III.9 Appendix 1

Table 9: Effects of the introduction of reference prices for statins, Fixed effect estimation with data from January 2004 - June 2006 with year indicators

	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Coefficient						
RP	-0.109***	-0.144***	-0.125***	-0.058	-0.120***	0.014
	(0.01)	(0.013)	(0.001)	(0.039)	(0.008)	(0.012)
RP*O	-0.273***	-0.273***	-0.265***	-0.281***	-0.278***	-0.466***
	(0.048)	(0.048)	(0.044)	(0.052)	(0.039)	(0.078)
RP*P	-0.074***	-0.074***	-0.094***	-0.159***	-0.098***	-0.234***
	(0.02)	(0.02)	(0.018)	(0.039)	(0.017)	(0.019)
Price Moratori-		-0.035***	-0.035***	-0.035***	-0.035***	-0.035***

[49] See Adams et al. (2006)

um						
		(0.005)	(0.005)	(0.005)	(0.005)	(0.005)
NC			-0.01***	-0.006*	-0.013***	0.003**
			(0.002)	(0.003)	(0.002)	(0.001)
NC*RP				-0.002*		-0.005***
				(0.001)		(0.001)
NC*B					0.005	-0.001***
					(0.003)	(0.002)
NC*RP*B						0.007*
						(0.004)
Year Indicators	Yes	Yes	Yes	Yes	Yes	Yes
Constant	-0.59***	-0.555***	-0.267***	-0.398***	-0.230***	-0.572***
	(0.008)	(0.011)	(0.048)	(0.08)	(0.048)	(0.031)
Observations	1,710	1,710	1,710	1,710	1,710	1,710
Number of products	57	57	57	57	57	57
R-squared	0.69	0.69	0.71	0.72	0.71	0.73

Columns 1 - 3 show the results of the Models (1) - (3), Columns 4 - 5 the results of the Models (4) and (5). Cluster robust standard errors are in parentheses. *** indicates significance at the 1 % - Level; ** indicates significance at 5 % - Level; * indicates significance at the 10 % -Level. Cluster robust standard errors in parentheses.

Table 10: Effects of the introduction of reference prices on prices of PPIs, Fixed effect estimation with data from January 2004 - June 2006 with year indicators

	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Coefficient						
RP	-0.155***	-0.258***	-0.248***	-0.163***	-0.132***	0.888***
	(0.007)	(0.01)	(0.011)	(0.035)	(0.014)	(0.086)

RP*O	0.036	0.036	0.034	-0.006	-0.102**	-1.071***
	(0.041)	(0.01)	(0.011)	(0.021)	(0.015)	(0.087)
RP*P	0.056	0.056	0.044	-0.011	-0.081**	-1.069***
	(0.034)	(0.009)	(0.011)	(0.024)	(0.014)	(0.088)
Price Moratori-um		-0.103***	-0.103***	-0.103***	-0.103***	-0.103***
		(0.009)	(0.009)	(0.009)	(0.008)	(0.008)
NC			-0.004**	0.001	-0.042***	-0.008***
			(0.002)	(0.002)	(0.003)	(0.002)
NC*RP				-0.005**		-0.057***
				(0.002)		(0.005)
NC*B					0.043***	0.013***
					(0.003)	(0.003)
NC*RP*B						0.051***
						(0.005)
Year Indicators	Yes	Yes	Yes	Yes	Yes	Yes
Constant	0.539***	0.642***	0.686***	0.633***	0.971***	0.684***
	(0.009)	(0.009)	(0.021)	(0.03)	(0.029)	(0.019)
Observations	1,140	1,140	1,140	1,140	1,140	1,140
Number of products	38	38	38	38	38	38
R-squared	0.63	0.67	0.68	0.68	0.71	0.73

Columns 1 - 3 show the results of the Models (1) - (3), Columns 4 - 5 the results of the Models (4) and (5). Cluster robust standard errors are in parentheses. *** indicates significance at the 1 % - Level; ** indicates significance at 5 % - Level; * indicates significance at the 10 % -Level. Cluster robust standard errors in parentheses.

Table 11: Effects of the introduction of reference prices for statins, Fixed effect estimation with data from January 2004 - June 2006 with quarter-year indicators

	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Coefficient						
RP	-0.057***	-0.202***	-0.170***	-0.105***	-0.164***	-0.039***
	(0.008)	(0.019)	(0.017)	(0.044)	(0.015)	(0.014)
RP*O	-0.273***	-0.273***	-0.265***	-0.282***	-0.280***	-0.472***
	(0.047)	(0.047)	(0.043)	(0.051)	(0.039)	(0.077)
RP*P	-0.074***	-0.074***	-0.094***	-0.160***	-0.099***	-0.237***
	(0.019)	(0.019)	(0.018)	(0.04)	(0.017)	(0.02)
Price Moratorium		-0.145***	-0.143***	-0.143***	-0.143***	-0.142***
		(0.017)	(0.017)	(0.017)	(0.017)	(0.017)
NC			-0.01***	-0.005*	-0.013***	0.006**
			(0.002)	(0.003)	(0.002)	(0.001)
NC*RP				-0.002*		-0.005***
				(0.001)		(0.001)
NC*B					0.006***	-0.001***
					(0.003)	(0.003)
NC*RP*B						0.007*
						(0.004)
Quarter-Year Indicators	Yes	Yes	Yes	Yes	Yes	Yes
Constant	-0.586***	-0.442***	-0.168***	-0.306***	-0.124***	-0.485***
	(0.009)	(0.023)	(0.055)	(0.086)	(0.056)	(0.044)
Observations	1,710	1,710	1,710	1,710	1,710	1,710
Number of products	57	57	57	57	57	57
R-squared	0.72	0.72	0.74	0.74	0.74	0.75

Columns 1 - 3 show the results of the Models (1) - (3), Columns 4 - 5 the results of the Models (4) and (5). Cluster robust standard errors are in parentheses. *** indicates significance at the 1 % - Level; ** indicates significance at 5 % - Level; * indicates significance at the 10 % -Level. Cluster robust standard errors in parentheses.

Table 12: Effects of the introduction of reference prices on prices of PPIs, Fixed effect estimation with data from January 2004 - June 2006 with quarter year indicators

	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Coefficient						
RP	-0.105***	-0.254***	-0.246***	-0.169	-0.104***	0.564**
	(0.014)	(0.014)	(0.016)	(0.163)	(0.027)	(0.251)
RP*O	0.036	0.036	0.035	-0.002	-0.095**	-0.719***
	(0.041)	(0.041)	(0.041)	(0.01)	(0.042)	(0.247)
RP*P	0.056	0.056	0.05	-0.001	-0.074***	-0.715***
	(0.033)	(0.033)	(0.032)	(0.111)	(0.022)	(0.255)
Price Moratorium		-0.148***	-0.145***	-0.145***	-0.117***	-0.107***
		(0.014)	(0.014)	(0.014)	(0.014)	(0.015)
NC			-0.002	0.003	-0.04***	0.014
			(0.003)	(0.01)	(0.006)	(0.011)
NC*RP				-0.005		-0.038**
				(0.01)		(0.014)
NC*B					0.04***	0.02
					(0.006)	(0.013)
NC*RP*B						0.032**
						(0.015)
Quarter-Year Indicators	Yes	Yes	Yes	Yes	Yes	Yes
Constant	0.542***	0.690***	0.707***	0.656***	0.959***	0.736***
	(0.015)	(0.021)	(0.034)	(0.108)	(0.037)	(0.089)
Observations	1,140	1,140	1,140	1,140	1,140	1,140
Number of products	38	38	38	38	38	38
R-squared	0.71	0.71	0.71	0.71	0.73	0.74

Columns 1 - 3 show the results of the Models (1) - (3), Columns 4 - 5 the results of the Models (4) and (5). Cluster robust standard errors are in parentheses. *** indicates significance at the 1 % - Level; ** indicates significance at 5 % - Level; * indicates significance at the 10 % -Level. Cluster robust standard errors in parentheses.

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IV. The impact of regulative instruments on the market share of generic drugs

IV.1 Introduction

The expenditures for prescription drugs in the German Statutory Health Insurance (SHI) system increased from 19.4 billion euro in 2000 and 2010 to 30.2 billion euro.[1] Therefore, drug expenditures are, after the expenditures for hospital treatments (58.1 billion euro in 2010), the second largest cost factor of the SHI system. Yet, different to the expenditures for hospital treatment or physicians in ambulant care, the expenditures for prescription drugs rose on a larger annual rate than the overall costs in the SHI system. While the total expenditures for health care services in the SHI system increased about 2.8 %, drug costs increased about 4.5 % annually.[2]

In response, the Federal Ministry of Health, the regulatory body of the SHI, pursuits several strategies to control pharmaceutical expenditures. While some strategies directly target the overall drug expenditures or the price of a prescription drugs, others influence the drug expenses indirectly.

A indirect strategy to lower the expenditures for prescription drugs is the support of the substitution of original drugs[3] by generic versions of the same active ingredient. As the development of generic products causes only a minimum of R&D expenditures, prices of generic drugs are generally lower than prices of original products containing the same active ingredient. In a competitive market the increasing utilization of generic drugs should trigger a decrease of the overall price

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1 See Bundesministerium für Gesundheit (2011)

2 See Bundesministerium für Gesundheit (2011)

3 The term off-patent original drug can be used synonymously for the term original drug.

level. This should lead to a decrease of expenditures for prescription drugs. During the observation period of the dataset of the paper (2004 to 2007), large savings through the exchange of original drugs with generic versions could be achieved. In 2004, 202.0 million euro were saved through the substitution of original drugs with generic versions. The number increased to 321 million euro in 2006 and dropped again slightly to 269.1 million euro in 2007.[4]

A major component of these savings was accomplished through the implementation of regulatory instruments. The three most important instruments are:

- The reference price system that establishes a maximum reimbursement limit for drugs included in a reference price group.
- The exemption of drugs in reference price groups from patient co-payments,[5] if the drug price is below a certain level.
- The possibility of rebate contracts between pharmaceutical producers and sickness funds and the associated preferred dispense of rebated drugs by the pharmacies.

The instruments and the way they affect market participants are explained in detail in Section IV.4.

This paper studies the effect on the demand of a generic drug subjected to one or more of these regulatory instruments. While there is a large body of literature studying the effects of the entry of generic drugs on the prices of original products,[6] studies on the impact of regulative instrument on the demand of prescription drugs are mostly restricted on the effects of reference pricing.[7]

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4 See Häussler et al. (2006), p. 32-33, Häussler et al. (2007), p. 22-23, and Häussler et al. (2008), p. 21-22.

5 Patients in the SHI system have normally to make a co-payment between 5 and 10 euro per prescription drug. If the drug price is below 5 euro, the patient has to pay the full price by himself.

6 See Cave et al. (1992), Grabowski and Vernon (1992), and Aronsson et al. (2001)

7 See Section IV.2 for a literature overview.

This study uses an empirical approach that belongs to a class of models introduced by Berry (1994) and Berry et al. (1995). Since the prescribing physician fulfills a central role in the choice of the dispensed drug, his decision behavior for prescribing drugs is modeled. Therefore a discrete choice approach with a random utility function is used as the starting point of the analysis. The approach is inspired by Dalen et al. (2006), but was substantially altered and extended to match the context of the paper.

The paper has three objectives.

First, the impact of the regulatory instruments on the demand of a generic drug will be estimated.

Second, the role of the price difference between generic drugs and the corresponding original drug on the demand of generic drugs will be examined.

At last, the heterogeneity in the generic drug market will be acknowledged by separating generic products in branded generic drugs and non-branded generic drugs.[8] Since different demand reactions are assumed for branded and non-branded generic drugs, the effects of the observed regulatory instruments on both kinds of generics will be analyzed.

The results of the paper indicate that a decrease of the price difference between generic drugs and the corresponding (more expensive) original drugs has a negative effect on the demand of a generic drug. Therefore, a price increase of the generic drug or a price decrease of the original drug decreases the demand for a generic drug. The effect is stronger for generic drugs that are part of reference price groups or are, in addition, exempted from patient co-payments. Interestingly, the effect of the price difference is reversed for drugs that are part of a rebate contract. This indicates the diminishing importance of the retail price for drugs participating in rebate contracts.

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[8] The differences between these two types of generic drugs will be explained in detail in Section IV.3.1.

Among the regulatory instruments, the strongest effect on the demand for a generic drug was estimated for drugs that become part of rebate contracts. The effect is stronger for non-branded generic drugs than for branded generic products. The demand of generic drugs that are exempted from patient co-payments also increased. The impact is weaker than in the case of rebate contracts and not significantly different for branded and non-branded generic drugs. The smallest, still positive, effect on the demand of a generic drug was observed following the implementation of reference price groups. This reaction was stronger for branded than for non-branded generics.

The paper is structured as follows. Section IV.2 gives an overview on the existing literature of physician prescription behavior and the influence of regulatory instruments on the demand and pricing of prescription drugs. Section IV.3 describes the dataset and contains the descriptive results for the observed markets. Section IV.4 presents a short overview about the institutional background of the SHI system and the role of the physicians. It also includes the description of the observed regulatory instruments as well as hypotheses about the impact of these instruments on the demand of a generic drug. The demand model and the estimation approach are presented in Section IV.5 and Section IV.6. The estimation results are shown in Section IV.7. Finally, Section IV.8 concludes the paper.

IV.2 Literature Review

The nature of competition in the market of pharmaceuticals was examined by various authors. Among different topics, the effects of the market entry of generic drugs after patent expiration have been investigated by several authors.

Grabowski and Vernon (1992) studied the effect of generic drug entry in the US market. They show that for 18 different active ingredients the original drug prices

increased in the years following the generic drug entry. In contrast, the prices of the generic drugs decreased substantially in the same time period.[9]

Frank and Salkever (1997) confirmed some of these results, also using data from the US drug market. For 32 drugs that had lost their patent protection between 1980 and 1985 they find that an increase in competition between generic producers reduced the prices of generic drugs. However, unlike the study of Grabowski and Vernon, the prices of original products are not affected by the competition between the generics.

Lexchin (2004) also studied the changes of original drug prices following the market entry of generic drug competition. Using data from Ontario, Canada, Lexchin compared the prices of 81 different original drugs without generic competition in 1990 that faced one or more generic competitors in 1998. The results indicate that the prices of original drugs did not change statistically significant when generic competition entered the market. The price development of original drugs was also not influenced by the origin of the generic drug (either produced by the same company that produces the original drug or not) or mandatory price freezes.

A theoretical model supporting these empiric results was developed by Königsbauer (2005). She used a vertical differentiation approach to explain the observed pricing behavior of generic and original drug producers.

Another group of authors studied the effects of regulative instruments on prices and demand of drugs.[10]

Most of the studies investigating the effects of regulatory instruments discuss the influence of reference price (RP) systems on the pricing of drugs. Theoretical papers on the topic were published by Danzon and Lui (1996), Zweifel and Crivelli (1997), and Brekke et al. (2007).

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9 Scherer (1993) called this finding the "generic competition paradox".

10 Literature surveys of the topic were made by Danzon and Ketcham (2004), Lopes-Casasnovas and Puig-Junoy (2000) and Puig-Junoy (2005).

Danzon and Lui (1996) used a kinked demand model to show that the prices of all drugs in a reference price group converge towards the reference price. This implies a decrease in the price of branded original products. In contrast, the prices of generics increases.

Zweifel and Crivelli (1997) developed a Bertrand duopoly model also using a kinked demand approach. They found two possible Nash equilibria. In the low price equilibrium the producers of the innovator drug (original drug) accept the reference price as given while the generic is priced below the reference price. In the high price equilibrium the original product is priced above the reference price, while the price of the generic drugs equals the reference price.

A recent theoretical approach by Brekke et al. (2007) compared the effects of generic reference pricing (GRP),[11] therapeutic reference pricing (TRP),[12] and the situation in the absence of reference pricing. The authors find that competition is strongest under therapeutic reference pricing, which thereby leads to the lowest drug prices. Moreover, as TRP implies the lowest profits for patent drug producers, it negatively affects the market entry of patent drugs in the theoretical model.

Empirical studies of the influence of reference pricing were conducted by Aronsson et al. (2001), Pavcnik (2002), Dalen et al. (2006), Brekke et al. (2009) and Augurzky et al. (2009).

Using data from Sweden, Aronsson et al. (2001) showed that the introduction of a reference price system has a strong negative impact on the prices of both original and generic drugs.

Pavcnik (2002) analyzed the impact of the introduction of therapeutic reference pricing in the German drug market on the prices of original and generic products. For two different therapeutic areas (antiulcerants and oral antidiabetics) Pavcnik

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[11] In the case of generic reference pricing only drugs with the same active ingredient are included in a common reference price group.

[12] In the case of therapeutic reference pricing, it is possible to assemble drugs of different active ingredients that are therapeutically or pharmacologically similar in a joint reference price group.

(2002) identified strong price decreases for both types of drugs. The prices of original drugs decreased more than the prices of their generic versions. Moreover, an increase of the number of generic competitors also reduces prices significantly.

The study of Dalen et al. (2006) investigated the effect of the implementation of an index price system[13] in Norway on demand and market power of generic drug producers. The results indicate that the index price system had led to an increase of the generic demand.

Brekke et al. (2009) investigated the relationship between pharmaceutical pricing strategies and the introduction of reference pricing. Their results indicate that reference prices reduced the prices of original drugs more than those of generic drugs. In addition, the results show a negative cross price elasticity for substitute drugs not included in the reference price system. The authors conclude that the reference price system is more effective in lowering prices than the already implemented price cap system.

Augurzky et al. (2009) examined the effects of the German reference price system on ex-factory prices. Their results indicate that market prices do not adjust fully after the implementation of reference prices, as a 1 % change in references prices only leads to a 0.3 % change in market prices. Moreover, the study shows a reduction of the market prices of about 7 % for drugs that are affected by the reference price system.

While the impact of (I) reference price systems on drug prices and demand is researched extensively, the literature concerning the effects of other regulative instruments in the German SHI system is less comprehensive. In particular, to the author's knowledge, the effects of (II) the possibility to exempt drugs from patient co-payment and (III) rebate contracts between pharmaceutical producers and sickness funds are not analyzed in the present literature.

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[13] This regulation approach is similar to a reference price system. For more information see Dalen et al. (2006) and Brekke et al. (2009).

In addition, the current research primary analyzes the different effects of regulatory mechanisms on original and generic drugs. This heterogeneity within the group of generic drugs has not been considered in the literature so far.

The presented study tries to close these gaps. First, the effects of (I) reference pricing, (II) the possibility to exempt drugs from patient co-payments and (III) rebate contracts on the demand of a generic drug will be investigated. Second, the heterogeneity of generic drugs will be considered. Therefore generic drugs are separated in branded and non-branded generic ones. Following this, the effects of the three regulatory instruments on the demand of branded and non-branded generic drugs are investigated.

IV.3 Dataset and descriptive results

IV.3.1 Dataset

The dataset provided by INSIGHT Health[14] (called "Nationale Versorgungs Information" (NVI)) covers the sales of all dispensed drugs for the six active ingredients that are used in the analysis. These six active ingredients were chosen for various reasons.

First, the included substances had to be affected by the three examined regulation instruments. Second, the chosen active ingredients should have a high significance in terms of sales and be used in the treatment of common diseases like heart problems or high blood pressure. Third, an original drug has to be on the market for the complete observation period.

While all drugs with the same active ingredient are automatically part of a reference price group,[15] the participation in the other two regulatory instruments is op-

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[14] INSIGHT Health is a private provider of SHI related drug data. The dataset of INSIGHT Health included over 99 % of the prescribed drug products in the SHI system. The data is collected from various data processing centers for pharmacies.

[15] The included active ingredients are either part of Level 1 or Level 2 Reference Price Groups.

tional for pharmaceutical producers.[16] Therefore, drugs that are part of a rebate contract or are exempted from patient co-payments are marked specifically in the dataset.

For drugs that were available in different strengths or package sizes, the pharmaceutical form with the highest quantity of sales in the observation period was used in the empirical analysis.[17] The dataset was also restricted to drugs that were available during the complete observation period.

Table 13 shows the analyzed active ingredients, identified by their ATC Code,[18] the name of the original drug producer and the therapeutic group of the drug.

Table 13: Sample of observed substances

ATC7 Code	**Name**	**Original drug producer**	**Therapeutic group**
A02BC01	Omeprazole	AstraZeneca®	Proton pump inhibitor
C09AA02	Enalapril	MSD Sharp&Dohme®	ACE inhibitor
C09AA05	Ramipril	AstraZeneca®	ACE inhibitor
C02AC05	Moxonidine	Solvay®	Central alpha agonist
C08CA02	Felodipine	Sanovi-Aventis®	Calcium channel blocker
C07BB07	Bisoprolol and Thiazides	Merck Pharma®	Beta blocking agent

Source: NVI

[16] Manufacturers can choose to exempt their products from patient co-payments or make rebate contracts with sickness funds.

[17] The mechanism was chosen with regard to the instrument variable regression method used in the analysis. Through the narrowing of the dataset to the drugs with the highest overall sales per producers in an ATC7 group, it is possible to use the prices of drugs from the same producers with different package size or strength as instruments. (See Section IV.6)

[18] The Anatomical Therapeutic Chemical (ATC) Classification System is used to classify drugs. It is published by the WHO Collaborating centre for Drug Statistics Methodology. The system divides drugs into different groups according to the organ or system on which they act. Also it considers the therapeutic and chemical characteristics of the classified drugs.

The balanced panel covers the monthly sales volume and the quantity of dispensed drugs in the SHI Market from January 2004 to December 2007 for the observed active ingredients. It contains data for 93 drugs over a time span of 48 periods, leading to 4,464 observations. The drugs can be separated in original drugs, branded generic drugs, non-branded generic drugs, and re-imported original drugs.[19]

Re-imports were only available for the active ingredients bisoprolol and thiazides as well as felodipine. Overall, only five out of 93 observed drugs were re-imports.

While the distinction between original and generic drug is common in literature,[20] the differentiation between brand name generic drugs and non-branded generics is made by the author to meet the specific market environment in the German SHI prescription drug market.

Following this categorization, generic drug producers can be differentiated by the level of activity in various therapeutic fields. In addition, manufacturers vary in their popularity by both patients and physicians, primarily triggered through intensive marketing activities.[21]

The first group, so-called "non-branded" generic producers concentrates their activities on a specific therapeutic field, offering only a very limited range of different drugs. They are also less known and popular by the user groups. An example for this kind of producers is Neurax Pharm®, concentrating on drugs in the therapeutic field of illnesses of the central nervous system.

Generic drug producers of the second category, so-called "brand generic" producers, cover a wide area of different therapeutic fields. They also often produce Over-the-counter (OTC) drugs. Especially through the legal advertisement for

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19 The dataset included 6 original drugs, 5 re-imported drugs, 21 brand name generic drugs and 61 non-branded generic drugs.

20 See Section IV.2 for more information.

21 For more information about how pharmaceutical marketing influence the physician prescription behavior, see de Laat et al. (2002).

OTC drugs[22] they are well-known and popular to both patients and physicians. In Germany, Norvartis®, Stada® and Merckle® and some of their subsidiary companies can be classified as branded generic drug producers.[23]

The sales volumes of all drugs are denoted in retail prices. The quantity of dispensed drugs is delivered as the number of sold packages. The number of sold packages per pharmaceutical form of each drug is transformed to the amount of dispensed Defined Daily Doses (DDD). The amount is calculated using the officially measured value of DDD per package from WiDO.[24] Following this, the data is used to calculate the sales in euro per DDD, from now on referred to as price.

The market share of each product was calculated as the quantity of dispensed DDD for each product divided by total quantity of dispensed DDD in the ATC7 group. Note that a balanced panel cannot take account of new products introduced during the observation period. Therefore, the monthly market shares are calculated considering all available products with sales in the relevant market. This procedure leads to competition adjusted market shares for each product.[25]

The dataset also includes the name of the producer, package size and strength of each drug. In addition, information about the status of a drug concerning the inclusion in a reference price group, the exemption from patient co-payment and the participation in a rebate contract were available.

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22 It has to be noted that advertisement for prescription drugs is forbidden in Germany.

23 See Appendix 3 in Section III.9 for the sales figures of branded generic producers, including their subsidiary companies in the observation period (2004 to 2007) Note that the subsidiary firms 1A Pharma, Ct-Arzneimittel and AbZ Pharma were not labelled as branded generic drugs in the data, as they are the non-branded subsidiaries of Novartis®, Stada® and Merckle®.

24 The "Wissenschaftliches Institut der Ortskrankenkassen" (WIdO) is the scientific institute of the Local Health Care Fund (AOK), Germany's largest health insurance company. One of its tasks is the adjustment of the international DDD levels, issued by the WHO on yearly base, for the German health care market.

25 The analysis was also conducted using non adjusted market shares. The results did not vary, as the observed markets were widely saturated. Therefore only a small number of new competitors entered the market during the observation period.

IV.3.2 Descriptive statistics

Appendix 1 depicts the market share development of original,[26] branded, and non-branded generic drugs for the six active ingredients within the observation period.

The descriptive results indicate that the combined market share of generic products was already considerably high even before the implementation of the examined regulatory instruments. Depending on the active ingredient the market share of generic drugs reached from 35 % to 90 % in January 2004 (See Figure 9 - Figure 14 in Appendix 1).

This is most evident for the active ingredients omeprazole, felodopine, bisoprolol and thiazides, and enalapril. The combined market shares of generic drugs for each of these substances accounted for about 90 % in January 2004 and remained on this level until December 2007. This can be explained by the high level of generic competition in the markets even before the implementation of the considered regulation schemes. In contrast, original drugs did not play an important role throughout the observation period.

The market picture was different for the active ingredients moxonidine and ramipril. The market shares of generic drugs were between 35 and 50 % at the beginning of the observation period in January 2004. They increased steadily during the observation period. At the end of 2007, the generic market shares added up to about 90 %. In contrast, the market shares of original drugs decreased strongly during the observation period to market shares between 7 and 10 % in December 2007.

The descriptive results also indicate the strong market position of brand name generics. For each of the observed substances, brand name generics achieved a larger market share than non-branded generics during the observation period.

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[26] For reasons of clarity, re-imported original drugs are not shown separately in the following descriptive figures. Re-imported drugs did not gain a mentionable market share during the observation period. Also, their prices did not differ substantially from the prices of original drugs.

However, the market position of brand name generic drugs was weakened following the implementation of rebate contracts in April 2007.

The development of the average prices[27] of original, brand name generic and non-branded generic drugs is depicted in Appendix 2. Figure 16 - Figure 20 indicate that the average price of original drugs was always higher than the average prices of any type of generic drug. This observation applies to all observed active ingredients.

In addition, the average price level of brand name generic and non-branded generic drugs was similar in all markets. However, for some of the active ingredients (e.g. omeprazole and ramipril), the average price of brand name generic drugs was slightly higher throughout the observation period.

For each active ingredient the average prices of all drug types decreased in the observation period. The price decrease was stronger for original drugs than for both types of generic drugs. The average price decline was similar for branded and non-branded generic drugs.

The descriptive results also indicate two strong price reductions in the observation period. The first considerable decline occurred after the implementation of reference price groups, affecting primarily the more expensive original drugs.[28] The second sudden decrease of average prices followed the recalculation of reference prices in July 2006. Unlike the introduction of reference price groups, the recalculation also lowered the average prices of generic drugs. However, the average prices of original drug decreased more than the prices of generic drugs. The effect of the reference price recalculation was similar for brand name and non-branded generic drugs.

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[27] As outliners could strongly bias the average prices, the prices were weighted with their monthly market share in the ATC7 group.

[28] The reference dates of the implementation of the reference price system for each market can be found in Figure 8.

IV.4 Regulatory instruments affecting demand for generic drugs

The regulatory body of the SHI, the Federal Ministry of Health, is responsible for the regulation of the market for prescription drugs. As a reaction to the increasing drug expenditures in the SHI system (the annually rate of expenditures for prescription drugs was 4.5 % between 2000 and 2010)[29] different cost control mechanisms were implemented. These regulative instruments target the prescription choices of physicians, the dispense behavior of pharmacies, and the pricing strategies of the pharmaceutical companies.

Physicians occupy a central position within the SHI system. They are the only authority allowed to prescribe drugs to patients. Due to their "therapeutic freedom" they are also free in their choice of a particular drug. However, this “therapeutic freedom” is constrained by various regulative instruments.

The most effective regulative instrument, the physician specific drug budget, was introduced in 2001. The drug budget restricts the drug expenditures per patient, depending, among other, on his age and gender. Physicians are encouraged to prescribe drugs with combined costs (in retail prices) that do not exceed this budget. If physicians are exceeding the budget they have to explain their prescription behavior to the Regional Association of Statutory Health Insurance Physicians.[30] In the worst case, the physician can be made liable for the sum exceeding the budget.

Thus, the drug budget encourages physicians to pay attention to the prices of the prescribed drugs. Consequently, the establishment of physician specific drug budgets increases the price sensitivity of physicians. It also promotes the prescription of cheaper generic versions of an active ingredient instead of the more expensive original drugs.

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29 See Bundesministerium für Gesundheit (2011)

30 The Regional Associations of Statutory Health Insurance Physicians (RASHIP) are responsible for the medical supply of compulsorily insured people. Each physician who wants to treat compulsorily insured persons has to be a member of the competent RAHSIP.

A regulatory instrument targeting both pharmacies and physicians was introduced in 1989. The so-called Aut-idem rule forces pharmacies to exchange the prescribed drugs with cheaper products of the same active ingredient, if they are available in the same strength and package size.[31] However, physicians are allowed, due to their "therapeutic freedom", to suspend this procedure by adding a reservation to the prescription. This reservation prohibits pharmacies to substitute the prescribed drug.

The only regulative instrument targeting patients that are member of statutory health insurance funds are prescription charges. Patients normally have to pay a prescription related co-payment between 5 and 10 euro depending on the price of the prescribed drug. Beside this co-payment, patients are fully reimbursed for the consummation of prescription drugs. Consequently, the price sensitivity of patients can be assumed to be weak. It has to be noted, that patients can be excluded from co-payments due to a high financial burden through prescription fees (f.e. patients that suffer from chronic diseases).

The presented regulations so far are the basis for any regulatory schemes targeting the pharmaceutical industry, as they make patients and in particular physicians more price-sensitive in their drug choices. The instruments addressing the pharmaceutical industry are at the focus of this study. They will therefore be explained in more detail.

Figure 8 gives an overview of the regulative instruments that affected pharmaceutical producers of included active ingredients during the observation period between January 2004 and December 2007. Our discussion of the instruments will be confined to this period.

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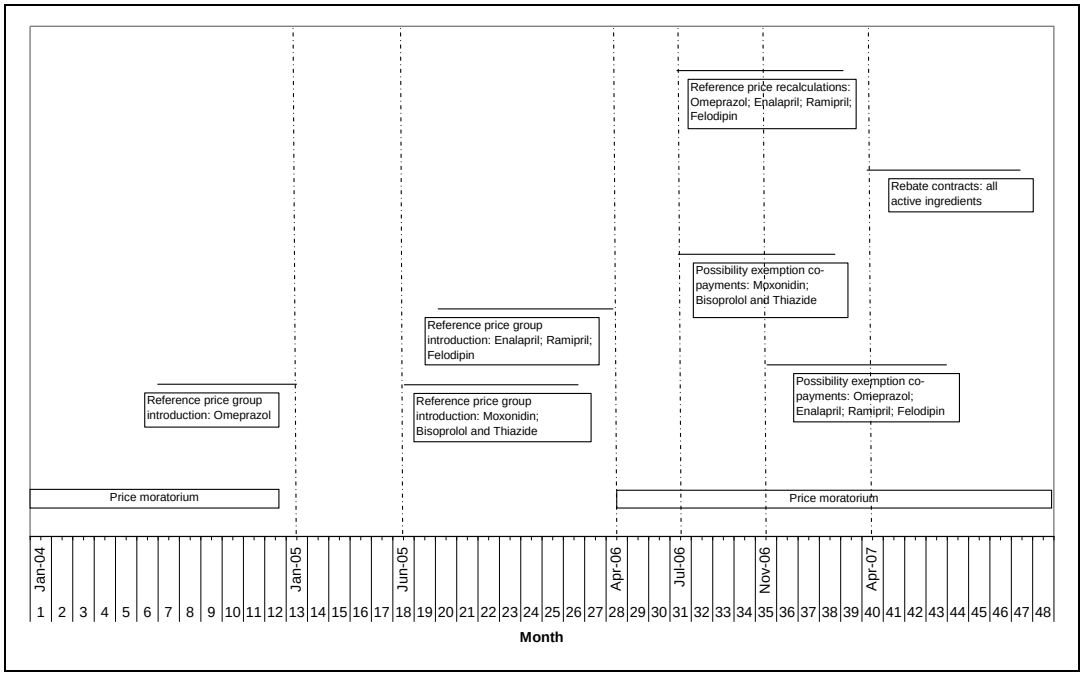
[31] By law the pharmacist has to choose between the three drugs with the lowest price. If the physician writes a specific drug name on the patient's prescription instead of the name of the chemical substance, the pharmacist is allowed to choose between the three cheapest drugs and the named drug.

Figure 8: Regulatory instruments targeting pharmaceutical producers of the observed active ingredients between 2004 and 2007



Source: Own illustration based on Book V of the Social Code

A popular regulative instrument implemented in the observation period are price moratoria, that means freezing drug prices on a specific level for a certain time period. Pharmaceutical companies are still allowed to set their prices freely, however, they are obliged to give any price increase within the price moratorium as an additional discount to the sickness funds of the SHI system.[32]

The effect of price moratoria on the demand of a generic drug is theoretically difficult to assess. It depends on the pricing strategies of both, the generic and corresponding original drug producers during the price moratoria. In addition, the coexistence of other regulative instruments could influence the effect of the price moratoria.

In 2007, price ceilings for drugs not included in the reference price system were generally allowed. The price ceilings have to be either negotiated between the pharmaceutical companies and the National Association of Health Insurance

[32] See Busse et al. (2005)

Funds[33] on a voluntary base or have to be set after a cost-benefit analysis. However, the system has not been applied so far. Consequently, possible effects on pharmaceutical products cannot be measured.

The reference price system was first implemented in 1989. Drugs that are part of a reference price group are only reimbursed to a specific limit by the sickness funds. This limit, called reference price, is determined in a complex process by the National Association of Statutory Health Insurance Funds. While the exact value of the reference price differs from group to group, it is always set lower than the price of original drugs. If the price of a product exceeds the reimbursement level, patients have to pay the difference between the reference price and the retail price by themselves.[34] Originally only original drugs and their generic versions were included in the reference price system. Since 2004 also patent protected drugs can become part of a reference price group. Such groups can consist either of various patent protected drugs or a mixture of patent, off-patent original drugs and their generic versions.

Reference prices are set by the National Association of Statutory Health Insurance Funds and revised annually. Currently, three different levels of reference price groups exist, differentiated by their formation directive as Level 1 Reference Price Groups, containing only drugs with the same active ingredient, Level 2 Reference Price Groups, containing drugs with therapeutically and pharmacologically similar active ingredients, and Level 3 Reference Price Groups, including drugs with comparable therapeutic effects, especially combinations.

In June 2006 the reference prices of Level 2 and Level 3 Reference Price Groups were recalculated. This resulted in a reduction of the reference prices of the affected groups below the previous level.

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[33] The National Association of Statutory Health Insurance Funds is the central lobby of the statutory health insurance and long-term care insurance funds. It shapes the outline conditions for healthcare in Germany and represents the interests of the SHI sickness funds in the Federal Joint Committee.

[34] See Stargardt et al. (2005)

In December 2007, 440 different reference price groups existed. The main part of it were Level 1 RP Groups (316) containing original drugs and their generics, followed by Level 2 RP Groups (66) which also include patent drugs, and Level 3 RP Groups (58) consisting mainly of drug combinations.[35]

The primary goal of reference pricing is the reduction of prices for expensive original products for which cheaper generic versions are available. In addition, as Merino-Castelló (2003) stated, the reference price system should also encourage price sensitive patients to replace expensive original drugs with cheaper generic versions. While this theory is acceptable for the Spanish reference price system, the situation is different for the German SHI market.

Since patients in Germany only have to provide a small co-payment between 5 and 10 euro, they can be assumed to be rather price-insensitive. Consequently, they should be less encouraged to urge their physician to prescribe cheaper drugs. The implementation of the reference price systems should increase the price sensibility of patients only for drugs that are priced above the reference price level. Thus, it can be expected that the price level of originals decreases to the reference price level. Still, since reference prices are located between the price of the original drug and the average price of generic drugs, generic drug prices remain the cheaper alternative. Yet, patients themselves have no real reason to choose them. It is the physician who, due to the constraints of their drug budget, should always try to prescribe the less expensive generic drugs.[36]

From a theoretical point of view, reference pricing can be expected to have a considerable impact on drug prices, especially on prices of expensive original drugs. However, it is less clear whether it also has an effect on the quantities sold.

The situation is similar for the reference price recalculation in 2006. While it can be expected that both original drug producers and generic producers will lower

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35 See GKV-Spitzenverband (2008)

36 The descriptive results shown in Appendix 2 in Section IV.9.2 confirm this thesis for the observed active ingredients.

their prices due to the new reference price, the market situation does not change. Therefore, it is unclear whether the recalculation has an effect on the quantity.

Based on the reference price system, an additional instrument specifically promoting the use of generic drugs was introduced in July 2006. Following the implementation of the "SHI Act of efficiency improvement in drug supply" it is possible for the Federal Association of Company Health Insurance Funds to exempt reference price groups from the requirement of the patient prescription charge. The producers of drugs that are part of such a reference price group can exempt their products from patient co-payments by lowering their prices to a certain level below the reference price.

The possibility to exempt drugs from patient co-payments was well received by the pharmaceutical industry. In December 2007, 12,371 primary generic drugs had been excluded from the so-called prescription charges.[37]

Although the exemption from co-payments can be obtained by every drug in the previous targeted reference price group,[38] the foremost target of the instrument are generic drugs as their main selling argument is their price. Since generic drug competition is primary price-driven, the “co-payment exemption level” can be characterized as a generic drug specific reference price. As patients have to make co-payments for drugs exceeding the “co-payment exemption level”, the demand for these generic drugs should decrease. Moreover, physicians should also prefer co-payment freed drugs due to the lower price. Consequently, the demand for a generic drug that is freed from patient co-payments should increase.

The newest regulative instrument are rebate contracts between statutory health insurance funds and pharmaceutical companies. The contracts contain arrange-

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37 See GKV-Spitzenverband (2008)

38 This means that the target reference price group has to be chosen by Federal Association of Company Health Insurance Funds to give pharmaceutical producers the possibility for get exemption from patient related co-payments by lowering their prices below 30 % of the reference price.

ments about additional discounts for drugs of certain active ingredients or the whole product portfolios.

Originally introduced in 2003, rebate contracts were not common until changes in legal agreements that were implemented through the "competition reinforcement law" in April 2007. These obliged pharmacists to dispense drugs covered by rebate contracts, if available. This directive even overwrites the previously described Aut-idem rule.[39] Following this legal change, the popularity of rebate contracts increased strongly.

The first round of rebate contracts in 2007 targeted only the generic market, leaving out original products. The majority of statutory sickness funds had at least one rebate contract.[40] In December 2007, 579 active ingredients with about 18,000 products were included in rebate contracts.[41]

The effects of rebate contracts on the utility of patients and physicians are assumed to be positive. Physicians can benefit from prescribing drugs that are part of the rebate contract by joining the specific rebate contracts. If they do, prices of rebated drugs are not fully taken into account in the physician specific drug budget. Patients also benefit from rebate contracts, since the legal changes in 2007 made it possible for health insurance funds to waive patient co-payments for rebated drugs. Therefore, the demand of drugs that are part of rebate contracts should increase.

IV.5 A theoretical demand model

In the following the utility function of a patient from, mediated by the physician's advice is described. The physician partly acts as agent of the patient. However, as we have seen in Section IV.4, price sensitivity is mainly (but not solely) introduced by the physician's incentive system. In the following, the term doc-

39 Physicians are still able to suspend the substitution of their prescribed drugs.

40 See Häussler et al. (2008), p. 71-73

41 See Häussler et al. (2008), p. 70

tor/patient refers to a pair of physician and patient making a prescription decision. It is assumed that a doctor/patient chooses drugs that maximize the utility of the patient. All doctors/patients are subject to a budget constraint. Moreover, they are assumed to gain the same deterministic part of utility through the chosen drug.

Following the model of Dalen et al. (2006), let $m = 1,2,..,M$ be the observed market that contains all drugs of a specific active ingredient, described by the corresponding ATC Code. If I_m is the number of drugs in market m, the utility from drug $i = 1,2,..,I_m$ in market m in time period $t = 1,..,T$, for doctor/patient d is random, and given by

$$U_{imdt} = g_{imt} + a_p P_{imt} + e_{imdt} \tag{1}$$

where P_{imt} is the price of drug i in market m in period t. The coefficient a_p captures the direct effect of the price of a drug on the utility. It is assumed to be the same across drugs, markets and periods and is expected to be negative.

The random variable e_{imdt} represents heterogeneity in the preferences of doctor/patient d and therefore stands for the unobserved part of the utility. It is assumed to be independently and identically (i.i.d) extreme value distributed across products, markets and periods.

The variable g_{imt} describes product specific effects, due to unobservable drug specific attributes. It consists of two parts:

$$g_{imt} = FE_{im} + v_{imt};\ i = 1,2,..,I_m \tag{2}$$

where FE_{im} is the fixed effect of drug i in market m that is assumed to be constant over time. Fixed effects are constants that capture unobserved drug specific effects. They are based on the assumption that even if drugs of the same market

consist of an identical active ingredient, differences concerning the packaging, the size, or the appreciation of specific drugs by physicians exist.[42]

The random variable v_{imt} captures drug related effects that can affect the utility perception of the product in a specific time period *t*. Examples for such effects are press articles or short term marketing activities. The variable v_{imt} is assumed to have zero expectation and a constant and equal variance across products, markets and time periods. Also, v_{imt} is assumed to be uncorrelated across products, markets and periods.

A physician d will choose drug i in market m in time period t, if and only if $U_{imdt} > U_{jmdt}$ for all $j \neq i$

As e_{imdt} is assumed to be independently and identically extreme value distributed, the probability (Pr) of the physician choosing drug i in market m in period t has the form of the logit: [43]

$$\Pr(\mathrm{U}_{imdt} = \max_j \mathrm{U}_{jmdt} \mid i, j = 1,2,..,I_m, m = 1,2,..,M) =$$

$$\varpi_{imt} = \frac{e^{(g_{imt} + a_p P_{imt})}}{\sum_{j=1}^{I_m} e^{(g_{jmt} + a_p P_{jmt})}}; i = 1,2,..,I_m, \ for \ m = 1,2,..,M \qquad (3)$$

where ϖ_{imt} is the probability for the choice of drug *i* in market *m* in time period *t*. Assuming that product $b \in \{1,2,..,I_m\}$ in all markets $m = 1,2,..,M$ is the original drug; the ratio of the relative probabilities of drug i to drug b can be described as:

$$\frac{\varpi_{imt}}{\varpi_{bmt}} = e^{((g_{imt} + a_p P_{imt}) - (g_{bmt} + a_p P_{bmt}))} \qquad (4)$$

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42 See Coscelli (2000) and Pavcnik (2002). Both authors have shown the relevance of unobserved drug related fixed effects.

43 See MacFadden (1974) on the discrete choice approach, especially the class of Generalized Extreme Value models.

Equation (4) indicates that original drugs are used as the base category or outside good option, measuring the substitution relation between generic and original drugs.[44]

As mentioned before, the deterministic part of the utility is assumed to be identical for all individuals. Thus, the logarithm of the relative probabilities given in (4) equals the logarithm of the respective market shares. Therefore equation (4) implies:

$$\ln \frac{MS_{imt}}{MS_{bmt}} = \Delta FE_{im} + a_p (P_{imt} - P_{bmt}) + \Delta v_{imt} \qquad (5)$$

where $\Delta FE_{im} = FE_{im} - FE_{bm}$ and $\Delta v_{imt} = v_{imt} - v_{bmt}$.

The variable MS_{imt} represents the market share of drug *i* in market *m* in time period *t*. MS_{bmt} stands for the market share of the corresponding original drug *b* in market *m* in time period *t*.

Note that the empirical observation of average prices of generic and original drugs in Section IV.3.2 leads to the proposition that generally $P_{imt} < P_{bmt}$ for all $i \neq b$.

IV.5.1 Implementation of regulative instruments

Section IV.4 described the most important regulative instruments that affect prescription drugs during the observation period.

The focus of this analysis is on reference pricing, on the possibility to exempt drugs from patient co-payments, and on rebate contracts. However, to avoid misinterpretations or miscalculation of the estimated effects, the impact of additional regulative schemes, that were present during the observation period, has to be controlled in the model.

As Figure 8 shows, two price moratoria were effective in the observation period. The first price moratorium was effective until December 2004.[45] A new price

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[44] See Berry (1994) for the importance of an outside good option.

freeze was introduced in April 2006, which lasted until the end of the observation period. To capture the possible effect of these price moratoria on the demand of a generic drug, the dummy variable PF_{imt} is introduced. It takes the value of 1 if the drug *i* in market *m* in time period *t* is part of a price moratorium, and 0 otherwise.

The reference price system will be considered first. Figure 8 in Section IV.4 shows that the time period of inception of the reference price system was different for the observed active ingredients. Thus, the dummy variable τ_{imt} is introduced. It takes the value of 1 if a drug *i* in market *m* is part of a reference price group in time period *t* and 0 otherwise.

In April 2006 a legal change modified the calculation of reference prices in Level 2 and Level 3 reference prices groups. This affected some of the observed active ingredients. Hence, the effect of the recalculation is captured by the dummy variable $RPRC_{imt}$. It takes the value of 1 if the drug *i* in market *m* was part of a reference price group whose reference prices were recalculated, and $t \geq$ April 2006. The variable is 0 in all other cases.

The second regulative scheme included in the estimation is the possibility for drugs to be exempted from patient co-payments. Similar to reference pricing, the implementation date of the instrument differ for the observed active ingredients.[46] Since pharmaceutical companies can choose to participate in this regulative scheme, the time period of co-payment exemption depends on the pricing decision of the manufacturer. The dummy variable η_{imt} covers this. It takes the value of 1 if a drug *i* in market *m* is exempted from patient co-payments in time period *t*, and 0 otherwise.

The newest regulatory instrument implemented in the SHI system are rebate contracts between pharmaceutical manufactures and sickness funds. Rebate contracts are optional for pharmaceutical producers. Thus the month a drug becomes part of a rebate contract depends on the negotiations with sickness funds. So, it is possi-

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45 See Busse et al. (2005)

46 See Figure 8

ble that drugs did not become part of rebate contracts instantly after the implementation of the instrument in April 2007.[47] Consequently, the dummy variable ξ_{imt} takes the value of 1 if a drug *i* in market *m* is part of a rebate contract in time period *t*, and 0 otherwise.

At last, a time trend parameter λ_q is implemented in the model. The time trend is modulated as quarterly dummies, taking the form of λ_q where $q = 1,..,16$. It captures time specific effects. For example it can be expected that the market share ratio of generic drugs to original drugs is generally increasing during the observation period. This can be justified by the cheaper price of generic drugs and the increasing acceptance of generic drugs by physicians and patients.

The inclusion of λ_q should separate the effects of the regulatory instruments from the expected general increase of the market share ratio within the observation period.

Including those elements into the basic expression (5), the "Basic Model" takes the following form:

$$\ln \frac{MA_{imt}}{MA_{bmt}} = \Delta FE_{im} + a_p(P_{imt} - P_{bmt}) + a_{RP} GD_{im} \tau_{imt} + a_{ECP} GD_{im} \eta_{imt} + a_{RC} GD_{im} \xi_{imt} + a_{PF} PF_{imt} + a_{RPRC} RPRC_{imt} + \lambda_q + \Delta v_{imt} \quad (6)$$

GD_{im} is a dummy variable, taking the value of 1 if drug i in market *m* is a generic drug, and 0 otherwise.

The parameters a_{PF} and a_{RPRC} capture the effects of price moratoria and reference price recalculations of the affected drugs on the market share ratio. The coefficient a_{RP} measures the total effect of the implementation of the reference price system on the market share ratio of a generic drug. The impact of the exemption from patient co-payments on the market share ratio of a generic drug, participat-

[47] See Figure 8

ing in the regulative scheme, is estimated by the coefficient a_{ECP}. The demand effect on a generic drug that is part of a rebate contract is measured by the variable a_{RC}.

IV.5.2 The Expanded Model for branded and non-branded generic drugs

Equation (6) explains the impact of drug prices and selected regulatory instruments on the demand of a generic drug. However, generic drugs appear as a homogenous group. But, as shown in Section IV.3.1, generics can be separated in branded and non-branded generic drugs.

Thus, the effects of the regulatory instruments on both types of generic drugs will be estimated in an extended model.

Consequently, the coefficients capturing the demand effect of reference pricing (a_{RP}), exemption from patient co-payments (a_{ECP}) and rebate contracts (a_{RC}) are expanded to:

$$a_{RP} = a_{RPNBG} + a_{RPBG}\upsilon_{BG} \tag{7}$$

$$a_{ECP} = a_{ECPNBG} + a_{ECPBG}\upsilon_{BG} \tag{8}$$

$$a_{RC} = a_{RCNBG} + a_{RCBG}\upsilon_{BG} \tag{9}$$

with υ_{BG} =1 if the generic drug is a branded generic and 0 otherwise.

The demand effect of the three regulations for non-branded generics is captured by the coefficients a_{RPNBG}, a_{ECPNBG} and a_{RCNBG}.

The total demand effect of the implementation of reference pricing on branded generics is estimated by $a_{RPNBG} + a_{RPBG}$. Alike, $a_{ECPNBG} + a_{ECPBG}$ describes the effect of the exemption from co-payments for participating branded generic drugs. At last, $a_{DCNBG} + a_{RCBG}$ captures the demand impact of rebated branded generics.

Incorporating the modifications of (7) – (9), the "Expanded Model" takes the following form:

$$\ln\frac{MA_{imt}}{MA_{bmt}} = \Delta FE_{im} + a_p(P_{imt} - P_{bmt}) + (a_{RPNBG} + a_{RPBG}\upsilon_{BG})GD_{im}\tau_{imt} + (a_{ECPNBG} + a_{ECPBG}\upsilon_{BG})GD_{im}\eta_{imt} \quad (10)$$
$$+(a_{RCNBG} + a_{RCBG}\upsilon_{BG})GD_{im}\xi_{imt} + a_{PF}PF_{imt} + a_{RPRC}RPRC_{imt} + \lambda_q + \Delta v_{imt}$$

IV.6 Estimation of the demand equation

The theoretical models of this study belong to the class of the so-called demand-price models.[48] The estimation of demand-price models is characterized by possible endogeneity problems. These are caused by the possible causality between the prices occurring on the right hand side of (10) and the market share ratio on the left hand side of (10), also known as the simultaneous causality problem. Therefore using ordinary least square methods (OLS) could lead to inconsistent estimates as the error terms could be correlated with the prices.

A standard solution for this problem is the use of instrument variables for the possible endogenous variable. Instruments are defined as variables that are correlated with the endogenous variable (in this case prices)[49] but not with the error term. The application of instruments variables concludes in the estimation of the coefficients of the demand equation using a two-stage least-square approach (TSLS).

Since the use of instruments is often criticized in the econometric literature, a Davidson-MacKinnon test of exogeneity[50] is used to determine the necessity of instrument variables for prices. However, the corresponding test statistic requires a TSLS regression and a standard OLS estimation to be carried out first.

Following Berry et al. (1995) and Hausmann-Taylor (1981), instrument variables for the TSLS approach should affect the supply side (the market share ratio) but have to be uncorrelated with the error terms in the demand equation. Thus, in-

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48 See Berry (1994)

49 See Berry (1994) for more information on the use of instrument variables in demand supply models.

50 See Davidson and MacKinnon (2003), p. 339-348

spired by Dalen et al. (2006) the following instrument variables for prices were chosen:

1. Prices per DDD of drugs from the same producers with the next smaller package size and equal strength.
2. Prices per DDD of drugs from the same producers with the next bigger strength and equal package size.

A Hausmann-test showed that a fixed effect model in favor of a random effect model should be used in the estimation process. The residuals were also tested on heteroskedacity[51] and serial correlation.[52] Since both effects occur, product level cluster robust standard errors are estimated, which are robust to group vice heteroskedasticity and arbitrary serial correlation.

Next, the quality of the instrument variables was tested. The results indicate that the instrument variables fulfill the requirements of identity and exogeneity i.e., instrument variables should be correlated with the endogenous variables, but not with the residual terms. In addition, the strength of the instruments was tested, as weak instruments (instruments that are only weakly correlated with the endogenous variables) could lead to poor estimators. The instrument variables also satisfy this demand.[53]

Following this, the Davidson-MacKinnon test of exogeneity in panel regression was conducted. The null hypothesis states that the error terms are uncorrelated with all regressors. A rejection of the null hypothesis indicates the need of instru-

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[51] A modified Wald-test for group vice heteroskedacity (most common form of heteroskedacity in panel data) has been conducted.

[52] A test for serial correlation in the idiosyncratic errors of a linear panel-data model was conducted, as discussed by Wooldridge (2003), p. 274-276. See Drukker (2003) for further details of the test statistic.

[53] The results of Anderson canonical correlation test show that the equation is identified for both the Basic and the Expanded Model. Tests based on the Cragg-Donald F statistic indicate that the instruments are not weak. The results of Sargan-Hansen test show that the instruments are exogenous, therefore not correlated with the residuals.

ment variables.[54] The test statistic for the present dataset computes a p-value < 0.05 (< 0.1 for the Expanded Model). Therefore, the application of instrument variables for prices is advised. Following these remarks, a TSLS model with robust standard errors was used to estimate the coefficients of the demand equations. The next section shows the results of the estimation process.

IV.7 Estimation results

IV.7.1 Basic Model

Table 14 shows the results of the TSLS estimations for the various variants of the Basic Model, following equation (6).[55] They include the estimated effects of the price difference between generic and original drugs $(P_{imt} - P_{bmt})$ and the regulative instruments on the demand of a generic drug. The demand is measured by the market share ratio of the generic drug to the corresponding original drug.

Following Figure 8, various regulative instruments were simultaneously active within the observation period. To avoid misinterpretations, Basic models (2) and (3) estimate the coefficients of the demand equation considering different sets of interaction variables.

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[54] For more information on both tests see Davidson and MacKinnon (2003), p. 339-348 and Wooldridge (2003), p. 483-484

[55] The missing value of the constant in the IV regression can be explained by the applied estimation procedure. The Two Stage Least Square estimation was performed using a user written stata command, called xtivreg2, see Schaeffer (2008). The command was used instead of the standard command (ivreg) because of the availably of additional test statistics concerning the validity of the used instruments. It also includes options for group vice heteroskedacity and serial correlation robust standard errors. However, it misses the option to report the value of the estimated constant.

Table 14: Estimated coefficients of the Basic Models

Coefficient[56]	**Basic Model (1)**	**Basic Model (2)**	**Basic Model (3)**
Price Difference (P_{imt} -P_{bmt})	-0.217	-0.519***	-0.505***
	(0.15)	(0.19)	(0.19)
Reference Price (RP)	0.095*	0.114**	0.106**
	(0.05)	(0.049)	(0.05)
Co-payment Exemption (CPE)	0.457***	0.234**	0.044
	(0.06)	(0.1)	(0.14)
Rebate Contract (RC)	0.854***	1.073***	1.001***
	(0.12)	(0.15)	(0.18)
Price Moratorium	-0.127***	-0.115***	-0.270***
	(0.045)	(0.045)	(0.041)
Reference Price Recalculation (RPRC)	0.330***	0.176	-0.0286
	(0.094)	(0.12)	(0.14)
Price-Difference*RP	-	-0.501**	-0.507**
		(0.23)	(0.23)
Price-Difference* CPE	-	-1.438***	-1.658***
		(0.41)	(0.37)
Price-Difference* RC	-	1.851***	10.53***
		(0.51)	(3.28)
Price-Difference* CPE*RC	-	-	-8.211***
			(2.88)
RP*Price Moratorium	-	-	0.067
			(0.059)

[56] Instead of the regression coefficient descriptions, the names of the variables, whose effects are estimated, are shown in Table 14 and Table 15. This was done to simplify the interpretation of the results.

CPE*RPRC	-	-	0.112
			(0.17)
RC*RPRC	-	-	0.217
			(0.21)
Constant	Yes	Yes	Yes
Quarterly Dummies	Yes	Yes	Yes
Observations	4,464	4,464	4,464
Number of Drugs	93	93	93
R-Square	0.50	0.51	0.51

Standard errors robust to any form of heteroskedacity and serial correlation are in parentheses. *** indicates significance at the 1 % - Level; ** indicates significance at 5 % - Level; * indicates significance at the 10 % - Level.

Results of Basic Model (1)

This model contains only the direct effects of the price difference and the regulative instruments on the demand of a generic drug. It should be noted that the measured coefficients indicate the change of the price difference about one euro. The average price differences between original and generic drugs were located between 0.10 and 0.20 euro, as the descriptive results indicate. Therefore the numerical value of the coefficients should be interpreted with care.

The effect of the price difference $(P_{imt}\text{-}P_{bmt})$ on the demand of generic drugs is negative but not significant in Basic Model (1). Although the effect becomes significant in Basic models (2) and (3), for reasons of clarity, the explanation of the effect is already given here. Given the estimated negative coefficient, in the common case of $P_{imt} < P_{bmt}$ for all $i \neq b$[57], an increase of the price difference (through the price increase of the original drug or the price decrease of the generic drug) leads to a rise of the demand for generic drugs. This supports the assumption that physicians try to prescribe generic drugs, if possible, due to the price advantage of the latter.

[57] Appendix 2 in Section IV.9.2 shows that generally generic drugs are cheaper than original drugs. This result is found for every observed market.

The introduction of reference pricing had a significant positive influence on the demand of generic drugs, as the positive coefficient of (RP) indicates. The estimated effect is rather small. Therefore the demand for cheaper generic drugs did not increase much following the implementation of reference prices. A possible explanation is that some physicians that previously preferred the more expensive original drug could be urged by patients to prescribe cheaper generic drugs, if the corresponding original drug is priced above the reference price. However, following the strong drug budget pressure, it can be assumed that the number of physicians prescribing larger amounts of original drugs is rather small. Consequently, the implementation of reference pricing leads to only a small effect on the demand of a generic drug.

The exemption from patient co-payments increased the demand for generic drugs that were part of the regulative scheme as the positive coefficient of (CPE) shows. This seems reasonable as physicians and patients benefit from co-payment freed drugs, as proposed in Section IV.5. Physicians prefer the cheaper co-payments exempted drugs, due to their incentive system. Patients, on the other hand, save the prescription fee between 5 and 10 euro when using co-payment exempted drugs.

The strongest positive demand effect, measured by the coefficient (RC), was estimated for drugs that were part of a rebate contract. The extent of the demand reaction can be explained by the quasi monopolistic position of rebate drugs, due to the fact that pharmacies are obliged to dispense rebated drugs, if available. Therefore, the market share of a rebate drug increases strongly, as assumed in Section IV.5.

The effect of price moratoria (Price Moratorium) on the market share ratio of a generic drug and the corresponding original drug is negative. A possible explanation is the absence of regulative instruments during the first price moratoria (see Figure 8). As the descriptive results indicate, market shares of original drugs are

higher during the first price moratorium compared with the later time periods.[58] This development is captured by the estimated coefficient for price moratoria, leading to a negative impact on the market share ratio.

The recalculation of reference prices in April 2006 (RPRC) increased the demand for a generic drug. This result is not self-evident, as the recalculation affected the prices of both original drugs and generic drugs, forcing both of them to reduce their prices to stay competitive. Consequently, the relative market situation might have remained stable. Still, similar to the case of reference pricing, it is possible that original drug producers do not decrease their prices to the new reference price level. This would explain the increase of the demand for the cheaper generic drugs. However, the coefficient is only significant in Basic Model (1).

For clarity reasons, the estimated coefficients of the quarter year indicators are not included in Table 14. They indicate an increasing demand for generics during the observation period.

Results of Basic Models (2) and (3)

Basic Model (2) and Basic Model (3) consider different sets of interaction variables. Basic Model (2) includes possible interactions between the regulative instruments and the price difference between generic and original drugs $(P_{imt}-P_{bmt})$. Basic Model (3) additionally includes all possible interaction variables between the included regulative instruments.[59]

Most results of Basic Model (1) are confirmed in the more elaborate models. Still, the significance and the strength of some effects changes in Basic Model (2) and (3). The direct effect of the price difference $(P_{imt}-P_{bmt})$ is stronger and also significant in these models. The coefficients measuring the effects of reference price

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58 See Appendix 2 in Section IV.9.2

59 As the results in Table 14 show, not every conceivable interaction variable is included in the estimation. In some cases, a specific reform was enacted for the complete observed time span of another regulative regime. Therefore the dummy capturing the interaction would always take the value of one (perfect multi-collinearity).

recalculations (RPRC) and the exemption from patient co-payments (CPE) have the same sign, but are insignificant in Basic Model (3).

In addition, the following results of Basic Models (2) and (3) are worth mentioning.

The interaction variables, capturing the effect of $(P_{imt}-P_{bmt})$ and the various regulative instruments, indicate that the magnitude of the direct price effect on the demand of a generic drug varies under the regulative regimes.

The estimated interaction coefficient Price-Difference*RP shows that the negative effect of $(P_{imt}-P_{bmt})$ is significantly stronger for generic drugs that are part of a reference price group. Moreover, the interaction coefficient Price-Difference* R*CPE indicates that the impact of $(P_{imt}-P_{bmt})$ increases even more for generic drugs that are additionally exempted from patient co-payment.[60] These results seem reasonable, as both reference pricing and exemption from patient co-payments are directed at decreasing drug prices.

At last, it should be noted that the estimated effect of $(P_{imt}-P_{bmt})$ is *positive* for generic drugs that are part of a rebate contract (Price-Difference*RC). This results appears counterintuitive, but can be explained by the nature of rebate contracts. Since pharmacies are obliged to dispend rebated drugs, if available, the importance of the retail price is reduced. Therefore, it is possible that the demand for a rebated generic drug rises, although the corresponding retail price increases. The estimated interaction coefficient (Price-Difference*CPE*RC) in Basic model (3) indicates that this effect is weaker for drugs participating in rebate contracts but are, in addition, exempted from patient co-payments.

Other interaction variables that were included in the model specification (3) to capture possible interaction effects between the regulative instruments are not significant or had to be dropped due to multi-collinerarity.

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60 As explained before, only drugs that are part of a reference price groups can be exempted from patient related co-payments.

IV.7.2 Expanded Model

The Expanded Model, following equation (10), separates the drug class of generic drugs to branded and non-branded generic drugs.

Table 15 shows the results of the estimation process using a similar set of models as for the basic model approach. Therefore, Expanded Model (1) estimates the effects of the price difference $(P_{imt}-P_{bmt})$ and the regulative instruments on the demand of branded and non-branded generic drugs. Expanded Models (2) and (3) include different sets of interaction variables.

Table 15: Estimated coefficients of the Expanded Models

Coefficient	**Expanded Model (1)**	**Expanded Model (2)**	**Expanded Model (3)**
Price Difference $(P_{imt}-P_{bmt})$	-0.195	-0.468***	-0.473***
	(0.14)	(0.18)	(0.18)
Reference Price*Non-Branded generic drug (RP)	0.01	0.021	0.025
	(0.055)	(0.052)	(0.061)
RP*Branded generic drug (BGD)	0.195***	0.240***	0.220**
	(0.049)	(0.059)	(0.092)
Co-payment Exemption*Non-Branded generic drug (CPE)	0.407***	0.151	-0.0827
	(0.072)	(0.11)	(0.15)
CPE*BGD	0.041	0.106	0.232
	(0.081)	(0.12)	(0.18)
Rebate Contract*Non-Branded generic drug (RC)	1.162***	1.548***	1.494***
	(0.15)	(0.19)	(0.22)
RC*BGD	-0.691***	-1.028***	-1.025***
	(0.15)	(0.21)	(0.27)
Price Moratorium	-0.126***	-0.120***	-0.268***
	(0.044)	(0.044)	(0.04)

Reference Price Recalculation (RPRC)	0.307***	0.152	-0.0195
	(0.09)	(0.11)	(0.14)
Price-Difference*RP	-	-0.531**	-0.512*
		(0.27)	(0.28)
Price-Difference*RP*BGD	-	0.383	0.29
		(0.31)	(0.34)
Price-Difference* CPE	-	-1.786***	-1.326**
		(0.48)	(0.52)
Price-Difference* CPE*BGD	-	0.681	-0.892
		(0.59)	(0.67)
Price-Difference* RC	-	3.098***	15.07***
		(0.71)	(4.53)
Price-Difference* RC*BGD	-	-2.651***	-1.727
		(0.95)	(1.09)
Price-Difference* CPE*RC	-	-	-12.06***
			(3.9)
Price-Difference* CPE*RC*BGD	-	-	-[61]
RP*Price Moratorium	-	-	0.098
			(0.06)
RP*Price Moratorium*BGD	-	-	0.0467
			(0.073)
CPE*RPRC	-	-	0.365*
			(0.19)
CPE*RPRC*BGD	-	-	-0.625***

[61] The dataset does not include brand name generics that were exempted from patient co-payments and are part of a rebate contract at the same time.

			(0.19)
RC*RPRC	-	-	0.0484
			(0.31)
RC*RPRC*BGD	-	-	0.234
			(0.38)
Constant	Yes	Yes	Yes
Quarterly Dummies	Yes	Yes	Yes
Observations	4,464	4,464	4,464
Number of Drugs	93	93	93
R-Square	0.52	0.53	0.54

Standard errors robust to any form of heteroskedacity and serial correlation are in parentheses. *** indicates significance at the 1 % - Level; ** indicates significance at 5 % - Level; * indicates significance at the 10 % - Level.

Results of Expanded Model (1)

The results of Expanded Model (1) show the direct effects of the price difference and the observed regulative instruments on the market share ratio. In contrast to the basic models, the demand effect of regulative instruments is estimated separately for branded and non-branded generic drugs. Possible explanations for the overall effects of the regulative instruments on the demand of a generic drug were already given in the results for Basic Model (1). Thus, the following explanations focus on the possible differences in the demand reactions for branded and non-branded generic drugs.

The direct effect of the price difference $(P_{imt}-P_{bmt})$ on the demand for generic drugs is negative and not significant. The result is similar to the case of Basic Model (1). Again, the result shows that physicians prefer cheaper drugs.

The impact of reference pricing on the demand of branded and non-branded generics is positive, but, similar to Basic Model (1), rather small. However, the results indicate that the demand effect is stronger for branded generic drugs

(RP*BGD)[62] than for non-branded generic drugs (RP). The stronger demand effect for branded generics can be explained by the higher popularity of branded generics among physicians and patients.[63]

The exemption from patient co-payments has a positive effect on the demand of both branded (RP*CPE*BGD)[64] and non-branded (RP*CPE) generic drugs that participate in the reform. The impact on the market share ratio is, like in Basic Model (1), stronger than in the case of reference pricing. However, the demand reaction is only significant in Expanded Model (1). It is also not significantly different for branded and non-branded generics. Therefore the stronger market position does not seem to increase the demand of a co-payment exempted branded generic drug.

In contrast, the demand effect differs strongly between branded and non-branded generic drugs that are part of a rebate contract. Rebate contracts have a positive and significant impact on the demand of non-branded generics (RC). The effect is weaker for branded generics (RC*BGD).[65] Therefore, non-branded generic producers gained more from rebate contracts than branded generic producers. This result can be explained by the different strategies of statutory health insurances concerning rebate contracts. In 2007, the group of sickness funds with the largest number of members, the local social health insurances (AOKs),[66] contracted only non-branded generic producers. Consequently, the demand of a non-branded generic drug that was part of rebate contracts increased strongly. The situation is different for branded generic producers that were not able to conclude contracts

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62 The total demand effect of reference pricing for a branded generic drug is RP+ (RP*BGD).

63 Appendix 1 in Section IV.9.1 shows that during the observation period for each active ingredient branded generic drugs had a higher market share than non-branded generics.

64 The total demand effect for a branded generic drug that is exempted from patient co-payments is RP*CPE+ (RP*CPE*BGD).

65 The total demand effect for a rebated branded generic drug is RC+ (RC*BGD).

66 The Local Health Care Funds (AOK) covered 35.5 % of all insured persons in the SHI system in 2007.

with the AOKs. Some of them made rebate contracts with other health insurance funds (BARMER, Techniker Krankenkasse or Deutsche Angestellten Krankenkasse). Based on these contracts, the demand of a rebated branded generic increased, although the effect was smaller than for non-branded generics. A possible reason for this could be the lower number of members of the contracted health insurance funds.

The demand impact of price moratoria (Price Moratorium) and the recalculation of references prices (RPRC) are comparable with the estimated effects of the basic models. Price moratoria have a negative effect on the demand of a generic drug while the effect of the reference price recalculation is positive. The explanations for both effects are the same as in the case of the basic models.

Results of Expanded Models (2) and (3)

The Expanded Models (2) and (3) include different sets of interaction variables. Expanded Model (2) incorporates interactions between the regulative instruments and the price difference between original and generic drugs. Expanded Model (3) additionally considers all meaningful interactions between the observed regulative instruments.

The majority of the findings of Expanded Model (1) are supported by the results of the Expanded Models (2) and (3). However, some differences have to be pointed out. The effect of the price difference $(P_{imt} - P_{bmt})$ on the demand of generic producers becomes stronger and also significant in the more elaborated expanded models. However, the influence of the recalculation of reference prices (RPRC) becomes insignificant. This is also the case for the demand effect of the exemption from patient co-payments (CPE).

In addition, the estimated effects of the interaction variables between the regulative instruments and the price difference $(P_{imt} - P_{bmt})$ should be noted. Similar to the results of the basic models, the price difference has a stronger negative impact on the demand of a generic drug if it is part of a reference price group (Price-Difference*RP). The effect is even stronger for drugs that are also exempted from

patient co-payments (Price-Difference*RP*CPE). Both interaction effects are not significantly different for branded and non-branded generic drugs.

Comparable to the estimated effect in the basic models, the interaction variable between $(P_{imt}-P_{bmt})$ and rebate contracts is positive (Price-Difference*RC). The positive interaction effect is significantly smaller for branded generic drugs (Price-Difference*RC*BGD). A possible reason for this is the attempt of branded generic producers to hold their market position in other submarkets.[67] Therefore, they cannot raise their prices in the same manner as smaller non-branded generic producers that never had a large market share in any submarket.

The demand effect of the price difference is weaker for rebated non-branded drugs that are, in addition, exempted from patient co-payments (Price-Difference*CPE*RC). This result can be explained by the legal framework for the exemption from patient co-payments. Based on these regulative settings, producers of drugs cannot increase their prices strongly without losing the co-payment exemption.

The quarterly time indicators capturing time specific effects are, similar to the estimates in the basic models, supporting the assumption that the market share of a generic drug increases over time. Other interaction variables included in the model specification (3) are not significant or had to be dropped due to multicollinerarity.

IV.8 Discussion

The promotion of generic drug use is one of the major strategies for the shareholders of the SHI to control the expenditures for prescription drugs. Different regulative schemes were implemented to support the use of generic drugs instead of original products. The most important instruments are the reference price sys-

[67] Submarkets are defined as the demand of patients that are insured by a health insurance fund that does not have made a rebate contract with the pharmaceutical company.

tem, the possible exemption from patient co-payments, and rebate contracts between drug producers and statutory health insurance funds.

This study analyzes the impact of these reforms and the role of the price difference between generic and original drugs on the demand of a generic drug. The demand of the generic drug is expressed by the ratio of the market share of the generic drug to that of the corresponding original drug.

As expected, the direct effect of the price on the generic demand is negative. Thus, an increase of the generic drug price leads to a reduction of the market share ratio. Interestingly, the strength of the price effect is affected by the regulatory instruments. The impact is stronger for drugs that are included in reference price groups or are, in addition, exempted from patient co-payments. However, the price effect is reversed for drugs that are part of a rebate contract. In this case, the demand is actually increasing with rising prices. This indicates the diminishing importance of the retail price for drugs under a rebate contract.

All three analyzed regulative instruments have a positive impact on the demand of generic drugs. The effect is strongest for generic products participating in rebate contracts. The possibility to exempt drugs from patient co-payments also significantly increases the market share ratio of affected generic drugs. Reference pricing had the smallest impact on the demand of a generic drug (though a strong impact on the overall price level).

In an Extended model, the effects of the price difference and the regulative instruments on different types of generic drugs are analyzed. To this end generic drugs are separated in branded and non-branded generic drugs.

In the Extended Model, similar to the Basic Model, rebate contracts have the largest impact on the demand of generic drugs. Interestingly, the demand effect is much stronger for non-branded generic drugs than for branded generics. Therefore, rebate contracts primarily helped smaller generic companies to increase their market share substantially. The demand reaction for drugs that are exempted from co-payments is, like in the Basic Model, positive but weaker than for rebate contracts. The effect is similar for branded and non-branded generics. Again, the

smallest demand effect is found for the regulative instrument of reference pricing. The results show that the branded generic drugs benefited more from the reference price implementation than non-branded ones.

The paper has several limitations that have to be considered when interpreting the results.

An important restriction for the analysis is the dataset that consists of only 93 different drugs distributed across six markets. The reason for this limitation is the requirement that the effects of the implementation of the considered regulatory instruments have to be examined for each of the three regulative instruments. Therefore the sample of active ingredients for which each instrument was implemented during the observation period was rather limited. Especially the criterion of the introduction of reference pricing narrowed the field of potential active ingredients considerably, since many active ingredients in the market were already part of a reference price group before the observation period started.

In addition, the instrument of rebate contracts was implemented towards the end of the observation period of the dataset. This also restricted the number of available active ingredients for the analysis. It can be expected that the number of rebate contracts will increase in the future, due to their great success. In principle, this would make it possible to include a larger variety of active ingredients in future analysis. However, it has to be noted that since 2007 it has become increasingly difficult to get full information on all rebate contracts as they are private agreements between the parties involved with an increasing level of complexity. This will make it more difficult to repeat a similar study in the future.

The results indicate that the observed regulatory instruments were successful in increasing the demand for generic drugs. However, at the end of 2007, the overall market share of generics has reached a high level in almost every observed active ingredient.[68] Therefore the implementation of new regulatory mechanisms targeting the demand of generic drugs cannot be expected to increase the market share

[68] See Appendix 1 Section IV.9.1

of generics much further. Consequently, only small expenditure savings can be expected through such regulative instruments.

Due to this fact, policy makers should establish new ways to restrict drug expenditures. Especially potential savings on the market of patent protect drugs might be evaluated as the importance of this market segment increases steadily. This is illustrated by the fast rising share of expenditures for patent protect original drugs (between 1993 and 2008 from 10.2 to 36.8 % of the total expenditures for prescription drugs in the SHI system).[69]

Savings on the market segment of patent drugs could be achieved in different ways. Policy maker can choose between mandatory regulations like the reference price system and competition-based regulations like rebate contracts.

The so-called "Early Benefit Evaluation" that will be implemented in 2011, belongs to the first category. It primary targets the prices of new patent drugs as it is used to evaluate the utility of new active ingredients.[70] The valuation will be performed by the Federal Joint Committee.[71] If an additional utility, in comparison with the existing alternative treatments is found, the price of the patent drugs[72] is negotiated between the National Association of Health Insurance Funds and the pharmaceutical producer. If an additional benefit cannot be proven, the patent drug is automatically included in a reference price group. In both cases, the prices for new patent protected drugs should decrease, leading to lower expenditures for new drugs.

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69 See Schwabe et al. (2009)

70 According to the schedule, early benefit analyzes will also be used for older active ingredients in the future.

71 The Federal Joint Committee is the highest decision -making body of the joint self-government of physicians, dentists, hospitals, and health insurance funds in Germany. It issues directives for the benefit catalogue of the SHI system and specifics which services in medical care are reimbursed by the SHI.

72 More precisely, an additional discount for all statutory health insurance funds is negotiated.

A possible approach, using more competition-orientated regulative instruments, is the extended use of rebate contracts for patent protected drugs. Beside the pure cost savings, the contracts could also include options of risk or cost agreements. These options would help to lower the financial risks of expensive drug treatments in therapeutic fields where the effectiveness of the drugs strongly depends on the singular patient. Also, additionally services by the pharmaceutical companies could be part of rebate contracts for patent protected drugs. This could also increase the quality of the treatment.

IV.9 Appendix

IV.9.1 Appendix 1

Figure 9: A02BC01 - Omeprazole market share

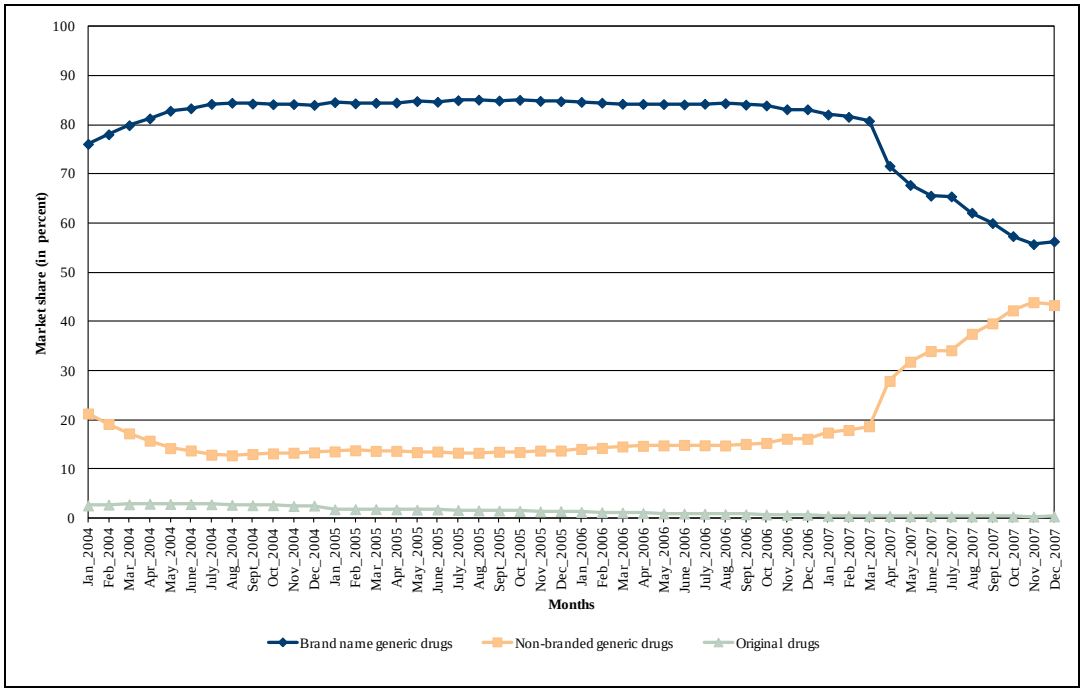


Figure 10: C02AC05 - Moxonidine market share

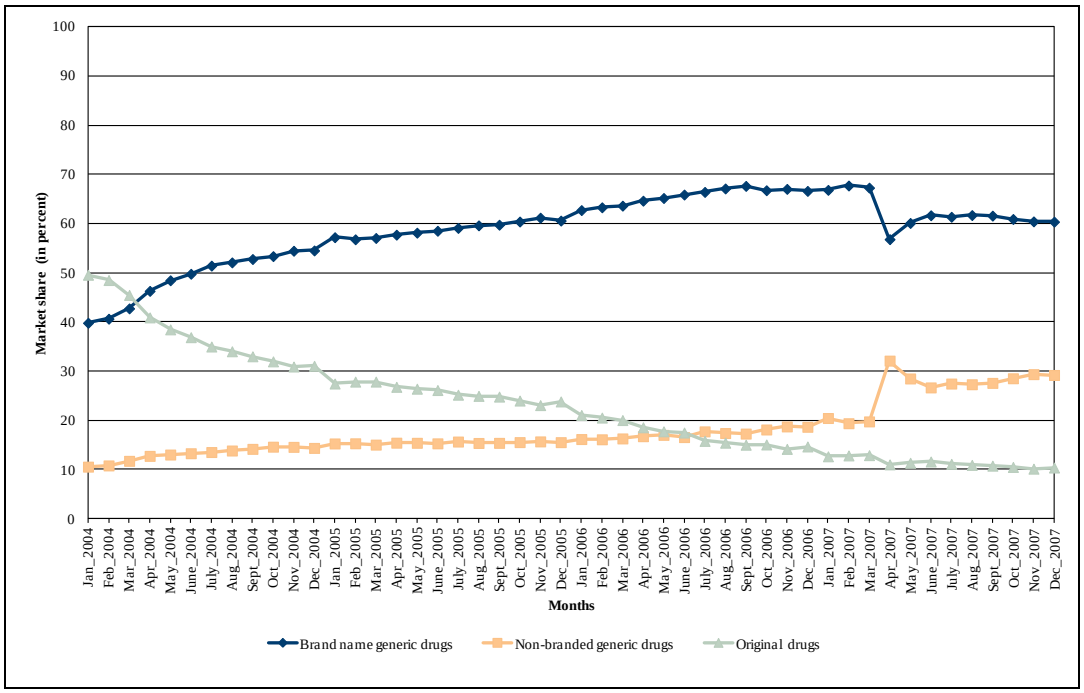


Figure 11: C07BB07 - Bisoprolol and Thiazides market shares

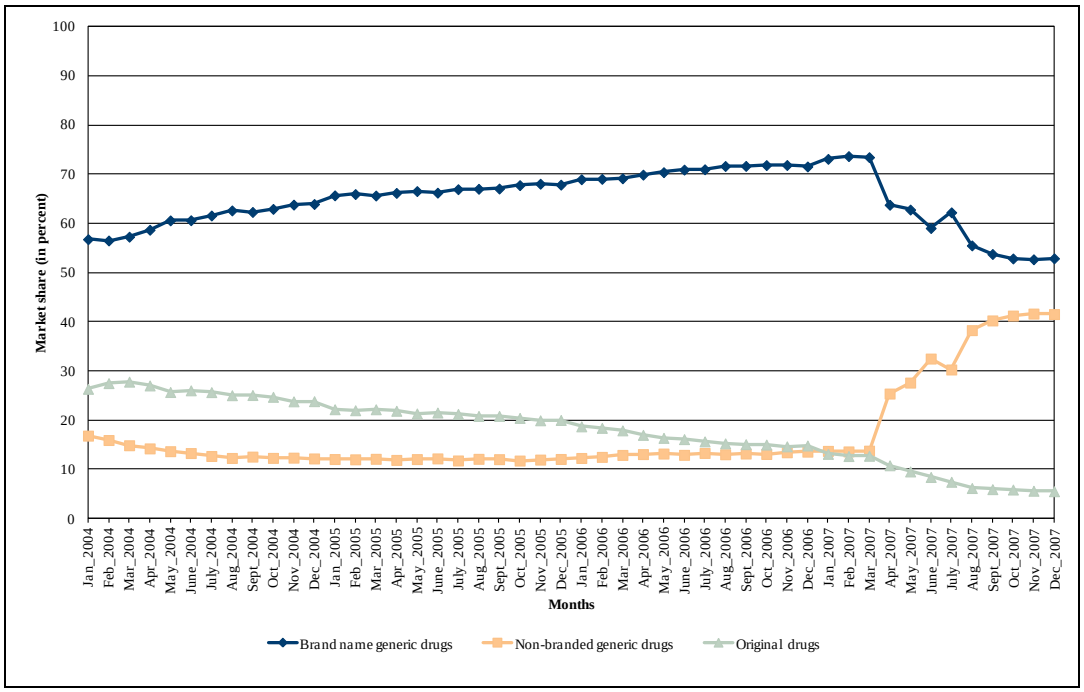


Figure 12: C08CA02 - Felodipine market share

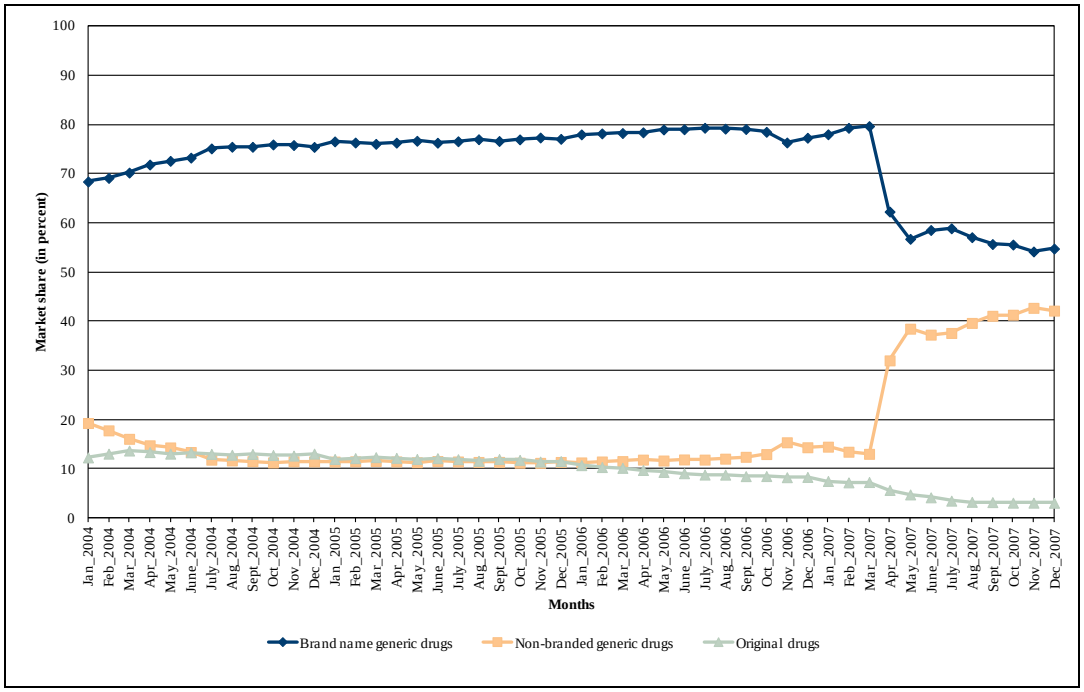


Figure 13: C09AA02 - Enalapril market share

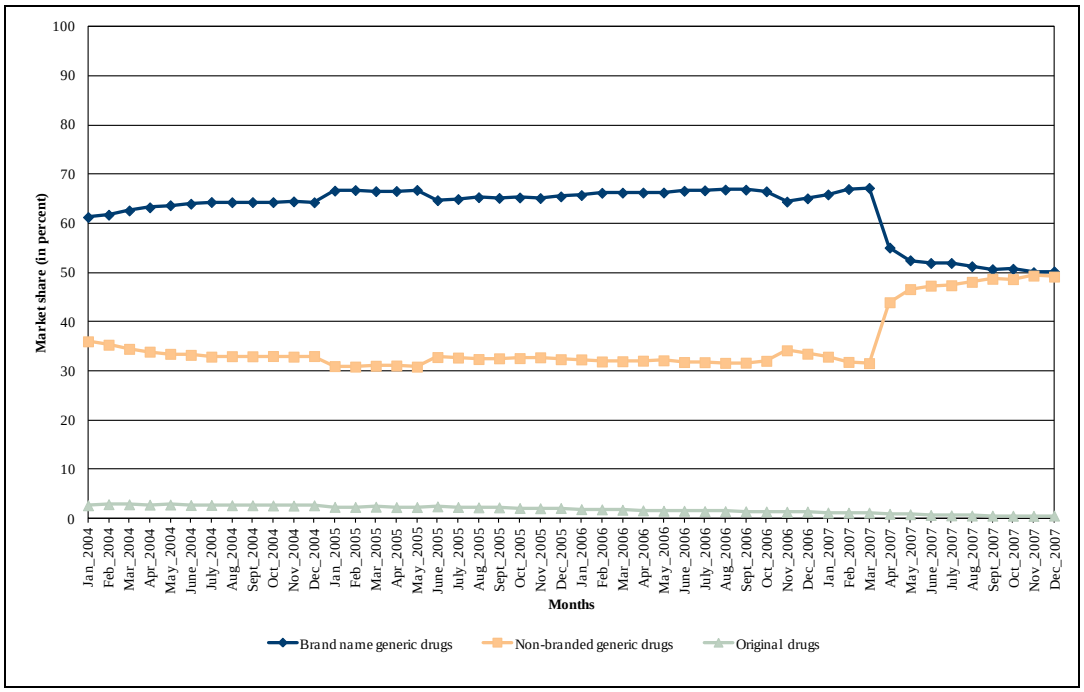
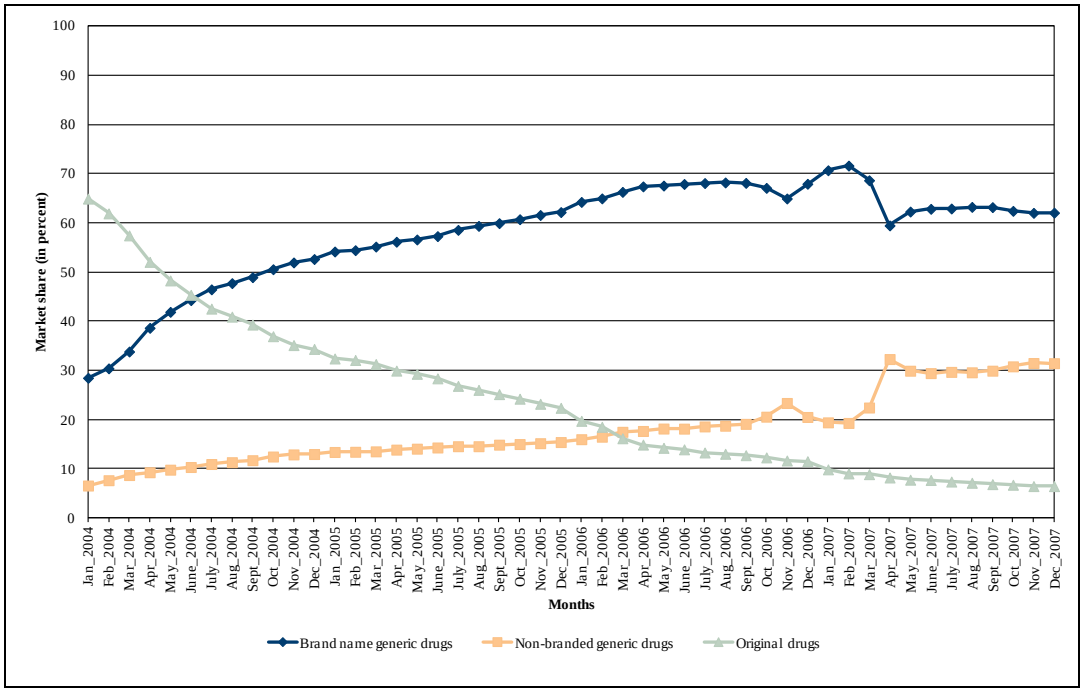


Figure 14: C09AA05 - Ramipril market share



IV.9.2 Appendix 2

Figure 15: A02BC01 - Omeprazol average prices

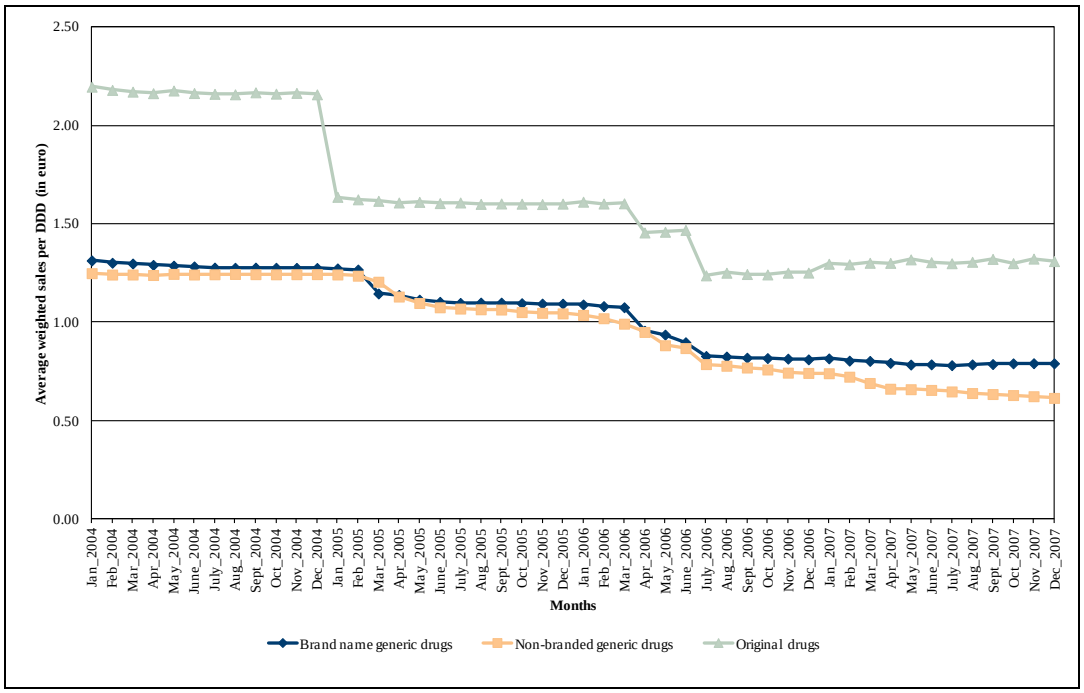


Figure 16: C02AC05 - Moxonidin average prices

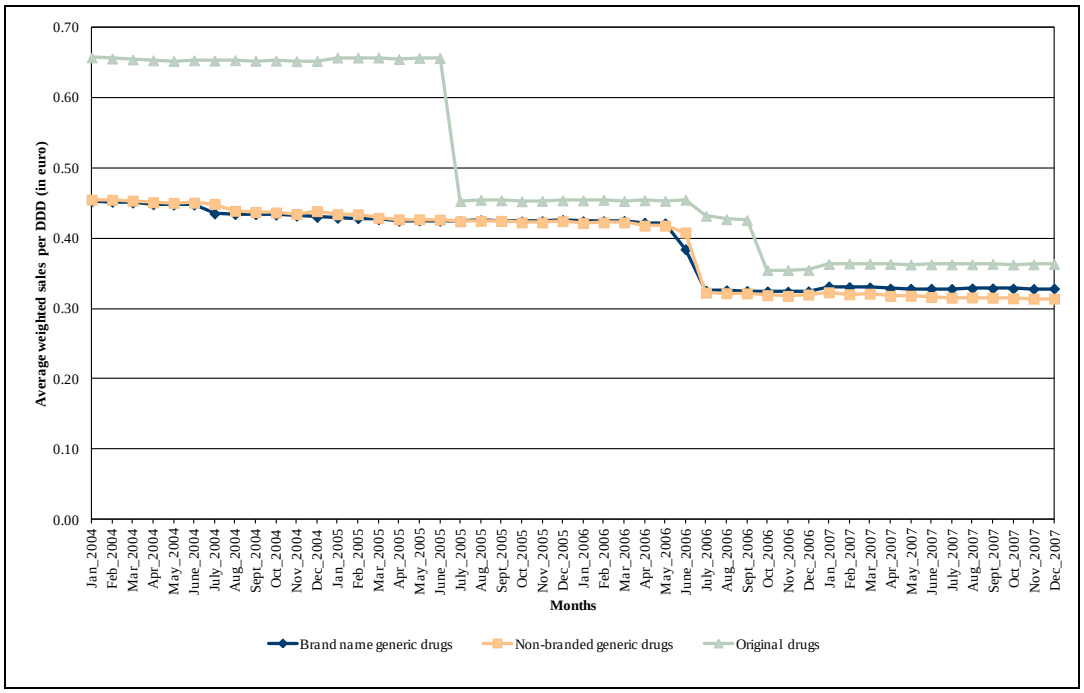


Figure 17: C02AC05 - Bisoprolol and Thiazide average prices

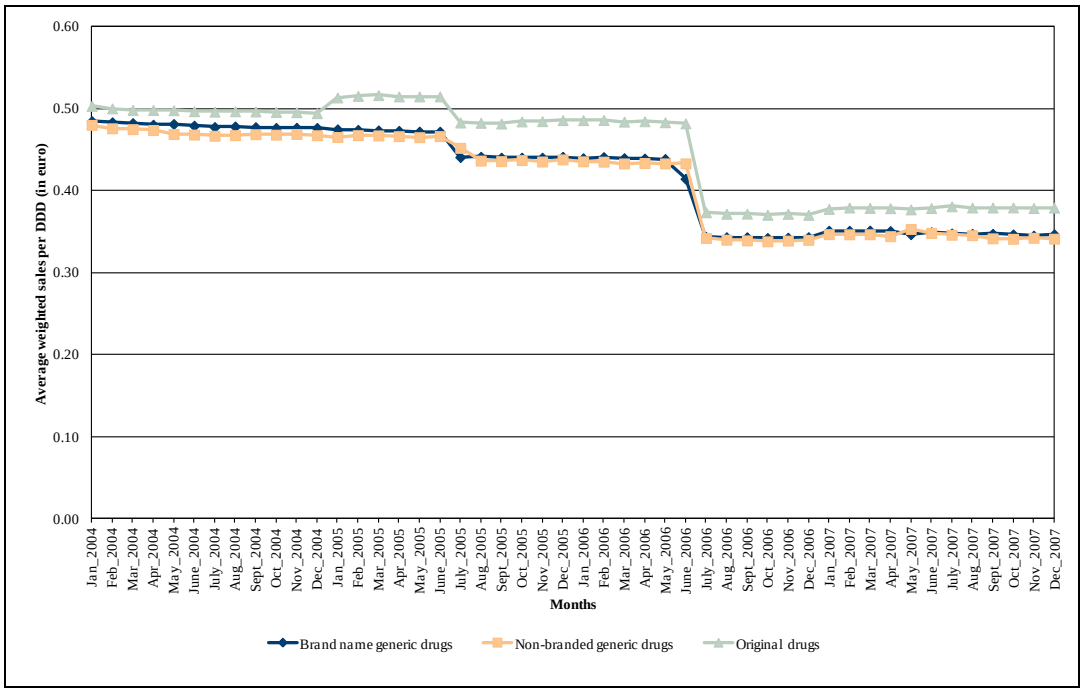


Figure 18: C08CA02 - Felodipine average prices

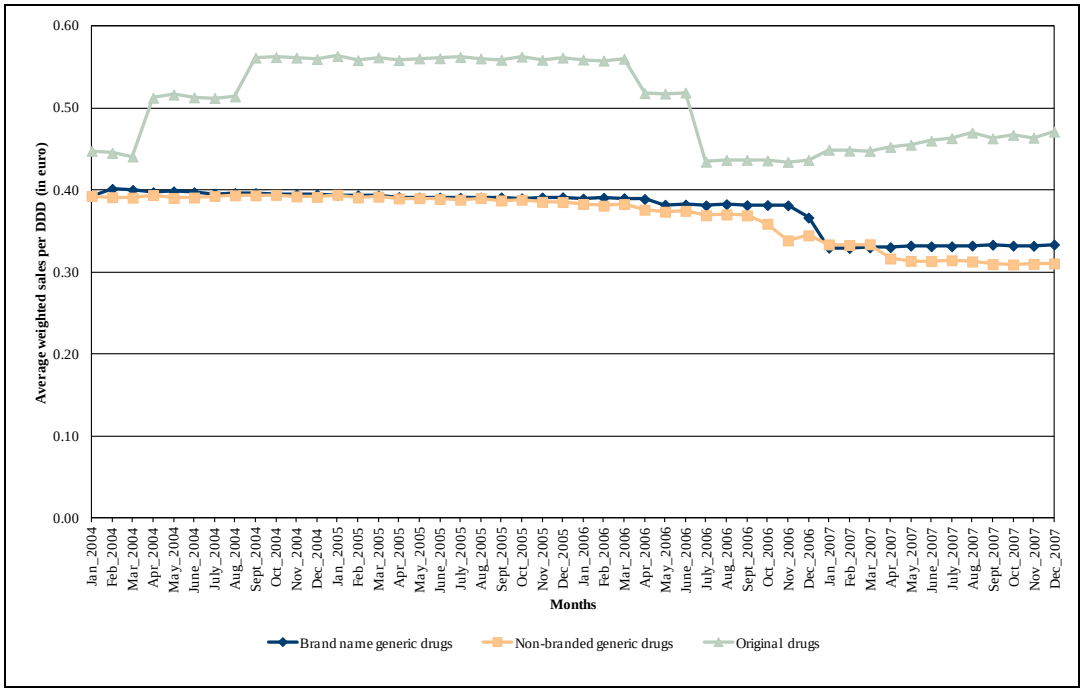


Figure 19: C09AA02 - Enalapril average prices

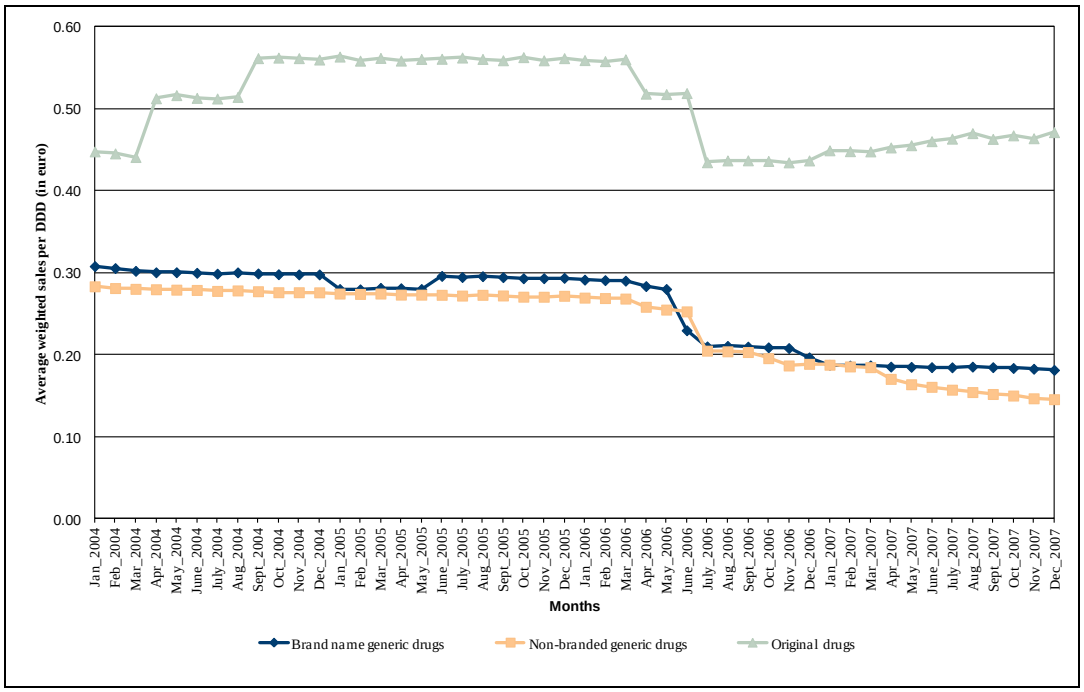
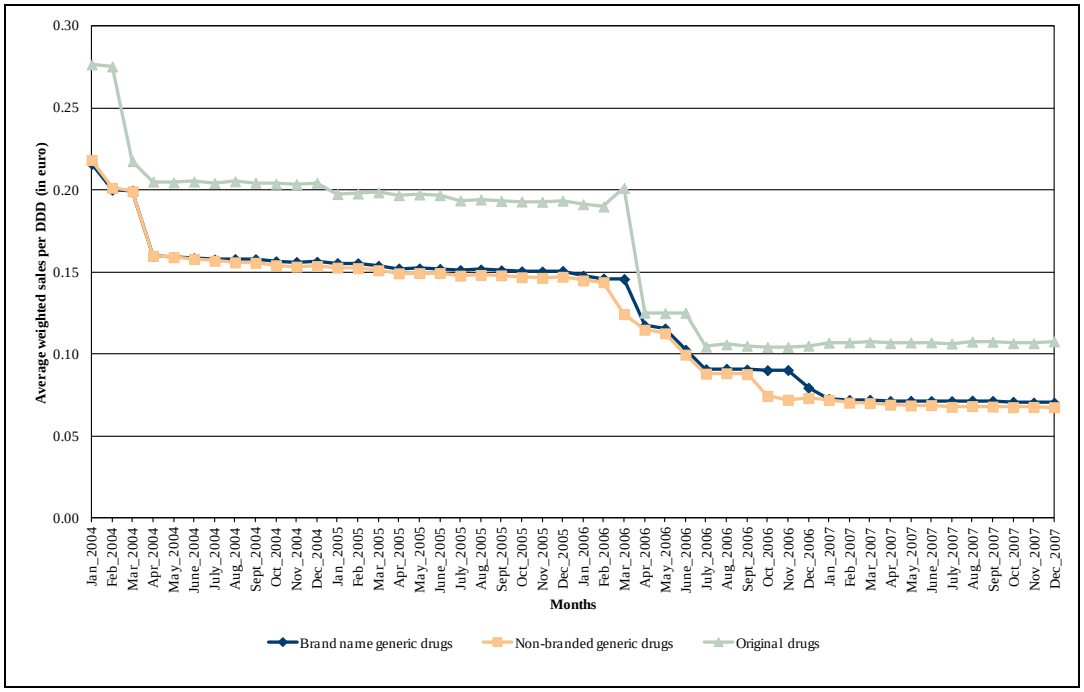


Figure 20: C09AA05 - Ramipril average prices



IV.9.3 Appendix 3

Table 16: Sales of the three biggest generic producers in the SHI market (in million euro) based on NVI data

	Sales 2004	Sales 2005	Sales 2006	Sales 2007
Novartis®[73]	1,479	1,792	1,988	1,975
Stada®[74]	683	746	832	921
Merckle®[75]	1,594	1,766	1,814	1,499

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[73] Aggregated sales of the subsidiary companies of Novartis®, producing generic drugs: Hexal®, Sandoz®, and 1A Pharma®

[74] Aggregated sales of the subsidiary companies of Stada®, producing generic drugs: Stadapharm®, and Aliud®

[75] Aggregated sales of the subsidiary companies of Merckle®, producing generic drugs: Ratiopharm®, Ct-Arzneimittel®, and AbZ-Pharma®

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V. Changes in drug dispense. Which factors determine what drug a patient receives?[76]

V.1 Introduction

In the German Statutory Health Insurance (SHI) System, patients often face switches of the drug dispensed to them. In the past, most these changes occurred between more expensive original drugs and bio-equivalent cheaper generic versions of the same active ingredient. The existing literature has found various determinants that affect these changes. Both, patient and physician characteristics, do play a role for the exchange of an original drug by a generic version, as shown by Hellerstein (1998), Coscelli (2000), and Decollogny et al. (2011). Furthermore the importance of the price differential between original and generic drugs has been shown.[77] Also, the impact of marketing activities on prescription behavior has been analyzed.[78]

However, the current literature is less extensive concerning switches between drugs of similar active ingredients and changes between generic drugs of the same active ingredients. In addition, the impact of regulatory instruments in the SHI system on the probability of a change in the dispensed drug has been analyzed to a lesser extent.[79]

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[76] This paper is a joint work with Christoph de Millas

[77] See Lundin (2000) and Furu et al. (2008)

[78] See Janakiraman et al. (2008)

[79] Furu et al. (2008) and Lundin (2000) incorporated aspects of regulative regimes in their analysis. In both cases, the considered regulatory instruments were similar to the German Reference Price system.

Unlike in other OECD countries with a smaller market share of generic drugs,[80] generic drugs are common in the German SHI prescription drug market. In 2009, 81 % of the dispensed active ingredients for which generic drugs were available, were generic drugs.[81] Only 19 % were original drugs without patent protection.[82] Thus, the relevance of drug switches from original to generic drugs is smaller in the German SHI market than in other OECD countries. In opposite, drug changes between generic drugs consisting of the same active ingredient are more present in the German SHI system than in countries with a lower generic drug share. Also the German drug market has a relatively high number of regulative instruments to encourage switches to cheaper active ingredients, whereas other European health systems prefer direct control by statutory pricing and positive lists.[83] Examples for such instruments are therapeutic reference pricing and the lead compound rule. Both instruments will be explained in detail in Section V.2.

Including these aspects in our analysis, we consider changes between drugs of the same active ingredient as well as changes between drugs of different, however pharmacologically similar, active ingredients. Avoiding possible misleading results due to changes based on different side effects of drugs, the therapeutic groups used in the analysis include only active ingredients that have a very similar range of side effects. Therefore, switches of drugs with different active ingredients resulting from side effects should only happen exceptionally.

The aim of this study is to estimate the effects of patient, physician, and drug specific characteristics on the prescription behavior of physicians. The paper contributes to the existing literature in various ways. First, while other authors narrow the focus on switches from original to generic drugs of the same active ingredient, we

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80 See Mrazek and Frank (2004) and Decollogny et al. (2011)

81 The overall market share of generics in 2009 was 63 %. See Pro Generika e.V. (2010)

82 See Pro Generika e.V. (2010)

83 See Vogler et al.(2008), p. 59 and p. 85

extend the analysis to include drug switches between generic drugs and switches between similar active ingredients.

Second, the large dataset includes at least 200,000 observations of prescriptions by physicians for each of the different therapeutic groups of drugs. Moreover, the analysis is conducted for three therapeutic groups separately with very similar results. Therefore a high degree of validity and robustness of our results can be assumed.

Third, the impact of the implementation of several important regulative instruments in the German SHI system on the probability for a drug switch will be estimated in this paper. Similar studies have been concluded for a singular instrument in the Swedish drug market by Lundin (2000) and in the Norwegian drug market by Furu et al. (2008), however only in the context of prescription changes of original to generic drugs. Yet, we are not aware of any study examining the effects of the implementation of regulative instruments in the German SHI market on changes of the prescription behavior of physicians. Thus, this study tries to close this gap.

The results of the paper show that patient and physician specific characteristics and habits have a strong impact on the likelihood for a change of the dispensed drug. Patient specific characteristics like the time span between prescriptions or the number of previous changes between drugs of the same or different active ingredients increase the probability of a drug change. In contrast, the number of visited physicians, the age of the patient and the previous number of drug prescriptions within an active ingredient have an negative effect on the likelihood of a drug change. Also, the preferences of physicians for a specific producer or active ingredient influence the probability of a drug switch. The preference for an specific active ingredient increases the probability of drug switch while the preference for a specific producer reduces it. Moreover, the price difference between two consecutively dispensed drugs has an impact on the likelihood of a prescription change. In addition, the nature of the active ingredient of the dispensed drug influences the drug choice. Several regulative instruments (reference pricing, co-

payment exemption for patients, and rebate contracts) also positively affect the probability for a change of the dispensed drug significantly.

The paper is organized as follows. Section V.2 describes the German SHI market, the main regulative instruments, and the role of the physician. Section V.3 provides an overview of the existing literature on the prescription behavior of physicians. This is followed by the dataset prescription and the descriptive results in Section V.4. Section V.5 introduces a theoretical approach for the physician prescription behavior. Section V.6 discusses an empirical estimation framework based on the theoretical approach. Section V.7 shows the estimation results as well as their interpretations. Section V.8 concludes.

V.2 The German Health Care System

In 2009, over 90 % of the German citizens were insured in the German Statutory Health Insurance (SHI) system.[84] These insurants received both outpatient (ambulant care) and inpatient (hospital care) services in various forms.

The most important fields of services, in terms of expenditures for the SHI system, are prescription drug expenses in the outpatient sector (30.2 billion euro in 2010), medical services provided by physicians in ambulant care (27.1 billion euro in 2010), and hospital treatments for the insurants (58.1 billion euro in 2010).[85]

While prescription drugs are the second strongest driver of expenditures in the SHI system, they are the sector with the largest growth rate between 2000 and 2010. While the expenditures for medical services in ambulant care and hospital treatments increased on average about 2.1 % and 2.8 % per annum, the annually growth rate of expenditures for prescription drugs was higher (4.5 %). Thus, be-

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84 See Bundesministerium für Gesundheit (2011) and Statistisches Bundesamt (2010)

85 See Bundesministerium für Gesundheit (2011)

tween 2000 and 2010, the expenditures for prescription drugs rose stronger than the total health care expenditures (2.8 %).[86]

In response to the rising drug expenditures, the German Federal Ministry of Health, responsible for the regulation of the drug market, implemented various cost control instruments.[87] Interestingly, unlike in other OECD countries with fixed prices or price caps,[88] pharmaceutical companies in Germany are still allowed to set their manufacturer price freely.

One of the most important roles in the SHI system is full field by the physician in ambulant care. He inhabits a central role for both patient but also for the various regulation schemes. Since a core objective of our analysis is the measurement of the effects of the implementation of various regulative instruments on the prescription behavior of physicians, the most important schemes will be described in detail in the following.

The first restriction for a physician is the drug budget, implemented in 1989. However, the calculation process was changed over the years by various reforms. The current calculation procedure came into effect in 2001. Following this, a physician is only allowed to prescribe a restricted value of prescription drugs per patient and quarter. This value is measured in retail prices and depends on the age, the employment status (pensioner or employee), and the gender of the patient. The sum of the patient related prescription volumes form the drug budget of the physician.[89] In case of overstepping the drug budget a physician has to face consequences by the Regional Association of Statutory Health Insurance Physicians.[90]

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86 See Bundesministerium für Gesundheit (2011)

87 See Denda (2010) for an overview of the regulative instruments in the SHI system.

88 See Mossialos et al (2004)

89 Physicians can shift drug budgets between patients. So they can use the idle budget of certain patients to subsidize other patients' drug demands.

90 The Regional Associations of Statutory Health Insurance Physicians (RASHIP) are responsible for the medical supply of compulsorily insured people. Each physician

These consequences range, depending on the amount of overstepping, from a formal discussion of the prescription behavior with the responsible RASHIP and the sickness funds to penalty payments equal to the difference between the drug budget and the values of the prescribed drugs in the quarter.

The second regulation instrument affecting the physician prescription decision is the "Aut-Idem" rule, implemented in 1989. This regulation scheme obliged pharmacists to substitute drugs by cheaper alternatives of the same active ingredient, if these are available in the same strength, package size and comparable form. Thus, it is possible that the drug a physician prescribes differs from the drug the patient receives from the pharmacist. However, physicians can prohibit the substitution by adding a reservation on the prescription.

The regulative instrument of reference pricing, first implemented in 1989, primarily targets the producers of drugs. It implements a maximum reimbursement limit for drugs that are part of a reference price group. As patients have to pay the positive difference between the reference price and the retail price, it seems reasonable that physicians try to prescribe drugs that do not require additional co-payments for patients. This is especially common for drugs where bioequivalent cheaper generic versions are available. At the same time, the prescription of cheaper drugs helps the physician to remain within the drug budget.

Since 2006 producers of drugs in specific reference price groups have the possibility to exempt their drugs from patient co-payments. To achieve this, pharmaceutical manufacturers have to lower their prices to a certain level below the reference price. The availability of these, cheaper, co-payment exempted drugs should affect both the prescription behavior of physicians due to the drug budget and the demand of patients for drugs without co-payments.

Another regulation, implemented in 2007, is the "lead compound" rule. Included in the regional drug agreements between sickness funds and the Regional Association of Statutory Health Insurance Physicians, the lead compound rule pro-

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who wants to treat compulsorily insured persons has to be a member of the competent RASHIP.

motes the prescription of specific active ingredients in selected therapeutic groups. This results in quotes for specific active ingredients that physicians are obliged to achieve in certain therapeutic groups.[91]

The latest major regulation scheme, also implemented in 2007, are rebate contracts between pharmaceutical producers and sickness funds. Following this regulation the Aut-Idem rule was modified. The pharmacies are now obliged to dispense primarily the rebated drug and not the cheapest drug. Consequently, physicians that persist on a specific drug for a patient, have to prohibit the substitution of the drug explicitly.

V.3 Literature review

The prescription decision of physicians was examined by various authors. However, the majority of the studies focused on prescription switches between brand name original drugs and corresponding generic versions.

Hellerstein (1998) used prescription data for multisource drugs from the US Food and Drug Administration[92] to examine determinants for the physicians' choices between generic drugs and branded originals. Her findings suggest that the preference of physicians for original brand name or generic drugs is fairly independent of observable patient specific characteristics. Thus, Hellerstein concludes that the heterogeneity in the prescription decision is due to unobserved physician characteristics. However, her analysis has several limitations. First, the dataset, which

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91 The rates are negotiated first at federal level and are modulated and/or expanded on the regional level in negotiations between the Regional Association of Statutory Health Insurance Physicians and the SHI sickness funds.

92 The Food and Drug Administration (FDA) is an agency of the United States Department of Health and Human Services. It is one of the United States federal executive departments, responsible for the protection and promotion of public health through the regulation and supervision of, among other areas, prescription and over-the-counter pharmaceutical drugs (medications), and medical devices. The FDA is also responsible for the market access of new drugs and the withdraw of drugs from the US market in cases of serious side-effects that were unknown at the time of the product launch.

were extracted from a physician survey, included data of only two weeks. Thus only two observations for each patient existed. Due to the short observation period and the small number of observations it was difficult to measure possible patient or physician habits. Especially the analysis of patient specific habits is not possible as patients appear only twice in the dataset. Second, the data did not contain information on prices. Therefore the impact of possible price differences on prescription decisions could not be measured. At last, the dataset did not include information about which drug was finally dispensed to a patient but only about the drug the physician prescribed.

The paper of Coscelli (2000) addressed two of the limitations of Hellerstein's study. Coscelli's dataset included all prescriptions for anti-ulcer drugs for a 10 % sample of the population of Rome on a monthly base for the years 1990 - 1992. In addition, Coscelli had exact information about the drug that was finally dispensed to the patient. This avoids possible misleading results because of unobserved substitutions by the pharmacist. His results support Hellerstein's hypothesis of consistent physician related prescription habits, using a number of variables to describe the physician. However, in addition to Hellerstein's results, he also finds evidence for patient related characteristics, that affect the prescription choice of the physician. Yet, like Hellerstein, the paper of Coscelli does not include price data to describe the influence of the price differences on prescriptions.

Lundin (2000) fixed this issue by using data from two pharmacies in a small Swedish municipality of Tierp for the years 1992 and 1993. The dataset contained information about the prices of the dispensed drugs as well as the amount that had to be paid for a drug by both, the patient and a third-party payer. The dataset also included exact information about which drug was dispensed. The results of Lundin (2000) confirm the existence of habit persistence among both patients and physicians. In addition, it shows that the price difference between the original and the generic version of a drug has an effect on the prescription decision. Inherently, an increase in the price difference results in an increasing frequency of physicians choosing the generic instead of the original drug.

Janakiraman et al. (2008) investigated the impact of promotion activities of pharmaceutical companies on the prescription decision of physicians. Their dataset included unique information on promotion related variables like the number of out-of-office meetings between physicians and representatives of pharmaceutical companies, symposium visits, and detailing visits by pharmaceutical representatives. The results indicate that a certain group of physicians, classified as "non-persistent" in their prescription behavior, are affected by detailing visits and by the number of symposium visits they are invited to. In opposite, physicians that are classified as "persistent" prescribers are only responsive to symposium visits. The results also imply that older doctors as well as physicians working in smaller practices are less likely to switch drug prescriptions. Physicians receiving more visits by pharmaceutical representatives, feature a higher willingness to change their drug prescriptions than physicians receiving fewer visits.

Furu et al. (2008) used a dataset from Norway, containing all prescriptions for 23 different active ingredients to determine explanatory factors for the prescription choice between original and generic drugs. Beside various patient and physician related variables, also price data was included in the estimation. The findings of the paper give further evidence on the importance of both physician and patient characteristics for the physician's prescription decisions. The results indicate that the probability for generic substitution is affected by the price difference as well as by the type of insurance coverage of the patient. In addition, the study points out the role of pharmacies for the patient's decision to substitute the more expensive original drug by a cheaper generic product.

Stargardt (2010) analysed the impact of the inclusion of statins in the German reference price system on drug switches of long term users between the more expensive active ingredient atorvastatin and other statins. Using patient data of a large German sickness fund his results concerning patient related socio-economic variables indicate that the probability of a patient to switch drugs decreases with older age and a larger number of hospital visits due to cardiovascular diseases in the baseline periods. Also patients with a high yearly income (> 41,800 euro) have a lower predicted probability to switch drugs compared to patients with a low in-

come (< 15,000 euro). In contrast, the predicted probability for a drug switch increases for patients that are exempted from co-payments due to low income or unemployment. In addition, the membership in a disease management program for diabetes also increases the predicted probability for a drug switch.

Decollogny et al. (2011) examined the influence of patients, physicians, and certain generic drug market characteristics on the generic substitution in Switzerland. They used reimbursement data of a large health insurer for three regions in Switzerland during 2003. Their results indicate that poor health status (described by older patients and complex treatments) is associated with lower generic drug use. Increasing generic drug use is associated with higher out-of-pocket payments, greater price differences between generic and original drugs and with the number of generic drugs in the market.

Our own results and their relation to the presented literature will be discussed in the final Section V.8.

V.4 Dataset and descriptive results

The dataset is provided by a large German sickness fund with more than 1.0 million members during the observation period included in the dataset (2004 - 2007). It was one of the largest sickness funds in the SHI system (among the top 15 out of 241 considering the number of members in 2007).[93] The insured are from different social backgrounds and income groups. Compared to total SHI population, the age structure of the insurants is younger and the share of unemployed persons is below the average.[94] The catalogue of benefits and the reimbursement of physicians in the German SHI system is more or less identical over all sickness funds.[95] Consequently it seems unlikely that patients in our dataset are treated differently

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93 See Beiträge zur Gesellschaftspolitik (2008)

94 See Holle et al. (2005) for more information about the historically rooted risk profiles of different types of sickness funds.

95 See Schulze Ehring and Köster (2010)

than patient in other sickness funds with a different age, mortality or gender structure.[96]

The data contains information about the complete prescription history of patients and their treading physicians between 2004 and 2007 on a monthly basis for three different therapeutic groups (HMG-CoA reductase inhibitors, ACE inhibitors, and proton pump inhibitors). The three therapeutic drug markets were chosen due to the high prevalence of the associated diseases and the significance of the associated expenditures for the SHI system. Also, each of the associated diseases is of chronic nature and requires constant treatment with drugs. Finally, all three therapeutic groups consist of active ingredients with and without patent protection.

The identity of patients and physician is made anonymous. Each patient is assigned a specific *patient_id*, while physicians are identified by a *prescriber_id* that is bestowed by the Regional Associations of Statutory Health Insurance Physicians. The dataset includes socio-economic variables like age, gender, and the status of the patient as an employed or an unemployed person. In addition, the data include information about the nature of the dispensed drug[97] (brand name, producer, strength, price per defined daily doses[98] and package size).

The initial overall dataset contains 2,617,017 observations for 73,032 physicians and 372,196 patients. We excluded patients in the dataset that received only one drug prescription in the observation period. Also, as the data contains some data errors, especially regarding invalid *prescriber_ids*, several observations had to be deleted. The two limitations reduced the number of observations included in the dataset only marginal (< 1%).

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96 See Grobe et al. (2005)

97 It has to be noted, that the prescribed drug and the dispensed drug can differ due to the "Aut-Idem" rule. We try to control this problem in our estimation using a specific variable that captures the effect of "Aut-Idem". See Section V.6.2.3.

98 The Defined Daily Doses (DDD) is a measurement for drug consumption. According to the definition by the WHO, it is “the assumed average maintenance dose per day for a drug used in its main indication in adults". See WHO Collaborating Centre for Drug Statistics Methodology (2011) for more information about the DDD system.

Also, similar to other panel datasets of dynamic nature, the dataset suffers from the so-called initial conditions problem. The problem arises as we do not have any information on the behavior of patients and physicians before the observation period. Therefore we cannot observe possible important information that forms the prescription decision in the later, observable, time periods. Following the advices found in the literature (Heckman (1981) and Coscelli (2000)) to solve this problem, it is assumed that the prescription is either a first time treatment or that the treatment is restarted if a patient has not received a prescription in the therapeutic group for six months. This assumption seems suitable for our dataset, since it only includes chronic diseases that require constant drug treatments and a physician visit every three to six months.

Consequently, only those patients were included in the estimation who received their first prescription after June 2004. Resulting from the above mentioned restrictions the number of observations is reduced to 998,841, containing 62,024 physicians and 248,203 patients.

Table 17 shows the number of observations, patients and physicians for all three therapeutic drug markets. It also includes the number of drug switches during the observation period for each market.

Table 17: Number of observations, patients, physicians and drug dispense changes

	HMG-CoA reductase inhibitors		**ACE inhibitors**		**Proton pump inhibitors**	
Variable name	**Number**	**%**	**Number**	**%**	**Number**	**%**
Observations	212,742	-	322,251	-	463,848	-
Patients	53,202	-	72,769	-	168,585	-
Physicians	29,783	-	35,841	-	53,315	-
Drug changes	45,393	21.3	58,803	18.2	80,973	17.5

Table 17 shows that at least 50,000 patients and at least nearly 30,000 physicians were observed in each therapeutic drug market. The total sum over all patients and

physicians is not identical to the numbers given before, as some patients and physicians are part of more than one therapeutic group. The total number of observations ranged from slightly above 200,000 drug prescriptions for HMG-CoA reductase inhibitors to about 460,000 prescriptions for proton pump inhibitors. The percentage of drug switches ranged between 17.5 % and 21.3 % in the three therapeutic groups in the observation period of four years.

The three indications, representing different therapeutic drug markets, are described by the 4-digit ATC Code (also called ATC5 Code).[99] An individual active ingredient is identified by a unique 5-digit ATC Code (also called ATC7 Code)[100]. They are shown in Table 18.

The first therapeutic drug market are HMG-CoA reductase inhibitors (ATC5 Code C10AA, containing active ingredients C10AA**) that are used to control hypercholesterolemia and prevent cardiovascular diseases.

The second therapeutic group are ACE inhibitors for the treatment of hypertension and congestive heart failure. The market is defined by the ATC5 Code C09AA. It includes active ingredients with the ATC7 Codes C09AA**).

The third therapeutic group are proton pump inhibitors (ATC5 Code A02BC) that are used to reduce the gastric acid production to decrease the pain from heartburn. The included active ingredients are identified by the ATC7 Codes A02BC**).

Table 18 also shows drug expenditures for the active ingredients between 2004 and 2007. The market data (called Nationale Verordnungsinformation (NVI)) are provided by the German market research company INSIGHT Health.

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99 The ATC code is an internationally used drug classification system. It is differentiated into five levels. The first level contains 14 main groups that are assigned to an anatomic main group (for example cardiovascular system) that is primarily affected by the drug. The next two levels describe the therapeutic group and its possible sub groups. The fourth and fifth level are classified by the chemical structure of the drug.

100 See WHO Collaborating Centre for Drug Statistics Methodology (2010) for more information.

Table 18: Market data of the observed therapeutic drug markets

Therapeutic group	Active ingredient	7-digit ATC code	Sales in million € 2004	Sales in million € 2005	Sales in million € 2006	Sales in million € 2007
HMG-CoA reductase inhibitors			**817.7**	**617.8**	**582.5**	**479.9**
	Simvastatin	C10AA01	286.6	375.3	374.8	352.9
	Lovastatin	C10AA02	18.0	14.3	11.9	8.5
	Pravastatin	C10AA03	83.6	78.6	74.5	44.3
	Fluvastatin	C10AA04	73.1	95.0	77.9	46.6
	Atorvastatin	C10AA05	356.4	54.6	43.4	27.6
ACE inhibitors			**557.2**	**575.1**	**480.5**	**356.6**
	Captopril	C09AA01	78.0	62.4	46.3	31.5
	Enalapril	C09AA02	201.5	198.9	163.5	115.1
	Lisinopril	C09AA03	107.1	104.5	90.8	59.1
	Perindopril	C09AA04	8.8	5.0	3.5	2.1
	Ramipril	C09AA05	118.0	167.6	150.5	131.1
	Quinapril	C09AA06	6.6	5.7	5.1	3.7
	Benazepril	C09AA07	11.4	9.6	6.7	4.7
	Cilazapril	C09AA08	2.8	2.3	1.8	1.1
	Fosinopril	C09AA09	11.7	9.5	6.7	4.9
	Trandolapril	C09AA10	1.6	1.1	0.8	0.5
	Spiralpril	C09AA11	7.8	6.8	3.7	2.1
	Moexipril	C09AA13	0.8	0.7	0.5	0.3
	Imidapril	C09AA16	1.1	1.0	0.6	0.4
Proton pump inhibitors			**993.7**	**1,090.1**	**993.0**	**985.1**
	Omeprazole	A02BC01	421.2	419.9	448.3	593.6
	Pantoprazole	A02BC02	297.4	354.1	286.9	204.1

Lansoprazole	A02BC03	41.9	35.9	35.6	28.1
Rabeprazole	A02BC04	13.4	15.0	12.5	10.5
Esomeprazole	A02BC05	219.8	265.2	209.7	148.8

Source: NVI

It has to be noted that the econometric analysis was conducted separately for each therapeutic group to improve the validity of the results.

In the next step, we will develop a theoretical approach that formalizes the decision making process of physicians for a drug prescription in a therapeutic group.

V.5 A theoretical approach for the prescription behavior of physicians

In this section, a model for the decision making behavior of physicians will be developed. A basic assumption is that physicians act partly as agents of their patients. Thus, they care about the latter's health status. In case of indications where various related active ingredients are available, the physician has a scope of options that lead to similar medical results. Therefore, the physician has to choose which drug he wants to prescribe.

As mentioned before, the three therapeutic groups (HMG-CoA reductase inhibitors, ACE inhibitors, and Proton pump inhibitors) will be analyzed separately; therefore we omit an additional index for the therapeutic group in our notion. Considering one therapeutic group, let $k = 1,..,K$ denote the drugs in this therapeutic group.

Let $DC_{ijkt} \in \{0,1\}$ denote whether a drug change to a drug *k* from any other drug in the therapeutic group has occurred ($DC_{ijkt} = 1$) or not ($DC_{ijkt} = 0$) by physician $j = 1,..,J$ for patient $i = 1,..,I$ in observation point $t = 1,..,T$.

In terms of panel data terminology, the physician is considered as the observed object with $j = 1,..,J$. He prescribes to his patient $i = 1,..,I$. The number of observed prescriptions to a specific patient is counted by $t = 1,..,T$. Therefore, the

counting of observation points $t = 1,..,T$ is individual for each physician/patient tuple.

Note that drug changes between products of a singular producer, for example the exchange of a smaller package by a bigger one, are not considered as drug switches in our analysis. Consequently, the binary depending variable only takes the value of 1, if a drug change is connected to a change of the producer.

Let $U_{ijlkt}(DC_{ijlkt} = 1)$ denote the physician's utility from the drug switch such that he will change the medication if, and only if $U_{ijlkt}(DC_{ijlkt} = 1) > 0$.

In particular, we will assume that the physician's utility of a drug switch is additively decomposed into several components as follows:

$$U_{ijlkt}(DC_{ijlkt} = 1) = u_{ijlkt} + \varphi(p_{kt} - p_{lt-1}) + PC_{jkt} + D_{kt} + \tau_m \quad (1)$$

Where the following variables are used: u_{ijkt} is a vector capturing patient specific variables; $\varphi(p_{kt} - p_{lt-1})$ describes the effect of retail prices on the physician's utility of a drug switch; the vector PC_{jkt} contains physician related variables; drug related attributes that could affect the prescription decision are included in the vector D_{kt}; the monthly time dummy $\tau_m \in \{1, \ldots, 48\}$ captures possible observed month specific effects. Note the difference between the observation point *t* and the month *m*. The index *t* counts the number of prescriptions of a physician *j* for a specific patient *i*. In contrast, *m* is the month, in which the prescription occurs. The distinction between these two subscripts becomes important for some of the variables used in the analysis.

The elements of equation (1) will be discussed and refined in turn in the following paragraphs.

In the case of multiple options for the medication of a medical condition with comparable effects, physicians take into account observable characteristics and attributes of the patient *i* for their prescription decisions. These are captured by the vector u_{ijkt}. It includes patient specific characteristics like age or gender. Also,

patient specific habits like the preference for a specific active ingredient are considered by the physician. The vector is parameterized as

$$u_{ijkt} = \beta X_{ijkt} + e_{ijkt} \quad (2)$$

where X_{ijkt} is the vector of observable patient related variables.

The corresponding parameter vector is denoted as β, while the unobservable portion of the patient's term is represented by e_{ijkt}. This residual is assumed to be independently and normally distributed over the observation points, patients, and physicians with $e_{ijkt} \in N(0,1)$.

Based on informational constrains and private motives, it cannot be assumed that physicians act as perfect agents for their patients. Thus, physicians will consider their own preferences and their information about available drugs.

An important aspect for the physician is the retail price of the prescribed drug. While patients are nearly fully reimbursed for drug expenditures, physicians have to consider the retail price of the prescribed drug due to their limited drug budget. The effect of the drug prices is estimated by the price difference between the dispensed drug $k \in \{1, \ldots, K\}$ in observation point t and the dispensed drug $l \in \{1, \ldots, K\}$, in observation point *t-1* as $\varphi(p_{kt} - p_{lt-1})$, with $l \neq k$. The coefficient φ captures the effect of the price difference.[101]

However, the retail price of a drug is only one of several factors affecting the prescription decision. It can be assumed that physicians also have a set of non-price related characteristics and habits concerning the prescription of drugs. For example, physicians might prescribe some drugs more frequently due to their specific patient clientele or their own preferences for a particular producer. Also, special-

[101] The price per DDD is used instead of the retail price to avoid possible miscalculations and misinterpretations. When using retail prices, the change of a drug that is related with a change in package size from a smaller package to a bigger one can result in a positive price difference, although the price per "pill" remains constant or even decreases. This problem is solved by the use of prices per DDD that make prices of drugs comparable and independent of package size or strength.

ized physicians could have different drug preferences compared to general practitioners. The variable vector PC_{jkt} captures such physician specific characteristics and habits. It is parameterized as

$$PC_{jkt} = \lambda S_{jkt} + \alpha_j \tag{3}$$

The vector of observable physician characteristics and habits is denoted S_{jkt} with the corresponding parameter vector λ. The unobserved part of the physician preferences, assumed to be persistent over *t* and *k*, is denoted as α_j.

In addition to physician specific factors, we assume that physicians also consider drug specific properties in their prescription decision. Therefore the vector D_{kt} contains information about the active ingredient and the popularity of the drug. Also the possible effects of the implementation of regulation schemes targeting specific drugs are considered as a part of the drug specific variable vector. It is modeled as:

$$D_{kt} = \eta DV_{kt} + \chi RI_{kt} \tag{4}$$

where DV_{kt} is a vector of drug related variables. The implementation of regulation instruments that target drug *k* in observation point *t* is captured in vector RI_{kt}. The corresponding parameter vectors are η and χ.

Therefore, the empirical model to be estimated has the following form:

$$\begin{aligned} PR\left[DC_{ijlkt} = 1\right] = PR\big[&\beta_0 + \beta X_{ijkt} + \varphi(p_{kt} - p_{lt}) + \lambda S_{jkt} + \\ &\eta DV_{kt} + \chi RI_{kt} + \tau_m + \alpha_j + e_{ijkt}\big] \end{aligned} \tag{5}$$

where $D_{ijlkt} = 1$ if physician *j* changes the prescription to drug *k* from any other drug in observation point *t* for patient *i*.

V.6 Empirical analysis

V.6.1 Estimation strategy

First, it has to be decided, whether a logit or probit approach should be used to estimate equation (5). For both models, the unobserved heterogeneity can be assumed as a fixed or a random effect.

- In fixed effects models, α_j is considered as a parameter, which can be estimated like other parameter vectors. In this case, no assumption about the relationship between α_j and the other independent variables is specified.
- In random effect models, α_j is treated as a random variable, which is described by a density function.

The use of the fixed effect approach can lead to the incidental parameters problem.[102] This can result in non-consistent estimators for the unobserved heterogeneity when estimating a fixed effect probit model.[103] However, the estimated coefficients of a fixed effect logit model[104] are not biased as the conditional distribution of the model does not depend on the unobserved heterogeneity α_j.[105]

In opposite to the fixed effect model approaches, random effect models[106] assume that the correlation between the independent observed variables and the unobserved heterogeneity α_j is zero. Similar to fixed effect models, both probit and logit models can be estimated. As simple estimators for the random effect logit model are not available,[107] the random effect probit model should be the preferred estimation approach.

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[102] See Neyman and Scott (1948), Arellano (2003), and Wooldridge (2003), p. 490-492

[103] See Honoré (2002)

[104] See Chamberlain (1980)

[105] See Wooldridge (2003), p. 491

[106] See Heckman (1981)

[107] See Wooldridge (2003), p. 490

Thus, the fixed effect logit model and the random effect probit model have been identified as suitable models for our estimation. Although the random effect probit model underlies stricter restrictions about the correlation between α_j and the independent, observable variables, it will be used to estimate equation (5). The reason is that the computation of a fixed effect logit model becomes excessive with a large number of observations. In addition, certain statistical problems arise in the calculation of partial effects in fixed effect logit models.[108]

The use of the random effect probit estimator leads to the correlation assumption of the following form $Corr(W_{ijkt}, \alpha_j) = 0$, where W_{ijkt} describes the variable vector containing all regressors of the model. This assumption is very stringent. Thus, a second empirical approach will be estimated that relaxes the correlation assumption.

In this second model, that follows Chamberlain (1980) and especially Mundlak (1978), the time-invariant unobserved heterogeneity α_j is allowed to correlate in linear form with the mean values of the time-varying regressors $\overline{W}_{ijk}$.[109] The unobserved effect α_j is assumed to have the linear form:[110]

$$\alpha_j = \kappa \overline{W}_{ijk} + \psi_j \tag{6}$$

The variable ψ_j is independent and normally distributed $\psi_j \backsim N(0, \sigma_\psi^2$. Also it is assumed that $E[\psi_j | \overline{W}_{ijk}] = E[\psi_j] = 0$ for all t. The modification of the random effect α_j leads to following model specification:

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[108] See Greene (1990), p. 656

[109] See also Wooldrigde (2003), p. 487

[110] The original approach, as it can be found in Wooldridge (2003), p. 487-490 and Mundlak (1978), contains a constant. Since we already included a constant in the random effect probit model, and both constants cannot be separated, we chose not to include the constant in equation (7).

$$PR\left[DC_{ijlkt} = 1\right] = PR\left[\beta_0 + \beta X_{ijkt} + \varphi(p_{kt} - p_{lt}) + \lambda S_{jkt} + \eta DV_{kt} + \chi RI_{kt} + \tau m + \kappa Wijk + \psi j + eijkt > 0\right] \quad (7)$$

Again, it should be remembered that the three therapeutic groups (HMG-CoA reductase inhibitors, ACE inhibitors, and proton pump inhibitors) will be analyzed separately.

V.6.2 Variable description

The dependent variable (SWITCH) is a binary variable, taking the value of 1, if patient *i* receives a drug *k* from physician *j* in observation point *t* that is different from the drug received in $t-1$, and 0 otherwise.[111] The different groups of independent variables are described in detail below. The selection of the included variables is based on various studies, especially Hellerstein (1998), Coscelli (2000), Lundin (2000), and Furu et al. (2008). In addition, if necessary, new variables were defined, f.e. to capture the effects of the implementation of regulatory instruments.

V.6.2.1 Patient related variables

The first category of independent variables are the patient related variables, shown in Table 19:

Table 19: Description of patient related independent variables

Variable name	Variable description
AGE	Age of the patient i
GENDER	Female = 1, male = 0
EAST GERMANY	Patient i receives treatment in East Germany = 1, Patient i receives treatment in West Germany = 0
WELFARE RECIPIENT	Patient i receives benefit payments in observation

[111] The exact definition of a drug switch in terms of our analysis is formulated in Section V.5.

	point t = 1, Patient i receives no benefit payments in observation point t = 0
NATIONALITY	Patient i is not a German citizen = 1, Patient i is a German citizen = 0
CITY AREA	Patient i lives in a city area = 1, Patient i lives in a rural area = 0
TIME LAPSE	Number of months between prescriptions in observation point t and t-1 for patient i
N PRESCRIPTIONS	Total number of prescriptions of the patient i
N ATC7 GROUPS	Total number of different ATC7 groups received by patient i
N PHYSICIANS	Number of different physicians that prescribed at least one drug to patient i
PAST SWITCHES BETWEEN ATC7 GROUPS	Number of switches between ATC7 group until observation point t for patient i
PAST SWITCHES WITHIN ATC7 GROUP	Number of drug switches within ATC7 group until observation point t for patient i
N PRESCRIPTIONS WITHIN ATC7 GROUP	Number of prescriptions within the same ATC7 group until observation point t for patient i

The first variables considered in the estimation process are the AGE and the GENDER of the observed patient. The location dummy EAST GERMANY captures possible differences in the prescription pattern between East and West Germany. The variable WELFARE RECIPIENT indicates whether a patient receives benefit payments by the government. NATIONALITY shows, whether the patient is a German citizen or not. CITY AREA describes whether the patient lives in a rural or in an urban area.

N PRESCRIPTIONS differentiates patients into heavy users (chronic users) and occasional users. The distinction of patients in heavy and light users is further described by the variable TIME LAPSE that counts the months between two following prescriptions of a drug in the therapeutic group, independent of the visited physician. N ATC7 GROUPS counts the number of different active ingredients a patient has received over all observation points. The number can be influenced by both physician and patient. As the physician tries to find a suitable treatment for

the patient, the number of different active ingredients in the sample can capture the difficulties to find one. In addition, the variable indicates the patient's willingness to change the treatment. N PHYSICIANS describes how many different physicians a patient has consulted during the observation period.

The next set of variables, also shown in Table 19, captures the persistence of patients to a specific drug or active ingredient. However, it has to be noted, that switches can also be affected by the choice of pharmacists or physicians, especially concerning the actually dispensed drug.

PAST SWITCHES BETWEEN ATC7 describes how many switches between different active ingredients a patient has experienced until observation point t. The variable N PRESCRIPTIONS WITHIN ATC7 GROUP, describes the continuous prescription of the same active ingredient until observation point t. The number of previous changes of the dispensed drug with an active ingredient is captured by the variable PAST SWITCHES WITHIN ATC7 GROUP.

V.6.2.2 Physician related variables

The next group of independent variables are the physician related covariates, described in Table 20.

Table 20: Description of physician related variables

Variable name	Variable description
N PATIENTS	Number of different patients that received at least one drug prescription from physician j
AGE PATIENTS	Average age of all patients that received at least one drug prescription from physician j
SPECIALIST	Physician j is a specialist = 1, physician j is a general practitioner = 0
QUANTITY PRESCRIPTIONS	Average quantity of prescriptions over the last 3 months of physician j
PERCENTAGE ATC7 GROUP	Average share of dispensed DDD of the prescribed active ingredient over the last 3 months (in percent) of physician j
HERFINDAHL-INDEX ATC7 GROUP	Herfindahl-Index across different active ingredients over the last 3 months (market shares measured in DDD) of physician j

HERFINDAHL-INDEX PRODUCERS	Herfindahl-Index across different producers over the last 3 months (market share measured in DDD) of physician j

The variables N PATIENTS and AGE PATIENTS are independent of the observation point t. They describe the total number of patients as well as the average age of patients that are treated by the physician, giving information about his patient clientele. They also capture possible experience effects resulting from the number of patients treated and age specific aspects for the prescription behavior of the physician. Possible differences between general practitioner and specialists are measured by the variable SPECIALIST.

QUANTITY PRESCRIPTIONS counts, for each observation point t, the average amount of defined daily doses (DDD) prescribed by the physician in the last three months. The variable separates doctors in heavy and light prescribers considering the specific therapeutic group. The importance of the dispensed active ingredient for the physician is indicated by the variable PERCENTAGE ATC7.

The variable HERFINDAHL-INDEX ATC7 GROUP describes the physician related diversity in prescribing different active ingredients for a specific indication.[112] The last physician related variable, HERFINDAHL-INDEX PRODUCERS captures possible preferences of physicians for specific drug producers.

V.6.2.3 Drug related variables

Table 21 shows drug specific variables that describe the properties of the dispensed drugs and the price difference between the dispensed drugs in observation point t and observation point t-1.

[112] The Herfindahl-Hirschman Index is the sum of squared market shares. For convenience the percentage values are multiplied with 100. The index ranges from 0 to 10,000.

Table 21: Description of drug related variables

Variable name	Variable description
PRICEDIFF	Price difference ((measured in price per DDD) between the dispensed drug in observation point t and the dispensed drug in observation point t-1 of patient i
MARKET SHARE PZN[113]	Market share of dispensed drug i (measured in DDD) related to the corresponding ATC7 group in observation point t of patient i (in percent)
ATC7 GROUP	Set of dummy variables, identifying the ATC7 group of the dispensed drug in observation point t of patient i
AUT-IDEM DRUG	Dummy variable with the value of 1, if dispensed drug is one of the 3 cheapest drugs of the active ingredient in observation point t of patient i, 0 if not

The variable PRICEDIFF captures the price difference (in price per DDD) between the dispensed drug in observation point t and its predecessor in t-1. MARKET SHARE PZN is an indicator for the popularity of a specific drug that is identified by its central pharmaceutical number (PZN). ATC7 GROUP is a set of dummy variables that captures drug specific effects based on characteristics of the corresponding active ingredient. The variable AUT-IDEM DRUG indicates, whether the dispensed drug was one of the three cheapest drugs within the corresponding active ingredient in observation point t. While the physician could have prescribed this drug explicitly, it is more likely that the pharmacist has exchanged the originally prescribed drug with the dispensed cheaper drug due to the Aut-Idem rule.

V.6.2.4 Implementation of regulative instruments

The last group of variables contains indicators for the effect of the implementation of regulatory instruments on the probability of a change of the dispensed drug.

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[113] The abbreviation PZN stands for the term "Pharma Zentral Nummer". The PZN is a 7-digit number, which identifies a drug clearly according to its name, pharmaceutical form, strength, and package size. Therefore, each drug in the Germany SHI market can be identified by its unique PZN.

Table 22: Description of regulatory instruments

Variable name	**Variable description**
Definition of the variables concerning the implementation of regulatory instruments	Dummy variable, taking the value of 1 if, for the first time the dispensed drug in observation point t of patient i is part of the implemented regulatory instrument, while it was not in observation point t-1 of patient i, 0 otherwise.
LEAD COMPOUND	Describes the implementation of the lead compound rule.
REFERENCE PRICE	Describes the implementation of the reference price system.
EXEMPTION FROM CO-PAYMENT	Describes the implementation of the possibility to exempt drugs from patient related co-payments
REBATE CONTRACT	Describes the implementation of rebate contracts between health insurances and pharmaceutical producers

The variable LEAD COMPOUND displays the influence of the lead compound rule that encourages physicians to prescribe a specific active ingredient instead of other therapeutic options. Note that since the therapeutic market of ACE inhibitors was not covered by the lead compound rule, no coefficient was estimated for this therapeutic group. The dummy variable REFERENCE PRICE captures changes in prescription as a result of the introduction of the reference price system. The variables EXEMPTION FROM CO-PAYMENT and REBATE CONTRACT[114] measure the effects of introduction of the two latest regulatory reforms on the drug dispense situation of the patient. The former variable captures the effect of the implementation of the possibility of drugs to become exempted from patient related co-payments. The latter dummy variable captures the impact of the intro-

[114] Since the dataset is restricted to a specific health insurance fund, only drugs which are part of rebate contracts of this health insurance fund are marked as rebated products.

duction of a rebate contract between the pharmaceutical company and the health insurance fund.

The definition, whether a regulation instrument existed in the month the observation point falls into, is based on the status in the pharmacy software. This is due to the fact, that only with the implementation in the official pharmacy software; the regulations become relevant for the prescription decisions of the physicians and the dispensing decision of the pharmacists. An exception is the variable LEAD COMPOUND. Here the agreed inception of the treaty between the Association of Statutory Health Insurance Physicians and the sickness funds is considered.

The considered regulations were implemented with a time lap of at least a year. Consequently, the effects of the implementation of each regulatory instrument should not overlap. Still there is a minority of cases where two or three of the described regulation dummies change values simultaneously. Although the number of these cases is very small,[115] we deleted the concerned observations and recalculated the models. The estimations results did not differ; therefore the original dataset was used.

The descriptive statistics of the variables for each therapeutic market are shown in Appendix 1.

V.7 Estimation results

V.7.1 Random effect probit model

In this section, the results of the standard random effect probit model and of the random-effect probit model, inspired by Chamberlain (1980) and Mundlak (1978), are presented. Both models were estimated by using 50 evaluation

[115] The maximum of cases was found for the combination of co-payment exemption and rebate contacts. For this combination, in 1.8 % of the observed cases both dummy variables took the value of one in the same observation period.

points.[116] The stability of the models was checked by running the models with 34 and 66 evaluation points. Comparing the results, the relative differences between the coefficients are always <1 %. Thus, the models can be assumed to be stable.[117]

A likelihood-ratio test, conducted between the standard and the Chamberlain/Mundlak random effect probit models indicates that the latter econometric approach should be the preferred option.[118] This result is confirmed by the calculated AIC and BIC scores.[119]

The economic interpretation of the results of the Chamberlain/Mundlak probit model is limited to the magnitude and the sign of the coefficients. The results of the estimation are shown in Table 32 in Appendix 2.[120] It turns out that the estimation results of the three therapeutic groups are qualitatively very similar. Therefore, we describe the results for all three groups simultaneously.

It should be noted that in the following sections the term “probability of drug change” or similar expressions will be used. This is not entirely accurate. Following the model specification in Section V.5, the estimated coefficients for both the random effect probit models and the corresponding marginal effects have to be interpreted as effects on the “probability of a change to the drug in question”. However, for reasons of readability, we will simply refer to “drug changes”.

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116 See Butler and Moffitt (1982) and Hellerstein (1998) for more information about the derivation of the full likelihood for the random-effects probit model.

117 The stability was checked by using the quadchk command in Stata®. Results are available on request.

118 The results of the standard random effect probit model are shown in Table 31 in Appendix 2 in Section V.9.2.

119 AIC stands for the "Akaike Information Criterion", while BIC stands for the “Bayesian Information Criterion”. Both criteria help to select a specific model within a class of parametric models that have a different number of parameters. Since the approaches are related, for both of them the rule can be stated, that the estimated model with the lower value of AIC or BIC should be chosen. For more information, see Akaike (1974) and Schwarz (1978).

120 To simplify the interpretation of the results, the estimated coefficients of the average values of the time variant variables as well as the estimates of the monthly dummy variables are not included. The results are available on request.

Patient related variables

The results of variables capturing the socio-economic status of patients indicate that the dispensed drug is less frequently switched for older patients than for younger patients (negative coefficient of AGE). The drug prescriptions of patients living in East Germany are more often switched than for patients living in West Germany (positive coefficient of EAST GERMANY). Both results can be found in all therapeutic areas. The gender of the patients has a negative impact on the switching probability. Therefore, women are less likely to get their drug prescription changed than man. However the effect is only significant for the therapeutic area of proton pump inhibitors. The variable CITY AREA is also only significant for ACE inhibitors, suggesting that drug prescriptions of patients living in larger cities are switched more often than for patients in rural areas of Germany.

The second set of patient related variables describe the habits and preferences of patients. The coefficient of TIMELAPSE is positive and significant for all therapeutic markets. It indicates that the longer the time gap between drug prescriptions, the more the dispensed drug of a patient is likely to get switched.

The total number of prescriptions a patient receives in the observation period (N PRESCRIPTIONS) has a significant positive effect on the drug change probability. Thus, patients receiving more prescriptions have a higher possibility to receive a different drug than patients with fewer prescriptions. Also the total number of different active ingredients (N ATC7 GROUPS) increases the likelihood of a drug change. This result is comprehensible, as patient that changes active ingredients more often automatically get their drug prescription changed more frequently.

The total number of different physicians a patient visits (N PHYSICIANS) has a negative effect on the switching probability. The positive coefficient of PAST SWITCHES BETWEEN ATC7 GROUPS indicates that patients who already had different active ingredients prescribed in the past have an increased likelihood for prescription changes in the future. This effect is relatively small for patients treated with proton pump inhibitors compared to the two other therapeutic groups.

A similar explanation can be given for PAST SWITCHES WITHIN ATC7 GROUPS. Patients with a bigger variety of different drugs within an ATC7 group have an increased probability to get switched again in the future. This effect is stronger for patients with HMG-CoA reductase inhibitors.

The number of past prescriptions within an active ingredient (N PRESCRIPTIONS WITHIN ATC7 GROUP) has a negative effect on the drug change probability for all three therapeutic markets. Therefore patients that are adapted to a specific active ingredient, through a larger number of prescriptions in this group, are less likely to get switched to another drug than patients with a shorter prescription history concerning the specific ATC7 group. The smallest effect was estimated for patients treated with ACE inhibitors.

Summarizing the results for patient related variables, we find that for the group of socio-economic factors only age and whether the patient lives in East or West Germany have a significant impact on the switch probability for all three therapeutic areas. However, all variables describing the previous history of drug dispenses have significant effects on the probability of a drug switch.

Physician related variables

The results for variables describing the characteristics of physicians show that the total number of treated patients (N PATIENTS), their average age (AGE PATIENTS), and training of a physician as a specialist (SPECIALIST) have a negative impact on the probability of a drug switch. Thus, physicians that are specialists, have a high number of patients or an older patient clientele change drug prescriptions less often than physicians that are general practitioners, treating a lower number of patients or have a younger patient clientele.

The second set of variables captured the prescription habits of physicians. The results show that the probability of a drug switch is lower for patients treated by physicians with a higher number of average prescriptions (QUANTITY PRESCRIPTIONS). A similar effect was found for patients receiving a drug with an active ingredient that is prescribed strongly by the corresponding physician

(PERCENTAGE ATC7 GROUP). Both effects are not significant for the therapeutic group of ACE inhibitors.

The estimates of the Herfindahl coefficients indicate the effects of physician related preferences for specific active ingredients (HERFINDAHL-INDEX ATC7 GROUP) or producers (HERFINDAHL-INDEX PRODUCER) in a therapeutic group. The results show that physicians concentrating their prescriptions on a fewer number of active ingredients, expressed through a high HERFINDAHL-INDEX ATC7 GROUP, are more likely to change their prescription behavior than physicians prescribing across active ingredients.

It has to be noted that the negative sign of PERCENTAGE ATC7 GROUP and the positive sign of HERFINDAHL-INDEX ATC7 GROUP seems to be a contradiction. However, although the variables appear to be similar in their meaning, they capture different attributes of the physician. The variable PERCENTAGE ATC7 GROUP measures the physician related average market share (in DDD) of the actual dispensed active ingredient over the last three months. The results indicate that a physician who prescribes a large amount of this active ingredient changes his prescriptions less often. Thus, the variable captures the possible preference for the actual dispensed active ingredient.

In contrast, HERFINDAHL-INDEX ATC7 GROUP shows the overall preference of a physician towards the different active ingredients in the therapeutic market. It is, in contrast to PERCENTAGE ATC7 GROUP, independent of the actual dispensed active ingredient in observation point t. A physician that prefers to concentrate his prescriptions on a fewer number of active ingredients, measured by a high HERFINDAHL-INDEX ATC7 GROUP, has a higher probability to switch his prescriptions than a doctor prescribing a larger variety of active ingredients, expressed by a lower Herfindahl index.

At last, independent of the therapeutic markets, physicians preferring specific drug producers, indicated through a high HERFINDAHL-INDEX PRODUCER, are less likely to switch the prescriptions of their patients.

The analysis of the physician related variables indicates that characteristics of the physician and his patient clientele both have an impact on the probability of a drug switch. The effects are similar in all observed therapeutic markets. Also, prescription preferences for specific active ingredients or producers affect the prescription behavior of physicians significantly.

While it seems that both patient and physician specific characteristics and habits play a role for the drug dispense, the influence of the properties of the dispensed drugs itself are captured by the set of drug related variables.

Drug related variables

The estimated coefficient of the PRICE DIFFERENCE between the dispensed drugs in observation points t and t-1 is negative in all therapeutic groups. Therefore, in the case a cheaper drug in observation point t compared to the drug in observation point t-1 is dispended, the negative price difference has a positive effect on the switch probability. In the case of a positive price difference, which corresponds to dispending a more expensive drug in t compared to t-1, the effect is negative.

The market share of the prescribed drug has a significant negative impact on the probability of a drug change. This result has to be interpreted cautiously as it could be a statistical artifact. It is less likely that patients are switched to drugs with a high market share since a large number of patients already receive this drug. Therefore, the probability of a change towards such a drug is affected negatively. The positive coefficient of the AUT IDEM variable is not surprising, as most drugs dispensed with the attribute Aut-Idem are the result of a substitution process by the pharmacists.

The dummies for the active ingredients[121] in the therapeutic markets indicate that there are significant differences across the active ingredients in the frequency of

[121] Note that the estimates for the active ingredient dummies have to be interpreted in comparison to the reference category.

drug changes. This shows that specific attributes (e.g. patent status) of the prescribed active ingredients have an effect on the choice of the dispensed drug.

The results of the estimation of the drug related variables showed that especially the price difference of drugs plays an important role. A negative price difference leads to a significant increase in the probability of a drug change, indicating the change from a more expensive drug to a cheaper one. Also the probability of a drug switch depends on the active ingredient of the dispensed drug.

Implementation of regulative instruments

The implementation of any regulative instrument considered had a positive impact on the probability of a drug change. The strongest impact was found for the implementation of rebate contracts (REBATE CONTRACTS) followed by reference pricing (REFERENCE PRICE) and the possibility to exempt drugs from patient co-payments (EXEMPTION CO-PAYMENT).

The statistic significant coefficients for the regulation variables indicate that beside patient, physician or drug related attributes, an additional impact on switches of the dispensed drug is the implementation of regulatory instruments.

V.7.2 Magnitude analysis

Since the coefficient estimates of the random effect probit models are very difficult to interpret in an economic sense, the marginal effects of the coefficients are estimated. Most papers[122] calculate the marginal effects at the means (MEM). Therefore, the sample means of the independent variables would be used as fixed values. Instead of using MEM, we computed the average of discrete or partial changes over all observations, therefore estimating average marginal effects (AME).[123]

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[122] Examples for the use of MEM can be found in Hellerstein (1998), Coscelli (2000) and Lundin (2000). For the calculation of MEM in STATA®, see Bartus (2005).

[123] The average marginal effects were calculated using the user written command margeff in STATA®. See Bartus (2005)

The main argument for the use of average marginal effects is the possibility of a more realistic interpretation of the results, especially for dummy variables.[124] Under the consideration of dummy variables, the calculation of MEM is delicate, as the used sample means refer to non-existing observations. Since the larger part of our independent variables are dummies, the use of AMEs is the preferred option.

The calculated AMEs have to be interpreted differently for continuous and dummy variables. For continuous variables, the AMEs indicate how a partial change (about 1 unit) of a variable changes the probability for the switch of the dispensed drug. The interpretation of marginal effects for dummy variables is different. They show the marginal impact on the probability for a drug dispense switch if the dummy variable changes its value from 0 to 1.

Table 23 shows the average marginal effects of patient related variables:

Table 23: Average marginal effects for patient related variables of the Chamberlain/Mundlak random probit model[125]

Dependent variable – SWITCH						
	HMG-CoA reductase inhibitors		**ACE inhibitors**		**Proton pump inhibitors**	
Variable name	**Coefficient**	**Standard Error**	**Coefficient**	**Standard Error**	**Coefficient**	**Standard Error**
AGE	-0.0257 ***	0.0030	-0.0230 ***	0.0023	-0.0113 ***	0.0014
GENDER	-0.0014 ***	0.0014	-0.0023 **	0.0011	-0.0003	0.0008
EAST GERMANY	0.0076	0.0021	0.0042 **	0.0017	0.0092 ***	0.0015
WELFARE RECIPIENT	0.0128	0.0433	0.0165	0.0309	0.0018	0.0255

[124] See Bartus (2005)

[125] Due to the complexity of the estimation and limitations in the calculating capacity, the marginal effects estimated for ACE inhibitors and proton pump inhibitors are based on an 80 % respectively 60 % sample. To confirm the results, we repeated the probit model estimation and drew several random samples (80 % or 60 % respectively) and calculated the marginal effects again. The results for the marginal effects do not differ much and are available on request.

NATIONALITY	0.0061		0.0043	0.0004		0.0034	0.0016		0.0021
CITY AREA	0.0001		0.0016	0.0003		0.0014	0.0039	***	0.0011
TIME LAPSE	0.0178	***	0.0003	0.0168	***	0.0003	0.0123	***	0.0002
N PRESCRIPTIONS	0.0092	***	0.0005	0.0070	***	0.0003	0.0024	***	0.0001
N ATC7 GROUPS	0.0553	***	0.0037	0.0552	***	0.0035	0.0764	***	0.0012
N PHYSICIANS	-0.0424	***	0.0011	-0.0361	***	0.0009	-0.0312	***	0.0006
PAST SWITCHES BETWEEN ATC7 GROUPS	0.1580	***	0.0044	0.1733	***	0.0049	0.0847	***	0.0012
PAST SWITCHES WITHIN ATC7 GROUP	0.1471	***	0.0012	0.1025	***	0.0009	0.0544	***	0.0006
N PRESCRIPTIONS WITHIN ATC7 GROUP	-0.0360	***	0.0009	-0.0230	***	0.0005	-0.0236	***	0.0003

*** indicates significance on the 1 % level, ** significance on the 5 % level and * shows significance on the 10 % level

The results indicate that for a one unit increase in the age of the patient (AGE) the likelihood for a switch of the dispensed drug decreases between 1.1 and 2.6 %. This shows that older patients are less likely to face a drug change than younger patients. Concerning the number of months between prescriptions (TIME LAPSE), we find that an increase of about one month increases the probability of a drug change for the patient between 1.2 and 1.8 %. Visiting one additional physician in the observation period (N PHYSICIANS) decreases the change probability on average about 3.1 to 4.2 %.

The increase of the previous number of switches between active ingredients (PAST SWITCHES BETWEEN ATC7 GROUPS) about one unit raises the switch probability between 8.5 and 17.3 %. An additional past drug switch within an active ingredient (PAST SWITCHES WITHIN ATC7 GROUPS) increases the likelihood of a drug switch between 5.4 and 14.7 %.

If patients receive drugs more constantly within a specific active ingredient (N PRESCRIPTIONS WITHIN ATC7 GROUP), the probability of a switch decreases between 2.3 and 3.6 % for each additional previous prescription within

this active ingredient. Table 24 shows the average marginal effects for the physician related variables.

Table 24: Average marginal effects for physician related variables of the Chamberlain/Mundlak random probit model

Dependent variable – SWITCH						
	HMG-CoA reductase inhibitors		ACE inhibitors		Proton pump inhibitors	
Variable name	**Coefficient**	**Standard Error**	**Coefficient**	**Standard Error**	**Coefficient**	**Standard Error**
N_PATIENTS	-0.0008 ***	0.0002	-0.0007 ***	0.0001	-0.0007 ***	0.0000
AGE PATIENTS	-0.0004 ***	0.0001	-0.0003 ***	0.0001	-0.0004 ***	0.0001
SPECIALIST	-0.0046 ***	0.0016	-0.0060 ***	0.0014	-0.0071 ***	0.001
QUANTITY PRESCRIPTIONS	-0.0055 ***	0.0015	-0.0012	0.001	-0.0037 ***	0.0007
PERCENTAGE ATC7 GROUP	-0.0005 ***	0.0001	0.0001	0.0001	-0.0006 ***	0.0001
HERFINDAHL-INDEX ATC7 GROUP	0.00001 ***	0.0001	0.00001 ***	0.0001	0.00002 ***	0.0001
HERFINDAHL-INDEX PRODUCERS	-0.00002 ***	0.0001	-0.00003 ***	0.0001	-0.00004 ***	0.0001

*** indicates significance on the 1 % level, ** significance on the 5 % level and * shows significance on the 10 % level

For the group of physician related variables, the dimension of the variables has to be considered, before interpreting the impact of a one unit change. While some marginal changes are highly significant in a statistical sense, the actual importance of such a change is rather low. An example is the average age of the patients treated by the physician in the observation period (AGE PATIENTS). Even if the average age would increase about ten years, the effect would still be lower than 1 %.

Since the issue of the dominance of statistical significance in contrast to substantive significance has already been discussed by various authors (e.g. Hoover and

Siegler (2008); Ziliak and McCloskey (2008); and Miller (2008)), it will be not addressed here in detail. Considering the underlying dimensions and the relation to the mean values of the variables that can be found in Table 28 in Appendix 1, only a number of physician related marginal effects are regarded as substantively significant.

Therefore only the Herfindahl indices seem to have a considerable impact on the dependent variable. At first glance, the actual effect of the Herfindahl indices on the change probability seems relatively small. Still, the effects should not be underestimated, as the coefficient only indicates the probability increase of a drug change if the Herfindahl-Hirschman-Index (HHI) increases about one unit. As the Herfindahl indices can take values up to 10,000, the small impact on the change probability of an increase about one unit are misleading.[126]

Following the results in Table 24, an increase of the HHI measuring the preference of physicians for a specific active ingredient (HERFINDAHL INDEX ATC7 GROUPS) raises the probability for a drug switch. The probability decreases for patients whose physicians show a high preference for specific drug producers (HERFINDAHL INDEX PRODUCERS). Both effects are strongest for the group of proton pump inhibitors.

The average marginal effects of drug related variables on the SWITCH variable are shown in Table 25.

[126] See Miller (2008) for more information about misleading interpretation of marginal effects because of different scales.

Table 25: Average marginal effects for drug related variables of the Chamberlain/Mundlak random probit model

Dependent variable – SWITCH						
	HMG-CoA reductase inhibitors		**ACE inhibitors**		**Proton pump inhibitors**	
Variable name	**Coefficient**	**Standard Error**	**Coefficient**	**Standard Error**	**Coefficient**	**Standard Error**
PRICEDIFF	-0.1568 ***	0.0068	-0.2150 ***	0.0069	-0.0339 ***	0.0020
MARKET SHARE PZN	-0.0038 ***	0.0002	-0.0003 ***	0.0001	-0.0019 ***	0.0001
AUT-IDEM DRUG	0.0561 ***	0.0042	0.0447 ***	0.0048	0.0404 ***	0.0031
ATC_C10AA01	0.0088	0.0065	-	-	-	-
ATC_C10AA02	Reference category		-	-	-	-
ATC_C10AA03	0.0229 ***	0.0070	-	-	-	-
ATC_C10AA04	-0.0500 ***	0.0061	-	-	-	-
ATC_C10AA05	-0.0660 ***	0.0068	-	-	-	-
ATC_C09AA01	-	-	0.0424	0.0293	-	-
ATC_C09AA02	-	-	0.0459	0.0285	-	-
ATC_C09AA03	-	-	0.0598 **	0.0302	-	-
ATC_C09AA04	-	-	-0.0669 ***	0.0231	-	-
ATC_C09AA05	-	-	0.0332	0.0266	-	-
ATC_C09AA06	-	-	0.0442	0.0304	-	-
ATC_C09AA07	-	-	-0.1746	1.2351	-	-
ATC_C09AA08	-	-	0.0158	0.0275	-	-
ATC_C09AA09	-	-	-0.0519	0.0435	-	-
ATC_C09AA10	-	-	-0.0089	0.0259	-	-
ATC_C09AA11	-	-	-0.1746	0.3350	-	-
ATC_C09AA13	-	-	-0.1746	1.2351	-	-
ATC_C09AA16	-	-	Reference category		-	-

ATC_A02BC01	-	-	-	-	-0.0318	***	0.0032
ATC_A02BC02	-	-	-	-	-0.0522	***	0.0027
ATC_A02BC03	-	-	-	-	-0.0096	**	0.0038
ATC_A02BC04	-	-	-	-	Reference category		
ATC_A02BC05	-	-	-	-	-0.0570	***	0.0027

*** indicates significance on the 1 % level, ** significance on the 5 % level and * shows significance on the 10 % level

The results of the marginal effects of the drug related variables show that the price difference seems to have a large impact on the probability of a drug change. The effect has to be interpreted differently for positive and negative price differences. The prescription of a cheaper (more expensive) drug in t compared to the drug in t-1 would lead to an average rise (decrease) of the switch probability between 3.4 and 21.5 % for an increase of the price per DDD about one euro. While this effect seems very large, it has to be noted, that the average price difference lies between 0.02 euro and 0.04 euro. Following this, the actual effect has to be considered much weaker.[127] A dispended drug that falls under the Aut-Idem rule increased the probability of a drug change between 4.0 and 5.6 %.

If the patient receive the HMG-CoA reductase inhibitor atorvastatin (ATC7 Code C10AA05), the likelihood of a drug switch decreases about 6.6 % in comparison to the reference active ingredient lovastatin (ATC7 Code C10AA02). In case of fluvastin (ATC7 Code C10AA04), the decrease is 5.0 %.

It has to be noted that during the observation period the active ingredients atorvastatin and fluvastin have been under patent protection whereas for lovastatin (ATC7 Code C10AA02), simvastatin (ATC7 Code C10AA01) and pravastatin (ATC7 Code C10AA03) generic versions were available. Thus, the results show that the probability for drug switches increases whether a physician changes the

[127] This is a further example for the importance of substantive significance as mentioned by Hoover and Siegler (2008), Ziliak and McCloskey (2008) and Miller (2008)

prescription to or within an active ingredient for which generic drugs are available.

The same holds for the therapeutic group of the ACE inhibitors. We find that patients treated with perindopril (ATC7 Code C09AA04) have a decreased probability (-6.7 %) for a change in their drug dispense. In opposite, for patients using lisinopril (ATC7 code C09AA03) the likelihood of a drug switch increases about 6 % compared to the reference active ingredient imidapril (ATC7 Code C09AA16).

In case of proton pump inhibitors, the results indicate that a drug change to or within one of the active ingredients with existing generics (omeprazole (ATC7 Code A02BC01), pantoprozole (ATC7 Code A02BC02), and lansoprazole (ATC7 Code A02BC03) is less likely than a change to or within the patent protected reference active ingredient rabeprazole (ATC7 Code A02BC04). The relative high probability for a switch to or within rabeprazole compared to the active ingredients with available generic drugs is unusual for a patent drug. The reason seems to be the relative high market share of parallel imports for rabeprazole during the observation period. In contrast, there are no parallel importers in the market for the patent protected active ingredient esomeprazole (ATC7 Code A02BC05). The results indicate that patients receiving esomeprazole have a reduced likelihood to experience a change in drug prescription (-5.7 %) compared to the reference drug rabeprazole.

Table 26 describes the average marginal effects of the introduction of major regulatory instruments between 2004 and 2007 on the probability of a drug switch.

Table 26: Results of the Chamberlain/Mundlak random effect probit estimation for the effects of the introduction of regulatory instruments

Dependent variable – SWITCH									
	HMG-CoA reductase inhibitors			ACE inhibitors			Proton pump inhibitors		
Variable name	**Coefficient**		**Standard Error**	**Coefficient**		**Standard Error**	**Coefficient**		**Standard Error**
LEAD COMPOUND	0.7962		50.3801	Not included in regulatory regime			0.8361		429.2979
REFERENCE PRICE	0.1124	***	0.0062	0.0542	**	0.0312	0.0577	***	0.0039
EXEMPTION FROM CO-PAYMENT	0.0088	**	0.0033	0.0638	***	0.0028	0.0791	***	0.0030
REBATE CONTRACT	0.2492	***	0.0048	0.4209	***	0.0048	0.3461	***	0.0045

*** indicates significance on the 1 % level, ** significance on the 5 % level and * shows significance on the 10 % level

The last category of covariates captures the effects of the implementation of regulatory instruments on the changes of the dispensed drug for patients. The results show, that the introduction of reference prices (REFERENCE PRICE) increased the probability for a change in the dispensed drug between 5.4 and 11.2 %. The introduction of the possibility for pharmaceutical companies to exempt their drugs from patient co-payments (EXEMPTION FROM CO-PAYMENT) also increased the probability for a drug switch between 0.9 % and 7.9 %. The implementation of rebate contracts had the largest impact on the likelihood of a drug switch. The probability increased between 24.9 and 42.1 % following the implementation of rebate contracts.

V.8 Discussion

The aim of this paper was to estimate the effects of patient, physician and drug related characteristics and habits on the probability of a switch of the dispensed drugs for chronic diseases in the German SHI system. Moreover, for the first time,

the impact of the implementation of regulative instruments in the German SHI system on the probability of drug switches was analyzed.

We evaluated the effects of the patient, physician, and drug related variables for three different therapeutic groups, namely, HMG-CoA reductase inhibitors, ACE inhibitors and proton pump inhibitors. These therapeutic groups range quite prominently among the treatments of chronic diseases. We used a dataset consisting of the prescription history of over 50,000 patients and an overall number of nearly one million drug prescription observations between January 2004 and December 2007.

Interestingly, the estimated effects are similar for all three therapeutic groups. Thus, our results seem to be quite robust, even more so in view of the fairly large datasets.

The results indicate that patient and physician specific characteristics and habits have a significant impact on the probability of a drug switch. In line with Hellerstein (1998) and Stargardt (2010), our results suggest that older patients are less often switched than younger patients. Similar to Coscelli (2000), we find that an increase in time between treatment episodes increases the probability of a drug switch. Also, patients with a higher total number of different active ingredients, a larger account of previous switches between active ingredients, and especially more previous drug changes within and between active ingredients are more likely to get switched in their prescription.

Contrary to the results of Coscelli (2000), patients visiting a greater number of different doctors have a reduced probability of a drug switch. A possible explanation is that a new physician has to assemble medical knowledge about the patient first. Therefore the physician will initially prescribe the drug previously prescribed by his predecessor to avoid possible side effects.

Considering physician related habits and characteristics, the results indicate that patients face an increased probability for a drug switch if their physician prefers specific active ingredients. A reason for this could be an increased knowledge of the physician concerning the active ingredient, leading to a better knowledge

about the range of drugs on the market to choose from. In contrast, patients treated by physicians that have a strong preference for a specific manufacturer are changed less likely.

The analysis also shows that a cheaper price of the dispensed drug and the fact that it is an Aut-Idem drug (i.e. among the three cheapest drugs of an active ingredient) increase the probability to switch to this drug significantly. Both results show that physicians include economic aspects in their decision making, obviously to evade possible punishment due to regulations like budgeting.

In the existing literature, the impact of regulatory instruments on the prescription decision of physicians has only been investigated by few authors (e.g. Furu et al. (2008) and Lundin (2000)). Since the German SHI prescription drug market is strongly regulated, we included variables to capture the effects of the implementation of regulative regimes. The results show that the introduction of reference pricing, the possible exemption from patient co-payments, and especially the implementation of rebate contracts had a strong positive impact on the likelihood for a switch to a drug included in these instruments.

Overall, we find strong evidence that patient and physician related characteristics and habits influence the probability for a drug switch for patients in the German SHI market. In addition, the results indicate a strong impact of economic factors on the prescription behavior of physicians. Especially the implementation of several regulative instruments increased the likelihood of a drug switch significantly.

In contrast to similar theoretical approaches, we do not incorporate parameters that represent the level of reimbursement by the sickness funds.[128] The reason is that prescription drugs in the German SHI system are nearly fully reimbursed. Patients only have to pay a small co-payment between five and ten euro. Therefore the question of cost sharing between the two parties is less important. However, the importance of drug prices for the physician due to the drug budget is acknowledged in the estimation process.

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[128] See Hellerstein (1998) and Lundin (2000)

The dataset includes only data of one specific (although large) health insurance fund. This could influence the representativity of the results. Especially the low number of unemployed persons in the data set should be noted. However, due the structure of the SHI system, the supply of health care services is irrespective of the income of the insurant. Therefore, the possible bias should be small. Unfortunately, an extension of the data sample is difficult, as most health insurance funds do not share patient related data, even for scientific research.

For further research it would be interesting to include information about marketing activities of pharmaceutical companies (e.g. number of visits by pharmaceutical representatives) in the German SHI system. Following Venkataraman and Stremersch (2007) and Janakiraman et al. (2008) such factors could have an impact on the prescription decision. Also further variables regarding doctors' characteristics, such as age or practice type (e.g. singular or group practice) are desirable. Finally, it would be interesting to analyze whether the income situation of patients affect the prescription behavior of physicians.

V.9 Appendix

V.9.1 Appendix 1

Table 27: Descriptive statistics of patient related variables

	HMG-CoA reductase inhibitors				**ACE inhibitors**				**Proton pump inhibitors**			
Variable name	**Mean**	**Std. Dev.**	**Min**	**Max**	**Mean**	**Std. Dev.**	**Min**	**Max**	**Mean**	**Std. Dev.**	**Min**	**Max**
AGE	60.62	11.02	0	99	58.97	13.21	0	102	52.00	16.01	0	101
GENDER	0.38	0.49	0	1	0.38	0.48	0	1	0.51	0.50	0	1
EAST GERMANY	0.15	0.36	0	1	0.16	0.37	0	1	0.13	0.34	0	1
WELFARE RECIPIENT	0.01	0.02	0	1	0.01	0.02	0	1	0.01	0.02	0	1
NATIONALITY	0.03	0.17	0	1	0.03	0.17	0	1	0.05	0.21	0	1

CITY AREA	0.34	0.47	0	1	0.33	0.47	0	1	0.30	0.46	0	1
TIME LAPSE	3.06	3.49	0	41	2.55	2.88	0	41	1.95	3.79	0	41
N PRESCRIPTIONS	6.64	3.90	2	38	7.98	5.19	2	38	6.86	6.52	2	62
N ATC7 GROUPS	1.19	0.43	1	4	1.07	0.27	1	3	1.42	0.62	1	5
N PHYSICIANS	1.42	0.70	1	7	1.48	0.75	1	8	1.60	0.88	1	11
PAST SWITCHES BETWEEN ATC7 GROUPS	0.13	0.40	0	9	0.05	0.25	0	9	0.33	0.77	0	14
PAST SWITCHES WITHIN ATC7 GROUP	0.88	1.33	0	35	1.05	1.52	0	17	0.97	1.67	0	27
N PRESCRIPTIONS WITHIN ATC7 GROUP	3.57	2.81	1	38	4.39	3.73	1	38	3.36	4.74	1	62

Table 28: Descriptive statistics of physician related variables

	HMG-CoA reductase inhibitors				**ACE inhibitors**				**Proton pump inhibitors**			
Variable name	**Mean**	**Std. Dev.**	**Min**	**Max**	**Mean**	**Std. Dev.**	**Min**	**Max**	**Mean**	**Std. Dev.**	**Min**	**Max**
N_PATIENTS	9.42	13.54	1	191	11.42	15.04	1	206	17.66	30.72	1	468
AGE PATIENTS	61.66	7.21	1	94	60.33	8.43	0	98	52.71	9.30	0	96
SPECIALIST	0.31	0.46	0	1	0.29	0.45	0	1	0.34	0.47	0	1
QUANTITY PRESCRIPTIONS	3.48	2.14	0.33	49.33	3.99	2.48	0.33	38.67	3.83	2.37	0.33	42.67
PERCENTAGE ATC7 GROUP	84.18	25.83	0.28	100.00	68.49	31.02	0.32	100.00	75.34	30.29	0.17	100.00
HERFINDAHL-INDEX ATC7 GROUP	8,360	2,226	2,000	10,000	6,629	2,685	1,528	10,000	7,686	2,498	2,000	10,000
HERFINDAHL-INDEX PRODUCERS	6,227	3,046	761	10,000	5,737	2,970	830	10,000	6,220	2,938	933	10,000

Table 29: Descriptive statistics of drug related variables

	HMG-CoA reductase inhibitors				ACE Inhibitors				Proton pump inhibitors			
Variable name	**Mean**	**Std. Dev.**	**Min**	**Max**	**Mean**	**Std. Dev.**	**Min**	**Max**	**Mean**	**Std. Dev.**	**Min**	**Max**
PRICEDIFF	-0.03	0.10	-2.83	2.01	-0.02	0.07	-3.42	2.00	-0.04	0.20	-7.99	8.03
MARKET SHARE PZN	4.71	8.23	0.00	51.12	4.70	7.92	0.00	98.55	4.77	6.67	0.00	36.3
AUT-IDEM-DRUG	0.11	0.31	0	1	0.03	0.18	0	1	0.14	0.34	0	1
ATC_C10AA01	0.78	0.41	0	1	-	-	-	-	-	-	-	-
ATC_C10AA02	0.01	0.12	0	1	-	-	-	-	-	-	-	-
ATC_C10AA03	0.09	0.29	0	1	-	-	-	-	-	-	-	-
ATC_C10AA04	0.07	0.26	0	1	-	-	-	-	-	-	-	-
ATC_C10AA05	0.04	0.19	0	1	-	-	-	-	-	-	-	-
ATC_C09AA01	-	-	-	-	0.05	0.22	0	1	-	-	-	-
ATC_C09AA02	-	-	-	-	0.27	0.44	0	1	-	-	-	-
ATC_C09AA03	-	-	-	-	0.15	0.36	0	1	-	-	-	-
ATC_C09AA04	-	-	-	-	0.00	0.04	0	1	-	-	-	-
ATC_C09AA05	-	-	-	-	0.51	0.50	0	1	-	-	-	-
ATC_C09AA06	-	-	-	-	0.01	0.08	0	1	-	-	-	-
ATC_C09AA07	-	-	-	-	0.01	0.08	0	1	-	-	-	-
ATC_C09AA08	-	-	-	-	0.00	0.03	0	1	-	-	-	-
ATC_C09AA09	-	-	-	-	0.01	0.07	0	1	-	-	-	-
ATC_C09AA10	-	-	-	-	0.00	0.02	0	1	-	-	-	-
ATC_C09AA11	-	-	-	-	0.00	0.05	0	1	-	-	-	-
ATC_C09AA13	-	-	-	-	0.00	0.02	0	1	-	-	-	-
ATC_C09AA16	-	-	-	-	0.00	0.02	0	1	-	-	-	-
ATC_A02BC01	-	-	-	-	-	-	-	-	0.57	0.49	0	1
ATC_A02BC02	-	-	-	-	-	-	-	-	0.22	0.41	0	1

ATC_A02BC03	-	-	-	-	-	-	-	-	0.03	0.16	0	1
ATC_A02BC04	-	-	-	-	-	-	-	-	0.01	0.11	0	1
ATC_A02BC05	-	-	-	-	-	-	-	-	0.17	0.37	0	1

Table 30: Descriptive statistics of regulatory instruments

	HMG-CoA reductase inhibitors				**ACE inhibitors**				**Proton pump inhibitors**			
Variable name	**Mean**	**Std. Dev.**	**Min**	**Max**	**Mean**	**Std. Dev.**	**Min**	**Max**	**Mean**	**Std. Dev.**	**Min**	**Max**
LEAD COMPOUND	0.01	0.08	0	1	-[129]	-	-	-	0.02	0.12	0	1
REFERENCE PRICE	0.04	0.19	0	1	0.00	0.02	0	1	0.02	0.15	0	1
EXEMPTION FROM CO-PAYMENT	0.10	0.30	0	1	0.09	0.28	0	1	0.06	0.23	0	1
REBATE CONTRACT	0.08	0.28	0	1	0.06	0.24	0	1	0.05	0.21	0	1

V.9.2 Appendix 2

Table 31: Results of the standard random effect probit model

Dependent variable -SWITCH								
	HMG-CoA reductase inhibitors			**ACE inhibitors**			**Proton pump inhibitors**		
Variable name	**Coefficient**		**Standard Error**	**Coefficient**		**Standard Error**	**Coefficient**		**Standard Error**
Patient related variables									
AGE	-0.0006		0.0005	-0.0002		0.0003	-0.024	***	0.0002
GENDER	-0.0802		0.0085	-0.0099		0.0072	-0.0043		0.006
EAST	0.0462	***	0.0125	0.0352	***	0.011	0.0771	***	0.0106

[129] The proton pump inhibitors were not part of the lead compound regime.

WELFARE RECIPIENT	0.0615		0.246	0.1170		0.1798	0.0112		0.179
NATIONALITY	0.0357		0.025	0.0038		0.0212	0.0048		0.0148
CITY AREA	-0.0026		0.0096	-0.0024		0.0087	0.0264	***	0.0077
TIME LAPSE	0.0918	***	0.0014	0.0938	***	0.0012	0.0849	***	0.0009
N PRESCRIPTIONS	0.0303	***	0.0019	0.0268	***	0.0012	0.0249	***	0.0008
N ATC7 GROUPS	0.1376	***	0.0172	0.1301	***	0.0182	0.3309	***	0.0069
N PHYSICIANS	-0.2800	***	0.0068	-0.235	***	0.0054	-0.2373	***	0.0041
PAST SWITCHES BETWEEN ATC7 GROUPS	0.4387	***	0.0161	0.4818	***	0.0178	0.2709	***	0.0048
PAST SWITCHES WITHIN ATC7 GROUP	0.6887	***	0.0046	0.5564	***	0.0032	0.3886	***	0.003
N PRESCRIPTIONS WITHIN ATC7 GROUP	-0.2158	***	0.0031	-0.1584	***	0.002	-0.1655	***	0.0018
Physician related variables									
N_PATIENTS	-0.001	***	0.001	-0.0085	***	0.0007	-0.0068	***	0.0003
AGE PATIENTS	-0.0096	***	0.0009	-0.003	***	0.0006	-0.005	***	0.0004
SPECIALIST	-0.02	***	0.01	-0.0384	***	0.0091	-0.0447	***	0.0078
QUANTITY PRESCRIPTIONS	-0.013	**	0.0061	0.0039		0.0042	-0.0229	***	0.0031
PERCENTAGE ATC7 GROUP	-0.0025	***	0.0004	-0.0001		0.0002	-0.0012	***	0.0002
HERFINDAHL-INDEX ATC7 GROUP	0.00005	***	0.0001	0.0001	***	0.0001	0.0001	***	0.0001
HERFINDAHL-INDEX PRODUCERS	-0.0001	***	0.0001	-0.0001	***	0.0001	-0.0002	***	0.0001
Drug related variables									
PRICEDIFF	-0.6938	***	0.0342	-1.0271	***	0.0356	-0.2198	***	0.012
MARKET SHARE	-0.0133	***	0.0009	-0.0008		0.0006	-0.0163	***	0.0007

PZN									
AUT-IDEM DRUG	0.14	***	0.0169	0.1763	***	0.0193	0.0656	***	0.0147
ATC_C10AA01	0.1031	***	0.038	-		-	-		-
ATC_C10AA02	Reference category			-		-	-		-
ATC_C10AA03	0.1295	***	0.0383	-		-	-		-
ATC_C10AA04	-0.3004	***	0.0435	-		-	-		-
ATC_C10AA05	0.6129	***	0.0532	-		-	-		-
ATC_C09AA01	-		-	0.4661	***	0.1434	-		-
ATC_C09AA02	-		-	0.481	***	0.1424	-		-
ATC_C09AA03	-		-	0.5541	***	0.1426	-		-
ATC_C09AA04	-		-	-0.4221	**	0.204	-		-
ATC_C09AA05	-		-	0.4163	***	0.1426	-		-
ATC_C09AA06	-		-	0.4425	***	0.1485	-		-
ATC_C09AA07	-		-	0.2535	*	0.1497	-		-
ATC_C09AA08	-		-	-6.6225		8448.975	-		-
ATC_C09AA09	-		-	0.2678	**	0.1495	-		-
ATC_C09AA10	-		-	-0.1773		0.3453	-		-
ATC_C09AA11	-		-	-0.073		0.1655	-		-
ATC_C09AA13	-		-	-7.5212		14014.42	-		-
ATC_C09AA16	-		-	Reference category			-		-
ATC_A02BC01	-		-	-		-	-0.1805	***	0.0244
ATC_A02BC02	-		-	-		-	-0.3727	***	0.0244
ATC_A02BC03	-		-	-		-	-0.0347		0.0287
ATC_A02BC04	-		-	-		-	Reference category		
ATC_A02BC05	-		-	-		-	-0.4788		0.0265
Regulatory instruments									

LEAD COMPOUND	8.3961		16280.15	Not included in regulatory regime			13.645		75122.87
REFERENCE PRICE	0.5152	***	0.024	0.2821	**	0.1403	0.3533	***	0.0179
EXEMPTION FROM CO-PAYMENT	0.0961	***	0.0173	0.3883	***	0.0125	0.6223	***	0.0133
REBATE CONTRACT	1.2066	***	0.0153	1.6827	***	0.0142	1.668	***	0.014
Controls									
Monthly Dummies	Yes			Yes			Yes		
Constant (β_0)	-1.3511	***	0.0903	-1.4963	***	0.163	-1.6894		0.0826
Log Likelihood	-67938.25			-104034.13			-126519.41		
Rho	0.061		0.0033	0.088		0.0029	0.081		0.0024
Number Observations	212,742			322,048			463,848		

*** indicates significance on the 1 % level, ** significance on the 5 % level and * shows significance on the 10 % level

Table 32: Results of the Chamberlain/Mundlak random effect probit estimation for patient related variables

Dependent variable -SWITCH									
	HMG-CoA reductase inhibitors			**ACE inhibitors**			**Proton pump inhibitors**		
Variable name	**Coefficient**		**Standard Error**	**Coefficient**		**Standard Error**	**Coefficient**		**Standard Error**
Patient related variables									
AGE	-0.1521	***	0.0179	-0.1413	***	0.0138	-0.0806	***	0.0102
GENDER	-0.0084		0.0085	-0.0141	**	0.0071	-0.0018		0.0060
EAST	0.0447	***	0.0122	0.0257	**	0.0106	0.0642	***	0.0104
WELFARE RECIPIENT	0.0738		0.2451	0.0980		0.1771	0.0129		0.1800
NATIONALITY	0.0360		0.0247	0.0025		0.0206	0.0115		0.0148
CITY AREA	0.0008		0.0094	0.0019		0.0083	0.0279	***	0.0075

TIME LAPSE	0.1052	***	0.0019	0.1034	***	0.0016	0.0877	***	0.0012
N PRESCRIPTIONS	0.0546	***	0.0028	0.0427	***	0.0019	0.0173	***	0.0010
N ATC7 GROUPS	0.3269	***	0.0220	0.3374	***	0.0210	0.5372	***	0.0081
N PHYSICIANS	-0.2509	***	0.0068	-0.2213	***	0.0052	-0.2220	***	0.0042
PAST SWITCHES BETWEEN ATC7 GROUPS	0.9260	***	0.0256	1.0353	***	0.0284	0.5937	***	0.0081
PAST SWITCHES WITHIN ATC7 GROUP	0.8628	***	0.0077	0.6218	***	0.0054	0.3852	***	0.0042
N PRESCRIPTIONS WITHIN ATC7 GROUP	-0.2127	***	0.0051	-0.1412	***	0.0032	-0.1679	***	0.0022
Physician related variables									
N_PATIENTS	-0.0049	***	0.0011	-0.0044	***	0.0008	-0.0046	***	0.0003
AGE PATIENTS	-0.0026	***	0.0008	-0.0021	***	0.0006	-0.0032	***	0.0004
SPECIALIST	-0.0271	***	0.0097	-0.0370	***	0.0088	-0.0513	***	0.0076
QUANTITY PRESCRIPTIONS	-0.0323	***	0.0092	-0.0073		0.0063	-0.0262	***	0.0052
PERCENTAGE ATC7 GROUP	-0.0031	***	0.0005	0.0005		0.0003	-0.0043	***	0.0003
HERFINDAHL-INDEX ATC7 GROUP	0.0001	***	0.0001	0.0001	***	0.0001	0.0001	***	0.0001
HERFINDAHL-INDEX PRODUCERS	-0.0001	***	0.0001	-0.0002	***	0.0001	-0.0003	***	0.0003
Drug related variables									
PRICEDIFF	-0.9287	***	0.0405	-1.3205	***	0.0427	-0.2415	***	0.0141
MARKET SHARE PZN	-0.0226	***	0.0012	-0.0020	**	0.0008	-0.0139	***	0.0010
AUT-IDEM DRUG	0.3073	***	0.0209	0.2523	***	0.0247	0.2665	***	0.0184
ATC_C10AA01	0.0525		0.0382	-		-	-		-

ATC_C10AA02	Reference category			-			-		-		
ATC_C10AA03	0.1313	***	0.0383	-			-		-		-
ATC_C10AA04	-0.3247	***	0.0442	-			-		-		-
ATC_C10AA05	-0.4498	***	0.0547						-		-
ATC_C09AA01	-		-	0.2406			0.1531		-		-
ATC_C09AA02	-		-	0.2682	*		0.1522		-		-
ATC_C09AA03	-		-	0.3368	**		0.1523		-		-
ATC_C09AA04	-		-	-0.4958	**		0.2120		-		-
ATC_C09AA05	-		-	0.2041			0.1524		-		-
ATC_C09AA06	-		-	0.2483			0.1572		-		-
ATC_C09AA07	-		-	0.0559			0.1585		-		-
ATC_C09AA08	-		-	-7.4554			19601.71		-		-
ATC_C09AA09	-		-	0.1581			0.59		-		-
ATC_C09AA10	-		-	0.3577			-1.02		-		-
ATC_C09AA11	-		-	0.1659			-0.34		-		-
ATC_C09AA13	-		-	-7.553			22793.93		-		-
ATC_C09AA16	-		-	Reference category					-		-
ATC_A02BC01	-		-	-			-		-0.2223	***	0.0246
ATC_A02BC02	-		-	-			-		-0.4037	***	0.0246
ATC_A02BC03	-		-	-			-		-0.0701	**	0.0288
ATC_A02BC04	-		-	-			-		Reference category		
ATC_A02BC05	-		-	-			-		-0.4577	***	0.0269
Regulatory instruments											
LEAD COMPOUND	8.9284		32,639	Not included in regulatory regime					13.9348		134,174
REFERENCE PRICE	0.5672	***	0.0271	0.2992	**		0.1563		0.3612	***	0.0216
EXEMPTION FROM CO-	0.0512	***	0.0189	0.3501	***		0.0135		0.4741	***	0.0154

PAYMENT									
REBATE CONTRACT	1.0815	***	0.0174	1.6367	***	0.0161	1.5157	***	0.0156
Controls									
Monthly Dummies	Yes			Yes			Yes		
Constant (β_0)	-1.4636	***	0.0920	-2.0371	***	0.1701	-1.4683	***	0.0580
Log Likelihood	-66404.947			-99182.028			-123373.96		
Rho	0.045		0.003	0.067		0.0027	0.064		0.0022
Number Observations	212,742			322,048			463,848		

*** indicates significance on the 1 % level, ** significance on the 5 % level and * shows significance on the 10 % level

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VI. A microeconomic approach of rebate contracts in the German health care system[1]

VI.1 Introduction

Prescription drugs are one major source of expenditures in the German Statutory Health Insurance (SHI) system. About 19 % of the SHI budget is spent for prescription pharmaceuticals. The expenditures for prescription drugs have grown stronger since 2005 (5.3 % per year) than the expenditures for hospitals (3.6 %) and physicians (5.0 %).[2] To reduce the expenditures for prescription drugs, various instruments were implemented in the SHI system.[3]

Among others, rebate contracts are considered as a way to reduce health care expenditures. A rebate contract between a sickness fund (or a group of sickness funds) and a producer of pharmaceuticals contains agreements about rebates on every drug consisting of an active ingredient that is dispensed in a pharmacy at the expense of the sickness fund. The German health care system allows rebate contracts between pharmaceutical firms and sickness funds since 2003. Thereby, the extent of the contract is not specified. It can include only a singular product or the whole portfolio of a pharmaceutical firm. However, rebate contracts were not used frequently until 2007 as the incentives for pharmaceutical producers were rather low. Due to a legal change in 2007, pharmacists are legally obliged to dispense rebated products instead of other drugs with the same molecule. Since then, pharmaceutical producers receive a legal priority for the supply of insured of the sickness fund with their products. In return, they have to grant rebates on their products. Consequently, the popularity of rebate contracts increased. While physi-

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1 This paper is a joint work with Christoph de Millas.

2 See Bundesministerium für Gesundheit (2004-2009)

3 See Denda (2010)

cians have the right to demand that a specific drug is dispensed, the denial of rebated drugs would affect their personal budget and they could be financially prosecuted for economic inefficiency.[4]

The economic effects of rebate contracts are still under discussion. Some parties argue that rebate contracts will increase competition and thereby reduce prices, since the current prices in the market include price mark-ups, resulting from price leadership and market domination of a few big generic producers. For supporters of these arguments the rebate contracts are an option to break this oligopoly structure.[5]

Other parties suggest that the rebate contracts will even increase the oligopolistic power in drug markets, as large firms will be able to offer a higher volume of rebates. Following this, they will be able to win the tenders. In the end, smaller producers will be driven out of the market and prices will rise again due to the increased concentration of the market.[6]

The goal of this paper is to analyze, with the help of a theoretical model, which of the two contrary opinions is more applicable.

Even though the concept of tendering is not uncommon in the pharmaceutical market,[7] the theoretical literature about rebate contracts in pharmaceutical markets is limited. So far, we are not aware of any paper that analyzed the German market for rebate contracts in a theoretical economic model.

Therefore a theoretical model for rebate contracts in the German SHI system will be developed in this paper. The model will include different types of generic producers and patient groups. Resulting from the inclusion of various types of patients, consumer preferences will play an important role in the model.

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4 See KV Sachsen (2011)

5 See Hermann (2007)

6 See Pro Generika e.V. (2010)

7 See Carradinha (2009) and Grabowski and Mullins (1997)

The results indicate an imbalance between larger and smaller pharmaceutical producers concerning their competitive position. The strong market position of larger generic drug producers remains following the introduction of rebate contracts. However, rebate contracts are successful in intensifying competition between producers and lowering the drug expenditures of sickness funds. Crucial factors for the success of rebate contracts are mismatch costs and market access. If the mismatch costs are too high or the market access is too expensive, the contestability of the market can be reduced.

The paper is structured as follows. Section VI.2 gives an overview about the existing literature and the theoretical background influencing the development of the model approach. Section VI.3 introduces the basic model and outlines the situation before the introduction of rebate contracts. In Section VI.4 we investigate the implementation of rebate contracts under different market conditions. In Section VI.5 the results and limitations of the models are discussed with respect to the German market. Section VI.6 concludes.

VI.2 Literature review

The literature on theoretical aspects of the German SHI rebate market is very limited. Most discussions about rebate contracts are focused on aspects like medicine, entrepreneurship, law, lobbying, and politics. As they are considered in the design of the theoretical model, a short outline concerning these aspects will be given in the following.

The paper of Pruszydlo et al. (2008) discusses the medical aspects of rebate contracts. Their paper analyzes the problems of interchangeability that can occur between different generics of the same active ingredient (AIP). The German law only allows substitution between drugs that are identical in terms of AIP, strength, package size, dosage form and indication. However, drugs can still differ in shape, color, divisibility or auxiliary substances. The results of the paper indicate that these factors are relevant for convenience and compliance of the therapy. Pruszydlo et al. (2008) find that in about a third of the cases two possible substitute

drugs in the German SHI market differ in one of the factors mentioned. The problem is aggravated by rebate contracts, as only one product is eligible. Therefore, problems with drug compliance due to rebate contracts are possible.

The discussion about legal aspects of rebate contracts refers primarily to the regulation of the corresponding tendering process. The main question is whether sickness funds are companies, an opinion represented by Badtke (2007) among others, or corporations under public law, as argued by Natz (2008). In case, sickness funds are considered as private companies, they would fall under the anti-trust laws. This would limit the possibilities of sickness funds to create buying syndicates. In opposite, if they were considered as corporations under public law, they would need to tender rebate contracts and need to consider specifications about the promotion of medium-sized businesses.

As a result of the rising popularity of rebate contracts, pharmaceutical firms have to adjust their business strategies to remain competitive. Especially the shifting of the target group of decision makers from physicians to sickness funds leads to new challenges for the pharmaceutical producers. As Zeiner (2008a, 2008b, 2008c) shows, producers of patent drugs try to intensify their relationship with sickness funds by not only offering medical products but also additional health services to the members of a sickness fund. These additional services can also be part of rebate contracts.

In addition, pharmaceutical producers also express their fear of market cannibalization as companies are excluded from large parts of the market, if they lose a tender.[8] For pharmacists rebate contracts can be a reason for higher costs, since the number of different drugs that needs to be stored might increase.[9]

The existing literature on rebate contracts helps us to understand the market environment and the affected parties. However, the development of the theoretical

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[8] See Pro Generika e.V. (2010)

[9] See Bauer (2008), p. 350

model was inspired by the existing literature on another popular regulatory instrument, namely reference pricing (RP).

Even though RP leads to another type of competition, we used some aspects of the theoretical discussion for our model approach. Zweifel und Crivelli (1996) model the introduction of reference prices in Germany in a Bertrand duopoly setting. In their model, they distinguish between two types of physicians that have different preferences for the original and the generic drug. Their results show that the producer of the original drug can charge a higher price than the generic drug producer after reference prices were introduced.

Cabrales (2003) uses a setting with vertically differentiated products that are chosen by the companies. The results indicate that the introduction of reference prices does not always work against the interest of the firms, as it can release the firms of the necessity to compete in quality.

Merino-Castelló (2003) develops a model with two horizontally differentiated firms that decide about quality and price of their products. One firm produces the branded original drug, the other one the generic version. Merino-Castelló uses scenarios of Bertrand and Stackelberg competition to show that reference pricing is not sufficient to increase the market share of generics. However, the results show that the market entry of generics is a credible threat and forces the brand producer to reduce prices.

Mestre-Ferrándiz (2003) models the introduction of reference prices in Spain. In a duopoly of two horizontally differentiated firms, the effect of the policy changes from drug related co-payments to a reference price scheme are analyzed. Due to the design of the Spanish reference price scheme, the price of the original drug is always located above the reference price while that of the generic drug is always below. The results indicate that a reference price scheme can lead to lower prices than a co-payment scheme.

Miraldo (2005) examines the possiblity of collusive behaviour of pharmaceutical companies in the case of reference pricing. In her model, drug producers, both horizontally and vertically differentiated, can determine ex ante the reference

price by their own pricing policy. Following this, it is possible for the producers to collude in their price setting, even without direct cooperation by taking the reference price as a focal point. In Miraldo's model, reference prices are not able to decrease prices to a lower level than without the reference pricing.

Brekke et al. (2007) develop a model with horizontal and vertical differentiation of products. In their approach, competition exists between a producer of an original (off-patent) drug, a generic drug producer, and a third firm that offers a therapeutically comparable but patent protected drug. The authors show that therapeutic reference pricing, including comparable active ingredients in a joint reference price group, increases competition but also discourages innovations to enter the market.

While our paper is inspired by the presented papers on reference pricing, we also incorporated a theoretical approach by Grilo et al. (2001). While the paper analyzes a different topic, the consumer behavior related to external factors of conformity and vanity, the presented spatial duopol model for consumer behavior can be used in our context. In their model, two shopping stores, that are horizontally differenated by their location, sell a homogenous product. The consumers are located on an interval between zero and one, however the possible position of the shops is not limited to this interval. If the position of one store was outside this range and prices were equal, it would lose the market. Hence, horizontal and vertical differentiation are incorporated in a single modelling approach.

In the spirit of Grilo et al. (2001), a horizontally and vertically differentiated Bertrand duopoly model will be used. In our model, decisions about costs and qualities are already made, therefore the firms compete only in price. The differentiation of the firms represent their position relative to the preferences of patients or sickness funds (horizontal differentiation), but also (biased) expectations about the characteristics of the products (vertical differentiation). In contrast to the other authors mentioned, we expand the market by introducing a second group of pa-

tients (respectively sickness funds) that are only price sensitive. Further details about the market setting will be discussed in the next section.

VI.3 The Basic Model

In this section, a simple model for the demand of generic drugs in the SHI market will be developed. The basic model provides the basis for the theoretical modeling of rebate contracts in the later part of this paper.

We assume the existence of a therapeutic market for an active ingredient that is only available on medical prescription only. The market is dominated by generic drugs, while the product of the original producer - whose patent has expired - is not relevant in terms of sales.

The consumers (patients) are heterogeneous in their demand behavior. Thus, the demand for the active ingredient can be separated into two markets.

- Market I is characterized by *biased consumers* who prefer one of the two products. The price is not the only criterion for their decision between the two products.
- Market II captures the *unbiased consumers* who only react to the price of the products. Patients on this market will always choose the product that offers the lower price

There are two producers A and B each offering a single product on both markets. For type I consumers, the products are differentiated in a horizontal-vertical fashion as follows:

- Firm A produces a branded generic drug that is well known by both physicians and patients. The popularity of the drug allows the producer to charge higher prices without losing its complete demand.
- Firm B produces a no-name generic drug. The only advantage of the no-name generic drug compared to the product of manufacturer A can be its lower price,

For both markets, the demand of a consumer is assumed to be one product per period. For purpose of simplicity, we assume that the production costs are zero for both firms. This seems a reasonable assumption as marginal costs are negligible in the case of pharmaceuticals.[10] In addition, as both firms are established in the market, fix costs are considered to be sunk.

VI.3.1 The market of the biased consumers (market I)

For consumers in market I the generic drugs of Firms *A* and *B* are differentiated products. Although considered as equal under therapeutic aspects, they are perceived differently by the consumers due to subjective factors. Such aspects are the popularity of the producers, the shape of a tablet or its color. Also, preferences of physicians can influence the perception of the patient for specific drugs.

To express the diversity of the consumer we use a Hotelling's location model and define the market similar to Grilo et al. (2001). As shown in Figure 21, the length of market I is assumed to be 2. Firm *A* is located at 0, while Firm *B* is located at 2. The consumers of market I are distributed uniformly on the segment [0,1]. The total mass of consumers in market I is assumed to be 1.

If a product differs in its characteristics from the position of a consumer, the deviance creates costs for the patient. These mismatch-costs are described by the factor $t > 0$, expressing the marginal loss in utility for every unit of difference between the position of the consumer and the location of the demanded product. As Figure 21 shows, all consumers would prefer the product of Firm *A*, if prices of the two products were identical. Thus, our model for the market of the biased consumers (market I) displays a combination of both vertical and horizontal product differentiation.

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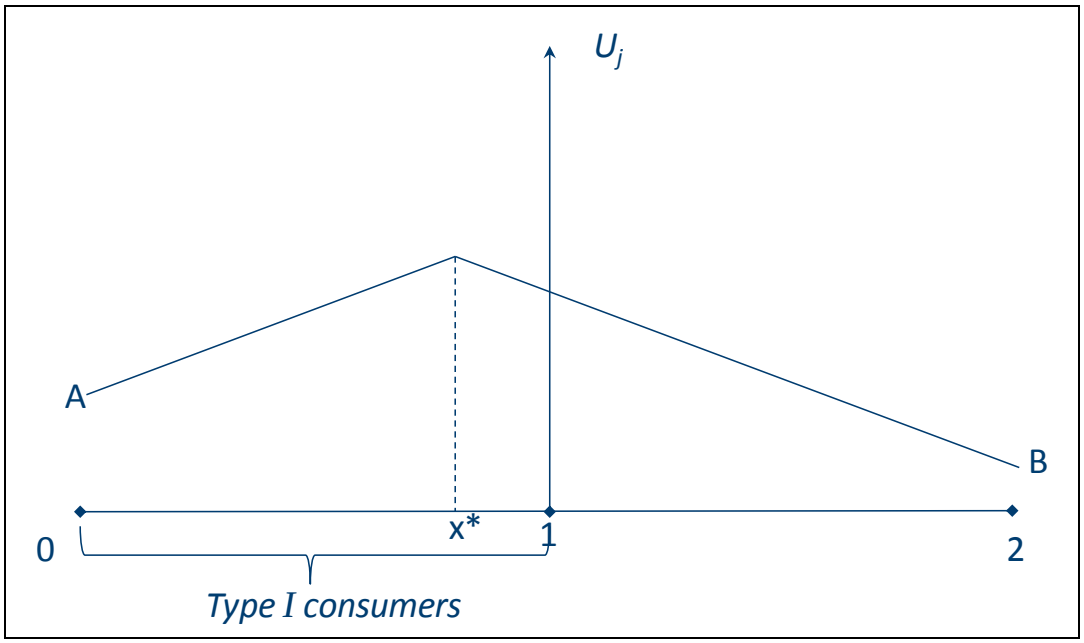
[10] See Schweitzer (2006), p. 144

Figure 21: The market for the biased consumers



The total utility U of the consumer $x \in [0,1]$ is

$$U = \begin{cases} u - tx - p_A & \text{if consuming product of Firm A} \\ u - t|x - 2| - p_B & \text{if consuming product of Firm B} \end{cases} \quad (1)$$

where u is the utility of the plain medical benefit of the active ingredient for consumers and p_A respectively p_B are the prices charged by the manufacturers.[11]

Excursus: Reason for the market position of Firm *B*

This excursus gives a variety of explanations for the differences in preferences by type I consumers. Except for the consumer on position $x = 1$, all consumers have a stronger preference for the product of Firm A than for the drug produced by Firm B. Consequently, in case of identical prices the consumers would always choose product A. However, from a clinical point of view, the products A and B are homogenous goods. Therefore, the difference arises from subjective factors. Possible explanations are:

[11] We assume that u is high enough so that every patient will have a positive utility from buying one of the products.

1. The separation between national pharmaceutical markets is relatively strong. Correspondingly, a firm that has its origins in the local market can establish a national image, which cannot be achieved by a foreign firm.
2. The effectiveness of a medical product also depends on the placebo effect. A lower confidence in Firm B and its product can reduce the healing effect, leading to a weaker market position of B.
3. Consumers might have gained a wider knowledge about Firm A due to other products. This leads to stronger confidence for product A.
4. Physicians, whose opinion might be biased because of advertising of Firm A, can influence the preferences of patients for the products.

VI.3.2 The market of the unbiased consumers (market II)

The second group of consumers that are included in the model (type II) are indifferent between the two generic products. Therefore, their consumption decision is solely based on the price p_i ($i = A, B$) and their "medical need" for the product expressed in value terms. Thus, if $p_i > \min\{p_A, p_B\}$, type II consumers will not buy products from firm i. Moreover, if the medical need, denoted by $y \in [0,1]$, is lower than $\min\{p_A, p_B\}$, the consumer or physician will choose an alternative therapy option, including self-treatment or no treatment at all. The medical need of the patient, described by y, is assumed to be uniformly distributed between 0 and 1. Similar to market I, we assume that each patient only consumes a singular product i per period. The total mass of consumers in market II is assumed to be unity.[12]

We can describe the utility U of a type II consumer as:

$$U = 1 - \mathrm{y} - \mathrm{p_i} \qquad (2)$$

[12] Therefore, the total mass of consumers in the model (type I and II) is two.

A consumer will buy the product if $U \geq 0$. It follows that the demand function in market II is:

$$D^{II}(p_{min}) = 1 - p_{min} \tag{3}$$

with $p_{min} = \min\{p_A, p_B\}$. If $p_A = p_B$, it is assumed that the firms will share the market on equal terms.

VI.3.3 Benchmarks: Market equilibria without rebate contracts

In a first step we investigate the *open market* and derive the market prices for the separate markets I and II, as well as the joint market without rebate contracts. If the firms were able to separate the different type of consumers, they could apply price discrimination and charge an individual price for each market. This will be shown in the following.

VI.3.3.1 Equilibrium in the market for biased consumers (market I)

For the indifferent consumer x^* the utility from consuming product A is equal to the utility gained from product B, i.e. $U(x^*, p_A) = U(x^*, p_B)$. The equation is fulfilled for:

$$x^* = \frac{p_B - p_A + 2t}{2t} \tag{4}$$

As defined in Section VI.3.1, the consumers are located between zero and one. However, in case of $p_A \leq p_B$, the position of the indifferent consumer would be larger than one. Therefore, we can derive the following demand functions for market I:

$$\begin{aligned} D_A^I &= \min(x^*, 1) \\ D_B^I &= 1 - D_A^I \end{aligned} \tag{5}$$

and in consequence the profit functions of the manufactures (recalling that cost are supposed to be zero) are

$$\pi_A = p_A D_A^I \tag{6}$$

$$\pi_B = p_B(1 - D_A^I) \tag{7}$$

Based on this, we can formulate the following lemma.

Lemma 1: If $p_A \leq p_B$ Firm B will never gain any of the biased consumers.

The firms will choose a price that maximizes their profits given the price of their opponent. This leads to following equilibrium prices and profits:

$$p_A = \frac{4t}{3}, p_B = \frac{2t}{3} \tag{8}$$

$$\pi_A = \frac{8t}{9}, \pi_B = \frac{2t}{9} \tag{9}$$

The indifferent consumer is located on $x^* = \frac{2}{3}$, irrespective of the mismatch costs t. Correspondingly the demand for Firm A is $D_A^I = \frac{2}{3}$ and the demand for Firm B is $D_B^I = \frac{1}{3}$ in the equilibrium.

The prices and profits are increasing in t and for all $t > 0$ it holds that $p_A = 2p_B > 0$ and $\pi_A = 4\pi_B > 0$.

The higher price of the product A results from the higher preferences of consumers for product A, compared to product B. Hence, the consumers accept a higher price.

VI.3.3.2 Equilibrium in the market of the unbiased consumers (market *II*)

Based on the demand function in equation (3) the two firms face three possible outcomes concerning their profits:

$$\pi_i = \begin{cases} p_i - p_i^2 & \text{if} \quad p_i < p_j \ (i \neq j) \\ \frac{1}{2}(p_i - p_i^2) & \text{if} \quad p_i = p_j \ (i \neq j) \\ 0 & \text{if} \quad p_i > p_j \ (i \neq j) \end{cases} \tag{10}$$

This is a classic Bertrand competition. Consequently, the equilibrium price for the firms are $p_A = p_B = MC = 0$. Since prices are identical, each firm will receive half of the demand, but profits are zero.

VI.3.4 Equilibrium in the combined market

In contrast to most other European countries, manufacturers in the German SHI market can set their sales prices for prescription drugs without restrictions. However, unless a rebate contract has been signed, they are bound to their official sales price. Also, the margins for pharmacists and wholesalers are set by legal regulations.[13] Therefore, only one nationwide market price exists for a prescription drug.

Given these regulations, we have to show how Firms A and B act when each of them has to charge the same price to all of their consumers. In the case of separated markets, equilibria in pure strategies have been found. This result does not necessarily hold for the combined market.

If the mismatch costs t are low, we have an equilibrium in pure strategies. We find, that $t^m = \frac{3}{16}\left(1 + \sqrt{17}\right) \approx 0{,}96$ are the minimum mismatch costs for an equilibrium in pure strategies to exist. This leads to our first proposition.

Proposition 1

If $t \geq t^m$, a unique Nash equilibrium in pure strategies with $p_A > p_B$ exists. In this equilibrium, Firm A serves most of the biased consumers. Firm B supplies only a small fraction of market I, and all unbiased consumers in market II. In the case of $t < t^m$ no equilibrium in pure strategies exists.

Proof of Proposition 1

Consider $p_A > p_B$. Following equation (3), Firm B receives the whole demand on market II. Moreover, $p_A > p_B$ implies that the profit functions of the firms are:

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[13] In case of over-the-counter pharmaceuticals (OTCs), pricing and margins are free. The price legislation does not apply for hospital pharmacies either.

$$\pi_A = p_A D_A^I \tag{11}$$

$$\pi_B = p_B \left(1 - D_A^I + (1 - p_B)\right) \tag{12}$$

Consequently the reaction functions lead to the following equilibrium prices and profits that are denoted by bars:

$$\bar{p}_A = t + \frac{3t}{3 + 8t} \tag{13}$$

$$\bar{p}_B = \frac{6t}{3 + 8t} \tag{14}$$

$$\bar{\pi}_A = \frac{2t(3 - 4t)^2}{(3 + 8t)^2} \tag{15}$$

$$\bar{\pi}_B = \frac{18t(1 + 2t)}{(3 + 8t)^2} \tag{16}$$

The indifferent consumer x^* of market I is located at:

$$x^*(\bar{p}_A, \bar{p}_B) = \frac{3 + 4t}{3 + 8t} \tag{17}$$

The initial condition $\bar{p}_A > \bar{p}_B$ is satisfied for all $t > 0$.

To prove the existence of a Nash equilibrium with the prices $\bar{p}_A$ and $\bar{p}_B$, it has to be shown that the firms have no incentive to deviate from the expected equilibrium prices.

We find that if Firm B sets a price $p_B \geq \bar{p}_A$, it would lose the whole market of unbiased consumers (type II) respectively half of it if $p_B = \bar{p}_A$. Also, following Lemma 1, B would also lose its market share in market I. Therefore, Firm B never has an incentive to deviate from $\bar{p}_B$.

In case of Firm A, the situation is different. In the above equilibrium candidate, Firm A relinquishes the competition market II. However, it is possible that Firm A can raise its profits by underbidding the price of Firm B.

Firm A prefers to underbid Firm B if:

$$\bar{\pi}_A < \bar{p}_B \left(\underbrace{1}_{\text{Market } I} + \underbrace{1 - \bar{p}_B}_{\text{Market } II} \right) \tag{18}$$

The right hand side of equation (18) is the profit of Firm A with a price that is infinitesimal lower than the price of Firm B: Firm A will then receive the whole market I (see Lemma 1) and in addition it gets the complete market II.

Solving equation (18) for *t* leads to:

$$t < \frac{3}{16}\left(1 + \sqrt{17}\right) = t^m \tag{19}$$

Thus, we have shown that for $t > t^m$, our equilibrium candidate is indeed an equilibrium. However, for $t < t^m$ Firm A has an incentive to lower its price below the price of Firm B. In reaction to the price reduction of Firm A, Firm B will also decrease its price. Consequently, the firms will start a process of underbidding. However, they will not reach a price level that equals the marginal cost, as at one point in the underbidding process, Firm A will gain higher profits by withdrawing from market II. The reason is that even for $p_B \to 0$, Firm A can make strictly positive profits in market I by setting a strictly positive price, whereas for $p_A \to 0$ its profits would vanish.

In the Nash equilibrium for $t \geq t^m$, Firm A serves only the biased consumers in market I and has no share in market II. With rising mismatch costs t, the market share of Firm A in market I falls to $\frac{1}{2}$ as $\lim_{t\to\infty} x^* = \frac{1}{2}$.

Correspondingly, Firm B receives a higher market share in market I as t increases. Note that for $t > \frac{3}{4}$ the price $\bar{p}_B$ is higher than $\frac{1}{2}$, which is the optimal price of the market II in a monopolistic setting.

VI.4 Introduction of rebate contracts

Section VI.3 described the characteristics of the markets where in Section VI.3.3 the equilibrium prices in the separate markets as well as the joint market were derived. As stated in Section VI.3.4, German laws do not allow different prices for the same prescription drug in the pharmaceutical market. Therefore, the equilibrium prices $\bar{p}_A$ and $\bar{p}_B$ are assumed to be the list prices of the product. They are assumed to be constant in the following.

The rebate prices of the firms are assumed to be a percentage r_i of the list prices $\bar{p}_i$ $(i = (A, B))$. For example, $r_i = 0.8$ denotes a rebate of 20 % by firm i concluding the rebate contract. We will refer to r_i as the *rebate element* in the following. Note that a higher rebate element means that a lower rebate is granted. In conclusion, the actual price paid by the sickness fund under a rebate contract is $r_i\bar{p}_i$.

The assumption of stable list prices in the following is not implausible. If we assume that the proportion between biased and unbiased consumers remains the same as in the case of the absence of rebate contracts, the list prices of the firms do not change. However, we assume that it is not possible or optimal for the firms to withdraw their products from the open market.

The introduction of rebate contracts creates new options for the firms. By closing a rebate contract with a sickness fund, the firm gains market exclusivity for this sickness fund's patients. Therefore, patients of the sickness fund receive products for which the sickness fund has a rebate contract.

Rebate contracts also change the demand side of the markets. Instead of patients, sickness funds are now assumed to represent the demand for prescription drugs. Assuming that sickness funds act as perfect agents of their members, we find that they are either preference orientated or price driven. Sickness fund I is assumed to be a representative of the biased consumers. In opposite, Sickness fund II represents the interests of the unbiased consumers.

Section VI.4.1 will describe the scenario for an active ingredient based rebate contract (*API contract*), where sickness funds issue a tender for the supply of their members with a specific active ingredient. Both Firms A and B can offer a contract for their respective products. Based on these offers, the sickness funds select the firm that offers the highest consumer surplus for their members.

Section VI.4.2 will expand the model and alter the characteristics of Firm A. Following this, Firm A will have the opportunity to give a rebate not only for a singular product but for its whole product portfolio, consisting of different active ingredients (*Portfolio contract*).

Due to the results of Section VI.3.4, the analysis is confirmed for the case $t \geq t^m$, since only under this condition an equilibrium in pure strategies exists in the open market.

VI.4.1 Active ingredient based rebate contracts

VI.4.1.1 Scenario 1a: Sickness fund I issues invitations to tender for an active ingredient (API) based rebate contract

As noted before, Sickness fund I represents the group of biased consumers. Since sickness funds act as perfect agents of their members, I will only accept a rebate agreement if it offers an equal or higher utility for its members compared to the utility without a rebate contract.

Therefore Firm A has to offer a price $r_A\bar{p}_A$ that fulfills:

$$\int_0^1 (u - tx - r_A\bar{p}_A)\,dx \geq \int_0^{x^*} (u - tx - \bar{p}_A)\,dx + \int_{x^*}^1 (u - t(2-x) - \bar{p}_B)\,dx \tag{20}$$

Similar, the condition for Firm B is:

$$\int_0^1 (u - t(2-x) - r_B\bar{p}_B)\,dx \geq \int_0^{x^*} (u - tx - \bar{p}_A)\,dx + \int_{x^*}^1 (u - t(2-x) - \bar{p}_B)\,dx \tag{21}$$

The right hand sides of the equations are identical, they express the cumulative utility of patients of Sickness fund I without rebate contract. The patients located between zero and x^* consume drug A. Patients between x^* and one consume drug B. The left sides of the conditions (20) and (21) represent the cumulated utility for all consumers under consideration of the offered rebate contracts of Firms A respectively B. Following the conclusion of a rebate contract, all members of Sickness fund *I* will either use drug *A* or drug B.

The following Proposition 2 describes the equilibrium in the market of type *I* with rebate contracts. We define the critical value for t, where we observe a switch in the rebate regime as:

$$\tilde{t} = \frac{3}{4}\left(1 + \sqrt{2}\right) \approx 1.81 \tag{22}$$

As $\tilde{t} > t^m$, both $t < \tilde{t}$ and $t > \tilde{t}$ are possible, given the assumption that $t \geq t^m$.

The equilibrium values of the rebate element r_A of Firm A in the different rebate regimes are denoted as:

$$\tilde{r}_A = \frac{9 + 36t + 24t^2}{9 + 36t + 32t^2}$$
$$\hat{r}_A = \frac{3 + 8t}{6 + 8t} \tag{23}$$

Note that $\tilde{r}_A < \hat{r}_A$ for all $t > \tilde{t}$ and $\tilde{r}_A \geq \hat{r}_A$ for all $t^m \leq t \leq \tilde{t}$.

Proposition 2

In case of an active ingredient based rebate contract (API contract), in equilibrium, Firm A offers a rebate element $\hat{r}_A$ if $t \leq \tilde{t}$ and a rebate element $\tilde{r}_A$ if $t > \tilde{t}$. In both cases Firm A will gain positive profits. Firm B offers a rebate of 100 %

($r_B = 0$). However, this rebate is not sufficient to make Sickness fund I choose Firm B compared to a contract with Firm A.

Proof of Proposition 2

Let $\tilde{r}_A$ and $\tilde{r}_B$ denote rebate elements of Firm A and B that just match the conditions in (20) respectively (21) with equality:

$$\tilde{r}_A = \frac{9 + 36t + 24t^2}{9 + 36t + 32t^2} \tag{24}$$

$$\tilde{r}_B = \frac{3(3 + 8t) - 2t^2}{6(3 + 8t)} \tag{25}$$

These two critical values are decreasing in t for all $t > t^m$. Also, it holds that $\tilde{r}_A - \tilde{r}_B > 0$ for all $t \geq t^m$. Therefore Firm B always has to offer a lower rebate element (meaning a higher rebate) than Firm A to compensate the higher mismatch costs of the patients.

While the rebate element of Firm A is always greater than zero with $\lim_{t\to\infty} \tilde{r}_A = \frac{3}{4}$, Firm B would need to offer a negative rebate element for $t > \frac{3}{4}(1 + \sqrt{2}) = \tilde{t}$. In this case, Firm B would incur a loss with a rebate contract and would refuse to compete in the tender process.

However, even though Firm B does not make an offer for a rebate contract, it can still be profitable for Firm A to conclude a rebate contract to gain market exclusivity.

Under the assumption of $t > \tilde{t}$, Firm A has to offer a rebate to Sickness fund I that fulfills equation (20) to win the tender. Following this, $\tilde{r}_A$ is the minimum and also the optimal rebate element for Firm A. A higher rebate would not expand the demand for drugs and thus only diminish profits.

As Firm A receives the whole market in case of a rebate contract, the profit is:

$$\tilde{\pi}_A = \tilde{r}_A \bar{p}_A = \frac{2t(9 + 36t + 24t^2)}{(3 + 8t)^2} \tag{26}$$

It can be shown that for all $t > t^m$, it holds $\tilde{\pi}_A > \bar{\pi}_A$. Consequently, Firm A will always offer a rebate contract even if it does not compete with Firm B. The reason for the higher profit is the increase in demand for their product and the possibility of Firm A to conduct a price discrimination between Sickness fund I and II.

In the case of $t^m < t \leq \tilde{t}$ the rebate contract is profitable for both firms. If the firms offered their critical rebate elements of $\tilde{r}_A$ and $\tilde{r}_B$ respectively in the first bidding round, the sickness fund would be indifferent and both firms would have a chance of $\frac{1}{2}$ to receive the rebate contract.

However, it is obvious, that this result cannot be an equilibrium. Both firms have an incentive to deviate from $(\tilde{r}_A, \tilde{r}_B)$ as the firm offering a slightly higher rebate will receive the whole market. Consequently, the other firm will counter with a higher rebate.

Thus, a Bertrand competition emerges, in which Firm A is in a better position than Firm B, due to the preference structure of Sickness fund I. Since members of I are assumed to have a preference for product A, the net price $(r_B\bar{p}_B)$ of Firm B must be lower than the net price $(r_A\bar{p}_A)$ of Firm A.

Given Firm B would offer a rebate of 100 % $(r_B = 0)$, the reaction of Firm A can be expressed as:

$$\int_0^1 (u - tx - r_A\bar{p}_A)\, dx \geq \int_0^1 (u - t(2 - x))\, dx \qquad (27)$$

The right hand side of the equation displays the utility of the consumers in case of a rebate contract with Firm B and $r_B\bar{p}_B = 0$. The left hand side is the utility for a contract with Firm A. Expression (27) leads to the critical

$$\hat{r}_A = \frac{3 + 8t}{6 + 8t} \qquad (28)$$

and the profit

$$\hat{\pi}_A = \hat{r}_A\bar{p}_A = t \qquad (29)$$

The rebate lies between $\frac{1}{2} \leq \hat{r}_A < 1$ and the profit $\hat{\pi}_A$ of Firm A is greater than zero. The results indicate that Firm A can outpace Firm B even if Firm B gives a 100 % rebate.

As shown in proof of scenario 1a, for $t > \tilde{t}$, Firm B would have to offer a rebate element $r_B < 0$ to win the tender. However, the maximum rebate element it will offer is $r_B = 0$, which is analogous to a rebate of 100 %. Firm A could offer a rebate element $\hat{r}_A$ to generate an equal utility for Sickness fund I. However, the sickness fund would not accept it. Firm A has to give the lower rebate element $\tilde{r}_A$ to make Sickness fund I indifferent to the open market situation.

For the case of $t \leq \tilde{t}$, Firm A faces the opposite situation. A rebate element $\tilde{r}_A$ would be sufficient to match the utility in the open market case. Yet, Firm A has to give $\hat{r}_A < \tilde{r}_A$ to outbid the offer of Firm B in this case.

VI.4.1.2 Scenario 1b: Sickness fund II issues invitations to tender for an active ingredient (API) based rebate contract

In this scenario, Sickness fund II offers an active ingredient based rebate contract. The sickness fund represents consumers whose consumption decision depends only on the price of the products.

Note that in market II the price reduction due to a rebate contract will increase the demand for the product. This means that Sickness fund II will transfer the savings of the rebate contract to the patients (in the form of lower co-payments or insurance premiums). Also, physicians will prescribe the drug more often because rebates are considered in the efficiency evaluation of their drug budgets. This implies welfare gains due to rebate contracts.

Considering this, the following Proposition 3 describes the equilibrium in the market of type II with rebate contracts.

Proposition 3

For all $t > t^m$ there exists a Nash equilibrium in pure strategies with $r_i = 0$ $(i = A, B)$ for both firms.

Proof of Proposition 3

Like sickness fund I, sickness fund II will only accept a rebate contract that offers at least the same utility for its members than in the situation without a contract.

If a rebate element r_i is granted and firm i is chosen, the consumer surplus of the sickness fund II is:

$$\int_0^{1-\bar{p}_i r_i} (1-q) - \bar{p}_i r_i \, dq \tag{30}$$

As Firm A is not present in market II before the introduction of rebate contracts due to its higher list price, it always has an incentive to offer a rebate to enter the market. Note that Firm B might also have an incentive to give a rebate. Firm B will only offer a rebate immediately, if the list price $\bar{p}_B$ is higher than the profit maximizing monopoly price $\frac{1}{2}$. This holds for all $t > \frac{3}{4}$ and as our model is limited to $t \geq t^m$ with $t^m > \frac{3}{4}$, Firm B will always offer a rebate element.

As every (reasonable) combination of strictly positive rebate element and list price will generate positive profits and increase the utility of the Sickness fund II, the firms will start a race of underbidding until they reach $r_A \bar{p}_A = r_B \bar{p}_B = MC = 0$. As a result, every firm will make zero profits and will conclude a rebate contract with Sickness fund II with a probability of $\frac{1}{2}$.

As we have seen so far, rebate contracts reduce net prices (rp). Yet, only in case of market II we reach a price equal to marginal costs and the firms have equal chances to win the contract. In contrast, on market I, Firm A keeps its advantage regarding the preferences of the consumers and will always win the bid. Thereby, the net prices on market I will not reach the level of the marginal cost.

However, API contracts are only one possible form of rebate contracts. Instead, some sickness funds do not offer tenders for a single ingredient, but for the whole

product portfolio of pharmaceutical producers. This kind of contracts, called portfolio rebate contracts, will be discussed in the next section.

VI.4.2 Portfolio rebate contracts

So far, we assumed that each firm produces only one single drug. Although the majority of generic producers sells only a small number of different drugs, there are a few large firms that have a portfolio up to over 200 different active ingredients.[14]

We now assume that Firm A is a brand name generic producer that also offers a variety of drugs besides product A. These other products are bundled as "product s" with price p_s. The combination of product s and product A forms the portfolio of Firm A. In contrast, Firm B is supposed to be a small producer that only has a single product in its portfolio. In consequence, only Firm A can offer portfolio rebate contracts to sickness funds.

On the open market the demand for the portfolio s is:

$$D^s(p_s) = 1 - p_s \tag{31}$$

We assume that $D^s(p_s)$ is the demand for the product s. If Firm A had a monopoly in the market, the price for product s would be $\frac{1}{2}$. Therefore, we assume $p_s \leq \frac{1}{2}$. Note that the maximum demand for product s is defined as one. This underlines the importance of our main products A and B compared to products represented by product s.[15]

In the following we compare the portfolio contract to the situation where the sickness funds offer a single API contract for product A or B and no contract for product s. Yet, an API contract for product s could also be possible. However,

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[14] See INSIGHT Health (2009)

[15] It is quite common that even large portfolio firms earn a major part of their overall profits from the sales of only a few products.

such kind of contract seems to be unlikely. There are several reasons for this assumption. In the case Firm A has a monopoly for product s, it has no incentive to offer any rebate because it will not increase its profits. If Firm A faces competition for product s, it might still not want to conclude a rebate contract for this product alone due to transaction cost. In contrast, a joint rebate contract for products A and s might save on transaction costs.

If Firm A offers a rebate contract, we assume that a rebate element r_s is chosen that is identical for product A and s. We also assume that a rebate leading to a lower net price will expand the demand for product s (similar to market II for product A).

VI.4.2.1 Scenario 2a: Sickness fund I issues invitations to tender for portfolio rebate contracts and Firm A can offer a portfolio contract

Similar to the previous scenarios, Firm A has to offer a rebate that will make Sickness fund I at least indifferent to the situation without a contract. Therefore, Firm A must fulfill the following condition (compare condition (20)):

$$\int_0^1 (u - tx - r_s\bar{p}_A)\,dx + \int_0^{1-p_s r_s} (1-q) - r_s p_s\,dq \geq \int_0^{x^*} (u - tx - \bar{p}_A)\,dx + \int_{x^*}^1 (u - t(2-x) - \bar{p}_B)\,dx + \int_0^{1-p_s} (1-q) - p_s\,dq \quad (32)$$

The term $\int_0^{1-p_s r_s}(1-q) - p_s r_s\,dq$ expresses the utility of the sickness fund for product s after the rebate. It can be expanded to:

$$\int_0^{1-p_s} (1-q) - p_s dq + \int_0^{1-p_s} (p_s - r_s p_s)\,dq + \int_{1-p_s}^{1-r_s p_s} (1-q) - r_s p_s dq \quad (33)$$

The first term expresses the utility of the sickness fund in the open market. The second is the utility gain through the lower price for the same quantity. The third term represents the utility gain through the higher amount of consumed products. The first term of (33) can be subtracted from both sides of condition (32) and the right side of the latter becomes identical to that of condition (20):

$$\begin{aligned}\int_0^1 (u - tx - r_s\bar{p}_A)\,dx \\ + \int_0^{1-p_s} (p_s - r_s p_s)\,dq + \int_{1-p_s}^{1-r_s p_s} (1-q) - r_s p_s dq \\ \geq \int_0^{x^*} (u - tx - \bar{p}_A)\,dx + \int_{x^*}^1 (u - t(2-x) - \bar{p}_B)\,dx\end{aligned} \tag{34}$$

Since Firm B only offers a single product, it faces the same condition (21) as in Scenario 1a.

Again there are two critical values $\tilde{r}_s$ and $\hat{r}_s$ (see equation (8) and respectively (43) in Appendix 1), with $\tilde{r}_s < \hat{r}_s$ for $t > \tilde{t}$, such that the following holds:

Proposition 4

Firm A will offer a portfolio contract with rebate element $\tilde{r}_s$ if $t > \tilde{t}$ and the rebate element $\hat{r}_S$ if $t^m \leq t \leq \tilde{t}$. In both cases Firm A will gain positive profits, even higher than under an API contract for product A and no rebate contract for product s. In contrast, Firm B cannot make a contract offer that makes sickness fund I better off compared to the portfolio contract proposal of Firm A.

Proof of Proposition 4

The critical rebate element $\tilde{r}_s$ for which (34) holds with equality can be seen in equation (43) in Appendix 1. It can be shown that $0 < \tilde{r}_s < 1$ holds for all $t > t^m$.

For Firm B the critical rebate elements remains $\tilde{r}_B$ (see equation (25). If $t > \tilde{t}$, we have shown in section VI.4.1.1, that the critical rebate element must be smaller than zero. Therefore, Firm B will not make a bid for the contract. If $t \leq \tilde{t}$, Firm B will lower its rebate element down to $r_B = 0$.

Because Firm B cannot offer a portfolio contract, Firm A has three choices. It could refrain from offering a rebate , offer an API contract for product A, or it could bargain a rebate contract for product A and product s.

The results of section VI.4.1.1 already indicated that an API rebate contract increases profits, compared to the situation without rebate contracts. Consequently, the decision is reduced to the choice between an API and a portfolio contract.

The Firm A will prefer the portfolio contract if:

$$\underbrace{(\tilde{r}_s\bar{p}_A + (1-\tilde{r}_S p_s)\tilde{r}_S p_s)}_{"portfolio\ profit"} - \underbrace{(\tilde{r}_A\bar{p}_A + (1-p_s)p_s)}_{"API\ profit"} \geq 0 \tag{35}$$

It can be shown that the portfolio profit is always higher than the API profit for $t > \tilde{t}$ and $0 < p_s \leq \frac{1}{2}$. The reason for the higher profits is the larger consumed amount of product s. In case of the API contract for product A, Firm A can compensate the utility loss of sickness fund I due to the switching from Firm B to Firm A, only through price reduction. With the portfolio contract, the sickness fund is also compensated by the demand expansion of the portfolio market. The results indicate a welfare increase on the market of product s. Firm A can sell product A for a higher price ($\tilde{r}_s\bar{p}_A$) and therefore overcompensate the profit loses for the remaining products of the portfolio.

For $t^m \leq t \leq \tilde{t}$ again an underbidding process between the two firms occurs, until the rebate element where Firm A can outpace Firm B.

Similar to (27) Firm A can offer a rebate that fulfills the following condition:

$$\int_0^1 (u - tx - \bar{p}_A r_s)\,dx + \int_0^{1-p_s r_s} (1-q) - p_s r_s\,dq \geq \int_0^1 (u - t(2-x))\,dx + \int_0^{1-p_s} (1-q) - p_s\,dq \tag{36}$$

The critical rebate $\hat{r}_s$ element that matches both sides is derived in equation (43) in Appendix 1.

Again Firm A makes higher profits with the portfolio contract compared to the API contract. In conclusion, Firm A will receive the whole market I, as a rebate factor $r_B = 0$ of Firm B would not lead to a higher benefit for the sickness fund.

A portfolio contract leads to higher profits for Firm A compared to an API contract or the open market. The reason is the increased demand on the market of product s. In case of an API contract Firm A can only increase the surplus of the consumers by lowering its price. It now sells more products (the ones sold before by Firm B), however the total amount of products stays the same. It can be shown that, if a price reduction on the market for product s led to no increase in demand, Firm A would be indifferent between an API contract and a portfolio contract. The profit gain due to the rebate contract for product A would be consumed by the loss for product s. With an increase in the demand the consumers are not only better off by the lower price but also more consumers are willing to buy product s. The increase of the demand for these products overcompensates the loss due to lower prices.

VI.4.2.2 Scenario 2b: Sickness fund II issues invitations to tender for portfolio rebate contracts and Firm A can offer a portfolio contract

In this scenario Firm A can offer a portfolio contract to Sickness fund II. The sickness fund will accept that offer if the following condition is fulfilled:

$$\int_0^{1-\bar{p}_A r_s} (1-q) - \bar{p}_A r_s \, dq + \int_0^{1-p_s r_s} (1-q) - p_s r_s \, dq \geq \int_0^{1-\bar{p}_B} (1-q) - \bar{p}_B \, dq + \int_0^{1-p_s} (1-q) - p_s \, dq \tag{37}$$

This means, the accumulated utility in case of a rebate contract (left hand side of (37) must be at least as high as in the market equilibrium without a rebate contract.

As before the firms will start a competition of underbidding and condition (37) can be changed to the case were $r_B = 0$:

$$\int_0^{1-\bar{p}_A r_S} (1-q) - \bar{p}_A r_s \, dq + \int_0^{1-p_s r_s} (1-q) - p_s r_s \, dq \geq \int_0^{1} (1-q)\, dq + \int_0^{1-p_s} (1-q) - p_s \, dq \tag{38}$$

As in the results of scenario 2a the term $\int_0^{1-p_s}(1-q) - p_s \, dq$ can be separated out of expression (38). Thus, the right side expresses the prescribed consumer surplus for Sickness fund $I\!I$ in condition (30) for the case when $r_i = 0$.

Therefore, we can express the condition for Firm A as:

$$\int_0^{1-\bar{p}_A r_S} (1-q) - \bar{p}_A r_s \, dq + \int_0^{1-p_s} (p_s - r_s p_s)\, dq + \int_{1-p_s}^{1-r_s p_s} (1-q) - r_s p_s dq \geq \int_0^{1} (1-q)\, dq \tag{39}$$

The following Proposition 5 describes the equilibrium in the market $I\!I$ if Firm A is able to offer a portfolio contract. Contrary to Proposition 3, the equilibrium value $\hat{\hat{r}}_s$ (see equation (45) in Appendix 2) of Firm A will now be greater than zero:

Proposition 5

Firm A will offer a portfolio rebate element $\hat{\hat{r}}_s > 0$ for all $t \geq t^m$ that will lead to positive profits for Firm A, even higher than in case of an API contract for product A and no rebate contract for product s. In contrast, Firm B cannot offer a rebate element $r_B \geq 0$ which generates a higher consumer surplus for Sickness fund $I\!I$ than the offer of Firm A.

Proof of Proposition 5

Similar to Section VI.4.1.2 the introduction of rebate contracts leads to an underbidding process. While Firm A can offer a portfolio rebate contract, Firm B cannot offer a comparable rebate due to the lack of a larger product portfolio.

Consequently, Firm A increases the utility for members of Sickness fund II and still realizes profits. Therefore, Firm A has to match condition (39). The right hand side of the equation shows the benefit of the sickness fund with a rebate offer $r_B = 0$ by Firm B. The left hand side shows the utility in case of a contract with Firm A. As a result we receive the critical rebate element $\hat{\hat{r}}_s$ of equation (45), which can be found in Appendix 2.

The rebate element $\hat{\hat{r}}_s$ lies between 0 and 1 for $t \geq t^m$ and $0 < p_s \leq \frac{1}{2}$. Firm A now gains a profit on the market for product A. Still, it has to be evaluated if the profit growth for drug A compensates the profit loss for products s. Thus, Firm A will offer the rebate $\hat{\hat{r}}_s$ if

$$\underbrace{(1-\hat{\hat{r}}_s\bar{p}_A)\hat{\hat{r}}_s\bar{p}_A + (1-\hat{\hat{r}}_s p_s)\hat{\hat{r}}_s p_s}_{profit\ of\ portfolio\ contract} \geq \underbrace{(1-p_s)p_s}_{profit\ of\ API\ contract} \qquad (40)$$

It can be shown that the left side of equation (40) is higher for all $t \geq t^m$ and $0 < p_s \leq \frac{1}{2}$. Therefore Firm A prefers the portfolio contract.

Compared to the offer by Firm ($r_B = 0$), Sickness fund II loses benefit on the market of product A (respectively B) if it accepts the bid of Firm A. But Firm A compensates the sickness fund with a benefit gain on the market for product s.

VI.4.3 Recapitulation of the results on rebate contracts

In the previous sections, we have shown four different scenarios for rebate contracts. Table 33 summarizes the results for each scenario. In three of them, Firm A receives the rebate contract and can increase its profits. In contrast, Firm B does not make any profit. Only in one scenario Firm B has a 50% chance of winning the tendering process for a rebate contract, but its profits would be zero.

The sickness funds improve their utility or are, at least, indifferent. In the market of Sickness fund I the increase of total welfare depends on the mismatch cost t. In the market of Sickness fund II total welfare always increases, independent of the value of t (note that following Proposition 1 our solutions considerations are confined to $t \geq t^m$).

Table 33: Summary of the tendering results

	Sickness fund I	**Sickness fund II**
API contract	Firm A wins and gains higher profit than without a rebate contract.	Firm A and Firm B have a chance of 50% to win the contract. They make no profits.
	For $t < \tilde{t}$ total utility of sickness fund increases, for $t \geq \tilde{t}$ total utility remains the same as without a rebate contract.	Sickness fund receives maximum consumer surplus of product A or B, independent of the value of t.
	Total welfare increases, if mismatch cost are high enough.	Sickness fund receives the maximum possible total welfare.
Portfolio contract	Firm A wins and gains higher profits than with API rebate contract.	Firm A wins and gains higher profits than with a API contract.
	For $t < \tilde{t}$ total utility of sickness fund increases, for $t \geq \tilde{t}$ total utility remains the same as without a rebate contract.	Sickness fund receives a surplus gain equal to to the API contract.
	Total welfare increases, if mismatch cost are high enough. In general, the total welfare is higher than under API contract due to higher profits of Firm A.	Total welfare increases, as the maximum total welfare of product A plus the former profit of Firm A for product s is shared between firm and sickness fund.

The results show that the biased consumers, represented by Sickness fund I, will always receive the product of Firm A. In contrast, the unbiased consumers represented by Sickness fund II will either receive product A or B.

Based on the results, Firm A will always prefer the portfolio contract because of the higher profits of this option. In contrast, the sickness funds are indifferent between the API and the portfolio contract. However due to the higher profits, Firm A obtains the possibility to convince the sickness funds to favor portfolio contracts by giving a slightly higher rebate.

Under these circumstances, the portfolio contract would always be the superior rebate contract option. Therefore, our analysis of the API contracts seems unnecessary. However, as we can see for the portfolio contract, Firm A would gain a monopolistic position not only for the API contract (where it is intended) but also for their remaining products consumed by the insurants of the sickness funds. In the long run this would lead to a monopolistic position for firm A in the whole SHI system. The legislature has recognized this issue and changed the legal framework for rebate contracts accordingly. Following 2009, portfolio contracts only fulfill the legal requirements for a rebate contract in very rare cases. We will discuss this in further detail in Section VI.5.

In regard to the total welfare of rebate contracts, the results are mixed. In the market of sickness fund I, the welfare gain depends on the value of the mismatch cost t. Firm B always loses its profits, independently of t. Firm A sells at a lower price but can increase its output and in sum increase its profits. The utility of the sickness fund increases when mismatch cost are low ($t \leq \tilde{t}$) and remain the same when mismatch cost are high ($t \geq \tilde{t}$). It can be seen from the profit functions (26) and (29) of Firm A that in case of the API contract profits are increasing in t. Consequently, the profit gain for Firm A, compared to the profit loss for Firm B, increases when *t* gets higher. This leads to a total welfare increase when t is larger than $\frac{3}{2}$. As we have shown in expression (40), the profits under a portfolio contract are always higher than under an API contract. Therefore, the profit gain of Firm A is even more higher relative to the profit loss of Firm B than in the case of the API contract. However, unlike for the API contract, the critical t, where the welfare increases, depends now also on price p_s of product s. If Firm A has a monopoly

for product ($p_s = \frac{1}{2}$), the total welfare is larger compared to the situation without rebate contracts when $t > 1.3514$.

In case of the market of sickness fund $\mathit{\Pi}$, the welfare effects are more intuitive. With the API contract, the actual price $r_i \bar{p}_i$ is zero. Therefore all patients with a medical need can consume the good and the sickness fund receives the maximum welfare in the market. When the model is extended to portfolio contracts, the welfare gain is even higher than under the API contract. In the case of portfolio contracts, Firm A needs to match with its offer the same consumers surplus as under the API contract as the actual price of Firm B will be again $r_B \bar{p}_B = 0$. Therefore, the total consumer surplus is the same as under the API contract, yet Firm A can increase its profits, since the gain for product A is higher than the loss for product s.

In the following section the political implications of these results will be discussed.

VI.5 Interpretation of the results in relation to the German pharmaceutical market

In a market for generics with free price setting, it is expected that prices are close to the marginal cost of production, as generic drugs are goods whose substitutability and (therapeutic and pharmacologic) homogeneity are the preconditions for market entry. But the need for regulatory instruments like reference pricing and the Aut-Idem rule[16] show that the market prices are usually above marginal costs. In reaction to reference pricing the firms are forced to lower their prices. Also, the

[16] Aut-Idem (latin: or the same) rule in Germany: As long as the physician has not explicitly excluded "Aut-Idem" on the receipt, the choice of the pharmacist is limited to the three cheapest drugs with the same active ingredient, package size, strength, application form and indication. If the physician has stated a specific drug on the receipt and not just the nonproprietary name (INN), the pharmacist may also dispense the drug on the receipt. When there is a rebate contract and Aut-Idem is not excluded by the physician, the pharmacist has to dispense the rebated drug (see Spitzenverband Bund der Krankenkassen (2009)

Aut-Idem rule intensifies the price competition between the different producers. But even then the firms have still the possibility to grant rebates in case of a rebate contract.

Hotelling's location model was used to explain the price differences between the various brands of a generic drug. The model was helpful to explain why the occurring prices lie above marginal costs by assuming the existence of subjective preferences of both patients and physicians for specific generic drugs.

As mentioned in the introduction, experts are divided between two different opinions how rebate contracts could change the market of the SHI system. One group expects an increase of competition and lower prices due to rebate contracts. The other fraction fears a squeeze out of small producers and therefore, in the long run, higher prices due to an oligopolistic or monopolistic market situation.

Our results show that both sides have reasonable arguments for their position. Our model predicts lower reimbursement prices for the sickness funds but also the tendency for monopolization. Of course, our model is only a simplification of the existing forms of contracts. In particular, we assume that firms just grant a simple rebate on the price of a drug. In reality, the German law allows far more complex rebate contracts. For example, firms are allowed to close contracts that include a general rebate on the price and an additional rebate for the increased amount of demand they generated due to the rebate contract. However, this does not alter the general requirement that the firms have to generate at least the same consumer surplus for the sickness funds as without a rebate contract. However, this condition again favors the bigger firms, as they can make better comprehensive offers. As a result, smaller producers could be discouraged to operate in the market.

In concern to the negative aspects of rebate contracts, we found that especially portfolio contracts reduce the chances for small producers. This danger was already acknowledged by the legal institutions in Germany. Since a 2009 court decision, sickness funds are considered as corporations under public law and there-

fore are obliged to tender Europe-wide.[17] Also they have to divide the contract in lots to make it easier for medium-sized businesses to participate in the tender. Consequently, the German Federal Social Insurance Authority prohibits portfolio contracts and appeals to the sickness funds to re-tender their rebate contracts.[18] Based on the court decision and the opinion of the German Federal Social Insurance Authority, the legislator concretized the Book V of the Social Code at the beginning of 2011. The duration of a contract should be two years. The variety of providers shall be taken into consideration. Our results indicate that these legal changes are reasonable.

While the legislator wants to avoid a declining number of producers in the market, a decrease in competition does not necessarily need to occur. Currently there are at least three pharmaceutical companies in Germany that correspond to the Firm *A* in our model (large portfolio and seen as a brand producer by consumers). With the introduction of rebate contracts, the firms would either underbid themselves to a rebate of 100 % or we might see a persistence of high prices (including rebate) when the German patients have a high preference (high mismatch cost) for specific branded generics.

A relatively high number of unbiased consumers could lower the power of the branded generics producers, because it gets more unattractive to give up the demand of the unbiased consumers in favor of higher prices charged to the biased consumers. However, they can use rebate contracts on the market of the unbiased consumers to improve their general market position. Before the rebate contract, only non-branded generic producers of type *B* supplied the consumers on the market. With the API contract firms of type *A* will still not make profits but neither will the former incumbent. Thereby branded generic producers can make it unattractive for small firms to compete on the German SHI drug market. If the brand firms can generate positive profits on other markets of their portfolio, they

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17 See Court of Justice of the European Communities (2009)

18 See Plate (2009)

might even accept losses on markets of unbiased consumers in the short run to drive small competitors out of the market. Hence, the market access for new firms is an import aspect for contestability of the generic market. As Natz (2008) points out, the existence of rebate contracts allows foreign pharmaceutical producers to enter the German market more easily, as they can focus their key account management on the sickness funds and not the heterogeneous mass of physicians. Therefore, even with no local firms of type B in the market, small foreign producers can be a continuous threat for the established market participants.

Another possible strategy for brand firms could be collusive agreements concerning rebate contracts. The larger, established firms in the market could agree that for every sickness fund only one of them offers a rebate. The result would depend on the number of repeated games (frequency of tenders, number of sickness funds), the potential of the firms to threat the (possible) competitors in the market, and the duration of a rebate contract. A deeper analysis is beyond the focus of this paper but it seems reasonable to expect that the options to collude diminish as market entry for new competitors becomes cheaper and the duration of a rebate contract decreases.

Reference pricing, which is an important aspect of the German generic market, was not addressed in this paper. Reference prices foremost influence the price setting on the open market. The German reference prices are based on the existing sales prices in the market and have to take into account that a minimum amount of different drugs is available for the intended reference price.[19] In our model, reference prices would set a maximum price for Firm A or a kink in the demand for product A. However, it would not change the general advantage of Firm A to set a higher price than Firm B. In addition, for the case of a discount contract the reference price does not play a role, as discounts are not considered in the calculation of the reference prices.

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[19] For further details about the calculation of the German reference prices see Schumacher and Greiner (2008) and Stargardt et al. (2005)

When we compare the results of the theoretical literature on reference pricing with our results, we find that the German rebate contracts are a radical regulation instrument. It exerts a stronger pressure on prices than reference pricing, but it cannot level out the differences in market power between the firms.

The analysis of the rebate contracts left out cases where the mismatch cost are $0 < t < t^m$. The reason is the non-existence of a stable list price $\bar{p}_i$ in the combined market without rebate contracts. A deeper analysis of this interval would have distracted from the intrinsic idea of this paper to show the interaction between the firms and the sickness funds in the rebate market. However, it should be noted that rebate contracts, if they are possible for values of t smaller than t^m, might stop the occurring circle of price decreases and increases, as with the existence of a rebate contract, changes in list price will not help to regain market share.

VI.6 Conclusion

Rebate contracts are a relatively new concept in the German market. Policy makers were immediately confronted with demands by the pharmaceutical industry to repeal them. Primarily installed to reduce the expenditures of the sickness funds, rebate contracts are able, under specific circumstances, to reduce the level of reimbursement of drugs to the level of marginal drug cost. However, in most cases a price markup will remain, because large and preferred producers can outperform smaller competitors before marginal costs are reached. Hence, rebate contracts bear the danger that smaller competitors are excluded from the market, leading to market concentration. Yet, it is questionable, whether these arguments are sufficient enough to withdraw the legislation for rebate contracts. But the legislator reacted with more specific frameworks and virtually forbid portfolio contracts.

The results of the paper indicate that the effects of rebate contracts depend on the market framework. By setting the proper regulatory framework, rebate contracts can lead to savings and avoid monopolistic market positions.

First, to prevent the negative aspects of rebate contracts, the contestability of a market has to be sustained. This can be difficult because the rebate contracts diminish the incentives of pharmaceutical companies to produce drugs when they do not participate in any of these contracts.

Second, only single active-ingredient contracts should be allowed. With portfolio contracts, smaller producers are heavily disadvantaged as they cannot compete with the diversity of the larger firms.

Third, the duration of a contract should not be too long, otherwise the excluded firms will most likely leave the market and new competitors cannot enter. The renegotiation of the contracts gives an incentive to remain in the market and the sickness fund might anticipate cost savings in the productions process through higher rebates.

Finally, also the demand side should be examined. It should be observed if the decreasing number of sickness funds, primary due to a number of mergers and the creation of buying syndicates by smaller sickness funds lead to oligopolistic structures on the demand side. However, as sickness funds are bound to regulations for governmental authorities the possible risks for a gross distortion of the pharmaceutical market should be small. It is also questionable whether one producer would have the capacity to supply medicines to about 70 million insurants in the SHI system.

In conclusion, we find that the rebate contracts have a great potential for savings, but possibly not to the expected extent. A sufficient framework is needed to unfold the potential. The market is still under development and in upcoming years, an empirical evaluation of the market is needed to show how the market picture is affected by this new regulatory instrument.

VI.7 Appendix

VI.7.1 Appendix 1

Rebate elements in Scenario 2a

In Section VI.4.2.1 we describe the Scenario 2a: Sickness fund I issues invitations to tender for portfolio rebate contracts and Firm A has the possibility to offer a portfolio contract. The rebate offer of Firm A depends on the possibility of Firm B to offer a rebate as well. For $t \leq \tilde{t}$ Firm B will submit a rebate element $r_B = 0$, but for $t > \tilde{t}$ Firm B could satisfy the condition in equation (21) only with a rebate element $r_B < 0$, therefore it will not participate in the tender. As a result the are at least two different outcomes for the rebate element r_s of Firm A.

In case of $t > \tilde{t}$, the rebate element r_s of Firm A has to satisfy the condition (34). Solving that condition at equality leads to two solutions:

$$r_s^1 = \frac{p_s+t+\frac{3t}{3+8t}-\sqrt{\frac{4t^2(3+4t)^2+4p_st(3+4t)(3+8t)-2p_s^3(3+8t)^2+p_s^4(3+8t)^2+p_s^2\left(9-4t\left(-3+4t(5+6t)\right)\right)}{(3+8t)^2}}}{p_s^2} \tag{41}$$

and

$$r_s^2 = \frac{p_s+t+\frac{3t}{3+8t}+\sqrt{\frac{4t^2(3+4t)^2+4p_st(3+4t)(3+8t)-2p_s^3(3+8t)^2+p_s^4(3+8t)^2+p_s^2\left(9-4t\left(-3+4t(5+6t)\right)\right)}{(3+8t)^2}}}{p_s^2} \tag{42}$$

But only r_s^1 satisfies the conditions of our model that $0 \leq r_s < 1$ for all $t \geq t^m$ and $0 < p_s \leq \frac{1}{2}$. Therefore r_s^1 is the only feasible solution and we define it as our critical value: $\tilde{r}_s = r_s^1$.

For $t \leq \tilde{t}$, the rebate element $r_s$of Firm A has to satisfy the condition in equation (36). There are two solutions for r_s that satisfy the condition:

$$r_s^3 = \frac{p_s+t+\frac{3t}{3+8t}-\sqrt{p_s^4-2p_s^3-2p_s^2(t-1)+2p_s\left(t+\frac{3t}{3+8t}\right)+\left(t+\frac{3t}{3+8t}\right)^2}}{p_s^2} \tag{43}$$

and

$$r_s^4 = \frac{p_s+t+\frac{3t}{3+8t}+\sqrt{p_s^4-2p_s^3-2p_s^2(t-1)+2p_s\left(t+\frac{3t}{3+8t}\right)+\left(t+\frac{3t}{3+8t}\right)^2}}{p_s^2} \quad (44)$$

As before only one of the solutions satisfies the conditions of our model. Here it is r_s^3 and we define it as the critical value, $\hat{r}_s = r_s^3$.

VI.7.2 Appendix 2

Rebate elements in Scenario 2b

In section VI.4.2.2 we describe the Scenario 2b: Sickness fund $\mathit{\Pi}$ issues invitations to tender for portfolio rebate contracts and Firm A has the possibility to offer a portfolio contract. The rebate offer of Firm A depends on the offer of Firm B. The two firms are in a race of underbidding. Due to its portfolio, Firm A has the advantage to outrun Firm B and still make profits. Hence, Firm A needs to satisfy the conditions about the consumers surplus of Sickness fund $\mathit{\Pi}$ in expression (39), where Firm B offers a rebate of 100% ($r_B = 0$). Solving at equality gives two solutions:

$$r_s^5 = \frac{p_s+t+\frac{3t}{3+8t}-\sqrt{\left(p_s+t+\frac{3t}{3+8t}\right)^2+p_s(p_s-2)\left(p_s^2+\left(t+\frac{3t}{3+8t}\right)^2\right)}}{p_s^2+\left(t+\frac{3t}{3+8t}\right)^2} \quad (45)$$

and

$$r_s^6 = \frac{p_s+t+\frac{3t}{3+8t}+\sqrt{\left(p_s+t+\frac{3t}{3+8t}\right)^2+p_s(p_s-2)\left(p_s^2+\left(t+\frac{3t}{3+8t}\right)^2\right)}}{p_s^2+\left(t+\frac{3t}{3+8t}\right)^2} \quad (46)$$

The condition $0 \leq r_s^5 < 1$ holds for all $t \geq t^m$ and $0 < p_s \leq \frac{1}{2}$. In case of r_s^6 the condition is only fulfilled for $t \geq \frac{1}{8}\left(5+\sqrt{73}\right) \approx 1.69$. In consequence, Firm A could choose between two possible rebate elements in this case. But naturally, as both rebate elements lead to the same consumers surplus for Sickness fund $\mathit{\Pi}$, Firm A would only offer the rebate element that leads to higher profits. As described in equation (40) the profit of Firm A is $(1-r_s\bar{p}_A)r_s\bar{p}_A + (1-r_sp_s)r_sp_s$. It

can be shown that for $t \geq \frac{1}{8}\left(5+\sqrt{73}\right)$ the rebate element r_s^5 always generates higher profits. Therefore, we can define r_s^5 as the critical rebate element $\hat{\hat{r}}_s = r_s^5$.

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VII. Concluding remarks

The goal of this study was the evaluation of the effects of the implementation of regulative instruments on key stakeholders of the SHI drug market. The study focused particularly on three regulative instruments which were implemented between 2004 and 2007. The thesis analyzed the effects of the implementation of reference pricing, of the possibility to exempt drugs from patient related co-payments, and of rebate contracts on pricing strategies and market shares of different types of pharmaceutical producers, the prescription behavior of physicians, and the strategic behavior of sickness funds in negotiations processes.

Thereby, the results indicate that the observed regulative instruments have lead to the desired results from the perspective of the legislator. However, it could be shown that these effects sometimes differ between sub-groups of the stakeholders.

The implementation of reference pricing was analyzed from various perspectives. As the regulative instruments primary aim at prices, pharmaceutical producers are the main target of the analysis. The results of the thesis show, that various types of pharmaceutical producers, in detail patent, original, and generic drug producers, are affected differently from the implementation of a joint reference price. Patent drug producers lower their prices to a smaller degree than original and generic drug producers. A possible explanation is a kind of (subjective) utility advantage of patent drugs, which original and generic drugs do not posses. Also, the results indicate that competition effects generic drugs stronger than patent or original drugs.

Beside the effects on the pricing behavior, the thesis also analyzed how the market shares of original and generic drugs are affected by the implementation of reference pricing. The results show, that reference pricing has a positive effect on the market shares of generic drugs, and therefore a negative one for the corresponding original drug. However, the demand effect is smaller than for the other analyzed

regulative instruments. Also, the results indicate that the demand reaction differs for sub-groups of generic drugs, as branded generic drugs benefit more than non-branded generic drugs.

Analyzing the implementation of reference pricing from the perspective of the prescribing physician, the results indicate, that the probability of a drug change increased after the reference price implementation. However, similar to the market share reactions, the effect was overall smaller in comparison to the effects of other regulative instruments.

Overall, as reference pricing was mainly targeting drug prices, it seems comprehensive that both the demand for drugs and the prescription behavior of physicians was not strongly affected. Therefore the analysis shows that the instrument has full field its goal, to force pharmaceutical producers to lower their drug prices.

Second, the effects of the implementation of the possibility to exempt drugs from patient related co-payments were analyzed. Observing from the perspective of the pharmaceutical producers, especially the targeted generic producers, the results indicate that the instrument has a positive effect on the demand for generic drugs that lower their prices below a certain level of the corresponding reference price to achieve the co-payment exemption.

Interestingly, while the effect on the demand of generic drugs partizpating in the possiblity of co-payment exemption is stronger than the effect of reference pricing, it is not significant different for branded and non-branded generic drugs. Shifting the perspective to the prescribing physicians, the results show that the implementation of the possibility to exempt drugs from patient related co-payments increased the probability of a prescription change for the patient more than reference pricing.

While the possibility of co-payment exemption also targeted the prices of pharmaceutical producers, the effects differ from reference pricing. This can be explained by the different focus group of the regime. Unlike reference pricing, co-payment exemption emphasized on low priced generic drugs. Consequently, this type of drugs should mainly benefit from the implemenation of the regulation.

The demand reactions estimated in the thesis confirm this. Also, the instrument also suggests to physicians to prescribe, if possible, co-payment exempted drugs to lower the financial burden of their patients. The positive effect on the probability of a change in drug prescription, that was estimated in the thesis, provides evidence that physicians follow this suggestion.

At last, the implementation of the newest major regulative instrument, rebate contracts between pharmaceutical producers and sickness funds, was analyzed from various perspectives. However, unlike in the case of the two previously studied regulative instruments, the effects are not only examined from the point of view of the pharmaceutical producer or the prescribing physician but also from the perspective of the involved sickness funds. This new perspective is necessary, as unlike before, sickness funds do play an active role in the configuration of the regulative instrument.

While rebate contracts also target the prices of pharmaceutical drugs, the effects are not observable, as the price reductions appear in form of discounts that are private information. In addition, the effects of rebate contracts are much different in comparison to the previous presented regulations. While both, reference prices and co-payment exemption, targeted only prices but did not affect the competitive mechanisms of prescription drug market, the situation is different for rebate contracts. In return for the offering of a discount, pharmaceutical producers, until now mostly generic drug producers, receive a quasi monopolistic market position for the market of insured persons of the contracted sickness fund.

Therefore, pharmaceutical producers that are part of a rebate contract should be able to increase their market position. The results of the thesis confirm this, as the effect of the implemenation of rebate contracts on the demand of partizipating generic drugs is strongly positive, yet weaker for branded than for non-branded generics. However, the demand increase for drugs under rebate contract is only possible through the extensive willingness of physicians to allow the exchange of prescribed drugs with rebated drugs. The analysis of the prescription behavior of physicians shows, that the implementation of rebate contracts lead to the single

largest increase of changes of the dispensed drug for the patient. Both the perspective of the pharmaceutical producers and the physician show that rebate contracts help to reduce drug expansions through the increase of the demand for rebated, and therefore, cheaper drugs.

However, critics of rebate contracts fear that the instrument will lead to an oligopolistic market structure and therefore to a fewer number of competitors and a higher price level in the future. The results of a theoretical analysis, conducted in this thesis, show that this danger is not completely unfounded. However, the results also indicate that pharmaceutical firms will not be able to use their (potential) monopolistic power by offering a large product portfolio, if mismatch and market access costs are low and portfolio contracts are not allowed. Under these rules, following the theoretical analysis, competition will not diminish but sickness funds will still receive the savings through rebate contracts. The current efforts by the legislator, especially concerning the rejection of portfolio rebate contracts, indicate that the political system is well aware of the risks for the competitiveness of markets through rebate contracts.

In conclusion, the empirical and theoretical analysis of the impact of the various regulative instruments on the different stakeholders shows that most of the instruments achieve their goals as expected. The analysis did not show any significant anomalies or flaws that lead to strong market malfunctionings. However, it should be noted, that the implemented instruments mainly affected the drug prices and not the demand for drugs. While the prices of drugs decreased constantly in the past years, in the same time period, the quantity of drugs prescribed and dispensed has increased strongly, leading to increasing drug expenses for the SHI system. While a part of this development has to be attributed to changes in morbidity or to catch-up effects, another part can be considered the result of induced demand. Therefore future regulative instruments should also consider the demand aspect instead of only focusing on drug prices.

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Erklärung über die (nicht) verwendeten Hilfsmittel

(gemäß §4, Abs. 4 der Promotionsordnung vom 15.8.2006)

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