Advertising, Competition, and Regulation in the Pharmaceutical Industry

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von:	Diplom-Volkswirt Moritz Suppliet geboren am 20.09.1984 in Herdecke
Erstgutachter:	Prof. Dr. Tomaso Duso
Zweitgutachter:	Jun.-Prof. Dr. Annika Herr
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– to my parents –
– for your unconditional love and support –

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Chapter 1

General Introduction

> *...economists must offer a rigorous analysis of how markets work, taking into account both the specificities of particular industries and what regulators do and do not know.*
>
> — Jean Tirole, 2015, p. 1666, *Bank of Sweden Prize in Economic Sciences in memory of Alfred Nobel*

Using the tools of empirical industrial organization, this thesis analyzes the pharmaceutical industry. Whether competition and regulation in pharmaceutical markets lead to efficient outcomes is a central question for health policy. Particularly, I focus on welfare effects and price changes due to policies concerned with advertising, parallel trade, and cost-sharing. Various forms of industry regulation trade off consumer surplus, for example via lower prices, and profits, for example via returns to investments (Tirole, 2015). The welfare effects of policy interventions calculated with full models of demand and supply, provide useful guidance for optimal regulation. The field of empirical industrial organization studies the structure of industries in the economy and the behavior of consumers and firm strategies. Recent advances in estimation techniques and data availability has motivated more structural empirical approaches, i.e., the combination of theoretical rationales and empirical work (Einav and Levin, 2010).

I am interested in the question of how patients and firms interact in the pharmaceutical market. The size of the pharmaceutical industry that constitutes about 1.7 % of GDP in Germany and about 2.1% in the US (both 2009) is large enough to warrant extended analysis (OECD, 2011). In recent years, pharmaceutical markets have increasingly been in the focus of public attention due to demographic changes and broader health insurance coverage. The market is growing and pharmaceutical sales in 2013 were more than US $800bn (in ex-factory prices) (Kyle and Scott Morton, 2012). Studies generally find that pharmaceuticals add large benefits to the social welfare of societies. The extreme complexity of pharmaceutical markets makes it especially difficult to analyze them with traditional methods. In particular, this thesis focuses on questions of how demand- and supply-side regulations shape demand patterns and firms' strategies. Robust policy evaluations rely on careful studies of market conduct. Structural econometric models incorporate these market principles by modeling consumer behavior and firm strategies.

Pharmaceutical products are experience goods and the matching process to find a suitable (or the best) treatment takes time and effort of patients and physicians. Patients and physicians as their agents are uncertain of the quality and efficacy of medical treatments or products (Ching, 2010; Crawford and Shum, 2005; Iizuka, 2004). Consumers are risk-averse to receiving a low-quality product or a non-matching

drug due to rather severe consequences. Typical risks of patients in pharmaceutical markets are bad health outcomes, such as no or low efficacy, or unintended severe side effects. Uncertainty about the characteristics of a product may sustain even after experiences with the product (Erdem, 1998). For some drugs it takes time to reveal their curative power, and for some preventive medicines, e.g., for chronic diseases, the curative power might never be completely revealed. Imperfect information about drugs, heterogeneous responses to medical treatments, and risk-averse consumers result in high switching costs for pharmaceuticals. One consequence is relatively brand-loyal consumers (Crawford and Shum, 2005). In particular, these demand-side characteristics have implications for cost-sharing policies and advertising regulations.

I methodologically apply recent empirical techniques to analyze market interactions in imperfectly competitive pharmaceutical markets. Advances in econometrics – in combination with structural assumptions from theory – more and better data have made empirical industrial organization much more useful. For example, new tools for demand estimations have improved the analysis of market outcomes (Pakes, 2003). I make use of a structural econometric modeling of demand and supply to unravel the impact of regulation in drug markets (Berry, Levinsohn, and Pakes, 1995; Berry, 1994). Understanding consumer behavior and firm strategies is of particular importance in complex and heavily regulated markets like pharmaceuticals (Berndt, McGuire, and Newhouse, 2011). On the demand side, I consider utility-maximizing patients who select treatments from a choice set of available drugs. Drugs are experience goods, the choice process is complex, and patients are heterogeneous, for example facing different cost-sharing (prices). Widespread (public) insurance coverage, moral hazard, and asymmetric information may not express the marginal benefits in health care demand curves (Berndt, McGuire, and Newhouse, 2011).

On the supply side, patent laws and federal regulation adds to the complexity of markets (Berndt, McGuire, and Newhouse, 2011). Therefore, I assume Bertrand-Nash competition with differentiated products in therapeutic drug markets (Dubois and Lasio, 2014; Kaiser, Mendez, Rønde, and Ullrich, 2014). The theoretical structure seems to be a good fit for off-patent molecules where originators compete with generic manufacturers. In Europe, originators also face competition for patented molecules by parallel imports. Therapeutic markets that are comprised of more than one molecule, either patented or off-patent, allow the patients to switch between molecules. Thus, the range of potential competition is large in many pharmaceutical markets. The supply side of the drug market is characterized by high (sunk) fixed costs for research and development and moderate costs of production,

approval, and advertising (DiMasi and Paquette, 2004). In particular the following chapters on parallel imports and the decision to advertise focuses on the outcomes of supply-side regulations.

To empirically study pharmaceutical markets, I collect unique and detailed data. The backbone of this thesis are the market level data of three therapeutic drug markets, namely anti-diabetes, anti-epileptics, and Alzheimer's disease drugs. Those are comprised of products that were reimbursed by German public health insurances between January 2004 and December 2010. Price and sales data are available at the package level and at the level of daily doses, which allows to compare products with different active substances and presentations. Each drug is characterized by name, active substance, company name, package size, strength, defined daily dosages, and an indication of whether the drug was exempt from co-payments. Data is provided by *IMS Health*, a private marketing and consulting firm, and extracted from their database *Pharmascope National*. The richness of information allows demand estimations and simulations, which are the premises for estimating welfare effects.

This product level database is merged with monthly firm-level direct-to-consumer advertising expenditures from *Nielsen Media Research Germany*. Advertising expenditures in euros include nationwide advertising in newspapers, journals, TV, radio, on billboards, and the internet. Advertising provides information on the strategic marketing behavior of firms. Furthermore, I collect epidemiological data of patients with diabetes in Germany from the *German Diabetes Association* and of patients with Alzheimer's disease from the *German College of General Practitioners and Family Physicians* and from the *European Collaboration on Dementia Project*. Additionally, I merge product level prices from Denmark to instrument for potentially endogenous prices. This approach assumes that prices in different geographical markets are driven by common cost drivers that are independent of country-specific demand shocks (Hausman-style instrumental variables). The prices of authorized pharmaceutical products in Denmark are publicly available.

To study the effects of cost-sharing and to evaluate the policy of co-payment exemptions for comparatively low priced drugs, I collect quarterly product level data on co-payment exemptions from January 2007 to December 2010 from the *Federal Association of Statutory Health Insurance Funds (FASHI)* in Germany. This information is merged with a quarterly database on reference prices from the *German Institute for Medical Documentation and Information (DIMDI)*. The final database contains prices, reference prices, and information on co-payment exemptions. The data covers 71.7% of all drug packages and 36.6% of all pharmaceutical expenses in Germany sold until the end of 2010.

I analyze competition and regulation in pharmaceutical markets in the three following chapters.

The second chapter is entitled **Umbrella Branding in Pharmaceutical Markets**. I investigate how advertising in the OTC drug market affects the decision to buy prescription drugs from a promoted brand, i.e., umbrella branding of pharmaceuticals. Pharmaceutical advertising is controversial and most governments restrict consumer-directed advertising of prescription drugs. Many firms offer a portfolio of prescription and non-prescription (over-the-counter or OTC) drugs and advertise the latter directly to patients due to fewer regulatory constraints. Exploiting the exogenous seasonality of OTC drug sales to identify a reduced-form estimation, I find significant positive effects of brand-name advertising on prescription drug sales. To explore the effect of consumer-directed advertising on firms' revenues and consumer surplus, I model discrete-choice demand with random coefficients and allow advertising spillovers as a product characteristic. Using monthly sales, prices, and advertising expenditures of Alzheimer's disease drugs in Germany, I find that patients value advertising positively. Sales increase with umbrella branding by 262k daily doses annually. In particular, generic manufacturers increase their annual sales with umbrella branding by 148k daily doses. Advertising spillovers are associated with a consumer surplus of €2.3m and additional revenues of €483k per year.

The third chapter is a joint work with Tomaso Duso and Annika Herr and entitled **The Welfare Impact of Parallel Imports: A Structural Approach Applied to the German Market for Oral Anti-diabetics**. The study utilizes a large panel data set containing monthly information on sales, ex-factory prices, and further product characteristics for all 649 anti-diabetic drugs sold in Germany between 2004 and 2010. We estimate a two-stage nested logit model of demand and recover the marginal costs and markups based on an oligopolistic model of multi-product firms. We finally evaluate the effects of parallel imports policy by calculating a counter-factual scenario without parallel trade. According to our estimates, parallel imports reduce the prices for patented drugs by 11% and do not have a significant effect on prices for generic drugs. This amounts to an increase in the demand-side surplus of €19 million per year (or €130 million in total) which is relatively small compared to the average annual market size of around €227 million based on ex-factory prices. The variable profits for the manufacturers of original drugs from the German market are reduced by €18 million (or 37%) per year when parallel trade is allowed, yet only one third of this difference is appropriated by the importers.

The fourth chapter is jointly written with Annika Herr and has the title **Pharmaceutical Prices under Regulation: Tiered Co-payments and Reference**

Pricing in Germany. This study analyzes the pricing strategies of generic, brand-name, and importing firms after the introduction of price limits below which drugs are exempt from co-payments. The new regulation incentivizes patients to buy cost-efficient products and firms strategically decide to adjust prices to the exemption limit. The policy affects drugs regulated by reference prices in Germany. We employ quarterly data from that market from 2007 to 2010. Identification relies on a difference-in-differences approach, instruments that proxy for regulation intensity, and the fact that the exemption policy was introduced successively in selected therapeutic markets (reference price groups) during this period. Our results show that the new policy leads to an average price decrease of 4.9% for generics while brand-name firms increase prices by 6.4%. We refer to these results as the "co-payment exemption paradox" and show that firms differentiate their products even in highly regulated markets.

Chapter 5 summarizes this dissertation and concludes.

The progress in analyzing firms and consumers in various markets settings resulted in the award of the 2014 Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel to Jean Tirole. This dissertation is meant to follow the two social responsibilities of the economists that Jean Tirole defined for the field of industrial organization: the rigorous analysis of how markets work and the participation in policy debate (Tirole, 2015). In the future, new market dynamics will challenge the efficiency of existing regulation. For example, the arrival of new technologies in health care provision poses challenges for existing market regulations, i.e., the imitation of bio-pharmaceutical active ingredients (Danzon, 2011). My dissertation aims at a better understanding of pharmaceutical markets to implement regulations that lead to efficient market outcomes and benefit consumers.

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Chapter 2

Umbrella Branding in Pharmaceutical Markets

The venerable admonition not to quarrel over tastes is commonly interpreted as advice to terminate a dispute when it has been resolved into a difference of tastes, presumably because there is no further room for rational persuasion. Tastes are the unchallengeable axioms of a man's behavior: he may properly (usefully) be criticized for inefficiency in satisfying his desires, but the desires themselves are data.

— Geroge J. Stigler and Gary Becker, 1977, p.76,
De Gustibus Non Est Disputandum

2.1 Introduction

Whether competition and regulation in pharmaceutical markets lead to efficient outcomes is a central question for health policy. Advertising plays a crucial role in shaping demand curves and in information diffusion from firms to consumers. Analyzing marketing strategies is important in industries where the regulation of advertising is heavily present, such as pharmaceuticals. When advertising, perceived product quality and consumers' utility are correlated, the demand effects have implications for consumers' choice problems, firms' marketing strategies, and market regulation. I investigate how advertising in non-prescription drug markets affects prescription drug demand.

Prescription and non-prescription drugs are marketed in two very distinct regulatory settings. Physicians and pharmacists are involved in prescription drug purchases and it is not allowed to advertise prescription drugs to patients in any OECD country other than the US and New Zealand, e.g., antibiotics. Non-prescription drugs (over-the-counter or OTC) drugs such as ibuprofen are sold without prescriptions in supermarkets and pharmacies. For OTC drugs, advertising toward patients (direct-to-consumer-advertising or DTCA) is an important industry feature (OECD, 2010). Spillover effects exist if patients use their knowledge of brand names from the OTC market to purchase prescription drugs from the same brand. The linkage of demand in prescription drugs and advertising in non-prescription drug markets allows me to identify the effects of umbrella branding across different pharmaceutical markets.

The prerequisite for spillovers – multi-product firms marketing prescription and OTC drugs – are a common phenomenon of pharmaceutical markets. For example, the firm *Bayer* is an innovative drug manufacturer and one of the largest OTC drug firms worldwide. *Bayer* heavily advertises its OTC products, for example, *Aspirin*, *Aleve*, and *Cleratine*. At the same time, the innovative drug branch of

Bayer offers prescription drugs like oral anti-diabetics, contraceptives, and cancer medication. Figures 2.1 and 2.2 show OTC and prescription drug packages, each of which depicts the *Bayer* brand logo. Umbrella branding is a strategy where firms extend their brand name beyond the original category to send signals about quality (Wernerfelt, 1988) or as a substitute for external certification (Hakenes and Peitz, 2009).

My work follows on from the growing literature of structural empirical market models where policy evaluations build on a rigorous analysis of consumer product choices. The complex market structure of the drug industry, which interacts with advertising regulation and firms' umbrella branding strategies, shapes prescription drug demand. Typically, drug consumers are not well-informed about available products and experts (physicians or pharmacists) suggest treatments. In markets of experience goods, the information about brand names might provide quality signals to consumers (Nelson, 1970; Erdem and Keane, 1996), for example, through umbrella branding (Miklos-Thal, 2012). This research helps to understand the role of regulation in industries with multiple regulatory constraints, for example, on advertising. Umbrella branding poses challenges for regulation if advertising is prohibited in one market and allowed in markets with very similar products, like OTC and prescription drugs in Europe. The problem is also complex for the US where two distinct institutions oversee pharmaceutical direct-to-consumer advertising: the *Federal Trade Commission* (*FTC*) is responsible for OTC drugs and the *Food and Drug Administration* (*FDA*) for prescription drugs.

Figure 2.1: *Bayer* OTC Drugs (Selection)

Advertising spillovers have implications for health policy-makers that are concerned with medical under- or over-treatment of diseases. If advertising spillovers have positive effects on demand and result in market expansion, under-treated patients would benefit. Alzheimer's is considered to be an under-treated disease. On the opposite side, market expansion through advertising is harmful for over-prescribed medications, such as antibiotics. Recently, several US-based medical

Figure 2.2: *Bayer* Prescription Drugs (Selection)

institutions and consumer protection agencies, including the *FDA*, the *Institute of Medicine* (*IOM*), and the *Institute For Safe Medication Practices* (*ISMP*) have added the topic of pharmaceutical branding to their agendas, e.g., brand-name extensions (FDA, 2014; Kohn, Corrigan, and Donaldson, 2000; ISMP, 2007). Umbrella branding is one way to extend brand-names and might pose a challenge to consumer protection. For pharmaceuticals, information diffusion and advertising become more important since more information is freely available for patients, e.g., on the internet. The European Commission has also launched approaches to provide more information to patients due to increasing interest in learning about medicine (Watson, 2011). My results are interesting for policy-makers and regulators who are concerned with information diffusion in prescription drug markets and patients' demand patterns.

Drug markets where patient-directed advertising is prohibited provide an ideal setting to test for spillovers. Therefore, my database focuses on the Alzheimer's disease (AD) drug market in Germany and includes sales, prices, and product characteristics from 2004 to 2010. Although the aim of this paper is to analyze welfare and structurally estimate a demand model, I start the empirical analysis with a reduced-form investigation. An endogeneity problem arises from firms strategically choosing advertising expenditures and media channels. To alleviate endogeneity issues, I implement instrumental variables for advertising, i.e., the seasonality of common illnesses treated with OTC products and its correlation with OTC advertising expenditures. The instruments rely on the exogeneity of OTC drug demand and its strong correlation with advertising. I find positive and significant spillover effects from OTC drug market advertising on prescription drug demand.

Next, I model individual demand, allow advertising spillovers from OTC markets, and estimate a discrete-choice demand system with random coefficients (Berry, Levinsohn, and Pakes (1995), henceforth BLP). Price and advertising coefficients are identified by optimal instruments in the sense of Chamberlain (1987) and Reynaert and Verboven (2014), seasonality of OTC drug markets, prices from Denmark

(Hausman-style instrumental variables), and BLP-style instruments. I find evidence that patients favor products from promoted brands. Due to umbrella branding, generic firms,[1] which spend comparatively more on advertising, increase their yearly sales by 146k daily doses. Originators' sales increase by 110k daily doses. Overall, the share of yearly treated patients increases by about 5 percent. Due to newly treated patients the yearly consumer surplus accumulates to €2.3m.

A comprehensive theoretical and empirical literature analyzes the effects of advertising (Bagwell, 2007). Various forms of pharmaceutical advertising seem to have mostly positive effects on drug demand and market shares. The advertising of pharmaceuticals in the US has produced a sizable literature that has been using varying identification strategies (Lakdawalla, Sood, and Gu, 2013; Avery, Eisenberg, and Simon, 2012; Ching, Clark, Horstmann, and Lim, 2015; Iizuka, 2004; Ling, Berndt, and Kyle, 2002). This is the first paper to analyze advertising spillovers from OTC drug advertising into prescription drug markets. Previous empirical work finds umbrella branding strategies in other industries (Balachander and Ghose, 2003) but evidence for pharmaceutical markets is rather incomplete. I draw on work on the spillovers of pharmaceutical advertising. Shapiro (2014) estimates the positive spillover effects from firms' individual advertising on the market level. Lakdawalla, Sood, and Gu (2013) find that the introduction of Medicare Part D boosts advertising expenditures which affect drug demand outside the Medicare program. The spillover effects of pharmaceutical advertising are also measured on compliance (Wosinska, 2002; Donohue, Cevasco, and Rosenthal, 2007), and on doctor visits (Iizuka and Jin, 2007). Ling, Berndt, and Kyle (2002) have investigated the link between prescription and non-prescription markets and find a positive effect of prescription drug advertising on demand in OTC drug markets in the US.

Although the empirical IO literature offers models that emphasize consumer heterogeneity (Berry, Levinsohn, and Pakes, 1995; Nevo, 2001), there are relatively few applications to the complex and diverse market structures of pharmaceuticals. Notable exceptions are Kaiser, Mendez, Rønde, and Ullrich (2014) who analyze a reference price policy in Denmark, Dubois and Lasio (2014) with a focus on price constraints in France, and Lasio (2015) who estimates the impact of de-listing from insurance coverage. Chintagunta (2002) includes advertising in a random coefficient

[1] In this paper, all drug types can advertise and become a *branded* drug. I differentiate between originators who invest in R&D and market innovative drugs, and generic firms who bring copies of no-longer-patented drugs to markets. In addition, imported versions of originators' drugs are available through parallel imports.

logit demand model. Other structural product-level discrete choice models, e.g., Dutta (2011), largely ignore the effect of advertising. Individual-level databases have triggered more research on advertising and demand (Yin, 2015; Dunn, 2012; Ackerberg, 2003). However, neither of the previous research streams calculate the welfare effects of umbrella branding nor do they focus on the role of brand-name spillovers from OTC markets.

Aside from pharmaceutical markets, some research is concerned with modeling advertising and consumers' utility (Dubois, Griffith, and O'Connell, 2014). Part of this literature is interested in the nature of advertising: information provision on the existence of products, about specific product attributes, and signaling product quality (persuasion). For example, in the context of drug markets, advertising could provide information on new drug therapies, about curative effects of specific drugs, and about brand names. Recent print advertisements for Alzheimer's disease drugs in the US contain elements of information and persuasion (Gooblar and Carpenter, 2013). However, in nations with restricted advertising the content of advertising spillovers is limited to brand-names. I model advertising as a product characteristic.

On the supply side, profit-maximizing firms observe demand curves, set prices, and decide to invest in umbrella branding. However, strategies differ for originators and generic manufacturers. As is shown in consequent sections, advertising is not a relevant strategy for importers.

Originators maintain their brand status by advertising and, thereby, make their products known to consumers and physicians. Drugs are advertised to differentiate from therapeutic alternatives or from imported versions and for life cycle management purposes (Bhattacharya and Vogt, 2003; Caves, Whinston, and Hurwitz, 1991). The European Commission (EUC, 2009) points out that advertising is a strategy of incumbents to react to generic entry. Firms tend to advertise more for products that are less price elastic (Rizzo, 1999). Thus, insurance plan coverage, like in the context of Medicare Part D, leads to an increase in advertising (and utilization) of drugs covered by health plans (Lakdawalla, Sood, and Gu, 2013). Indeed, originators spending the most on advertising (see Table 2.1). My welfare analysis examines the profit increases of originators due to advertising, although the relative increase seems to be larger for generic firms.

Advertising allows generic manufacturers to increase awareness of generic substitutes. Generic firms inform patients of alternative brands in former monopolistic therapeutic fields (Königbauer, 2007; Hurwitz and Caves, 1988), overcome brand loyalty, and switching costs (Shum, 2004). For example, the German OTC commercials of the generic firm *ratiopharm* show twins asking for lower-priced drug

alternatives in pharmacies. Generic firms could differentiate their products through advertising and persuading patients of lower prices or superior quality. This idea follows the work on *branded generics*, a strategy to avoid cannibalization (Berndt and Newhouse, 2010; Reiffen and Ward, 2007). Many health care systems have policies to steer patients, physicians or pharmacists toward low-priced drugs. Advertising would allow generic firms to differentiate and create *branded generics*. Indeed, my findings suggest that generic firms benefit from OTC drug advertising spillovers since their sales increase through advertising by about 80 percent (or 146k daily doses).

The remainder of the paper is structured as follows. Section 2.2 describes pharmaceutical advertising and the Alzheimer's disease (AD) drug market. The advertising and market data are laid out in section 2.3. In section 2.4 I present the economic model of demand and supply and describe the simulation and welfare calculation. Results are presented in section 2.5 and discussed in section 2.6.

2.2 Pharmaceutical Markets and Advertising

Pharmaceutical Advertising differs in many aspects from marketing in other industries. The political and academic debate on the social benefits of consumer-directed advertising in prescription drug markets is controversial and has produced a sizable literature (Avery, Eisenberg, and Simon, 2012).

About 60 percent of global drugs are marketed in countries where consumer-directed advertising is not permitted (Efpia, 2013). Traditionally, consumer-directed advertising for prescription drugs is restricted in Europe and has been regulated by a Council Directive since 1992 (EUC, 2009).[2] Drug advertising is common in the OTC industry. In 2010 in Germany, the OTC industry spent 12.6 percent of sales (€772m) on advertising (Nielsen Media, 2012).

Drug advertising in Europe targets mainly physicians and is regulated either by law, e.g., Germany and France, or by industry self-regulation, e.g., the UK and Sweden. Promotional activities comprise sales representative visits to physicians (detailing), free samples, and sponsored marketing conferences. While free samples are a pure economic incentive, detailing and conferences provide physicians with

[2]Direct-to-consumer advertising for prescription drugs is allowed in the US and New Zealand. US firms' advertising expenditures were US $4.37bn in 2010 (Kornfield, Donohue, Berndt, and Alexander, 2013). At the same time in the US, OTC drug sales were US $30bn (CHPA, 2015) and advertising spending was around US $3.2bn (Paek, Lee, Praet, Chan, Chien, Huh, and Cameron, 2011).

information (Ching and Ishihara, 2010) and persuade them to prescribe a specific drug (Berndt, Bui, Reiley, and Urban, 1995). Earlier work shows that detailing may have business stealing effects and may impact sales, while consumer-directed advertising is considered to have a market-expanding effect (Ling, Berndt, and Kyle, 2002; Iizuka, 2004; Iizuka and Jin, 2007; Ching, Clark, Horstmann, and Lim, 2015). Results of previous studies are difficult to transfer to pharmaceutical markets with strict advertising regulation and universal health insurance coverage. The overall role of pharmaceutical advertising in regulated countries is unclear, not least due to data limitations. This paper is the first to shed light on advertising in this context.

Drug Markets in Germany are in the center of this study which focuses on the public health system in Germany that covers about 70 million insurees or about 85 percent of the total population during the study period (BMG, 2012). In contrast to the US, insurance plans do not differ among insurees[3] and they reimburse products and services directly to the provider. In addition, a uniform incentive and payment scheme for all pharmacists and physicians across Germany mitigate agency problems associated with third-party payers. Expenditures for prescription pharmaceuticals were €29bn, about 18.3 percent of the total budget of the public health system in 2011. The OTC drug market was €4.3bn, 10 percent of pharmacies' revenues, and 42 percent of all sold packages (ABDA, 2012).

Pharmaceutical firms freely set their prices during the study period and prices are uniform across all German pharmacies. Until 2011, all drug prices were unrestricted and were reimbursed by the public health insurance. Reimbursement policies set incentives for firms to decrease the prices of generic drugs, e.g., reference prices or co-payments. Reference prices define the reimbursement levels of the public health insurance and induce competition in generic markets. However, some firms differentiate their products by setting prices above the reference prices (Herr and Suppliet, 2012).

Patients co-pay 10 percent per package, with a minimum of €5 and a maximum of €10. There are no deductibles or coverage gaps in the insurance plans. Pharmacists hand out prescription drugs and are reimbursed with a flat fee and a variable fee (3 % of the package price). There are regulations in place that encourage pharmacists to act as the patient's perfect agent and to consider limited resources, e.g., by offering one of the cheapest products. There are no drug sales in German supermarkets or

[3] Patients may augment their uniform public health plan with a private health plan. However, public health plans cover nearly all pharmaceutical expenses and I abstract from the idea that additional private health plans influence drug purchases.

in physician offices.[4] This implies that the actual place and procedure to receive an OTC drug is the same as for prescription drugs. These features particularly allow to study effects at the border of prescription and OTC drugs in the German drug market. The need for a prescription and health insurance coverage are the main differences between the two drug types. OTC drugs are available without prescriptions and are chosen by patients from the shelf space or after expert advice from the pharmacist.

Physicians are free in their drug choices and can either prescribe a specific product (and package size and strength) or an active ingredient. With an indication on the prescription they can prohibit substitution in the pharmacy. Physicians face a non-binding prescription cost benchmark with neighboring colleagues, which was brought into effect in 2001. However, benchmarks are individually re-negotiated, adjusted to patients' morbidity, and are poorly enforced (Korzilius, 2011). I argue that the prescription benchmark is a weak incentive for physicians to prescribe lower-priced pharmaceuticals. Physicians' reimbursement is independent of their prescription behavior and is uniform across Germany.

Alzheimer's Disease is a form of dementia characterized by memory loss and cognitive decline. It is the most common form of dementia and the disease typically follows a progressive course resulting from various central neurodegenerative and ischemic processes (Qaseem, Snow, Cross Jr, Forciea, and Hopkins Jr, 2008). Scientists still do not fully understand what causes AD, but most likely factors include a mix of genetic, environmental, and lifestyle factors. Preventive actions, for example omega-3 fatty acid supplementation or physical activity, show modest therapeutic potential, if any (Winslow, Onysko, Stob, and Hazlewood, 2011). There are several reasons why this paper focuses on the market for Alzheimer's disease drugs. First, Alzheimer's disease prevalence is strongly driven by age. Research on age-related diseases, like Alzheimer's disease, are of growing importance due to the aging Baby Boom generation and medical innovations. Second, the economic and social burdens of Alzheimer's disease on societies with aging populations are enormous: Zissimopoulos, Crimmins, and St.Clair (2014) use micro-simulations to predict 9.1 million patients, each with annual costs of US $71,303 for the year 2050 in the US. Drugs that delay onset could significantly lower the prevalence and associated costs of AD.

[4] All OTC drugs are also behind-the-counter products and are only available in pharmacies. Dietary supplements and very low-dosage herbal molecules are available in drug drugstores.

Alzheimer's Disease Drug Market constitutes of six different molecules, two off-patent and four patented active ingredients. The drugs comprise patented originators, imported patented originator drugs,[5] and generics. All international clinical guidelines recommend the first-line pharmacological treatment options cholinesterase inhibitors (*donepezil, galantamine* and *rivastigmine*) and *memantine* (DGPPN (2009) for Germany; Winslow, Onysko, Stob, and Hazlewood (2011); Rabins, Schneider, Tariot, and Anzia (2007); Qaseem, Snow, Cross Jr, Forciea, and Hopkins Jr (2008) for the US; NICE (2011) for the UK). *Piracetam* is frequently prescribed and reimbursed as a medical therapy for AD patients in Germany, although it is not recommended in every clinical guideline. The drug is associated with increasing blood flows in parts of the brain but its therapeutic value for dementia is under discussion (and is not approved by the FDA) (DGPPN, 2009; Flicker and Evans, 2004). Non-pharmacological treatments, for example, cognitive training or physical activity, are suggested as additional therapy, some of them with limited evidence (Ballard, Khan, Clack, and Corbett, 2011).

In addition, some guidelines mention evidence of treatments with *selegiline*, *testosterone*, or *ginkgo biloba* (Winslow, Onysko, Stob, and Hazlewood, 2011; DGPPN, 2009). *Ginkgo biloba* is reimbursed by the public health insurance in Germany if prescribed for AD patients and is included in the data. The herbal active ingredient is available as prescription drug and also available without a prescription. This double classification is rooted in the reimbursement system of the German public health insurance. Few OTC products are eligible for reimbursement if they are prescribed by a physician. The list of eligible drugs is limited and all other OTC drugs are not covered by any public plan. Examples of covered OTC drugs are *acetylsalicylic acid* to prevent myocardial infarction and *ginkgo biloba* for dementia. In order to receive reimbursement for covered OTC drugs from the German public health insurance, patients have to follow the procedure as if they had received a prescription drug: patients hand their prescription to the pharmacist, co-pay, and receive the OTC drug. Pharmacies are reimbursed as if *ginkgo biloba* was a prescription drug. Those hybrid markets allow firms to advertise reimbursed OTC drugs directly to consumers. I discuss possible issues in section 2.6. Sometimes pharmaceuticals switch their status from prescription to non-prescription (so-called *Rx-to-OTC Switch*). Prominent examples in the US and Germany are *proton pump inhibitors (PPI)* against heartburn and emergency contraceptives. There are no *Rx-to-OTC Switches* in the Alzheimer's disease market.

[5]Imported originator drugs (parallel imports) are the result of free trade and public pharmaceutical price regulation in the European Union (Duso, Herr, and Suppliet, 2014).

2.3 Data and Reduced-Form Evidence

Monthly data from the Alzheimer's disease drug market from Jan 2004 to Dec 2010 comes from the *Pharmascope National* database of *IMS Health* (IMS Health, 2012). The dataset contains information on sales and price at the product level for all products reimbursed by the German public health insurances. Information on the defined daily doses (DDD) allow comparisons across different molecules. Monthly firm-level, direct-to-consumer advertising expenditures from Jan 2002 to Dec 2010 were collected by *Nielsen Media Research Germany*. Advertising spending in euros include nationwide advertising in newspapers, journals, TV, radio, on billboards and the internet.

2.3.1 Summary Statistics: Advertising

OTC drug markets in Germany as in most other OECD countries traditionally have a high market share of brand name products (Carrera and Villas-Boas, 2014). A list of the top-20 advertising firms over the sample period is presented in Table 2.1. Total expenditures span from €404m to €40m and total market expenditures amounted to €5.6bn. The sample includes eight originators that advertise OTC products, e.g., *Pfizer* or *GSK*; five generic firms that advertise their OTC products, e.g., *Hexal* or *ratiopharm*; and eight OTC firms that do not sell prescription drugs, for example, *MCM Klosterfrau*. In 2011, most advertising was placed in TV (56 %) and newspapers (34 %), with internet advertising showing the highest growth rates. The most advertised product categories are cough and cold medications (€141m), followed by analgesics (€108m), and relaxant agents (€81m)(Nielsen Media, 2012).

Consumers keep marketing activities in mind, which allows advertising to have a longer lasting effect on demand. Firm reputation depends possibly on all advertising expenditures in past periods, an idea that has been used in a number of empirical research (Lakdawalla, Sood, and Gu, 2013; Berndt, Pindyck, and Azoulay, 2003). Advertising stocks cannot be observed directly. To take the wave-like character of OTC advertising into account I assume dynamic effects on demand and construct advertising stocks as the depreciated expenditure of past periods plus current advertising expenditures (Dubois, Griffith, and O'Connell, 2014).

Formally, the advertising vector of firm f in period t, a_{ft}:

$$a_{ft} = \lambda a_{ft-1} + e_{ft} = \sum_{\tau=0}^{t} \lambda^{\tau} e_{ft}, \tag{2.1}$$

Table 2.1: Umbrella Branding of Top-20 Advertising Drug Firms

Rank	Firm	[€, m]	Product Portfolio
1	MCM Klosterfrau	404	OTC only
2	Bayer	397	Prescription drugs & OTC
3	Boehringer Ingelheim	328	Prescription drugs & OTC
4	Johnson & Johnson***	274	OTC only
5	Novartis	219	Prescription drugs & OTC
6	Pfizer	207	Prescription drugs & OTC
7	Dr. Willmar Schwabe	173	OTC only
8	GlaxoSmithKline	157	Prescription drugs & OTC
9	Hexal	143	Prescription drugs (generics) & OTC
10	Biomedica	132	OTC only
11	Spitzner	126	OTC only
12	ratiopharm	118	Prescription drugs (generics) & OTC
13	Medice	85	Prescription drugs (generics) & OTC
14	Hermes	83	OTC only
15	Merck	72	Prescription drugs & OTC
16	Stada	69	Prescription drugs (generics) & OTC
17	Dr. Wolff	57	OTC only
18	Pohl-Boskamp	52	OTC only
19	Nycomed	51	Prescription drugs & OTC
20	Engelhard	40	Prescription drugs (generics) & OTC
	Total	5,600	

Notes: The column Product Portfolio indicates if firms sell prescription and OTC drugs under the same brand name. This table presents the top-20 firms in total OTC drug market advertising from 2004 to 2010. Own calculation with data from Nielsen. Firms without pharmaceutical sales are excluded (e.g. opticians or cosmetics producers). ***One of Johnson & Johnson's subsidiaries, Janssen-Cilag, is an innovative drug manufacturer but does not advertise under the J&J brand.

where last period's stocks, a_{ft-1}, depreciates with rate λ and this period's advertising expenditures are denoted e_{ft}. For this paper, I assume λ to be constant across firms. For the remaining estimations I assume the depreciation rate to be .1 per month, which is in range of other research.[6] Results are barely sensitive to the overall depreciation rate since the rate remains the same for all firms.[7] Different depreciation rates across firms would affect the results differently and are a promising venue for future research.

My model of advertising allows spillovers between drugs from the same firm but not to competitors' drugs. This is different in industries where advertising spillovers contain information about the promoted product. These spillovers can result in competitors' free-riding in advertising (Shapiro, 2014). The molecule *ginkgo biloba* can be advertised directly to patients because it is an OTC drug. Advertising for drugs with that molecule can have spillover effects on the class of Alzheimer's drugs, for example, through comparative effects between molecules. In section 2.5 I empirically test for these spillover effects.

2.3.2 Summary Statistics: AD Pharmaceuticals

The market for Alzheimer's disease drugs in Germany includes 106 different products that were marketed by 54 different firms between 2004 and 2010. The sample contains information about seven drugs from innovators, 45 imported innovative drugs, and 54 generics which sell six molecules: *donepezil, galantamine, ginkgo biloba, memantine, piracetam,* and *rivastigmine* (WHO, 2015).

Descriptive statistics by originator drugs, imports, and generics are presented in Table 2.2. The statistics show the importance of OTC advertising plays for generic drug manufacturers. On average, 48 percent of originator firms and 67 percent of generic firms invest in advertising. However, the amount of advertising stock differs substantially: originators show an average advertising stock of €2.2m and generic firms of €7.3m, importers advertise substantially less with a stock of about

[6] Dubois, Griffith, and O'Connell (2014) assume a depreciation rate of .25 per month, Berndt and Donohue (2008) of .2 per month and Azoulay (2002) of .05 per month. Alternatively, the depreciation rate can be estimated by a grid search which best fits the data, for example, Ling, Berndt, and Kyle (2002); Berndt, Pindyck, and Azoulay (2003); Lakdawalla, Sood, and Gu (2013). This procedure estimates market share equations with step-wise alternating depreciation rates and selects the depreciation rate that minimizes a measure of the model fit, e.g., mean squared errors. Results for optimal depreciation rates from this method are from 30 percent per year to 13 percent per month. I abstract from the grid search method because the model fit of a reduced-form market equation is not in the focus of this paper.

[7] For example, estimations with depreciation rates of .2 and .3 show very similar results in magnitude of the advertising coefficient.

Table 2.2: Summary Statistics by Type of Drug

Drug type	Originator	Import	Generic	All
N	588	1,547	3,107	5,242
Advertising [%]	48	47	67	59
	(50)	(50)	(47)	(49)
Advertising stock [€, m]	2.26	.07	7.30	4.94
	(4.74)	(.08)	(11.85)	(10.31)
s_{jt} [%]	7.80	.44	1.01	1.60
	(5.97)	(.91)	(1.80)	(3.33)
Price [€/DDD]	2.62	3.19	.42	1.49
	(1.5)	(2.12)	(.23)	(1.81)
Firm [N]	6.00	8.18	26.8	2.49
	(.00)	(3.08)	(4.05)	(9.89)
Patented [%]	71	76	-	30
	(45)	(43)	-	(46)

Notes: This table displays Alzheimer's disease drug data by type (originator, import, generic) from Jan 2004 to Dec 2010. Own calculations with data from IMS Health and Nielsen Media Research. Std. dev. in parentheses.

€70,000. Importing firms focus on trade with high-price on-patent products and, to my knowledge, there is no importing firm marketing OTC products. However, some firms also import medical equipment which they might advertise sparsely.[8]

Most originators' and imported originators' drugs (71% and 76% respectively) are sold in markets under patent protection. This market structure results in almost eightfold higher prices for originators' drugs than those of generic manufacturers. For the latter, there are on average 26 competitors in the molecule market.

Table 2.3: Monthly OTC Advertising

Firm	Mean [€]	Min [€]	Max [€]
Klosterfrau	4,978,668	458,345	14,600,000
Novartis	2,709,205	370,886	6,035,431
Schwabe	2,137,257	176,662	4,099,485
Hexal	1,772,860	116,966	6,510,396
Spitzner	1,574,603	11,506	3,986,249
Ratiopharm	1,461,147	83,859	4,135,006
Stada	849,239	21,160	2,556,131
Sandoz	412,636	0	2,018,179
Salus Pharma	317,506	6,771	1,234,252
Merz	230,945	0	1,207,864
Verla Pharm	336,121	774	1,107,999
Bionorica	126,439	0	1,982,847
Betapharm	91,595	0	1,477,524
UCB	41,452	0	350,921
Hevert	28,555	0	481,901
Eurim-Pharm	19,683	0	69,449
Aliud Pharma	18,527	0	399,254
ABZ Pharma	15,428	0	34,234
CT Arzneimittel	14,382	0	54,532
Janssen-Cilag	13,937	0	364,116

Notes: This table presents the top-20 advertising firms in the German Alzheimer's Disease Drug Market from 2004 to 2010. Statistical means of mean, min, and max are per period. Own calculations with data from Nielsen Media Research.

[8] Since billboards are included in our advertising, for example, the sponsoring of local sports events might also be reflected in the advertising expenditures.

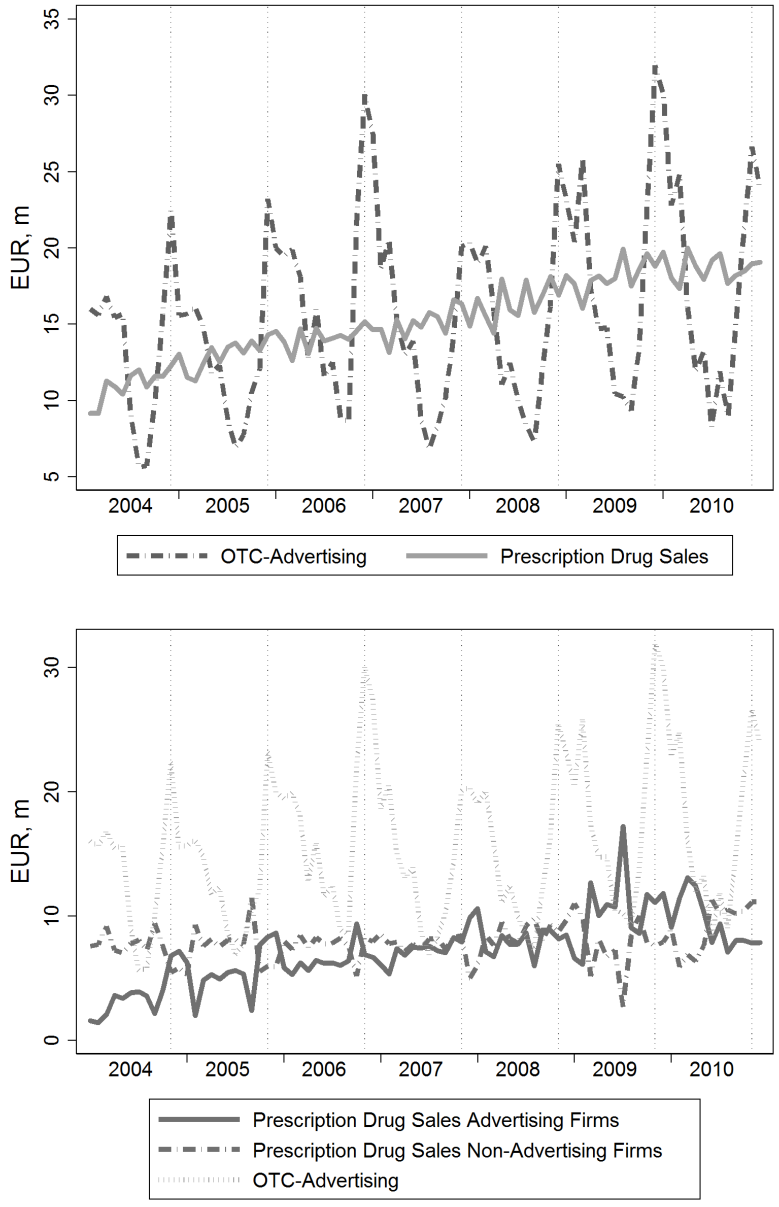
Table 2.3 presents the descriptive statistics for monthly OTC drug advertising expenditures for firms in the Alzheimer's disease drug market from 2004 to 2010. The OTC firm *Klosterfrau* spends, on average, almost €5m per month on advertising, followed by the originators *Novartis* and the OTC firm *Schwabe*. Firms tend to adjust advertising to market dynamics. The table shows a large variance of DTCA expenditure across firms and over time. Some firms invest only in selected months. For example, the firm *Sandoz* has zero expenditure in some months while more than €2m in others. To incorporate the effect of brand-name reputation on consumers' demand patterns, I use advertising stocks which have a longer-lived effect than monthly expenditures (Dubois, Griffith, and O'Connell, 2014).

Figure 2.3 presents OTC drug advertising and prescription drugs over time. The upper graph shows a strong seasonal trend of aggregated monthly advertising: expenditures peak in fall (November) when a colder season starts and colds are a common phenomenon.[9] Advertising seems to be correlated with seasonal demand pattern in the OTC market. Total advertising expenditures increase over the years 2004 to 2010. Sales of AD prescription drugs do not show seasonal demand shocks. Alzheimer's disease drug sales are also increasing over time but overall sales do not seem to be affected by monthly peaks in advertising expenditures. The lower graph in Figure 2.3 differentiates Alzheimer's prescription drug sales by firms that invest in advertising (solid line) and non-advertising firms (dashed line). Sales of advertising firms increase during peaks advertising periods. Sales of non-advertising firms show a reverse trend. The pattern is not that clear from 2009 onward. However, two advertising peaks in Nov 2008 and Mar 2009 correlate with two lagged peaks in sales of advertising firms in mid-2009. The observed advertising waves are common in many consumer packaged goods industries and are referred to as *pulsing strategy*, whereby advertising peaks within a few weeks are followed by a period of low or zero advertising (Dubé, Hitsch, and Manchanda, 2005). I use the seasonality of OTC sales and advertising to create instrumental variables for the reduced-form and the structural demand estimation, as explained in section 2.3.3.

Individual-level purchase decisions and advertising exposure, e.g., number and length of watched commercials, would allow me to identify the effect of advertising spillovers directly. I assume an evenly distributed advertising exposure which is constant over time. The elderly, as the most frequent consumer of AD drugs, show more homogeneous media consumption and are unlikely to change their behavior over time. In addition, individual-level purchase and media exposure data are rarely

[9] A second, smaller peak can be identified for spring (March) when hay fever and, again, colds are common.

Figure 2.3: Prescription Drug Sales and OTC Advertising



Notes: The upper graph shows monthly prescription drug sales in the Alzheimer's disease market and advertising expenditures in the OTC market from Jan 2004 to Dec 2010. Vertical lines indicate Novembers, the months when spending peaks each year. The lower graph shows sales of advertising firms and non-advertising firms, and advertising expenditures. Data: IMS Health and Nielsen Media Research.

available. I assume media exposure to be exogenous and rule out that patients who search for prescription drug information are more exposed to OTC advertising.

As a first step of analysis, I investigate the link between sales and advertising expenditures descriptively. The upper picture in Figure 2.4 graphs yearly advertising expenditures in the OTC market over time, AD drug market sales of advertising firms, and AD drug market sales of firms that do not advertise. Advertising expenditures and sales of firms that advertise show an increasing trend between 2004 and 2010. Sales of firms that do not advertise are constant over time.

The bottom picture in Figure 2.4 graphs market shares of advertised vs. non-advertised drugs. Market shares are calculated based on yearly sales and shows an increasing sales trend for advertising firms. Very similar patterns can be shown for means based on sold quantities. Although causal links cannot be made from this graph the positive correlation between OTC advertising and sales or market shares is a first sign of advertising spillovers. To investigate this link in more detail section 2.3.3 presents a reduced-form analysis and section 2.4 a full structural model of demand and supply.

2.3.3 Instrumental Variables and Reduced-Form Evidence

This section evaluates whether spillover effects from OTC advertising into the Alzheimer's disease prescription drug market exist and, if so, how they influence sales and market shares. The overall effect of brand-name advertising spillovers is unknown a priori.

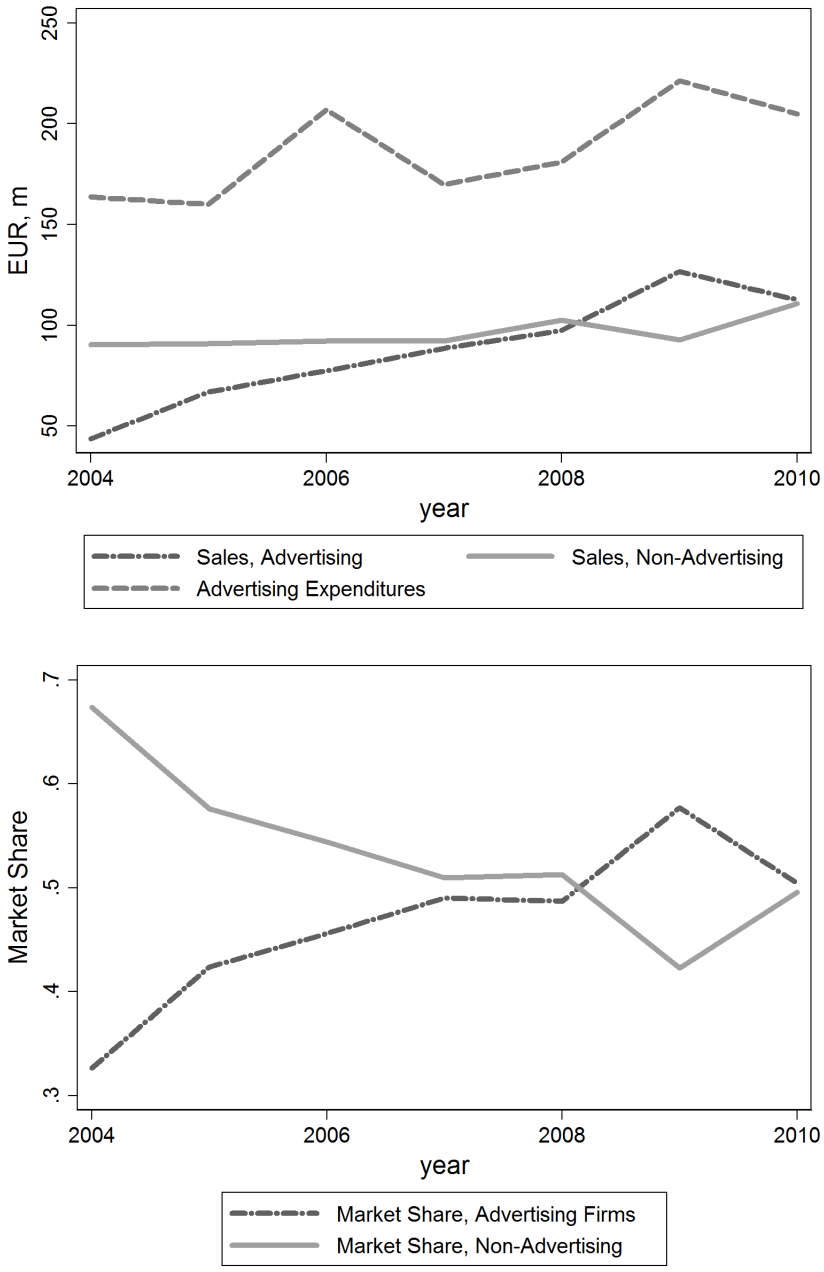
The analytic framework is straightforward and similar to Dave and Saffer (2012). For the reduced-form estimation, sales of product j in time t, S_{jft} are a function of advertising of firm f, a_{ft}:

$$\ln S_{jft} = \omega \ln a_{ft} + \psi_t + \chi_{jf} + \epsilon_{jft} \tag{2.2}$$

where time fixed-effects are captured by ψ_t and product fixed-effects by χ_{jf}. ϵ_{jft} are error terms. S_{jft} are measured in €.

If firms invest in OTC advertising to strategically influence prescription drug sales the endogeneity of advertising poses difficulties for identification. Detailing (physician-directed advertising) is unobserved and potentially correlated with drug sales and consumer-directed advertising. A priori, the direction of the IV bias is not clear: while unobserved firm strategies lead to an underestimation of the coefficient, the omitted variable bias might inflate OLS results. I reduce endogeneity with an

Figure 2.4: Sales and Market Shares of Advertising vs Non-Advertising Firms



Notes: The upper graph shows sales of advertising and non-advertising firms in the AD drug market between 2004 and 2010. The bottom picture displays market shares of advertising and non-advertising firms in the AD drug market from 2004 to 2010. Data from IMS Health and Nielsen Media Research.

IV approach where instruments take advantage of seasonal OTC advertising. The seasonality of common illnesses, like colds, drives demand and advertising in OTC markets, as described in Figure 2.3. I assume that the main driver of OTC drug market advertising is OTC drug market seasonality. In the same figure it is shown that overall monthly sales of AD drugs do not follow seasonal trends.

Since this study focuses on the effect of advertising stocks on drug demand, my instruments need to account for the long-lasting effects of advertising. I approximate the distance to the last November by constructing a stock of seasons. This variable is calculated on the firm-level and captures the number of *peak advertising seasons* in which a firm is in the market. The variable captures the number of times firm had the possibility to advertise its brand name in the past. By the same rationale, as the dummy variable season is correlated with monthly advertising expenditures, the stock of seasons is correlated with the stock of consumer-directed advertising. Formally, I define seasonality dummy variables which equal one in November and zero otherwise. The stock of seasons is created by a sum over the seasonality dummy variable with a depreciation rate of 10 percent per month. Both measures – season and stock of season – are independent of the error terms of prescription drug sales in Equation 2.2. There is no reasonable explanation as to why seasonality or the stock of seasonality (the depreciated stocks of Novembers) would have any explanatory power for the stock of detailing, the unobserved variable.

Table 2.4, columns (FE) and (IV) show the effects of advertising on sales. Results of the first-stage estimation are provided in the last column. The specification controls for product fixed-effects and instruments for advertising in column IV. Results indicate a statistical significant positive effect of advertising on sales: a 10 percent increase in advertising stocks increase sales by about 1.1 percent.

Moreover, the effects of OTC advertising on market shares are very similar: a 10 percent increase in advertising is associated with an 1 percent higher market share. The coefficients double when instrumenting for advertising expenditures. Estimations with a binary advertising variable as an explanatory variable yield very similar results. The complete list of results are available from the author upon request. Results are similar for a larger dataset, the positive spillover effect is persistent across different drug markets. I estimate the reduced-form equation (2.2) with data on oral anti-diabetics, anti-epileptic, and AD drugs. Results are presented in Appendix 2.8. I find in the descriptive analysis and in the reduced-form results suggestive evidence that umbrella branding has positive effects on sales and market shares. The results do not allow statements about consumer surplus and welfare. Therefore, I turn to a full structural econometric model in the next section.

Table 2.4: Reduced-form Evidence of Advertising on Sales

	Sales (€, ln)		first stage
	FE	IV	Advertising
Advertising (stock, €, ln)	.072***	.11***	
	(.01)	(.03)	
Season (stock)			4.50***
			(.42)
Constant	7.94***	7.56***	5.97***
	(.18)	(.35)	(.53)
Product FE	yes	yes	yes
Time FE	yes	yes	yes
N	5,242	5,242	5,242
R^2_{adj}	.91	.90	.98
$F-test$			109.97

Notes: The columns Sales present the effect of advertising (stock) on sales in €. Market Share columns present the effect of advertising (stock) on market shares. Instrumental variables for advertising stocks are the stocks of season (columns IV). Robust standard errors in parentheses. * $p < .10$, ** $p < .05$, *** $p < .01$.

2.4 Economic Model

The structural model analyzes the effects of umbrella branding on prescription drug demand. The demand model allows individual advertising spillovers from OTC markets on consumers' utility and captures individual price-sensitivity. On the supply side, I assume oligopolistic competition, calculate elasticities, margins and marginal costs. In the counter-factual analysis, I calculate equilibrium outcomes – like price, quantities, and consumer surplus – in a market without advertising spillovers and make a comparison to the status quo.

2.4.1 Pharmaceutical Demand

This section models demand and allows advertising spillovers from OTC advertising on patient's utility and prescription drug demand. Drugs are differentiated by observable characteristics like active ingredients or package sizes. The demand model captures vertical product differentiation by product fixed-effects. At the same time, some consumers have a preference for specific drugs. Horizontal differentiation is allowed by an idiosyncratic error term. I estimate a random coefficient logit demand model which accommodates heterogeneous consumers and allows identifying realistic substitution patterns (Berry, Levinsohn, and Pakes, 1995).

The decision to purchase a drug is not straightforward. Demand structures are complex and several parties are involved. Aggregate data, like in this study, include the preferences of all decision makers during the purchasing process. For example, patients might be covered by insurances and rely on physicians recommendations. Physicians might have their own preferences for particular brands or active ingredients. And patients might respond differently to advice from physicians or pharmacists. I assume that patients, given individual insurance coverage, maximize utility jointly with their physician and pharmacist by selecting one product from the $(J+1)$ choice set. Reimbursement for physicians does not depend on the number of prescriptions or on drug prices, they have incentives to prescribe drugs that are effective or which they believe to be effective. Regulation weakly incentivizes doctors to take drug prices into account. Pharmacists hand out the indicated drug on the prescription or substitute it if the drug is not in stock or not wanted by the patient. However, their potential to switch drugs without the confirmation of the doctor or the patient is limited. Pharmacists incentives depend weakly on prices, their reimbursement is a fixed fee and is 3 percent of the list price. My model captures heterogeneous demand parameters in a random coefficient and is, due to its

flexibility, a particular good fit to estimate pharmaceutical demand from aggregate data (Dubois and Lasio, 2014).

The decision of patient $i = \{1, ..., I\}$ to buy drug $j = \{1, ..., J\}$ is the result of utility maximization in time $t = \{1, ..., T\}$. In the German pharmaceutical market, prescription drug advertising is prohibited. Firms cannot provide information on new treatments or the product characteristics of prescription drugs. However, patients consume the advertising of OTC drugs, including information on brand names. Patients have two options to influence drug consumption. First, patients may believe in the superior efficacy of a particular brand name, maybe due to advertising, and might ask their doctors to prescribe a product from a specific brand. Physicians' prescription behavior is shaped by patients' requests (Berndt and Donohue, 2004; Soumerai, McLaughlin, and Avorn, 1989; Kravitz, Epstein, Feldman, Franz, Azari, Wilkes, Hinton, and Franks, 2005). Reports from the US state that 78 percent of primary care physicians are asked by their patients for specific drugs which they have seen directly advertised (ISMP, 2007). Most likely, the effect is smaller for advertising spillovers. Second, patients could choose a particular brand (or package) in the pharmacy if alternatives are available. Both choice options can be driven by advertising spillovers.

Patients' utility is modeled in the spirit of Lancaster (1971), which means that individual preferences depend on product characteristics. Consumers maximize utility over bundles of characteristics. Utility is defined as:

$$u_{ijft} = -\alpha p_{jt} + \sigma p_{jt} \nu_{ijt} + \gamma a_{ft} + \beta X_j + \xi_{jt} + \epsilon_{ijt}, \tag{2.3}$$

where the advertising of firm f in the OTC market is denoted a_{ft}, price of product j is p_{jt}, X_j are drug characteristics, ξ_{jt} are unobserved effects on utility, and ϵ_{ijt} are a consumer-product-specific error terms. Individual (dis-)utility for prices is captured by the term $\sigma p_{jt} \nu_{ijt}$. Utility can be decomposed into an individual specific part, $\sigma p_{jt} \nu_{ijt} + \epsilon_{ijt}$, and the mean utility which is the same for all patients: $\delta_{jft} = -\alpha p_{jt} + \gamma a_{ft} + \beta X_j + \xi_{jt}$. Then, utility can be summarized to:

$$u_{ijft} = \delta_{jft} + \sigma p_{jt} \nu_{ijt} + \epsilon_{ijt}. \tag{2.4}$$

The time-invariant drug characteristics, X_j, include observable drug characteristics, for example, active ingredient or brand name. I control for time-invariant unobserved drug characteristics by product fixed-effects. The unobserved part of utility, ξ_{jt}, is observed by firms and patients, but not by the econometrician. Since the model incorporates product and time fixed-effects, the unobserved part of utility

can be re-defined as the product-time-specific deviation, $\Delta\xi_{jt}$. Advertising, a_{ft}, enters as a state variable which consists of current and past advertising expenditures. Patients observe product attributes, including prices and advertising.

Prices, p_{jt}, are manufacturers' prices per defined daily dose (DDD).[10] They are the more accurate variable in terms of decision making although consumers bear only co-payments, at a fraction of the list prices. Co-payments are a kinked function of manufacturer prices. Also, manufacturer prices are the strategic variable of firms. Moreover, all parties involved, such as physicians, health insurances, and pharmacists, base their decision (partially) on manufacturer prices. The random coefficient allows heterogeneous individual specific preferences for prices.

In the context of BLP demand estimations, most authors define advertising as part of consumers' utility, for example, Murry (2015) for automobile demand, Nevo (2001) for cereals, or Chintagunta (2002) for analgesics. Ignoring advertising as a product characteristic in discrete-choice demand estimations leads to biased price coefficients and wrong predictions if advertising is a strategic variable, e.g., in merger simulations (Tenn, Froeb, and Tschantz, 2010).

Assuming utility maximization and the error term ϵ_{ijt} to be independently and identically extreme value type I distributed,[11] the choice probability of drug j for consumer i in time t is:

$$s_{ijft}(X, p, a; \theta) = \frac{\exp(\delta_{jft} + \sigma p_{jt}\nu_{ijt})}{1 + \sum_J \exp(\delta_{jft} + \sigma p_{jt}\nu_{ijt})}, \tag{2.5}$$

where $\theta = [\alpha, \beta, \gamma, \sigma]$. The assumption that ν is distributed with p.d.f. dP_ν allows to sum up individual choice probabilities and result in the market share equations:

$$s_{jft}(X, p, a; \theta) = \int_{\nu_t} \frac{\exp(\delta_{jft} + \sigma p_{jt}\nu_{ijt})}{1 + \sum_J \exp(\delta_{jft} + \sigma p_{jt}\nu_{ijt})} dP_\nu(\nu_t). \tag{2.6}$$

Section 2.4.2 describes in more detail the numerical solution of the integral 2.6 and the role of unobserved characteristics, ξ_{jt}.

[10] Although the use of manufacturers prices does not allow to calculate traditional consumer surplus I calculate demand-side surplus as an approximation.

[11] Logit demand models (or nested logit demand models) are simplified versions of the random coefficients models and assume $\sigma p_{jt}\nu_{ijt} = 0$. Estimates for utility under the assumption of a simple logit error term are presented as a benchmark case in section 2.5 and depend on the linear mean utility and on the error term: $u_{ijft} = \delta_{jft} + \epsilon_{ijt}$.

This logit model includes an option *not to buy Alzheimer's disease drugs* which is a composite outside good. The outside good includes the option to buy other treatments, such as cognitive training applications or personal memory training, and it has a normalized indirect utility $u_{i0t} = \epsilon_{i0t}$.

The total market size, M, is calculated by daily doses potentially consumed by all Alzheimer's disease patients per month. As the main risk factor for Alzheimer's disease is age, I collected historic age-specific prevalence rates from the German College of General Practitioners and Family Physicians (Degam, 2008) and the European Collaboration on Dementia Project (Eurocode, 2015) to determine the number of patients per month. About 5 percent of the population aged over 65 and 20 percent of the population aged over 80 are diagnosed with dementia, whereof about 65 percent are associated with the Alzheimer's disease (Degam, 2008; Eurocode, 2015). The total market size increased from about 900k to 1.1m patients from 2000 to 2010 and results in about 30m potentially consumed DDD per month. The actual market size in my data is smaller due to non-diagnosed or non-medically treated patients. To choose a broader/narrower definition of the total market size does not affect the estimated coefficients from the demand estimation but result in proportionally lower/higher demand elasticities.

2.4.2 Identification and Estimation

The estimation strategy for the demand model in 2.4.1 follows the algorithm of Berry, Levinsohn, and Pakes (1995) and extends and modifies it in several dimensions (Reynaert and Verboven, 2014; Hess, Train, and Polak, 2006).

I address the endogeneity of the structural model by using instrumental variables and estimate the model with Generalized Method of Moments (GMM). My moment condition relates the structural error term, ξ_{jt}, and a set of instrumental variables:

$$E[\xi_{jt}|X_{jt}(\theta), Z_{jt}], \tag{2.7}$$

where $X_{jt}(\theta)$ contains all observable characteristics and Z_{jt} are instrumental variables which I explain in more detail in the following.

First, I focus on the identification of σ. The random coefficient reflects the variance of the taste distribution across consumers' unobserved taste shocks. Variation of sales over time and changing choice sets (due to entry and exit) help to identify the random coefficient (Sovinsky, 2008). Additionally, I use optimal instruments in the sense of Chamberlain (1987), namely the expected value of derivatives of the

product-specific unobserved quality with respect to the random coefficient parameter σ:

$$z_{jt} = E[\frac{\partial \xi_{jt}(\alpha, \beta, \gamma, \sigma)}{\partial(\sigma)\prime}|x_{jt}] \tag{2.8}$$

I follow the approximation of optimal instruments of Reynaert and Verboven (2014) to calculate the instruments. I predict prices from a first-stage estimation with instrumental variables, Z_{jt}, and calculate derivatives of the mean utility with respect to the variance coefficient σ in the form $\frac{\partial \delta_{jft}(\hat{s_{jft}}, \sigma)}{\partial \sigma}$.

A second concern are potentially endogenous advertising expenditures. Advertising expenditures in the market for OTC drugs are driven by demand patterns that depend on seasonality, like flu and colds. I instrument for OTC drug advertising and exploit the seasonality of OTC drug markets, as explained in section 2.3.3.

Third, I use pharmaceutical prices for Alzheimer's disease drugs from another country, Denmark, as instrumental variables for prices. Nevo (2001) applies Hausman-style IV in the BLP framework, and Berndt, Pindyck, and Azoulay (2003) in pharmaceutical markets. This approach assumes that prices in different geographical markets are driven by common costs and are independent of country-specific demand shocks. The prices of all authorized pharmaceutical products marketed in Denmark are publicly available at `http://medicinpriser.dk/`. I replace the Danish drug price with means of therapeutically equivalent products if the same product is not available in Denmark.

Fourth, in order to utilize instruments that are correlated with prices but not with unobserved quality, I construct the statistical means of competitors' products characteristics (Berry, Levinsohn, and Pakes, 1995). Product fixed-effects fully account for the time-invariant correlation between prices and unobserved characteristics (Nevo, 2001). For time-product-specific unobservables, $\Delta\xi_{jt}$, I use traditional BLP-style instruments. The main assumption is that competitors' product characteristics – and, in particular, the product's location in the characteristics space – are exogenous. Endogenous quality choice of firms, e.g., the choice of product characteristics (Crawford, 2012), is not an issue in the pharmaceutical industry since products are either an outcome of an uncertain investment in research or due to regulatory changes, e.g., patent duration. Specifically, I include the mean DDD per package of all competitors in the active ingredient class, the mean product age of all competitors, the mean package size of all competitors, and quadratic polynomials of all variables.

Tests of the set of instrumental variables in the first stage confirm their strength, e.g., F-values of excluded instruments are 33.46 (prices) and 34.89 (advertising).

Also, the tests for joint instrument significance are above the critical value of ten (Stock, Wright, and Yogo, 2002). The demand model is estimated with monthly product-level data on all AD drug sales in Germany from 2004 to 2010. The sample includes 106 products marketed by 54 firms. The market share from Equation 2.6 need to be calculated numerically.[12]

2.4.3 Supply Model

I model the supply of prescription drugs as an oligopoly game where firms strategically choose prices and advertising expenditures. This analysis abstracts from entry and exit considerations and takes market structure as given.[13]

The oligopoly models of imperfect competition seem to be a good fit for therapeutic drug markets where patented and generic drugs compete for market shares (Dubois and Lasio, 2014; Kaiser, Mendez, Rønde, and Ullrich, 2014). Also, originators compete with imported drugs (Duso, Herr, and Suppliet, 2014). The supply side of drug markets is characterized by high (sunk) fixed costs for research and development and moderate costs of production, approval, and advertising (DiMasi and Paquette, 2004).

Firms maximize their profits by setting prices in the prescription drug market and by defining their advertising expenditures. The latter are freely set by firms depending on their OTC drug portfolio, and due to strategic considerations. If firms internalize the spillover effects of OTC advertising into the prescription drug market, OTC advertising becomes a strategic variable for profit maximization in the prescription drug market. The German pharmaceutical market is characterized by free price-setting during my data period. However, the reimbursement policies of the public health insurances, such as reference pricing or co-payments, set incentives for price competition in off-patent markets.

I assume advertising to be a fixed cost of production which is sunk after investment. Firms decide each period to increase their advertising stock. Advertising stocks are modeled as the geometric sum of current and past advertising expenditures with a depreciation rate of .1. The decision to invest in advertising expenditures recurs every period. In the following, supply is modeled as a static game.[14]

[12] I use 5,000 pseudo-random draws using Modified Latin Hypercube Sampling (Hess, Train, and Polak, 2006). Several starting values confirm the results.

[13] In this sample only generics and imports enter the market, which indicates regulation to be the main driver of market structure, e.g., patent duration or reference pricing.

[14] A static framework is also estimated in Murry (2015) and Sovinsky (2008). Theoretical dynamic considerations are presented in Cohen and Rabinowitz (2013); Shapiro (2014); Dubois, Griffith, and O'Connell (2014).

Firms' overall profits depend on revenues from all marketed products, including OTC drugs and non-medical drugs. In this paper, I model firms' revenues from the Alzheimer's disease market. The market consists of F firms, each of which markets a subset $\mathcal{F}_f$ of the $j = \{1, ..., J\}$ drugs in market $t = \{1, ..., T\}$. The profit functions of multi-product firm's f over prescription drugs are denoted:

$$\Pi_{ft} = \sum_{j \in \mathcal{F}_{ft}} (p_{jt} - mc_{jt}) M_t s_{jft}(\boldsymbol{p_t}, \boldsymbol{a_t}) - exp_{ft} - C_f, \tag{2.9}$$

where p_{jt} is the price of product j and mc_{jt} the marginal costs of the same drug. The vectors of advertising stocks in time t are denoted by $\boldsymbol{a_t}$ and exp_{ft} presents the advertising expenditures of firm f. The vectors of all prices in time t are denoted $\boldsymbol{p_t}$. Market shares of products j are given by $s_{jft}(\boldsymbol{p_t}, \boldsymbol{a_t})$, total market size is denoted M_t, and C_f are fixed costs of production. Note that market shares are a direct function of the vectors of all prices, $\boldsymbol{p_t}$, and of all advertising stocks, $\boldsymbol{a_t}$, in time t.

After observing demand factors, firms maximize revenues by setting optimal prescription drug prices and advertising expenditures. In a pure-strategy Bertrand-Nash equilibrium, under the assumption of strictly positive support, every price for product j must satisfy the first-order condition:

$$s_{jft}(\boldsymbol{p_t}, \boldsymbol{a_t}) + \sum_{k \in \mathcal{F}_{ft}} (p_{kt} - mc_{kt}) \frac{\partial s_{kft}(\boldsymbol{p_t}, \boldsymbol{a_t})}{\partial p_{jt}} = 0. \tag{2.10}$$

By definition, products are substitutes, cross-price derivatives are negative, and $(p_{kt} - mc_{kt})$ are markups on marginal costs. The assumptions about the industry's code of conduct in the pharmaceutical industry allow to derive markups and marginal costs for every product. I use the first-order condition of prices for simulation and marginal costs as starting values for numerical optimization.

2.4.4 Simulation

In this section, I explain how to quantify the welfare effects of umbrella branding and advertising spillovers from OTC drug markets on prescription drug markets by comparing the equilibrium without advertising spillovers to the status quo. In the following, I consider a counter-factual scenario where the effects of umbrella branding are zero. This assumption allows to calculate the value of advertising by comparing two market outcomes. Such a scenario is highly stylized but not unre-

alistic. In practice, such an approach would imply plain packaging of prescription drugs without any printed brand names.[15]

In my model, plain packaging for prescription drugs would still allow brand-name advertising for OTC drugs. However, decisions on advertising expenditures would only be relevant for the OTC markets and would not need to be modeled in the counter-factual market of prescription drugs. Without advertising, the set of strategic variables in the prescription drug market is limited to prices. In the new equilibrium without spillovers, advertising affects neither patients' utility nor firms' set of strategic variables. In line with previous research, other variables are assumed to be unaffected by the policy, including marginal costs (Nevo, 2001) and physician-directed advertising like detailing. These assumptions hold in the short run because firms cannot immediately adjust product portfolios. However, firms adjust their marketing strategies in the longer run. For example, if firms increase physician-directed advertising expenditures due to the ban of consumer-directed advertising, I would overestimate positive effects on demand.

Formally, the new price equilibrium, denoted by $\boldsymbol{p_t^0}$, must fulfill for all products j at time t the first-order conditions:

$$s_{jft}(\boldsymbol{p_t^0}, 0) + \sum_{k \in \mathcal{F}_{ft}} (p_{kt} - mc_{kt}) \frac{\partial s_{kft}(\boldsymbol{p_t^0}, 0)}{\partial p_{jt}} = 0, \tag{2.11}$$

where advertising stocks are zero, $\boldsymbol{a_t} = 0$. Market shares for product j at time t are given by:

$$s_{jft}(X^0, \boldsymbol{p_t^0}, 0; \theta) = \int_\nu \frac{\exp(\delta_{jft}^0 + \sigma p_{jt}^0 \nu_{ijt})}{1 + \sum_J \exp(\delta_{jft}^0 + \sigma p_{jt}^0 \nu_{ijt})} dP_{\nu_t}(\nu_t), \tag{2.12}$$

where $\boldsymbol{a_t} = 0$ and prices are optimal prices in the non-advertising state, $\boldsymbol{p^0}$. The set of product characteristics, X^0, does not contain advertising stocks. For the counter-factual price equilibrium, I solve for equations 2.11 and 2.12 numerically.

In the following, I approximate the demand-side surplus. Since patients are not fully exposed to the full price and the demand side of pharmaceuticals is also influenced by physicians, pharmacists, and health insurances, traditional consumer

[15] Most countries have enacted laws or guidelines for pharmaceutical packaging and labeling. For example, policy-makers focus on brand-name extensions to avoid confusing information (FDA, 2014). Since plain packaging is mandatory for tobacco products in selected countries, for example in Australia since 2011, some drug companies are worried about similar regulations for pharmaceuticals (WIPR, 2014).

surplus cannot be calculated. Using the new simulated equilibrium for every period ($\boldsymbol{p_t^0}$ and $\boldsymbol{s_t^0}$) and the estimated demand system, I compute a monetary value of welfare of the advertising ban, the Hicksian compensation variation. The compensation variation can be measured by solving the integral over the differences in maximum expected utilities using numerical simulation (Small and Rosen, 1981; Kaiser, Mendez, Rønde, and Ullrich, 2014):

$$CV_t = \int \frac{1}{\alpha + \nu_{it}} \left[ln \sum_j exp(\delta_{jft}^{pre} + \theta p_{jt}^{pre} \nu_t) - ln \sum_j exp(\delta_{jft}^{post} + \theta p_{jt}^{post} \nu_t) \right] dP_\nu(\nu_t) \tag{2.13}$$

where $\delta_{jft}^{post} = \delta_{jft}^0$ and $p_{jft}^{post} = p_{jft}^0$ are counter-factual equilibrium values for mean utility and prices, respectively. For a more complete welfare analysis, I report revenues and public health insurance expenditures for the two scenarios. The welfare analysis is limited to the AD market. Formally, the change in producer surplus in the AD market is:

$$PS_t = (\boldsymbol{p_t} * \boldsymbol{q_t}) - (\boldsymbol{p_t^0} * \boldsymbol{q_t^0}) \tag{2.14}$$

and $\boldsymbol{p_t}$ and $\boldsymbol{q_t}$ are vectors of all prices and quantities ($\boldsymbol{s_t} * M_t$).[16] Respectively, vectors from the counter-factual scenario are denoted $\boldsymbol{p_t^0}$ and $\boldsymbol{q_t^0}$.

2.5 Results

In this section, I present and discuss parameter estimates from the demand model, elasticities, and counter-factual outcomes. Table 2.5 presents results for Logit demand estimates, for Logit demand using instruments for prices and advertising, and for Logit demand with random coefficients.

Results of the first column in Table 2.5, *Logit-OLS*, have the underlying assumption of homogeneous patient preferences with respect to prices. The price coefficient is negative, indicating a disutility for prices, and the coefficient for advertising is positive and significant. The latter indicates a positive valuation of brand names by consumers. The second column, *Logit-IV*, presents the results for a model that uses instruments for prices and advertising. Controlling for changes in unobserved

[16] Advertising spending, exp_{ft}, affects the demand of all products of firm f, particularly of OTC drugs, and are part of the overall profit function. Since it is impossible to say what part of advertising expenditure is accrued by the AD market, by assumption, $exp_{ft} = 0$ in the AD market. Advertising expenditures are fixed costs and assumed to be sunk.

product characteristics increases the negative price coefficient and the positive advertising coefficient. Both effects are statistically significant. The model is still restrictive and assumes homogeneous patients.

The last column in Table 2.5 show results of the random coefficient model and allows individual-specific disutility for prices, i.e., price sensitivity. Results indicate a mean price coefficient of -3.21. The random coefficient of .6, the standard deviation from the mean product valuation, indicates substantial variation in the price sensitivity. The coefficient for umbrella branding is positive and statistically different from zero.

Price coefficients have the expected signs, advertising coefficients are positive, and both are statistically significant. All specifications are estimated with product and time fixed-effects. To assess the magnitude of the advertising effect, I present elasticities in section 2.5.1.

Table 2.5: Logit and Random Coefficient Logit Demand Results

	Logit Demand		Logit with
	OLS	IV	random coefficients
Price	-.53***	-2.12***	-3.21***
	(.04)	(.16)	(.49)
RC Price			.60***
			(.17)
DTCA	.02***	.14***	.14***
	(.004)	(.03)	(.03)
Constant	-9.97***	-1.70***	-9.94***
	(.17)	(.57)	(.65)
Product FE	yes	yes	yes
Time FE	yes	yes	yes
N	5,242	5,242	5,242
R^2_{adj}	.87	.74	

Notes: Logit IV and Logit with random coefficients use instruments for prices and advertising, F-values of first stage regressions are 33.46 (prices) and 34.89 (DTCA). The estimation RC Logit uses 5,000 modified latin hypercube sampling draws to simulate market shares. Robust standard errors are presented in parentheses; * $p < .1$, ** $p < .05$, *** $p < .01$.

2.5.1 Elasticity

Given the number of draws of individual demand shocks, ns, own-price elasticities of market shares, s_{jft}, with respect to prices, p_{jt}, are calculated by:

$$\varepsilon^{p}_{jkft} \equiv \frac{\partial s_{jft}}{\partial p_{kt}} \frac{p_{kt}}{s_{jft}} = \begin{cases} \frac{p_{kt}}{s_{jft}} [\frac{1}{ns} \sum_{i=1}^{ns} (\alpha_{jt} + \nu_{ijt}\sigma^{opt}) s_{ijft}(1 - s_{ijft})] & \text{if } j{=}\, k \\ \frac{p_{kt}}{s_{jft}} [-\frac{1}{ns} \sum_{i=1}^{ns} (\alpha_{jt} + \nu_{ijt}\sigma^{opt}) s_{ijft} s_{ikft}] & \text{otherwise.} \end{cases} \tag{2.15}$$

The optimal value for σ from the BLP estimation is denoted σ^{opt}. Own- and cross-elasticities of market shares with respect to advertising are calculated by:

$$\varepsilon^{a}_{f\tilde{f}} \equiv \frac{\partial s_{ft}}{\partial a_{\tilde{f}t}} \frac{a_{\tilde{f}t}}{s_{ft}} = \begin{cases} \gamma a_{ft}(1 - \sum_{k \in f} s_{jt}) = \gamma a_{ft}(1 - s_{ft}) & \text{if } f{=}\, \tilde{f} \\ \gamma a_{\tilde{f}t} s_{\tilde{f}t} & \text{otherwise.} \end{cases} \tag{2.16}$$

Advertising elasticities are calculated on the firm level because I observe advertising expenditures by firms. Cross-advertising elasticities are calculated between firms f and $\tilde{f}$. Formula 2.16 shows that advertising elasticities are constrained by variation only across firms and by elasticities proportional to own-firm advertising.

Mean and median own- and cross-price elasticities, and mean semi-elasticities over the three demand specifications, are presented in Table 2.6. The mean own-price elasticity of the random coefficient logit model is -4.38. The estimation simulates heterogeneous patients and their individual valuation of prices. My results are close to estimated own-price elasticities from other random coefficient logit demand models in pharmaceutical markets. Kaiser, Mendez, Rønde, and Ullrich (2014) report mean own-co-payment elasticities of -1.19, Chintagunta (2002) of -2.5, Duso, Herr, and Suppliet (2014) of -6.6 and Dubois and Lasio (2014) of -3.49. My results indicate rather price-sensitive patients. This is not surprising given the fact that almost 70 percent of all AD drugs are sold on generic markets. In Germany, patent-free markets might be more competitive due to reference pricing (Kaiser, Mendez, Rønde, and Ullrich, 2014) and tiered co-payments (Herr and Suppliet, 2012).

Beside patients' price-sensitivity, another driver of price elasticities in logit demand models is the almost linear dependencies of prices and elasticities (Björnerstedt and Verboven, 2012; Nevo, 2001). The problem is even more prevalent in markets with large price differentials. For example, in my data drug prices of originators are on average 2.62 and are more than sixfold of generic prices (0.42). The random coefficient, σ, alleviates the problem by allowing price sensitivity to depend

Table 2.6: Elasticity of Prices and Advertising Spillovers

	OLS		IV		Random Coeff	
	Own-Price	Cross-Price	Own-Price	Cross-Price	Own-Price	Cross-Price
Mean Price	-.78	.004	-3.14	.016	-4.38	.020
Median Price	-.32	.001	-1.28	<.001	-1.99	<.001
Median Advertising	.060	< -.001	.243	< -.001	.243	< -.001

Notes: This table displays the mean, median, and semi-elasticity of own- and cross-price changes over all periods and products between Jan 2004 to Dec 2010. It also displays the median elasticity of own- and cross-advertising changes over all periods. Own calculation with IMS Health and Nielsen Media Research data.

not only on the mean coefficient. Given the large price distribution, median price elasticities might also be an accurate measure – the median own-price elasticity is -1.99. The median own-advertising elasticity, the percentage change of demand when advertising increases, is .24 across all advertising firms.

2.5.2 Welfare Effects of Umbrella Branding

Welfare effects of umbrella branding are calculated by comparing prices, quantities, revenues, and consumer surplus in two equilibria: markets with and without advertising spillovers. By eliminating advertising stocks as a choice variable of consumers and as a strategic variable of firms, I calibrate counter-factual market outcomes without advertising spillovers. Comparison to the status quo allows the identification of welfare effects due to umbrella branding. Recall that advertising is defined as a product attribute. Welfare effects depend on how patients value advertising. Given the positive advertising coefficient, one would expect to see positive effects for consumers and firms after allowing advertising spillovers. Consumers would observe a new characteristic to maximize utility and firms would differentiate their products by advertising.

The key welfare effects shown in Table 2.7 are the following. First, umbrella branding has an impact on the number of treated patients. About 1.8m more daily doses are sold with advertising compared to the same market without advertising. Sold daily doses of generics increase by about 1m, followed by originators and 769k daily doses. The change of 22k in sales for imports is of minor importance. From a health policy perspective, the overall increase in daily doses might have a significant

effect on the health status of the population. In particular, the patient population of under-treated conditions would benefit from more medication. Also the Alzheimer's disease is considered to be under-treated (Sano, Amatniek, Feely, Sinyak, Holton, Ascher, and Finkel, 2005). However, the health status of over-treated patients, e.g., by antibiotics, would be harmed by market expansion for that molecule.

Table 2.7: Welfare Effects of Umbrella Branding

	All		Originators		Imports		Generics	
	Δ	Δ %	Δ	Δ %	Δ	Δ %	Δ	Δ %
Price (mean, €, DDD)	-.016	-.011	-.038	-.014	-.042	-.016	.003	.007
Shares (mean)	.001	.262	.003	.151	<.000	.03	.001	.80
Quantities (sum, 1'000)	1,834	.262	769	.151	22.1	.03	1,042	.80
Expenditures (sum, 1'000)	4,645	.186	3,649	.171	141.1	.049	855	1.12
Revenues (sum, 1'000)	3,387	.177	2,790	.169	103	.047	492	1.31
Consumer Surplus (year)	2,384,479							

Notes: This table presents the effect of umbrella branding calculated by changes from the simulated equilibrium (no advertising spillovers) to the status quo. Absolute changes and percentage changes are reported. Mean values for monthly changes from Jan 2004 to Dec 2010. Estimated parameters of the random coefficient logit model are used to predict the counter-factual equilibrium.

Second, OTC drug advertising spillovers in the demand for prescription drugs increase generic firms market shares by approximately 80 percent, followed by originators with 15.1 percent. In my sample, generic firms and originators possess high stocks of advertising expenditures, on average €4.9m and €2.26m, respectively. Thus, the gains through advertising are accrued by firms that advertise the most. The effect on market shares is small for imports (3 %) with an average stock of €.07m.

Third, the surprisingly high increase in generic market shares is driven by the active ingredient *ginkgo biloba*. This OTC drug is reimbursed by the public health insurance if prescribed by a physician. OTC drugs, like *ginkgo biloba* products, can be directly advertised toward patients. Possibly, the effects of advertising, γ, are stronger because firms actually advertise on the product level. Calculating separate statistics by active ingredients (not reported) shows a fourfold increase of sold drugs with the active ingredient *ginkgo biloba*. Most other therapeutic classes show much more moderate effects. Direct advertising of Alzheimer's disease drugs with the molecule *ginkgo biloba* can have an market expansion effect through advertising spillovers on the drug class (Shapiro, 2014). I test empirically for the effect of the

herbal ingredient by excluding it from the demand estimation. Results are very similar, the advertising coefficient is positive and statistically significant. Since I only observe firm-level advertising expenditures, I cannot disentangle the direct and the umbrella branding effect of *ginkgo biloba*. Firms might have higher advertising expenditures due to marketing of the OTC drugs other than *ginkgo biloba*. If advertising for non-*ginkgo biloba* drugs is driven by seasonality, my results are identified. For example, the firms *Klosterfrau* or *Stada* have large product portfolios which include cold medications. Furthermore, advertising for *ginkgo biloba* seems to be small compared to seasonal OTC markets. The top-10 advertised therapeutic OTC markets do not include dementia drugs. Without having detailed information, the maximum share of *ginkgo biloba* could only be less than 1.8 percent of total OTC drug advertising expenditures (Nielsen Media, 2012).

Fourth, price changes reflect firms' strategic behavior with and without advertising. Overall, price responses to the product attribute advertising are minor, negative for originals and imports, and positive for generics. At first, the results seem puzzling. However, with umbrella branding, generic manufacturers are able to differentiate their products along dimensions other than the pricef. Some generic firms might promote their products as high-quality alternatives and the high advertising expenditures of generic firms need to be recovered, partially by higher prices. Using umbrella branding, originators have a channel through which to market their products as high-quality drugs. Instead of signaling high quality only through prices, firms could signal high quality through advertising expenditures. Also, competition by heavily advertising generics lead to originator's prices decreases with advertising.

Fifth, the increase in daily doses affects public spending. Total expenditures of the public health insurance increase yearly by €665k by allowing advertising spillovers into prescription drug markets. The effect is driven by a 17 percent increase of expenses for originators. Although expenditures for generics more than double, the average yearly costs increase by €122k, a fraction of originators' costs increases. Expenditures of the public health insurance include pharmacy reimbursement and sales tax.

Sixth, on the supply side, firms' revenues increase with advertising by an average of 17 percent. Firms sell more products with advertising and revenues from the Alzheimer's disease drug market increase by €3.3m. Originators' revenues increase by €2.7m and generic firms' by €492k – an increase of 131 percent for the latter.

Seventh, the utility gain of potential consumers can be accumulated to about €2.38m per year. This figure compares to the Alzheimer's disease market which was €223m in 2010. AD drugs become more attractive compared to the outside good. Additionally, original drugs and imported originals become more attractive

with lower prices. Although the public health insurances face higher expenses due to advertising, there might be benefits from an increase in treated (and healthier) patients if diseases are under-treated.

I find that advertising spillovers from OTC markets increase the total quantity of prescription drugs. Expenditures of the public health insurance and patients' utility increase, the share of medically treated patients increase by about 5 percent of the potential market size. Lacking information on the OTC drug market and on more prescription drug markets makes a complete welfare analysis very difficult. I am approximating yearly total welfare in the AD market by adding gains in consumer utility and additional revenues, and subtracting additional health insurance expenditures. Yearly welfare gains in the Alzheimer's disease market are €2,211,194. Welfare effects were approximately 1 percent of the total Alzheimer's disease market size of €223m in 2010.

2.6 Interpretation and Discussion

Using data from the Alzheimer's disease prescription drug market and advertising expenditures from OTC markets, I find that consumer-directed umbrella branding has a significant impact on prescription drug markets. Results of a reduced-form estimation exploit the exogenous seasonality of OTC drug market advertising and finds positive spillover effects. The structural demand model incorporates advertising as a product characteristic. Using the demand estimates, I recover marginal costs, margins, and simulate a counter-factual market equilibrium. Total consumer surplus increases by 2.3m per year, mainly due to more medically treated patients. The overall increase of 1.8m daily doses is equivalent to the treatment of 5 percent more patients.

Under-treated conditions would benefit most from market expansion. Some researchers see Alzheimer's disease as also being under-treated (Sano, Amatniek, Feely, Sinyak, Holton, Ascher, and Finkel, 2005). Further expenditures for additional or higher-priced drugs would be justified by more treated patients. This problem is especially relevant for preventive therapies or for widespread chronic diseases. In these cases, the treatment of an acute outbreak can result in severe conditions and extremely high costs, for example, Alzheimer's disease or diabetes. For pharmaceutical markets, the welfare effects due to market expansion should be evaluated with caution. Some therapeutic markets are already over-treated, such as antibiotics. In this context, market expansion would be harmful to patients. Since the introduction of Medicare Part D, many prescription drugs are now covered by health insurances.

Patients cover minimal co-payments, if any, and are not exposed to the full drug price. Welfare calculation in the presence of intermediates between patients and products, such as health insurances and physicians, is challenging.

Another aspect of this work is the strategic implication for firms. Generic firms in particular might be able to internalize positive spillovers. For some markets, like the AD drug market, the advertising effects might be larger for generic firms than for originators. I observe that generic sales increase by up to 80 percent due to advertising. The effect is smaller for originators. However, originators are more expensive and total expenditures accumulate to €3.6m, compared to €855k for generics. A health policy implication for this market would be to allow advertising for generic drugs in order to increase their market shares.

One caveat of this study is the lack of knowledge of the actual drivers of additional sales. I cannot make statements about total welfare. The debate about pharmaceutical advertising is controversial. Arguments in favor are that DTCA might inform consumers about a new medication and motivate physician visits to treat symptoms (Ching, 2010; Bradford, Kleit, Nietert, Steyer, McIlwain, and Ornstein, 2006; Calfee, Winston, and Stempski, 2002; Berndt and Donohue, 2004). My findings seem to empirically support the market expansion effect of advertising, even for the case of umbrella branding. Benefits from advertising spillovers might also include positive health effects through higher drug compliance (Donohue, Cevasco, and Rosenthal, 2007; Wosinska, 2005). Advertising spillovers can have a very limited effect on therapy compliance because umbrella branding does not deliver any form of information on the product itself.

Other researchers have pointed out more critical views: advertising might provide misleading information on the quality or efficacy, and might motivate people to utilize more products which are expensive but not necessarily of a higher quality (Iizuka, 2004). My results show that advertising leads to increases in generic sales, the lower-priced alternatives in the market. Although generic prices increase due to advertising, the total effect on the expenditures of public health insurance is moderate for generics, compared to expenditures for patented originators. Additional generic sales are also generated by the cost-controlling regulations of public health insurances. Sometimes, health insurances implement direct controls, such as price caps or mandatory substitution. Sometimes, they implement incentives for firms and patients to control costs, such as reference prices. If data limitations were alleviated, the interaction of advertising and market regulation would be a promising venue for future research.

If regulatory institutions are interested in effectively banning advertising or in preventing unintended advertising spillovers they might adapt their institutional design of drug market regulation. Policy-makers could cooperate to adapt guidelines for drug packaging, like the *Federal Trade Commission* (*FTC*) and the *FDA*. If patients are confused by the similarity of product names or by the umbrella branding of a product portfolio, clear guidelines for product packaging and marketing could ultimately assist consumers. The existence of spillovers urges the development of guidelines for drug labeling, for example, the prominent display of active ingredients on the front package label (ISMP, 2007). Reports state that 67 percent of primary care physicians sometimes grant patients' requests for medications that are not clinically indicated (ISMP, 2007). If advertising was more informative, more targeted, and less persuasive it could contribute to a better match between patients and medications. From a theoretical point of view, firms choose their strategies, including advertising, to either maximize or minimize the dispersion of consumers (Johnson and Myatt, 2006). Advertising that persuades consumers and informs them of the product's existence focuses on unambiguous features of the product, targets the mass market, and shifts demand outward. If advertising contains product information, consumers learn about the product and demand rotates. The latter strategy focuses on niche markets (Johnson and Myatt, 2006). Advertising spillovers from OTC to prescription drugs shift demand outward and expands market size, as shown in this study. If umbrella branding allows pharmaceutical firms to differentiate their products at minimal costs an effective ban on advertising would reduce overall welfare (Milgrom and Roberts, 1986).

My findings are potentially relevant to patients, regulators, and firms. The overall benefits of umbrella branding are driven by more consumers buying generic Alzheimer's disease drugs. Consumer surplus also increases because prices for some original drugs decrease with the introduction of umbrella branding. If high prices are a signal of high quality in a world without advertising, firms might decrease prices and invest in advertising when umbrella branding is available. I do not control for the brand-name effects of long-term established brands in the drug market. Some brands, such as *Pfizer*, have been in the market for several decades while others are newly established brand names, e.g., through mergers. To disentangle the effects of established brand names and of advertising is a promising topic for future research.

European pharmaceutical markets are characterized by three types of drugs, originators, generics, and parallel imports. Parallel imports are original drugs legally imported from another European country. This arbitrage trade is facilitated by

national drug price regulation and free trade in the European Union (Duso, Herr, and Suppliet, 2014). I observe minor investments in advertising and very limited effects of umbrella branding for parallel imports. Another interesting research question for future projects would be the impact of the drug advertising of originators on demand for the imported version of the original brand.

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2.8 Appendix

To extend the economic significance, I estimate the reduced-form equation (2.2) with data of all drugs in the therapeutic markets of oral anti-diabetics, anti-epileptic, and AD drugs. Results are presented in Table 2.8. The column IV uses instrumental variables, namely seasonality as in section 2.3.3. Advertising has a positive effect on sales for the OLS and IV specification: a ten percent increase in brand-name advertising increases sales by .7 percent.

Table 2.8: Extension to a Larger Dataset

	Sales (€, ln)	
	OLS	IV
DTCA (€, ln)	.05***	.07***
	(.01)	(.02)
Constant	11.55***	11.37***
	(.15)	(.23)
Product FE	yes	yes
Time FE	yes	yes
N	31,538	31,538
R^2_{adj}	.84	.84

Notes: This table presents results from a reduced-form estimation for all drugs in the therapeutic markets of oral anti-diabetics, anti-epileptic, and AD drugs. Standard errors in parentheses are clustered on the product level. * $p < .05$, ** $p < .01$, *** $p < .001$.

The results hold for a large number of observation and across three distinct drug markets. The magnitude of advertising spillovers are about the same size as for AD drugs. Firms have to invest in DTCA only once to realize spillovers in every pharmaceutical market where firms market their products. Potentially, spillovers create additional revenues in every market where the firm is active. In addition, firms realize revenues from OTC drug markets. The total benefit of spillovers for firms are probably larger than estimated in this paper. This also explains the high advertising expenditures compared to sales in AD drug markets.

Chapter 3

The Welfare Impact of Parallel Imports: A Structural Approach Applied to the German Market for Oral Anti-diabetics

Co-authored with Tomaso Duso and Annika Herr

> *The industry is also characterized by extensive regulation of almost every activity, from product development through manufacturing and marketing. Some of these regulations have unintended consequences as a result of strategic responses by firms.*
>
> — Fiona Scott Morton and Margaret Kyle, 2012, p.762, *Markets for Pharmaceutical Products*

3.1 Introduction

The controversial welfare effects of parallel trade in pharmaceutical markets have been critically debated in health economics and policy (e.g., Ganslandt and Maskus, 2004; Dutta, 2011). The core of this policy debate is the tension between achieving price reductions that directly or indirectly benefit consumers in the short-run and long-run incentivising innovation into new products as well as securing the safety of drugs.

Since most drug manufacturers are active in international markets, both production and R&D activities are typically carried out at the global level. Yet, intellectual property rights (IPR) on active substances are generally exhausted at the national level, which creates entry barriers across geographical (national) markets. These barriers try to eliminate arbitrage gains, which would be possible in pharmaceuticals since the prices for the same drugs differ across countries as a response to heterogeneous national demand and income conditions and as a reaction to different national regulations (Kyle, 2011).

In this context, parallel imports – i.e., a drug made or sold legally in other countries, which is imported without the permission of the intellectual property rightholder (e.g., the patent owner) by licensed trading firms – are expected to generate some downward pressure on price levels. In theory, the welfare effects of parallel trade are ambiguous and depend on the differences in the national price regulations (Bennato and Valletti, 2014; Jelovac and Bordoy, 2005), the patients' preferences (Jelovac and Bordoy, 2005) and the vertical integration of the trade firms (Ganslandt and Maskus, 2007) among other reasons. If the cross-country price differentials do not reflect true discrepancies in the efficiency of production and they are rather the outcome of different regulatory policies, parallel imports may lead to a price convergence that constitutes a mere welfare transfer from consumers in low-price countries to consumers in high-price countries and most likely benefits arbitrageurs (Danzon, 1998). Furthermore, the loss in profits for patent holders may lead to decreased R&D investments (Rey, 2003). However, even from a theoretical point

of view, these mechanisms are not unequivocally clear. Parallel imports might well have positive effects on the innovation intensity due to the different incentives firms and regulators face when IPRs are internationally rather than nationally exhausted (e.g., Bennato and Valletti, 2014; Grossman and Lai, 2008). Hence, the assessment of the welfare effects of parallel trade is essentially an empirical issue. To identify causal effects, however, it is necessary to observe situations where parallel trade is allowed.

To this aim, the process of European integration provides a great policy experiment. The European Court of Justice commonly supports the community-wide exhaustion of IPR which allows free trade within the EU and prohibits the trade of patented products from and to non-European countries.[1] Indeed, drug trade mostly emerges from low-price countries such as Portugal, Spain, and Greece to high-price countries such as the UK, Sweden, and Germany (Kyle, 2011; Grossman and Lai, 2008). In 2012, parallel trade amounted to about €5.3bn in the EU and to €2.9bn (based on ex-factory prices) in Germany (Murray and Weissenfeldt, 2013). The total market shares of parallel imports ranged in 2010 from 24% in Denmark, to 11% in Germany, 10% in the Netherlands, and 7% in the UK (EFPIA, 2013). In the market for patented drugs, parallel imports covered 25% of the sales in Germany in 2010 (Deutscher Bundestag, 2010), whereby Germany is by far the largest European market for pharmaceuticals and the heaviest parallel importer in the EU (Murray and Weissenfeldt, 2013).

Our paper aims at adding to this controversial discussion by analysing the effect of parallel trade in the German anti-diabetics market. We estimate a structural model of demand and supply for a large panel data set containing all oral anti-diabetic drugs sold between 2004 and 2010. We focus on this indication for four reasons: First, changes in demographics and lifestyles made diabetes type 2 one of the most widespread diseases in Western countries. For instance, between 2000 and 2009 the number of German diabetes patients increased by 49% (Köster, Schubert, and Huppertz, 2012). Second, we observe the coexistence of original drugs, generics, and parallel imports across the different active substances. Third, oral anti-diabetics are prescribed exclusively for the treatment of this single disease, which makes a definition of the potential market size easier to identify. Finally, the prescription procedure for a particular drug package can be modelled more easily in this market than in other pharmaceutical markets.

[1] Parallel imported products are generally allowed in Europe and only differ in terms of packaging or colour, as the trading firms have to add package inserts and provide labelling in German either by a new package or by a sticker overlay. As an example, see Figures 3.1 and 3.2.

Figure 3.1: Figure Of The Imported Drug Package Of *Stilnox* Produced By *Sanofi-Synthelabo* And Marketed By *kohlpharma*. Source: Federal High Court Of Justice [Bundesgerichtshof, Decision I ZR 173/04].

Figure 3.2: Figure Of The Original Drug Package Of *Stilnox* Produced By *Sanofi-Synthelabo*. Source: Federal High Court Of Justice [Bundesgerichtshof, Decision I ZR 173/04].

The data that we use are provided by *IMS Health* and entail monthly information on sales, ex-factory prices, and further product characteristics such as package size, producer and re-seller names, and market entry. We model demand through a two-stage nested logit approach (e.g., Berry, 1994; Verboven, 1996; Stern, 1996), where the upper-nest corresponds to the chemical group (ATC4) and the lower-nest corresponds to the active substance (ATC5). This two-level structure based on the chemical groups and active substance covers the most relevant aspects of patient heterogeneity as well as the most relevant decisions' criteria of the physicians and the patients.

We build on Björnerstedt and Verboven (2012) and expand their approach to the estimation of different price coefficients for different chemical groups (Slade, 2004).[2]

While own price elasticities vary across chemical groups and active substances as well as over time, we estimate a mean own-price elasticity of -6.6 and mean cross-price elasticities that range from 5.082 to 0.002. Based on an oligopolistic model of multi-product firms, we then recover the marginal costs and, accordingly, relative markups on prices, which range between 22% and 86% depending on the specific drug type. Using these estimated demand- and supply-side parameters, we then simulate the new equilibrium prices, market shares, and changes in demand-side surplus and producers' variable profits that would result absent parallel trade.[3] According to our estimates, parallel imports strongly decrease the average price of patented drugs by 11% while they only imply a limited increase by 0.7% for the price of generic drugs that are subject to intense competition also without parallel imports. The overall increase in demand-side welfare due to parallel trade is estimated to be €130 million over seven years, which amounts to an increase by around 4% of the total demand side surplus calculated in the market for oral anti-diabetics absent parallel trade. The corresponding decrease in variable profits in Germany due to parallel trade for the manufacturers of original drugs amounts to €125 million over the seven sample years.[4] Parallel importers only appropriate a small fraction (€41 million) of this rent.

[2] For a general discussion on the benefits of alternative modelling alternatives for discrete choice models of demand see also Grigolon and Verboven (2014). However, Björnerstedt and Verboven (2012) conclude that – even in the specifically regulated pharmaceutical industry – the nested logit model seems to be strongly supported for use in competition analysis.

[3] We talk about demand-side welfare instead of consumer welfare because, given the structure of the German health care markets, this surplus is shared among the patients, physicians, and the statutory health care system.

[4] This number must be taken cautiously since our data does not contain information on profits original producers gain by selling their drugs to parallel traders outside of Germany (compare Subsection 3.3.5).

Our study contributes to the growing empirical literature on the effects of parallel imports on prices and welfare, whose results are still controversial.[5] While some of these studies find that parallel trade achieves only limited price reductions (e.g., Ganslandt and Maskus, 2004; Granlund and Köksal, 2011; West and Mahon, 2003), Kanavos and Vandoros (2010) even identify a small tendency of price increases after the entry of parallel imports in six European countries. Kyle (2011) explains the relative small price reductions as the outcome of the strategic reaction of the original producer. Kanavos and Costa-Font (2005) and Enemark, Pedersen, and Sørensen (2006) conclude that in the early 2000s, parallel imports led to rather small cost reductions for the German health insurances but to high losses in market shares and profits for the original producers.[6] Yet, all of these studies are mostly descriptive price or entry regressions and/or based on reduced-form price equations, which neither allow a careful modelling of the complex market structure nor an assessment of the effect of parallel trade on welfare.

Hence, to make a more precise assessment of the welfare implications of different policy interventions, our approach builds on recent developments in the empirical health economic literature that estimates structural models of demand and supply. The most recent studies in this strand of literature analyse the market entry of generic and "me-too" drugs in the U.S. (Ching, 2010; Branstetter, Chatterjee, and Higgins, 2011; Arcidiacono, Ellickson, Landry, and Ridley, 2013; Bokhari and Fournier, 2013). Almost all these papers show that the entry of generic drugs benefits consumers more than it harms the producers by decreasing prices of the former patented drug. Furthermore, there seems to exist substitutability not only across brand-names and generics or "me-toos" of the same molecule but also among different molecules (Branstetter, Chatterjee, and Higgins, 2011; Bokhari and Fournier, 2013). Since parallel imports are not allowed and patented drugs' prices are relatively high in the U.S., comparisons to Europe are difficult.

Probably the papers closest to our study are those by Dutta (2011) and Chaudhuri, Goldberg, and Jia (2006).[7] They model the effects of stricter intellectual property rights on welfare in India. Both measure substantial loss in consumer welfare from patent enforcement and price deregulation but quite limited gains for foreign patent holders. These results cannot be transferred directly to the European

[5] For an overview of studies about parallel trade see the EU Report "Competitiveness of the EU Market and Industry for Pharmaceuticals" (European Commission, 2009).

[6] In an earlier study, Kyle (2007) found fewer market entries of innovative products in low-price countries where parallel import is allowed and concluded that parallel trade indeed hinders innovation activities.

[7] Our results are in line with the conclusions by Méndez (2013) who uses a framework similar to ours to analyze the market for Danish statins.

case since in the EU patent enforcement is so strict that cheaper copies from other producers are not available in markets for patented drugs. Instead, parallel imports of the original drug from low-price to high-price countries exist. Hence, our research adds to this growing literature by looking for the first time at the welfare effect of parallel trade in the largest European market for oral anti-diabetics. Furthermore, it constitutes the first attempt to estimate a structural demand model for the German pharmaceutical market.

The paper is organised as follows. Section 2 describes the institutional details of the regulations in the German drug markets and the characteristics of the market for oral anti-diabetics. Section 3 sets up our modelling strategy, while Section 4 describes our data. Section 5 presents the results of our estimation and simulation. Section 6 concludes with a discussion of the results and their policy implications.

3.2 Diabetes and the German Market for Oral Anti-diabetic Drugs

Diabetes is a metabolic chronic disease in which either the body does not produce enough insulin (type 1 diabetes) or it does not respond to the insulin that is produced (type 2 diabetes). Usually, the disease results in hyperglycaemia, or high blood sugar, and leads to damages of the body's systems, e.g., nerves and blood vessels (WHO, 2013).

The causes of type 1 diabetes are unknown and the disease is unpreventable. The treatment includes medication with insulin. We focus on type 2 diabetes which accounts for 90% of all patients with diabetes (WHO, 2013). Type 2 diabetes differs substantially from type 1 diabetes and its causes include obesity, tobacco use, and physical inactivity. In Germany, 6 to 7 million patients are estimated to have suffered from type 2 diabetes in 2010 and a large number of unknown cases is assumed. Thus, diabetes type 2 is estimated to affect around 8% of the German population (Rathmann and Tamayo, 2012).

The German market for oral anti-diabetic drugs is large. In 2010, it amounted to about €572 million in pharmacy selling prices and €249 millions in ex-factory prices (own calculations). The treatment of type 2 diabetes ranges from dietary nutrition and physical activity to oral anti-diabetic drugs and, in severe cases, insulin. Seven chemical groups of oral anti-diabetics were available between 2004 and 2010 comprising 22 active substances. The drugs either suppress glucose production by the liver (*biguanide*), delay glucose absorption of the blood (*alpha-glucosidase inhibitors*), stimulate the production of insulin (*sulfonylureas*, *glinides*), increase

the physiological function of insulin (*thiazolidinediones*), or decreases blood glucose levels indirectly by increasing incretin levels (*Dipeptidyl peptidase 4 (DPP-4) inhibitors*). Furthermore, a range of drugs that combine groups of active substances (so-called combinations, e.g., *biguanide* and *thiazolidinediones*) were also available in the market. Each chemical group comprises several active substances that can be divided into either off-patent markets with free access for generic products or markets for patented drugs with strictly regulated access. However, independently of the specific regulation of reimbursement and disposal, all firms are free to set prices.

Cost-sharing and the distribution of parallel imports

More than 85% of the German population – around 69.8 million people – are covered by the statutory health insurance system (BMG, 2013). We only consider this group in our analysis. These insureds face a co-payment of 10% per package (minimum €5, maximum €10) on pharmaceutical prices for prescription drugs, which are uniform across all German pharmacies as prices are. Moreover, most off-patent markets are regulated by reference pricing where the patient additionally pays the positive difference of the drug's price to the reference price, if applicable. Thus, off-patent markets face fierce competition by generic drugs and reference pricing (e.g., Herr and Suppliet, 2012). Rebate contracts do not play a big role in our analysis since they only became available in 2008 and not relevant for patented drugs or parallel imports.

In Germany, the distribution of parallel imports is supported by the regulator. Pharmacists need to fulfil a specific quota: the share of total turnover gained by parallel imports per patented active substance has to exceed 5% (BMG, 2013).[8] Furthermore, the parallel imported drug's price has to be at least 15% or €15 below the original product's package price to be considered as a parallel imported drug in the 5% quota. However, in our data, these thresholds are only met by a small fraction of parallel imports and we observe both prices below and above them.

3.3 Empirical Strategy

To empirically analyse the extent of competition in the German market for oral anti-diabetic drugs, we follow the existing literature (e.g., Crawford and Shum, 2005; Dunn, 2012; Dutta, 2011; Kaiser, Méndez, Rønde, and Ullrich, 2013) and derive a demand function from the joint utility maximization of the two main agents – the

[8] Additionally, this must hold for each health insurance and quarter.

patient and the physician – who participate in the decision process.[9] In this sense, the demand-side of our model is a reduced form of a more complex decision making structure. We approximate this process by using a two-level nested logit model described below.

3.3.1 Demand Model

We observe one geographical market (Germany) over $t = 1, ..., 84$ months from 2004 to 2010. For each month, we calculate the potential market size, M_t, as the number of defined daily doses (DDD) for all diabetes patients in Germany. The potential market size is about twice as large as the actual market due to patients that either choose a non-prescription drug or other therapies to treat type 2 diabetes. The following specification of the demand estimation closely follows previous work from Berry (1994); Verboven (1996), and Slade (2004).

Joint utility maximization

The I agents, $i = 1, ..., I$, in each market/month t choose one out of J_t products, $j = 1, ..., J_t$.[10] In our setting, the agent's choice is represented by the joint decision of the two stakeholders: the patient and the physician.

The patient first provides information on her health status and, after discussing with the physician the most suitable chemical group and active substance, she finally chooses which specific product and package to buy at the pharmacy. We expect patients to show price-sensitive behaviour and have a preference for drugs that are fully exempt from co-payments. We also assume that patients respond to prices, as co-payments are a monotonic transformation of them, but to a smaller extent than doctors given the nature of the regulatory system and the limited amount of the co-payments.

The doctor is assumed to mostly decide in the patient's interest with respect to medical needs and other preferences, such as price sensitivity or taste. However, physicians are also assumed to purse their own utility as they are encouraged to consider economic aspects in their prescription behaviour even though they are

[9] Potentially, pharmacists and health insurers also are involved in this decision process, yet their influence in the determination of the demand for specific drugs is expected to be limited.

[10] Discrete choice models such as the nested-logit do not allow modelling of complementary goods. In our context, this might be problematic since a mix of drugs is sometimes prescribed. However, we specifically consider a chemical group which contains drugs combining different groups of active substances. We are therefore able to ease the complementarity problems by defining bundles of drugs which can be seen as substitutes to single drugs entailed in other nests.

not directly punished or compensated based on their decisions. Only if physicians exceed their individual drug budgets do they have to justify it to their supervising organization. Still, they should prefer to prescribe less expensive drugs such as generics (if available) to avoid audits and ease their overall budget constraint.

The model incorporates the option that agents might decide not to buy any drug or/and another product. This so-called outside good $j = 0$ extends the choice set to $J_t + 1$ products. The agent i's conditional indirect utility function for drug j is assumed to be:

$$u_{ijt} = -\alpha_g p_{jt} + \beta x_{jt} + \xi_{jt} + \upsilon_{ijt}, \tag{3.1}$$

where p_{jt} is the price of product j in time/market t, and x_{jt} is the vector of other observed product characteristics, such as the active substance, the strength, or the package size. Among these other characteristics, we also consider whether the drug is exempt from co-payments. This should capture an important aspect of the patients' decision, i.e. the preference not to pay to get a drug. We use a more flexible specification compared to the standard nested-logit model and allow the price coefficients α_g to depend on the characteristics of the product, namely on the chemical groups $g = 1, ..., G$ (Slade, 2004).[11] The first reason for this modelling assumption is that we assume preferences on prices and thus elasticities to differ by different patients' medical needs, severity of illness, medical history, age, etc. which is reflected by the choice of different chemical groups. Second, this approach helps to ease the well-known issue in logit models that elasticities –and thus markups and marginal costs – depend on products' prices in a linear fashion (Berry, Levinsohn, and Pakes, 1995; Nevo, 2000).[12] The vector ξ_{jt} contains characteristics that are observed by the firms, the patients, and the physicians but are unobserved by the researcher and might include brand perception, marketing expenditures, or publicly unknown interactions with other drugs. The random utility terms υ_{ijt} reflect the influence of individual-specific taste. We assume that each agent maximises utility,

[11] In a robustness check, we additionally insert the co-payments into this utility function to try to better disentangle the physician's and the patient's utilities. Yet, this is problematic from a theoretical viewpoint. Moreover, it would induce multicollinearity problems in almost all ATC4 groups. In the only sensible specification, where we do not estimate group-specific price and co-payment coefficients and after controlling for full co-payment exemption, the co-payment variable is not significant while the price is. Therefore, it does seem that the demand side's price sensitivity is mostly due to the physicians' economic incentives as well as patients' preference for full exemption. The results are available upon request.

[12] The linear dependency results in larger elasticities for more expensive products, which is not consistent with economic intuition.

u_{ijt}, given the characteristics of the product. The mean utility of product j in time/market t is:

$$\delta_{jt} = -\alpha_g p_{jt} + \beta x_{jt} + \xi_{jt} \tag{3.2}$$

and the mean utility of the outside good $j = 0$ in each time/market is normalised to zero: $\delta_{0t} = 0$.

Nesting structure

In the market for oral anti-diabetics, there is a natural order of choices, which we exploit in our nesting structure. First, the physician chooses the chemical group and second the active substance suitable to the patients' physical condition (e.g. body weight), individual preferences, medical history, co-morbidities, side-effects, and age. It is well understood that physicians make this choice in a hierarchical order with respect to both across and within chemical groups and active substances. For instance, the guidelines of the National Institute for Health Care and Excellence in the UK clearly advise initiating oral glucose control therapies for type 2 diabetes with *metformin*, followed by *insulin secretagogues* or *acarbose*, then other oral agents such as *exenatide*, and finally *thiazolidinediones*. When exactly the physician is expected to switch across groups depends on the patient's health status.[13]

Based on the specific decision structure described above, we define hierarchical nests of products by using ATC4 as the upper nest and ATC5 as the lower nest. We believe that the nesting parameters for the groups and the subgroups cover some of the most relevant aspects of the physicians' and patients' decisions and heterogeneity in these markets while the product's continuous characteristics play a less fundamental role to capture heterogeneity (e.g., Grigolon and Verboven, 2014). The continuous characteristics are time invariant and are mostly captured by the product fixed-effects in our setting.[14]

[13]For the German guidelines see `http://www.deutsche-diabetes-gesellschaft.de/fileadmin/Redakteur/Leitlinien/Evidenzbasierte_Leitlinien/EBL_Dm_Typ2_Update_2008.pdf` p. 51-53 and for UK compare e.g., `http://www.nice.org.uk/nicemedia/live/12165/44320/44320.pdfhttp://www.nice.org.uk/nicemedia/live/12165/44320/44320.pdf` p. 13-18.

[14]Since diabetes type 2 is a chronic disease, package size does not play an important role. The active substance's strength may be an important characteristic for the drug's choice, but there is not much variation within the active substances considered here. Yet, as a robustness check, we consider the active substance's concentration as an exogenous demand factor in the specification where we use firm-level fixed-effects (Firm FE.IV).

The first level of nests are G different chemical groups, $g = 1, ..., G$. The second level of nests consists of H_g, $h = 1, ..., H_g$, different active substances within the chemical group g. The specific composition of the nests is given in Table 3.1. We then apply a standard two-level nested logit model and assume a variance component error structure of the agent-specific error term, υ_{ijt}. Following Verboven (1996), we derive the estimation equation for each period t:

$$\ln(s_{jt}) - \ln(s_{0t}) = -\alpha_g p_{jt} + \beta x_{jt} + \xi_{jt} + \sigma_1 \ln(s_{j|hg,t}) + \sigma_2 \ln(s_{h|g,t}), \tag{3.3}$$

where $s_{jt} = q_{jt}/M_t$ and $s_{0t} = 1 - \sum_{j=1}^{J_t}[q_{jt}/M_t]$ are the market shares of drug j and of the outside good, respectively, q_{jt} are sales in defined daily doses [DDD] and p_{jt} is the price per DDD in EUR in month t. Inner-group market shares are defined as $s_{j|hg,t} = \frac{q_{jt}}{\sum_{j \in H_g} q_{jt}}$ and $s_{h|g,t} = \frac{\sum_{j \in H_g} q_{jt}}{\sum_{g=1}^{G} \sum_{j \in H_g} q_{jt}}$.

3.3.2 Identification

The unobserved characteristics of product j at time t are assumed to be known to the firms, the patients, and the physicians but not to the researchers, and they are captured by ξ_{jt}. When firms set their prices they most likely use this information, which in turn implies that prices and inner-group market shares are correlated with this structural error term. Thus, they are endogenous. To partially alleviate this problem, we assume a two-way error component model by $\xi_{jt} = \xi_j + \xi_t + \omega_{jt}$. We then capture part of the unobserved heterogeneity by means of a large set of fixed-effects: the component ξ_j is captured by 649 product fixed-effects and ξ_t is captured by 84 time dummies similar to Nevo (2001). The remaining error term ω_{jt} is defined as a product-and-time-specific error term.[15] In our main specification, the identification condition is therefore $E[p_{jt}|\omega_{jt}] = 0$.

This does not seem to be a particularly restrictive assumption since it is difficult to imagine systematic sources of correlation among prices and *the changes* in unobserved product characteristics. Yet, in order to assess the robustness of our findings, we adopt a second identification strategy and estimate a specification where we use firm-specific fixed-effects together with product-specific, mostly time-invariant,

[15] For a discussion of the inclusion of product fixed-effects see Dube, Chintagunta, Petrin, Bronnenberg, Goettler, Seetharaman, Sudhir, Thomadsen, and Zhao (2002); Kaiser, Méndez, and Rønde (2010).

characteristics and we instrument the German prices for drug j at time t by means of the Danish prices for the same drug in the same time period.[16]

This strategy also has an additional advantage. Since we use ex-factory prices, one might claim that they are measured with error due to the existence of rebate contracts among generic producers and health insurance companies. This might in turn create endogeneity problems if the contracted rebates are systematically correlated with the temporal change in unobserved characteristics of the products (our error term). While we do not think that this should be a major problem in our case, the IV approach would nonetheless allow us to obtain consistent estimate.[17]

In our setting, inner group market shares are also potentially endogenous. Hence, we use an instrumental variable approach to obtain unbiased estimates for the parameters σ_1 and σ_2. Following Berry (1994) and Dutta (2011) we use nine standard instruments which account for the crowdedness in the product space.[18] The identifying assumption is therefore that the instruments, which are correlated with the inner-group market shares and prices through the markups, are uncorrelated with the product-specific error term.

Finally, to account for the potential serial correlation of the error terms due to the relatively high-frequency time structure of the data, we cluster the standard errors at the product-level.

3.3.3 Elasticities

We follow Berry (1994) and Verboven (1996) by calculating own-price elasticities and cross-price elasticities that are different for drugs in the same sub-nest, H_g, of active substances, for drugs in the same nest, G, of chemical groups, and for drugs

[16] This approach is similar to Hausman, Leonard, and Zona (1994) and Nevo (2001). It assumes that prices in different geographical markets are driven by common cost drivers that are independent of country-specific demand shocks. The prices of all authorised pharmaceutical products marketed in Denmark are publicly available at `http://medicinpriser.dk/`.

[17] Since first, rebate contracts in Germany only became used starting in 2008, second, they only play a major role for generic drugs and, third, among these, only for a small fraction of the largest companies, we do not think that measurement problems due to rebates are an issue in our sample. Furthermore in a robustness check, we restrict our sample to the years 2004 to 2007. Coefficient estimates are quite similar, but a bit less precise than in our preferred model. Only for two ATC4 groups (1 and 4) the price coefficients' estimates are smaller and not significantly different from zero since generic competition started later in these groups (results available upon request).

[18] Our instruments are: the number of different packages a firm offers per product, the number of firms active in the product specific ATC5 group and in all other ATC5 as well as ATC4 groups, the number of products within each chemical group (total and by firm), and the number of products without the own firm's products within the same active substance and the same chemical group. All variables are inverted and log-linearised (e.g., Björnerstedt and Verboven, 2012).

in different groups. W e can compute one matrix of price elasticities for all products sold in each month. This results in 84 ($J_t \times J_t$) matrices of elasticities. We follow Berry (1994) and Verboven (1996) and calculate the own-price elasticities as

$$\frac{\partial q_{jt}}{\partial p_{jt}} \frac{p_{jt}}{q_{jt}} = -\alpha_g p_{jt} \left(\frac{1}{1-\sigma_1} - \left(\frac{1}{1-\sigma_1} - \frac{1}{1-\sigma_2} \right) s_{j|h_g,t} - \left(\frac{\sigma_2}{1-\sigma_2} \right) s_{j|g,t} - s_{jt} \right) \quad (3.4)$$

The cross-price elasticities for drugs in the same sub-nest, h_g, of active substances are defined by:

$$\frac{\partial q_{jt}}{\partial p_{kt}} \frac{p_{kt}}{q_{jt}} = -\alpha_g p_{jt} \left(- \left(\frac{1}{1-\sigma_1} - \frac{1}{1-\sigma_2} \right) s_{j|h_g,t} - \left(\frac{\sigma_2}{1-\sigma_2} \right) s_{j|g,t} - s_{jt} \right) \quad (3.5)$$

Similarly, the cross-price elasticities for drugs in the same nest, g, of chemical groups are given by:

$$\frac{\partial q_{jt}}{\partial p_{kt}} \frac{p_{kt}}{q_{jt}} = -\alpha_g p_{jt} \left(- \left(\frac{\sigma_2}{1-\sigma_2} \right) s_{j|g,t} - s_{jt} \right) \quad (3.6)$$

Finally, we derive the cross-price elasticities with all drugs outside the own chemical group to be:

$$\frac{\partial q_{jt}}{\partial p_{kt}} \frac{p_{kt}}{q_{jt}} = \alpha_g p_{jt} s_{jt} \quad (3.7)$$

Even though the nested-logit model is restrictive in the representation of substitution patterns within or outside groups, it is quite flexible when it comes to the asymmetry of cross-price elasticities across products or groups as these only depend on the structural parameters and the price and market shares of the substitute good/group. This is particularly important in our context where the substitution among different chemical groups is mostly hierarchical and cannot be assumed to be symmetric.

3.3.4 Supply-side

In our analysis, we assume that firms in pharmaceutical markets sell a range of differentiated products and compete in prices. Typically, differentiation in drug markets stems from the active substance, strength, package size, and branding. In

our sample 62 firms sell 649 products either in the same or in different classes of active substances. Hence, we assume that all these drugs (patented, imported, or generic) are, to some extent, substitutes one of the other. Indeed, our demand estimation approach enables us to recover all possible cross-price elasticities among them. Further, we use the observed ownership structure to account for the fact that multi-product firms internalise the competitive externalities that each of their products exerted on the demand of their other products.

Finally, we assume that firms compete in prices. This is the standard assumption made in the relevant literature (e.g., Dunn, 2012; Dutta, 2011) and reflects the observation that pharmaceutical firms do not compete in quantities when producing chemical drugs.[19] In off-patent markets, such as *metformin*, market entry is a common phenomenon and demand-side regulation supports price competition, e.g., by reference pricing or co-payments. In markets for patented drugs, like the one for *thiazolidinediones*, the patent holder is granted a short run monopoly. However, since in our model we explicitly allow for parallel imports and model the competition patented drugs face from similar active substances, we believe that Bertrand-Nash behaviour with differentiated goods is a reasonable approximation to describe the market for patented oral anti-diabetics.

The profit functions of the multi-product firm f ($f = 1, \ldots, 62$) active in time/market t that manufacture a subset F_{ft}, of the J products is:

$$\Pi_{ft} = \sum_{j \in F_{ft}} (p_{jt} - c_{jt}) q_{jt}(\mathbf{p}_t) - C_f, \tag{3.8}$$

where $q_{jt}(\mathbf{p}_t)$ is the sold quantity of product j in time/market t as a function of the vector of all prices, $\mathbf{p}_t$, here defined as $q_{jt}(\mathbf{p}_t) = s_{jt} \times M_t$. This definition allows us to include the market share of the outside good as well as to keep the market size fixed in our simulation while at the same time enabling the total quantity of products sold to increase (Nevo, 2000). We assume constant marginal costs c_{jt} – yet we allow them to vary over time – and we denote the fixed costs with C_f.

Furthermore, we also assume that a Bertrand-Nash equilibrium in prices exists and that the prices that support it are strictly positive (e.g., Nevo, 2000). In each time/market t, the price vector, $\mathbf{p}_t$, has to satisfy the following J_t first-order conditions (in matrix notation):

[19] Other ways to model conduct in this market would be to assume joint profit maximization due to collusion or a Stackelberg pricing game, where the producers of original drugs are the price leaders and generics are the followers. However, these would be also very particular assumptions, which had not been identified to hold in general for this market.

$$\mathbf{q}_t(\mathbf{p}_t) + (\Omega_t^F \otimes \Delta(\mathbf{p}_t))(\mathbf{p}_t - \mathbf{c}_t) = 0, \tag{3.9}$$

where $\mathbf{q}_t(\mathbf{p}_t)$, $\mathbf{p}_t$, and $\mathbf{c}_t$ are $J_t \times 1$ vectors of quantities, price, and marginal costs, respectively. Ω_t^F is the firms' product ownership matrix $(J_t \times J_t)$ with elements $(\Omega_t^F(j,k))$ equal to 1 if product j and k are produced by the same firm in time/market t, and 0 otherwise. The $(J_t \times J_t)$ matrix of first derivatives $\Delta(\mathbf{p}_t) = \frac{\partial \mathbf{q}_t(\mathbf{p}_t)}{\partial \mathbf{p}_t'}$ is multiplied element-by-element with the ownership matrix. To identify the marginal cost $\mathbf{c}_t$, Equation (3.9) can be rearranged into

$$\mathbf{c}_t = \mathbf{p}_t - (\Omega_t^F \otimes \Delta(\mathbf{p}_t))^{-1}\mathbf{q}_t(\mathbf{p}_t). \tag{3.10}$$

Clearly, the identification and the estimation of the marginal costs rely on our demand estimates and on the assumption of Bertrand-Nash competition.

3.3.5 Simulation

To quantify the welfare effects of parallel imports in Germany we compare the status quo market with parallel imports versus a hypothetical market without parallel imported drugs. We motivate this hypothetical situation by the fact that firms constantly try to avoid parallel trade (Kyle, 2007), for instance by not entering low-price countries or by offering slightly different versions (in package size or strength) in different countries. Furthermore, as Desogus (2010) shows discussing the Adalat Case, quantity restrictions on intra EU trade –limiting the availability of parallel imports– have been interpreted as a unilateral conduct by the EU. The situation is different in the U.S., where re-imports are prohibited mostly because of patient's safety issues but also because they are expected to harm innovative firms.[20] Kanavos and Vandoros (2010) conclude that *"Drawing on the European evidence, [...] opening the US market to parallel imports will not necessarily lead to competition and enhance pharmaceutical cost containment."* Nevertheless, there is an ongoing debate in the U.S. about disadvantages and advantages, for example by stopping illegal imports from Canada or Mexico.

Hence, we assume that the choice set in the counterfactual situation is different to that in the status quo. Specifically, similar to the structural models that estimate the value of the introduction of new products (e.g., Petrin, 2002), we define the

[20] Golec and Vernon (2006) show that U.S. firms are more profitable, earn higher stock returns, and spend more on research and development (R&D) than manufacturers in the EU.

counterfactual choice set where parallel imported drugs are excluded as $J_t^{sim} = J_t - I_t$, where I_t is the number of parallel imports in time/market t. Accordingly, we define the J_t^{sim} nested-logit demand functions as:

$$q_{jt}(\mathbf{p}_t^{sim}, \hat{\delta}_t) = M_t \cdot s_{jt}(\mathbf{p}_t^{sim}, \hat{\delta}_t) \cdot s_{j|hg,t}(\mathbf{p}_t^{sim}, \hat{\delta}_t) \cdot s_{h|g,t}(\mathbf{p}_t^{sim}, \hat{\delta}_t) \tag{3.11}$$

Similarly, the J^{sim} first-order conditions are:

$$\mathbf{q}_t(\mathbf{p}_t^{sim}, \hat{\delta}_t) + (\Omega_t^F \otimes \Delta_t(\mathbf{p}_t^{sim}, \hat{\delta}_t))(\mathbf{p}_t^{sim} - \hat{\mathbf{c}}_t) = 0, \tag{3.12}$$

We then determine the equilibrium simulated prices ($\mathbf{p}_t^{sim}$) and simulated quantities ($\mathbf{q}_t(\mathbf{p}_t^{sim})$) by using a Newton algorithm on Equation (3.12). With the new simulated equilibrium ($\mathbf{p}_t^{sim}$ and $\mathbf{q}_t(\mathbf{p}_t^{sim})$) and the estimated structural parameter ($\hat{\delta}_t$ and $\hat{\sigma}$) we calculate the demand-side surplus (e.g., Dutta, 2011):[21]

$$DS_t(\mathbf{p}_t^{sim}) = \frac{1}{\hat{\alpha}_g} M_t ln(1 + \sum_{g=1}^{G} (\sum_{h=1}^{H_g} D_{h|g,t}^{\frac{(1-\hat{\sigma}_1)}{(1-\hat{\sigma}_2)}})^{(1-\hat{\sigma}_2)}), \tag{3.13}$$

where $D_{h|g,t} = \sum_{j \in h|g} exp\left(\frac{\delta_{jt}}{1-\sigma_1}\right)$ and the firms' variable profits are:

$$VP_t(\mathbf{p}_t^{sim}) = \sum_{j \in F_{ft}} (p_{jt}^{sim} - \hat{c}_{jt}) q_{jt}(\mathbf{p}_t^{sim}) \tag{3.14}$$

We finally compare them with the status quo welfare measures calculated by using the observed instead of the simulated prices and quantities.

3.4 Data

Our data set contains monthly sales and prices of all oral anti-diabetic drugs sold in Germany between January 2004 and December 2010. Price and sales data are available at the package level and at the level of defined daily doses (DDD)[22], thus allowing us to compare products with different active substances and presentations.

[21] The demand-side surplus corresponds to the typical consumer surplus calculated for a nested logit model. As we mentioned above, since only a part of this surplus goes directly to the consumers, we prefer to use the notation demand-side surplus.

[22] The WHO Collaborating Centre for Drug Statistics Methodology in Oslo provides a list of DDD for each active substance on a yearly basis.

Each of the drugs is characterised by the name, active substance, company name (either producer or parallel importer), package size, strength, defined daily dosages, and an indication if the drug was exempt from co-payments. All data were provided by *IMS Health*, a private marketing consulting firm, and extracted from their database *Pharmascope National* which is restricted to the German Statutory Health Insurance (SHI) market (IMS Health, 2012).

The strength, or concentration, varies considerably by active substances (in total from 0.5 mg to 1000g), which motivates the use of DDD as the basic metrics. The ex-factory prices per daily dose range from €0.01 to €0.27 and reflect the fact that some products are sold in markets for patented drugs while others are sold in off-patent markets.

To calculate the size of the potential market, M_t, we collect epidemiological data about the number of patients with diabetes in Germany from the German Diabetes Association (DDG, 2011; Giani, Janka, Hauner, Standl, Schiel, Neu, Rathmann, and Rosenbauer, 2004) and from Hauner, Köster, and Schubert (2007). Annual information about diabetes patients are transformed into monthly values using average growth rates. We estimate our demand specification with the two- and threefold quantity of sold DDD as a robustness check and yield very similar results.

To ensure homogeneous market conditions, we only include in our sample products that are covered by the German SHI. A complete classification of the drugs analysed in this study is given in Table 3.1. In our estimations, we only include packages with a market share within the subgroup of active substances (ATC 5) larger than 0.1%.[23] Furthermore, we exclude the chemical substance *exenatide* due to its sub-dermal administration (pens, 158 obs.) and 83 observations of retard tablets (belonging to *gliclacides*). Finally, we also exclude *DPP-4 inhibators* (287 observations) and the combination of one of them (sitagliptin) with *metformin* (116 obs.) as well as *glimepiride & pioglitazone*, *gliclazide*, and *gliquidone* since they form a special group of late innovations with very high prices, which would constitute an extreme outlier not suitable for estimating a general model for the entire market (compare Table 3.1).[24]

Table 3.2 gives an overview of the 24,603 observations included in the final estimation by firm type (originator drug manufacturer, parallel importer or generic man-

[23] The preferred demand model leads to similar results when excluding all drugs with an overall market share below 0.001% or not excluding by market shares at all. However, it proved very difficult to correctly simulate very small market shares. The reduced sample still covers 92% of the market in terms of sales in 2006.

[24] The demand estimation does yield similar results when not excluding this group but, again, it proved very difficult to predict the market shares and prices of such an extreme outlier using our average coefficient estimates.

Table 3.1: Anatomical Therapeutic Chemical (ATC) Classification System For The Therapeutic Class *Blood Glucosidase Lowering Drugs, Excl. Insulin* (A10B) (= Oral Anti-diabetics) Marketed In Germany 2004-2010

ATC4: chemical (sub-) group	**ATC5: active substance / chemical substance**	**Total # of products**	**Total # of firms**
1. Alpha glucosidase inhibitors	Acarbose	34	12
	Miglitol	8	5
2. Biguanides	Metformin	173	45
3. Combinations of oral blood glucosidase lowering drugs	Metformin & Rosiglitazone	28	11
	Glimepiride & Rosiglitazone	19	6
	Metformin & Pioglitazone	10	8
	Glimepiride & Pioglitazone*	4	1
	Metformin & Sitagliptin*	4	1
	Metformin & Vildagliptin	15	3
4. Other blood glucosidase lowering drugs, excl. insulin (here: glinides)	Repaglinide	66	19
	Nateglinide	4	3
	Exenatide*	7	3
5. Sulfonylurea	Glibenclamide	53	28
	Glibornuride	3	3
	Gliquidone*	2	1
	Gliclazide*	4	2
	Glimepiride	212	31
6. Thiazolidinediones	Pioglitazone	27	9
	Rosiglitazone	6	4
Dipeptidyl peptidase 4 (DPP-4) inhibitors	Sitagliptin*	8	6
	Vildagliptin*	4	2
	Saxagliptin*	4	3

Oral anti-diabetics (OAD) marketed in Germany between 2004 and 2010. Several OAD are not available in Germany and hence not reported in the table. The symbol [*] denotes that the group is excluded from our estimation.

Table 3.2: Number Of Observations Used In Final Estimation By ATC4 Class And Firm Type, 2004-2010

ATC4	Orignals	Imports	Generics	Total
1. Alpha glucosidase inhibitors	338	1,434	48	1,820
2. Biguanides (metformin)	275	421	7,211	7,907
3. Combinations	353	988	-	1,341
4. Other (glinides)	322	1,586	312	2,220
5. Sulfonylurea	589	766	9,030	10,385
6. Thiazolidindiones	399	531	-	930
Total	2,276	5,726	16,601	24,603

Oral anti-diabetic drugs in Germany over 84 months (2004-2010). Final sample with data from *IMS Health*.

ufacturer) and chemical group. We observe quite heterogeneous competitive conditions across groups as the *biguanides* and *sulfonylurea* groups face severe generic competition while the other groups are much smaller and under patent protection, so that the competitive constraints are mainly those imposed by parallel imported drugs or potential market entry by innovations.

Table 3.3 reports the descriptive statistics for the most important variables used in this study, including the different prices, the overall market shares (s_{jt}), the market shares of the products within the inner nest ($s_{j|h,t}$) as well as the market shares of the inner nests within the outer nest ($s_{h|g,t}$). The variables are presented by firm type. In our preferred specification we control for the patients' preference not to pay for the chosen drugs. This is captured through the dummy *co-payment exemption* that takes on the value of 1 if drugs are fully exempt from co-payments. This happens when their price undercuts a certain threshold, which is set at 70% of the reference price. In our sample, it only occurs in one of the ATC4 groups (*sulfonylurea*).[25] Prices, sales per product, as well as market shares vary considerably across manufacturer types. In the lowest part of the table, we report the number of firms and products within groups and sub-groups, which are used to construct the instrumental variables for the inner-group market shares.

[25]Specifically, only 3,766 among the 10,504 observations in the ATC4 group *sulfonylurea* correspond to co-payment exempt drugs. Some drugs change status (from non-exempt to exempt and vice versa) across the sample periods which allows us to identify the effect of the co-payment exemption in our regressions with product-specific fixed-effects.

Table 3.3: Summary Statistics, Oral Anti-diabetic Drugs (2004-2010)

	Total		Originals		Imports		Generics	
	mean	s.d.	mean	s.d.	mean	s.d.	mean	s.d.
Market shares								
s_{jt} [in ‰]	0.03	[0.09]	0.09	[0.20]	0.01	[0.01]	0.04	[0.07]
$s_{j\|h,t}$ [in %]	0.03	[0.07]	0.13	[0.17]	0.03	[0.05]	0.01	[0.03]
$s_{h\|g,t}$ [in %]	0.78	[0.26]	0.66	[0.31]	0.74	[0.27]	0.82	[0.24]
Price/package [EUR]	21.61	[29.74]	47.48	[47.15]	43.05	[39.25]	10.67	[10.22]
Price/DDD [EUR]								
Total	0.33	[0.42]	0.79	[0.60]	0.75	[0.44]	0.12	[0.11]
1. Alpha gluc. inh.	0.88	[0.23]	1.04	[0.26]	0.85	[0.21]	0.75	[0.18]
2. Big. (metformin)	0.12	[0.06]	0.16	[0.04]	0.18	[0.10]	0.12	[0.05]
3. Combinations	0.77	[0.24]	0.79	[0.24]	0.76	[0.24]	-	-
4. Other (glinides)	0.90	[0.42]	1.31	[0.55]	0.85	[0.35]	0.74	[0.30]
5. Sulfonylurea	0.10	[0.04]	0.18	[0.07]	0.13	[0.05]	0.09	[0.03]
6. Thiazolidinediones	1.50	[0.26]	1.52	[0.30]	1.48	[0.22]	-	-
Co-pay exemption	0.15	[0.36]	0.00	[0.00]	0.02	[0.13]	0.22	[0.41]
# of firms in ATC5	23	[10]	13	[11]	12	[9]	27	[6]
# of firms in ATC4	25	[10]	17	[11]	14	[9]	30	[4]
# of products in ATC5	80	[48]	42	[45]	36	[38]	100	[37]
# of products in ATC4	99	[55]	58	[52]	46	[45]	124	[40]
Danish prices [in EUR]	0.37	[0.48]	0.84	[0.71]	0.87	[0.47]	0.13	[0.14]

We report the descriptive statistics for the 649 oral anti-diabetic drugs in Germany over 84 months (2004-2010). Nest g is defined at the chemical group level (ATC4), nest h is defined at the active substance level (ATC5). We use 6 different chemical groups (ATC4): 1. Alpha glucosidase inhibitors, 2. Biguanides (metformin), 3. Combinations, 4. Other (glinides) 5. Sulfonylurea, 6. Thiazolidinediones. s_{jt} is the overall market share of product j in month t, $s_{j|h,t}$ is the market share of the product within the inner nest (ATC 5), $s_{h|g,t}$ is the market share of the inner nest (ATC5) within the outer nest (ATC4). All prices are ex-factory and in EUR. All values are based on our own calculations with data from *IMS Health*. 24,603 observations.

3.5 Results

3.5.1 Demand-side Estimation

Table 3.4 displays the results of the two-level nested logit demand estimation presented in Equation (3.3). In the first two columns, we present the results for the specification that only includes product fixed-effects [FE], the following two columns then report the instrumental variables estimation that accounts for the potential endogeneity of the inner group market shares [FE.IV]. Finally, model [Firm FE.IV] presents the results obtained including firm-specific fixed-effects and product characteristics (rather than product-specific fixed-effects) and instrumenting the prices by means of the Danish prices. The coefficients σ_1 and σ_2 measure the correlation of agents' preferences within the nests of active substances and chemical groups, respectively, and the six price coefficients $[\alpha_g]$ represent the average effect of the price on the market shares for each of the chemical groups. In all specifications, all parameters (except of two) are significant and have the expected signs.

As conjectured, the mean utility positively and significantly depends on the co-payment exemption which therefore confirms the importance to control for patients' preferences. Moreover, both coefficients measuring the correlation of preferences within the two nests [σ_1 and σ_2] are consistent with random utility theory ($0 \leq \sigma_2 \leq \sigma_1 \leq 1$) across all three models. They are considerably smaller after controlling for possible endogeneity, as expected. Model Firm FE.IV additionally shows that the demand significantly increases if the drug stems from the originator manufacturer or a parallel importer as opposed to the generic manufacturer, capturing the preference for branded products.

From here on we focus on our preferred specification [FE.IV]. The six price coefficients are negative and statistically significant from zero. The coefficients cannot be interpreted as marginal effects but they show that substitution indeed differs by chemical group: group 2 represents an off-patent market with several generic competitors which results in a price coefficient of -4.2 and group 4 represents a market with patented active substances and a considerably lower price coefficient of -0.5.

For a clear interpretation of these estimates in terms of substitution patterns, we then need to calculate elasticities. The mean value of own- and cross-price elasticities of all products across all months are presented in Table 3.5. The own price elasticities vary considerably across groups (-37 to -1, mean: -6.65), while the average cross-price elasticity within the same nest of active substances (0.45) is larger than within the upper nest of the respective chemical group (0.26) and indicates a strong substitution among products in similar nests. The mean cross-price elasticity for products outside the chemical group is small (0.004 on average) and reflects

Table 3.4: Demand Estimation Results

$\ln s_{jt} - \ln s_{0t}$	FE		FE.IV		Firm FE.IV	
σ_1 [active substance]	0.987***	(0.005)	0.854***	(0.031)	0.991***	(0.052)
σ_2 [chemical group]	0.609***	(0.045)	0.598***	(0.055)	0.604***	(0.069)
Price, ATC4, group 1	-4.450***	(0.492)	-4.407***	(0.478)	-11.586***	(2.273)
Price, ATC4, group 2	-4.145***	(0.245)	-3.992***	(0.308)	-7.503***	(1.002)
Price, ATC4, group 3	-6.636***	(1.164)	-7.989***	(1.322)	-7.591***	(1.653)
Price, ATC4, group 4	-0.508***	(0.134)	-0.789***	(0.213)	-4.805***	(0.388)
Price, ATC4, group 5	-1.493***	(0.303)	-1.421***	(0.400)	-5.680***	(1.138)
Price, ATC4, group 6	-0.523**	(0.177)	-0.952***	(0.265)	-2.938***	(0.291)
Co-pay exemption	0.038***	(0.005)	0.087***	(0.013)	0.017	(0.041)
Original					0.510***	(0.114)
Import					0.056	(0.078)
Constant	-1.297***	(0.065)			-1.854***	(0.260)
Observations	24,603		24,603		24,603	
Product fixed effects	yes		yes		no	
Time fixed effects	yes		yes		yes	
Firm fixed effects	no		yes		no	
Concentration dummies	no		no		yes	
IV [σ_1,σ_2]	no		yes		yes	
IV [p_{jt}]	no		no		yes	
Adj. R-squared	0.971		0.954		0.950	
F-test excl. IV [σ_1 / σ_2]			18.55 / 120.99		36.72 / 121.96	
F-test excl. IV [p_{1t} / p_{2t}]					2.15 / 25.31	
F-test excl. IV [p_{3t} / p_{4t}]					2.21 / 82.51	
F-test excl. IV [p_{5t} / p_{6t}]					137.00 /0.89	

In the first two columns, we report the parameter estimates for the OLS (FE) and instrumental variable (FE.IV) estimations of equation (3.3). The specification (FE.IV) is used for the simulation. Column (Firm FE.IV) reports the results from an IV specification with firm fixed effects (without product fixed effects) and where the prices p_{jt} are instrumented with the corresponding Danish prices. The dependent variable in all specifications is $\ln s_{jt} - \ln s_{0t}$, where s_{jt} = quantity sold of drug j in month t/potential market size in month t and s_0 = market share of the outside option in month t/potential market size in month t. The heterogeneous price coefficients α_g are reported separately for the 6 different chemical groups (ATC4) listed in the Table 3.1: 1. Alpha glucosidase inhibitors, 2. Biguanides (metformin), 3. Combinations, 4. Other (glinides) 5. Sulfonylurea, 6. Thiazolidinediones. The clustered (product level) standard errors are reported in parentheses. The symbols *, **, *** represent significance at the 1%, 5%, and 10% levels, respectively.

the low substitutability among drugs from different chemical groups. The high correlation among preferences for drugs of the same chemical group is reasonable and reflects the fact that the grouped active substances differ only slightly in their molecule structure, which allows patients to easily substitute among them. The even larger correlation among drugs containing the same active substance might be driven by the same reasoning. Here, the drugs differ only in strength, dosage form, manufacturer, colour, package size, etc. Furthermore, it is a common finding in the literature that patients tend to substitute toward similar drugs, (e.g., Ellison, Cockburn, Griliches, and Hausman, 1997; Dutta, 2011).

Table 3.5: Product-level Price Elasticities

	OPE mean [std]	CPE, ATC5 mean [std]	CPE, ATC4 mean [std]	CPE, all mean [std]
Total	-6.652	0.452	0.258	0.004
	[10.624]	[1.399]	[0.734]	[0.004]
ATC 4				
1. Alpha glucosidase inhibitors	-24.689	1.837	0.988	0.007
	[6.751]	[1.198]	[0.078]	[0.007]
2. Biguanides (metformin)	-3.478	0.031	0.031	0.002
	[1.049]	[0.001]	[0.001]	[0.000]
3. Combinations	-37.349	5.028	4.126	0.009
	[16.284]	[3.275]	[1.584]	[0.002]
4. Other (glinides)	-4.818	0.300	0.142	0.003
	[2.461]	[0.603]	[0.021]	[0.001]
5. Sulfonylurea	-0.991	0.023	0.011	0.003
	[0.409]	[0.030]	[0.003]	[0.000]
6. Thiazolidinediones	-8.685	0.945	0.526	0.004
	[2.409]	[0.527]	[0.115]	[0.001]
Original	-18.026	2.309	0.957	0.009
	[14.226]	[3.166]	[1.320]	[0.007]
Import	-15.572	0.968	0.636	0.006
	[14.630]	[1.280]	[0.706]	[0.006]
Generic	-2.321	0.030	0.025	0.002
	[1.895]	[0.049]	[0.035]	[0.001]

We report the mean values and standard deviations over 84 period of the the product-level's own- (OPE) and cross-price elasticities (CPE) based on the estimated parameters from specification (FE.IV) of equation (3.3) and the formulas (3.4) to (3.7). 24,603 observations.

We can now use Equation (3.10) to retrieve the marginal costs and the corresponding markups for each of the 84 sample months. Table 3.6 presents marginal

costs and markups as a mean percentage over all drugs across all time periods. On average, marginal costs are 33% of prices and tend to be higher for patented drugs and lower for generic products. This result, which is mostly driven by the chosen nested logit demand model to estimate elasticities, is a bit surprising as marginal costs are reported to be low in the pharmaceutical industry. A possible explanation is that high marginal costs for patented drugs reflect that innovative firms utilise more sophisticated production technology than generic companies. The reported marginal costs might also partially reflect investments in research and development that are not captured by fixed costs.

Table 3.6: Marginal Costs And Markups

	Total mean [std]	Original mean [std]	Import mean [std]	Generic mean [std]
Marginal cost [EUR/DDD]	0.26	0.87	0.66	0.04
	[0.40]	[0.39]	[0.41]	[0.10]
Marginal cost [% of price]	0.33	0.76	0.78	0.14
	[0.59]	[0.18]	[0.25]	[0.59]
Markup [EUR/DDD]	0.11	0.28	0.10	0.08
	[0.10]	[0.20]	[0.08]	[0.06]
Markup [% of price]	0.67	0.24	0.22	0.86
	[0.59]	[0.18]	[0.25]	[0.59]

We report the absolute and and percentage mean values (with st.d.) over all 84 months of the estimated markups and marginal costs, which are based on the Jacobians calculated with the estimated parameters from specification [FE.IV] of equation (3.3). 24,603 observations.

3.5.2 Simulation

The final step of our empirical analysis consists of simulating the new equilibrium in prices and quantities that one would observe, had parallel imports not been allowed. By comparing this counterfactual scenario to the status quo prices and corresponding demand-side surplus and variable profits, we can estimate the value of parallel imports.

Table 3.7 shows the estimated changes in prices (mean) and quantities (total) due to the existence of parallel imports over all 84 months in our sample. Prices of originator drugs decrease on average by ca. 11% and prices of generic drugs increase on average by only 0.7% due to parallel trade in the German market for oral antidiabetics. The overall average price in the market increases by ca. 10% because

of the existence of parallel imports, which are more expensive drugs with respect to generics. Hence since the entire price distribution changes, one cannot make a clear comparison with respect to the situation without parallel trade. In order to do that, we also report the average price of original drugs and generics excluding parallel imports. Clearly, this average price decreases as a consequence of increased competition. Moreover, we observe an expansion of demand by 2.7% due to the introduction of new goods through parallel trade. Specifically, the reduction of over 218 million DDD generics (-0.5%) and over 7 million DDD original drugs (-2.5%) is overcompensated by the sales of 428 million DDD of parallel imports.

We then calculate the change in demand-side surplus and variable profits generated by the introduction of parallel trade, which are shown in Table 3.8. The change in demand-side surplus amounts to about €130 million in total (3.7% of the level without parallel trade) or ca. €19 million per year. These figures do not seem to be particularly large in comparison to the average annual market size of €227 million based on ex-factory prices.

The average demand-side effect comes mostly from the lower price level for original drugs, but is also strongly influenced by the demand expansion as well as the behaviour of the marginal consumer. First, the prices of original drugs are lower and, second, some patients substitute away from original products to parallel imports, which are even cheaper. However, these positive demand-side effects are partially outset by a decrease in demand-side surplus from generics. The price reduction for these drugs is minimal and several patients substitute away from the cheaper generic drugs to the more expensive parallel imports. These patterns are confirmed when we look at how the change in demand-side surplus breaks down among the different chemical groups.[26] Large gains from parallel trade are observed in those chemical groups where generic competition is not severe, while surplus losses are measured in the *biguanides (metformin)* and *sulfonylurea* groups, where several generic products are sold. A side remark on this result is that, apparently, competition by generics does indeed work. When we look at the time evolution in Figure 3.3, we also observe some variation in the changes of demand-side surplus over time. Specifically, we observe a substantial jump in the change in demand-side surplus created by parallel trade after 2007.[27]

[26] Please notice that the sum of the levels and differences of demand-side surplus across drugs types are not equal to the total. This is due to the fact that the demand-side surplus is calculated as a non-linear function of the mean utilites according to equation (3.13).

[27] We also compared the mean co-payment with and without parallel trade. Since we neither observe reference prices or contracted rebates for the two ATC4 groups with generic competition nor the exemption for specific individuals, this average co-payment potentially entails some measurement error. For the entire sample, the mean co-payments are on average around 2% lower

Table 3.7: Effects Of Parallel Imports On Mean Prices And Total Quantities By Product Types And Chemical Groups – 2004-2010

Price [EUR/DDD]	status quo mean	w/o imports mean	Difference in %
Total	0.36	0.27	10.0
Total, w/o imports	0.25	0.27	-5.9
Original	1.15	1.29	-11.0
Import	0.76	-	-
Generic	0.128	0.127	0.7
ATC 4			
1. Alpha glucosidase inh.	0.88	1.09	-19.4
2. Biguanides (metformin)	0.13	0.13	1.7
3. Combinations	0.79	0.82	-3.6
4. Other (glinides)	0.95	1.64	-41.9
5. Sulfonylurea	0.11	0.10	4.8
6. Thiazolidinediones	1.48	1.66	-10.5
Cumulated quantity [DDD]	**status quo in mio**	**w/o imports in mio**	**Difference in %**
Total	7,778.0	7,574.8	2.7
Original	1,369.0	1,376.2	-0.5
Import	428.7	-	-
Generic	5,980.3	6,198.5	-3.5
ATC 4			
1. Alpha glucosidase inh.	139.9	71.0	97.0
2. Biguanides (metformin)	3,194.0	3,259.0	-2.0
3. Combinations	1,142.9	984.7	16.1
4. Other (glinides)	236.0	159.9	47.6
5. Sulfonylurea	2,813.3	2,897.5	-2.9
6. Thiazolidinediones	252.0	202.5	24.4

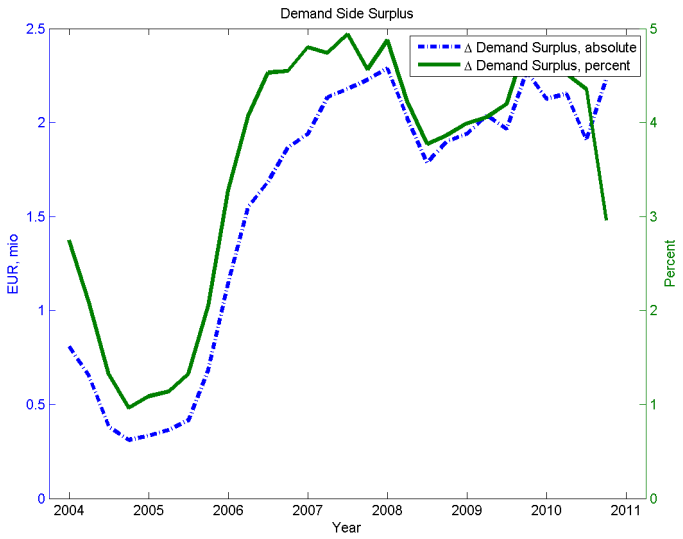
We report the mean values and percentage changes over all 84 months of the observed prices and total sum of quantities vs. their simulated counterparts, based on the estimated parameters from specification [FE.IV] of equation (3.3). Column *status quo* reports the observed values from our data while column *w/o imports* displays our simulated results. 24,603 observations.

Table 3.8: Effects Of Parallel Imports On Demand-side Surplus And Variable Profits By Firm Types And Chemical Groups – Sum Over 84 Months (2004-2010)

Demand-side surplus	status quo in mio EUR	w/o imports in mio EUR	Difference in %
Total	3,674.0	3,544.1	3.7
ATC 4			
1: Alpha glucosidase inh.	87.5	43.7	100.2
2: Biguanides (meformin)	1,773.5	1,773.7	-0.01
3: Combinations	707.1	601.4	17.6
4: Other (glinides)	148.9	100.4	48.2
5: Sulfonylurea	1,585.8	1,597.6	-0.7
6: Thiazolidinediones	158.8	123.7	28.4
Variable profits	**status quo in mio EUR**	**w/o imports in mio EUR**	**Difference in %**
Total	829.7	931.7	-10.9
Original	208.3	333.5	-37.5
Import	41.5	-	-
Generic	579.9	598.3	-3.1
ATC 4			
1: Alpha glucosidase inh.	6.1	10.5	-42.2
2: Biguanides (meformin)	127.7	129.9	-1.7
3: Combinations	70.6	83.0	-15.0
4: Other (glinides)	62.6	107.0	-41.5
5: Sulfonylurea	451.7	460.7	-1.9
6: Thiazolidinediones	111.0	140.6	-21.1

We report the aggregated values and percentage changes over all 84 months of the demand-side surplus and variable profits due to parallel import. All figures are calculated based on the estimated parameters from specification [FE.IV] of equation (3.3). Column *status quo* reports values based on the observed data while column *w/o imports* displays values based on the simulated results. 24,603 observations.

Figure 3.3: Absolute And Relative Difference Between Simulated And Status Quo Demand-side Surplus Over 28 Quarters. 84 monthly values averaged to 28 quarters. Left axis in EUR, right axis in %.



The final step of our welfare analysis regards the gains and losses for manufacturers. Since we do not have a measure of fixed costs, we only analyse the effect of parallel trade on variable profits realised in Germany and hence measure an upper bound to the possible decrease in the incentive to invest in R&D for originators. On average, as shown in the lower part of Table 3.8, variable profits decrease by about €102 million over the seven sample years. This figure is mostly determined by the severe decrease in variable profits for the manufacturers of original drugs by €125 million (not taking into account sales in foreign countries, which would be (re-)imported). Notice, however, that parallel trade most likely increase the profits of these multi-national firms due to the increased sales of their products to parallel importers in other countries. Only a small part of these lost profits, €41 million, is transferred to parallel importers. Furthermore, producers of generic drugs face a reduction of their variable profits by about €18 million.

Unfortunately, we cannot derive a complete welfare analysis absent a reasonable measure of fixed costs as well as the profit effects of parallel trade in other countries where firms active in Germany also operate. Moreover, our results are clearly affected by the existence of other extensive demand-side and price regulations that affect health care markets in Germany and might eventually reduce the ability of parallel trade to exert effective competitive pressure on prices. E.g., given a demand-side policy that strictly promotes parallel imports Méndez (2013) reports an increase in consumer surplus of 111% on average for Denmark. To this extent, one could try to simulate other counterfactual scenarios by changing other key parameters of the parallel imports policy – such as for instance the distribution rule's threshold. These simulations exceed the scope of this paper.

3.6 Conclusion

In this paper, we study the effect of parallel trade on welfare in the German market for oral anti-diabetics. To this aim, we develop and estimate the first structural demand model of the German pharmaceutical market. The estimated demand for anti-diabetic drugs seems to be quite elastic, with an average own-price elasticity of -6.65. These results are mostly driven by the broad availability of generic products in various chemical groups. Indeed, several demand-side policies –such as tiered co-payments and the reference pricing system– support generic competition

in our simulated data (€5.46) than in our observed data (€5.56). This reflects the same logit as discussed above and it is driven by the fact that the price of parallel imports is higher than the price of generics. While the co-payments for generics are very similar in the two scenarios, the co-payments for original products are almost 50 EUR cents per package lower due to parallel trade.

in the off-patent market. Moreover, physicians and pharmacists are also made more price-sensitive through other specific cost-containment regulations. These findings contrast with the common wisdom that the broad insurance coverage of drug costs tends to generate quite price-inelastic behaviour (e.g., Kaiser, Méndez, Rønde, and Ullrich, 2013). The estimated cross-price elasticities support the existence of some degree of market segmentation. Substitution seems to mainly take place across drugs within the same active substance and less within the same chemical group. The fact that patients barely substitute across chemical groups is very much in line with the physicians' behaviour in oral glucose control therapies for type 2 diabetes.

The main focus of our analysis is the measurement of the welfare effect of parallel imports. We therefore need to simulate the situation where parallel imports are not allowed. By comparing the status quo to the simulated scenario we measure a price decrease of 11% for original drugs and no change for generics due to parallel trade. Several patients switch from the original products to the parallel imports, which increases demand-side surplus. Yet, this increase is limited to €130 million over the seven sample years since some patients who would consume generics in the absence of parallel imports switch to these more expensive drugs when they come to the market. Furthermore, the modest average price reaction is most likely driven by other institutional details of the existing parallel import policy in Germany (e.g., Kyle, 2011). In particular, it might be driven by the minimum parallel import quotas of 5% in pharmacy sales. Under this regulation, pharmacists do not have any incentive to hand out cheaper parallel imports other than those which undercut the price threshold to be counted in the quota (15% or €15 below the original's price). We expect the price effect to be larger, if there were other distribution rules, e.g., if the rules were similar to those applied in the off-patent market where pharmacists have to hand out one of the three cheapest drugs if there is no rebate contract for the patient's health insurance drug combination and the physician has not ruled out a substitution of the prescribed drug. These alternative scenarios could be further investigated within our framework at the cost of imposing a more complex and potentially restrictive structure.

An important discussion that we did not address in this study is how the policy of parallel imports affect investments in research and development. This is closely related to the ability to measure profits changes for innovative manufacturers. By definition, parallel traders gain arbitrage profits and do not conduct any investments in R&D. Thus, one effect of the policy is to transfer profits from innovative firms that invest, at least partially, into R&D toward firms that do not invest in R&D at all. Our results partially confirm this view. The manufacturers of original drugs face severe losses in the German market by over €125 million due to the introduction of

parallel trade. This loss in variable profit is, however, only to a small fraction (€41 million) transferred to parallel importers and it rather benefits the statutory health insurance. Yet, to get a complete picture of parallel trade's effects on manufacturers profits and incentives to innovate we would need to consider the global nature of production and R&D. While original drugs' manufacturers lose some profits in markets with parallel trade due to increased competition, they most likely increase their profits in other markets by selling their drugs to parallel importers. Which effect prevails is unclear especially because it seems that parallel trade, by decreasing the overall price level, also has the effect to expand overall demand. Hence to carefully answer these questions, we would need a much richer model of multi-country competition and a much more extensive dataset.

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Chapter 4

Pharmaceutical Prices under Regulation: Tiered Co-payments and Reference Pricing in Germany

Co-authored with Annika Herr

The logic and limitations of ideal competitive behavior under uncertainty force us to recognize the incomplete description of reality supplied by the impersonal price system.

— Kenneth J. Arrow, 1963, p.967,
Uncertainty and the Welfare Economics of Medical Care

4.1 Introduction

In markets with insurance coverage, insurees are not exposed to the full price of their consumption. Cost-sharing regulations of insurances exploit consumers' price sensitivity to control for ex-post moral hazard and steer consumption to preferred products or services. Two instruments for health insurances to control health care expenditures via the demand-side are tiered co-payments and reference pricing, for example, in the pharmaceutical market (Berndt, McGuire, and Newhouse, 2011). Tiered co-payments differentiate cost-sharing by drug types or by patients. Cost-sharing takes on various functional forms, e.g., a linear function of prices or fixed fees. With fixed-fee co-payments, insurees have a very limited incentive to search for a lower-priced product or service. Reference pricing defines the maximum drug reimbursement of the health insurance using competitors prices. This paper analyzes the combined effects of tiered co-payments and reference pricing and evaluates the effects of co-payment exemptions on pricing strategies.

In Germany, selected drugs are exempt from co-payments if firms set prices 30% or more below the reference price. The policy can be interpreted as the introduction of a more differentiated cost-sharing, i.e., tiered co-payments. The incentive for patients to switch to lower-priced drugs impacts pricing strategies of firms: they decide on a lower price for their consumers by decreasing their prices. Our paper exploits the institutional features of the newly introduced exemption policy, its application to pharmaceuticals with reference pricing, and its successive implementation in therapeutic markets (reference price clusters).

In the US, tiered co-payments are the favorite approach to steer drug demand to low-price substitutes. For example, most Medicare Part D Prescription Drug Plans (PDP) differentiate co-payments by drug type: median cost-sharing across all insureds was $5 for generics, $41 for preferred brands, and $92 for non-preferred brands in 2012 (Hoadley, Summer, Hargrave, Cubanski, and Neuman, 2012).

Reference pricing defines a maximum reimbursement limit for groups of chemical, pharmacological or therapeutically equivalent substitutes. Patients share 100 percent of the costs when a drug price exceeds the maximum reimbursement. This regulation is a prominent cost-sharing regulation in Europe and seems to be more

common in public health care systems, for example, in Spain, the Netherlands or Germany. The empirical literature regularly finds that (internal) reference pricing has a price-decreasing effect for all products in the respective therapeutically market (Pavcnik, 2002; Brekke, Grasdal, and Holmas, 2009; Brekke, Holmas, and Straume, 2011; Kaiser, Mendez, Ronde, and Ullrich, 2014; Augurzky, Göhlmann, Gress, and Wasem, 2009). In the US, several insurances and governmental agencies also define a maximum reimbursement based on a list of generic equivalents. For example, the maximum allowable costs (MAC) are similar to reference pricing in that patients bear the full costs of drug prices above the maximum reimbursement level.[1] (Scott Morton and Kyle, 2012).

This study exploits a policy change in the German pharmaceutical market which is characterized by homogeneous market conditions, such as uniform prices across all pharmacies and the same co-payment scheme for all publicly insured (Pavcnik, 2002; Ziebarth, 2010). We utilize quarterly price data of all prescription drugs that are reimbursed by reference pricing in Germany from 2007 to 2010. The study evaluates the effect of co-payment exemptions using a difference-in-differences approach and exploits the sequential introduction of the co-payment exemption level (CEL) in selected therapeutic markets. Our identification strategy relies on instruments for reference prices: a proxy for regulation intensity, i.e., the change in the reference prices in other groups. We find negative price effects of reference prices in general and evidence of market segmentation: prices decrease by 4.9 percent for generics while prices of brand name drugs increase by 6.4 percent. We refer to this finding as the "co-payment exemption paradox." A simple back-on-the-envelope counterfactual simulation approximates potential savings. Assuming that this reform had been introduced for the first time for all drugs simultaneously in 2010, it would have lead to savings of about €242m.

Off-patent drugs are a cornerstone of pharmaceutical markets: in 2011 more than 80 percent of all prescriptions in the US and more than 50 percent of all drugs in Europe were filled by generics (GPhA, 2012; EGA, 2012).Little is known about the overlap and combination of demand-side regulations. Some authors raise concerns that a high level of regulation may drive competition out of the market (Danzon and Chao, 2000), others have outlined the efficiency of demand-side regulations (Berndt, McGuire, and Newhouse, 2011).

[1] The average sales price (ASP) calculated by Medicare follows a similar approach (Scott Morton and Kyle, 2012). Furthermore, Danzon and Ketcham (2004), Scott Morton and Kyle (2012) and Huskamp, Rosenthal, Frank, and Newhouse (2000) discuss the implementation of reference pricing for comprehensive Medicare drug benefit plans in the US.

This paper adds to the literature on competition and regulation in pharmaceutical markets. We show that co-payment exemption levels foster competition for lower-priced drugs. In pharmaceutical markets, the empirical literature identifies a negative price effect of competition (through generic entry) on generic drug prices (Reiffen and Ward, 2005; Wiggins and Maness, 2004). For example, the "generic competition paradox" shows that prices of formerly patented drugs increase when generics enter the market (Grabowski and Vernon, 1992; Frank and Salkever, 1997; Regan, 2008). Our set-up allows to analyze the policy effects on generics and brand-name drugs separately. Thereby, we provide independent empirical evidence that the economics of the "generic competition paradox" (Scherer, 1993) hold even in generic markets with demand-side regulations. Explanations for the price increase of brand-name drugs after generic entry include the firms' strategies to focus on less price elastic, brand-loyal consumers (Regan, 2008). As Richard and Van Horn (2004) show, brand characteristics explain a large part of the choices consumers make. If there are consumer segments with different preferences for (observed) quality, price discrimination would indeed maximize consumer and overall welfare (Alexandrov and Deb, 2012).

The remainder of this paper is structured as follows. We briefly explain the German market for pharmaceuticals and its regulatory framework in section 4.2. Section 4.3 condenses the theoretical ideas of the generic and original firms' price-setting behavior. In section 4.4 we discuss our data, the estimation strategy, and the identification of our key parameters. Sections 4.5 presents and discusses our results, and section 4.6 concludes.

4.2 The German Market for Pharmaceuticals

More than 69.5 million people (or about 85 percent of the population) are covered by the public health insurance which also reimburses medical expenses. Lifestyle pharmaceuticals and OTC drugs are not reimbursed. Potential selection problems due to different types of statutory insurance are not relevant in our sample. In 1989, Germany was the first country to introduce internal reference pricing with the aim to lower pharmaceutical expenses. Since 2006, co-payment exemption levels (CEL) have been introduced successively in several therapeutic markets (reference price clusters).

Drug prices are uniform across all German pharmacies. Incentives to hand out more expensive drugs are low due to regulated wholesale and pharmacy margins. For example, pharmacists receive a fixed fee per package and a fraction of the drug price (3%) directly from the health insurance. The drug choice can be influenced

by physicians, health insurances, patients, and by pharmacists. The market can be characterized as homogeneous (Pavcnik, 2002).

Reference Pricing[2] means that health insurances specify a maximum reimbursement for each drug and patients bear the price differential to the drug price. Reimbursements are calculated by a price comparison mechanism to similar products in two steps.[3]

First, product groups of therapeutic markets are defined and comprise generics and originator drugs. These products are defined as perfect substitutes (Zweifel and Crivelli, 1996) and named *reference price cluster*. In Germany during the period 2007 to 2010, patented and off-patent drugs could be regulated by reference prices if the patented product does not add any medical benefit ("me-too drugs").

Second, maximum reimbursement levels, the reference prices, are defined. After the normalization of prices according to package size, dosage form, and concentration, the reference price has to lie within the smallest 30 percent of the previous year's price interval. In addition, at least 20 percent of all packages and of all prescriptions must be available for prices equal to or below the reference price at the time of implementation. Products with a market share of less than 1 percent are not considered in the calculation. The procedure bases on the previous year's prices. The Statutory Health Insurance Funds in Germany (FASHI) reviews and adjusts reference prices regularly. By law, reviews are supposed to take place every year. However, in the real-world reference prices are effectively adjusted in different intervals, mostly more than 12 months. Pharmaceutical companies can neither negotiate the assignment to a specific reference price clusters nor the reference price itself. The whole procedure is exogenous to the producers, as is the timing of possible adjustments. Although the actual design of internal reference pricing differs across countries, empirical studies find, on average, decreasing drug prices due to the policy.[4]

Co-payments in Germany are 10 percent of the pharmacy's selling price (p_i) with a minimum of €5 and a maximum of €10. Patients below 18 years and low-

[2] In the following, we use the notion reference pricing for internal reference pricing as opposed to external reference pricing, where reimbursement limits are set comparatively to prices in other countries.

[3] Stargardt, Schreyögg, and Busse (2005) provide a detailed description of the German reference price scheme.

[4] For example, in Norway (Brekke, Grasdal, and Holmas, 2009; Brekke, Holmas, and Straume, 2011), Spain (Puig-Junoy, 2007), Germany (Pavcnik, 2002; Augurzky, Göhlmann, Gress, and Wasem, 2009), and Denmark (Kaiser, Mendez, Ronde, and Ullrich, 2014). The success of internal reference pricing in enhancing price competition crucially depends on the definition of the reference price. Puig-Junoy (2010) provide a comprehensive review of the effect of regulation on prices in Europe.

income insurees with catastrophic health care costs do not co-pay. Reference pricing increases cost-sharing for those patients who prefer more expensive drug alternatives with prices exceeding the reference price. Compared to other European countries and to the US, the fraction of drug co-payments is small in Germany (Arcidiacono, Ellickson, Landry, and Ridley, 2013; Baicker and Goldman, 2011). Drug co-payments added up to €1.76 billion (€2.40 per package) in 2010 (ABDA, 2011).[5]

Co-payment Exemptions are introduced to some therapeutic markets of reference priced drugs since July 2006. If firms decrease prices below the exemption levels patients do not co-pay for these drugs. The maximum price of an exempt drug (the co-payment exemption level (CEL)) must lie at 30 percent below the respective reference price. The FASHI is supposed to decide on CEL based on expected savings. Basically, the new policy is similar to the introduction of a tiered co-payment system where firms can strategically decide on co-payments of their products.

4.3 Firm Strategies and Patients' Incentives

To analyze the effect of co-payment exemption levels, the theoretical section follows the idea of Frank and Salkever (1992) and derives testable hypotheses. We assume that firms maximize profits and are free in setting prices. We further assume that there is one brand name producer who is a Stackelberg leader in terms of price setting. This setting is realistic since we argue that consumers differ by preferences for brands. As Gorecki (1986) shows for Canada, pioneering drugs indeed have advantages in prices and market shares compared to later entries, which cannot always be explained by quality differences. He argues that physicians are brand-loyal in this case.

In our model, the Stackelberg leader sets p_b to maximize profits, assuming that the number of generic firms n is exogenous at that time period. The n generic firms in the market follow suit by setting prices according to a Nash equilibrium with respect to the brand price p_b and to the number of identical generic firms n in the market. Departing from Frank and Salkever (1992), we introduce the binary indicator $cel \in (0, 1)$, which is equal to one if a co-payment exemption level (CEL) is available and zero otherwise. Furthermore, we assume that the CEL also increases competition among the exogenous number of generic producers and reduces

[5] Many important studies are based on the RAND Health Insurance Experiment (Manning, Newhouse, Duan, Keeler, and Leibowitz, 1987) and estimate an overall elasticity of medical spending in the range of -0.2 to -0.6, similar for the elderly (Chandra, Gruber, and McKnight, 2010), for Medicare beneficiaries (Li, Guh, Lacaille, Esdaile, and Anis, 2007), and for families with lower income (Gruber, 2006).

the average generic price similar to additional generic competitors. To ease the derivations, we assume that the number of firms entering is independent of the availability of a CEL, and vice versa. More specifically, and without loss of generality, the number of generic competitors n is fixed.

The demand side is modeled to consist of loyal consumers who always purchase the branded drug irrespective of the generic price and the cross-price sensitive segment whose demand is influenced by both prices.[6] In the pharmaceutical market, generics can be viewed as very close substitutes. However, loyal customers may have high switching costs for several reasons: lack of switching experience, risk aversion, good experience with branded drugs, preferences for brands, or lack of information.

We now analyze a heterogeneous market with two consumer segments.

The brand-name producer's demand function is $Q_b = D_L(p_b) + D_S(p_B, p_G)$ with D_L the demand of the loyal segment only depending on the brand-name price and D_S the demand of the price-sensitive segment for the brand-name drug depending on both prices.

Since prices are set sequentially and we apply the Nash equilibrium concept, the game is solved by backward induction. In the second stage, the market demand function for n identical firms is $D_G(p_g, p_b, n, cel)$ and the equilibrium value of p_g is $p_g(cel, p_b, n)$. We assume that the generic price p_g decreases with the availability of a CEL and the number of generic firms and increases with the brand-name price. Furthermore, we assume that $\frac{\partial D_S}{\partial p_b} < 0$ and $\frac{\partial D_S}{\partial p_g} > 0$. The latter implies that the demand for the branded drug by price-sensitive consumers increases in the generic price.

In the first stage, substituting p_g into Q_b and assuming that the brand-name's producer has zero costs[7], we write the brand-name firm's profit function as

$$\pi = p_b \cdot [D_L(p_b) + D_S(p_b, p_g(cel, p_b, n))] = p_b \cdot Q_b(p_b, cel, n) \tag{4.1}$$

where $Q_b(p_b, cel, n)$ can be viewed as the reduced-form demand curve for the brand-name drug for given values of $cel \in [0, 1]$ and n.

Maximization of (4.1) with respect to p_b yields the first-order condition

$$\frac{\partial \pi}{\partial p_b} = p_b \cdot \left(\frac{\partial D_L}{\partial p_b} + \frac{\partial D_S}{\partial p_b} + \frac{\partial D_S}{\partial p_g} \cdot \frac{\partial p_g}{p_b} \right) + Q_{p_b} = 0 \tag{4.2}$$

Since demand Q_{p_b} is assumed to be non-negative, the first part of (4.2) must be negative for the first-order condition to hold.

[6] This assumption first appeared in Varian (1980), who distinguishes between informed and uninformed consumers in a homogeneous duopoly.

[7] In contrast, Frank and Salkever (1992) assume costs to depend on the drugs' quantities.

While we assume that the generic price decreases after the introduction of a CEL ($\frac{\partial p_g}{\partial cel} < 0$), the effect of a CEL on brand-name price, $\frac{dp_b}{dcel}$, can be assessed by a total differentiation of Equation 4.2.

The implicit function theorem gives us that $\frac{dp_b}{dcel} = -[\frac{\partial^2 \pi}{\partial p_b^2}]^{-1} \cdot \frac{\partial^2 \pi}{\partial p_b \partial cel}$. With $\frac{\partial^2 \pi}{\partial p_b^2} \leq 0$ for the equilibrium to be a maximum (second-order condition), solving the second multiplier it suffices to identify the sign of this equation.

$$\frac{\partial^2 \pi}{\partial p_b \partial cel} = \frac{\partial D_S}{\partial p_g} \cdot \frac{\partial p_g}{\partial cel} + p_b \cdot \left(\frac{\partial^2 D_S}{\partial p_b \partial p_g} \cdot \frac{\partial p_g}{\partial cel} + \frac{\partial^2 D_S}{\partial p_g^2} \cdot \frac{\partial p_g}{\partial cel} \cdot \frac{\partial p_g}{\partial p_b} + \frac{\partial D_S}{\partial p_g} \cdot \frac{\partial^2 p_g}{\partial p_b \partial cel} \right) \tag{4.3}$$

The sign of this equation is unclear a priori. The first term is negative by assumption. However, the term in brackets may be positive and exceed the size of the first term which would translate into a price increase of brand-name drugs due to a CEL. We now assume that $\frac{\partial^2 p_g}{\partial p_b \partial cel} < 0$, which means that generic prices react less to changes in brand-name prices if a CEL is in place. We further assume that $\partial p_g / \partial p_b > 0$, which makes the reduced-form demand curve $Q_b(p_b, cel)$ less own-price elastic than the ordinary demand curve for the brand-name drug. We further assume that $\frac{\partial^2 D_S}{\partial p_g^2} > 0$ holds, which means that the price-sensitive demand for the brand-name drug has a less elastic reaction to generic price increases the lower the generic price. It then crucially depends on the shape and the extent of the change of the cross-price sensitive demand curve D_S ($\frac{\partial^2 D_S}{\partial p_b \partial p_g}$) whether the branded price increases or decreases due to the introduction of a CEL. This specific term is negative if the demand for the branded good is more elastic for lower branded prices if p_g decreases than for higher prices. This means, that the demand curve for the brand-name drug with respect to p_b is rotated toward zero if p_g decreases.

This is similar to Frank and Salkever (1992) who identify one realistic condition to explain the observed generic competition paradox. They argue that entry must make the reduced-form demand curve steeper (less elastic). "If, for example, the purchasers with the strongest own-price response are more likely to reduce their purchases [of the branded drug] to zero as p_g falls, this will result in a steeper slope for the reduced-form demand curve [for the branded drug] since the remaining cross-price sensitive purchasers have (by assumption) weaker price responses."(Frank and Salkever, 1992) Under the assumptions above, there may be an equivalent effect for the introduction of a CEL. We thus hypothesize:

> The CEL will increase the price gap between drugs from innovators and generic firms if the demand curve becomes steeper due to a CEL. While

generic firms will compete even more in the low-price segment, innovative firms will not decrease prices and may even increase prices.

4.4 Estimation Strategy and Data

Estimation Strategy We investigate the effects of the co-payment exemption policy on firm's pricing strategies with a reduced-form price regression. We identify the results by a difference-in-difference approach and instruments for reference prices. The price equation for each drug is given by:

$$\begin{aligned} \ln p_{it} &= \beta_0 + \beta_1 \ln rp_{it} + \beta_2(gen_i \times CEL_{it}) \\ &\quad + \beta_3(brand_i \times CEL_{it}) + \beta_4(imp_i \times CEL_{it}) \\ &\quad + \beta_5 m_{it} + \sum_{t=2}^{15} \delta_t \tau_t + \alpha_i + \epsilon_{it} \end{aligned} \tag{4.4}$$

where i denotes drugs $i = 1, ..., I$ and t denotes quarters $t = 1, ..., T$. The price for each drug, $\ln p$, first depends on its reference price, $\ln rp$, and on the co-payment exemption policy, CEL. The variable *cel* is one from the quarter in which the co-payment exemption policy was introduced for the respective reference price cluster, and zero before. To identify effects by firm-type, the 364 companies are classified according to their websites into three unique groups: generic firms, brand-name originators, and importers.[8] To differentiate the effects by firm type, the policy dummy is interacted with firm-type: *gen* (generic), *brand* (brand-name), and *imp* (importing). We include the number of firms within the reference price cluster, m, to capture market size and proxy for competition. Time dummy variables, τ_t, control for quarter-specific shocks. Product fixed-effects (α_i) are constant over time (such as [observed] quality, package size or side effects, efficacy, the firm's management quality or the drug type), and ϵ_{it} are time and product normally distributed error terms.

Reference prices are an important predictor of prices. Their non-regular adjustments cannot be foreseen and they are published one to three months before the new reference price is binding to allow for price adjustments. Reference prices are based on prices that are lagged by 12 months on average. Prices of drugs with a less than 1 percent market share are not considered and at least 20 percent of all products

[8] A table with the classification is available from the authors upon request.

must be available at the reference price. The regulation is meant to rule out strategic price setting to influence the calculation of the reference price. By definition, reference prices depend on (lagged) prices in the same therapeutic market (reference price cluster). To control for potential endogeneity issues, we use instruments, i.e., a proxy for regulation intensity across different therapeutic markets.

We apply a difference-in-differences approach to estimate causal effects of the treatment. The treatment group consists of those reference price clusters in which co-payment exemption thresholds were introduced between Q2 2007 and Q3 2010, after the first period and before the last period of the sample. The control group consists of drugs that are treated in the last quarter, i.e., are affected by the CEL policy in the last quarter. The rationale for that choice is that both groups become treated over time and differ only in the timing of the introduction. Descriptive statistics and empirical tests confirm the validity and quality of the control group and are presented in the paragraph *Identification*. As robustness checks, we present also the results for another control group: clusters which had been treated already before 2007 (CEL before Q2).

Data We collect quarterly prices, reference prices, and characteristics at the product level of prescription drugs in Germany for the years 2007 to 2010. The sample includes all drugs for which reimbursement is defined by a reference price and which are potential candidates for a co-payment exemption. By the end of 2010, our data covered 71.7 percent of all drug packages sold and 36.6 percent of all pharmaceutical expenses in Germany (ProGenerika, 2011). Comparatively low prices are explained by the high share of generic drugs that fall under the regulation of reference pricing. Prices (p), reference prices (rp), and exemption levels CEL are at the level of pharmacy selling prices, including VAT and pharmacists reimbursements (which both remain unchanged over the study period). Products are identified with a unique identification number (PZN), by active ingredient, package size, strength, form of administration, and reference price cluster. The data set on reference prices is publicly available from the German Drug Regulatory Authorities.[9]

The data set of prices and reimbursements is merged with information about co-payments and exemptions thereof. Product-specific co-payment exemption levels are published by the Federal Association of Statutory Health Insurance Funds (FASHI) in Germany (FASHI, 2011).

The final sample comprises 2,105 packages of which there were 1,451 generic drugs, 362 drugs of brand-name firms, and 292 imports. Table 4.1 presents the tim-

[9] In cooperation with the German Drug Regulatory Authorities the German Institute for Medical Documentation and Information (DIMDI) quarterly updates a central information platform for pharmaceutical products and reference prices in Germany (DIMDI, 2011).

ing of the treatment. Co-payment exemption levels are introduced in 284 reference price clusters between Q2 2007 and Q4 2010. The heterogeneity in cluster size becomes clear in quarter 5, where 9 clusters and 260 drugs are treated, versus quarter 14 (242 drugs in 55 clusters).

Table 4.1: Newly Introduced Co-payment Exemption Limits

Quarter	Q3	Q5	Q7	Q9	Q14	Q16
# Packages	716	260	135	23	242	698
# clusters	34	9	10	3	55	167

Own calculations with data from the Federal Association of Statutory Health Insurance Funds, Q1 2007 to Q3 2010. Column Q16 presents the preferred control group treated in Q4 2010.

Table 4.2 presents descriptive statistics of the treatment group by the three product types before and after the treatment. Prices and reference prices are inflation adjusted to the base year 2007. On average, drug prices are lower after the reform on average and off-patent brand name products always have the highest price. More than 70 percent of the observations are drugs from generic manufacturers. The average number of firms decreases after the policy introduction.

The statistics in Table 4.3 investigate the pricing pattern in more detail. 97 percent of generic firms set prices below the reference price both before and after the policy. About 25 percent of the brand-name firms increase their prices to above the reference price after the reform. Before the treatment, all firm types set prices between 37 percent and 8 percent below the reference price. However, after the policy implementation, brand-name firms and importers set prices above the reference price. The last column of Table 4.3 ($P<CEL$) shows that a majority of generic drugs are exempt from co-payments while only a small fraction of brand-name drugs and imports are exempt. Around 14 percent of the original and imported packages would have been exempt one quarter before the introduction while only 6 percent are exempt after the introduction.

Identification The treatment group comprises all therapeutic markets in which the exemption policy was introduced between Q2 2007 and Q3 2010. The control group CEL(late) consists of all drugs that are treated in the last quarter, i.e., are affected by the CEL policy in the last quarter. Both groups become treated over time and differ only in the timing of the policy introduction. We present also the results for an alternative control group of therapeutic markets that were treated before 2007 (CEL early) as a robustness check.

Table 4.2: Descriptive statistics of the treatment group

	N		Price		Ref. price		# firms	
CEL	Before	After	Before	After	Before	After	Before	After
Generics	3,433	9,033	39.67	22.56	52.78	25.83	7.44	3.56
			(57.92)	(28.23)	(74.74)	(31.22)	(3.73)	(1.68)
Brand	797	2,007	75.21	44.06	79.48	36.28	6.18	4.86
			(106.8)	(63.08)	(117.1)	(59.23)	(2.35)	(1.69)
Importer	774	1,681	39.38	35.32	41.79	31.85	4.18	1.72
			(31.13)	(28.97)	(36.02)	(32.22)	(2.43)	(.90)

Descriptive statistics (means and standard deviations in parentheses) of the treatment group from Q1 2007 to Q3 2010, by firm class before/after the introduction of co-payment exemption thresholds. Average # of firms per reference price cluster. Data source: FASHI.

Table 4.3: Co-payment Exemptions and Prices

	(p-rp)/p		P<RP		P<CEL	
CEL	Before	After	Before	After	Before*	After
Generics	-.37	-.16	.97	.98	.49	.55
	(.45)	(.15)	(.15)	(.10)	(.50)	(.49)
Brand	-.09	.11	.91	.69	.14	.06
	(.37)	(.26)	(.28)	(.46)	(.35)	(.24)
Importer	-.08	.08	.90	.76	.12	.008
	(.19)	(.23)	(.29)	(.42)	(.32)	(.09)

This table displays means and standard deviations (in parentheses) of pricing patterns around the policy introduction of the treatment group from Q1 2007 to Q3 2010. * indicates hypothetical exemptions one period before the introduction of the policy. Data source: FASHI.

Table 4.4 presents descriptive statistics for the treatment and control group. Additionally, summary statistics for all drugs in the sample and for the alternative control group are shown. To investigate how similar therapeutic markets in the treatment and control groups are, we compare prices, reference prices, and co-payment exemption levels. The treatment and late control group (CEL late) show very similar prices and price-to-reference price ratios. Prices of the earlier treated control group (CEL early) are a bit higher but more drugs are priced below the reference price.

Table 4.4: Descriptive Statistics of Treatment and Control Groups

Sample	Price	Price<RP	Price<CEL	CEL (1=yes)	N
	mean	mean	mean	mean	
	(std)	(std)	(std)	(std)	
All	45	.94	.51	.76	373,056
	(115)	(.22)	(.49)	(.42)	
Treatment	32	.92	.41	.71	17,725
	(47)	(.26)	(.49)	(.45)	
CEL late	34	.92	.	.	6,533
	(29)	(.26)			
CEL early	55	.96	.52	1	256,743
	(133)	(.19)	(.49)	(0)	

Own calculations with data from the Federal Association of Statutory Health Insurance Funds, Q1 2007 to Q3 2010. All: all drugs in a reference price cluster (with and without CEL) from Q1 2007 to Q3 2010. Treatment: drugs facing a CEL introduction after Q1 2007 and before Q4 2010, CEL late: the preferred control group treated in the last quarter. CEL early: the control group treated before 2007.

Figure 4.1 shows mean prices for the treatment and control group and provides first descriptive evidence on the policy's effect on prices. The six largest treated therapeutic markets show decreasing mean prices due to the policy. The graph also provides evidence on the quality of the control group. The treated clusters show similar constant pre-policy price-trends as the control group.

The identifying assumption for the difference-in-difference approach is that the treatment and the control group do not differ in unobserved characteristics over time. For example, the group of drugs would differ if they show different time trends. We empirically test for the independent time trends of the treatment and the control group and regress prices prior to the treatment on time trends and on the interaction between time trends and treatment (Pavcnik, 2002). The variable *Quarter x Treatment* interacts quarter and an indicator for treated drugs. The results in Table 4.5 indicate a negative price trend over time [*Quarter*] and no

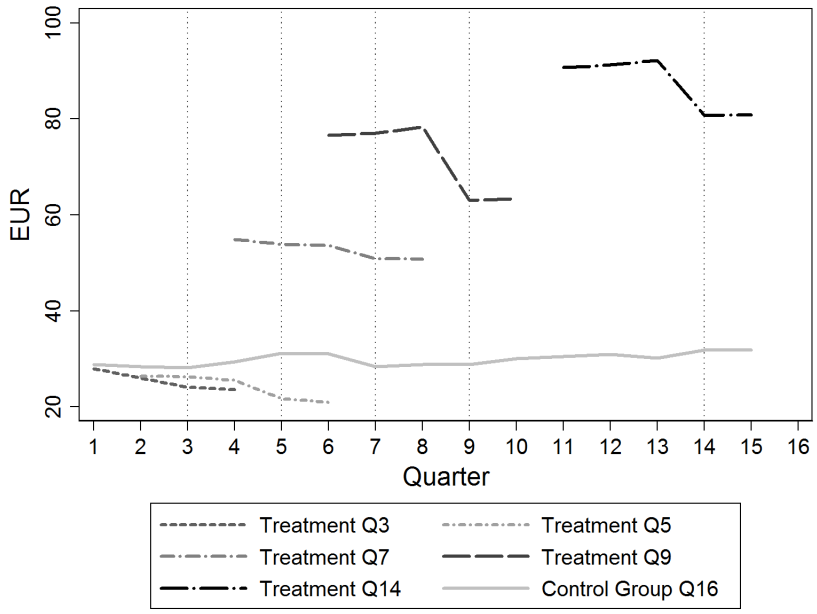

Figure 4.1: This graph shows mean prices of the five largest groups treated at different points in time two quarters before and one after the introduction of a CEL. The solid lines are mean prices over 15 periods of the control group CEL late.

statistical significant difference between the time trend of the treatment group and of the control group. In addition, CEL are introduced successively at different points in time. Time and product fixed-effects control for time-invariant drug attributes and time fixed-effects.

Table 4.5: Price Trends Prior to Treatments

	Price [ln]
Reference Price [ln]	.244***
	(.038)
Quarter	-.348***
	(.056)
Quarter × Treatment	.079
	(.056)
Constant	27.87***
	(1.822)
N	12,035
R^2_{adj}	.284

Clustered standard errors in parentheses; * $p < .05$, ** $p < .01$, *** $p < .001$; Sample includes only observations for pre-CEL periods. Data source: FASHI.

In Germany, an institution exogenous to the pharmaceutical market decides to implement CEL based on the legislative goal to generate savings. We could not find any pre-defined rules when to introduce CEL to which group, which was confirmed by the decision committee and business professionals. The implementation is an administrative bargaining result which can be characterized as a black box. The main identification assumption for Equation 4.4 is the exogeneity of the CEL introduction and of the reference price $[CEL|\epsilon = 0; rp|\epsilon = 0]$. We empirically test for drivers of the decision to introduce the policy. Therefore, we regress the treatment decision (one from the beginning of the policy, zero otherwise) on potential drivers of the introduction. Since the political goal of the policy is to generate savings, potential variables of interest are reference prices, prices, and market size approximated by the number of firms. Co-payment exemption levels are introduced at the level of therapeutic markets. Thus, we collapse our data on the therapeutic market (mean). Table 4.6 presents results of this estimation for the preferred control group (CEL late) in column (1) and for the alternative control group (cel early) in column (2). None of the variables in (1) is statistically different from zero which indicates that none of the variables has an effect on the decision to implement the policy. Results are similar for the alternative control group of early treated, although the number

of firms is statistically significant and positive. The latter results indicate an effect of market size on the decision to implement the policy. To control for the effect of market size, we include the number of firms in our price regression.

Internal reference prices depend on lagged competitors' prices. We instrument reference prices with changes in the reference price in all other therapeutic markets. How often and by how much reference prices change in other therapeutic markets depends on the focus of the regulator, i.e., the intensity of regulation. Policy makers might have a focus on particular therapeutic markets or some drug markets might attract attention due to special circumstances. Taking limited resources of the regulatory body into account, the regulatory activity in one market can indicate how much the regulator focuses on all other markets. The more a regulator focuses on one market, the lower the prices are in this market. Thus, we would expect a negative correlation of reference prices and reference prices in other therapeutic markets. F-tests of excluded instruments indicate that the instrument is relevant.

To address concerns about colluding firms: on average 23 firms are active in one therapeutic market (reference price cluster). A stable mechanism to collude in such an environment seems not very credible.

Table 4.6: Drivers of the Decision to Introduce CEL

	Treatment Decision	
	CEL late	CEL early
$ReferencePrice(ln)$	-0.33	-0.49
	(2.48)	(2.07)
$Price[ln]$	0.31	0.78
	(2.50)	(2.09)
$\#Firms$	0.58	0.90***
	(0.31)	(0.24)
Constant	-0.95	-3.71***
	(1.06)	(0.94)
N	103	251

Logistic regression; data collapsed on reference price group; panel variables: reference price group and quarter; 351 groups dropped because of all positive or all negative outcomes; * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$; Data Source: FASHI.

4.5 Results

This section provides empirical results on the effects of the co-payment exemption levels on pricing strategies and it presents robustness checks for our identifica-

tion strategy. Table 4.7 presents OLS and instrumental variable estimation results. Columns (1) and (2) show the overall effects of co-payment exemptions levels and columns (3) and (4) differentiate the effects by firm-type. Table 4.8 provides robustness checks.

4.5.1 Effects of the Co-payment Exemption Policy

OLS results in Table 4.7, column (1) indicate 2.8 percent lower prices after the co-payment exemption policy. Prices decrease by 2.1 percent if reference prices decrease by 10 percent. Once we use instruments for reference prices in column (2), the effect becomes more negative and prices decrease by 2.4 percent after a 10 percent decrease in reference prices. Controlling for unobservables decreases the effect of the exemption policy to 2 percent, as indicated in column (2).

When we differentiate the effect of co-payment exemptions by firm-type in columns (3) and (4). Prices for generics decrease by 4.9 percent and brand-name firms increase their prices by 6.4 percent on average. It turns out that generic firms respond more to the incentives of lower prices. Brand-name firms are able to charge higher prices, controlling for the insurance's reimbursement level. The policy does not affect prices of importing firms.

Since our results show similar effects as the "generic competition paradox," we name our findings the "co-payment exemption paradox" (Regan, 2008). Both mechanisms work in a similar way, i.e., brand-name firms increase their prices due to policies introducing more incentives for firms to compete in prices. The results above indicate a strong market segmentation which allows branded drugs to maintain higher prices, even with additional competition-enhancing instruments. Several papers have analyzed the paradox. As presented in section 4.3, we follow Frank and Salkever (1992), Kong and Seldon (2004) and Regan (2008) who explain their results in a Stackelberg framework. Other studies explain the phenomenon by heterogeneous health insurance coverage (Ferrara and Missios, 2012; Ferrara and Kong, 2008) and imperfect substitution between original and generic drugs (Nabin, Mohan, Nicholas, and Sgro, 2012) which is both unlikely in the German case. The joint analysis of reference prices and tiered co-payments through additional co-payment exemption levels gives insight into the effects of combining both policies. Our estimates confirm earlier findings of price decreases due to (changes in) reference prices (Regan, 2008; Pavcnik, 2002; Augurzky, Göhlmann, Gress, and Wasem, 2009).[10] The

[10] Augurzky, Göhlmann, Gress, and Wasem (2009) use similar price data and estimate an (ex-factory) price increases of 0.29 percent when the reference prices increases by 1 percent. Pavcnik

Table 4.7: Effects of the Copayment Exemption Policy

	(OLS-1) Price [ln]	(IV-2) Price [ln]	(OLS-3) Price [ln]	(IV-4) Price [ln]
Reference Price (ln)	.211***	.244***	.199***	.254***
	(.014)	(.022)	(.014)	(.021)
CEL	-.028***	-.020***		
	(.005)	(.006)		
# of firms (ln)	-.017***	-.018***	-.019***	-.020***
	(.006)	(.006)	(.006)	(.006)
CEL × generic			-.062***	-.049***
			(.007)	(.008)
CEL × innovator			.054***	.064***
			(.008)	(.010)
CEL × importer			.004	.012
			(.011)	(.011)
Constant	2.51***		2.56***	
	(.049)		(.050)	
Quarter FE	Yes	Yes	Yes	Yes
N	24,258	24,258	24,258	24,258
R^2_{adj}	.44	.38	.46	.40
F test excl IV		134		135

The columns IV use the average change in reference prices in other therapeutic markets as instrument for own reference prices. Standard errors are clustered at the product level and presented in parentheses; * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$; CEL: co-payment exemption level.

negative price effect of the number of firms is small but significant and underlines the negative price effect of competition and market size.

4.5.2 Robustness Checks

In this section we present and discuss alternative estimation techniques and approaches. In particular, we present results for an alternative control group and for a first-difference estimation. The latter controls for first-order serial correlation of the error terms of the reduced-form price equation. All estimates confirm our results from Section 4.5.

Table 4.8: Robustness Checks

	CEL early		FD	
Price [ln]	FE	IV	FE	IV
Reference Price [ln]	.306***	.269***	.160***	.209***
	(.005)	(.019)	(.014)	(.021)
CEL × generic	-.072***	-.080***	-.092***	-.079***
	(.006)	(.007)	(.006)	(.007)
CEL × innovator	.041***	.035***	.019***	.031***
	(.009)	(.009)	(.006)	(.008)
CEL × importer	-.010	-.015	-.027**	-.016
	(.012)	(.012)	(.011)	(.012)
# of firms	-.033***	-.034***	-.011***	-.011***
	(.003)	(.003)	(.004)	(.004)
Quarter FE	Yes	Yes	Yes	Yes
N	274,468	274,468	22,127	22,127
R^2_{adj}	.39	.38	.21	.20
F	829.92	827.05	101.23	100.57

The columns IV use the average change in reference prices as instrument for own reference prices. Standard errors are clustered at the product level and presented in parentheses; * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$; CEL: co-payment exemption level.

Table 4.8, columns (1) and (2), show in our preferred model that the general results hold for another control group: clusters which had been treated between Q3 2006 and Q1 2007 (CEL early). We observe only slight changes in magnitudes and

(2002) finds decreases in prices after a potential rise of the patients' out-of-pocket payments due to newly introduced reference prices.

standard errors. Prices and reference prices are still positively correlated and the effect of the co-payment exemption policy has a negative effect on prices of generic drugs and a positive effect on prices of brand-name drugs. Results of a first-difference regression show a more negative effect of co-payments as presented in column (3) and (4) of Table 4.8. The effect of the policy is -7.9 percent for generics and +3.1 percent for brand name products in the IV specification.

4.6 Discussion

This study utilizes data of all German drugs regulated by reference pricing between 2007 and 2010 and evaluates the introduction of co-payment exemption levels. We are the first study to analyze the policy and show that the co-payment exemption policy has a significant negative effect of -4.9 percent on generic prices (up to -7.9 percent, depending on the empirical specification). Brand-name drugs increase prices by 6.4 percent due to the new regulation. Analogously to the price increases of brand-name drugs after generic entry ("generic competition paradox"), we call this phenomenon the "co-payment exemption paradox." Our results are in line with previous findings in the way that we find signs of significant market segmentation despite multiple demand-side regulations in place (Regan, 2008). Furthermore, the results of this study do not suggest regulation overload (Danzon and Chao, 2000). The discussed combination of reference prices with co-payment exemption levels seems to foster price competition.

It is crucial to understand how demand-side instruments steer drug demand toward cost-efficient products. While reference pricing means that consumers of comparatively more expensive drugs have higher co-pays, the new policy rewards lower-priced drug users with zero co-pays. The CEL is defined as 70 percent of the reference price and we show that the introduction of another co-payment tier leads to lower prices on average.

We can distinguish two groups of patients in the market: one group is brand-loyal and the other is price sensitive and switches to cheaper drugs. The two policies, co-payment exemptions and reference pricing, seem to have different implications for both groups. While the reference price scheme leads to lower prices in general, the co-payment exemption policy allows firms to separate the two segments with respect to their price sensitivity. Higher priced drugs meet the demand of the brand-loyal consumers. Overall, it seems that the reference pricing scheme has a larger effect on prices.

This study does not observe sales or utilization of drugs. The success of the co-payment exemption policy depends also on the substitution behavior of patients.

The key question remains how many consumers switch to products without co-payments and how many patients are willing to bear higher co-pays. Our results indicate how firms respond to changes in market demand and to regulation. To be able to make more general statements about substitution, an analysis using sales data would complement our study.

In a first back-of-the-envelope calculation that quantifies the effect, we multiply the overall effect of CEL (2 percent) with the total spending of the public health insurance on prescription drugs regulated by reference pricing of €12,14bn in 2010. Assuming that this reform was introduced for the first time for all drugs simultaneously in 2010, the reform would have led to savings of about €242m. Analyzing the social welfare effects of the policy one would need information on sales to observe substitution behavior after the policy change. However, this would not be sufficient: international prices, data on physician or hospital visits, and follow-up costs would also have to be taken into account for a more complete welfare analysis.

The US approach to steer drug demand by co-payments seems to lead to higher generic penetration rates (Berndt and Aitken, 2011). However, the US health care system is different to the German institutions. For example, drug co-payments are significantly higher in the US than they are in Germany, where insurees co-pay 10 percent of the price (maximal €10) per package, regardless of the drug type. Nevertheless, the price effects of the CEL policy and of the adjustment of reference prices indicate a considerable demand elasticity. We may underestimate the real effect of co-payment exemption levels due to private information about rebate contracts between health insurances and generic producers who directly negotiate lower prices given a certain demand. However, it is a strong sign that we observe negative price effects even in list prices. The relevance of the policy during our observation period is supported by additional information from the FASHI which indicates that most exempt products (12,887) were sold in March 2010 (numbers were increasing steadily since 2006) while the overall number of products in the market remained constant (FASHI, 2011).

To rationalize regulations like reference prices or co-payment exemptions, these have to be more efficient than possible alternatives. The procedures and statistical measures of the reference price calculations vary significantly across countries and health insurances. For example, Italy, the Netherlands, and Poland set the maximal reimbursable price equal to the lowest price in the reference price cluster (Puig-Junoy, 2010). Some countries regulate generic markets with a strict generic substitution policy, for example, Norway (Kanavos, Costa-Font, and Seeley, 2008). The comparison of different reference price systems in terms of their effectiveness in lowering pharmaceutical expenditure is an interesting avenue for future research.

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Chapter 5

Conclusion

This dissertation applies recent empirical approaches to investigate market outcomes in the pharmaceutical industry. Methodologically, I apply structural models from the field of empirical industrial organization that combine theoretical rationales and empirical methods. Recent empirical advances give information on demand patterns, marginal costs, and margins; counterfactual results derive price changes and welfare outcomes.

The first chapter focuses on advertising spillovers from non-prescription drug markets on prescription drug demand. I find that positive and statistically significant spillovers from advertising in OTC drug markets influence the demand of prescription drugs from the same brand. Patients place a positive value on advertising and buy more Alzheimer's disease drugs from advertising brands. Since consumer-directed advertising is forbidden in most prescription drug markets, the findings have important implications for the optimal marketing regulations in drug markets. Observing an increase in medically-treated consumers with advertising and an increase in consumer surplus raises the question of whether advertising might be an instrument to increase demand for under-treated diseases.

The second chapter analyzes the welfare effects of parallel imports – legally imported drugs by a licensed trading firm which are available parallel to the approved original drug without the permission of the right's holder. Results show that the demand side, i.e., patients and health insurances, benefits from parallel imports while innovative firms incur profit losses. Generics seem to be less affected by the policy. We calculate an annual demand-side surplus of €19m.

The third chapter evaluates an insurance policy of tiered cost-sharing for pharmaceuticals. The German public health insurance exempts drugs from all co-payments if firms set a price 30% below the reference price, the maximum reimbursement of the health insurance. The policy impacts pricing strategies since firms can choose to decrease prices and let patients be exempt from co-payments. The results give insight in firms' strategies and show that generic prices decrease and brand-name drug prices increase as a result of the policy.

To conclude, this dissertation provides an in-depth analysis of the pharmaceutical industry by applying the most recent methodological techniques. My results help to understand how market regulations affect consumption patterns and the strategic interactions of firms. Policy advice from this dissertation supports the creation of more efficient regulations that benefit consumers.