Entry and Competition in the Pharmaceutical Market following Patent Expiry

Evidence from Macro and Micro Data

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Für meine Großmutter
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Preface

"Happiness is Nothing more than Good Health and a Bad Memory."
(Albert Schweitzer, 1875 - 1965)

The pharmaceutical industry has made substantial contributions to public health, putting immense financial resources into the discovery and development of novel drugs. Medications have improved the quality of health care, both changing the progression of diseases and increasing survival rates from serious illness (e.g. cardiovascular disease and cancer). The death rates for cardiovascular disease fell dramatically by 26.4% from 1999 to 2005 (Lloyd-Jones *et al.*, 2009). Since 1980, life expectancy for cancer patients has increased by about 3 years (Sun *et al.*, 2008). Lichtenberg (2004) shows that medicines account for 50% to 60% of increases in cancer survival rates since 1975. The *European Federation of Pharmaceutical Industries and Associations* (*EFPIA*) states that an average of 10-13 years will have elapsed since the first synthesis of the new active substance by the time a medical product reaches the market (EFPIA, 2010). According to the most recent estimate by DiMasi and Grabowski (2007), pharmaceutical companies devote on average $1.318 Bn. (in year 2005 dollars) to the research and development of one new chemical entity.[1] Drug development cost estimates typically include the costs of preclinical research and failed tests incurred for "product failures" (Scherer, 2004).[2] "Only about 21-23% of the new chemical entities that are subjected to human testing emerge at the end of the process with marketing approval; the rest fail at various stages" (Scherer, 2004).[3] According to the *EFPIA*, 3 out of 10 marketed

[1] PhRama (2010) report drug development costs of $1.3 Bn. as of 2005, $802 Mio. as of 2001, and $318 Mio. as of 1987. The reported drug development time is 10-15 years.

[2] Scherer (2004) emphasizes that drug cost estimates need to be regarded with a bit of caution. In case of the 2001 estimate of $802 Mio., for instance, only about half the estimated price tag entailed actual out-of-pocket costs; the remainder was an estimated 11% annual cost of financial capital invested in research and testing. The voluntary sample from which the estimates were drawn numbered only 10 companies which also placed a disproportionate emphasis on drugs for chronic diseases. Drugs used to treat acute symptoms and those directed toward small "orphan" markets are developed at a much lower average cost.

[3] EFPIA (2010) report that on average only one or two of every 10,000 substances synthesized in laboratories, will successfully pass all the stages to become marketable medicines.

drugs return revenues that match or exceed R&D costs prior to patent expiration.[4] The top-selling medications (blockbuster drugs) allow pharmaceutical companies to recoup R&D investments (also those of failed products) and earn a profit. The European Commission reports that the top-ten blockbuster drugs in the 27 European Member States as of 2007, accounted for a tremendous share of companies' global turnover of up to 55% (EUC, 2009).[5]

Medical products are usually subject to patent protection. The basic statutory patent life is 20 years. About 12-13 years of basic product patent life remain by the time a medical product reaches the market (Scherer, 2004).[6] Several blockbuster medicines went off-patent[7] in recent years and many more will lose patent protection in the next few years (EUC, 2009). Most pharmaceutical companies have difficulties to refill the drug pipeline with new products[8], especially with products offering major improvements over existing medications[9].

Upon patent expiry, generic firms typically enter the market with medicines that are equivalent to the original (brand) drug. The revenues from brand-name drug manufacturers tend to erode massively only within a few months of generic competition. According to the *European Generic Medicines Association* (*EGA*) generic products sell at a 20-90% price differential to the off-patent brand product, generating €25 Bn. in drug cost savings each year for the European health care systems.[10] EUC (2009) emphasize that generic competition is essential to keep public budgets under control and to facilitate widespread access to novel medicines at the same time. During the past decade, health care spending has increased steadily, and pharmaceuticals have been a key factor driving the growth in health care costs (EUC, 2009). In the German statutory health care system – the largest in Europe – drug expenditures increased from €17.7 Bn. to €27.8 Bn. alone over the period 1998-2007.[11]

[4] www.efpia.eu/Content/Default.asp?PageID=407&IsNewWindow=True; According to PhRama (2010) only 2 out of 10 marketed drugs return revenues that match or exceed R&D costs.

[5] EUC (2009) find that blockbuster medicines offered profit margins of up to 80%. The therapeutic areas addressed by the main blockbusters are cardiovascular system, respiratory system and nervous system.

[6] Pharmaceutical companies customarily apply for patent protection on new chemical entities shortly before clinical tests in humans commence (Scherer, 2004). EUC (2009) report an average (effective) protection period of 12.5 years in the EU member states from 2000 to 2007, as counted from the market launch of the drug to first generic entry in a national market.

[7] In Germany, for instance, the blockbuster drugs *Zocor* (Merck & Co), *Norvasc* (Pfizer), *Risperdal* (Johnson & Johnson) lost patent protection in 2003, 2004 and 2007 respectively.

[8] From 1995 to 1999 an average of 40 novel molecular entities were launched worldwide per year. From 2000 to 2007 the average was only 27 (EUC, 2009).

[9] Many of the drugs that are being invented are of the "me–too" variety-variants of existing drugs; www.newyorker.com/archive/2004/02/16/040216ta_talk_surowiecki (accessed: Nov 15th 2010).

[10] www.egagenerics.com/gen-geneurope.htm (accessed: Nov. 15th 20010).

[11] www.gesundheitspolitik.net/04_medikamente/apotheke/oeffentlich/GEK-Arzneimittelreport-2009.pdf.

To fully benefit from the potential savings brought about by generic products, effective price competition among generic firms has to be ensured (EUC, 2009). Generic entry must not be deterred or delayed, and demand should respond to price differentials (EUC, 2009).

There is an ongoing debate both in Europe and the U.S. (FTC, 2002; EUC, 2008; FTC, 2009; EUC, 2009) whether brand-name drug manufacturers impose barriers to generic entry by increasingly filing secondary patents[12] and authorizing generic entry prior to patent expiry. Introducing a generic version of the brand drug prior to patent expiry, brand-name drug producers extract a large fraction of generic firms' revenues over the following years. First generic entrants enjoy a substantial and long-term first-mover advantage over subsequent entrants. EUC (2009) state that generic entrants focus on blockbuster products, which are "often the backbone of many originator companies, [and] which they aim to defend".

For prescription medicines, the ultimate consumer (patient) differs from the decision maker (physician or pharmacist) and very often also from the bearer of the costs (health care system). As a consequence, decision makers' and patients' price sensitivity is considered to be rather limited (EUC, 2009). Without appropriate financial incentives on the demand side, EUC (2009) fear that demand shifts away from the cheapest medicine supplied towards more expensive alternatives. So far, however, there is no compelling evidence of how the given peculiarities on the demand side influence the effectiveness of generic price competition.

On the supply side, the discussion has centered on optimal price control mechanisms as "competition between generic firms, (⋯) broadly speaking takes place on the basis of price" (EUC, 2009). Manufacturing costs account on average for 51% of firms' annual turnover with prescription drugs in 2007. Marketing and promotion costs by contrast account for 13% (EUC, 2009). Generic and originator companies' cost structures differ notably.[13] Nevertheless, the assumption that generic firms merely compete on price may be too simplified.

Examining entry and competition in pharmaceuticals following patent expiry, this thesis provides novel insights into the dynamics of intra-generic competition and the effectiveness of generic price competition. Chapter 1 investigates how strongly authorized generic entry

[12] Secondary patents are filed for different dosage forms, the production process or for particular pharmaceutical formulations.

[13] The ten largest originator companies in the EU spent over €40 Bn. per year on global marketing and promotion activities. This is more than twice the global turnover of the ten largest generic companies in the EU. Both manufacturing and marketing/promotion costs account on average for 21% of originator companies' annual turnover with prescription medicines in 2007. R&D costs account for 18% (EUC, 2009).

affects the entry decisions of generic firms, and thus generic entry patterns in off-patent drug markets. Based on a macro analysis of generic market shares and a micro analysis of patients' switching behavior among generic products, Chapter 2 delivers evidence on the price sensitivity of demand for generic drugs. Chapter 3 studies the variation in prices across generic firms to evaluate the importance of cost differences and product differentiation.

The three Chapters are closely related to each other. The empirical analyses are all directed to the German generic drug market, which is the world's second-largest market for generic drugs after the United States.[14] Therefore, industry and regulatory setting remain the same in all studies. The analyses also rely in parts on the same data. The studies in Chapter 2 and Chapter 3 both make use of generic product panel data. Patient tracking data are additionally made use of in the empirical study presented in Chapter 2. The study described in Chapter 1 resorts to micro (firm) data as well. Conducting analyses both at the macro and micro level, important generic drug industry dynamics are uncovered in the three Chapters, all of which are self-contained and can be read independently of each other.

In recent years, brand-name drug manufacturers have increasingly often introduced a generic version of the brand (original) drug prior to patent expiry. Doing so, they obtain a notable share of profits made in the generic market segment, and can mitigate the erosion of the brand-name drug's revenues following generic entry. First generic entrants apparently enjoy a substantial and sustainable first-mover advantage over subsequent generic entrants (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Hollis, 2002). Both in Europe and the U.S. (FTC, 2002; EUC, 2008; FTC, 2009; EUC, 2009) there has been an ongoing debate over whether authorized generic entry substantially lowers incentives for independent generic entry, impairing generic price competition and putting at risk drug expenditure savings.

A few empirical studies (Hollis, 2003; Reiffen and Ward, 2007; Berndt *et al.*, 2007a,b) investigate the impact of authorized generic entry – treated as exogenous – on independent generic entry, yet arrive at different conclusions. There is overall no comprehensive empirical evidence based on recent data that would show authorized generic entry to have had a delaying or deterring effect on generic entry (Berndt *et al.*, 2007a). Except for the study by Berndt *et al.* (2007a), peer-reviewed analyses rely on data from the late 80s, early and mid 90s. Hollis and Liang (2006); FTC (2009) also note that set of drug markets experiencing

[14] www.nytimes.com/2010/03/19/business/global/19drugs.html (accessed: Nov. 15th 2010).

authorized generic entry is not a random selection of markets. Giving rise to selection bias and inconsistent estimates, authorized generic entry should not be treated as exogenous.

Assessing the impact of authorized generic entry on independent generic entry, the study presented in Chapter 1 is the first to employ recent micro data and to account for the endogeneity of authorized generic entry. The study examines the independent generic entry decisions made in the course of patent expiries in the German pharmaceutical market from 2002 to 2007. The German pharmaceutical market experienced the largest number of authorized generic entries of all European generic drug markets from 2000 to 2007 (EUC, 2009).

The results unambiguously show that authorized generic entry has no significant effect on the likelihood that a generic firm enters the drug market following patent expiry. Drug markets' pre-entry revenues turn out to have a significantly positive and the largest impact on generic entry decisions. Like previous studies (Morton, 1999), I also find that generic firms' therapeutic and drug form experience influence generic entry decisions positively.

The fact that intermediate-sized and high-revenue drug markets experienced authorized entry proportionally more often, indicates that originators authorized generic entry prior to patent expiry first and foremost fueled by rent-seeking rather than strategic entry-deterrence motives (Fisher Ellison and Ellison, 2007). Government scrutiny would be necessary if small drug markets experienced authorized generic entry more frequently in the future.

Chapter 2 provides a fundamental motivation for why first generic entrants enjoy a substantial and long-term first-mover-advantage over subsequent generic entrants, or in other words, for why brand-name drug producers authorize generic entry prior to patent expiry.

Looking at identical active ingredients, drug forms and dosage sizes, prices vary notably across generic firms, yet market shares are largely persistent over time. Evidently, consumers' sensitivity to price differentials is low. The previous literature provides little evidence of how persistent generic market shares are, and of how strongly they are affected by prices (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Hollis, 2002), which is in turn is indispensable to evaluate the efficiency of generic price competition. Resorting exclusively to macro data, the studies identify important trends in generic prices and market shares but not the factors influencing generic market shares' persistence. Related micro studies focus on physicians' prescribing behavior (Hellerstein, 1998; Coscelli, 2000; Paraponaris *et al.*, 2004), and do not investigate pharmacists' and patients' choice among generic products, in particular their

sensitivity to price differentials. As a result of generic substitution laws, pharmacists and patients make the choice among bio-equivalent drug products in the vast majority of cases.

The empirical study presented in Chapter 2 provides recent and comprehensive evidence of how strongly generic market shares are affected by prices over time, employing both macro and micro data. Generic product panel data allow me to examine at macro level the effect of generic prices on market shares and the persistence of the latter. The chosen estimator addresses the problem of dynamic panel and simultaneity bias. Patient tracking data facilitate a micro analysis of patients' switching behavior among generic products in response to price differentials. The analysis accounts for patient and drug characteristics as well as for treatment specificities. Both micro and macro analysis are directed to generic products in 35 drug markets, where drugs went off-patent in Germany over 2002-2006.

The macro analysis shows that generic market shares are quite persistent over time. Generic prices have a strikingly small and decreasing impact on market shares over time. After about 32 months of generic competition, a price change has essentially no impact on the market share of the generic firm. The micro analysis indicates further that patients habitually receive the same generic product. The longer patients receive a particular drug, the lower is the probability that they switch among generic products. The persistence of generic market shares observed at macro level can, however, also be attributed to patients' and pharmacists' low price sensitivity. Pharmacists and patients are largely insensitive to the price differentials across generic products, and they are only slightly more cost sensitive as the size of the generic price differential increases. This phenomenon may explain why generic prices have a small and slightly decreasing effect on market shares over time.

One implication of this finding is that patients will switch more infrequently among lower-cost generic products, where price differentials are small. Price competition could be stimulated if insurance providers', pharmacists' and patients' financial interests were to be aligned more closely. If patients, for instance, participate more proportionally in the financial consequences of their drug choices, they should have a greater incentive to save on drug costs. A revision of the current copayment and dispensing fee structures seems to be necessary.

Whereas Chapter 2 studies how strongly the demand for generic drugs responds to price differentials, Chapter 3 investigates which supply side factors potentially drive the latter.

Generic drugs are therapeutically equivalent (bio-equivalent) to off-patent brand-name drugs, and generic firms' marketing expenditures are relatively low. Not only in public debates but also in the economic literature (Morton, 2002; Hollis, 2005), generics firms are often regarded as Bertrand competitors, offering an undifferentiated drug product at identical cost (Reiffen and Ward, 2005) and competing exclusively on price. The Bertrand model of competition with undifferentiated goods predicts zero price variation as soon as two or more generic entrants compete in one drug market, which is not consistent with empirical evidence.

Generic firms presumably have cost advantages in the production, storage and promotion of generic drugs (economies of scope), which allows them to be more competitive in price (Natz, 2008). Moreover, companies appear to be able to claim higher markups the more reputation and brand recognition they enjoy among consumers. Generic firms establish brand recognition in the German generic drug market, building umbrella brands through the corporate branding of generic drug products. Several theoretical papers show that umbrella branding can have a positive impact on both firms' investment in product quality and the price consumers are willing to pay. Only a few empirical studies investigate the price variation in individual drug products (Grabowski and Vernon, 1992; Wiggins and Maness, 2004; Kanavos *et al.*, 2008). Economists attribute the variation in generic prices to perceptions of quality differences among firms (brand loyalty) and differences in product variety, yet they deliver no direct evidence of how cost or reputation differences affect generic prices.

This study examines the variability in generic prices to evaluate the importance of cost differences and product differentiation (umbrella branding), and to reassess the validity of the Bertrand assumption. Generic firms' drug portfolio size provides a measure of cost advantage. The size of the umbrella brand facilitates in turn a measure of firm reputation. Generic product panel data allow me to measure the impact of drug portfolio and umbrella brand sizes on generic prices in 35 off-patent drug markets, where generic products were launched from 2002 to 2007. Among other important price determinants, I control for package size differences and firms' market share. I employ several estimators, to first replicate essential results of the previous studies, and to investigate endogeneity issues in the second step.

This study shows that the variability of generic price can largely be attributed to differences in firms' drug portfolio and umbrella brand size, providing evidence of economies of scope and brand recognition in the generic drug industry. Generic firms claim a higher

price premium the more umbrella branded drugs they supply. In spite of the price premium, generic manufacturers charge overall lower prices the broader their drug portfolio is.

Brand-name markups for generic products are not necessarily desirable. Generic products carry only the international non-proprietary name of the active ingredient in the US and UK pharmaceutical market. A pure INN marketing strategy for generic drug products might also be a viable and beneficial solution for Germany. Similar studies targeting other important pharmaceutical markets would be useful to corroborate and supplement the current study's findings, and to obtain additional evidence of the validity of the Bertrand assumption.

The structure of the pharmaceutical industry is unique and very complex. There are many stakeholders – pharmaceutical and generic companies, health care insurance providers, physicians, pharmacists and patients to name some of the most important actors. Governments are also closely involved, and there is high degree of regulation. The regulations aim to support innovation, ensure a high degree of public health, and to keep health care budgets under control. Generic competition is essential in this context as it "enables sustainable treatment of more patients with less financial resources" (EUC, 2009). There is a great public debate on whether generic firms can compete effectively in off-patent drug markets.

This thesis contains several empirical studies all of which make a substantial contribution to this debate. Overall, the studies show that generic firms do not effectively compete on price as the demand for generic drugs is very inelastic. Originators' practice to authorize generic entry prior to patent expiry does not deter generic entry. The implementation of rebate contracts in Germany in April 2007 was likely motivated by both pharmacists' and patients' low price sensitivity. Rebate contracts practically force patients to switch to a possibly cheaper generic product which their statutory health care insurance provider contracted for. Rebate contracts provide a natural experiment to study the persistence of generic market shares and the dispersion of generic prices. How generic drug industry dynamics changed after April 2007 is an important research question and will be the subject of future work.

Chapter 1

Authorized Generic Entry prior to Patent Expiry: Reassessing Incentives for Independent Generic Entry

1.1 Introduction

As blockbuster drugs lose patent protection and drug pipelines have run dry, "Big Pharma" seeks ways to limit profit erosion following generic entry.[1] One increasingly common practice has become the introduction of a generic version of the original drug prior to the loss of exclusivity – expiry of patent or supplementary protection certificate (SPC)[2] –, either through a subsidiary or licensee/supply partner (early entry). The increasing frequency of early entry has raised policy concerns (FTC, 2002; EUC, 2008; FTC, 2009; EUC, 2009). First-movers enjoy a sustainable competitive advantage over subsequent entrants (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Hollis, 2002), and anticipated early entry may reduce incentives for generic entry and put at risk drug expenditure savings. The prevailing assumption is that generic firms anticipate early entry based on drug markets' characteristics and past experiences. A few empirical studies (Hollis, 2003; Reiffen and Ward, 2007; Berndt *et al.*, 2007a,b) investigate the impact of early entry – exogenously given – on generic entry, arriving at different conclusions. Berndt *et al.* (2007a) concede that authorized generic entry prior to patent expiry may reduce incentives to generic firms, yet they emphasize that there

[1] *The Economist*, January 24^{th} 2008: "The bitterest pill".

[2] A certificate that allows for an extension of market exclusivity for up to five years after patent protection which – depending on the life cycle of the drug – is granted by the national patent office.

is no comprehensive empirical evidence based on recent data that would show early entry to have had a delaying or deterring effect on generic entry. Except for the study by Berndt *et al.* (2007a), peer-reviewed analyses rely on data from the late 80s, early and mid 90s. This study is the first to employ recent micro data to examine generic and early entry decisions.

The previous debate has largely centered on the effect of anticipated authorized generic entry on generic firms' incentives to pursue paragraph IV challenges prior to patent expiry. In the U.S., the first generic manufacturer to file for market approval with a successful paragraph IV certification (claim of patent non-infringement or patent invalidity) is granted a 180-day exclusivity period where no other generic firm (except for the authorized generic) is entitled to market the same version of the drug. If authorized generic entry drastically lowered generic firms' incentives to file paragraph IV certifications, generic entry could be delayed. The 180-day exclusivity period is an institutional feature specific to the U.S. pharmaceutical market. Moreover, only a fraction of generic applications seek entry prior to patent expiry.[3] Whether early entry broadly impaired generic entry in recent years, remains an open question. Providing a complete answer to this question requires the modeling of original drug producers' early entry decisions which are endogenous. Original drug producers appear to decide on early arrangements on a case-by-case basis most often in the year prior to loss of exclusivity (EUC, 2009). Hollis and Liang (2006) and FTC (2009) emphasize that set of drug markets experiencing early entry is not a random selection of markets.

This study accounts for the endogeneity of early entry and provides comprehensive empirical evidence on the impact of early entry on generic entry decisions made in the course of recent patent expiries. The analysis relies on a unique micro data set comprising pharmaceutical market and exclusivity data (patents and SPCs) for the German pharmaceutical market, the second largest generic drug market in the world, experiencing the largest number of early entries of all European generic drug markets from 2000 to 2007 (EUC, 2009). 75 substances[4] lost exclusivity (patent or SPC protection) between 2002 and 2007. By the end of 2007, 87 generic firms entered in 48 markets[5], resulting in a total of 724 market entries[6]

[3]From 1998 to 2000, 20% of generic applications included a paragraph IV certificate (FTC, 2002).

[4]Throughout the paper the term substance is equivalently used for mono-substance, i.e. a substance that contains one active ingredient only. As the allocation of all relevant patents and supplementary protection certificates to mono-substances is delicate, the analysis is confined to mono-substances.

[5]Other studies report similar rates of generic entry, e.g. Magazzini *et al.* (2004).

[6]As one firm typically enters in more than one market, this yields 724 generic entries in total.

by independent generic firms. Of the 48 drug markets experiencing generic entry, 16 markets were affected by early entry from 2002 to 2007. Early entry occurred on average four months prior to loss of exclusivity. I estimate univariate and recursive bivariate probit models of entry to quantify the impact of early entry. Treating early entry as exogenous (univariate probit model) may give rise to a selection problem and inconsistent estimates if early entry occurs in markets that are more attractive than given market characteristics suggest, or in other words, if there is a spurious correlation between early entry and generic entry decisions. Bivariate probit estimates indicate that early entry decisions are endogeneous. The identification strategy in the bivariate probit model relies on the assumption of normality and the fact that I model sequential entry decisions. Exclusion restrictions are not necessarily required to achieve identification in recursive bivariate probit models (Wilde, 2000; Greene, 2008). I do impose one exclusion restriction to improve identification. As early entry decisions are arguably motivated by pioneers' financial distress, I add a count of originators' further losses of exclusivity between 2002 and 2007 as an instrumental variable to the early entry equation. As Evans and Schwab (1995), I provide tentative empirical evidence on the suitability of the instrument, showing that the instrumental variable has no significant effect on independent generic entry decisions. Determining the average marginal effect of early entry in the bivariate probit model, I compute the average change in the probability of generic entry conditional on early entry having and having not occurred. Standard errors are computed using the delta-method (Papke and Wooldridge, 2005). Regardless of the identifying assumption made, early entry turns out to have no significant impact on the probability of generic entry. Originators appear to authorize generic entry prior to loss of exclusivity to extract revenues rather than to deter generic entry. Drugs' pre-entry market size has the strongest impact on generic entry decisions. A 1% increase in pre-entry revenues induces on average a 14-18% increase in the likelihood of generic entry. Furthermore, the number of off-patent drug substitute affects entry negatively, whereas the length of the exclusivity period and firms' therapeutic and drug form experience influence generic entry decisions positively.

The organization of the paper is as follows: Section 1.2 provides relevant industry information. Section 1.3 reviews the literature on early entry. Section 1.4 describes the data, and Section 1.5 specifies the empirical implementation. Section 1.6 presents and discusses the empirical findings. Concluding remarks follow in Section 1.7.

1.2 Industry Background

With a market size of €4.5 Bn. and a generic penetration (efficiency[7]) rate of about 20% (68%) as of 2007, Germany is the second largest generic drug market in the world, and the largest generic drug market in Europe, experiencing the largest number of generic and early entries between 2000 and 2007 (EUC, 2009). Hence, it is one of the most important pharmaceutical markets to examine when seeking insights into generic and early entry decisions. The following paragraph outlines the market approval process of generic drugs and the regulatory framework in Germany, shaping generic competition post patent expiration.

Generic drugs are therapeutically equivalent to the off-patent, brand (original) drug: they contain the same active ingredient, have identical quality and performance characteristics, the same strength and the same or a similar route of administration. Originator's market share typically drops quickly as generic firms enter. The case of Pfizer's bestseller product Norvasc illustrated in Appendix [1.1] is only one prominent example. As a result of price competition and lower R&D outlays, generic firms offer large price discounts of up to 95%.[8] Instead of expensive safety and efficacy tests, generic firms conduct bioequivalence studies.[9] In drug stability studies, they prove further that the drug product remains within the established specifications and maintains its identity, strength, quality and purity throughout the expiration dating period of typically two or three years. To obtain market approval on time, generic firms prepare for market entry at least three years ahead of entry.[10] Generic entry usually occurs as soon as the patent or supplementary protection certificate (SPC)[11] for the brand drug expires. Occasionally, originators also authorize generic entry prior to loss of exclusivity[12] and launch a generic version of the brand drug through a generic subsidiary or a licensee/supply partner (early entry).[13] Independent generic firms file abridged applications for market approval, referring to the reviews of experts and clinical test results obtained in the course of the brand drug's approval process. Current law entitles generic

[7]The generic efficiency rate indicates the fraction of multi-source drug prescriptions dispensed as generic. Own calculations based on *Insight Health* prescription data.

[8]Own calculations based on generic price data for 35 drug markets in Germany from 2002 to 2007.

[9]Generic firms prove in bioequivalence studies that the rate and extent of absorption of the active ingredient is identical to that of the reference drug. It takes at most four month to conduct such studies.

[10]Interviews with industry experts provided further, detailed information on the stages and time frame involved in the generic drug approval process.

[11]If an originator applies within six month after the brand drug's market approval for a SPC and the national patent office approves the request, the exclusivity period will be extended by up to five years.

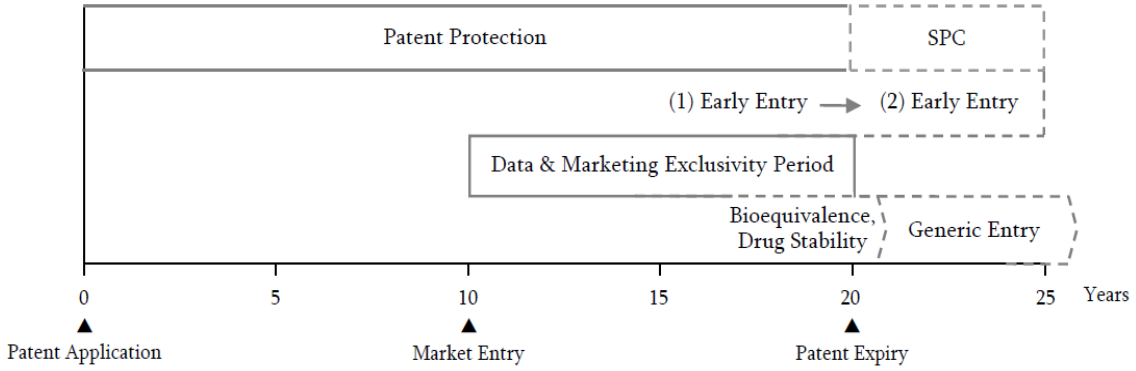
[12]EUC (2008), pp. 11, 246; *The Economist*, August 6^{th} 2009: "Friends for Life"; "Something Rotten".

[13]Original drug producers appear to decide on early arrangements on a case-by-case basis most often in the year prior to loss of exclusivity to generate substantial profits (EUC, 2009).

firms to cite such documents without notice or permission of the originator once eight years have passed since the brand drug's launch (data exclusivity period).[14] If the data exclusivity period elapsed, generics may conduct bioequivalence studies while the reference drug is still patent-protected. However, generic drugs are not be marketed until 10 years have passed since the brand drug's launch (marketing exclusivity period).[15] A centralized application procedure has increasingly been used by generic firms in recent years, providing a single market authorization for the European community (EUC, 2008).[16] Applications are submitted for evaluation to the *European Medication Evaluation Agency (EMEA)*, which gives a recommendation to the European Commission within 270 days unless major objections are identified. The European Commission grants market approval and informs the applicant.

In summary, generic firms decide upon market entry at least three years prior to loss of exclusivity. Due to the disclosure of generic applications until shortly before the grant of market approval[17] generic firms sink entry costs simultaneously and can only form expectations about competitors' actions.[18] Figure 1.1 below outlines the various exclusivity mechanisms. At the discretion of originators early entry may either occur prior to patent (1) or SPC expiry (2). Independent generic firms enter after patent (or SPC) expiry, depending on the duration of bioequivalence studies and timing of generic drugs' market approval.

Figure 1.1: From Patent Application to Generic Entry



[14] With the implementation of the *Bolar provision* in German law, "working under patent" became legal. For applications filed in Germany prior to November 2005 the data exclusivity period amounts to 10 years.

[15] If the originator obtains market approval for at least one additional indication within eight years after market entry, the marketing exclusivity period is extended for another year (8+2+1-Rule).

[16] The centralized procedure has been accessible to generic firms since 2005. Alternatively, generics can file national applications at the *Bundesinstitut für Arzneimittel und Medizinprodukte*. Via the mutual-recognition procedure, the national market authorization can be extended to other EU countries.

[17] EUC (2008), pp. 15, 271; Accenture (2005): Market approval is often granted later than expected.

[18] Entry costs comprise the costs of conducting bioequivalence studies – \$40.000-150.000 (WHO, 2005), market approval fees – at the EMEA, an annual fee of €21.700 in addition to a basic fee of €94.100 (EUC, 2008) – and legal costs in the event of litigation, settlements etc..

An increase in generic substitution has been achieved through the enforcement of the *Act for the Limitation of Drug Expenditures* (*Arzneimittelausgaben-Begrenzungsgesetz, AABG*) in February 2002, introducing the *Aut-idem* regulation for prescription drugs. If doctors do not exclude substitution by checking the *Aut-idem* box on the prescription pad, a pharmacist is encouraged to sell one of the 30% lowest priced (generic) drug products to the patient. Since January 2004, dispensing fees on prescription drugs[19] consist largely of a fixed component[20], reducing pharmacists' incentive to sell high-priced drugs. In the same year, reimbursement practices were also altered. Patients covered by statutory health insurance have been prompted to make a co-payment for each drug product they purchase. The co-payment amounts to 10% of the retail price, the minimum contribution is €5 and €10 is the maximum. As most drugs are sold in packages priced below €50, patients are often inclined not to search for a cheaper drug with the same active ingredient (Accenture, 2005). Patients generally get prescription drug coverage up to a predetermined reference price and must pay for any extra costs in addition to the co-payment. As of May 2006, co-payments become obsolete if a drug product is priced 30% or more below the reference price.[21] In April 2007 the *Statutory Health Insurance Competition Reinforcement Act* (*Gesetz zur Stärkung des Wettbewerbs in der gesetzlichen Krankenversicherung , GKV-WSG*) was enforced, legally authorizing the use of rebate contracts. Ever since statutory insurance providers have been permitted to close exclusive supply contracts with the generic firm offering the lowest price for a particular medical product. Thereafter, pharmacists must provide patients with that specific generic drug product, unless patients insist on another generic drug product and incur the additional expenses. Except for rebate contracts, previous regulations seem to have provided generally few incentives to switch between identical generic drugs as long as price differences are minor, conferring a sustainable advantage to generic first-movers.

1.3 Literature Review

The distinctive features of competition in off-patent drug markets have attracted the attention of various economists. Previous empirical studies prove pre-entry market size (Morton, 1999; Saha *et al.*, 2006), firm and drug characteristics (Morton, 1999), and the

[19] Around 78% of pharmaceutical sales are made on prescription drugs (BPI Pharma-Daten 2008).

[20] Pharmacies receive a fixed fee of €8.10 on each product sold, plus 3% of the product's purchase price.

[21] To secure fair competition practices, companies have also been prohibited from giving discounts in kind to pharmacies since May 2006. Financial rebates have been restricted to non-prescription drugs.

brand-name drug's goodwill stock (Hurwitz and Caves, 1988; Hudson, 2000) to be important influencing factors of generic entry. A few empirical studies address the issue of early entry – also known as authorized, branded or pseudo-generic entry – gauging its potentially anti-competitive impact on independent generic entry. Early entry is a common phenomenon in both Europe and the USA. Generic first-movers have been shown to enjoy a long-lasting advantage over subsequent generic entrants (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Hollis, 2002).[22] Not only can the first generic entrant serve the market for a longer period of time – with fewer competitors and higher generic profits after patent expiry – but it can also capture and sustain a substantially larger market share over a period of several years. On these grounds early entry may drastically reduce incentives for generic entry and harm off-patent competition. Prior studies draw different conclusions about the effect of early entry on generic entry decisions. Whereas Hollis (2003) argues that early entry has a deterring effect on generic entry and substantial welfare effects, Reiffen and Ward (2007) and Berndt *et al.* (2007a) hold a more moderate view on the ultimate impact of early entry.

Hollis (2003) explains that patients' unwillingness to switch between medications, search and "persuasion" costs on parts of doctors, and the administrative costs of pharmacies when stocking several (identical) generic drugs result in switching costs. Switching costs are not easy to overcome as generic drugs are bio-equivalent and competitors match prices immediately as soon as one firm lowers its price. Referring to a related study (Hollis, 2002) establishing evidence on first-mover advantages in the Canadian generic market, he concludes that brand-controlled pseudo-generics substantially lower incentives for generic entry.

Reiffen and Ward (2007) examine the motivation of original drug manufacturers in the USA to introduce authorized generics pre-patent expiry, addressing the issue of entry deterrence. Based on structural estimates from earlier empirical studies (Caves *et al.*, 1991; Reiffen and Ward, 2005), they calculate the effect of authorized generic entry on generic industry profits and the number of generic entrants in equilibrium, which in turn affects generic and brand prices, and eventually original drug producers' profits. Their calculation shows that the anticipation of (exogenously given) authorized generic entry crowds out between 1.7 to 2.4 generic entrants depending on the size of switching costs but independent of market size. Reiffen and Ward (2007) argue that original drug producers introduce authorized generics

[22] Berndt *et al.* (2002) provide similar evidence for Rx-to-OTC switches of antiulcer and heartburn drugs.

in large drug markets fueled by rent-seeking motives, i.e. to capture generic profits without substantially affecting the number of generic entrants or generic prices. In small and medium-sized markets on the contrary, entry deterrence motives play an important role as the impact on generic entry and prices is relatively large. Reiffen and Ward (2007) argue that early entry is least problematic and also most profitable in high-revenue drug markets.

Recent evidence on the consumer welfare effects of authorized generic entry in the USA has been provided by Berndt *et al.* (2007a,b). The studies examine the impact of (exogenously given) authorized generic entry on the filing of Abbreviated New Drug Approvals (ANDA)[23] with a paragraph IV certification (claim of patent non-infringement or invalidity), i.e. they look at generic entrants' incentives to enter timely and not necessarily at the actual market entry decision. Under the Hatch-Waxman Act of 1984, the first generic firm to file an ANDA with a successful paragraph IV certification is granted a 180-day exclusivity period where no other firm (except for the authorized generic) is entitled to market the same version of the drug. Berndt *et al.* (2007b) point out that several factors besides authorized generic entry may limit the profitability of the 180-day exclusivity period.[24] They show that in spite of the increase in authorized generics since 2003, there is little change in the total number of paragraph IV certifications, paragraph IV certifications per drug, and timing of filings relative to approvals of new chemical entities. Based on a review of descriptive statistics, they conclude that the effect of authorized generic entry on independent generic entry and consumer welfare in the U.S. is likely to be small. Berndt *et al.* (2007a) emphasize also that there is no comprehensive empirical evidence based on recent data that would show early entry to have had a delaying or deterring effect on independent generic entry.

1.4 Data

Through a matching of national pharmaceutical market and exclusivity data, a unique data set has been created, tracking substances' losses of exclusivity and generic entry between 2002 and 2007. *Insight Health* provides pharmaceutical market, patent and SPC data.[25] The

[23] Abbreviated New Drug Approval: application process for generic entrants in the USA, where therapeutic equivalence to the original drug and quality of the manufacturing process has to be proven.

[24] Multiple entrants are awarded 180-day exclusivity given they apply for the same dose at the same day.

[25] *Insight Health* has obtained exclusivity data from the national patent and trademark office since 2005. I accessed the PATDPASPC, Esp@cent Patent, Derwent and Open Drug database, Thomson's Current Patent Gazette, the FDA Orangebook, and online patent expiry reports to complement and verify the data.

pharmaceutical market data comprise information on drugs[26], medical products and manufacturers. Additionally, they provide product-level information on prices, turnover and revenues generated in the German retail segment. Exclusivity data give information about patent holders, originators, the date of patent and SPC application, the date of first market approval. The analysis is limited to human medications containing one active ingredient to ensure a high matching quality of pharmaceutical and exclusivity data.[27] Moreover, it is confined to data on retail revenues, i.e. wholesale and direct purchase transactions of public pharmacies. I disregard hospitals sales due to data availability constraints. In Europe, the turnover generated with prescription medications is significantly larger in the retail segment. In 2007 the retail turnover was approximately three times as large as the turnover generated in the hospital segment(EUC, 2008). As a result of quantity discounts, prices charged to hospitals are also typically much lower than retail prices. Thus, for the vast majority of drugs in this study (prescription drugs), retail revenues provide a sufficiently reliable measure of markets' attractiveness. Furthermore, I have not been able to obtain data on advertising expenditures. Pharmaceutical firms spend a substantial fraction of profits on advertising[28], yet these data are private and for researchers almost impossible to acquire. Pre-expiration brand advertising may not be a barrier to generic entry (Morton, 2000) – original drug producers' intensity of advertising decreases drastically as exclusivity expires (Berndt *et al.*, 2003; Janakiraman *et al.*, 2008; EUC, 2009)–, and generic advertising may be rare (Scherer, 2000; Berndt *et al.*, 2003), the lack of advertising data is certainly a limitation of this study.

79 drugs experienced a loss of exclusivity between 2002 and 2007. Four drugs are excluded from the sample given their uncommon routes of administration (lung, eye and systemic use)[29], confining the analysis to 75 markets with a predominantly oral, topical or parenteral drug form use. SPC extensions were granted for 60 drugs. By the end of 2007, 87 generic firms entered in 48 out of the 75 markets[30], resulting in a total of 724 generic entries.[31] As

[26]Strength, drug form and therapeutic field(s) of indication are specified. The drug form classification follows the New Form Code (NFC) Classification established by the *European Pharmaceutical Market Research Association (EphMRA)*, the classification of therapeutic fields in turn rests upon the Anatomical Therapeutic Chemical (ATC) Classification System which was introduced by the *WHO* in 1976.

[27]The consistency of generic entry and exclusivity data was verified. If generic entry occurred prior to patent or SPC expiry, investigations were carried out to find evidence on early entry or patent invalidity cases that would explain entry prior to the official date of patent or SPC expiry.

[28]Direct advertising of prescription medications to consumers is illegal in the European Union.

[29]Only Formoterol attracts generic entry (route of administration: lung).

[30]Other studies report similar rates of generic entry, e.g. Magazzini *et al.* (2004).

[31]As one firm typically enters in more than one market, this yields 724 generic entries.

generic firms tend to focus on high revenue markets several entry opportunities attract no entry (Morton, 1999; Hollis, 2003). Of the 48 drug markets experiencing generic entry, 16 were affected by early entry – on average four months prior to loss of exclusivity. Licensing/supply agreements were the preferred mode to arrange for early entry. A generic version of the original drug was launched through a generic subsidiary in the case of two drugs only. A total of 26 early entries took place as originators would often cooperate with two generic firms. Table 1.1 outlines important characteristics of the 75 entry opportunities arising between 2002 and 2007: pre-entry market revenues (in € Mio., evaluated at producer prices, two years prior to loss of exclusivity), the extent of generic entry, the duration of monopoly (number of years from original drug's market approval to loss of exclusivity) and the number of off-patent drugs available (substitutes) treating the same indication(s)[32].

Table 1.1: Generic Entry Opportunities 2002–2007

	Markets	Pre-Entry Market Size		Entries	Monopoly (Yrs.)		Substitutes	
	N	Mean	Median	N	Mean	Median	Mean	Median
Generic Entry	48	47.8	32.9	724	12.3	12.5	50.7	43.5
Early Entry	16	55.6	39.8	301	12	12.5	45.9	33.5
No Early Entry	32	43.9	25.2	423	12.5	12.5	53.1	45.5
No Generic Entry	27	0.6	0.2	0	11.7	13	42.9	35
Total	75	32.7	14.8	724	12.1	12.5	47.9	39

Notably, very small markets experience no generic entry. The average pre-entry market size of drug markets experiencing generic entry amounts to of € 47.8 Mio.. Also, early entry appears to be focused on high revenue markets comparing either mean or median pre-entry market sizes of the given markets. Grouping the 25 smallest, the 25 intermediate-sized and 25 largest drug markets with an average pre-entry market size of € 2.2 Mio., € 17.6 Mio. and € 78.3 Mio., I find evidence for a monotonic relationship between generic entry (early entry) and pre-entry market size. Generic entry (early entry) occurs in 4 (1) small-revenue, in 21 (4) intermediate-sized and in 23 (11) high-revenue markets. Differences in the duration of monopoly are generally minor. Original drug producers exclusively supplied drug markets for approximately 12 years on average. Generic entrants also appear to enter more "crowded" (profitable) therapeutic fields. The number of available, off-patent drugs (substitutes) treating the same indication(s) – a measure of the intensity of off-patent competition prior to generic entry – tends to be larger in the 48 markets experiencing generic entry. Appendix

[32]Therapeutic fields are classified by the ATC System at the second level of aggregation (ATC2).

[1.2] illustrates the patterns of losses of exclusivity, generic entry and early entry from 2002 to 2007 and it sketches the highly left-skewed distribution of pre-entry market sizes.

The unit of observation in the analysis is the market entry decision of a generic firm. Observing firms that decided to enter, one remains agnostic about those firms which refrained from entry. For an examination of generic entry decisions, negative entry decisions (zero-entries) need to be accounted for, however. As in Morton (1999), sets of potential entrants are constructed for each substance to identify generic firms that could have entered but decided not to do so.[33] The pharmaceutical data set lists around 985 firms that supplied the German pharmaceutical market between 1999 and 2007. By restricting the set of potential entrants to manufacturing firms (no re-import[34]) with at least half of the retail form portfolio being classified as "generic", 395 firms remain. By limiting the set of potential entrants further to those firms with a portfolio of at least 50 retail forms the number of firms is reduced to 101. These 101 firms manufactured 94.4% of all generic retail forms available on the German market between 1999 and 2007. The first set of potential entrants is defined for each drug market by including only those firms that are in business as exclusivity expires (Data Set 1). The criteria might seem arbitrary at first, yet they turn out to predict generic entry decisions very well. In 672 out of 724 generic entries between 2002 and 2007 (92.8%), generic entrants fulfilled these criteria. Thus, the criteria should be similarly apt to identify potential entry candidates which eventually refrained from entry. A further restriction of entry candidates may be warranted as not all of those firms were similarly likely to have decided upon each of the 75 entry opportunities. Morton (1999) finds that generic firms therapeutic and drug form experiences influence entry decisions positively. Two further sets of potential entrants are created for each and every drug market to account for potential entrants' experiences.

The second set of potential entrants limits entry candidates in the first set of potential entrants to those firms which prove to be experienced in the relevant fields of indication as exclusivity expires, having marketed a positive number of retail forms in the given therapeutic fields (Data Set 2). The third set of potential entrants lastly restricts the second set of entry candidates to those firms which additionally have expertise in manufacturing the relevant drug form(s) as exclusivity expires, having launched a positive number of particular drug

[33] Kyle (2007) determines market entry opportunities in a similar context. See also Kyle (2006).

[34] As of 2007 re-import firms have supplied only a minor fraction of 3.9% of all generic retail forms.

forms (Data Set 3). Table 1.2 below summarizes the sets of criteria employed to identify potential entrants, providing an overview of the three data sets accordingly generated.

Table 1.2: Outline Data Set Construction

	Data Set 1	Data Set 2	Data Set 3
Definition	Active generic firms (share generic retail forms ≥50%) supplying at least 50 retail forms (no re-import firms).	Firms in Data Set 1 which are active in the relevant field(s) of indication (ATC2).	Firms in Data Set 2 with drug form experience (NFC1).
Potential Entrants			
Total	127	126	126
Mean	100.2	37.4	33.7
Median	101	38	34
Zero-Entries			
Total	6793	2080	1807
48	4081	1251	1058
27	2712	829	749
Mean	90.6	27.7	24.1
48	85.0	26.1	22.0
27	100.4	30.7	27.7
Median	93	23	21
48	85.5	22	19
27	101	31	30
Generic Entries			
Total	724		
Mean	15.1		
Median	14		
Sample Size (N)	7517	2804	2531

Notes: Statistics for generic entries refer to the 48 drug markets experiencing generic entry by 2007, whereas statistics for potential entrants and statistics for zero-entries are presented for all 75 drug markets in the sample. Latter statistics are additionaly disaggregated by drug markets with (48) and without (27) generic entry.

With an increasing limitation of the total number of potential entrants from data set 1 to data set 3, the average and median number of potential entrants declines notably.[35] The same applies to the number of zero-entries and sample sizes. There are on average about 100, 37 and 34 potential entrants for one drug market. Given that there are around 50-60 generic firms in Germany, and given that innovative pharmaceutical firms would supply generic drugs in various instances (acis Arzneimittel GmbH, 2007), too, these numbers appear to be reasonable. Between 2002 and 2007, 48 drug markets experienced generic entry. A total of 724 generic entries occurred in the given time period. Approximately 15 generic firms entered

[35]Whenever firms which are not tracked in the sets of potential entrants enter markets, the total number of potential entrants increases from 101 to 127, and to 126 respectively.

into one drug market. Appendix [1.3] provides an overview of the distribution of generic entries and negative entry decisions (zero-entries) over the 75 drug markets. Depending on the established criteria for sets of potential entrants, a fraction of 9.6%, 26% and 29% of the various entry opportunities are realized. Morton (1999) examines 123 firms and 363 drug markets (drug and drug form combinations) and uses a similar methodology, yet somewhat different criteria to identify potential entrants. Having created substantially more entry opportunities in each of the three data sets (N_1=42059, N_2=33979, N_3=23811), Morton (1999) finds that only a fraction of 2%, 3.5% and 7% of observations experience generic entry. As such, my criteria are not necessarily less restrictive than the criteria employed in the previous study.[36] In general, the more restrictive criteria I employ, the smaller become not only the sets of potential entrants assigned to drug markets but also the fractions of identified, positive generic entry decisions. Some generic firms enter unknown therapeutic fields and a few firms also launch new drug forms. Using the second (third) set of criteria to identify potential entrants, I can trace back 78.7% (76.5%) of positive generic entry decisions. Any of the criteria employed to identify potential entrants in the specific drug markets seem to predict generic entry decisions sufficiently well. Therefore, any of the criteria should be similarly suitable to identify generic firms which decided not to enter. Using all of the three data sets in the empirical analysis allows me to verify the robustness of results.

1.5 Empirical Implementation

Using the three cross-sectional micro data sets, I examine the impact of early entry on independent generic entry decisions. Generic first-movers have been shown to enjoy a long-lasting competitive advantage over subsequent generic entrants (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Hollis, 2002) as a result of doctors', patients' and pharmacists' switching costs (see Section 1.2 & 1.3). Along those lines, early entry is likely to diminish the expected profitability of subsequent generic entry (EUC, 2009). As generic firms are uncertain about competitors' entry decisions until the latter obtain market approval, they can only form expectations about the event of early entry when deciding upon market entry. The underlying assumption made in all related studies is that generic firms are apt to predict early entry

[36] Examining 1444 unique molecules produced by 278 firms in 134 therapeutic classifications over the time period 1980-1999 in 28 European countries, Kyle (2007) identifies 299567 entry opportunities (drug-country-class-year observations), out of which 7,630 had a product launch (2.5%).

(Hollis, 2003; Reiffen and Ward, 2005; Berndt *et al.*, 2007a,b). Given the frequent occurrence of early entry – firms presumably learning from past experiences – this assumption appears to be reasonable. Industry experts also assured me that generic firms must essentially expect early entry in high-revenue drug markets. The hypothesis pursued in this study, is specified below. I make no further assumptions about the size of the early entry effect.

Hypothesis: Early entry prior to loss of exclusivity has a negative effect on independent generic entry decisions (deterrence effect).

Both generic entry and early entry are dichotomous variables. One observes market entry but not the profits generic firms or early entrants (original drug producers) expected to reap upon entry (latent variable), which in turn motivated firms' entry decision. For the majority of generic firms early entry is practically "exogenously" given, i.e. they have no means to directly influence original drug producers' decisions. Yet, there is no reason to believe that early entry is truly exogenous. The set of drug markets in which early entry occurs is not a random selection of drug markets (Hollis and Liang, 2006; FTC, 2009). Unobserved factors determine expected market profits, and thus both the likelihood of generic and early entry. For instance, therapeutic innovations change the future competitive landscape and may let entry into a certain market appear less attractive than observed market characteristics suggest. On the contrary, long-term clinical studies may reveal that a substance is very effective in a specific therapeutic field, and entry becomes more attractive. Demographic trend projections possibly affect expected profits as well. If generic and early entry occur in selective drug markets which are more attractive than given market characteristics suggest – the most likely scenario –, there will be a spurious correlation between early entry and generic entry decisions. The selection effect may understate the effect of early entry, basically counterbalancing the presumably negative effect of early entry. In other words, the early entry dummy may to some extent pick up drug markets' (unobserved) attractiveness.

Ignoring endogeneity issues, I estimate a univariate probit model in the first step to obtain a basic insight into the impact of early entry (ee_i) on the generic entry decision of firm j in market i (g_{ij}). As previous empirical studies on generic entry (Hurwitz and Caves, 1988; Morton, 1999; Hudson, 2000; Saha *et al.*, 2006; Moreno-Torres *et al.*, 2009), I control for pre-entry market size, the duration of monopoly, the number of off-patent substitute active ingredients, therapeutic field, drug form and year fixed effects ($\mathbf{X}$). I also account for

potential entrants' capabilities, i.e. their therapeutic and drug form experiences ($\mathbf{C_{ij}}$). Firms' experiences influence generic entry decisions (Morton, 1999; Kyle, 2006). In all regressions standard errors are robust to heteroscedasticity and clustered at firm level. Firms' entry decisions are arguably not independent. The univariate probit model is specified below.

$$g_{ij} \;=\; 1[g^*_{ij} > 0] \quad \textit{where} \quad g^*_{ij} \;=\; \mathbf{X}\boldsymbol{\beta} + \mathbf{C_{ij}}\boldsymbol{\alpha} + \delta ee_i + \epsilon_{ij}$$

In order to allow for a correlation (ρ) between generic entry and early entry decisions over the error terms and to provide evidence for selection, I estimate a recursive bivariate probit model in the second step. The bivariate probit model is a natural extension to the univariate probit model. The error terms ϵ_{ij} and μ_i are assumed to be distributed bivariate normal, with $E(\epsilon_{ij}) = E(\mu_i) = 0$, $Var(\epsilon_{ij}) = Var(\mu_i) = 1$ and $Cov(\epsilon_{ij}, \mu_i) = \rho$. Evans and Schwab (1995) adopt this empirical approach in a seminal paper. Various studies in health economics trying to gauge the impact of a binary endogenous treatment on a binary outcome rely on the recursive bivariate probit model (Goldman *et al.*, 2001; Jones *et al.*, 2006). Bhattacharya *et al.* (2006) conduct a Monte Carlo exercise to evaluate the consistency of multivariate probit, two-stage probit and two-stage least squares estimators when examining the impact of a binary treatment on a binary outcome in a non-randomized setting. Bhattacharya *et al.* (2006) point out that the results argue in favor the multivariate probit, especially when the average probability of the dependent variable is close to 0 or 1, or when the data generating process is not normal. The identification strategy in the bivariate probit model relies on the assumption of normality and the fact that I am modeling sequential entry decisions. Exclusion restrictions are not necessarily required to achieve identification in recursive bivariate probit models (Wilde, 2000; Greene, 2008)[37]. I do impose one exclusion restriction, however, to improve identification. As early entry decisions are arguably motivated by original drug producers' financial distress, I add a count of each original drug producers' further losses of exclusivity in the time period 2002 to 2007 as instrumental variable to the early entry equation ($\mathbf{I}$). Past losses of exclusivity are included. Original drug producer's financial distress is expected to have a positive effect on the likelihood of early entry. Original drug producers who do not experience many patent expiries in the given time period are ceteris paribus financially better off and depend less on current income streams

[37]Review also online material provided by William Greene (accessed December 2009): pages.stern.nyu.edu/∼wgreene/DiscreteChoice/Lectures/Part5-Bivariate&MultivariateProbit.ppt

and their preservation. Out of the 19 originators in the sample, 11 originators conclude early entry agreements facing on average 3.4 further losses of exclusivity, whereas the remaining 8 originators experience on average only 0.5 further losses of exclusivity between 2002 and 2007. The number of original drug producers' further losses of exclusivity is exogenously given, forming only a small subset[38] of all entry opportunities in the given time period. The high frequency of further losses of exclusivity also suggests that originators could make use of early entry arrangements primarily to mitigate the loss of monopoly profits. Original drug producers' advertising efforts in a given market are known to decline around the time of patent expiry and to drastically decline thereafter (Berndt *et al.*, 2003; Janakiraman *et al.*, 2008; EUC, 2009), suggesting that advertising is not an alternative channel through which original drug producers' financial distress would impact independent generic entry decisions.

If, after controlling for other observed drug market and firm characteristics, *Financial Distress* is correlated with generic firms' unobserved propensity to enter into a given market, it will not provide a valid exclusion restriction. One straightforward way to address this issue, yet not a formal test, is to include the instrumental variable in the single-equation probits. Single-equation models are misspecified if there is selection, but they still offer a a clear sense of the patterns in the data (Evans and Schwab, 1995). Besides this tentative empirical evidence for the suitability of the instrument, I conduct a likelihood-ratio test of the restricted versus unrestricted recursive bivariate probit model showing that the instrument improves identification and the model's goodness of fit. The recursive bivariate probit model's specification is given below. It is identical to the univariate probit model except for the second equation – the early entry decision ee_i – which is now additionally to be estimated. Due to lack of variation in the data, drug form effects are not accounted for in the early entry equation. Early entry occurs in drug markets with oral drug form use only.

$$\begin{aligned} g_{ij} &= 1[g_{ij}^* > 0] \quad \textit{where} \quad g_{ij}^* = \mathbf{X_1}\boldsymbol{\beta_1} + \mathbf{C_{ij}}\boldsymbol{\alpha} + \delta ee_i + \epsilon_{ij} \\ ee_i &= 1[ee_i^* > 0] \quad \textit{where} \quad ee_i^* = \mathbf{X_2}\boldsymbol{\beta_2} + \mathbf{I}\boldsymbol{\tau} + \mu_i \end{aligned}$$

The dependent variable of particular interest in all regressions is *Generic Entry*, denoting the market entry decision of an independent generic firm. *Generic Entry* is coded as 0-1 dummy and it takes on the value one if an independent generic firm decides to enter a

[38] Original drug producers face on average 2.2 further losses of exclusivity between 2002 to 2007.

specific drug market post loss of exclusivity. The *Early Entry* dummy regressor – introduced to generic entry equations to examine the effect of early entry on generic entry decisions – similarly takes on the value one if a generic version of the original drug is launched in a specific drug market prior to loss of exclusivity. *Pre-Entry Market Size* is a fundamental control variable in generic (early) entry equations (Berndt *et al.*, 2007a; Fisher Ellison and Ellison, 2007; Reiffen and Ward, 2007). *Pre-Entry Market Size* denotes the annual revenues in logarithms in a given market two calendar years prior to loss of exclusivity (evaluated at producer prices, in € Mio). I use a lagged version of the variable to avoid endogeneity issues. *Monopoly Duration* and *Substitutes* are two further, important control variables in generic (early) entry equations. *Monopoly Duration* measures the number of years from the original drug's first market approval to loss of exclusivity. Previous studies have shown that the effective duration of monopoly has a negative effect on generic entry, mainly arguing that original drug producers' goodwill stocks are larger (Hurwitz and Caves, 1988; Hudson, 2000). *Substitutes* proxies the intensity of off-patent competition in therapeutic fields, indicating the number of off-patent substitute active ingredients available in a particular therapeutic field. Whenever off-patent drugs fall into the same ATC2 class as the drug in question, they are counted as substitutes[39], a common approach in the literature (Kyle, 2007). The intensity of off-patent competition is assumed to affect generic (early) entry decisions negatively (Moreno-Torres *et al.*, 2009). The variables *Field Experience* and *Form Experience* are introduced in generic entry equations to account for potential entrants' capability to enter specific markets. *Field Experience* serves a proxy for potential entrants' therapeutic experience, denoting the number of retail forms the generic firm has launched in the relevant therapeutic fields prior to loss of exclusivity. Similarly, *Form Experience* is a count of the number of retail forms the generic firm has marketed of a specific drug form, proxying the firm's drug form experience.

Remember that the variable *Financial Distress* is introduced in early entry equations only, providing an exclusion restriction and facilitating identification in recursive bivariate probit regressions. *Financial Distress* indicates the number of further losses of exclusivity original drug producers' have to face in the time period 2002 to 2007. The more financial losses original drug producers experience the larger is presumably the likelihood of early entry.

[39]Of course, substances in the same ATC2 class are not necessarily perfect substitutes. Nevertheless, one obtains a first insight into the degree of off-patent competition in a certain therapeutic field; see Kyle (2007).

Therapeutic field, (drug form)[40] and year fixed effects are accounted for by introducing sets of dummy variables to generic entry and early entry equations. Table 1.3 provides a summary of definitions for all variables employed in the analysis. Other variables measuring, for instance,

Table 1.3: Definition of Variables

Variable Name	Definition
Generic Entry	0-1 dummy variable,=1 if independent generic firms decided to enter drug market post loss of exclusivity (patent or SPC expiry).
Early Entry	0-1 dummy variable,=1 if early entry occurs prior to loss of exclusivity.
Pre-Entry Market Size	Annual drug market revenues in logarithms two calendar years prior to loss of exclusivity, in € Mio., evaluated at producer prices.
Monopoly Duration	Number of years from dugs' market approval to loss of exclusivity.
Substitutes	Count of off-patent substitute active ingredients, listed in the same therapeutic field(s) (ATC2 Class.) by the time exclusivity expires.
Field Experience	Count of potential entrants' retail form launches prior to loss of exclusivity, in therapeutic field(s) (ATC2 Class.) the drug is applicable in.
Form Experience	Count of potential entrants' retail form launches prior to loss of exclusivity, having an identical route of administration (NFC2 Class.).
Financial Distress	Count of further losses of exclusivity which original drug producers' experience between 2002 and 2007.
Therapeutic Field	0-1 dummy variable,=1 if drug is applicable in therapeutic field prior to loss of exclusivity (13 ATC1 classes/dummies).
Drug Form	0-1 dummy variable,=1 if drug has been primarily administered orally, parenterally or topically prior to loss of exclusivity.
Year Expiry	0-1 dummy variable,=1 if loss of exclusivity occurs in 2002, $\cdots$, 2007.

drugs' therapeutic applicability, or the number of losses of exclusivity (entry opportunities) in a given year, proved insignificant. Hence, only a parsimonious set of variables is presented. Summary statistics for Data Set 3 are presented in Table 1.4 below. Appendices [1.4] and [1.5] provide summary statistics for Data Sets 1 and 2. Given the different composition of the three data sets (see Section 1.4), the distribution of variables differs. For instance, with the number of zero-entries decreasing from Data Set 1 to Data Set 3, the fraction of positive generic decisions increases. So does the fraction of independent generic entry decisions affected by early entry. The fraction of positive generic entry decisions amounts to roundabout 29% in Data Set 3. About 24% of generic entry decisions are affected by early entry. The average generic entry decision is made for a drug market with pre-entry revenues of € 37.5 Mio., where original drug producers enjoyed a duration of monopoly of about 11.9 years[41], and faced roughly three further losses of exclusivity over the time period 2002 to 2007. Potential generic entrants decide on drug launches in therapeutic fields with on average 54 off-patent, available substitutes prior to drugs' loss of exclusivity. Before entry

[40] As early entry occurs in drug markets with oral drug form use only, drug form fixed effects cannot be controlled for in early entry equations.

[41] Grabowski and Kyle (2007) find similar average market exclusivity periods for the same time interval.

Table 1.4: Summary Statistics Data Set 3

Variable Name	Mean	Median	Min.	Max.	Sd.	N
Generic Entry	0.29	0	0	1	–	2531
Early Entry	0.24	0	0	1	–	2531
Pre-Entry Market Size (€ Mio.)	37.5	20.1	0	187	44.5	2531
Pre-Entry Market Size (log)	16.08	16.82	0	19.05	3.20	2531
Monopoly Duration	11.86	12.5	5	20	3.0	2531
Substitutes	53.97	44	8	204	36.28	2531
Field Experience	26.38	12	0	374	37.43	2531
Form Experience	178.8	85	0	1679	224.97	2531
Financial Distress	2.92	2	0	6	2.47	2531

opportunity arose, potential entrants marketed on average 26 retail forms in the relevant therapeutic fields, and 179 retail forms using the specific drug's routes of administration.

1.6 Results

In order to provide basic insights into the impact of early entry on independent generic entry decision, a univariate probit model, ignoring any endogeneity issues, is estimated at first. An overview of the estimates obtained from each of the three data sets is given in Table 1.5 below. Coefficients look remarkably similar, even though the composition of the data sets varies. Univariate probit estimates indicate that early entry has an adverse effect on generic entry decisions, the size and precision of the estimate notably decreasing from Data Set 1 to Data Set 3. The early entry effect obtained for Data Set 3 is not significant anymore.

Generic entry decisions are significantly and positively influenced by pre-entry market sizes in turn, regardless which regression estimates one refers to. *Monopoly Duration* also has a significantly positive impact on independent generic entry decisions, which is a rather striking result. Previous studies show that the effective duration of monopoly has a negative effect on generic entry, arguing that original drug producers' goodwill stocks are larger (Hurwitz and Caves, 1988; Hudson, 2000). One explanation for the different result is that the two earlier empirical studies rely on data from the 80s and 90s. Given the recent institutional and legal changes in Germany (e.g. the enforcement of the *Aut-idem* regulation in 2002), the U.S. and many other pharmaceutical markets to foster generic substitution, the length of the exclusivity period may not necessarily serve as a good proxy for the accumulated goodwill of pioneers anymore.[42] The various initiatives taken to promote generic substitution likely

[42]Results are robust to the exclusion of *Monopoly Duration* from generic entry and early entry equations.

Table 1.5: Univariate Probit – Coefficients

	Data Set 1 (N=7517) *Generic Entry*	Data Set 2 (N=2804) *Generic Entry*	Data Set 3 (N=2531) *Generic Entry*
Early Entry (0/1)	-0.2159***	-0.1554*	-0.1392
	(0.055)	(0.074)	(0.076)
Pre-Entry Market Size (log)	0.5796***	0.7311***	0.7740***
	(0.045)	(0.049)	(0.049)
Monopoly Duration	0.1215***	0.1441***	0.1484***
	(0.013)	(0.016)	(0.017)
Substitutes	-0.0018	-0.0081***	-0.0079***
	(0.001)	(0.001)	(0.001)
Field Experience	0.0139***	0.0078***	0.0075***
	(0.002)	(0.002)	(0.002)
Form Experience	0.0030***	0.0022***	0.0021***
	(3.1e-04)	(3.4e-04)	(3.4e-04)
Therap. Field (0/1)	*yes*	*yes*	*yes*
Drug Form (0/1)	*yes*	*yes*	*yes*
Year Expiry (0/1)	*yes*	*yes*	*yes*
Const.	-11.4171***	-13.1081***	-13.6092***
Prob > chi2(23)	<0.001	<0.001	<0.001
Log-Likelihood	-1403.64	-978.15	-914.91

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is the decision of a generic firm to enter a drug market post loss of exclusivity (generic entry). Heteroscedasticity-robust and clustered standard errors in parentheses. Oral drugs in parasitology and sense organs with loss of exclusivity in 2002 form the reference group in generic entry equations.

neutralized pioneers' reputation advantage, and as a result generic manufacturers will benefit first and foremost if medications are well-established. The number of available off-patent substitutes – a measure of the intensity of off-patent competition – appears to affect independent generic entry decisions negatively. The effect of *Substitutes* is significant except for the estimate obtained for Data Set 1. Both therapeutic and drug form experience encourages generic entry. The effects are generally positive and significant. Therapeutic field, drug form and year fixed effects are significant in any of the univariate probit regressions.

Remember that if generic entry and early entry occur in selective drug markets which are more attractive than given market characteristics suggest, there will be a spurious correlation between early entry and generic entry decisions, i.e. univariate probit estimates will be inconsistent. In order to allow for a correlation between generic entry and early entry decisions through unobservables, I estimate a recursive bivariate probit model in the second step. The variable *Financial Distress* is added as instrument to the early entry equation to facilitate identification. Univariate probit estimates provide tentative empirical evidence that

Financial Distress provides a valid exclusion restriction. Once added to the single-equation probit regressions, it turns out not significantly impact generic entry decisions. Appendix [1.6] presents the estimates. Note also, that the exclusion restriction is not required to achieve identification, yet it improves identification notably. Appendix [1.7] provides the bivariate probit estimates, relying on a functional form identification strategy. The recursive bivariate probit estimates are generally robust to the identification strategy pursued, i.e. results do not critically hinge on the exclusion restriction. Likelihood-ratio tests of the restricted versus unrestricted bivariate probit model suggest, however, that the inclusion of the instrument improves identification and the model's overall goodness of fit. The results of the Likelihood-ratio tests are reported in Appendix [1.8]. As *Financial Distress* appears to be a suitable instrument, improving the bivariate probit model's identification, I confine the following interpretation of results to the estimates of the unrestricted recursive bivariate probit model. Table 1.6 provides the according estimates. The (residual) correlation between generic and early entry decisions, denoted by the correlation coefficient ρ, is large and significantly positive. Wald–Tests show that the null hypothesis of $\rho = 0$ can be rejected.

The finding is robust to the various criteria established for identifying potential entrants. Unobserved factors (favorable market characteristics) appear to stimulate both independent generic and early entry decisions, suggesting that there is a selection effect, or in other words, that early entry is endogenous. Univariate probit estimates turn out to be inconsistent. The coefficient of early entry is significantly negative in any of the bivariate probit regressions. Unless selection is accounted for, the early entry dummy apparently picks up drug markets' (unobserved) attractiveness, counterbalancing and weakening its negative effect on independent generic entry. The coefficient of *Financial Distress* generally has the expected sign, the effect turning out to be highly significant. The more financial losses original drug producers experience between 2002 and 2007, the larger is the likelihood of early entry. The sign and relative size of all other coefficients in the generic entry equation changes little in comparison to the univariate probit estimates. Generic entry decisions are strongly driven by pre-entry revenues (*Pre-entry Market Size*). The length of the exclusivity period (*Monopoly Duration*) also has a significantly positive impact on independent generic entry decisions. *Substitutes* – the number of available off-patent substitutes measuring the intensity of off-patent competition – generally affects independent generic entry decisions negatively. Both therapeutic

Table 1.6: Bivariate Probit – Coefficients

	Data Set 1 (N=7517)		Data Set 2 (N=2804)		Data Set 3 (N=2531)	
	Generic Entry	*Early Entry*	*Generic Entry*	*Early Entry*	*Generic Entry*	*Early Entry*
Early Entry (0/1)	-1.6490***		-1.5845***		-1.5531***	
	(0.079)		(0.057)		(0.060)	
Pre-Entry Market Size (log)	0.8145***	0.7986***	0.9221***	0.8822***	0.9841***	0.9386***
	(0.035)	(0.010)	(0.043)	(0.038)	(0.043)	(0.043)
Monopoly Duration	0.1092***	0.0511***	0.1459***	0.0878***	0.1583***	0.1155***
	(0.009)	(0.001)	(0.012)	(0.011)	(0.013)	(0.012)
Substitutes	-0.0035***	-0.0011***	-0.0060***	0.0017*	-0.0069***	0.0004
	(8.7e-04)	(1.6e-04)	(0.001)	(0.001)	(0.001)	(0.001)
Field Experience	0.0123***	–	0.0068***	–	0.0067***	–
	(0.002)		(0.001)		(0.001)	
Form Experience	0.0022***	–	0.0017***	–	0.0016***	–
	(2.7e-04)		(2.5e-04)		(2.6e-04)	
Financial Distress	–	0.0676***	–	0.0691***	–	0.0689***
		(0.004)		(0.011)		(0.010)
Therap. Field (0/1)	*yes*	*yes*	*yes*	*yes*	*yes*	*yes*
Drug Form (0/1)	*yes*	*no*	*yes*	*no*	*yes*	*no*
Year Expiry (0/1)	*yes*	*yes*	*yes*	*yes*	*yes*	*yes*
Const.	-15.0238***	-15.0655***	-16.4721***	-17.0777***	-17.4244***	-18.1747***
Prob > chi2(36)	<0.001		<0.001		<0.001	
Log-Likelihood	-3870.52		-1903.42		-1775.53	
ρ	0.8996***		0.9478***		0.9437***	
Wald Test: chi2(1)	34.04		60.75		46.25	
Prob > chi2(1)	<0.001		<0.001		<0.001	

* p<0.05, ** p<0.01, *** p<0.001

Notes: In columns (1), (3) and (5) an observation in the regression is the decision of a generic firm to enter a drug market post loss of exclusivity (generic entry). In columns (2), (4) and (6) the occurrence of early entry prior to loss of exclusivity denotes the dependent variable. Heteroscedasticity-robust and clustered standard errors in parentheses. Oral drugs in parasitology and sense organs with loss of exclusivity in 2002 form the reference group in the generic entry equation. The Wald Test is conducted for the null hypothesis of $\rho = 0$, i.e. absence of correlation in the model.

and drug form experience encourages generic entry. Early entry decisions in turn are also strongly driven by *Pre-entry Market Size*. The duration of monopoly affects early entry decisions positively, providing further evidence that *Monopoly Duration* is not necessarily a good proxy for pioneers' goodwill but rather another market value correlate. Early entry decisions also appear to be negatively affected by the intensity of off-patent competition. The effect of *Substitutes* is negative, mostly significant, yet smaller in size. Therapeutic field, drug form and year effects are significant in any of the bivariate probit regressions.

Table 1.7 provides the average marginal effects obtained from the univariate and recursive bivariate probit regressions. The interpretation of average marginal effects facilitates the

assessment of the size and economic relevance of the early entry effect. Average marginal effects are reported for the 16 drug markets experiencing early entry between 2002 and 2007, i.e. for the subset of generic entry decisions affected by early entry. The prevailing assumption is that generic manufacturers are apt to correctly anticipate early entry given drug markets' characteristics and past experiences. As a result, early entry impairs generic entry only in drug markets which experience early entry. Appendix [1.9] provides the average marginal effects computed for all drug markets. The results and conclusions are similar.

Table 1.7: Univariate and Bivariate Probit – Average Marginal Effects

	Data Set 1 (N=1581)		Data Set 2 (N=633)		Data Set 3 (N=599)	
Dep.: Generic Entry	*Univariate Probit*	*Bivariate Probit*	*Univariate Probit*	*Bivariate Probit*	*Univariate Probit*	*Bivariate Probit*
Early Entry (0/1)	-0.0440***	-0.0522	-0.0450*	-0.0601	-0.0402	-0.0507
	(0.009)	(0.0344)	(0.021)	(0.0316)	(0.022)	(0.0314)
Pre-Entry Market Size (log)	0.1089***	0.1384***	0.2113***	0.1762***	0.2244***	0.1847***
	(0.012)	(0.019)	(0.012)	(0.025)	(0.012)	(0.026)
Monopoly Duration	0.0228***	0.0208***	0.0417***	0.0389***	0.0430***	0.0370***
	(0.003)	(0.004)	(0.004)	(0.007)	(0.005)	(0.008)
Substitutes	-0.0003	-0.0007***	-0.0023***	-0.0030***	-0.0023***	-0.0030***
	(2.1e-04)	(2.3e-04)	(3.9e-04)	(6.2e-04)	(4.0e-04)	(6.3e-04)
Field Experience	0.0026***	0.0029***	0.0023***	0.0028***	0.0022***	0.0028***
	(3.7e-04)	(5.5e-04)	(5.5e-04)	(7.3e-04)	(5.6e-04)	(7.5e-04)
Form Experience	0.0006***	0.0005***	0.0006***	0.0007***	0.0006***	0.0007***
	(5.6-05)	(9.3e-05)	(8.0e-05)	(1.4e-04)	(8.3e-05)	(1.4e-04)

* p<0.05, ** p<0.01, *** p<0.001

Notes: Average marginal effects are reported for the subset of sixteen drug markets experiencing early entry between 2002 and 2007. Average marginal effects presented for the univariate (recursive bivariate) probit model denote average, ceteris paribus changes in the likelihood of independent generic entry (conditional on early entry having occurred).

The (relative) size of average marginal effects is generally robust to the micro data employed, i.e. the estimates obtained from Data Set 1, Data Set 2 and Data Set 3 reveal a consistent pattern. Univariate probit estimates suggest that early entry lowers the marginal probability of generic entry by about 4% on average. Except for the estimate obtained for Data Set 3, the average marginal effects are significant at least at a 5% level. Given the (residual) correlation between generic entry and early entry decisions, univariate probit regressions do not provide consistent estimates, whereas the recursive bivariate probit estimates are consistent. Unlike the average marginal effects obtained from the univariate probit model, the average marginal effects reported for the bivariate probit model denote changes in conditional and not marginal probability of generic entry. When determining the average marginal effect of early entry in the recursive bivariate probit model, interest

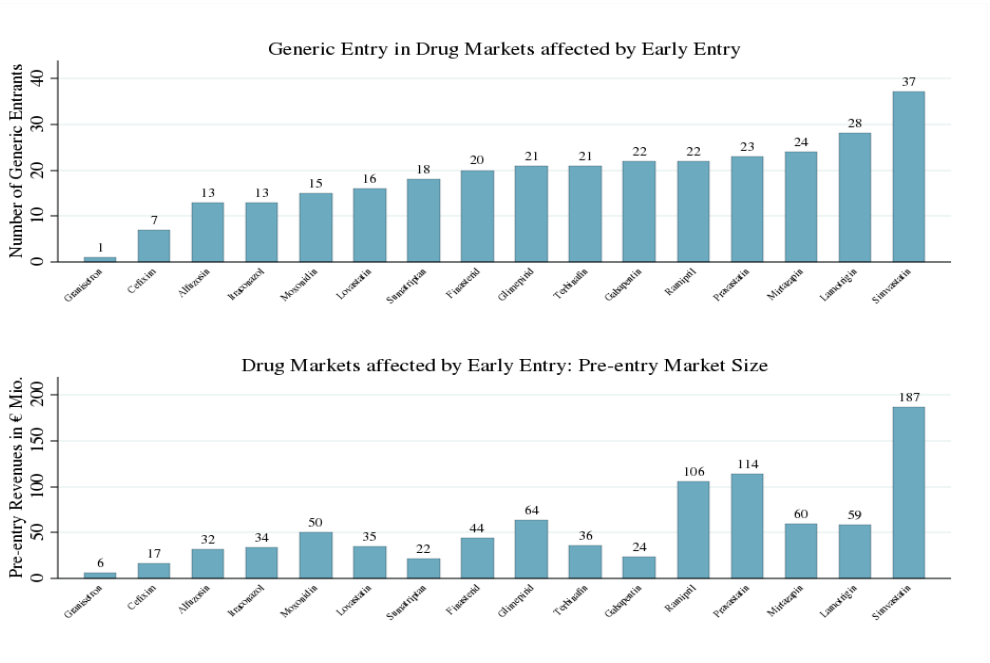
lies in the average change in the probability of generic entry conditional on early entry having occurred ($P(G = 1|E = 1)$) and the counterfactual – early entry having not occurred ($P(G = 1|E = 0)$). The average marginal effects of the other covariates similarly denote changes in probability of generic entry given that early entry occurred ($P(G = 1|E = 1)$). I compute standard errors of the average marginal effects using the delta-method (Papke and Wooldridge, 2005). The relative size of average marginal effects reported for the univariate and recursive bivariate probit models tends to be similar. The average marginal effect of early entry obtained from the recursive bivariate probit regressions is insignificant at a 10% (5%)[43] level, however. Accounting for selection, I obtain even stronger evidence that early entry does not significantly lower incentives for independent generic entry. The recursive bivariate probit estimates prove again that *Pre-entry Market Size* has the strongest impact on generic entry decisions. A mere 1% increase in drug markets' pre-entry revenues induces on average a 14-18% increase in the (conditional) probability of independent generic entry. In drug markets experiencing early entry a one standard deviation increase in pre-entry revenues relative to mean pre-entry revenues corresponds to a 4.25% (Data Set 1: 4.5%) increase in pre-entry revenues, boosting the likelihood of generic entry by roughly 60-76%.

Furthermore, the (conditional) probability of independent generic entry tends to increase on average by 0.3% (0.07%) with each retail form launched prior to loss of exclusivity in drug relevant therapeutic fields (having the particular drug's route(s) of administration). Morton (1999) finds positive effects from therapeutic and drug form experience of a similar magnitude. Given the variation in potential entrants' experience (retail form launches), the economic effect of either therapeutic or drug form experience may not be negligible. A one standard deviation increase in the number of retail form launches in the relevant therapeutic fields[44] increases the likelihood of generic entry by 7.6-11.2%. Similarly, a one standard deviation increase in the number of retail forms launched having the same route of administration[45] increases the likelihood of generic entry up to 15.8%. An increase in the duration of the exclusivity period by one year in turn raises the (conditional) probability of generic entry by 2-4% on average. Given a standard deviation of 1.75 years on drug market level, the effect tends to be small. Lastly, an increase in the number of off-patent substances

[43]The average marginal effect obtained for Data Set 2 is marginally significant at a 10% level.
[44]The standard deviation amounts to 25.4, 36.5 and 37.4 retail form launches in Data Set 1, 2, and 3.
[45]The standard deviation amounts to 157, 218.7 and 225.9 retail form launches in Data Set 1, 2, and 3.

by one, reduces the generic entry probability by about 0.1-0.3% on average. The effect still turns out to be moderate given the fairly large variation[46] in the number of off-patent substitutes. The results suggest overall that independent generic entry is primarily influenced by drug markets' pre-entry revenues. Early entry turns out to have no significant effect on generic entry decisions. Figure 1.2 displays the generic entry patterns in the high-revenue drug markets experiencing early entry. The generic entry patterns observed confirm the notion that drug markets' pre-entry revenues stimulated independent generic entry greatly.

Figure 1.2: Generic Entry in Drug Markets experiencing Early Entry



I computed generic firms' market shares in the bestseller segment – the dosage and drug form yielding the largest generic revenues by 2007 – for drug markets experiencing at least one year of off-patent competition. Comparing the turnover and revenue market shares of first-movers entering post loss of exclusivity and those of early entrants, the latter appear to obtain a considerably larger market share with respect to both turnover and revenue. Multiple first generic entry, occurring in the majority of drug markets in Germany post loss of exclusivity, appears to reduce first-mover advantages. Plotting turnover market shares of generic firms against firms' order of entry – including and excluding early entrants in the sample of firms – one finds that generic first-movers entering post loss of exclusivity tend to nevertheless have a considerable market share advantage over subsequent entrants.

[46]The standard deviation amounts to roughly 34, 37 and 37 substances in Data Set 1, 2, and 3.

Thus, even first-movers entering post loss of exclusivity pose a threat to subsequent generic entrants' profits. Appendix [1.10] provides the according graphs. This finding may in turn explain why early entry does not significantly deter independent generic entry. Examining the U.S. pharmaceutical market, Berndt *et al.* (2007a) find that additional generic entrants after the first four or five generic entrants do not significantly affect long-run generic-to-brand price ratios. A relevant implication of this finding is that a reduction in the number of independent generic firms as a result of early entry is unlikely to substantially impair generic price competition, unless it results in fewer than four or five generic entrants. The generic entry patterns in the majority of drug markets satisfy this criterion, suggesting that the welfare effects of early entry are most likely to be minor. The monotone relationship of early entry and pre-entry market revenues – intermediate-sized and high-revenue markets experience early entry proportionally more often – indicate also that original drug producers authorized generic entry prior to loss of exclusivity first and foremost fueled by rent-seeking rather than strategic entry-deterrence motives (Fisher Ellison and Ellison, 2007).

1.7 Conclusion

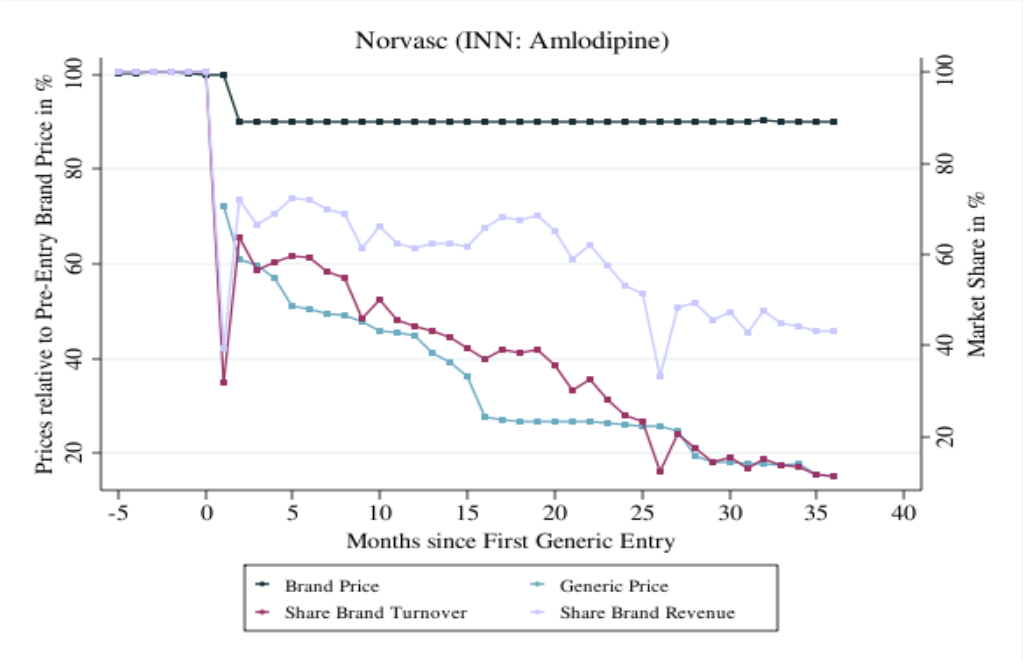
This study provides recent empirical evidence on the impact of early entry – also known as authorized, branded or pseudo-generic entry – on independent generic entry decisions accounting for the endogeneity of early entry decisions. The results strongly suggest that independent generic entry decisions are primarily influenced by drug markets' pre-entry revenues. Early entry turns out to have no significant impact on independent generic entry decisions. Originators appear to authorize generic entry prior to loss of exclusivity to extract generic profits rather than to deter generic entry. The European Commission's survey of originators conducted in course of its *Pharmaceutical Market Sector Inquiry* supports this conclusion. Generic first-movers have been shown to enjoy a long-lasting advantage over subsequent generic entrants (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Hollis, 2002) as a result of doctors', patients' and pharmacists' switching costs. Some economists accordingly argue that anticipated early entry has an anti-competitive, deterring effect on independent generic entry. Based on a unique micro data set comprising pharmaceutical market and exclusivity data, I examine the impact of early entry on independent generic entry decisions in the German pharmaceutical market within the time period 2002-2007. If generic and early

entry occurs in selective drug markets which are more (or less) attractive than given market characteristics suggest (Hollis and Liang, 2006; FTC, 2009), there will be a spurious correlation between early entry and generic entry decisions. Accounting for the endogeneity of early entry decisions, I employ unique micro data and estimate univariate and recursive bivariate probit models of entry. Recursive bivariate probit estimates indicate that early entry decisions are endogenous, rendering univariate probit estimates inconsistent. The identification strategy in the bivariate probit model relies on the assumption of normality and the fact that I model sequential entry decisions. As early entry decisions are arguably motivated by pioneers' financial distress, I add a count of each original drug producers' further losses of exclusivity between 2002 and 2007 as an instrumental variable to the early entry equation which improves identification. Regardless of the identifying assumption made, I find no evidence that early entry significantly reduces the likelihood of generic entry.

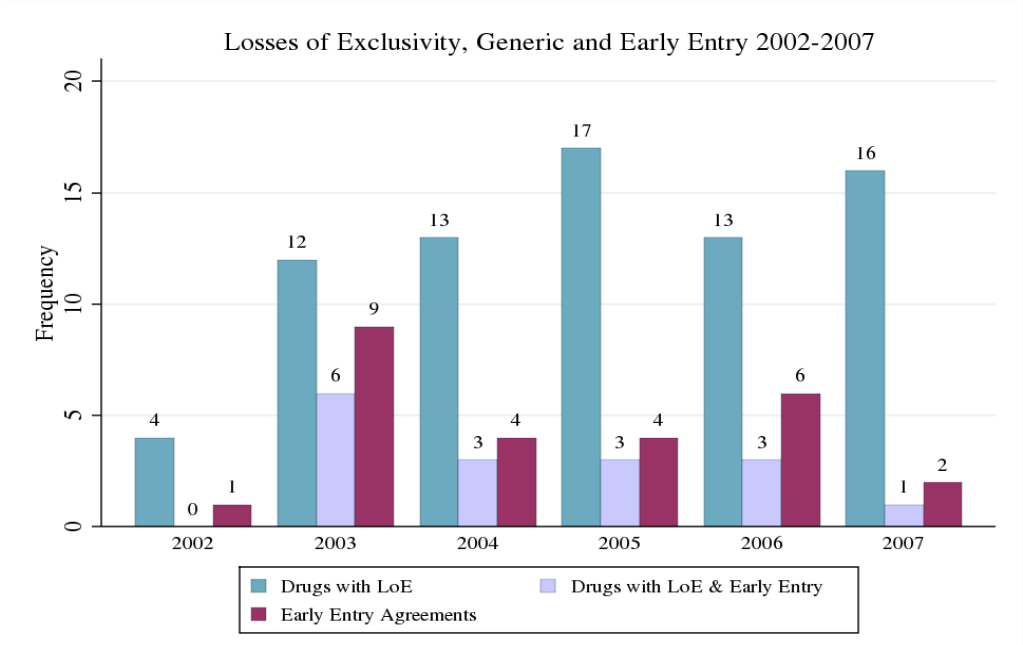
Drug markets' pre-entry revenues influence both independent generic entry and early entry decisions most strongly. Just like previous related studies on generic entry, I also show that the degree of off-patent competition affects generic entry decisions negatively, whereas firms' therapeutic and drug form experiences encourage generic entry. Monopoly duration surprisingly influences generic entry decisions positively and not negatively, indicating that the length of the exclusivity period is not necessarily a good proxy for pioneers' accumulated goodwill stock as suggested by Hurwitz and Caves (1988); Hudson (2000). Generic manufacturers appear to benefit first and foremost if medications are well-established. Government scrutiny targeting early entry would be appropriate if small drug markets turned out to experience early entry more frequently in the future. Further research is also warranted to assess the welfare effects of early entry. Early entry may not impair generic entry decisions, yet it could adversely affect competition in off-patent pharmaceutical markets. Gauging the impact of early entry on generic manufacturers' prices and market shares, and the rate of price erosion, are important areas of research which I intend to examine in the future.

1.8 Appendix 1

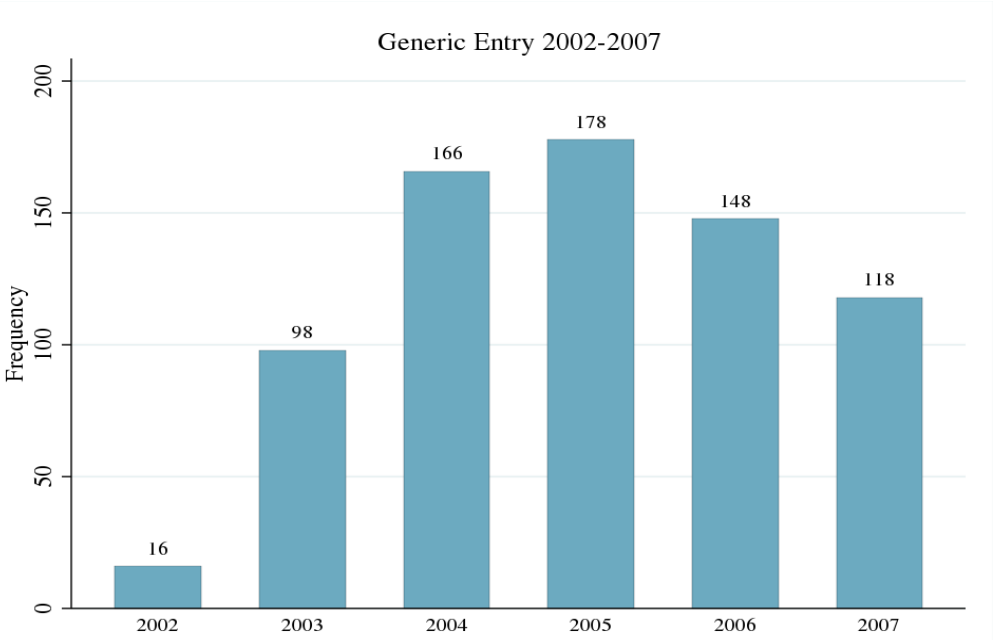
1.8.1 Brand Market Share post Generic Entry: Pfizer

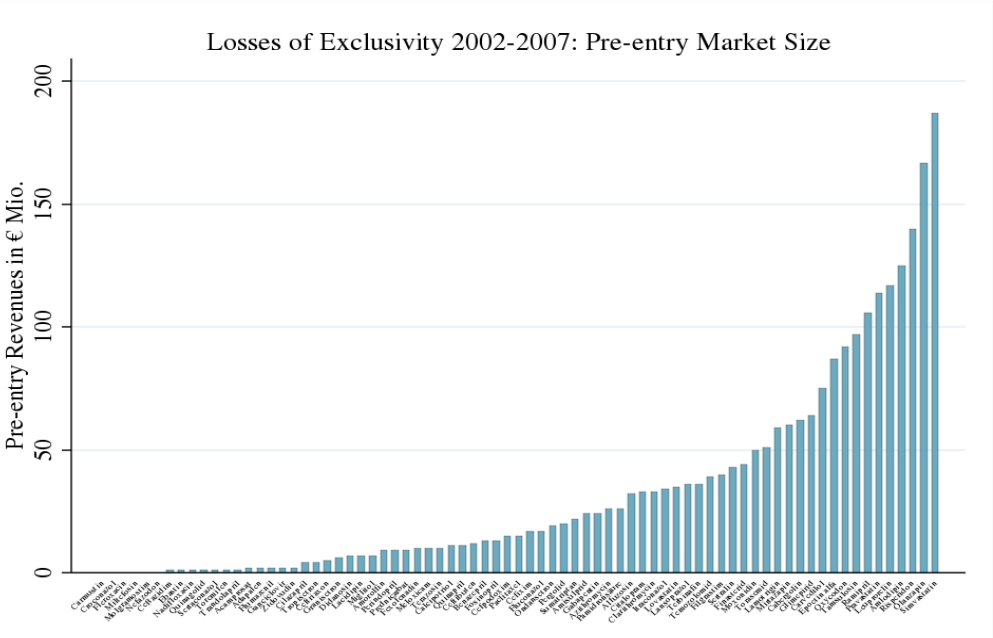


1.8.2 Patent Expiry, Early Entry and Generic Entry 2002-2007



1.8.2 Patent Expiry, Early Entry and Generic Entry 2002-2007





1.8.3 Allocation Generic Entries and Zero-Entries to Drugs

				Data Set 1		Data Set 2		Data Set 3	
Substances	Generic Entry	Early Entry	Generic Entries	Zero-Entries	Total	Zero-Entries	Total	Zero-Entries	Total
Acamprosate	no	no	0	100	100	16	16	11	11
Adapalene	no	no	0	101	101	23	23	11	11
Alfuzosine	yes	yes	13	87	100	21	34	20	33
Amisulpride	yes	no	13	86	99	41	54	41	54
Amlodipine	yes	no	32	70	102	22	54	18	50
Amorolfine	no	no	0	100	100	34	34	33	33
Azithromycin	yes	no	17	84	101	44	61	44	61
Benazepril	yes	no	8	92	100	37	45	37	45
Cabergoline	yes	no	8	93	101	29	37	22	30
Calcipotriol	yes	no	3	98	101	10	13	10	13
Carmustine	no	no	0	101	101	16	16	15	15
Carvedilole	yes	no	25	75	100	22	47	22	47
Cefixime	yes	yes	7	89	96	51	58	51	58
Cefpodoxime	yes	no	10	90	100	49	59	47	57
Ceftazidime	yes	no	6	95	101	52	58	14	20
Ceftibuten	no	no	0	101	101	61	61	59	59
Ceftriaxone	yes	no	10	92	102	48	58	12	22
Cilazapril	no	no	0	100	100	45	45	45	45
Citalopram	yes	no	28	70	98	12	40	12	40
Clarithromycin	yes	no	18	83	101	42	60	42	60
Croconazole	no	no	0	100	100	34	34	33	33
Didanosine	no	no	0	101	101	22	22	21	21
Ebastine	no	no	0	100	100	31	31	30	30
Epoetin alfa	yes	no	3	98	101	20	23	5	8
Fexofenadine	no	no	0	100	100	31	31	30	30
Filgrastim	no	no	0	101	101	4	4	3	3
Finasteride	yes	yes	20	80	100	24	44	16	36
Fleroxacin	no	no	0	101	101	60	60	57	57
Fluconazole	yes	no	19	81	100	3	22	3	22
Flumazenile	yes	no	5	98	103	15	20	6	11
Fosinopril	yes	no	3	97	100	42	45	42	45
Gabapentin	yes	yes	22	76	98	10	32	8	30
Ganciclovir	no	no	0	101	101	34	34	34	34
Glimepirid	yes	yes	21	79	100	20	41	20	41
Granisetron	yes	yes	1	97	98	18	19	17	18
Itraconazole	yes	yes	13	85	98	5	18	5	18

1.8.3 Allocation Generic Entries and Zero-Entries to Drugs

				Data Set 1		Data Set 2		Data Set 3	
Substances	Generic Entry	Early Entry	Generic Entries	Zero-Entries	Total	Zero-Entries	Total	Zero-Entries	Total
Lacidipine	no	no	0	101	101	54	54	50	50
Lamotrigine	yes	yes	28	71	99	22	50	20	48
Lansoprazole	yes	no	13	88	101	37	50	35	48
Leuprorelin	yes	no	2	99	101	31	33	1	3
Lovastatin	yes	yes	16	81	97	19	35	14	30
Meloxicam	yes	no	11	89	100	47	58	46	57
Miglitol	no	no	0	98	98	37	37	37	37
Miltefosine	no	no	0	101	101	17	17	3	3
Mirtazapine	yes	yes	24	74	98	19	43	19	43
Molgramostim	no	no	0	101	101	4	4	3	3
Moxonidine	yes	yes	15	83	98	14	29	14	29
Nadifloxacin	no	no	0	101	101	23	23	11	11
Nefazodone	no	no	0	101	101	45	45	44	44
Olanzapine	yes	no	7	94	101	49	56	49	56
Ondansetron	yes	no	20	88	108	11	31	10	30
Oxycodone	yes	no	4	97	101	60	64	54	58
Paclitaxel	yes	no	10	92	102	7	17	6	16
Pamidron acid	yes	no	7	93	100	5	12	1	8
Pergolide	yes	no	9	90	99	19	28	19	28
Perindopril	no	no	0	98	98	43	43	43	43
Pravastatin	yes	yes	23	74	97	15	38	12	35
Prednicarbate	yes	no	2	96	98	22	24	22	24
Quinagolid	no	no	0	101	101	22	22	16	16
Quinapril	yes	no	9	90	99	35	44	35	44
Ramipril	yes	yes	22	77	99	22	44	22	44
Risperidone	yes	no	29	72	101	30	59	29	58
Sertaconazole	no	no	0	101	101	34	34	33	33
Sertraline	yes	no	25	76	101	19	44	18	43
Simvastatin	yes	yes	37	66	103	7	44	4	41
Sumatriptan	yes	yes	18	81	99	44	62	37	55
Tamsulosin	yes	no	27	76	103	11	38	10	37
Temozolomide	no	no	0	101	101	16	16	5	5
Terazosin	yes	no	20	79	99	22	42	22	42
Terbinafine	yes	yes	21	80	101	21	42	19	40
Torasemide	yes	no	20	80	100	26	46	26	46
Toremifene	no	no	0	98	98	29	29	29	29
Trandolapril	no	no	0	101	101	49	49	49	49
Tropisetron	no	no	0	101	101	23	23	22	22
Zidovudine	no	no	0	101	101	22	22	22	22

1.8.4 Summary Statistics Data Set 1

Variable Name	Mean	Median	Min.	Max.	Sd.	N
Generic Entry	0.10	0	0	1	–	7517
Early Entry	0.21	0	0	1	–	7517
Pre-Entry Market Size (€ Mio.)	32.8	14.8	0	187	41.5	7517
Pre-Entry Market Size (log)	15.76	16.51	0	19.05	3.40	7517
Monopoly Duration	12.12	12.5	5	20	3.27	7517
Substitutes	47.86	39	8	204	34.91	7517
Field Experience	9.39	0	0	374	25.40	7517
Form Experience	84.19	26	0	1679	157.00	7517
Financial Distress	2.95	2	0	6	2.43	7517

1.8.5 Summary Statistics Data Set 2

Variable Name	Mean	Median	Min.	Max.	Sd.	N
Generic Entry	0.26	0	0	1	–	2804
Early Entry	0.23	0	0	1	–	2804
Pre-Entry Market Size (€ Mio.)	37.3	19.1	0	187	44.6	2804
Pre-Entry Market Size (log)	16.05	16.76	0	19.05	3.15	2804
Monopoly Duration	12.12	12.5	5	20	3.23	2804
Substitutes	54.51	44	8	204	35.81	2804
Field Experience	25.18	11	0	374	36.50	2804
Form Experience	165.21	75	0	1679	218.67	2804
Financial Distress	2.94	2	0	6	2.46	2804

1.8.6 Univariate Probit (incl. Instrument) – Coefficients

	Data Set 1 (N=7517) *Generic Entry*	Data Set 2 (N=2804) *Generic Entry*	Data Set 3 (N=2531) *Generic Entry*
Early Entry (0/1)	-0.2157***	-0.1534*	-0.1390
	(0.055)	(0.074)	(0.076)
Pre-Entry Market Size (log)	0.5797***	0.7328***	0.7743***
	(0.045)	(0.049)	(0.049)
Monopoly Duration	0.1218***	0.1441***	0.1482***
	(0.014)	(0.016)	(0.017)
Substitutes	-0.0018	-0.0084***	-0.0079***
	(0.001)	(0.001)	(0.001)
Field Experience	0.0139***	0.0078***	0.0075***
	(0.002)	(0.001)	(0.002)
Form Experience	0.0030***	0.0023***	0.0022***
	(3.1e-04)	(3.4e-04)	(3.4e-04)
Financial Distress	0.0015	-0.0168	-0.0020
	(0.012)	(0.014)	(0.015)
Therap. Field (0/1)	*yes*	*yes*	*yes*
Drug Form (0/1)	*yes*	*yes*	*yes*
Year Expiry (0/1)	*yes*	*yes*	*yes*
Const.	-11.4209***	-13.0998***	-13.6102***
Prob > chi2(24)	<0.001	<0.001	<0.001
Log-Likelihood	-1403.63	-977.68	-914.90

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is the decision of a generic firm to enter a drug market post loss of exclusivity (generic entry). Heteroscedasticity-robust and clustered standard errors in parentheses. Oral drugs in parasitology and sense organs with loss of exclusivity in 2002 form the reference group in generic entry equations.

1.8.7 Bivariate Probit (excl. Instrument) – Coefficients

	Data Set 1 (N=7517)		Data Set 2 (N=2804)		Data Set 3 (N=2531)	
	Generic Entry	*Early Entry*	*Generic Entry*	*Early Entry*	*Generic Entry*	*Early Entry*
Early Entry (0/1)	-1.6293***		-1.5228***		-1.5034***	
	(0.062)		(0.053)		(0.054)	
Pre-Entry Market Size (log)	0.7987***	0.7867***	0.9086***	0.8634***	0.9739***	0.9209***
	(0.033)	(0.011)	(0.044)	(0.037)	(0.043)	(0.043)
Monopoly Duration	0.0531***	0.1053***	0.1430***	0.0888***	0.1551***	0.1160***
	(0.009)	(0.002)	(0.012)	(0.010)	(0.013)	(0.011)
Substitutes	-0.0035***	-0.0022***	-0.0064***	0.0003	-0.0071***	-0.0011
	(0.001)	(1.7e-04)	(0.001)	(0.010)	(0.001)	(0.001)
Field Experience	0.0121***	–	0.0069***	–	0.0068***	–
	(0.002)		(0.001)		(0.001)	
Form Experience	0.0021***	–	0.0016***	–	0.0016***	–
	(2.7e-04)		(2.5e-04)		(2.6e-04)	
Therap. Field (0/1)	*yes*	*yes*	*yes*	*yes*	*yes*	*yes*
Drug Form (0/1)	*yes*	*no*	*yes*	*no*	*yes*	*no*
Year Expiry (0/1)	*yes*	*yes*	*yes*	*yes*	*yes*	*yes*
Const.	-14.5317***	-14.6976***	-16.0689***	-16.5732***	-17.0781***	-17.6726***
Prob > chi2(35)	<0.001		<0.001		<0.001	
Log-Likelihood	-3903.83		-1919.02		-1789.76	
ρ	0.9209***		0.9363***		0.9382***	
Wald Test: chi2(1)	52.02		101.04		90.55	
Prob > chi2(1)	<0.001		<0.001		<0.001	

* p<0.05, ** p<0.01, *** p<0.001

Notes: In columns (1), (3) and (5) an observation in the regression is the decision of a generic firm to enter a drug market post loss of exclusivity (generic entry). In columns (2), (4) and (6) the occurrence of early entry prior to loss of exclusivity denotes the dependent variable. Heteroscedasticity-robust and clustered standard errors in parentheses. Oral drugs in parasitology and sense organs with loss of exclusivity in 2002 form the reference group in the generic entry equation. The Wald Test is conducted for the null hypothesis of $\rho = 0$, i.e. absence of correlation in the model.

1.8.8 Likelihood-ratio test: Restricted vs. Unrestricted Model

	Data Set 1 (N=7517)		Data Set 2 (N=2804)		Data Set 3 (N=2531)	
Model	*Restricted*	*Unrestricted*	*Restricted*	*Unrestricted*	*Restricted*	*Unrestricted*
Log-Likelihood	-3903.83	-3870.52	-1919.02	-1903.42	-1789.76	-1775.53
LR chi2(1)	66.62		31.20		28.45	
Prob > chi2	<0.001		<0.001		<0.001	

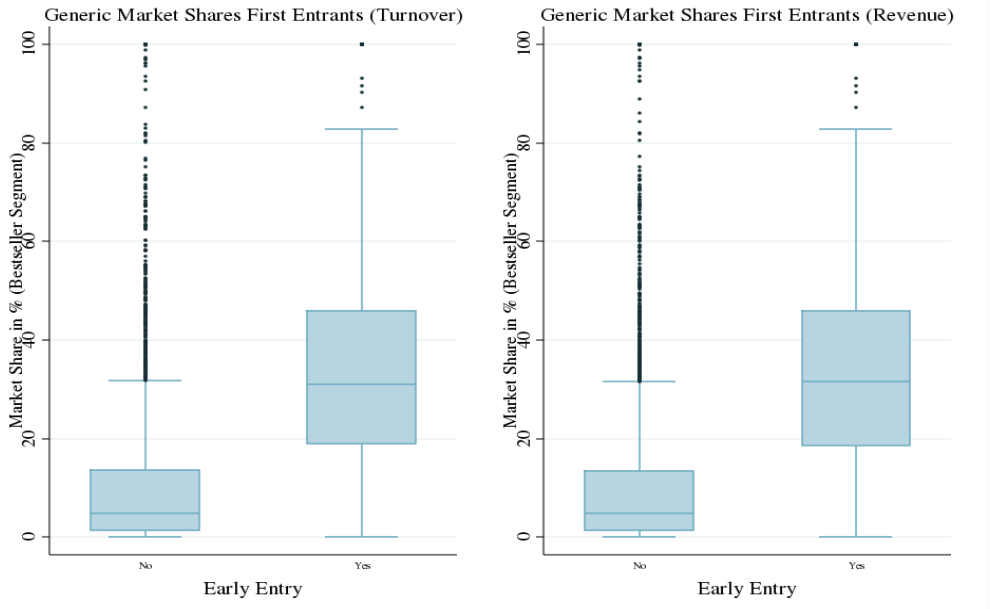
1.8.9 Probits – Average Marginal Effects (All Drugs)

	Data Set 1 (N=7517)		Data Set 2 (N=2804)		Data Set 3 (N=2531)	
Dep.: Generic Entry	*Univariate Probit*	*Bivariate Probit*	*Univariate Probit*	*Bivariate Probit*	*Univariate Probit*	*Bivariate Probit*
Early Entry (0/1)	-0.0215***	-0.0122	-0.0298*	0.0375	-0.0278	0.0484
	(0.005)	(0.019)	(0.014)	(0.045)	(0.015)	(0.045)
Pre-Entry Market Size (log)	0.0597***	0.0676***	0.1441***	0.1230***	0.1578***	0.1328***
	(0.006)	(0.016)	(0.010)	(0.025)	(0.009)	(0.026)
Monopoly Duration	0.0125***	0.0110***	0.0284***	0.0310***	0.0303***	0.0286***
	(0.002)	(0.002)	(0.003)	(0.009)	(0.003)	(0.008)
Substitutes	-0.0002	-0.0003*	-0.0016***	-0.0026***	-0.0016***	-0.0027***
	(1.2e-04)	(1.4e-04)	(8.5e-04)	(7.8e-04)	(8.5e-04)	(7.5e-04)
Field Experience	0.0014***	0.0016***	0.0015***	0.0025**	0.0015***	0.0025**
	(1.9e-04)	(4.1e-04)	(3.6e-04)	(8.7e-04)	(2.8e-04)	(8.9e-04)
Form Experience	0.0003***	0.0003***	0.0004***	0.0006**	0.0004***	0.0006**
	(2.9e-05)	(7.4e-05)	(5.7e-05)	(1.9e-04)	(6.1e-05)	(1.9e-04)

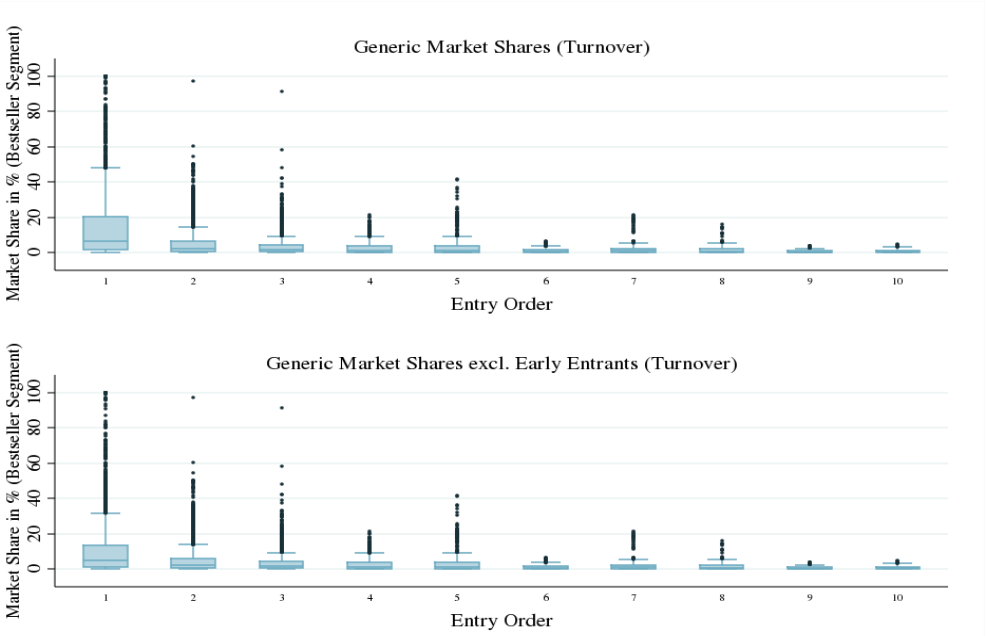
* p<0.05, ** p<0.01, *** p<0.001

Notes: Average marginal effects are reported for the 75 drug markets experiencing a loss of exclusivity between 2002 and 2007. Average marginal effects presented for the univariate (recursive bivariate) probit model denote average, ceteris paribus changes in the likelihood of independent generic entry (conditional on early entry having occured).

1.8.10 Generic Market Shares and Timing of Entry



1.8.10 Generic Market Shares and Timing of Entry



Chapter 2

Generic Market Share Dynamics post Patent Expiry: Gauging the Impact of Generic Price Differentials

2.1 Introduction

As in many industrial nations, drug expenditures have rapidly increased in the German statutory healthcare system over the last decade. Amounting to €27.8 Bn. in 2007, drug expenditures make up the second largest cost factor after expenditures on hospital services in the statutory health care system.[1] Generic firms generate substantial savings in drug expenditures, offering large price discounts on off-patent drugs.[2] Interestingly, generic prices vary notably across firms. Looking at identical active ingredients, drug forms and dosage sizes, price variations on a scale of 10 percentage points are common in the German generic drug market. Nevertheless, market shares are largely persistent, suggesting that consumers' sensitivity to generic price differentials is relatively low. The observed price differentials alone correspond to forgone drug cost savings of roughly €11 Bn. from 2002 to 2007.[3] The previous literature on intra-generic competition provides no recent and reliable evidence[4] of

[1] www.gesundheitspolitik.net/04_medikamente/apotheke/oeffentlich/GEK-Arzneimittelreport-2009.pdf.

[2] Generic firms offer price discounts of up to 95% within three years of generic competition (own calculations based on generic price data for 35 drug markets in Germany from 2002 to 2007).

[3] These drug cost savings could have been ideally realized if all generic drug products had been sold at the minimum monthly generic price observed in each of the 35 drug markets in the sample.

[4] Only Hollis (2002) examines specifically the impact of generic prices on market share, not accounting for the simultaneity bias which arises from the introduction of prices in the market share equation. He obtains either an insignificant or a significantly positive price effect. The estimates are overall disputable.

how persistent generic market shares are, and of how strongly they are affected by prices (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Hollis, 2002). Profound evidence of how strongly generic market shares are influenced by prices is indispensable to evaluate the intensity and efficiency of generic competition. Notably, the studies identify important trends in generic prices and market shares but not the underlying factors provoking generic market shares' persistence, resorting exclusively to macro data. The previous micro studies focus in turn on physicians' prescription decisions (Hellerstein, 1998; Coscelli, 2000; Paraponaris *et al.*, 2004), and do not investigate pharmacists' and patients' choice among generic products, and especially their sensitivity to price differentials. As a result of generic substitution laws, multi-source drug choices are nowadays made in vast majority of cases by pharmacists and patients. Due to largely fixed copayments and dispensing fees, they both have a low financial incentive to switch among generic products unless price differentials are large.[5]

Employing both macro and micro data, this study is the first to provide recent and comprehensive evidence of the small and decreasing impact of generic prices on market shares over time. Generic product panel data allow me to examine at macro level the effect of generic prices on market shares and the persistence of the latter. Patient tracking data in turn facilitate a micro analysis of patients' switching behavior among generic products in response to price differentials. Generic prices generally denote ex-factory per-pill prices.

The micro and macro analysis are directed to generic products in 35 drug markets, where drugs went off-patent between 2002 and 2006. At macro level, I examine the monthly market shares and prices of 605 generic products launched between 2002 and 2007. Generic prices are normalized by pre-entry brand prices in the macro analysis to obtain a comparable measure of generic price variations across drug markets. In order to gauge the impact of generic prices on market shares and the persistence of the latter, I estimate a dynamic panel data model and resort to the System GMM estimator to tackle dynamic panel and simultaneity bias. Except for the dynamic component, the empirical model's specification rests on the previous empirical work on competition in off-patent pharmaceutical markets (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Frank and Salkever, 1997; Bhattacharya and Vogt, 2003; Reiffen and Ward, 2005; Saha *et al.*, 2006; Regan, 2008). At micro level, I investigate how

[5]EUC (2009) assert that doctors, pharmacists and patients are typically not very price sensitive for prescription medicines. "Neither the patient, nor the prescriber or the dispenser directly bear most of the costs, as these are generally covered and/or reimbursed largely $(\cdots)$ by national health (insurance) schemes."

price differentials influence patients' switching behavior among generic products within each of the 35 drug markets. Employing unique patient tracking data available for the year 2007, the micro analysis is confined to 88432 repeat-purchase patients who obtained their first diagnosis in 2007. Only for those patients I can unambiguously identify all generic product switches. I resort to a pooled probit estimation to gauge the impact of generic price differentials on the probability of a product switch. Following Hellerstein (1998) and Coscelli (2000), I control for patient and drug characteristics as well as for treatment specificities.

Consistent with previous findings (Grabowski and Vernon, 1992; Hollis, 2002), GMM estimates indicate that generic market shares are largely persistent over time. Also, the number of generic entrants influences market shares notably: the entry of one generic firm lowers market shares by about 0.6 percentage points, the effect decreasing by 0.01 percentage points with each additional entrant. Strikingly, prices affect generic market shares only minimally: a 10 percentage point lower generic-to-brand price ratio leads to a market share increase of roughly 1 percentage point. Moreover, the impact of a price cut declines by 0.0032 percentage points in each month of generic competition. After roundabout 32 months the effect is essentially zero. Lastly, the GMM estimates do not indicate that generic firms broadly positioned across drug markets obtain higher market shares, and there also is no evidence of intermolecular competition. The probit estimates in turn show that the chances of a generic product switch increase in the size of the price differential, which may explain why prices affect market shares by less and less over time. Unless generic price differentials are extremely large, however, patients will habitually receive the same generic product. A 1 Cent per-pill price discount increases the probability that a patient switches to another generic product by merely 0.8%. As per-pill prices vary on average by 6 Cent in the first month of generic entry, and by 2 Cent after three years of generic competition, generic price differentials have practically a negligible impact on multi-source[6] drug choices. The persistence of generic market shares observed at macro level can evidently be attributed to patients' and pharmacists' low sensitivity to generic price differentials as well as to habit persistence. The longer patients receive a particular drug, the lower is the probability that they switch among generic products. The likelihood of a product switch decreases by roughly

[6]Drugs are classified as single or multi-source, which refers to the number of manufacturers of the drug. Single-source drugs become multi-source drugs as brand drugs go off-patent.

1.4% with each additional month that has elapsed since the first diagnosis. Notably, patients tend to receive the particular medications for several years once they have fallen ill.

The organization of the paper is as follows: Section 2.2 provides background information on the German generic drug industry. Section 2.3 reviews the literature on first-mover advantages in generic drug markets, and the related literature on generic drug prescriptions. Section 2.4 describes the macro and micro data employed in this study. Section 2.5 presents the econometric model and findings of the macro analysis. Section 2.6 presents the econometric model and results of the micro analysis. Concluding remarks follow in Section 2.7.

2.2 Industry Background

The German pharmaceutical market is one of the most important drug markets. With a market size of €4.5 Bn. and a generic penetration (efficiency[7]) rate of about 20% (68%) as of 2007, the German generic drug market is the second largest market in the world. As the largest generic market in Europe, it experienced the highest number of generic entries from 2000 to 2007 (EUC, 2009). The following paragraph describes the fundamental dynamics of generic drug competition. Moreover, it outlines Germany's regulatory framework which governs the prescribing and dispensing of prescription (Rx) drugs post patent expiration.

Generic drugs are therapeutically equivalent (bio-equivalent) to the off-patent, brand (original) drug: they contain the same active ingredient, have identical quality and performance characteristics, the same dosage size and the same or a similar route of administration. Instead of safety and efficacy tests, generic firms conduct bioequivalence studies to show that the rate and extent of absorption of the active ingredient is identical to that of the reference drug. It takes at most four months to conduct such studies. In drug stability studies, they prove further that the drug product remains within the established specifications and maintains its identity, strength, quality and purity throughout the expiration dating period of typically two or three years. The market approval process usually takes another six to nine months. It is generally impossible to predict exactly when market approval will be granted.[8] To obtain market approval on time, generic firms prepare for market entry at least three

[7]The generic efficiency rate indicates the fraction of multi-source drug prescriptions dispensed as generic. Own calculations based on *Insight Health* prescription data.

[8]The German or European market authorization agency may, for instance, identify major objections in the generic application, delaying the market approval process by a few months until issues are resolved. Market approval is often granted at a later date than expected; see EUC (2008), p. 271; Accenture (2005).

years ahead of entry.[9] Generic entry typically occurs as soon as the patent or supplementary protection certificate (SPC)[10] for the brand drug expires. Generic drugs are most frequently marketed as INN-generics in Germany: the international-non-proprietary name (INN) of the active ingredient and a company suffix identify the drug product.[11] Carrying the corporate name or an abbreviated version thereof, many generic products are umbrella branded.

Occasionally, originators also authorize generic entry prior to loss of exclusivity and launch a generic version of the brand drug through a generic subsidiary or a licensee/supply partner (early entry). The German pharmaceutical market experienced 26 early entries between 2002 and 2007. First generic entrants, especially early entrants, appear to enjoy a substantial first-mover advantage, achieving on average a market share of 9.9% (35.9%) over the time period 2002 to 2007. Subsequent entrants obtained a market share of merely 3.8% within the generic market segment. Universally, generic firms offer large price discounts relative to the brand drug whose price remains constant or declines little post patent expiry. There is no direct price regulation of producer (ex-factory) prices in Germany. In the first month of generic entry, (turnover-weighted) average generic prices tend to be 25% lower than pre-entry brand prices. Continuously declining as new firms enter, generic prices are on average 60% lower than pre-entry brand prices within three years.[12] In Germany, off-patent pharmaceutical markets experience rapid entry, and attract numerous generic entrants.

In a series of health care reforms over the time period 2002 to 2007, the German government introduced several regulations to foster generic competition. A major increase in generic substitution has been achieved through the enforcement of the *Act for the Limitation of Drug Expenditures* (*Arzneimittelausgaben-Begrenzungsgesetz, AABG*) in February 2002, introducing the *Aut-idem* regulation for prescription drugs: pharmacists are encouraged to sell one of the 30% lowest priced generic drug products to the patient unless the physician excludes generic substitution by checking the *Aut-idem* box on the prescription pad.[13] Latest figures obtained by *Insight Health* for the year 2008 indicate that the *Aut-idem* quota

[9]Interviews with industry experts provided further, detailed information on the stages and time frame involved in the generic drug approval process.

[10]If an originator applies within six month after the brand drug's market approval for a SPC and the national patent office approves the request, the exclusivity period will be extended by up to five years.

[11]www.stada.de/english/investorrelations/glossary/definitionpharmamarkt.asp (accessed: Jul 30th 2010).

[12]Own calculations. Saha *et al.* (2006) report similar figures for the U.S. pharmaceutical market.

[13]Until the following health care reform which was implemented in January 2004, generic substitution was also prohibited once the prescribed medical product was listed among the group of the 30% lowest priced products, or once the latter group did not consist of five or more drug products.

– fraction of non-substitution prescriptions – amounts to 14%[14], demonstrating that in the vast majority of cases physicians leave the dispensing decision to the pharmacist and patient.

Since the enforcement of the *Statutory Health Insurance Modernization Act* (*Gesetz zur Modernisierung der Gesetzlichen Krankenversicherung, GMG*) in January 2004, dispensing fees on Rx drugs[15] consist mainly of a fixed component. Pharmacies charge a fixed fee of €8.10[16] for each dispensed product independent of its package size, plus a markup of 3% of product's purchase price (producer price incl. wholesale markup). Due to the fixed compensation structure, pharmacists' incentives to sell high-priced products have been reduced.

Patients covered by statutory health insurance (GKV) – 86% of the German population as of 2007[17] – generally get prescription drug coverage up to a predetermined reference price.[18] When purchasing a medical product, GKV patients pay only for any extra costs above the reference price. Furthermore, patients have been prompted to make a copayment for each medical product as of January 2004. The copayment amounts to 10% of the pharmacy selling price, the minimum contribution is €5 and €10 is the maximum.[19] Notably, as most medical products are sold in packages priced below €50, patients are often not inclined to search for a cheaper product containing the same active ingredient (Accenture, 2005).

With the enactment of the *Law for the Economic Provision of Pharmaceutical Products* (*Arzneimittelversorgungs-Wirtschaftlichkeitsgesetz, AVWG*) in May 2006, patient copayments become obsolete once drug products are priced at least 30% below the current reference price, putting further downward pressure on generic prices. Pharmaceutical companies in Germany can update prices at the *Institute for Pharmaceutical Products* (*Institut für Arzneimittelspezialitäten*) in Frankfurt on the 1st and 15th of each month. Pharmacies usually obtain an electronic update of official prices on the same day. Thus, pharmacists can

[14] www.insight-health.de/upload/MVF_01-2009_Zahlen.pdf (accessed: Aug. 2nd 2010).

[15] Around 78% of pharmaceutical sales are made on prescription drugs (BPI Pharma-Daten 2008).

[16] Since the *Statutory Health Insurance Competition Strengthening Act* enforced in April 2007, pharmacists must grant patients covered by statutory health insurance a discount of €2.30 on the product's pharmacy selling price, independent of its package size, reducing the fixed component of the dispensing fee's to €5.80.

[17] Own calculations based on data obtained from the federal health monitoring information system (www.gbe-bund.de) and from the German association of private health insurance website (www.pkv.de).

[18] Reference prices were introduced in Germany with the enforcement of the *Health Care Reform Act* (*Gesundheitsreformgesetz, GRG*) in 1989. The central association of health care providers determines the reference prices for specific groups of medical products. Reference prices for groups of medical products containing the same active ingredient must be in the price range of the 30% lowest priced products. Reference prices get updated quarterly (www.aok-bv.de/lexikon/f/index_00338.html; accessed: Aug 2nd 2010).

[19] GKV-Patients pay for medical products priced below €5 themselves.

immediately determine which medical products will not require a copayment.[20] As of May 2006, pharmaceutical companies have also been prohibited from giving discounts in kind to public and hospital pharmacies, improving the transparency of price competition. Financial rebates have been restricted to non-prescription (over-the-counter, OTC) drugs. As the last major health care reform enacted in April 2007, the *Statutory Health Insurance Competition Strengthening Act* (*Gesetz zur Stärkung des Wettbewerbs in der gesetzlichen Krankenversicherung , GKV-WSG*) legally authorized the use of rebate contracts. Statutory insurance providers have ever since been permitted to close exclusive supply contracts with the generic firm offering the lowest price for a particular medical product. Thereafter, pharmacists must provide patients with that specific generic drug product, unless patients insist on another generic drug product and incur the additional expenses. Except for rebate contracts, previous health care reforms appear to have provided few incentives to both pharmacists and patients to switch among generic products as long as price differences are not strikingly large.

2.3 Literature Review

The distinctive dynamics of generic competition have attracted the attention of various economists. The previous empirical studies generally show that first generic entrants enjoy a substantial and long-term competitive advantage over later generic entrants (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Hollis, 2002), even charging higher prices (Grabowski and Vernon, 1992). Overall, however, there is no recent and reliable evidence of how persistent generic market shares are, and of how strongly they are affected by prices. Employing exclusively macro data, the studies identify important trends in generic prices and market shares but not the underlying factors provoking generic market shares' persistence.

Caves *et al.* (1991) show that the entry of an additional generic firm depresses generic prices more severely than the price of the brand-name drug. As a result of the strong decline in generic prices, Caves *et al.* (1991) assert that first movers make ultimately larger profits than subsequent generic entrants, charging higher prices for a certain amount of time.

Focusing solely on the retail drugstore segment and comparing the prices and market shares of generic products over the 1984-87 time period, Grabowski and Vernon (1992) are the first to exploratively investigate the variability of generic prices and market shares. In

[20] www.gkv.info/gkv/index.php?id=661 (accessed: Oct. 15th 2010).

half of the 18 generic drug products in their sample, the maximum price observed is over 50% greater than the minimum price one year after initial generic entry. Interestingly, these firms obtained a significant market share even though they charged a higher price. Grabowski and Vernon (1992) suspect that first-mover advantages come into play. In practically all generic drug markets, the market leader is a first-mover, where the initial lead time is often not more than a month or two. Grabowski and Vernon (1992) explain that, "once pharmacies begin stocking a particular generic supplier's product, they will have a preference to continue using that product given its recognizable shape, size, and color to repeat-purchase customers", and they conjecture that first movers will have an advantage in sustaining high market shares.

Using pooled cross-section data for the Canadian pharmaceutical market over the time period 1994-1997, Hollis (2002) examines the effect of being first or second generic entrant on firms' sales market share within the generic market segment[21], as measured after the first, second, third and fourth year following first generic entry. Controlling for the number of generic entrants, a time trend, the generic product's price relative to the average generic price and for the average generic price relative to the pre-entry brand price, Hollis (2002) runs an Ordinary Least Squares (OLS) regression for each of the four time periods. The relative timing of entry and the number of generic entrants at each point in time are treated as exogenous. The OLS results show that first generic entrants obtain a roughly 20-35% larger market share over a period of at least four years. Hollis (2002) explains that patients' unwillingness to switch among medications, search and "persuasion" costs on parts of doctors, and the administrative costs of pharmacies when stocking several generic drugs result in switching costs which in turn give rise to first-mover advantages. Providing tentative evidence of the retainability of first-mover advantages, Hollis (2002) obtains no estimate of how persistent generic market shares are. Furthermore, he ignores the simultaneity bias arising from the introduction of generic prices in the market share equation. The effect of generic products' price on market share is insignificant except for the first year regression estimate, where Hollis (2002) obtains a significant and positive coefficient. The positive effect contradicts economic intuition and casts doubt on the consistency of the OLS estimate.

[21] Hollis (2002) defines a market as a drug formulation (dosage size and drug form) in a Canadian province.

Giving rise to a moral hazard problem in the market for insurance, the lack of price sensitivity among physicians and patients has been identified as one major explanatory factor of the historically slow uptake of generic drugs (Hellerstein, 1998; Paraponaris *et al.*, 2004), and more generally of the persistence of prescription decisions (Coscelli, 2000). Physicians are considered not to be fully price sensitive as they usually have little knowledge of actual drug prices[22], and do not benefit financially from the prescription choices. Not bearing the full cost of treatment, risk-averse patients have an incentive to receive the brand-name rather than the cheaper generic drug. Both Hellerstein (1998) and Paraponaris *et al.* (2004) assert that moral hazard in the market for health care insurance has likely hindered the surge in generic prescriptions, yet the studies do not explicitly investigate physicians' or patients' sensitivity to price differentials across therapeutically equivalent drugs. Hellerstein (1998) finds that physicians generally vary their prescription decisions. The reasons for why some physicians are more likely to prescribe generic drugs are largely left unexplained. Observable patient characteristics, such as age or sex, influence physicians' generic versus brand-name prescription choices very little. Paraponaris *et al.* (2004) in turn show that physicians who have access to a computer, who regularly read medical journals and who collaborate with other physicians are more willing to prescribe generic drugs. In contrast to Hellerstein (1998) and Paraponaris *et al.* (2004), Coscelli (2000) focuses on physicians' prescription choices among therapeutically equivalent tradename drugs. Controlling for patient and doctor attributes, she examines the tradename drug choices among six anti-ulcer drugs in Italy from 1990 to 1992. Coscelli (2000) finds a strong time-dependence in physicians' prescription choices which she links to the persistent differences in firms' market share. Noting that the Italian reference price system forces vendors of therapeutically equivalent drugs to set identical prices, she does not account for price differentials. She further points out that pharmacists had no power to substitute generic for brand-name drugs during the sample period.

Many industrial nations have enforced generic substitution laws by now, shifting the choice over therapeutically equivalent drugs to the pharmacist and patient. Pharmacists know medical products' prices and can inform the patient about saving possibilities. None of the previous studies investigates pharmacists' and patients' choice among generic products and their sensitivity to price differentials. Generic prices vary evidently not only in the U.S.

[22]Temin (1980) and Kolossa (1995) provide further details on physicians' awareness of actual drug prices.

pharmaceutical market (Grabowski and Vernon, 1992) but also in pharmaceutical markets with a long-established reference price regime (e.g. Germany). An analysis of how strongly price differentials affect patients' switching behavior among generic products will shed light on the underlying factors provoking the observed generic market share dynamics.

2.4 Data

The study relies on national pharmaceutical market and exclusivity data, tracking the evolution of generic prices and market shares in 35 off-patent drug markets between 2002 and 2007. Moreover, it relies on unique micro data, tracking the monthly medication history of 88432 newly diagnosed repeat-purchase patients over the year 2007. *Insight Health* provides pharmaceutical market, patent, SPC and patient tracking data. The following two subsections give an overview of the two data sets employed in the empirical study.

2.4.1 Macro Data: Generic Product Panel

The retail pharmacy data reflect wholesale and direct purchase transactions of public pharmacies and contain detailed information on medical products supplied in the German pharmaceutical market.[23] The macro analysis is confined to human medications containing one active ingredient to ensure a high matching quality of pharmaceutical and exclusivity data.[24] Drugs are classified by the current status of patent and SPC protection, the availability of generic and re-import versions of the drug and by therapeutic field(s) of indication[25]. Medical products in turn are categorized as "patent-protected brand, off-patent brand or generic" and as "original or "re-import" product. Information on medical products'

[23]Similar data for the German hospital segment are not available. As a result of quantity discounts, prices charged to hospitals are generally much lower than prices charged to public pharmacies. However, the turnover generated with prescription drugs tends to be considerably smaller in the hospital segment. In 2007, for instance, the retail turnover in Europe was roughly three times as large as the turnover generated in the hospital segment (EUC, 2009). Thus, for the majority of prescription drugs in this study, retail pharmacy prices should nevertheless provide a reliable indicator of actual market prices.

[24]*Insight Health* has obtained exclusivity data from the national patent and trademark office since 2005. I accessed the PATDPASPC, Esp@cent Patent, Derwent and Open Drug database, Thomson's Current Patent Gazette, the FDA Orangebook, and online patent expiry reports to complement and verify the data. If generic entry occurred prior to patent or SPC expiry, investigations were carried out to find evidence of early entry or patent invalidity cases that would explain entry prior to loss of exclusivity.

[25]The classification of therapeutic fields rests upon the Anatomical Therapeutic Chemical (ATC) Classification System which was introduced by the *WHO* in 1976.

trade name, active ingredient(s), the manufacturer, the availability of various drug form(s)[26], dosage(s) and package size(s) is available. Dates of launch are provided at retail form level, i.e. for each drug form, dosage and package size of the medical product. Monthly price and sales data are available at retail form level as well. Lastly, there is a lack of generic advertising data. Such data are private and almost impossible to acquire for researchers. The overall level of generic advertising is known to be low (Scherer, 2000; Berndt *et al.*, 2003).[27] Nevertheless, the lack of generic advertising data is certainly a limitation of this study.

Overall 48 drugs went off-patent between 2002 and 2007.[28] 724 generic entries have occurred in these markets by 2007. Assuring the comparability of results, I confine the analysis to drug markets with oral drug form use (39 drugs) which have experienced at least one year of off-patent competition by December 2007 (42 drugs).[29] 35 drug markets meet both criteria. Overall 640 generic products were launched in these markets. Notably, most drugs are available in multiple dosages and package sizes. Like Caves *et al.* (1991), Grabowski and Vernon (1992), Bhattacharya and Vogt (2003) and Regan (2008), I determine generic prices for the most "popular" dosage size to ensure a constant unit of observation. This dosage size has generated the largest generic revenue stream in a drug market by 2007.[30] Note that generic firms usually offer different and not necessarily the same package sizes for one specific dosage size. Hence, it is impossible to determine a constant unit of observation at package size level without losing a substantial fraction of observations. Confining the analysis to one market segment does not turn out to be disadvantageous on the other hand as the majority of generic firms launch the bestselling dosage size. The total number of generic entries (generic products) declines slightly to 622, and the average generic entry pattern in the 35 drug markets and bestseller segments is astonishingly similar. At last, I restrict the sample to 605 generic products where market share and price observations are available for a period of at least six months, as I require higher order lags of the variables in selected estimations.[31]

[26]The drug form classification follows the New Form Code (NFC) Classification established by the *European Pharmaceutical Market Research Association (EphMRA)*.

[27]Direct advertising of prescription medications to consumers is illegal in the European Union.

[28]Other studies report similar rates of generic entry, e.g. Magazzini *et al.* (2004).

[29]Saha *et al.* (2006) and Regan (2008) similarly confine their analyses to oral medications.

[30]Monthly revenues in the bestseller segment make up on average 62% of total drug market revenues.

[31]I include market share and price lags of third order in the macro analysis. The follow-up study on generic price dispersion (see Chapter 3) requires lags of higher order, however. For the two studies to be directly comparable, I use the same restriction and the same sample of generic products.

Unit of observation in the macro analysis is firms' monthly turnover share in the generic bestseller segment. Generic prices denote average per-pill prices. I aggregate the ex-factory[32] per-pill prices of different package sizes, computing a turnover-weighted[33] average price *per pill* for each generic product[34]. Per-pill prices vary slightly across different package sizes.[35]

As drugs' losses of exclusivity and generic entries occur at different points in time, I obtain an unbalanced data panel. Selection and attrition issues are likely to be minor, however. The dates of patent and SPC expiries are exogenously given, and within a period of a few months at least, generic entry timing is plausibly exogenous. Generic firms decide upon market entry at least three years prior to loss of exclusivity, and the legal process of obtaining market approval makes it generally impossible to predict exactly when approval will be granted (see Section 2.2). The majority of generic entries (395) eventually occurred within a narrow time window of six months[36], and generic companies did not exit drug markets. Price and turnover – indicators of supply activity – are never missing after generic firms' entry in the bestseller segment. Table 2.1 provides an overview of the data sample, outlining important characteristics of drug markets, generic firms and generic products.

Table 2.1: Overview Generic Drug Markets – Bestseller Segment

	N	Mean	Median	Min.	Max.	Sd.
Drug Markets						
Months off-patent Generic Competition	35	39.9	43	12	70	15.1
Accumulated Generic Entry by Dec. 2007	35	17.7	17	3	39	8.3
Initial Monthly Revenues (in €Mio.)	35	3.8	2.3	0.1	22.7	0.5
Generic Firms						
Drug Portfolio Size by Dec. 2007	68	70.3	44.5	1	304	67.9
Rx Drug Portfolio Size by Dec. 2007	68	57.4	34	1	246	56.6
Umbrella Brand Size by Dec. 2007	68	43.1	18	0	300	63.1
Generic Products						
Months off-patent Generic Competition	605	34.5	31	6	70	14.1
Initial Generic Price Cuts (in %)	605	37.7	36.3	-71.3	89.2	17.7
Initial Generic Market Share (in %)	605	7.4	0.3	0	100	19.2

Notes: Price and revenue statistics are based on producer prices. Initial monthly revenues in the bestseller segment are measured in the first month of generic entry. The umbrella brand of a generic manufacturer comprises all products which carry the (un)abbreviated corporate name of the firm. Generic firms' initial price cuts in the first month of entry are reported relative to the brand price observed in the month prior to first generic entry.

[32]Ex-factory prices are the selling prices charged by generic firms which neither include the fixed wholesale and pharmacy markup nor the value added tax, providing an informative measure of firms' profit streams.

[33]If a product yielded zero turnover, I compute a package size-weighted average price instead.

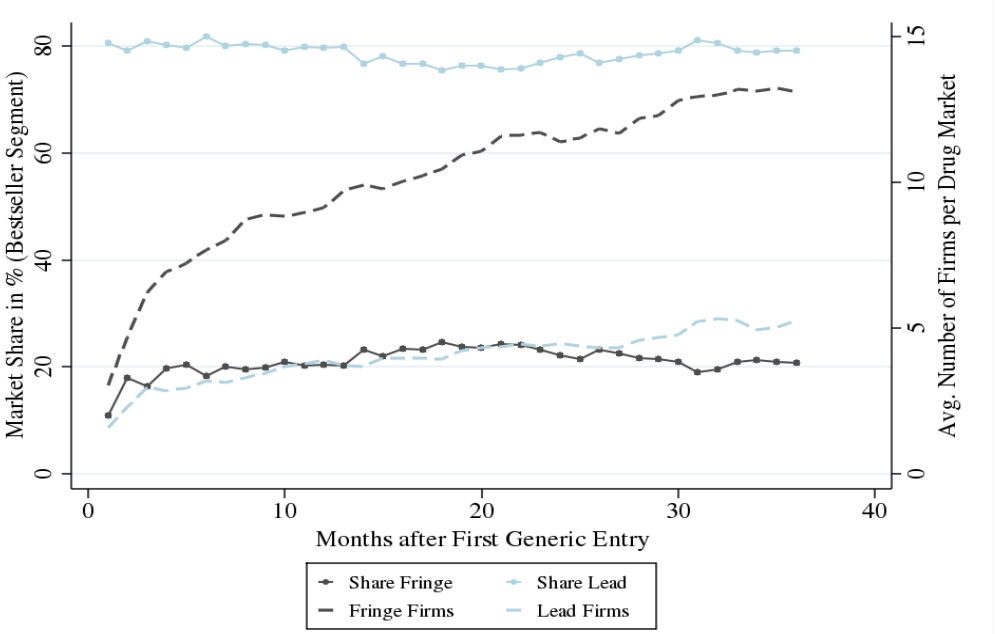
[34]The terms generic product and generic drug are used interchangeably as firms tend to launch one product per drug. Else products' prices are aggregated at drug-firm level using turnover/package size weights.

[35]I account for the additional price variation across package sizes by controlling for the (turnover-weighted) average package size of each generic product in the bestseller segment.

[36]24 generic products were launched in 15 drug markets prior to patent or SPC expiration (early entry).

Overall 68 generic firms entered in the 35 bestseller segments. As of December 2007, these firms offer 70.3 drugs on average, supplying primarily Rx drugs. Firms' portfolio of umbrella branded drugs is smaller than their overall drug portfolio as firms have occasionally pursued a (non-INN) premium brand strategy. On average, I track generic products for 34.5 months (T). Examining the market shares of 605 generic products (G), I obtain a total of 20888 observations (GxT). In the first month of entry, generic products are on average offered at a price discount of 37.7% relative to the pre-entry brand price.[37] Generic firms obtain on average a market share of 7.4% in the first month, yet there is a strong variability in market shares across firms. Notably, generic firms with above average market shares (lead firms) appear to be able to sustain their favorable market position over the long-run. Figure 2.1 below depicts the average aggregate market shares of lead and fringe firms, the latter achieving below average market shares within the generic market segment. Moreover, it plots

Figure 2.1: Aggregate Market Shares, Turnover: Lead vs. Fringe Firms



the average number of lead and fringe firms in each drug market (bestseller segment) over time. Roughly five firms achieve above average market shares and supply on average 80% of all generic pills, tablets or capsules. Whereas the average number of lead firms remains quite stable over time, the average number of fringe firms increases notably from roughly four to

[37] The implied average generic price ratio in the first month of entry (62.3%) varies from the previously reported average generic price ratio of 75% (Section 2.2) for several reasons: (1) The given generic price ratio denotes an unweighted average price across the 605 generic products and not an unweighted average of the (turnover-weighted) average generic price across the 35 drug markets. (2) The initial price cut refers to the first month of product launch which must not coincide with the first month of off-patent generic competition.

fourteen firms within three years of generic competition. In spite of this large increase, fringe firms do not supply more than roughly 20% of generic oral solids at any point in time.

Not surprisingly, fringe firms tend to charge comparatively higher prices than their competitors. Appendix [2.1] shows that fringe firms deviate strongly and positively from the average generic-to-brand price ratio observed in a given drug market and month. However, price deviations in the range of 10 percentage points are also common for lead firms. Appendix [2.2] illustrates that generic price differentials tend to decline over time as generic prices become smaller. The standard deviation[38] of generic prices drops by almost 60% within three years of generic competition, even looking at lead and fringe firms separately. The previously described pattern of aggregate market shares suggests that market shares are indeed persistent, and not heavily influenced by the observable price deviations.

2.4.2 Micro Data: Patient Tracking

The patient tracking data provide a monthly medication history for a random sample of about 7 Mio. patients in Germany over the year 2007. About 4100 drugs were dispensed in total. Whenever patients received more than one drug, multiple patient-drug (treatment) observations are given. The data are unbalanced as they report a different number of drug dispensing events for the treatments. Patients received very rarely more than one prescription for a specific drug in a single month. One drug was typically dispensed to the patient in several, not necessarily succeeding months. For instance, the drug *Amlodipine* could have been dispensed to patient A three times in 2007 (e.g. in March, April and August), whereas patient B could have received *Amlodipine* two times in 2007 (e.g. in April and July).

The 35 off-patent drugs were consumed by roughly 2 Mio. patients, out of which 1.8 Mio. patients received generics and could have potentially switched among products. Being unaware of patients' medication history prior to 2007, I confine the analysis to patients who obtained their first diagnosis in 2007. Only for those patients I can unambiguously identify all generic product switches. By definition those patients have not consumed the medical product before January 2007. About 430000 patients obtained their first diagnosis in 2007. Price

[38]The average generic price (standard deviation of generic prices) denotes a turnover-weighted average of generic prices (generic price deviations from the turnover-weighted average generic price) within a drug market. The standard deviation is set from zero to missing as long as one firm supplies the bestseller segment, where the standard deviation of generic prices will automatically be zero. This event must be distinguished from the case where at least two generic firms compete and set equal prices.

data are in turn only available for generic products in drug markets' bestseller segment[39] (see Section 2.4.1), which were dispensed to 283151 patients. I am only able to identify a switch among generic products once at least two drug dispensing events were recorded for a patient-drug observation. Recall that patients usually received not more than one prescription per drug in a single month. 115200 treatments, and respectively 100708 patients meet this criterion. Lastly, the analysis is confined to 88432 newly diagnosed, repeat-purchase patients (J), given that information on both age and sex of the patient is specified. As some of the patients started to consume more than one of the 35 drugs (M) in 2007, I obtain overall 101096 patient-drug or treatment observations (JxM). Two dispensing events were recorded for 55223 out of the 101096 treatments (54.6%), and three dispensing events were recorded for another 28141 treatments (27.8%). As patients tend to repeatedly purchase generic products, generic firms' pricing decisions have an immediate and fundamental impact on patients' purchase and product switching decisions. The data comprise overall 279171 drug dispensing events, recording several follow-up drug dispensing events (D_F) for some of the treatments. As the micro analysis is directed to generic product switches, I only make use of the 178075 follow-up drug dispensing event observations (JxMxD_F). By definition generic product switches do not occur at the time of the first drug dispensing event.

The patient tracking data indicate the active ingredient, drug form, dosage and package size, and therapeutic indication of the dispensed generic product. Note that the medical product dispensed by the pharmacist must not necessarily coincide with the product prescribed by the physician. The data neither indicate whether the physician prohibited generic substitution, nor whether the statutory health care insurance provider of the patient had closed a rebate contract for the particular medial product. As physicians predominantly allow for generic substitution, the lack of information on prescribed medical products or the possibility of substitution is not a severe restriction. On the contrary, data on dispensed medical products are a prerequisite for the identification of switches among generic products. Indicating the statutory health care insurance provider of the patient, the data allow the researcher to control at least indirectly for closings of rebate agreements. Notably, the data do not reflect differences in reimbursement practices across insurers, given that the prescrip-

[39]Notably, drug markets can be fragmented into patient segments with distinct drug usage profiles. In 90.6% of all generic product switches, newly diagnosed patients switched among generic products of the same drug form (NFC1 Class.) and dosage size. In 85.6% of all generic product switches within the 35 drug market bestseller segments, product package sizes were also identical.

tion drug coverage is uniform within the German statutory health care insurance system. The data specify further patients' age, sex, the date of the first diagnosis and the affiliated physician group of the prescribing doctor. Information on income or similar characteristics of the patient are not available, and the identity of the pharmacy dispensing the generic product is kept confidential. The patient tracking data indicate, however, from which physician group patients received their prescriptions. Thus, I have at least a weak indication for whether the patient visited the same doctor and potentially bought the generic product at the same pharmacy. Pharmacies are often located close to medical centers or clusters of private practices, and especially elderly patients develop a preference for one pharmacy within their reach.[40] Notably, patients received 109839 of the 178075 follow-up drug prescriptions from a general practitioner (61.7%). The German *Family Physician Model*[41] provokes that patients predominantly consult general practitioners, and likely the same physician.

Table 2.2 below provides an overview of the patients and treatments examined in the micro analysis. The average patient is 66 years old. Most prevalent among patients are

Table 2.2: Overview Patients and Treatments – Bestseller Segment

	N	Mean	Median	Min.	Max.	Sd.
Patient Age (in Years)	88432	66.1	68	1	108	16.6
Patient Sex (=1 for female)	88432	0.5	0	0	1	–
Medications Prescribed in 2007	88432	6.8	6	1	46	4.6
Month of First Diagnosis	101096	4.2	4	1	11	2.5
Monthly Prescriptions per Drug	101096	1.0	1	1	10	0.2
Follow-up Drug Dispensing Events	101096	1.8	1	1	11	1.1
Follow-up Drug Dispense: 1st Switch	38824	1.3	1	1	9	0.7
Month since First Diagnosis: 1st Switch	38824	4.8	4	1	11	2.4

diseases of the cardiovascular system, which predominately appear in older adults. 49.4% of patients are female. Patients consumed on average seven drugs, which may include any of the 4100 drugs dispensed in 2007. They obtained the first diagnosis on average in April 2007

[40] TNS Infratest conducted 3300 nationally representative interviews with purchasers of over-the-counter (OTC) products between April and May 2009. 57% of the respondents indicated that they buy medical products at one specific pharmacy only. Further 35% of interviewees indicated that they buy medical products at the pharmacy closest within their reach. Elderly patients in particular turn out to have a strong preference for one specific pharmacy, organizing their shopping activities in account of the reachability of the pharmacy. (www.tns-infratest.com/Presse/pdf/autorenbeitraege/02_07_AB_TNS_Infratest_Brohl_Gern-Coprian_Schnaeppchenjagd_RR_01_2010.pdf; accessed: Oct. 15th 2010.)

[41] Statutory health care insurance providers in Germany are required by law to offer a *Family Physician Model* tariff to patients. Enrolled patients generally have to consult their general practitioner first once they develop a disease, and obtain a special tariff in return. The general practitioner will refer the patient to a specialist if necessary. Purpose of the *Family Physician Model* is to save on health care expenditures, avoiding multiple physical examinations. See also www.handelsblatt.com/politik/deutschland/gesundheitswesen-hausarztmodell-wohl-auf-der-streichliste;2599929 (accessed: Oct. 30th 2010).

and at the latest in November 2007. Recall that the analysis is confined to newly diagnosed patients who received drugs in at least two different months. Per treatment, 1.8 follow-up drug dispensing events were recorded on average (Median: 1). Strikingly, patients hardly switched among generic products. In fact, the majority of patients (59.1%) always received the same generic product. Generic product switches can be observed in 38824 out of 101096 treatments (38.4%), and in 49389 out of 178075 follow-up drug dispensing events (27.7%). Interestingly, generic product switches occurred early on: first-time product switches usually took place in the course of the first follow-up drug dispensing event. At that time, patients had on average been in treatment for roughly 5 months (Median: 4). Unfortunately, I remain uninformed about whether the patient or pharmacist initiated the product switch. Thus, I can only make a global statement on the price sensitivity of patients and pharmacists.

2.5 Macro Analysis of Generic Market Shares

Lacking evidence of how effectively generic firms compete on price in off-patent drug markets, economists can neither assess the intensity nor efficiency of generic competition. The macro analysis investigates how strongly generic market shares are affected by price differentials, accounting for their persistence. The aggregate market share and price patterns in 35 drug markets indicate that market shares are persistent and largely uninfluenced by the price differentials observed across generic products. Based on the empirical evidence, the macro analysis pursues the first hypothesis of the study which is given below. The econometric model and the results of the macro analysis are presented in the next subsections.

Hypothesis 1: Generic prices (generic-to-brand price ratios) have a small and marginally decreasing impact on generic market shares over time.

2.5.1 Macro Analysis: Empirical Implementation

Generic prices ($P_{g_{itm}}$) are normalized by pre-entry brand prices – as observed in the month prior to first generic entry – to obtain a comparable measure of generic price variations across drug markets.[42] The generic-to-brand price ratio ($P^{Ratio}_{g_{itm}}$) and market share ($M_{g_{itm}}$) of firm i – as observed in month t following first generic entry in drug market m – are potentially correlated with firm i's advertising expenditures. The lack of data on generic advertising

[42] A log-transformation is unneeded. Generic-to-brand price ratios are quite close to normally distributed.

expenditures may give rise to omitted variable (ov) bias. Given that generic advertising is very limited (Hellerstein, 1998; Scherer, 2000; Berndt *et al.*, 2003)[43], Berndt *et al.* (2003) hypothesize that marketing-to-sales ratios are close to zero. I assume that advertising expenditures are potentially non-zero but time-constant (ov_i) as generic advertising is directed to firms' drug portfolio rather than individual drug products (Berndt *et al.*, 2003).[44]

I include both the generic-to-brand-price ratio and a one month lag of the dependent variable ($M_{g_{itm}}.l1$) in the generic market share equation, examining the impact of generic prices on market shares and the persistence of the latter. The lagged dependent variable is necessarily correlated with the omitted (unobserved) effect (ov_i) in the composite error term v_{it} ($v_{it} = u_{it} + ov_i$), which gives rise to dynamic panel bias in an Ordinary Least Squares (OLS) regression framework.[45] The OLS coefficient estimate for lagged market share turns out to be inflated, as predictive power of the unobserved effect is incorrectly being attributed to the dependent lagged variable. Based on the previous assumption of potentially non-zero but time-invariant generic advertising expenditures, I am able to eliminate the unobserved effect from the composite error term v_{it} ($v_{it} = u_{it} + ov_i$) using either first differencing or a within-transformation of the data.[46] The Fixed Effects (FE) estimator applies a mean-deviation transformation (within-transformation) to each variable. However, causing a negative correlation between the transformed lagged dependent variable and the transformed error term, the within-transformation does not eliminate dynamic panel bias. The FE coefficient estimate for lagged market share accordingly turns out to be deflated.[47] Nevertheless, FE and OLS estimates provide useful bounds between which good estimates of the true parameter should lie in or be in the near range of (Bond, 2002). The General Method of Moments Difference (DIFF GMM) estimator theoretically tackles the problem of dynamic panel bias, using first-differencing to remove time-invariant unobserved effects and instrumenting the endogenous, first-differenced variables with appropriately lagged levels (Holtz-Eakin *et al.*,

[43]Generic firms hardly engage in physician detailing (promotional visits) and do a modest amount of journal advertising (Berndt *et al.*, 2003; Gupta and Yu, 2008).

[44]The average (median) generic firm launches nine (four) new drugs between 2002 to 2007. As generic firms likely direct advertising efforts to newly off-patent drugs and less to older drug products, advertising may be targeted to a different selection of drugs over time but should nevertheless remain roughly constant.

[45]The positive correlation between the regressor and error term violates the orthogonality assumption which is a necessary condition for the consistency of OLS.

[46]Time-invariant, unobserved firm effects (c_i), e.g. managerial quality, will be similarly wiped out.

[47]The transformed lagged dependent variable can also not be instrumented with higher order market share lags as those are similarly correlated with the transformed error term. The FE transformation can only be used once strictly exogenous and time-variant instruments are available (Wooldridge, 2002).

1988; Arellano and Bond, 1991). Depending on the order of autocorrelation in the v_{itm}'s – indicated by the Arellano-Bond autocorrelation test – different lags will be appropriate. Practically however, DIFF GMM will perform poorly if the dependent variable is highly persistent.[48] In this case, past levels provide only weak instruments for first differences. The System GMM estimator developed by Blundell and Bond (1998) offers substantial efficiency gains in situations where the standard DIFF GMM estimator performs poorly. In addition to lagged levels as instruments for first differences, the System GMM estimator uses lagged differences as instruments for levels, imposing restrictions on the initial conditions process.[49]

As generic market shares appear to be highly persistent, I employ the System GMM estimator to cope not only with dynamic panel bias but also with the simultaneity bias arising from the introduction of prices in the market share equation (Saha *et al.*, 2006). Like related empirical studies (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Frank and Salkever, 1997; Bhattacharya and Vogt, 2003; Reiffen and Ward, 2005; Saha *et al.*, 2006; Regan, 2008), I control for the number of generic entrants (N_{tm}), the number of off-patent (generic) and on-patent therapeutic substitutes ($\mathbf{S_{tm}}$), for a time trend (T_{tm}) and for year effects ($\mathbf{Y_{tm}}$). Adding the square of the number of entrants (N_{tm}^2) to the market share equation, I allow for a non-linear effect of generic entry. I follow Reiffen and Ward (2005)[50] and Saha *et al.* (2006), assuming that the number of generic entrants is strictly exogenous. Given the time frame of the market approval process and the frequent delays in the grant of market approval, the number of generic entrants is plausibly strictly exogenous (see Section 2.2). Recall also that generic manufacturers did not exit from any of the 35 drug markets.

The first specification includes further the size of firm i's drug portfolio (dp_{it}) and umbrella brand (ub_{it}) as well as generic products' average package size (ps_{itm}). Industry evidence suggest that the size of generic firms' drug portfolio and umbrella brand are critical factors for success in intra-generic competition (Accenture, 2005). The package size of generic products within one drug market differs notably, and might provide a competitive advantage to some

[48] Alonso-Borrego and Arellano (1996) show in simulation studies that DIFF GMM has large finite sample bias and poor precision in dynamic panel data models where the autoregressive parameter is moderately large and the number of time series observations is moderately small.

[49] Instruments are being differenced to make them exogenous to the unobserved effect, which is valid under the assumption that changes in the instrumental variable are uncorrelated with the latter. This assumption can hold only under certain initial conditions on the data generating process (see Blundell and Bond (1998)).

[50] Reiffen and Ward (2005) test for endogeneity using a Hausman test and cannot reject the null hypothesis that market structure is exogenous.

firms if pharmacists or patients have preferences for smaller or larger packages. The first specification is estimated by System GMM as well as by FE and OLS to obtain a bound for the true parameter estimate for $M_{g_{itm}}.l1$. As generic firms' pricing decisions across drug markets and within drug markets over time are likely not independent, standard errors are generally clustered at firm level (68 clusters). The OLS and FE standard errors are robust to heteroscedasticity, whereas the (two-step) System GMM standard errors are robust to both heteroscedasticity and arbitrary autocorrelation within panels (generic products). The Windmeijer-correction of standard errors reduces the typically inherent downward bias in the two-step System GMM standard errors. The first specification is given below.

$$\begin{aligned} M_{g_{itm}} &= \alpha M_{g_{itm}}.l1 + \beta P_{g_{itm}}^{Ratio} + \gamma_1 N_{tm} + \gamma_2 N_{tm}^2 + \\ &\quad \mathbf{S_{tm}}\boldsymbol{\delta} + \theta T_{tm} + \mathbf{Y_{tm}}\boldsymbol{\eta} + \mu dp_{it} + \nu ub_{it} + \lambda ps_{itm} + v_{itm} \end{aligned}$$

Examining whether the impact of generic prices on market shares changes over time, the generic-to-brand price ratio is lastly interacted with the time trend ($P_{g_{itm}}^{Ratio} * T_{tm}$), and the interaction term is added to the market share equation. The second, extended specification is estimated by System GMM. Appendix [2.3.1] contains a summary of definitions for all variables employed in the panel data analysis. Summary statistics[51] are presented in Table 2.3 below, which again show that the vast majority of generic firms achieved only a small market share between 2002 and 2007. Appendix [2.4] provides a further, more disaggregate

Table 2.3: Summary Statistics – Generic Product Panel

Variable Name	Mean	Median	Min.	Max.	Sd.	GxT
Generic Market Share ($M_{g_{itm}}^{Ratio}$)	6.66	2.42	0	100	12.04	20888
Generic-to-Brand Price Ratio ($P_{g_{itm}}^{Ratio}$)	41.94	40.30	5.57	173.40	18.32	20888
Generic Entry	19.96	20	1	39	7.97	20888
Branded Substitutes	5.68	4	0	23	5.15	20888
Generic Substitutes	15.86	12	0	65	13.30	20888
Drug Portfolio Size	127.95	130	0	304	78.23	20888
Umbrella Brand Size	97.14	101	0	300	79.91	20888
Package Size	78.26	87.55	2	284	34.63	20888
Time Trend	26.75	25	1	70	15.35	20888

overview of the data, decomposing variables' standard deviation into its between and within components. The statistics indicate that there is a by far larger variation in market shares across generic firms than over time, suggesting that market shares are indeed quite persistent.

[51] Summary statistics are weighted by the number of entrants (N_{tm}) markets have attracted in month t.

2.5.2 Macro Analysis: Results

Examining at macro level the impact of generic prices on market shares and the persistence of the latter, I estimate a dynamic panel data model and employ the FE, OLS and System GMM estimator. Appendix [2.5] presents the FE and OLS estimates obtained for the first specification. Table 2.4 below contains the System GMM estimates. For the most

Table 2.4: System GMM – Coefficients

	$M_{g_{itm}}.l1$, $P^{Ratio}_{g_{itm}}$ and $P^{Ratio}_{g_{itm}}$xT instrumented using 3^{rd} Lags:	
Dep.Variable: $M_{g_{itm}}$	*Spec.1*	*Spec.2*
Lag Generic Market Share ($M_{g_{itm}}.l1$)	0.7593***	0.7392***
	(0.069)	(0.062)
Generic-to-Brand Price Ratio ($P^{Ratio}_{g_{itm}}$)	-0.0741**	-0.1020**
	(0.029)	(0.032)
$P^{Ratio}_{g_{itm}}$ * Time Trend: ($P^{Ratio}_{g_{itm}}$xT)	–	0.0032**
		(0.001)
Generic Entry	-0.5321*	-0.6140*
	(0.251)	(0.243)
Generic Entry^2	0.0084	0.0120*
	(0.004)	(0.005)
Branded Substitutes	-0.0579*	-0.0210
	(0.029)	(0.017)
Generic Substitutes	0.0169	0.0025
	(0.015)	(0.013)
Drug Portfolio Size	0.0080	0.0136
	(0.014)	(0.011)
Umbrella Brand Size	0.0011	-0.0044
	(0.013)	(0.009)
Package Size	0.0027	0.0057
	(0.003)	(0.003)
Time Trend	-0.0040	-0.1391**
	(0.005)	(0.049)
Year (2002,$\cdots$,2007)	*yes*	*yes*
Arellano-Bond test AR(1)	0.000	0.000
Arellano-Bond test AR(2)	0.017	0.018
Arellano-Bond test AR(3)	0.616	0.595
Hansen test: chi2(2)/chi2(3)	0.094	0.299
Instruments (Overid. Restr.)	18 (2)	20 (3)
Wald chi2(15)/(16)	1332.59	1743.45
Prob > chi2	<0.001	<0.001
G x (T-1)	20283	

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is the monthly turnover share of a generic product within the bestseller segment. Two-step standard errors robust to heteroscedasticity and autocorrelation, clustered at firm level (68 clusters), in parentheses. The Windmeijer correction for two-step standard errors has been employed. The reference year is 2002.

part, the same explanatory variables turn out to have a significant effect. Whereas the size of the effects varies somewhat across the three estimations, the direction of the effects is the same. Notably, the GMM coefficient of the lagged dependent variable lies well in the range of the FE and OLS estimate. Recall that the FE and OLS estimates provide a useful bound for the true parameter estimate for the lagged dependent variable ($M_{g_{itm}}.l1$). Given a second order autocorrelation of the error terms – as indicated by the Arellano-Bond autocorrelation test – I use market share lags of third order as instruments in the GMM regression.[52] The Hansen-test of over-identifying restrictions does not reject the joint null hypothesis that instruments are valid and that excluded instruments are correctly excluded from the estimated market share equation. The estimated coefficient of the lagged dependent variable's amounts to roughly 0.76, indicating that generic market shares are quite persistent over time.

Consistent with empirical evidence, this result implies that first-mover advantages can be substantial in generic drug markets. Independent generic first-movers (early entrants) achieved on average a market share of 13.6% (59.1%) in the first month of entry. After one year generic first-movers (early entrants) had retained on average a market share of 10.5% (39.2%). After two years they had retained on average a market share of 10.2%, and 31.3% respectively. Even after three years of generic competition, independent generic first-movers (early entrants) had still retained a market share of 8.1% (29.5%) within the generic bestseller segment. The small impact of generic prices on market shares proves to be one important explanatory factor of market shares' persistence. Just like lagged market shares, generic-to-brand price ratios are instrumented using third order lags. The coefficient of the generic-to-brand price ratio variable amounts to roughly -0.07, which implies that generic manufacturers achieve only a 0.7 percentage point higher market share by offering a 10 percentage point lower price. Given a standard deviation of 14.9 percentage points across generic products (see Appendix[2.4])[53], generic prices tend to affect market shares very little.

The entry of one generic firm reduces the market share of other generic firms by roughly 0.5 percentage points. Between three and 39 generic companies have entered the 35 drug markets by December 2007. With a standard deviation of roundabout eight generic entrants, the effect of entry on firms' market shares is large, considering that the vast majority of generic firms obtain a small market share only. The number of on-patent, branded sub-

[52] Effectively, I use market share lags of second order as instruments for the lagged dependent variable.

[53] Appendix[2.1] also illustrates that generic price deviations on a scale of 10 percentage points are common.

stitutes also has a significantly negative impact on market shares in the first specification. An additional branded drug in the same ATC1 therapeutic field lowers market shares by about 0.06 percentage points. Given a standard deviation of 5 branded substitutes, the effect explains hardly any variation in the data. All other effects are insignificant at a 5% level. The number of off-patent, generic substitute drugs in the same ATC1 therapeutic field has no impact on generic market shares. Neither does the size of firms' drug portfolio or umbrella brand, or products' package size. There is no evidence of a time trend in market shares.

In the second specification generic-to-brand price ratios are further interacted with the time trend to examine the impact of generic prices on market shares over time. The interaction term is instrumented for using third order lags. Its inclusion in the empirical model does not alter the results notably. The coefficient of the lagged dependent variable decreases slightly to 0.74, confirming that market shares are persistent over time. The effect of generic-to-brand price ratios increases somewhat. Firms achieve a 1 percentage point higher market share by offering a 10 percentage point lower price. Given a standard deviation of 14.9 percentage points across products, the impact of prices on market shares is again very small. Moreover, their effect diminishes by 0.0032 percentage points in each month of generic competition. After roughly 32 months the effect of a price change is essentially zero. Overall, I find support for the first hypothesis, stating that differences in generic-to-brand price ratios have a small and marginally decreasing impact on generic market shares over time.

The entry of one generic firm has in turn again a negative, yet slightly larger and non-linear effect on firms' market share. The entry of one generic firm lowers market shares by about 0.6 percentage points, and the effect is decreasing by 0.01 percentage points with each additional entrant. Given a standard deviation of roughly eight entrants, the effect is notable. Recall that the most firms obtain a minuscule market share only. Except for the time trend, all other effects are again insignificant. The coefficient of the time trend amounts to -0.14, indicating that market shares drop by about 0.1 percentage points in each month of generic competition. Given a standard deviation of roughly 15 months, the effect does not explain much of the variation in the data. Overall, estimates show that the previous market share and the number of generic entrants determine firms' market share most strongly. Generic prices affect market shares only minimally, and their effect is decreasing over time.

2.6 Micro Analysis of Patients' Switching Behavior

Patients' and pharmacists' low sensitivity to price differentials may be one important explanatory factor of patients' rare switching among generic products, and the persistence of generic market shares at macro level. As a result of largely fixed copayments and dispensing fees, patients and pharmacists do not fully internalize the marginal cost of treatment and the financial benefit of switching to a cheaper generic product. If price differentials between two generic products – identical in active ingredient, drug form and dosage size – are not very large, patients' prescription drug expenses will be equally covered and the copay amount will also be similar. In this line of reasoning, patients' financial incentive to switch among generics should decline as price differentials become smaller. Since pharmacists' variable pay component is very small, their financial incentive to encourage a switch among generic products should similarly decline as the size of price differentials decreases. Suspecting that pharmacists and patients are largely insensitive to price differentials (EUC, 2009), the micro analysis pursues the second hypothesis of the empirical study which is specified below. The econometric model and the results of the micro analysis are presented in the next subsections.

Hypothesis 2: Price differentials have a small impact on patients' switch among generic products, whereby the size of the effect increases in the size of the price differential.

2.6.1 Micro Analysis: Empirical Implementation

Assessing the price sensitivity of patients and pharmacists, I measure how differences in generic prices ($P_{g_{itm}}$) affect patients' switching behavior among generic products.[54] The related studies on physicians' prescription choices by Hellerstein (1998) and Coscelli (2000) examine the switch from the brand to a generic product, and the switch among therapeutically equivalent drugs respectively. Employing prescription panel data, both studies resort to the RE probit estimator, whereby Coscelli (2000) runs a pooled probit estimation as baseline model. Given the overall small time dimension[55] of the available patient panel data, I resort to a pooled probit estimation. One important advantage of the univariate probit estimator over the RE probit estimator is that heteroscedasticity-robust and clustered standard errors can be computed. Clustering standard errors at drug level is necessary, as product switches

[54]The results of the analysis are robust to the normalization of generic prices by pre-entry brand prices.

[55]For 55223 (54.6%) out of overall 101096 treatment observations I only observe one follow-up drug dispensing event. For another 28141 treatments (27.8%) I observe two follow-up dispensing events.

within one drug market are likely not independent. Patients might be generally more willing to switch because the particular drug has few or minor side effects. Patients' drug choices over time or across drugs[56] may also be dependent. As a robustness check, I cluster standard errors not only at drug level (35 clusters) but also at patient level (88432 clusters).[57] As the number of patient clusters is very large and the number of observations within one cluster accordingly small[58], the differences in standard errors should be minor (Moulton, 1990).

Generic Product Switch (S^G_{jitm}) denotes the dependent variable in the micro analysis. The dummy variable takes the value zero whenever patient j's generic product i, dispensed in month t of off-patent competition in drug market m, is manufactured by the same generic company as the previously dispensed generic drug product. It will take in turn the value one if generic product i is supplied by a different generic manufacturer than the previously dispensed generic drug product. Notably, each follow-up drug dispense d_f coincides with one specific month t of off-patent competition in drug market m. In conformity with the notation in the macro analysis, I use from now on the latter index to indicate both the time of the follow-up drug dispensing event and the size of the micro data sample (JxMxT).

In order to gauge the impact of generic price differentials on the likelihood of a generic product switch, I include the explanatory variable *Price Differential* in the product switch equation. The variable measures the per-pill price difference between the monthly average price and the price of the currently dispensed generic product i in Cent: Avg($P_{g_{itm}}$)-$P_{g_{itm}}$. Ideally, researchers would want to compare the generic price of product i and the previously dispensed product as observed in month t. Whenever patients do not switch among generic products, however, this price difference is automatically zero. Put differently, a price difference specified in that way contains the same information as the dependent variable itself, which disqualifies it as explanatory variable. The average generic price in turn facilitates a valid and reasonable reference point, and the interpretation of the price effect is essentially the same: patient j switched to (did not switch from) generic product i as it provided drug cost savings relative to the average generic price observed in drug market m in month t. Notably, generic product switches over the year 2007 are unlikely to be triggered by generic firms' promotional activities. Recall that direct advertising of prescription medications to

[56] 77388/9567/1318/142/17 patients receive 1/2/3/4/5 drug(s) out of the 35 drugs in the sample.

[57] A program written by Jingling Guan and Mitchell Petersen facilitates a probit estimation with two-way clustering; www.kellogg.northwestern.edu/faculty/petersen/htm/papers/se/probit2.ado.

[58] I observe on average 3.2 follow-up drug dispensing events for one particular patient (Median: 2).

consumers is illegal in the European Union. Furthermore, financial rebates for prescription drugs and discounts in kind to public pharmacies have been prohibited since May 2006.

Switches among generic products potentially occur more likely the more generic products are available. Also, patients may be more inclined to switch as they have gained confidence in the quality of generic drugs over time. Hence, I control for the number of generic entrants (N_{tm}) in drug market m as well as for a time trend (T_{tm}). Following Hellerstein (1998) and Coscelli (2000), I control for patient and drug characteristics, and for the specificities of the treatment. I control for patient's age (Age_j), sex (Sex_j) and statutory health care insurer ($\mathbf{I_{jt}}$)[59], and for generic product i's therapeutic field/indication ($\mathbf{TF_{jim}}$)[60]. Moreover, I account for the number of months that have elapsed since the first diagnosis (FD_{jtm}), and for the number of months that have elapsed since the last drug dispense (LD_{jtm}). Patients may become more reluctant to switch the more chronic their disease turns out to be, developing a "habit" for one medical product. Controlling for the duration and progression of the disease, I take account of habit persistence. Lastly, I control for the number of prescriptions the patient receives for the specific drug in month t ($Pres_{jtm}$), and for the number of drugs the patient receives in month t (Med_{jt}). Both provide a measure of patients' overall health status and their monthly drug expenses. The first specification is given below.

$$\begin{aligned} S^G_{jitm} &= \alpha(Avg(P_{g_{itm}}) - P_{g_{itm}}) + \beta N_{tm} + \gamma T_{tm} + \delta Age_j + \epsilon Sex_j + \\ &\quad \mu FD_{jtm} + \nu LD_{jtm} + \kappa Pres_{jtm} + \lambda Med_{jt} + \mathbf{I_{jt}}\boldsymbol{\eta} + \mathbf{TF_{jim}}\boldsymbol{\theta} + v_{jimt} \end{aligned}$$

Knowing from which physician group patients receive a prescription, I have a weak indication for whether the patient visited the same doctor and potentially bought the medical product at the same pharmacy. If pharmacies stock the same selection of generic drugs over time (Hollis, 2002), patients will habitually receive the same generic product. To further examine the impact of habit persistence, I estimate a second specification, where I account for whether the previously and currently prescribing doctor belong to the same physician group (SPG_{jitm}). Moreover, I control for the physician group of the prescribing doctor (PG_{jitm})[61].

[59] Patients are covered by 21 statutory health care insurers. 12 insurers (Arb, BG, BKN, BUN, LKK, PB, POL, PRI, Pos, SOZ, SEE, VdA) are grouped and classified as "OTHER" as they cover only few patients.

[60] There are seven therapeutic indications (ATC1 Class.). Two therapeutic fields (alimentary tract and metabolism, musculo-skeletal system) are grouped and classified as "OTHER" given their rare incidence.

[61] 17 out of 23 physician groups (anesthetists, eye specialists, surgeons, gynecologists, ear-nose-throat specialists, pediatricians, laboratory physicians, oral and maxillofacial surgeons, neurologists, neurosurgeons, nuclear surgeons, orthopedic specialists, pathologists, psychotherapists, radiologists, primary care physicians, dentists) are grouped and classified as "OTHER" as they treat only few of the patients in the sample.

Appendix [2.3.2] contains a summary of definitions for all variables employed in the analysis of patients' switching behavior. Summary statistics[62] are presented in Table 2.5.

Table 2.5: Summary Statistics – Patient Tracking Data

Variable Name	Mean	Median	Min.	Max.	Sd.	JxMxT
Generic Product Switch	0.28	0	0	1	–	178075
Price Differential (Cent/Pill)	-0.02	-0.24	-87.4	54.6	3.46	178075
Generic Entry	26.19	25	3	39	7.34	178075
Time Trend	44.91	46	3	70	11.50	178075
Patient Age	67.51	69	1	108	16.01	178075
Patient Sex	0.50	0	0	1	–	178075
Months since first Diagnosis	5.28	5	1	11	2.56	178075
Months since last Dispense	2.76	3	1	11	1.56	178075
Prescriptions per Month	1.03	1	1	10	0.18	178075
Medications per Month	3.42	3	1	23	2.18	178075
Same Physician Group	0.96	1	0	1	–	178075

Receiving the previously dispensed generic product in about 72% of follow-up drug dispensing events, patients hardly switched among generic drugs. Evidently, patients forgo small drug cost savings in order to receive a particular generic product. At pill level, generic products are on average priced 0.1 Cent above the corresponding average generic price (Median: 0.2 Cent). At most, drug cost savings of 55 Cent (87 Cent) per pill were (not) realized. The large average number of generic entrants supplying drug markets indicates that patients were predominantly consuming drugs which have been off-patent for some time. On average drugs have lost patent protection since 45 months, which in turn explains why the observed generic price differentials are relatively small. Noteworthy further is that patients almost exclusively received their prescriptions for a particular drug from doctors of the same physician group. This strongly suggests that patients typically consulted the same physician and probably purchased generic products at the same pharmacy at different points in time.

2.6.2 Micro Analysis: Results

The analysis of patients' switching behavior among generic products provides a fundamental motivation for the decreasing effect of generic price differentials over time. Table 2.6 presents the pooled probit estimates obtained for the two specifications outlined in Section 2.6.1. Appendix [2.6] contains the univariate probit estimates with two-way clustered standard errors. The significance of effects is generally unaffected by the two-way clustering of

[62] Summary statistics are weighted by the number of follow-up drug dispensing events per treatment.

standard errors. As conjectured in *Hypothesis 2*, patients switch more likely to new generic drug products the larger the price differentials are relative to average generic prices. Patients and pharmacists turn out to be less sensitive to smaller per-pill price differentials.

Table 2.6: Univariate Probit – Coefficients

Dep.Variable: S^G_{jimt}	*Spec.1*	*Spec.2*
Price Differential	0.0255*	0.0254*
	(0.012)	(0.013)
Generic Entry	0.0134***	0.0143***
	(0.004)	(0.004)
Time Trend	0.0029	0.0030
	(0.003)	(0.003)
Patient Age	0.0003	0.0006
	(5.7e-04)	(5.0e-04)
Patient Sex (0/1)	0.0104	0.0089
	(0.011)	(0.010)
Months since first Diagnosis	-0.0415***	-0.0422***
	(0.006)	(0.006)
Months since last Dispense	0.0982***	0.0967***
	(0.009)	(0.008)
Prescriptions per Month	0.2466***	0.2284***
	(0.048)	(0.048)
Medications per Month	0.0107***	0.0075**
	(0.003)	(0.002)
Same Physician Group (0/1)	–	-0.4544***
		(0.061)
Insurance Provider (0/1)	*yes*	*yes*
Therapeutic Field (0/1)	*yes*	*yes*
Physician Group (0/1)	*no*	*yes*
Const.	-1.5596***	-1.1173***
Prob > chi2	<0.001	<0.001
Log-Likelihood	-102745.89	-102139.48
J x M x T	178075	

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is a follow-up dispensing event, where either the previously dispensed generic product (S^G_{jimt}=0) is dispensed to the patient, or a new generic product (S^G_{jimt}=1) supplied by a different generic firm. Generic products generally contain the same active ingredient and have an identical drug form and dosage size. The insurance group "Techniker Krankenkasse", the physician group "General Practitioners" and the therapeutic field "Cardiovascular System" form the reference group. Heteroscedasticity-robust standard errors, clustered at drug level (35 clusters), in parentheses.

The likelihood that a patient receives a new generic product increases with the entry of a generic firm. The larger the selection of generics products, the more likely is the patient to find another, equally desirable product to switch to. Interestingly, there appears to be no

time trend: patients are not more or less likely to switch to another generic product in drug markets which recently went off-patent or those that have been off-patent for some time.

The follow-up generic drug dispensing decisions can also not be explained by observable characteristics of individual patients. Neither the age nor the sex of the patient has a significant impact on the probability of a generic product switch. Hellerstein (1998) similarly finds that very little of prescription decisions can be explained by patients' age and sex.[63] Consistent with the empirical evidence that generic product switches occur predominantly in the early phase of the treatment (see Table 2.2), I find that patients switch less likely among generic products the more months have passed since the disease diagnosis. Like Coscelli (2000), I also find that patients are more likely to receive another generic product the more months have elapsed since the current and previous drug dispense. Apparently, patients develop a "habit" for one generic drug product the longer and more frequently they receive a particular drug. The more prescriptions patients receive for the drug in one month, the greater are in turn the chances that patients switch among generic products. Patients are more cost sensitive the higher the monthly expenditures (copayments) for one medication are. The effect of the total number of medications patients receive in a given month goes into the same direction. Patients are more likely to switch among generic products the more medications they receive, and the higher their potential monthly drug expenditures are.

The estimates obtained for the second specification are very similar. In the latter, I further account for the physician group of the currently prescribing doctor, and control for whether the patient received the current and previous drug prescription from doctors of the same physician group. Receiving the previous and current drug prescription from doctors of the same physician group, patients switch less likely among generic products. Patients possibly visit the same doctor and buy generic products at the same pharmacy which is likely located in the vicinity of the practice. As pharmacies tend to stock the same selection of generic drugs over time (Hollis, 2002), patients habitually receive the same generic product.

Table 2.7 below presents the average marginal effects obtained for the two probit regressions, which facilitate an assessment of the economic importance of the identified effects. A 1 Cent price differential at pill level increases the probability of a generic product switch by 0.8%. Evidently, the chances of a product switch increase in the size of the price differen-

[63] Coscelli (2000) provides only the (significant) probit coefficients for age and sex. Thus, it is impossible to evaluate the size of the two identified effects.

tial. Given a standard deviation of 3.5 Cent (see Table 2.5), price differentials tend to have a minor effect, however. With an average marginal effect of roughly 0.5% and a standard deviation of about seven generic entrants, the effect of generic entry is similarly small.

Table 2.7: Univariate Probit – Average Marginal Effects

Dep.Variable: S^G_{jimt}	*Spec.1*	*Spec.2*
Price Differential	0.0084*	0.0083*
	(0.004)	(0.004)
Generic Entry	0.0045***	0.0047***
	(0.001)	(0.001)
Time Trend	0.0010	0.0010
	(0.001)	(0.001)
Patient Age	0.0001	0.0002
	(1.9e-04)	(1.6e-04)
Patient Sex (0/1)	0.0034	0.0029
	(0.004)	(0.003)
Months since first Diagnosis	-0.0136***	-0.0137***
	(0.002)	(0.002)
Months since last Dispense	0.0321***	0.0314***
	(0.003)	(0.003)
Prescriptions per Month	0.0807***	0.0743***
	(0.016)	(0.016)
Medications per Month	0.0035***	0.0025**
	(0.001)	(0.001)
Same Physician Group (0/1)	–	-0.1626***
		(0.023)

* p<0.05, ** p<0.01, *** p<0.001

Notes: Average marginal effects reported for the univariate probit model denote average, ceteris paribus changes in the likelihood that a repeat-purchase patient with first diagnosis in 2007 switches to an identical generic product which is manufactured by a generic firm different from the generic manufacturer of the previously dispensed generic product.

Notably, the likelihood that a patient receives a different generic product declines by about 1.4% with each additional month that has elapsed since the first diagnosis. Observing at most 11 follow-up drug dispensing events for patients with first diagnosis in 2007, the standard deviation amounts to 2.6 months only. Not surprisingly, the effect appears to be moderate. Taking into account, however, that patients with first diagnosis prior to 2007 have consumed generic products on average for 32.8 months (Sd.: 17.0), the effect should have quite a large bearing in reality. With each month that has elapsed since the last drug dispense, the chances of a product switch increase by roughly 3.2%. Given a standard deviation of about 1.6 months, the effect does not explain much of the variation in the data.

The chances of generic product switch also increase with each additional prescription patients receive for the drug in one month, namely by about 8%. Given a standard deviation of 0.18 additional prescriptions, the effect is practically negligible. The same holds for the effect of the total number of medications patients receive in one month.[64] Whether the previously and currently prescribing doctor belong to the same physician group has a large impact on the likelihood of a product switch. In this case, chances are 16.3% lower that patients switch among generic products. In summary, results indicate that patients habitually consume the same generic product. Pharmacists and patients are largely insensitive to the price differentials across generic products, and they are only slightly more cost sensitive as the size of the price differential increases. This phenomenon may in turn explain why generic prices have a small and slightly decreasing effect on market shares over time. One implication of this finding is that patients will switch more infrequently among lower-cost generic products, where per-pill price differentials are small. Whereas the relative size of generic price differentials decreases in the amount of the per-pill price (see Appendix [2.7]), their absolute size increases (see Appendix [2.8]). Showing that the lack of price sensitivity and habit persistence at patient level translate into the persistence of generic market shares at drug market level, the micro and macro analysis augment and support each others findings.

2.7 Conclusion

Employing both macro and micro data, this study is the first to provide recent and comprehensive evidence of the small and decreasing impact of generic prices on market shares over time. In spite of the observable price variations across generic firms, market shares are largely persistent. Patients' and pharmacists' low sensitivity to generic price differentials proves to be one important explanatory factor of patients' seldom switching among generic products which evidently translates into the persistence of market shares at macro level.

As a result of generic substitution laws, multi-source drug choices are made in vast majority of cases by pharmacists and patients. Due to largely fixed copayments and dispensing fees, both have a low financial incentive to switch among generic products unless price differentials are very large. In many industrial nations, dispensing fees have only a small variable component, and patients' copayments for medical products are also often largely fixed.

[64] Both the average marginal effect (0.35%) and the variation in the data (Sd.: 2.18) are only small.

The two analyses are confined to generic products in 35 drug markets, where drugs went off-patent between 2002 and 2006. At macro level, I examine the monthly market shares and prices of 605 generic products from 2002 to 2007. Resorting to the System GMM estimator, I estimate a dynamic panel data model to measure the impact of generic prices on market shares, and the persistence of the latter. The System GMM estimates indicate that market shares are persistent over time. Generic prices turn out to affect market shares little: a 10 percentage point lower generic-to-brand price ratio leads to a market share increase of roughly 1 percentage point. The effect also declines by 0.0032 percentage points in each month of generic competition. After about 32 months the effect of a price change is essentially zero.

At micro level, I investigate in turn how price differentials affect patients' switching behavior among generic products within each of the 35 drug markets. Employing patient tracking data for the year 2007, the micro analysis is confined to 88432 repeat-purchase patients who obtained their first diagnosis in 2007. I resort to a pooled probit estimation to gauge the impact of generic price differentials on the probability of a product switch. The univariate probit estimates show that the chances of a generic product switch increase in the size of the price differential, which may in turn explain why prices affect generic market shares by less and less over time. Patients habitually receive the same generic product, however, unless price differentials are extremely large. A 1 Cent per-pill price discount increases the probability of a product switch by merely 0.8%. Per-pill prices vary on average by 6 Cent in the first month of generic entry, and by 2 Cent after three years of generic competition.

The small per-pill price variations imply substantial forgone drug cost savings at the aggregate level. A preliminary calculation shows that monthly savings of on average €2.2 Mio. (Median: €1.6 Mio.) could have been ideally realized in the German statutory health care system if the 605 generic products had been sold at the minimum monthly price observed in each drug market. This corresponds to a monthly expenditure reduction of on average 7.2% (Median: 4.8%). The forgone savings from 2002 to 2007 amount to €11 Bn., coming up to a total expenditure reduction of 8.8%. Assuming that there are no capacity constraints, this estimate provides an upper bound for the potentially forgone drug cost savings.

The low sensitivity to the small generic price differentials likely motivated the implementation of rebate contracts in Germany in April 2007. Rebate contracts stimulated generic competition, essentially forcing patients to switch to a possibly cheaper generic product

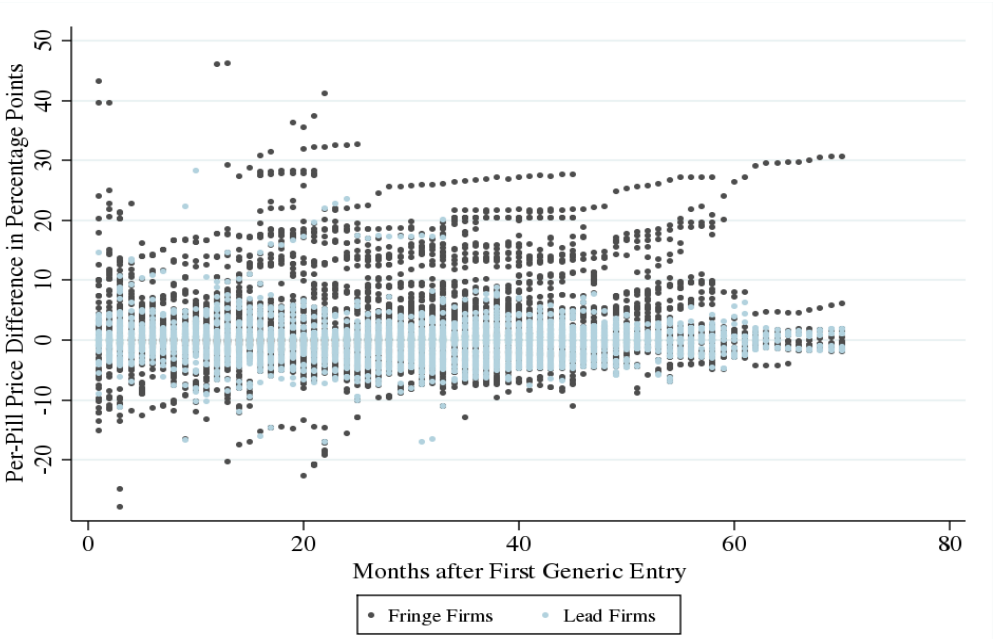
which their statutory health care insurance provider contracted for. As the largest statutory health care insurer in Germany, covering almost one third of the population, the *Allgemeine Ortskrankenkasse* (*AOK*) recently announced that it will save €520 Mio. in generic drug expenditures alone in 2010 due to the closure of rebate contracts.[65] This figure is in line with the estimated forgone average, annual savings of €1.6 Bn. between 2002 and 2007.

A less intrusive and more global stimulation of price competition across on-patent and off-patent drug markets could be achieved by aligning insurance providers' and patients' financial interests more closely. The adoption of flexible co-insurance rather than co-payment agreements, where the co-share decreases from lower to higher price brackets might be one viable solution. In co-insurance agreements, patients assume a specific percentage of drug costs and not a co-payment fee, which is practically fixed over a certain price range. Participating more equally in the financial consequences of their drug choices, patients have a greater financial incentive to save on drug costs. An examination of how the use of rebate contracts has influenced both the persistence of generic market shares and the variation in generic prices seems to be worthwhile. Notably, which factors ultimately drive the observed price variations requires still an investigation. Also, similar studies on generic competition in other important pharmaceutical markets (e.g. the U.S. pharmaceutical market) are warranted to corroborate and supplement the current study's findings. This would allow in particular for an assessment of how different reimbursement schemes (copay vs. co-insurance) affect multi-source drug choices. All these questions open up new avenues of research.

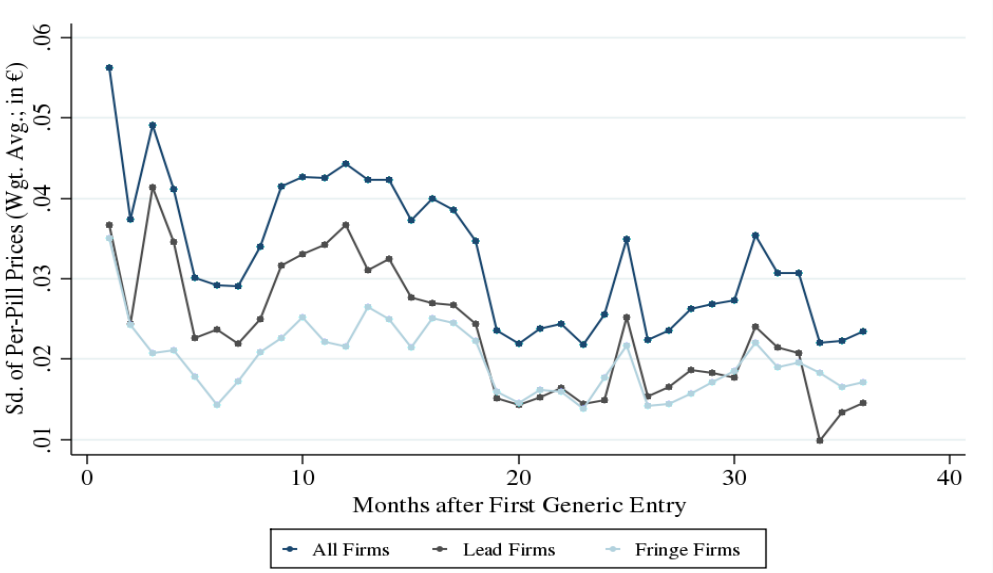
[65] www.aok-bv.de/politik/wettbewerb/index_02091.html (accessed: Oct. 15th 2010).

2.8 Appendix 2

2.8.1 Percentage Point Price Deviations from Avg(P^{Ratio}_{gitm})



2.8.2 Standard Deviation of Generic Prices over Time in €



Note: Standard deviations of generic prices denote turnover-weighted averages of generic price deviations from the turnover-weighted average generic price. The standard deviation of generic prices attributable to fringe firms is smaller, as lead firms achieve notably larger market shares.

2.8.3 Defintion of Variables

2.8.3.1 Generic Product Panel

Variable Name	Definition
Generic Market Share ($M_{g_{itm}}$)	Monthly turnover share within the generic bestseller segment: fraction of pills sold by the generic manufacturer (in %).
Generic-to-Brand Price Ratio ($P^{Ratio}_{g_{itm}}$)	Generic firms' monthly (turnover/package size-weighted) average per-pill price for the bestselling dosage size relative to the brand price charged in the month prior to first generic entry (in %).
Generic Entry	Accumulated number of generic entrants in a drug market and month.
Branded Substitutes	Number of available, on-patent drugs listed for the same therapeutic field(s) of indication (ATC2 Class.) as the drug in question.
Generic Substitutes	Number of available, off-patent generic drugs listed for the same therapeutic field(s) of indication (ATC2 Class.) as the drug in question.
Drug Portfolio Size	Number of generic products (drugs) launched by the generic firm.
Umbrella Brand Size	Number of generic products (drugs) launched by the generic firm whose tradename incorporates the (un)abbreviated corporate name.
Package Size	Monthly, turnover-weighted average package size of a generic product.
Time Trend	Count of months since first generic entry in a given drug market.
Year (2002,$\cdots$,2007)	0-1 dummy variable,=1 for all observations in 2002, $\cdots$, 2007.

2.8.3.2 Patient Tracking Data

Variable Name	Definition
Generic Product Switch	The follow-up dispense of a generic product which is manufactured by a generic firm different from the generic manufacturer of the previously dispensed generic product, but which contains the same active ingredient and has an identical drug form (NFC1 Class.) and dosage size.
Price Differential	Difference between the monthly average generic price and the price of the currently dispensed generic product (in Cent/Pill): Avg($P_{g_{itm}}$)-$P_{g_{itm}}$. Average generic prices at drug level denote a turnover-weighted mean.
Generic Entry	Accumulated number of generic entrants in a drug market and month.
Time Trend	Count of months since first generic entry in a given drug market.
Patient Age	Age of the Patient in Years.
Patient Sex	0-1 dummy variable,=1 for female patients.
Months since first Diagnosis	Number of months between first diagnosis and current drug dispense.
Months since last Dispense	Number of months between last dispense and current drug dispense.
Prescriptions per Month	Number of prescriptions for one specific drug in a given month.
Medications per Month	Number of medications (drugs) received by a patient in a given month.
Same Physician Group	0-1 dummy variable,=1 if the prescribing doctor of the current and previous drug prescriptions is associated with the same physician group.
Insurance Provider	0-1 dummy variable,=1 if the patient is insured by the particular insurance group (10 insurance group dummies).
Therapeutic Field	0-1 dummy variable,=1 if the generic product is effective for the particular therapeutic indication (6 ATC1 group dummies).
Physician Group	0-1 dummy variable,=1 if the prescribing doctor is associated with the particular physician group (7 physician group dummies).

2.8.4 Decomposition Standard Deviation: Generic Product Panel

Variable Name	Mean	Sd.	GxT	G	T (⌀)
Generic Market Share ($M_{g_{itm}}^{Ratio}$)	6.66	12.04	20888		
		10.15		605	
		4.97			34.53
Generic-to-Brand Price Ratio ($P_{g_{itm}}^{Ratio}$)	41.94	18.32	20888		
		14.87		605	
		10.75			34.53
Generic Entry	19.96	7.97	20888		
		7.23		605	
		2.91			34.53
Branded Substitutes	5.68	5.14	20888		
		5.00		605	
		0.73			34.53
Generic Substitutes	15.86	13.30	20888		
		14.34		605	
		0.88			34.53
Drug Portfolio Size	127.95	78.22	20888		
		78.51		605	
		10.90			34.53
Umbrella Brand Size	97.14	79.91	20888		
		79.65		605	
		11.69			34.53
Package Size	78.26	34.63	20888		
		37.30		605	
		7.87			34.53
Time Trend	26.75	15.35	20888		
		10.84		605	
		12.26			34.53

Notes: The within and between standard deviations may not sum up for two reasons. (1) The overall mean (mean of the panel means weighted by number of observations) is different from the mean of the panel means due to unbalanced nature of the data. (2) The reported standard deviation estimates are biased-corrected estimates which are multiplied by a factor of $\sqrt{G*T/(G*T-1)}$, and $\sqrt{G/(G-1)}$ respectively.

2.8.5 Ordinary Least Squares and Fixed Effects – Coefficients

Dep.Variable: $M_{g_{itm}}$	Estimates obtained for Spec.1: *FE*	*OLS*
Lag Generic Market Share ($M_{g_{itm}}.l1$)	0.6484***	0.9105***
	(0.045)	(0.013)
Generic-to-Brand Price Ratio ($P^{Ratio}_{g_{itm}}$)	-0.0357***	-0.0058*
	(0.009)	(0.003)
Generic Entry	-0.7828***	-0.2012***
	(0.185)	(0.046)
Generic Entry^2	0.0122***	0.0037***
	(0.003)	(0.001)
Branded Substitutes	-0.1751	-0.0107
	(0.105)	(0.006)
Generic Substitutes	0.197	0.0025
	(0.113)	(0.004)
Drug Portfolio Size	-0.0622	0.0034
	(0.064)	(0.002)
Umbrella Brand Size	0.0479	0.0004
	(0.040)	(0.002)
Package Size	0.0226**	0.0013
	(0.008)	(0.001)
Time Trend	0.0106	0.0010
	(0.015)	(0.003)
Year (2002,$\cdots$,2007)	*yes*	*yes*
Const.	10.8701***	2.4480**
R^2 within	0.6431	–
R^2 between	0.7429	–
R^2 overall	0.7619	0.9339
F(15,67)	98.66	5362.23
Prob > F	<0.001	<0.001
G x (T-1)	20283	

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is the monthly turnover share of a generic product within the bestseller segment. Standard errors robust to heteroscedasticity and autocorrelation, clustered at firm level (68 clusters), in parentheses. The reference year is 2002.

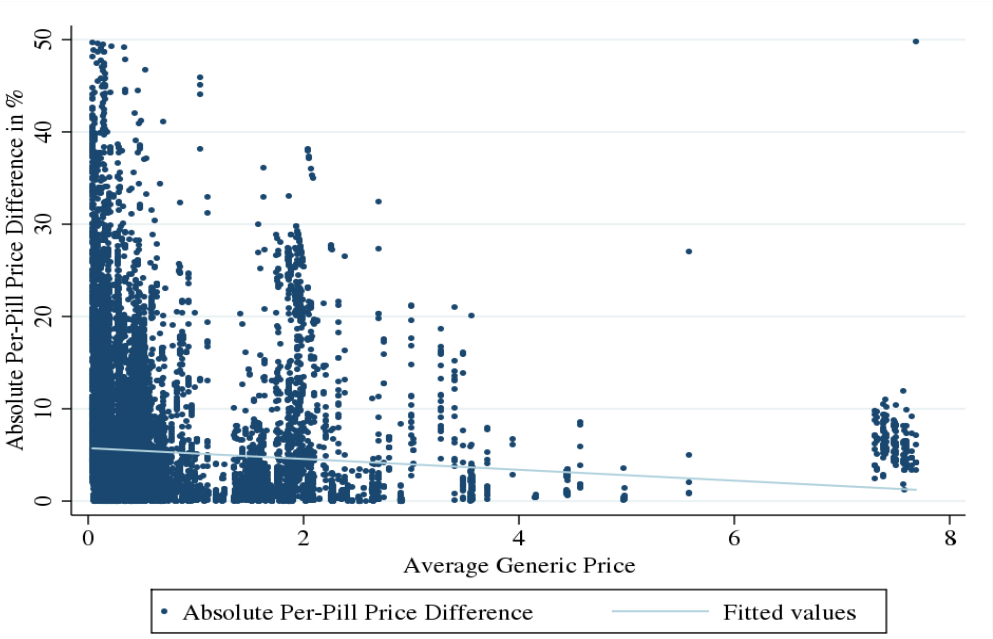
2.8.6 Univariate Probit (Two-way Clustering) – Coefficients

Dep.Variable: S^G_{jimt}	*Spec.1*	*Spec.2*
Price Differential	0.0255*	0.0254*
	(0.011)	(0.011)
Generic Entry	0.0134***	0.0143***
	(0.003)	(0.003)
Time Trend	0.0029	0.0030
	(0.003)	(0.003)
Patient Age	0.0003	0.0006
	(4.8e-04)	(4.1e-04)
Patient Sex (0/1)	0.0104	0.0089
	(0.010)	(0.009)
Months since first Diagnosis	-0.0415***	-0.0422***
	(0.004)	(0.004)
Months since last Dispense	0.0982***	0.0967***
	(0.007)	(0.007)
Prescriptions per Month	0.2466***	0.2284***
	(0.043)	(0.042)
Medications per Month	0.0107***	0.0075**
	(0.003)	(0.003)
Same Physician Group (0/1)	–	-0.4544***
		(0.055)
Insurance Provider (0/1)	*yes*	*yes*
Therapeutic Field (0/1)	*yes*	*yes*
Physician Group (0/1)	*no*	*yes*
Const.	-1.5596***	-1.1173***
J x M x T	178075	

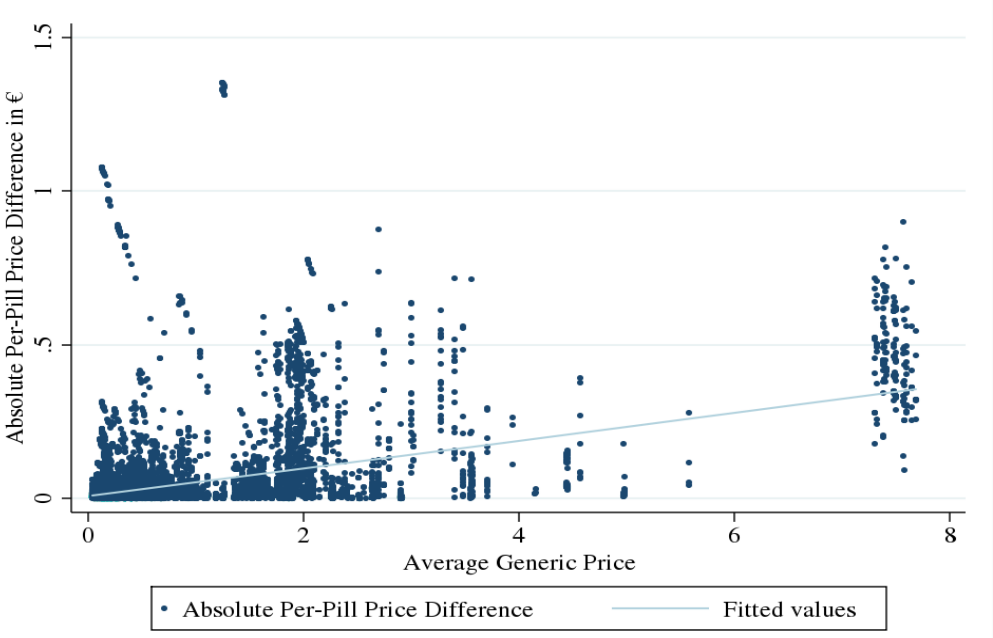
* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is a follow-up dispensing event, where either the previously dispensed generic product (S^G_{jimt}=0) is dispensed to the patient, or a new generic product (S^G_{jimt}=1) supplied by a different generic firm. Generic products generally contain the same active ingredient and have an identical drug form and dosage size. The insurance group "Techniker Krankenkasse", the physician group "General Practitioners" and the therapeutic field "Cardiovascular System" form the reference group. Heteroscedasticity-robust standard errors, clustered at drug (35 clusters) and patient level (88432 clusters), in parentheses.

2.8.7 Generic Price Deviations across Price Levels in %



2.8.8 Generic Price Deviations across Price Levels in €



Chapter 3

Generic Price Dispersion post Patent Expiry: Revisiting the Assumption of Bertrand Competition

3.1 Introduction

Generic drugs are therapeutically equivalent (bio-equivalent) to off-patent brand-name drugs. Due to bio-equivalence and negligible marketing-to-sales ratios (Hellerstein, 1998; Scherer, 2000; Berndt *et al.*, 2003), generics firms are often regarded as Bertrand competitors (Morton, 2002; Hollis, 2005), offering an undifferentiated product at identical cost (Reiffen and Ward, 2005) and competing solely on price. The Bertrand model of competition with undifferentiated goods predicts zero price variation as soon as two or more generic entrants compete in one drug market, which is not consistent with empirical evidence. Looking at identical active ingredients, drug forms and dosage sizes, price variations on a scale of 10 percentage points are common in the German generic drug market. Industry insiders confirm that there are strikingly large price variations and profit margins in the generic drug market.[1] They point out that generic firms do not necessarily have identical cost structures or enjoy the same reputation among consumers. Supplying a large drug portfolio, firms presumably have cost advantages in the production, storage and promotion of generic drugs

[1]The anti-blood clotting drug *Clopidogrel* was sold by Hexal and Ratiopharm for €180.82 in September 2009. In September 2010, Stada charged €50.50 for the same product. As of October 2010, TAD Pharma provides the medical product to patients covered by the German statutory health care insurance provider *AOK* for roughly €18, which corresponds to a 60% price discount relative to the cheapest generic competitor. www.spiegel.de/spiegel/print/d-73892381.html (accessed: Oct. 30th 2010).

(economies of scope), and they are also more competitive in price (Natz, 2008). Building up umbrella brands through corporate branding, companies further establish brand recognition (Accenture, 2005)[2], which apparently allows them to extract higher markups[3]. Therefore, it seems necessary to revisit the Bertrand assumption[4] to ensure an accurate modeling of generic competition, and to eventually provide useful and sustainable policy recommendations.

The previous empirical literature on competition in off-patent pharmaceutical markets focuses on aggregate (average) generic price patterns (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Frank and Salkever, 1997; Bhattacharya and Vogt, 2003; Reiffen and Ward, 2005; Saha *et al.*, 2006; Regan, 2008). Only a few studies investigate the price variation in individual drug products (Grabowski and Vernon, 1992; Wiggins and Maness, 2004; Kanavos *et al.*, 2008), identifying both a large markup of brand-name over generic products (Wiggins and Maness, 2004) and a large variability in generic prices (Grabowski and Vernon, 1992). Economists attribute the variation in generic prices to perceptions of quality differences among firms (brand loyalty) and differences in product variety. Exploratively investigating generic prices (Grabowski and Vernon, 1992) and accounting for generic firms' aggregate product differentiation efforts (Kanavos *et al.*, 2008)[5], previous studies provide no direct evidence of economies of scope or brand recognition in the generic drug industry.

To my knowledge, this is the first study to examine the variability in generic prices, accounting for economies of scope and brand recognition. Generic firms' drug portfolio size provides a measure of their cost advantage. The size of the umbrella brand facilitates in turn a measure of firm reputation.[6] Based on industry evidence, I hypothesize that generic companies have a greater cost advantage the more drugs they supply, which in turn allows them to charge lower prices. Furthermore, I assume that generic firms enjoy a higher level of brand recognition and loyalty the more umbrella branded drugs they supply, which

[2]www.progenerika.de/downloads/1312/PM040929leitlinien.pdf; www.publicis-vital-pr.de/uploads/media/05_Vortrag_Roehrer_PharmaTrends2009.pdf (accessed: Oct. 30th 2010).

[3]www.handelsblatt.com/unternehmen/industrie/generika-sektor-vor-weiteren-konsolidierungen;1267628 (accessed: Oct. 30th 2010).

[4]The assumption of Bertrand competition would also fail if there were capacity constraints. The previous literature has not widely discussed this issue so far. As marginal production costs are very low in the pharmaceutical industry, economists tend to abstract from capacity constraints (Brekke and Straume, 2008).

[5]Kanavos *et al.* (2008) explore how strongly generic prices are affected by the total number of drug formulations (e.g. pills, injectables) and package sizes introduced by generic firms in a given drug market.

[6]The size of the overall drug portfolio and umbrella branded drug portfolio (umbrella brand) do not coincide. The latter tends to be notably smaller as generic firms do not always pursue a corporate branding strategy, in particular in the Over-the-Counter (OTC) market segment.

possibly pushes generic prices upward. Theoretical papers by Cabral (2009) and Miklòs-Thal (2010) show most recently that umbrella branding can have a positive impact on both firms' investment in product quality and the price consumers are willing to pay. The generic industry offers a unique setting to study the impact of umbrella branding on prices. Due to their bio-equivalence, generic drug products are at least in theory homogenous goods.

Using unique panel data on 605 generic products launched in 35 off-patent drug markets from 2002 to 2007, I examine the impact of generic firms' drug portfolio and umbrella brand size on monthly ex-factory prices. The analysis is confined to identical oral solid dosage sizes to assure a constant unit of observation. Generic prices are normalized by pre-entry brand prices to obtain a comparable measure of price variations across drug markets. Drug portfolio and umbrella brand sizes are likely correlated with firms' advertising expenditures on which I lack data. I assume that advertising expenditures are potentially non-zero but time-constant as generic advertising is directed to firms' drug portfolio rather than individual products (Berndt *et al.*, 2003)[7]. Moreover, I assume that drug portfolio and umbrella brand sizes are strictly exogenous, as firms decide on both market entry and the branding strategy for a product years ahead of entry. They also have not exited the 35 drug markets by 2007.

Employing the Fixed Effects (FE) and First-Difference (FD) estimator I tackle the issue of omitted variable bias and replicate essential results of previous empirical studies. If FE and FD estimates differ notably, the strict exogeneity assumption may in fact not hold. Among other important price determinants, I control for package size differences and generic firms' market share. Whereas FE and FD estimates for firms' drug portfolio and umbrella brand size are very similar, market share coefficients differ strongly, indicating that simultaneity bias is present. In order to tackle and assess the severity of the bias, I reestimate the specification using the Difference GMM (DIFF GMM) estimator. Like the FE and FD estimates, GMM estimates show that generic-to-brand price ratios are about 0.3 percentage points lower (0.2 percentage points higher) with each (umbrella branded) drug generic firms' additionally supply. Given a standard deviation of 80 (umbrella branded) drugs, I predict a net variation (reduction) in generic-to-brand price ratios of 8 percentage points. Observing price deviations on a scale of 10 percentage points and higher, these estimates are plausible. The GMM estimates indicate further that generic price variations can also be attributed to

[7]As generic advertising is rare, Berndt *et al.* (2003) assume marketing-to-sales ratios to be close to zero.

market share differences: a generic firm with a 10 percentage point higher market share, has a roughly 5-6 percentage point lower generic-to-brand price ratio. In line with previous studies, I show that the entry of a generic firm lowers generic-to-brand price ratios by roughly 2 percentage points. Package size differences cannot explain the variation in prices across firms. Providing evidence of economies and brand recognition in the generic drug industry, the study contests the assumption of Bertrand competition frequently made in the literature.

The organization of the paper is as follows: Section 3.2 provides background information on the German generic industry and the regulation of prescription drug prices. Section 3.3 reviews the literature on competition in off-patent pharmaceutical markets. Section 3.4 describes the data. Section 3.5 specifies the empirical implementation, and Section 3.6 presents and discusses the empirical findings. Concluding remarks follow in Section 3.7.

3.2 Industry Background

With a market size of €4.5 Bn. and a generic penetration (efficiency[8]) rate of about 20% (68%) as of 2007, the German generic drug market is the second largest, and one of the most important generic drug markets in the world. As the biggest generic drug market in Europe, it experienced the largest number of generic entries between 2000 and 2007 (EUC, 2009). The following paragraph outlines the dynamics of generic competition and reviews the underlying (indirect) price regulation of off-patent, prescription (Rx) drugs in Germany.

Instead of safety and efficacy tests (clinical trial tests), generic firms conduct bioequivalence studies in a period of at most 4 months to show that the rate and extent of absorption of the active ingredient is identical to that of the reference drug. Being therapeutically equivalent (bio-equivalent) to the off-patent brand drug, generic drugs contain the same active ingredient, have identical quality and performance characteristics, the same dosage size and the same or a similar route of administration. In drug stability studies, firms prove further that the drug product remains within the established specifications and maintains its identity, strength, quality and purity throughout the expiration dating period of typically two or three years. It takes another six to nine months to obtain market authorization. However,

[8]The generic efficiency rate indicates the fraction of multi-source drug prescriptions dispensed as generic. Own calculations based on *Insight Health* prescription data.

it is generally impossible to predict exactly when market approval will be granted.[9] Generic firms prepare for market entry at least three years ahead of entry in order to obtain market approval on time.[10] As soon as the patent or supplementary protection certificate (SPC)[11] for the brand (original) drug expires, generic manufacturers will typically enter the market.

As in many industrial nations[12], generic drugs are most frequently marketed as INN-generics in Germany: the international-non-proprietary name (INN) of the active ingredient (generic name) and a company suffix identify the generic product.[13] As a result of the INN-name convention, many generic products are umbrella branded, carrying the corporate name or an abbreviated version thereof. Designating generic products with a unique logo such as "lich" (Winthrop) or "gamma" (Wörwag Pharma) is another, yet less frequently pursued strategy to build umbrella brands. Lastly, generic products may also be launched under a distinct tradename such as "Simvacor" (Lindopharm) which is unrelated to the corporate name or logo. According to industry experts generic firms adopt the last strategy mainly in the non-prescription (over-the-counter, OTC) segment to establish a premium brand.[14]

Importantly, an invented tradename for a medical product may be too similar to an existing tradename according to trademark law or from the standpoint of the (supra)national market authorization agency for medical products[15] which seeks to ensure that names will not be confused. An expert on trademark law explained to me that pharmaceutical companies spend several hundred thousand Euro in addition to trademark search fees in order to find a suitable tradename which they will register a trademark for. At the German patent and trademark office (*Deutsche Patent- und Markenamt*) the registration of national trademarks will usually take seven to eight months if the office has no further inquiries.[16] At the

[9]The German or European market authorization agency may, for instance, identify major objections in the generic application, delaying the market approval process by a few months until issues are resolved. Market approval is often granted at a later date than expected; see EUC (2008), p. 271; Accenture (2005).

[10]Interviews with industry experts provided further, detailed information on the stages and time frame involved in the generic drug approval process.

[11]If an originator applies within six month after the brand drug's market approval for a SPC and the national patent office approves the request, the exclusivity period will be extended by up to five years.

[12]Myrtha Hurtado Rivas (Global Head of Trademarks & Domain Names, Sandoz): *Trade Marks in a Generic World*, Pharmaceutical Trade Marks Group 81^{st} Group Conference, Athens, Oct 1st 2010.

[13]www.stada.de/english/investorrelations/glossary/definitionpharmamarkt.asp (accessed: Jul 30th 2010).

[14]Myrtha Hurtado Rivas (Global Head of Trademarks & Domain Names, Sandoz): *Trade Marks in a Generic World*, Pharmaceutical Trade Marks Group 81^{st} Group Conference, Athens, Oct 1st 2010.

[15]Whereas, the *Bundesinstitut für Arzneimittel und Medizinprodukte* issues national market authorizations, the *European Medicine Evaluation Agency* grants market approval for the European Community.

[16]See also www.dpma.de/marke/faq/index.html#a6 (accessed: Oct. 20th 2010).

Office for Harmonization in the Internal Market (*OHIM*), it will currently take at least six months[17] from the date of filing to have a community trademark registered if no opposition of the trade mark application arises.[18] Due to the time-intensive naming process, generic firms must determine the branding strategy for a new generic product essentially at the same time they decide on market entry to avoid delays in the market authorization process.

In 2005, the consulting company Accenture surveyed 40 industry representatives to identify key trends in the German generic drug market. In the view of increasing cost and competitive pressure, generic firms' corporate brand and size of drug portfolio are said to play a decisive role in intra-generic competition. Evidently, firms focus on building (corporate) umbrella brands rather than individual product brands to establish brand recognition (Accenture, 2005)[19], which enables them to extract higher markups[20]. Industry insiders also confirmed to me in interviews that broadly positioned firms have cost advantages. Generic firms save on costs, buying input goods such as drug additives, drug carrier particles or packaging materials in bulk. Moreover, they can use the full capacity of the drug production line and storage facility, and they can jointly promote or cross-promote generic drug products.[21]

Generic firms tend to offer large price discounts relative to the brand drug whose price typically does not decline much post patent expiry. The German government does not directly regulate the producer (ex-factory) prices of pharmaceutical companies. Appendix [3.1] provides an overview of the average generic price and generic entry pattern in 35 drug markets, where drugs went off-patent in Germany from 2002 to 2006. Alone in the first month of generic entry, (turnover-weighted) average generic prices are 25% lower than pre-entry brand prices. On average five firms compete in one drug market. Continuously declining as firms enter, generics prices are on average 60% lower than pre-entry brand prices after three years of competition.[22] Drug markets have on average attracted 19 generic firms by then.

[17] See also oami.europa.eu/ows/rw/pages/CTM/regProcess/regProcess.de.do (accessed: Oct. 20th 2010).

[18] Between 1996 and 2004, it took on average 1.76 years (Min.: 11 months) to register a community trademark at the *OHIM*, looking at unopposed trademark applications (von Graevenitz, 2007).

[19] www.progenerika.de/downloads/1312/PM040929leitlinien.pdf; www.publicis-vital-pr.de/uploads/media/05_Vortrag_Roehrer_PharmaTrends2009.pdf (accessed: Oct. 30th 2010).

[20] www.handelsblatt.com/unternehmen/industrie/generika-sektor-vor-weiteren-konsolidierungen;1267628 (accessed: Oct. 30th 2010).

[21] The British Office of Fair Trading published a market study on "The Pharmaceutical Price Regulation Scheme" in Great Britain in 2007, revealing that pharmaceutical firms with a broad product portfolio are better apt to spread the effect of an imposed price cut over their portfolio; http://cvu.rediris.es/pub/bscw.cgi/d869624/PharmaPriceUK.pdf (accessed: Aug 2nd 2010).

[22] Saha *et al.* (2006) report similar figures for the U.S. pharmaceutical market.

Introducing the *Aut-idem* regulation for prescription drugs, the enforcement of the *Act for the Limitation of Drug Expenditures* (*Arzneimittelausgaben-Begrenzungsgesetz, AABG*) in February 2002 has achieved a substantial increase in generic substitution: unless the physician checks the *Aut-idem* box on the prescription pad and excludes substitution, pharmacists are prompted to sell one of the 30% lowest priced generic drug products to the patient. Pharmaceutical companies update prices at the *Institute for Pharmaceutical Products* (*Institut für Arzneimittelspezialitäten*) in Frankfurt on the 1st and 15th of each month.

In order to reduce pharmacists' incentives to sell high-priced products, the *Statutory Health Insurance Modernization Act* (*Gesetz zur Modernisierung der Gesetzlichen Krankenversicherung, GMG*) implemented a new dispensing fee structure. As of January 2004 dispensing fees on prescription drugs[23] have consisted mainly of a fixed component: pharmacies charge a fixed fee of €8.10[24] for each dispensed product independent of its package size, plus a markup of 3% of product's purchase price (producer price incl. wholesale markup).

When purchasing a medical product, patients covered by statutory health insurance (GKV) – 86% of the German population as of 2007[25] – get generally prescription drug coverage up to a predetermined reference price.[26] They pay only for any extra costs above the reference price. As of January 2004 patients have further been prompted to make a copayment for each medical product they purchase. The copayment amounts to 10% of the pharmacy selling price, the minimum contribution is €5 and €10 is the maximum.[27]

With the enactment of the *Law for the Economic Provision of Pharmaceutical Products* (Arzneimittelversorgungs-Wirtschaftlichkeitsgesetz, AVWG) in May 2006, patients have been exempted from making a copayment once the medical product is priced at least 30% below the prevailing reference price.[28] In order to increase the transparency of price competition,

[23]Around 78% of pharmaceutical sales are made on prescription drugs (BPI Pharma-Daten 2008).

[24]Since the *Statutory Health Insurance Competition Strengthening Act* enforced in April 2007, pharmacists must grant patients covered by statutory health insurance a discount of €2.30 on the product's pharmacy selling price, independent of its package size, reducing the fixed component of the dispensing fee's to €5.80.

[25]Own calculations based on data obtained from the federal health monitoring information system (www.gbe-bund.de) and from the German association of private health insurance website (www.pkv.de).

[26]Reference prices were introduced in Germany with the enforcement of the *health care Reform Act* (*Gesundheitsreformgesetz, GRG*) in 1989. The central association of health care providers determines the reference prices for specific groups of medical products. Reference prices for groups of medical products containing the same active ingredient must be in the price range of the 30% lowest priced products. Reference prices get updated quarterly (www.aok-bv.de/lexikon/f/index_00338.html; accessed: Aug 2nd 2010).

[27]GKV-Patients pay for medical products priced below €5 themselves.

[28]Pharmacies usually obtain an electronic update of official prices on the same day as pharmaceutical companies update their prices. Thus, pharmacists can immediately determine which medical products will not require a copayment. www.gkv.info/gkv/index.php?id=661 (accessed: Oct. 15th 2010).

pharmaceutical companies have further been prohibited from giving discounts in kind to public and hospital pharmacies, and financial rebates have been restricted to OTC drugs.

As the last major health care reform enacted in April 2007, the *Statutory Health Insurance Competition Strengthening Act* has authorized statutory health care insurers to close exclusive supply contracts with the generic firm offering the lowest price for a medical product. Unless patients insist on a different product and pay for the additional expenses, pharmacists are required to dispense that specific generic product. Except for rebate contracts, previous health care reforms seem to have provided few incentives to both pharmacists and patients to switch among generic products as long as generic price differentials are not very large. Put differently, generic firms have likely been able to vary prices somewhat over the time period 2002 to 2007, without necessarily experiencing an immediate loss in market share.

3.3 Literature Review

Generic firms are often referred to as Bertrand competitors (Morton, 2002; Hollis, 2005), offering a undifferentiated product at identical cost and competing solely on price. Hollis (2005), for instance, states that "the price of generic drugs within a group is almost always identical, since it is difficult for generics to differentiate themselves from each other", concluding that "competition among generics is $(\cdots)$ accurately described as repeated Bertrand competition, where firms are forced to meet the lowest price in the market or suffer a large discrete decrease in market share". Scale economies are deemed to be unimportant in drug manufacturing. Caves *et al.* (1991) explain that "the fermentation technologies extensively used to produce the active chemical entities are batch processes carried out on small scales. Both quality control considerations and the small absolute quantities of active ingredients produced discourage large-scale continuous-process technologies". Production cost are assumed to be identical across generic firms (Reiffen and Ward, 2005). The previous empirical literature focuses on aggregate (average) generic price patterns in the U.S. pharmaceutical market (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Frank and Salkever, 1997; Bhattacharya and Vogt, 2003; Reiffen and Ward, 2005; Saha *et al.*, 2006; Regan, 2008). Only a few studies investigate the price variation in individual (generic) drug products (Grabowski and Vernon, 1992; Wiggins and Maness, 2004; Kanavos *et al.*, 2008), providing, however, no direct evidence of economies of scope or brand recognition in the generic drug industry.

Grabowski and Vernon (1992) are the first to explore the variation in prices across generic products in the retail drugstore segment from 1984 to 1987. Grabowski and Vernon (1992) define prices as the average cost per unit paid by drugstores and hospitals for the most frequently consumed dosage size of each drug.[29] In half of the 18 generic products in their sample, the maximum price is over 50% greater than the minimum price as observed one year after generic entry. Interestingly, firms obtained a significant market share even though they charged a notably higher price. Grabowski and Vernon (1992) suspect that first-mover advantages and perceptions of quality differences among generic firms come into play.

The more recent studies by Wiggins and Maness (2004) and Kanavos *et al.* (2008) also examine the price variation across individual drug products. Wiggins and Maness (2004) measure the impact of brand-name recognition on the prices of anti-infectives in the 1984-90 period. They measure the price of a product as price per prescription, arguing that doctors normally write an anti-infective prescription for a quantity of medication designed to cure a disease. However, they concede that for other pharmaceuticals, a pill or a daily dose might be more relevant. Arguing that brand recognition is likely to be an important price determinant, Wiggins and Maness (2004) include a brand dummy for products sold by innovative firms in the price equation. Estimating Weighted Least Squares regressions, they identify a brand-name mark up of roughly 50% over generic products, which they attribute to the differentiated nature of brand products. They explain that brand products appeal to quality conscious customers, whereas generic firms compete exclusively on price.

In contrast to Wiggins and Maness (2004), Kanavos *et al.* (2008) assert that product differentiation plays also an important role in the generic drug market. They explain that differentiation can take a variety of forms. It can be related to the brand and the loyalty it may command among prescribers, pharmacists and patients, but also to the different dosage sizes and package sizes which generic firms supply.[30] Based on quarterly, retail pharmaceutical market data for twelve molecules and seven countries (the UK, Germany, France, Italy, Spain, the US, and Canada) over the 2000-2005 period, they examine the variation in generic firms' (average) price for one mg of active ingredient. Estimating Fixed Effects

[29] Caves *et al.* (1991); Regan (2008) similarly determine prices for the most "popular" strength (dosage size) to ensure a constant unit of observation when comparing medical products' prices.

[30] Kanavos *et al.* (2008) note that there is little other product differentiation occurring at this point, since all generic products containing the same molecule are bio-equivalent to the originator molecule, and, thus, they have, in principle, similar side effect profiles.

regressions, they find a very small and positive effect of product differentiation on generic prices. Product differentiation is measured by the total number of drug formulations (e.g. pill, capsule, injectable or suppository) and package sizes which generic firms introduced in a given country. Kanavos *et al.* (2008) treat the number of formulations and package sizes launched as exogenous. Even though they emphasize that product variety and brand loyalty are likely to be important price determinants, they only account for generic firms' aggregate product differentiation efforts and abstract from economies of scope and firm reputation.

Providing an overview of current developments in the German health care market, Natz (2008) observes that generic manufacturers with broad product portfolios dealt more successfully with the increasing price pressure after the implementation of rebate contracts in April 2007. Companies with a narrow product spectrum were less able to compete on price, and often experienced a large decrease in market share. The phenomenon suggests that there are scope economies in the production and distribution of generic drugs. Economies of scope are cost saving externalities between product lines, which may, however, not only "relate to production in the narrow sense but to all the services that accompany production $(\cdots)$" (Teece, 1980; Tirole, 1988).[31] Referring to Tauber (1988), Cabral (2009) states that "umbrella branding is a form of economies of scope, as it economizes on the costs of creating a new brand". He adds, however, that umbrella branding also has an important informational role in situations where consumers repeatedly purchase experience goods and are uncertain about products' characteristics. As consumers can only observe quality ex-post, firms have a short-run incentive to reduce quality and save on costs. Cabral (2009) shows that umbrella branding may assure that firms invest in the quality of products for which consumers in turn pay a higher price. Umbrella branding signals a positive correlation between the qualities of the products to consumers. All products under the umbrella contribute to the brand's reputation. If a firm offers one lower-quality product, costumers will update their beliefs about the other products, and won't pay a high price for its products anymore. Wernerfelt (1988), Choi (1998), Hakenes and Peitz (2008), Hakenes and Peitz (2009) and Miklòs-Thal (2010) provide similar results. Empirical studies show for oral hygiene products (Tülin, 1998) and for cars (Sullivan, 1990) that consumers quality perceptions of one product are correlated with their assessment of other products marketed by the firm under the umbrella brand.

[31] Economies of scale (product-specific economies) exist when the production cost of a single product decreases with the number of units produced (Tirole, 1988).

3.4 Data

This study relies on national pharmaceutical market and exclusivity data, providing a record of generic products' prices and market shares in off-patent drug markets from 2002 to 2007. *Insight Health* provides pharmaceutical market, patent and SPC data.[32]

To ensure a high-quality match of pharmaceutical market and exclusivity data, the analysis is confined to human medications containing one active ingredient. The retail pharmacy data reflect wholesale and direct purchase transactions of public pharmacies. Similar data for the German hospital segment are not available. As a result of quantity discounts, prices charged to hospitals are usually much lower than prices charged to public pharmacies. Yet, the turnover generated with prescription drugs is considerably smaller in the hospital segment. In 2007, for instance, the retail turnover in Europe was roughly three times as large as the turnover generated in the hospital segment (EUC, 2009). Thus, for the majority of prescription drugs in this study, retail pharmacy prices should provide a reliable indicator of actual market prices. The retail pharmacy data contain detailed information on drugs and medical products. The current status of patent and SPC protection, the availability of generic and re-import versions of the drug and the therapeutic field(s) of indication[33] is specified for each drug. Medical products are classified as "patent-protected brand, off-patent brand or generic" and as "original or "re-import" product. The data further indicate medical products' tradename, the active ingredient(s), the manufacturer of the product and the availability of various drug form(s)[34], dosage sizes and package sizes. The date of launch is provided at retail form level, i.e. separately for each drug form, dosage and package size. Monthly price and sales data are available at retail form level, too. Generic advertising data are confidential and were impossible to acquire. Importantly, direct advertising of prescription medications to consumers is illegal in the European Union, and also the overall level of generic advertising is known to be very limited (Hellerstein, 1998; Scherer, 2000; Berndt *et al.*, 2003). Nevertheless, the lack of generic advertising data is a limitation of this study.

[32] *Insight Health* has obtained exclusivity data from the national patent and trademark office since 2005. I accessed the PATDPASPC, Esp@cent Patent, Derwent and Open Drug database, Thomson's Current Patent Gazette, the FDA Orangebook, and online patent expiry reports to complement and verify the data.

[33] The classification of therapeutic fields rests upon the Anatomical Therapeutic Chemical (ATC) Classification System which was introduced by the *WHO* in 1976.

[34] The drug form classification follows the New Form Code (NFC) Classification established by the *European Pharmaceutical Market Research Association (EphMRA)*.

Between 2002 and 2007, 48 drug markets experience a total of 724 generic entries following loss of exclusivity.[35] The analysis is directed at 35 oral medications to ensure the comparability of results.[36] Those drug markets had experienced at least one year of generic competition by December 2007. Overall 640 generic products were launched in these markets. Most drugs are available in different dosages sizes, yet the prices of different dosage sizes cannot simply be aggregated as the relationship between the price of a medical product and the amount of active ingredient it contains is non-monotonic (Fisher Ellison and Ellison, 2007). Like Caves *et al.* (1991), Grabowski and Vernon (1992), Bhattacharya and Vogt (2003) and Regan (2008), I determine generic prices for the most "popular" dosage size to ensure a constant unit of observation. This dosage size has generated the largest generic revenue stream in a drug market by 2007.[37] As generic firms generally offer different and not necessarily the same package sizes for one specific dosage size, it is impossible to determine a constant unit of observation at package size level without losing a large fraction of observations. Directing the analysis to one market segment does not turn out to be disadvantageous on the other hand, as nearly all firms launch this dosage size. The average generic entry pattern in the 35 drug markets and bestseller segments is astonishingly similar (see Appendix [3.2]) given that the total number of generic entries (generic products) declines only slightly to 622. Looking just at the generic entry pattern, the bestseller segment gives a complete picture of generic competition. In the majority of cases (615 generic entries), firms launch the bestselling dosage size right at market entry and before they launch any other dosage sizes. This highlights the economic importance of the bestseller segment. As I require higher order market share lags in selected estimations, I restrict the sample to 605 generic products, for which I observe market shares and prices for a period of at least six months.

Unit of observation in the analysis is monthly generic price charged by a generic firm in the bestseller segment. Generic prices denote average per-pill prices. Computing a turnover-weighted[38] average *per-pill* price for each generic product[39], I aggregate the ex-factory per-pill prices of different package sizes. Ex-factory prices are manufacturers' selling prices which

[35]Other studies report similar rates of generic entry, e.g. Magazzini *et al.* (2004).
[36]Saha *et al.* (2006) and Regan (2008) similarly confine their analyses to oral medications.
[37]Monthly revenues in the bestseller segment make up on average 62% of total drug market revenues.
[38]If a product yielded zero turnover, I compute a package size-weighted average price instead.
[39]The terms generic product and generic drug are used interchangeably as firms tend to launch one product per drug. Else products' prices are aggregated at drug-firm level using turnover/package size weights.

neither include the fixed wholesale and pharmacy markup nor the value added tax. Thus, they provide an informative measure of firms' profit streams. Per-pill prices vary slightly across different package sizes. Controlling for the (turnover-weighted) average package size of each generic product, I account for the price variation across different package sizes.

The panel data are unbalanced as drugs' losses of exclusivity and generic entries occur at different points in time over the 2002-2007 period. The dates of patent and SPC expiries are exogenously given. Given that generic firms decide upon market entry at least three years prior to loss of exclusivity, and given that the legal process of obtaining market approval makes it generally impossible to predict exactly when approval will be granted (see Section 3.2), the timing of generic entry is plausibly exogenous, at least within a period of a few months. The majority of 395 generic entries occurred within a narrow time window of six months. Also, generic firms have not exited the 35 drug markets by 2007. Price and turnover – indicators of supply activity – are never missing after firms' entry in the bestseller segment. Overall, selection and attrition issues are likely to be minor. Table 3.1 outlines fundamental characteristics of the drug markets, generic firms and generic products. Limiting

Table 3.1: Overview Generic Drug Markets – Bestseller Segment

	N	Mean	Median	Min.	Max.	Sd.
Drug Markets						
Months off-patent Generic Competition	35	39.9	43	12	70	15.1
Accumulated Generic Entry by Dec. 2007	35	17.7	17	3	39	8.3
Initial Monthly Revenues (in €Mio.)	35	3.8	2.3	0.1	22.7	0.5
Generic Firms						
Drug Portfolio Size by Dec. 2007	68	70.3	44.5	1	304	67.9
Rx Drug Portfolio Size by Dec. 2007	68	57.4	34	1	246	56.6
Umbrella Brand Size by Dec. 2007	68	43.1	18	0	300	63.1
Generic Products						
Months off-patent Generic Competition	605	34.5	31	6	70	14.1
Initial Generic Price Cuts (in %)	605	37.7	36.3	-71.3	89.2	17.7
Initial Generic Market Share (in %)	605	7.4	0.3	0	100	19.2

Notes: Price and revenue statistics are based on producer prices. Initial monthly revenues in the bestseller segment are measured in the first month of generic entry. The umbrella brand of a generic manufacturer comprises all products which carry the (un)abbreviated corporate name of the firm. Generic firms' initial price cuts in the first month of entry are reported relative to the brand price observed in the month prior to first generic entry.

the analysis to drug markets with at least one year of off-patent competition, I observe at least of 12 months of generic competition. On average I observe off-patent drug markets for 39.9 months. By December 2007, drug markets have on average attracted 17.7 generic firms. At least three and a at most 39 firms entered in one drug market. The different timings of patent (SPC) expirations and the strong variation in drug markets' (pre-entry) revenues

explain the large variation in the number of generic entrants across drug markets. In the first months of generic entry, €3.8 Mio. in revenues accrue on average in one bestseller segment. The largest revenues of €22.7 Mio. are generated by the blockbuster drug *Simvastatin*.

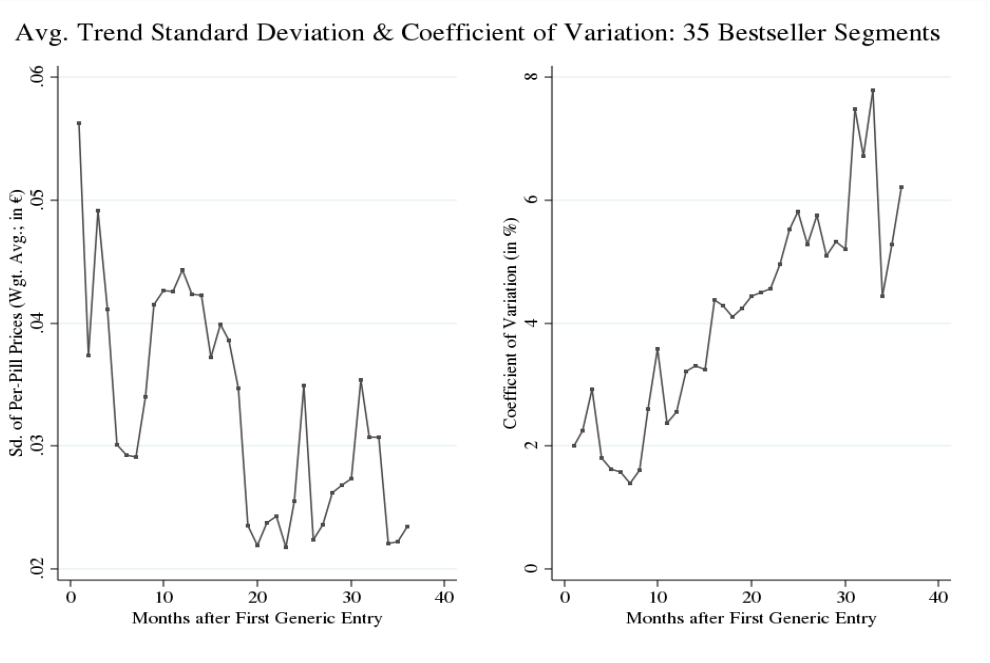
Overall 68 generic manufacturers entered in the 35 bestseller segments. Firms' drug portfolio sizes vary strongly. As of December 2007, generic firms have been active in 70.3 drug markets on average, supplying primarily Rx drugs. The generic firm with the smallest (largest) drug portfolio has been active in 1 (304) drug market(s). The portfolio of umbrella branded drugs is smaller than the overall drug portfolio as generic firms have occasionally adopted a (non-INN) premium brand strategy. Also the sizes of the umbrella branded drug portfolio vary significantly, suggesting that firms have achieved a different level of brand recognition among physicians, pharmacists and patients. I track generic products on average for 34.5 months (T) and obtain a total of 20888 observations (GxT), examining the market shares of 605 generic products (G). In the first month of entry, generic firms offer their products on average at price discount of 37.7% relative to the pre-entry brand price[40], and obtain a market share of 7.4%. There is a strong variability in market shares across firms.

Strikingly, there is also a considerable variation in generic prices across firms within the bestseller segment. Figure 3.1 below plots the average trend of the standard deviation and the coefficient of variation of generic prices. The standard deviation of generic prices is reported as soon as at least two generic manufacturers have entered the bestseller segment.[41] Per-pill prices vary on average by roughly 6 Cent in the first month of generic competition. Both generic prices and the standard deviation of generic prices decline over time. After three years of generic competition, per-pill prices vary only by about 2 Cent. The coefficient of variation indicates the ratio of the standard deviation of generic prices relative to the average generic price within one bestseller market segment. The standard deviation of generic prices makes up on average an increasingly large fraction of average generic price over time of up to 8%. Importantly, both measures of price variation are non-zero at any point in time.

[40]The implied average generic price ratio in the first month of entry (62.3%) varies from the previously reported average generic price ratio of 75% (Section 3.2) for several reasons: (1) The given generic price ratio denotes an unweighted average price across the 605 generic products and not an unweighted average of the (turnover-weighted) average generic price across the 35 drug markets. (2) The initial price cut refers to the first month of product launch which must not coincide with the first month of off-patent generic competition.

[41]The standard deviation is set from zero to missing as long as only one generic firm serves the bestseller segment. If only one generic firm is active the standard deviation of generic prices will automatically be zero. A standard deviation of zero is uninformative once only one generic firm supplies the market, and this case must be distinguished from the event where at least two generic firms compete and set equal prices.

Figure 3.1: Generic Price Variation within Bestseller Segments

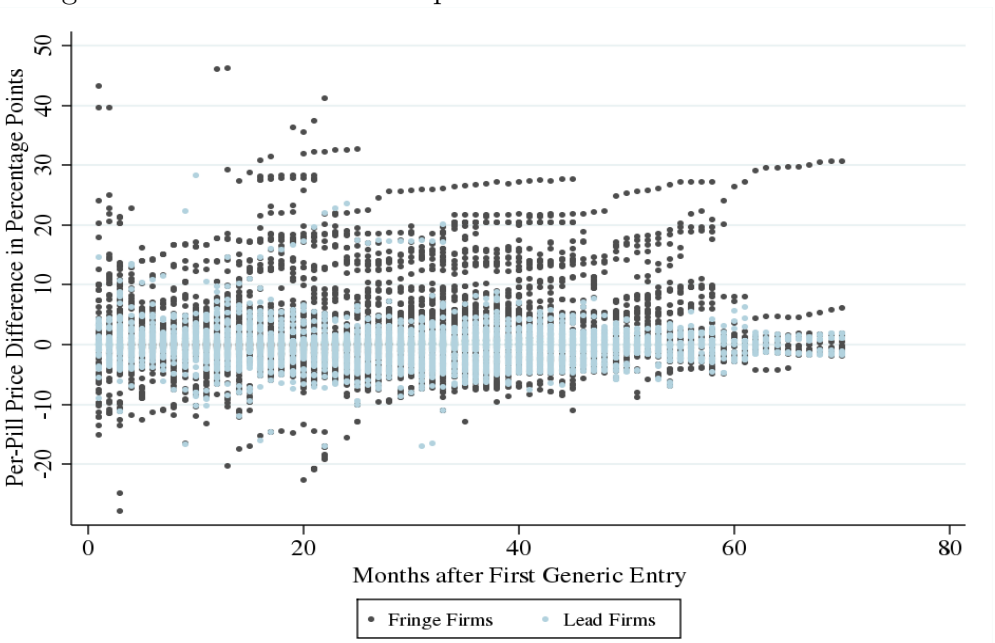


The pattern in generic prices clearly contradicts the assumption of Bertrand competition with undifferentiated goods, which predicts zero variation in generic prices as soon as at least two generic manufacturers have entered the drug market (bestseller segment). As the standard deviation of generic prices denotes the turnover-weighted average deviation in generic prices from the turnover-weighted average generic price as observed in one bestseller segment, the variation in generic prices cannot be fully attributed to fringe firms which achieve below average market shares and charge disproportionately high prices. Especially firms with a small market share might find it worthwhile to maintain high prices (markups) at the expense of a potentially slight decrease in market share if the demand for generic drug products is relatively inelastic.[42] Figure 3.2 below plots the monthly generic price deviation from the current average generic price for each of the 605 generic products in the sample. Observation points of fringe firms take on a grey color, whereas observation points of generic firms achieving above average market shares (lead firms) are highlighted in light blue.

In comparison to fringe firms, "market leaders" tend to deviate less strongly from the average generic price observed in a given market segment and month. However, price deviations on a scale of 10 percentage points can also be observed for lead firms. Put differently,

[42]In a related study (Chapter 2), I find that patients habitually receive the same generic product. Being largely insensitive to price differentials, patients will hardly switch among products of different generics firms, even if they contain the same active ingredient and have an identical drug form and dosage size.

Figure 3.2: Generic Price Dispersion conditional on Market Share



the variation in generic market shares cannot fully explain the observed variability of generic prices. Due to price regulation or legal contractual commitments (e.g. supply agreements, fixing prices in the short run), generic prices could potentially be sticky. If some generic companies cannot immediately adapt their prices as other economic factors have changed (e.g. after a substantial price decrease by competitors), one will necessarily observe a variation in generic prices. However, generic prices turn out to change (decline) each and every month. Generic firms lowered the prices of the 605 generic products on average by 2%/6%/11% within one/three/six month(s)[43], and they lowered prices on average by 8%/15%/20% within the first month/first three months/first six months[44] following market entry. In brief, the variation in generic prices observed within the bestseller segment is unlikely to stem from the stickiness of prices. Industry evidence suggests that economies of scope and differences in firm reputation partially explain the variability of generic prices. Drug portfolio and umbrella brand sizes differ significantly across companies and may affect generic prices.[45]

[43]The median generic product's price has been lowered by 0.1%/1%/6% within one/three/six month(s).

[44]The median generic product's price has been lowered by 2%/9%/16% within the first month/first three months/first six months following market launch. Price changes denote % and not percentage point changes.

[45]There is hardly any variation in the branding strategies generic firms pursue. The majority of the 605 generic products is umbrella branded: 500 (62) generic products have a tradename that incorporates the firms' (un)abbreviated name (a logo), whereas only 43 generic products have a distinct tradename.

3.5 Empirical Implementation

Generic manufacturers presumably have cost advantages in the production, storage and promotion of generic drugs (economies of scope). Generic firms' drug portfolio size provides a measure of their cost advantage, which apparently enables them to be more competitive in price. Building up umbrella brands through corporate branding, generic firms attempt in turn to establish brand recognition. The size of the umbrella branded drug portfolio facilitates a measure of firm reputation. The umbrella brand comprises all generic products (drugs) which carry the (un)abbreviated corporate name. Theoretical models show that umbrella branding can have a positive impact on firms' investment in quality and the price consumers are willing to pay. Signaling that the qualities of the firms' umbrella branded products are positively correlated, umbrella branding alleviates information asymmetries between sellers and buyers and provides a bond for quality. The more generic products are marketed under the same umbrella, the greater is the bond for quality, for which consumers will accordingly pay more. If brand recognition pushes prices upward, it will attenuate if not neutralize the price lowering effect of economies of scope. I do not question altogether that generic firms compete on price but that they exclusively compete on price. The demand for generic drugs appears to be quite inelastic[46], such that price deviations on a certain scale will not result into an immediate loss of market share. This study pursues the following two hypotheses which are presented below. The first hypothesis rests on the economic theory of economies of scope. The second hypothesis builds on theoretical models of umbrella branding.

Hypothesis 1: The broader a generic firm's overall drug portfolio is, the lower are the prices it will charge relative to generic competitors in the bestseller segment.

Hypothesis 2: The larger a generic firm's umbrella brand is, the higher are the prices it will charge relative to generic competitors in the bestseller segment.

Generic company i's price ($P_{g_{itm}}$), drug portfolio (dp_{it}) and umbrella brand (ub_{it}) size as observed in month t following first generic entry in drug market m, are likely to be correlated with firm i's advertising expenditures. The lack of generic advertising data potentially gives rise to omitted variable (ov) bias. Berndt *et al.* (2003) hypothesize that generic marketing-to-sales ratios are close to zero as generic advertising is known to be very limited (Hellerstein,

[46] In a related empirical study, I show that price differentials have a negligibly small impact on pharmacists' and patients' choice among therapeutically-equivalent generic drug products (see Chapter 2).

1998; Scherer, 2000; Berndt *et al.*, 2003)[47]. Given that generic advertising is directed to firms' drug portfolio rather than individual generic drug products (Berndt *et al.*, 2003), I assume that advertising expenditures are potentially non-zero but time-constant (ov_i).[48]

Based on the previous assumption, I am able to eliminate the omitted (unobserved) effect (ov_i) from the composite error term v_{it} ($v_{it} = u_{it} + ov_i$) using either first differencing or a within-transformation of the data.[49] By removing the unobserved effect from the composite error term, I eliminate one potential source of endogeneity. Whereas the Fixed Effects (FE) estimator applies a mean-deviation transformation (within-transformation) to each variable, the First-Difference (FD) estimator uses first-differencing. Allowing for an arbitrary correlation between the explanatory variables and time-invariant omitted (unobserved) effect, both the FE and FD estimator assume that explanatory variables are strictly exogenous.[50] In other words, the explanatory variables are uncorrelated with the idiosyncratic error term u_{it} throughout time. If unobserved price shocks within the first three years following market entry influenced the current or future entry (exit) decisions in new (old) drug markets and thus, the drug portfolio size of the firm, the assumption of strict exogeneity would not hold. Notably, generic firms have not exited from the 35 drug markets (bestseller segments) by 2007, and they very rarely exited from an old drug market.[51] The correlation between price shocks in one drug market and exit decisions in old drug markets seems to be minor. As generic firms also prepare for a new market entry at least three years prior to loss of exclusivity, firms' drug portfolio and umbrella brand size[52] are effectively predetermined at

[47]Generic firms hardly engage in physician detailing (promotional visits) and do a modest amount of journal advertising (Berndt *et al.*, 2003; Gupta and Yu, 2008).

[48]The average (median) generic firm launches nine (four) new drugs between 2002 to 2007. As generic firms likely direct advertising efforts to newly off-patent drugs and less to older drug products, advertising may be targeted to a different selection of drugs over time, and are thus assumed to remain roughly constant.

[49]Time-invariant, unobserved firm effects (c_i), e.g. managerial quality, will be similarly wiped out.

[50]The FE and FD estimator rely on a less stringent assumption and are typically more robust than the Random Effects (RE) estimator which assumes strict exogeneity but hypothesizes the correlation between the explanatory variables and the constant unobserved effect to be zero. The Breusch-Pagnan Lagrange-Multiplier test indicates that unobserved effects are present. The absence of a constant unobserved effect is statistically equivalent to the null hypothesis of no serial correlation in the composite error terms v_{it}, which can be rejected regardless of which specification I employ. Both the Hausman test and an asymptotically equivalent test for RE vs. FE clearly reject the null hypothesis of no systematic difference between the RE and FE estimates. Assuming that strict exogeneity holds, explanatory variables correlate with the constant unobserved effect which renders RE estimates inconsistent. The Hausman-like test relies on an augmented regression and performs a simple Wald test, dropping the assumption that either estimator is fully efficient.

[51]Over the six year time period the 68 generic firms exited on average from two drug markets (Median: 1). Once firms exit a drug market I neither observe price nor turnover data for the generic product.

[52]Due to the time-intensive naming process, generic firms must determine the branding strategy for a new generic product essentially at the same time they decide on market entry to avoid delays in the market authorization process (see Section 3.2).

the time of market entry, and they are plausibly strictly exogenous at least in the first three years following market entry. For now, I assume that both the size of the drug portfolio and umbrella brand are strictly exogenous. I employ both the FE and FD estimator to verify the robustness of results. If FE and FD estimates differ in ways that cannot be attributed to sampling error, the strict exogeneity assumption is unlikely to hold.[53] As a primary "test" of the assumption, I further investigate how robust the final estimates are to the limitation of the data sample to price observations collected in the first three years following market entry, where firms' drug portfolio and umbrella brand size are arguably strictly exogenous.

Examining aggregate (average) generic prices in off-patent pharmaceutical markets, previous empirical studies (Caves *et al.*, 1991; Grabowski and Vernon, 1992; Frank and Salkever, 1997; Bhattacharya and Vogt, 2003; Reiffen and Ward, 2005; Saha *et al.*, 2006; Regan, 2008) often resort to a FE or RE estimation. The studies typically control for the number of generic entrants, the number of therapeutic substitutes, a time trend and year effects. Employing the FE and FD estimator, I replicate essential results of the previous studies in the first step to verify the consistency of the data. Thereby, I ignore the potential effects of economies of scope and brand recognition on generic prices. I examine how the number of generic entrants (N_{tm}), the number of off-patent (generic) and on-patent therapeutic substitutes ($\mathbf{S_{tm}}$), the passage of time – number of months following first generic entry – (T_{tm}), and year effects ($\mathbf{Y_{tm}}$) affect generic-to-brand price ratios $P^{Ratio}_{g_{itm}}$. I obtain a more comparable measure of generic price deviations across the 35 off-patent drug markets, normalizing generic prices ($P_{g_{itm}}$) by pre-entry brand prices as observed in the month prior to first generic entry. A log-transformation is dispensable as generic-to-brand price ratios follow a normal distribution quite closely (see Appendix [3.3]).[54] Moreover, I include the square of the number of generic entrants (N^2_{tm}) in the price equation to allow for a non-linear effect of generic entry.

I follow Reiffen and Ward (2005)[55] and Saha *et al.* (2006), assuming that the number of generic entrants is strictly exogenous. Given the time frame of the market approval process and the frequent delays in the grant of market authorization, the number of generic entrants is plausibly strictly exogenous (see Section 3.2). Recall also that generic manufacturers have

[53] If the time series process is appropriately stable and weakly dependent, the inconsistency from using FE (FD) will be of order T^{-1} (will not depend on T) and may be minimal with large T (Wooldridge, 2002).

[54] By contrast generic prices are highly right-skewed. The majority of pills is priced around €1.

[55] Reiffen and Ward (2005) test for endogeneity using a Hausman test and cannot reject the null hypothesis that market structure is exogenous.

not exited the 35 bestseller segments by 2007. The number of on-patent and off-patent (generic) drugs, listed for identical therapeutic indications, are also assumed to be strictly exogenous. Dates of patent/SPC expirations are exogenously given. Moreover, new drug launches constitute strategic, large-scale R&D investments made at least ten years prior to the actual launch of the drug (EUC, 2009). The date of market approval is eventually determined by the (supra)national market authorization agency. Standard errors are robust to heteroscedasticity in both FE and FD regressions. As generic companies' pricing decisions across drug markets and within drug markets over time are likely not independent, standard errors are clustered at firm level (68 clusters). The first specification is given below.

$$P_{g_{itm}}^{Ratio} = \alpha_1 N_{tm} + \alpha_2 N_{tm}^2 + \mathbf{S_{tm}}\boldsymbol{\beta} + \theta T_{tm} + \mathbf{Y_{tm}}\boldsymbol{\eta} + v_{itm}$$

The second specification incorporates the size of firm i's drug portfolio (dp_{it}) and umbrella brand (ub_{it}) to measure the effect of economies of scope and brand recognition in generic drug markets. Furthermore, I control for generic products' turnover-weighted average package size (ps_{itm}) to account for the possible variation in generic prices due to different package sizes. The analysis has so far been directed to the bestselling oral solid dosage size within a drug market. If patients easily switch among different drug forms or dosage sizes, generic prices might be affected by generic manufacturers' introduction of other oral solid dosage sizes and other types of oral solids (e.g. oro-dispersible pills) containing the same dosage size. Allowing for substitution effects, I also take into account the number of alternative oral solid dosage sizes and alternative types of oral solids containing the same dosage size ($\mathbf{A_{tm}}$), both of which were launched by generic entrants. The second specification is denoted below.

$$\begin{aligned} P_{g_{itm}}^{Ratio} = {} & \alpha_1 N_{tm} + \alpha_2 N_{tm}^2 + \mathbf{S_{tm}}\boldsymbol{\beta} + \theta T_{tm} + \mathbf{Y_{tm}}\boldsymbol{\eta} + \\ & \delta_1 dp_{it} + \delta_2 ub_{it} + \lambda ps_{itm} + \mathbf{A_{tm}}\boldsymbol{\gamma} + v_{itm} \end{aligned}$$

Lastly, the variation in generic prices may partially stem from generic firms with below average market shares and disproportionately high prices. Thus, I need to verify how robust estimates are to the inclusion of firms' market share ($M_{g_{itm}}$) in the price equation. Generic firms' drug portfolio size and market share are modestly correlated[56]. Saha *et al.* (2006) emphasize generic prices and market shares are determined simultaneously, mean-

[56]The Bravais-Pearson correlation coefficient amounts to 0.4631.

ing that market shares cannot be considered strictly exogenous. Instrumental variable (IV) estimators in a FE (FD) setting require strictly (sequentially) exogenous and time-variant instruments which are redundant in the price equation. Lacking a time-variant instrumental variable that would be both sufficiently correlated with market shares and uncorrelated with prices (conditional on other explanatory variables), I resort to the two-step Difference General Method of Moments Difference (DIFF GMM) estimator to solve the simultaneity problem.[57] The DIFF GMM estimator uses first-differencing to remove time-invariant unobserved effects and instruments the endogenous, first-differenced variable ($\triangle M_{g_{itm}}$) with appropriately lagged levels (Holtz-Eakin *et al.*, 1988; Arellano and Bond, 1991). Depending on the order of autocorrelation in the v_{itm}'s – indicated by the Arellano-Bond autocorrelation test – different lags will be appropriate. I use several lag structures to assess the sensitivity of the GMM estimates. The two-step standard errors are robust to heteroscedasticity and arbitrary autocorrelation within panels (generic products), and they are clustered at firm level (68 clusters). The Windmeijer-correction of standard errors reduces the typically inherent downward bias in the two-step DIFF GMM standard errors. The third specification is estimated by FE, FD and GMM in order to assess the severity of the simultaneity bias. Only the DIFF GMM estimator tackles both the problem of unobserved heterogeneity and simultaneity, thereby providing a relevant benchmark for the true parameter values.

$$\begin{aligned} P_{g_{itm}}^{Ratio} &= \alpha_1 N_{tm} + \alpha_2 N_{tm}^2 + \mathbf{S_{tm}}\boldsymbol{\beta} + \theta T_{tm} + \mathbf{Y_{tm}}\boldsymbol{\eta} + \\ &\quad \delta_1 dp_{it} + \delta_2 ub_{it} + \lambda ps_{itm} + \mathbf{A_{tm}}\boldsymbol{\gamma} + \mu M_{g_{itm}} + v_{itm} \end{aligned}$$

Appendix [3.4] contains a summary of definitions for all variables employed in the panel data analysis. Table 3.2 provides summary statistics.[58] Table 3.2 shows that generic products were priced on average roughly 60 percentage points below pre-entry brand prices over the time period 2002 to 2007. There is quite a large variation in generic-to-brand price ratios (Sd.: 18.3 percentage points). Appendix [3.5] provides a further, more disaggregate overview of the data, decomposing variables' standard deviation into its between and within components. The statistics indicate that there is a large variation in generic-to-brand-price ratios both

[57] Alonso-Borrego and Arellano (1996) show in simulation studies that DIFF GMM has large finite sample bias and poor precision in dynamic panel data models where the autoregressive parameter is moderately large and the number of time series observations is moderately small. In a static panel data model, however, the DIFF GMM may in fact have a smaller finite sample bias than the System GMM estimator when the endogenous variable ($M_{g_{itm}}$) is persistent (Windmeijer and Bun, 2009).

[58] Summary statistics are weighted by the number of entrants (N_{tm}) markets have attracted in month t.

Table 3.2: Summary Statistics – Generic Product Panel

Variable Name	Mean	Median	Min.	Max.	Sd.	GxT
Generic-to-Brand Price Ratio ($P^{Ratio}_{g_{itm}}$)	41.94	40.30	5.57	173.40	18.32	20888
Generic Market Share ($M^{Ratio}_{g_{itm}}$)	6.66	2.42	0	100	12.04	20888
Generic Entry	19.96	20	1	39	7.97	20888
Branded Substitutes	5.68	4	0	23	5.15	20888
Generic Substitutes	15.86	12	0	65	13.30	20888
Alternative Strengths	2.86	3	0	6	1.67	20888
Alternative Drug Forms	0.39	0	0	4	0.72	20888
Drug Portfolio Size	127.95	130	0	304	78.23	20888
Umbrella Brand Size	97.14	101	0	300	79.91	20888
Package Size	78.26	87.55	2	284	34.63	20888
Time Trend	26.75	25	1	70	15.35	20888

across time and across firms. Drug portfolios (umbrella brands) comprise on average roughly 128 (97) drugs, yet there is also a substantial variation in drug portfolio and umbrella brand sizes across firms. It is worthwhile to examine whether the variation in generic prices can at least in parts be attributed to differences in drug portfolio and umbrella brand sizes.

3.6 Results

Estimating three differently specified price equations, I investigate to what extent economies of scope (*Hypothesis 1*) and brand recognition (*Hypothesis 2*) are able to explain the observed variation in generic prices. Table 3.3 below provides an overview of the estimates obtained from the FE regressions. The first column of Table 3.3 reports the estimates obtained for the first specification, where I replicate essential results of previous empirical studies on generic prices. The entry of one firm is associated with a 1.55 percentage point decrease in generic-to-brand price ratios. The previous studies (Caves *et al.*, 1991; Frank and Salkever, 1997; Reiffen and Ward, 2005; Saha *et al.*, 2006) often find a negative effect of entry on generic prices, however, the size of the effect varies to some extent. Saha *et al.* (2006) similarly confine their analysis to the "most popular dosage size" and examine average generic-to-brand-price ratios instead of (unnormalized) average generic prices. They find a somewhat larger decrease in average generic-to-brand price ratios of 2.3 percentage point due to generic entry. Consistent with past studies on intermolecular competition (Fisher Ellison *et al.*, 1997; Wiggins and Maness, 2004; Regan, 2008), I find no evidence that therapeutic substitutes affect generic prices. Lastly, prices tend to fall by 0.48 percentage points in each month of generic compe-

Table 3.3: Fixed Effects – Coefficients

Dep.Variable: $P_{g_{itm}}^{Ratio}$	*Spec.1*	*Spec.2*	*Spec.3*
Generic Market Share ($M_{g_{itm}}$)	–	–	-0.1059*
			(0.050)
Generic Entry	-1.5496***	-1.3940***	-1.6070***
	(0.204)	(0.193)	(0.161)
Generic Entry^2	0.0038	-0.0029	0.0006
	(0.003)	(0.003)	(0.003)
Branded Substitutes	-0.3789	-0.3265	-0.3746
	(0.235)	(0.203)	(0.189)
Generic Substitutes	-0.2345	-0.0840	-0.0253
	(0.255)	(0.233)	(0.209)
Alternative Strengths	–	3.1506***	3.0755***
		(0.276)	(0.237)
Alternative Drug Forms	–	-3.3062***	-3.2408***
		(0.730)	(0.687)
Drug Portfolio Size	–	-0.3047*	-0.3241*
		(0.141)	(0.138)
Umbrella Brand Size	–	0.1906*	0.2035*
		(0.085)	(0.085)
Package Size	–	-0.0603*	-0.0547*
		(0.027)	(0.025)
Time Trend	-0.4765***	-0.4097***	-0.3988***
	(0.024)	(0.051)	(0.051)
Year (2002,$\cdots$,2007)	*yes*	*yes*	*yes*
Const.	0.7360***	0.9133***	0.9421***
R^2 within	0.6513	0.6656	0.6676
R^2 between	0.3499	0.0801	0.0673
R^2 overall	0.4167	0.1934	0.1714
F(10/15/16,67)	326.28	674.08	1334.24
Prob > F	<0.001	<0.001	<0.001
G x T		20888	

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is the monthly generic-to-brand price ratio of a generic product. Standard errors robust to heteroscedasticity and autocorrelation, clustered at firm level (68 clusters), in parentheses. The reference year is 2002.

tition. The time trend in generic prices may capture the (quarterly) adjustment of reference prices, creating downward pressure on prices. The second specification additionally controls for generic firms' drug portfolio and umbrella brand size, the package size of the product, and for alternative oral solid dosage sizes and types of drug forms containing the same dosage size. The size and significance of the previously identified effects practically remain unaltered by the extension of the model. The number of alternative oral solid dosage sizes introduced by generic firms seems to soften price competition. Each additional strength introduced

increases generic-to-brand price ratios by about 3.2 percentage points, suggesting that different dosage sizes are not substitutes for one another.[59] The number of alternative types of oral solids launched by generic firms intensifies price competition on the contrary: each oral solid introduced lowers generic-to-brand price ratios by 3.3 percentage points. Different types of oral solids (e.g. oro-dispersible vs. chewable pills) appear to be substitutes for one another.

Drug portfolio and umbrella brand sizes also affect generic prices significantly. Generic-to-brand price ratios are about 0.3 percentage points lower with each drug firms additionally supply. Economies of scope – cost advantages in the production, storage and promotion of generic drugs – can explain the superior price competitiveness of generic firms with a broad drug portfolio. The standard deviation of firms' drug portfolio size amounts to roughly 79 drugs (see Appendix [3.5]), implying a per-pill price variation (reduction) of about 24 percentage points. The size of generic firms' umbrella brand attenuates this effect to a large extent. With each umbrella branded drug firms supply additionally, generic-to-brand price ratios are about 0.2 percentage points higher, indicating that there is a also brand-name markup (price-premium) in the generic drug market. Overall, however, manufacturers charge lower prices the larger their drug portfolio. The standard deviation of firms' umbrella brand size amounts to about 80 drugs (see Appendix [3.5]), implying a per-pill price variation (increase) of around 16 percentage points. Taken together, the estimates predict a net variation (reduction) in generic-to-brand price ratios of roughly 8 percentage points. As I observe price deviations on a scale of 10 percentage points and higher (see Figure 3.2), these estimates turn out to be plausible. Lastly, package sizes appear to affect generic prices as well. Oral solids supplied in bulk are slightly cheaper: with each pill the package additionally contains, the generic-to-brand price ratio will be about 0.06 percentage points lower. Given a standard deviation of roundabout 37 pills between generic products (see Appendix [3.5]), the variation in generic-to-brand price ratios tends to be in the range of 2.2 percentage points. Overall, package size differences explain a small fraction of the variation in generic prices.

The inclusion of market shares in the price equation (Spec. 3) does not substantially alter the results. The sign, relative size and level of significance of most effects remain unchanged. The coefficient of generic firms' market share ($M_{g_{itm}}$) is negative as expected. Firms with a higher market share, charge lower prices. For instance, a generic firm with a 10 percentage

[59] A patient requiring a 10mg dosage size may be different from patients requiring higher dosage sizes.

point higher market share has a roughly 1 percentage point lower generic-to-brand price ratio. The effect of market shares appears to be minuscule. However, this estimate needs to be interpreted with caution given the potentially inherent simultaneity bias. Recall that FE and FD estimates will differ in ways that cannot be attributed to sampling error if the strict exogeneity assumption does not hold. Appendix [3.6] presents the according FD estimates. The FD market share estimate is about 75% smaller and statistically insignificant, confirming the notion that market share estimates are affected by simultaneity bias. The FD estimates obtained for firms' drug portfolio and umbrella brand size are in turn very similar to the FE estimates. The sign and relative size of the other coefficients also remain largely unchanged. Except for *Alternative Strength* and *Alternative Drug Forms*, the covariates still have a highly significant effect on generic prices. In contrast to the FE estimates, FD estimates indicate that the number of on-patent substitutes influences generic prices. As the number of on-patent therapeutic substitutes increases by one, generic-to-brand price ratios increase by roughly 0.3 percentage points. Also, generic entry now affects generic prices in a non-linear fashion, its effect decreasing by 0.01 percentage points with each additional entrant. Given a standard deviation of five on-patent therapeutic substitutes and a standard deviation of eight generic firms (see Appendix [3.5]), the two effects are essentially negligible. Even though many estimates turn out to be similar, the divergence in the market share estimate leaves no doubt that simultaneity bias is present, distorting the FE and FD estimates.

Using first-differencing to remove constant unobserved effects and instrumenting the endogenous, first-differenced variable ($\triangle M_{g_{itm}}$) with appropriately lagged levels, the DIFF GMM estimator tackles the simultaneity problem. Table 3.4 below reports the two-step DIFF GMM estimates obtained for the third specification. Note that the Arellano-Bond test for autocorrelation is applied to the differenced residuals. Autocorrelation of order one – AR(1) – is expected in those residuals as they share the idiosyncratic error term $u_{i,t-1}$. Due to autocorrelation, specific market share lags will still be correlated with the error term, and will thus fail to provide valid instruments. The Arrelano-Bond tests of autocorrelation provide weak evidence of AR(2), casting doubt on the validity of using market share lags of second order as instruments. Using second market share lags of second order as instruments, the Arrelano-Bond test clearly rejects the null hypothesis of no autocorrelation of second

Table 3.4: GMM First Differences (Spec.3) – Coefficients

Dep.Variable: $P_{g_{itm}}^{Ratio}$	$\triangle M_{g_{itm}}$ instrumented using Lags of $M_{g_{itm}}$: *Lags (3-4)*	*Lags (3-5)*	*Lags (4-5)*	*Lags (4-6)*
Generic Market Share ($M_{g_{itm}}$)	-0.4816	-0.4880*	-0.5336*	-0.5302*
	(0.260)	(0.235)	(0.237)	(0.236)
Generic Entry	-1.9685*	-1.9955**	-1.9417**	-1.9413**
	(0.900)	(0.737)	(0.680)	(0.648)
Generic Entry^2	0.0336	0.0341*	0.0329*	0.0330*
	(0.019)	(0.016)	(0.014)	(0.013)
Branded Substitutes	0.2725***	0.2713***	0.2507***	0.2510***
	(0.072)	(0.069)	(0.068)	(0.067)
Generic Substitutes	-0.0225	-0.0227	-0.0007	-0.0017
	(0.129)	(0.129)	(0.126)	(0.124)
Alternative Strengths	-0.0211	-0.0208	-0.0490	-0.0579
	(0.492)	(0.494)	(0.515)	(0.470)
Alternative Drug Forms	-0.3141	-0.3271	-0.2016	-0.2035
	(0.572)	(0.518)	(0.533)	(0.520)
Drug Portfolio Size	-0.3327*	-0.3294*	-0.3079*	-0.3101*
	(0.158)	(0.142)	(0.143)	(0.140)
Umbrella Brand Size	0.2058*	0.2035*	0.1926*	0.1935*
	(0.103)	(0.093)	(0.091)	(0.090)
Package Size	-0.0197	-0.0195*	-0.0181	-0.0182
	(0.010)	(9.6e-03)	(9.5e-03)	(9.4e-03)
Time Trend	-0.6853***	-0.6853***	-0.6980***	-0.6976***
	(0.034)	(0.034)	(0.033)	(0.032)
Year (2002,$\cdots$,2007)	*yes*	*yes*	*yes*	*yes*
Arellano-Bond test AR(1)	0.023	0.018	0.020	0.020
Arellano-Bond test AR(2)	0.082	0.085	0.112	0.109
Arellano-Bond test AR(3)	0.553	0.537	0.540	0.546
Hansen test: chi2(1/2)	0.103	0.270	0.340	0.619
Instruments (Overid. Restr.)	17 (1)	18 (2)	17 (1)	18 (2)
Wald chi2(16)	6310.46	6269.13	6500.74	6638.93
Prob > chi2	<0.001	<0.001	<0.001	<0.001
G x (T-1)	20283			

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is the monthly generic-to-brand price ratio of a generic product in the bestseller segment. Two-step standard errors robust to heteroscedasticity and autocorrelation, clustered at firm level (68 clusters), in parentheses. The Windmeijer correction for two-step standard errors has been employed. The reference year is 2002.

order at a 1% level. Yet, it cannot identify autocorrelation of any higher order.[60] Conservatively, I employ lags of third and higher order to assure the validity of instruments. In total, I use only one or two lags since a proliferation of instruments can greatly weaken the Hansen test of over-identifying restrictions as result of which it generates p-values close to one (Roodman, 2008). The joint null hypothesis states that instruments are valid and that excluded

[60]The according GMM estimates can be obtained from the author upon request.

instruments are correctly excluded from the estimated equation. The null hypothesis cannot be rejected independent of the lag structure and number of over-identifying restrictions I use, indicating that the selected lags of market shares provide valid instruments for market shares in first-differences ($\triangle M_{g_{itm}}$). The GMM estimates prove to be quite insensitive to the lag structure used. The market share coefficient increases roundabout fivefold, and the effect is generally significant at a 5% level. A generic firm with a 10 percentage point higher market share – the standard deviation of market shares between generic products amounts to roughly 10 percentage points (see Appendix [3.5]) –, has a roughly 5-6 percentage point lower generic-to-brand price ratio. This estimate is more plausible than the FE or FD estimates given the strikingly larger price variations observed for fringe firms (see Figure 3.2).

The entry of one generic firm is also associated with a notably higher decrease in generic prices of 2 percentage points, which is more in line with the estimate by Saha *et al.* (2006) who also account for the simultaneity of generic prices and market shares. The effect of generic entry decreases marginally by 0.04 percentage points with each additional entrant, which has practically, however, no bearing (cp. discussion FD estimates). The coefficient of the time trend increases as well: generic prices fall by 0.7 percentage points in each month of generic competition. Recall that the (quarterly) adjustment of reference prices potentially creates further downward pressure on generic prices over time. Overall GMM estimates provide only weak evidence that therapeutic substitutes have a sustainable impact on generic prices. Generic prices increase by roughly 0.2 percentage points as the number of on-patent therapeutic substitutes increases by one. Given a standard deviation of five on-patent substitute drugs the effect is practically negligible. The GMM estimates provide no further evidence that alternative dosage sizes, alternative types of oral solids and package size differences affect generic prices.[61] All effects are insignificant independent of the lag structure used. Lastly, the GMM estimates indicate that generic-to-brand price ratios decrease by about 0.3 percentage points with each drug generic firms additionally supply. Again, the size of generic firms' umbrella brand attenuates this effect to a large extent. With each umbrella branded drug generic companies additionally supply, generic-to-brand price ratios are about 0.2 percentage points higher. Thus, GMM estimates predict a similar net variation in generic-to-brand price ratios of 8 percentage points at pill level. Generic firms charge overall lower

[61] FE, FD and GMM estimates are robust to the exclusion of the three variables from the model.

prices the larger their drug portfolio is. Notably, the GMM estimates are robust to the limitation of the data sample to price observations collected in the first three years following market entry, where the sizes of companies' drug portfolio and umbrella brand are likely exogenous. Appendix [3.7] presents the according estimates. Market share, drug portfolio and umbrella brand size again turn out to be key influencing factors of the variation of generic prices across firms. The direction and size of the effects remain largely unchanged by the restriction of the observation period. Generic manufacturers with a small market share tend to charge higher prices, whereas firms broadly positioned across drug markets set significantly lower prices, independent of any brand-name markup they may able to claim. Notably, package size differences are not able to explain the variation in generic prices.

3.7 Conclusion

This study shows that the variability of generic price can largely be attributed to differences in firms' drug portfolio and umbrella brand size, providing evidence of economies of scope and brand recognition in the generic drug market. Firms claim a higher price premium the more umbrella branded drugs they supply. In spite of the price premium, generic manufacturers charge altogether lower prices the broader their overall drug portfolio is.

Industry insiders assert that generic firms have cost advantages in the production, storage and promotion of generic drugs, which allows them to be more competitive in price. There is also industry evidence that generic companies can charge higher markups the more reputation and brand recognition they enjoy among consumers. Generic firms establish brand recognition, building up umbrella brands through the corporate branding of generic drug products. Theoretical models show that umbrella branding can have a positive impact on firms' investment in quality and the price consumers are willing to pay for the product.

Studying the impact of firms' drug portfolio and umbrella brand size on generic prices, I investigate the monthly ex-factory prices of 605 generic products in 35 off-patent drug markets over the time period 2002 to 2007. Assuming that drug portfolio and umbrella brand sizes are strictly exogenous, I resort to a FE and FD estimation. The strict exogeneity assumption is unlikely to hold if FE and FD estimates differ notably. Like the previous empirical literature on (average) generic prices, I account for the number of generic entrants, the number of therapeutic substitutes, a time trend and year effects. Among other impor-

tant price determinants, I further control for package size differences and the market share of the generic firm. Whereas FE and FD estimates for firms' drug portfolio and umbrella brand size are very similar, market share estimates differ strongly, pointing at simultaneity bias. In order to eliminate the simultaneity bias and verify the robustness of the results, I reestimate the specification using the DIFF GMM estimator. First-differenced market shares are instrumented with lagged levels. Like the FE and FD estimates, GMM estimates show that generic-to-brand price ratios are about 0.3 percentage points lower (0.2 percentage points higher) with each (umbrella branded) drug generic firms additionally supply. Given a standard deviation of 80 (umbrella branded) drugs, I predict a net variation (reduction) in generic-to-brand price ratios of 8 percentage points. Observing per-pill price deviations on a scale of 10 percentage points and higher, these estimates are plausible. Importantly, estimates are robust to the limitation of the sample to price observations collected in the first three years after market entry, where drug portfolio and umbrella brand sizes are arguably exogenously given. The GMM estimates indicate further that the variability of generic price can also be linked to market share differences: a generic firm with a 10 percentage point higher market share has a roughly 5-6 percentage point lower generic-to-brand price ratio. Consistent with previous studies, I show that generic entry lowers generic-to-brand price ratios by roughly 2 percentage points, and I find no evidence of intermolecular competition. Package size differences are likewise not able to explain the variation in generic prices.

Overall, the study shows that the common approach to aggregate generic prices results in a loss of valuable information, as price variation at firm level is neglected. Providing evidence of economies of scope and brand recognition in the generic drug industry, the study also calls into question the assumption of Bertrand competition frequently made in the literature.

In light of the large and ever-increasing drug expenditures in the German statutory health care system[62], the German government seeks constantly to identify sources of drug cost savings. The prices of generic drugs supplied in Germany are considered to be notably higher than in neighboring countries, accounting for differences in value-added-tax rates.[63] The study shows that generic companies claim price-premia by building up umbrella brands and

[62]Drug expenditures have rapidly increased in the German statutory healthcare system over the last decade. As of 2007, drug expenditures amount to € 27.8 Bn. and make up the second largest cost factor after expenditures on hospital services. www.gesundheitspolitik.net/04_medikamente/apotheke/oeffentlich/GEK-Arzneimittelreport-2009.pdf.

[63]http://wido.de/fileadmin/wido/downloads/pdf_arzneimittel/wido_arz_pk_avr2008_0908.pdf.

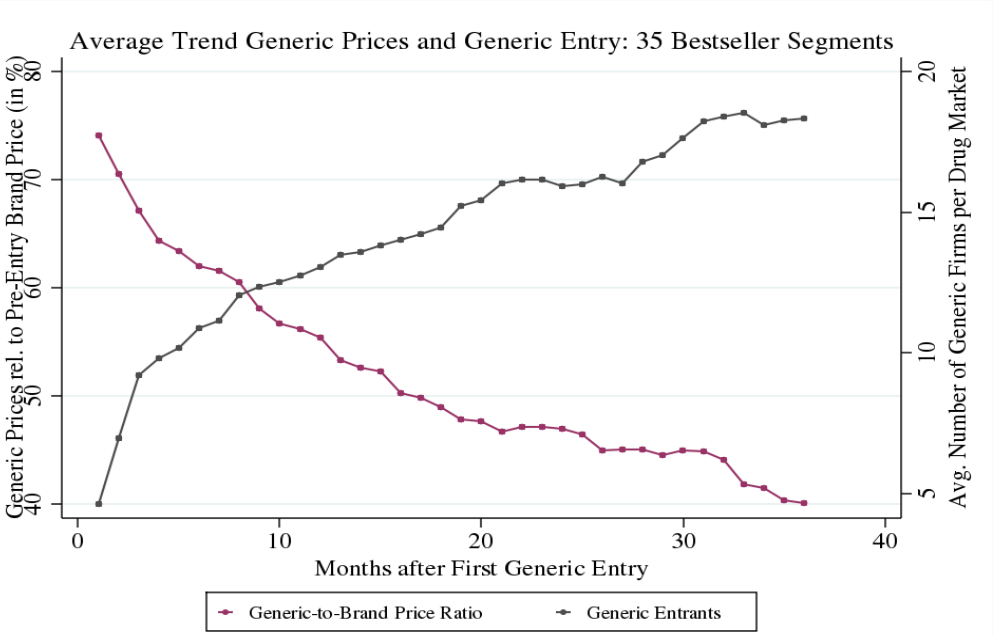
brand recognition. Brand-name markups for generic products are not necessarily desirable. Generic products carry only the international non-proprietary name of the active ingredient in the US and UK pharmaceutical market.[64] A pure INN marketing strategy for generic drug products might also be a viable and beneficial solution for Germany. If generic firms are legally restricted from building up brand reputation, generic brand premia may erode.

Similar studies on off-patent competition in other important pharmaceutical markets, in particular the U.S. pharmaceutical market, would be useful to corroborate and supplement the study's findings. Reassessing the validity of the Bertrand assumption, both empirical and theoretical analyses will provide deeper insights into the dynamics of intra-generic competition. How various aspects of product differentiation, especially generic advertising, affect generic prices remains to be investigated and opens up a new avenue of research.

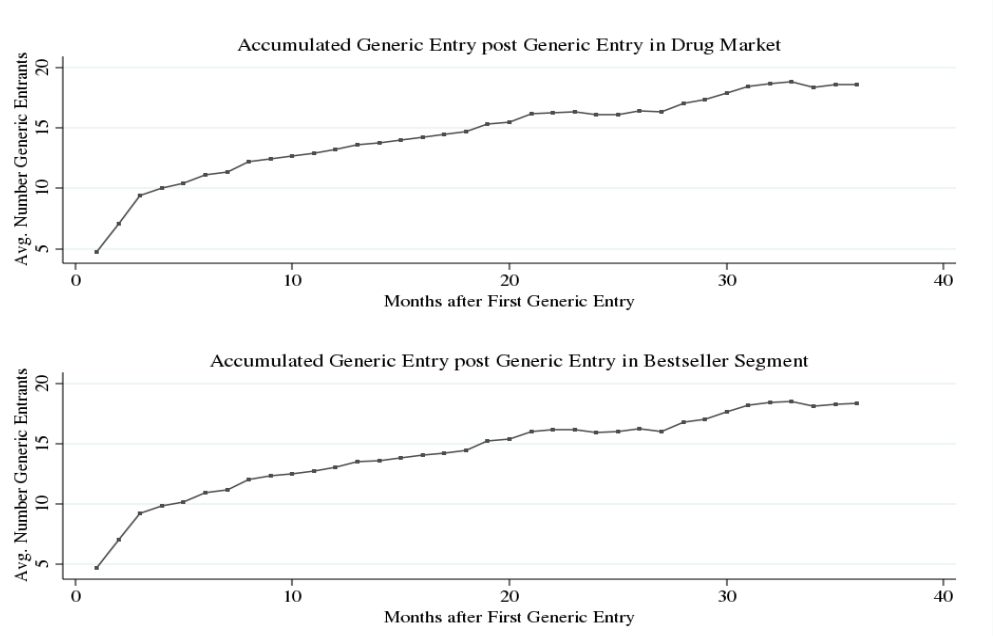
[64]Myrtha Hurtado Rivas (Global Head of Trademarks & Domain Names, Sandoz): *Trade Marks in a Generic World*, Pharmaceutical Trade Marks Group 81^{st} Group Conference, Athens, Oct 1st 2010.

3.8 Appendix 3

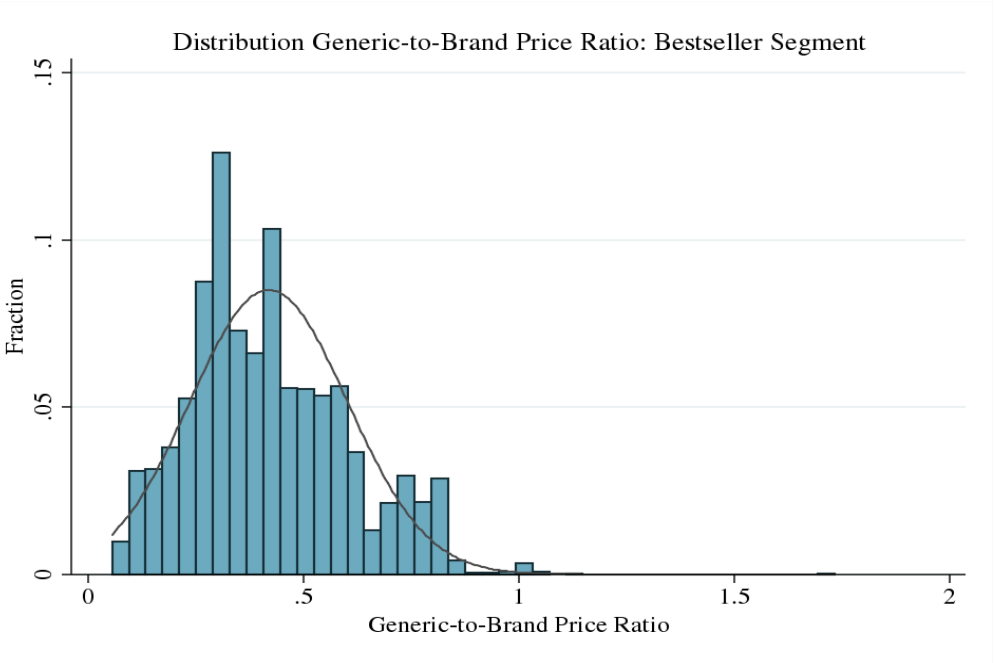
3.8.1 Overview Generic Price and Generic Entry Pattern



3.8.2 Generic Entry: Drug Market vs. Bestseller Segment



3.8.3 Distribution Generic-to-Brand Price Ratios



3.8.4 Definition of Variables: Generic Product Panel

Variable Name	Definition
Generic-to-Brand Price Ratio ($P_{g_{itm}}^{Ratio}$)	Generic firms' monthly (turnover/package size-weighted) average per-pill price for the bestselling dosage size relative to the brand price charged in the month prior to first generic entry (in %).
Generic Market Share ($M_{g_{itm}}$)	Monthly turnover share within the generic bestseller segment: fraction of pills sold by the generic manufacturer (in %).
Generic Entry	Accumulated number of generic entrants in a drug market and month.
Branded Substitutes	Number of available, on-patent drugs listed for the same therapeutic field(s) of indication (ATC2 Class.) as the drug in question.
Generic Substitutes	Number of available, off-patent generic drugs listed for the same therapeutic field(s) of indication (ATC2 Class.) as the drug in question.
Alternative Strengths	Number of other oral solid dosage sizes introduced by generic firms.
Alternative Drug Forms	Number of oral solid subtypes (oro-dispersible, chewable pills etc.) available in the same dosage size and introduced by generic firms.
Drug Portfolio Size	Number of generic products (drugs) launched by the generic firm.
Umbrella Brand Size	Number of generic products (drugs) launched by the generic firm whose tradename incorporates the (un)abbreviated corporate name.
Package Size	Monthly, turnover-weighted average package size of a generic product.
Time Trend	Count of months since first generic entry in a given drug market.
Year (2002,$\cdots$,2007)	0-1 dummy variable,=1 for all observations in 2002, $\cdots$, 2007.

3.8.5 Decomposition Standard Deviation: Generic Product Panel

Variable Name	Mean	Sd.	GxT	G	T (⌀)
Generic-to-Brand Price Ratio ($P_{g_{itm}}^{Ratio}$)	41.94	18.32	20888		
		14.87		605	
		10.75			34.53
Generic Market Share ($M_{g_{itm}}^{Ratio}$)	6.66	12.04	20888		
		10.15		605	
		4.97			34.53
Generic Entry	19.96	7.97	20888		
		7.23		605	
		2.91			34.53
Branded Substitutes	5.68	5.14	20888		
		5.00		605	
		0.73			34.53
Generic Substitutes	15.86	13.30	20888		
		14.34		605	
		0.88			34.53
Alternative Strengths	2.86	1.67	20888		
		1.68		605	
		0.34			34.53
Alternative Drug Forms	0.39	0.72	20888		
		0.79		605	
		0.17			34.53
Drug Portfolio Size	127.95	78.22	20888		
		78.51		605	
		10.90			34.53
Umbrella Brand Size	97.14	79.91	20888		
		79.65		605	
		11.69			34.53
Package Size	78.26	34.63	20888		
		37.30		605	
		7.87			34.53
Time Trend	26.75	15.35	20888		
		10.84		605	
		12.26			34.53

Notes: The within and between standard deviations may not sum up for two reasons. (1) The overall mean (mean of the panel means weighted by number of observations) is different from the mean of the panel means due to unbalanced nature of the data. (2) The reported standard deviation estimates are biased-corrected estimates which are multiplied by a factor of $\sqrt{G*T/(G*T-1)}$, and $\sqrt{G/(G-1)}$ respectively.

3.8.6 First Differences (Specification 1-3) – Coefficients

Dep.Variable: $P_{g_{itm}}^{Ratio}$	*Spec.1*	*Spec.2*	*Spec.3*
Generic Market Share ($M_{g_{itm}}$)	–	–	-0.0246
			(0.022)
Generic Entry	-1.0611***	-1.0282***	-1.0783***
	(0161)	(0.158)	(0.181)
Generic Entry^2	0.0148***	0.0144***	0.0154***
	(0.003)	(0.003)	(0.004)
Branded Substitutes	0.2579***	0.2551***	0.2536***
	(0.054)	(0.055)	(0.054)
Generic Substitutes	-0.1251	-0.0813	-0.0781
	(0.121)	(0.120)	(0.120)
Alternative Strengths	–	0.1544	0.1479
		(0.160)	(0.170)
Alternative Drug Forms	–	-0.0675	-0.0794
		(0.243)	(0.250)
Drug Portfolio Size	–	-0.3170***	-0.3136***
		(0.077)	(0.078)
Umbrella Brand Size	–	0.1881***	0.1862**
		(0.050)	(0.051)
Package Size	–	-0.0296**	-0.0290**
		(0.009)	(0.009)
Time Trend (dropped)			
Year (2002,$\cdots$,2007)	*yes*	*yes*	*yes*
Const.	-0.0080***	-0.0072***	-0.0072***
R^2	0.0269	0.0327	0.0332
F(9/14/15,67)	15.54	18.07	17.53
Prob > F	<0.001	<0.001	<0.001
G x (T-1)	20283		

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is the monthly generic-to-brand price ratio of a generic product in the bestseller segment. Standard errors robust to heteroscedasticity and autocorrelation, clustered at firm level (68 clusters), in parentheses. The reference year is 2002.

3.8.7 GMM First Differences – Robustness Check

Dep.Variable: $P_{g_{itm}}^{Ratio}$	*Restriction Data:* $P_{g_{itm}}^{Ratio}$, where $t \leq 36$ $\triangle M_{g_{itm}}$ instrumented using Lags of $M_{g_{itm}}$: *Lags (3-4)*	*Lags (4-5)*
Generic Market Share ($M_{g_{itm}}$)	-0.5234	-0.5618*
	(0.317)	(0.277)
Generic Entry	-2.0912	-2.0106**
	(0.893)	(0.805)
Generic Entry^2	0.0369	0.0352*
	(0.023)	(0.017)
Branded Substitutes	0.2711**	0.2517**
	(0.087)	(0.080)
Generic Substitutes	0.0054	0.0426
	(0.145)	(0.146)
Alternative Strengths	0.0250	-0.0026
	(0.579)	(0.613)
Alternative Drug Forms	-0.2584	-0.1319
	(0.607)	(0.564)
Drug Portfolio Size	-0.3394*	-0.3216*
	(0.155)	(0.139)
Umbrella Brand Size	0.2145*	0.2059*
	(0.101)	(0.088)
Package Size	-0.0191	-0.0175
	(0.011)	(0.010)
Time Trend	-0.7680***	-0.7829***
	(0.037)	(0.038)
Year (2002,$\cdots$,2007)	*yes*	*yes*
Arellano-Bond test AR(1)	0.047	0.038
Arellano-Bond test AR(2)	0.122	0.139
Arellano-Bond test AR(3)	0.491	0.499
Hansen test: chi2(1)	0.117	0.335
Instruments (Overid. Restr.)	17 (1)	17 (1)
Wald chi2(16)	7199.40	7406.11
Prob > chi2	<0.001	<0.001
G x T^*	16992	

* p<0.05, ** p<0.01, *** p<0.001

Notes: An observation in the regression is the monthly generic-to-brand price ratio of a generic product in the bestseller segment. Two-step standard errors robust to heteroscedasticity and autocorrelation, clustered at firm level (68 clusters), in parentheses. The Windmeijer correction for two-step standard errors has been employed. The reference year is 2002. DIFF GMM estimates are presented for Specification 3.

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