Reference pricing and cost-sharing: Evidence on anti-epileptics *

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Abstract

This paper evaluates the impact of reference pricing on prices, copayments, and overall expenses in the market for off-patent pharmaceuticals. We use data of the German market for anti-epileptics for the years 2007 to 2010 at the package level and at the aggregate level (by active agent). We exploit that the reference price has been adjusted during that time span in some of the active agents but not in others in a difference-in-differences framework. At the package level, we find that lower reference prices induce price reductions both for brand-name drugs and for generics, but lead to higher copayments, especially for brand-name drugs due to the copayment structure when reference pricing is in place.

To analyze overall effects of these changes, we aggregate the package level data at the active agent level. We find that stricter reference prices lead to savings for

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health insurances which come from three sources. First, due to lower prices revenues of pharmaceutical companies go down. Second, we also find evidence that lower reference prices lead to substitution from higher priced brand-name products to cheaper generics. Third, via lower reference prices, the health insurers shift a share of the costs toward direct payments by patients (in the form of higher copayments). The latter and its effects should be considered by regulators before adjusting the reference price.

Keywords: Pharmaceuticals; drugs; regulation; reference pricing; cost-sharing; anti-epileptics

JEL Classification: I11, I18, L65, L15

1 Introduction

Medical expenditures have been increasing for decades and a number of policy debates have centered around cost containment policies while still preserving incentives for providing high quality and innovation. This applies, in particular, to pharmaceutical markets which are also characterized by an extensive health insurance coverage in many countries.

Reference pricing has become an established tool to control pharmaceutical expenditures for off-patent drugs (Kanavos, 2001). The basic idea of reference pricing is that, while firms are free in their price setting, the maximal amount covered by the health plan is limited to a certain threshold. The potentially positive difference between the price and the reference price has to be covered out-of-pocket, in addition to other possible copayments. This policy aims at increasing the price elastic behavior of insured individuals, fostering substitution by cheaper drugs and thus increasing competition across pharmaceutical firms.[1] Our study empirically analyzes whether the instrument of reference prices is effective in contributing to these goals, namely in increasing price competition in the market and in containing cost for the health insurers.

Existing studies show that reference pricing can lead to more intense price competition and lower prices, which are the main aims of reference prices. On average, prices decrease after the introduction of reference pricing, for example, for Germany (Pavcnik, 2002), Denmark (Kaiser et al., 2014) or Norway (Brekke et al., 2009, 2011). However, the

[1]The famous RAND Health Insurance Experiment (HIE) with 2,000 US families conducted over the years 1971-1986 showed that the demand for pharmaceuticals behaves price-elastic: individuals reduce health care expenditure when co-insurance rates increase (Gruber, 2006).

magnitude of lowering the reference price on prices seems rather modest. For example, Augurzky et al. (2009) report that a downward adjustment of the reference price by 1 percent leads, on average, to a price decrease of about 0.3 percent.

In this study we focus on the German market for anti-epileptic drugs. This allows us to estimate the effects of reference prices in a market where a reference pricing system has been long established. Moreover, in contrast to most existing studies we also study effects beyond drug pricing, such as patients' copayments or the overall effects on spending by public health insurances. While the price reducing effect of reference pricing at a package level is well understood, the aggregate effects on, in particular, cost shifting and cost containment are less understood. Therefore, our study focuses explicitly on aggregate effects of reference pricing. How large are the savings by the health insurance due to reference pricing? And to what extent do come these savings from lower firm revenues and to what extend do they come from higher out-of-pocket payments by patients?

We use quarterly data for all anti-epileptic drugs provided by IMS Health for the years 2007 to 2010, which we merge with information on reference prices. Epileptics is one of the most common chronic diseases affecting 0.5-1 percent of the German population where annual sales of around €740 mio in 2009 range among the top 10 drug classes (Schwabe, 2010). Anti-epileptics help to control and reduce seizures and are the preferred way of treatment.

We observe price as well as the total quantities at package level that are sold to patients covered by the statutory health insurance (comprising around 86 percent of the German population in 2016).[2] Our identification strategy relies on a difference-in-differences analysis where we exploit the fact that reference prices have been changed in three out of five active agents under consideration.

Our empirical analysis comes in two parts. First, we analyze the effects at the package level to investigate the effects on prices sold. In a second step, we aggregate our data at the level of the active agent. This allows to estimate the overall effects of reduced reference prices on spending by the health insurances and on firm revenues. Importantly, this analysis also allows us to investigate how the total out-of-pocket-payments by patients are affected taking substitution behavior between higher-priced brand-name products and lower-priced generics into account. From a policy perspective it is of interest to explore to what extent reference prices shift the costs between health insurances

[2]Source: https://www.vdek.com/presse/daten/b_versicherte.html

and consumers so that consumers are left to carry a larger share of the price (see also Brekke et al., 2011) and to what extent it leads to overall cost savings for the health care system.

At the package level we report price reductions of about 0.9 percent for brand-name drugs and of about 0.5 percent for generic drugs for a reference price reduction of one percent. This is slightly higher than in earlier findings. Copayments for brand-name drugs increase by about 1.48 percent. They do not increase for non-exempt generic drugs but the probability that a generic drug is exempt from copayments (price below a certain exemption level) shrinks.

At the aggregate level, we show that a one percent reference price reduction leads to significant savings for the health insurers of around 0.3 percent. In particular, payments towards brand producers decrease substantially by around 2.5 percent. Payments to generic producers also decrease, though to a smaller extent (around 0.2 percent). This can be explained by substitution effects from brand-name to generic drugs which we observe in our data. Our analysis also permits to investigate the sources of these cost savings. Here, we find that firm revenues decrease, in particular, of brand-name firms. However, we also observe that a significant part of health insurance cost savings comes from higher consumer payments. A one percent reduction in the reference price leads to 2.2 percent higher out-of pocket payments for generics. Thus, our analysis suggests that a large part of the savings are not derived from total cost reductions, but can rather be attributed to cost-shifting to patients.

Our paper contributes to the empirical literature on reference pricing. In contrast to existing studies we focus on the effects of reference pricing in a market where such a system has been in place for a long time. The two closest paper to our empirical analysis are the studies by Brekke et al. (2011) and Herr and Suppliet (2017).

Brekke et al. (2011) evaluates the the switch from a price-cap regulation to internal reference pricing in Norway in 2003. They find significant negative effects on average prices and brand-name market shares, suggesting significant cost-savings for the health care system. They estimate an average copayment reduction of about 12 percent which stems both price reduction for generic and brand name drugs and from substitution to cheaper generic drugs. In contrast, in our study we evaluate the effects of further reference price reductions in a system where reference prices have been in place for 30 years. Our results suggest that the effects of ever lower reference prices can be quite different from the introduction of a reference price. In particular, we find that price reductions are only

modest, and hence, the main implication is that cost savings by health insurances can be attributed to cost-shifting to patients via higher out-of-pocket payments.

Our study is complementary to Herr and Suppliet (2017) who examine the effects of introducing copayment exemption levels on prices in the German market. In contrast, in this paper we analyze firms' responses and the implications for consumers if reference prices are reduced when copayment exemption levels, which are defined and adjusted relative to the reference price, have already been implemented. Besides showing differentiated price effects for generics and brand-name drugs, Herr and Suppliet (2017) present evidence that also price elasticity differs between these two drug types. Thus, we also differentiate between brand-name and generic drugs and look at them separately.

Augurzky et al. (2009) analyze the effects of repeated adjustments of the reference price for the German market. However, in contrast to this study they do not consider the effects on different firm types. Moreover, they do not examine the effects on copayments which is essential to fully understand the implications of those policies. Additionally, we also examine the interaction with a different regulatory scheme (copayment exemptions).

The rest of the paper is organized as follows. In Section 2 we describe the institutional framework for the German market while in Section 3 we present our data set. Section 4 describes the estimation strategy and Section 5 presents our main empirical findings. Section 6 concludes.

2 Institutional background

In Germany, reference pricing for off-patent drugs has been in place since 1989. In reference price markets, patients need to copay the absolute difference between the drug's price and the reference price if the drug's price exceeds it. This leads to the following copayment structure. Since January 2004, consumers have been paying 10 percent of the pharmacy's selling price or the reference price within the minimum of €5 and the maximum of €10. The positive difference between the price and the reference price is added to this, if applicable.[3]

[3]However, low-income insureds with health care costs exceeding an household-income related threshold (1-2 percent) and insureds younger than 18 years old do not need to copay for social reasons.

First, a reference price group is defined by the Federal Joint Committee (Gemeinsamer Bundesausschuss). It most often comprises drugs with the same or similar active agents (e. g., originals and their generics).[4] The reference price is set by the Federal Association of Statutory Health Insurance Funds (FASHI) for each reference price group. After the normalization of prices according to package size, dosage form, and concentration, the reference price has to lie within the smallest 30 percent of the price interval. In addition, at least 20 percent of all packages and of all prescriptions must be available for prices equal to or below the reference price at the time of implementation. Products with a market share of less than 1 percent are not considered. The FASHI reviews reference prices irregularly and adjusts them, if identified to be necessary, e.g. due to generic entry, based on the prices around 12 months before the revision. Revisions typically cannot be foreseen by firms and are announced one quarter before the adjustment.

Since 2006, the FASHI has also been able to introduce copayment exemption levels (CEL) in selected groups of reference priced drugs. In general, the maximum price of an exempt drug lies 30 percent below the respective reference price (rp). If firms decrease the price below this exemption level, consumers do not need to copay for the drug. Pricing strategies in groups with CELs are very different, and the introduction of such a CEL constitutes a structural break (Herr and Suppliet, 2017). Basically, this policy is similar to the introduction of a tiered copayment system where firms can strategically decide on the copayment (either 0, general, or above reference price). For two illustrative examples of the copayment scheme compare Figure 2 in the Appendix. The figure also makes clear that reductions in the reference price have two effects. If the price is not significantly adjusted, copayments are likely to increase. The price either lies above the new reference price for high price drugs or above the new exemption level for low price drugs when it was below before the respective threshold before. It is an empirical question by how much prices are reduced relative to the reduction in the reference price and whether consumers substitute to cheaper drugs to circumvent higher copayments. The overall effects on copayments are not clear a priori and will be analyzed in the following.

[4]Since 2011, on-patent drugs may also be grouped into reference price groups if they cannot prove significant advantages compared to off-patent drugs. Furthermore, in Germany it is possible that drugs with similar (but not the same) chemical compounds are grouped in one group (level 2) or with similar therapeutic effects or combinations of active agents (level 3).

Table 1: Treatment and control group and timing of the adjustments

active agent	rp adjusted in	rp adjusted in	market share	N	N firms
treatment group					
gabapentin	Q3-2008	Q2-2010	.52	5,707	34
lamotrigine*	-	Q2-2010	.19	2,322	38
valproate	Q3-2008	Q2-2010	.20	2,913	24
control group					
carbamazepine	-	-	.19	4,228	27
primidone	-	-	.02	144	3

market share measured as revenue per active agent relative to revenues of the five active agents per quarter. Data: 2007-2010
* enters sample in Q1-2009, 2 quarters after rp has been introduced.

3 Data

We observe quarterly data at the package level for all anti-epileptic drugs provided by IMS Health (IMS Health, 2012) for the years 2007 to 2010.[5] The data contains information on prices (ex-factory and retail) per defined daily dose (DDD), quantities sold in DDD, active agent (following the Anatomical Therapeutic Chemical (ATC) classification system by the WHO we look at the chemical substance, fifth level), package characteristics and indicators whether there had been a reference price or a CEL defined.

Seven of the 21 active agents face reference pricing out of which five also face co-payment exemption levels (carbamazepine, gabapentin, lamotrigine, primidone, valproate). We drop those observations without a CEL to not confound the effects of reference pricing and copayment exemptions (336 observations of clonazepam + 144 observations of phenytoin).

The data has been augmented with public information on reference prices (DIMDI, 2011) and product-specific co-payment exemption levels (GKV-Spitzenverband, 2011), where applicable (compare Herr and Suppliet (2017)). A reference price group is defined by grouping four variables: active agent, strength, package size, and dosage form. Copayments are calculated according to the above explained rules, which hold for all members of the statutory health insurance who are not exempt from co-payments.

In three out of the five active agents the reference price was adjusted between Q1-2007 and Q4-2010. Table 1 shows that reference price adjustments took place in quarters

[5]This data is also used by Herr and Suppliet (2017) who study the effects of the introduction of co-payment exemptions on pricing behavior and demand.

Q3-2008 and Q2-2010 when, to our knowledge, no other regulation had been changed. Lamotrigine enters the sample in Q1-2009. On average the reference price decreases by around €22.70, if any.[6] However, the distribution is very skewed. 50% of the decreases lie below €6 and 25% below €3.

4 Estimation Strategy

4.1 Effects at package level, all anti-epileptic drugs with CEL

We exploit the fact that the reference price has not been adjusted in two of the five active agents in a difference-in-differences framework. The idea behind this method is that the non-treated groups serve as a control group capturing all other influences on the variables of interest except of the change in the reference price. For this, we need to assure that the control group behaved similar before the change. Since the reference price has only been adjusted once for lamotrigine in Q2-2010, we drop all observations of this agent from before 2009 to not interfere control and treatment groups.

Figure 1 presents logged mean prices over time for the three treated active agents and for the control group comprising the other two non-treated agents with reference prices and a CEL. All treatment groups and the control group show similar pre-policy price trends. We also empirically test for parallel price trends in the treatment and the control group. Following Pavcnik (2002) and Herr and Suppliet (2017), we regress logged prices prior to the treatment on time trends (*Quarter*), on the interaction of time trends and treatment groups (*Quarter* $\times$ *Treat*) and on product fixed effects. We split the 16 quarters in two sub-samples and test whether trends were parallel (1) before the first adjustment in Q3-2008 and (2) between the first and the second adjustment (between Q3-2008 and Q2-2010) . The results for all variables at package level, except for the probability to be exempt, show that the interaction between the time trend and the treatment group is not significantly different from zero (Table 6 and Table 7 in the Appendix).[7] At aggregate level, there is no difference between treatment and control group in the changes of any of the outcome variables (available upon request).

Equation (1) shows that we are mainly interested in changes in the reference price while

[6] That is, by around 35% given an average reference price of €65 before the adjustment took place.

[7] The probability to be exempt is different though, since this depends highly on relative price and reference price levels and not on trends.

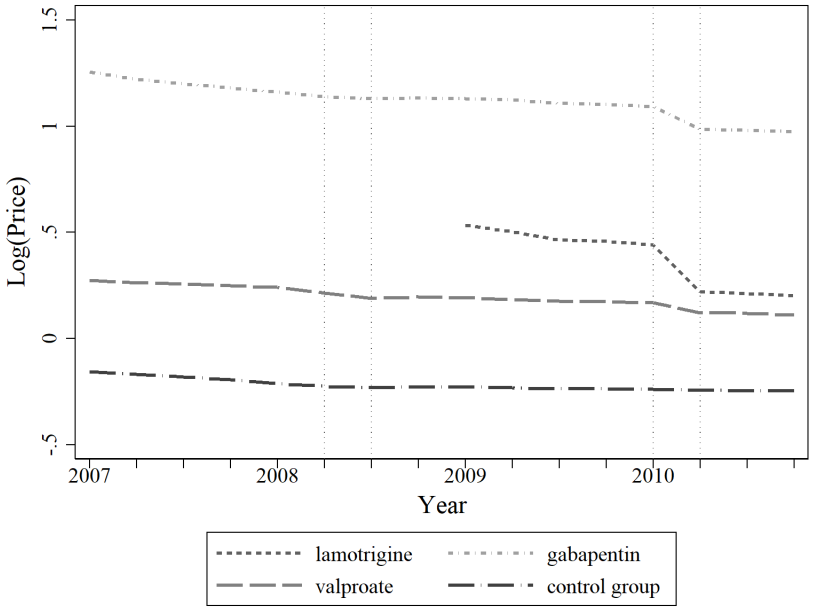

Figure 1: Mean logged prices by treatment quarter across active agents. The dash-dotted line shows the mean logged prices of the control group. Data Source: FASHI. Own calculations.

controlling for time fixed effects and all time-independent unobserved effects, such as price level or quality, using package fixed effects.

$$\ln(y)_{it} = \ln(refprice)_{i,t} + \tau_t + \alpha_i \tag{1}$$

where the dependent variable y varies: (1) ex-factory price per DDD, (2) pharmacy retail price per DDD (including taxes, pharmacists' reimbursment), (3) co-payments per DDD (if non-zero), and (4) the probability to be exempt (linear probability model). Standard errors are clustered at the reference price group level (same active agent, form of administration, package size, and concentration).

In our analysis, we differentiate between two sub-samples: brand-name drugs (former originals and parallel imports) and generics since, following the literature, we postulate different effects on these two types of drugs. We estimate the model for the three samples, i) all drugs, ii) only generics, iii) only brand-name drugs, separately.

In a second step, we control for the fact that the treatment itself may be endogenous, which would invalidate the difference-in-difference analysis. Reference prices might be correlated with time-varying unobservable factors captured by the error term which may also systematically influence our dependent variables. Thus, we use two instrumental variables and only exploit the variation in the reference price which can be explained by these exogenous factors (Herr and Suppliet, 2017).

First, we argue that if the regulator focuses on one active agent, resources do not allow to focus on the others simultaneously. That is why if a reference price in other active agents is adjusted, e.g. due to generic entry, the reference price in the group of interest is probably not. Thus, these the reference price in other active agents should be negatively correlated with the own reference price. Furthermore, since substitution across anti-epileptics is difficult and mostly dependent on medical conditions as opposed to prices or copayments, we argue that this instrument, the average reference price per defined daily dose (ddd) in all other active agents, is valid. Second, with a similar reasoning, we use the average number of products in all other reference price groups, where the correlation should be positive since an increase in products in the other reference price groups is likely to lead to a decrease in their reference price. However, the two instruments are highly correlated with the active agent dummies and with each other. For example, entry may occur in markets where the reference price is higher. We face the problem of perfect predictions in the first stage and extremely high F-values. Thus,

we decided not to use both in the final regression. Instead, we construct a new instrument. We regress the first instrument, the *average reference price in all other reference price groups*, on the second instrument, the *number of products in all other reference price groups*, quarter dummies, and active agent dummies. The predicted values are very similar to the original variable with mean 0.81 and standard deviation of 0.37 instead of 0.39. This instrument is stronger than the average reference price in other groups alone without causing problems of multicolinearity in the first stage. For the instrumental variables regressions, we use $STATA14$ and apply $xtivreg2$ by Schaffer (2010).

4.2 Effects at aggregate level, all anti-apileptic drugs with reference price

In the second part of the analysis, we collapse the package level data at active agent level j overall and by drug type. We estimate the following model for the three samples separately.

$$\ln(y)_{jnt} = \ln(refprice)_{jnt} + \tau_t + \alpha_j \tag{2}$$

where $n \in$ {all,generic,brand-name} and the dependent variable y varies: (1) total firms' revenues (ex-factory price times quantities sold measured in DDD), (2) quantities sold, (3) total co-payments, (4) total expenses of the statutory health insurance, and (5) overall expenses (which is (3)+(4)). For the instrumental variables regressions, we use $STATA14$ and apply $ivreg2$ by Baum et al. (2002) with the same predicted instrument for the reference price as before and with active agent fixed effects. Since the number of observations is reduced to 72, we bootstrap the standard errors in a robustness check.[8]

5 Descriptive statistics and results

5.1 Descriptive statistics

Table 2 presents the descriptive statistics by drug type at package level. It becomes clear that brand-name drugs are more expensive, less often exempt and induce higher copayments than generic drugs. The average copayment lies below €5 since 63 percent of the packages are exempt (zero copayments). The reference price and the CEL are

[8]The OLS results present bootstrapped standard errors, the 2SLS results not yet.

Table 2: Descriptive statistics at package level by drug type and total

	Total		Generic		Brand-name	
	mean	sd	mean	sd	mean	sd
Retail price	30.15	35.34	27.92	31.27	42.56	50.76
Pharmacy price	49.11	45.83	46.21	40.54	65.23	65.87
Ref. price	65.70	65.66	65.36	65.40	67.59	67.06
Exemption level	47.16	43.44	46.82	43.14	49.04	45.06
Copayment	3.80	5.95	3.02	3.61	8.11	11.77
Exempt $= 1$	0.63	0.48	0.71	0.45	0.16	0.37
N	15,145		12,839		2,306	

Data: Pharmascope, IMS Health, Q1-2007 to Q4-2010. At package level.
Own calculations.

Table 3: Descriptive statistics at active agent level by active agent

active agent	gabapentin		lamotrigine		valproate		carbamazepine		primidone	
variable	mean	sd	mean	sd	mean	sd	mean	sd	mean	sd
Firm revenues [€ 1000]	14315	649	5514	1.163	5577	245	5220	590	512	30
Quantities [1000 ddd]	8340	977	6740	538	10651	583	15126	1.053	1283	54
Copayments [€ 1000]	862	662	785	171	1344	206	1077	428	210	45
Expenses SHI [€ 1000]	21111	1423	8137	1.604	8674	477	8945	646	880	45
Total Expenses [€ 1000]	21973	997	8922	1438	10018	379	10022	1043	1089	62
N	16		8		16		16		16	

Data: Pharmascope, IMS Health, Q1-2007 to Q4-2010. At active agent level. Own calculations.
total firms' revenues = ex-factory price times quantities sold measured in DDD,
total expenses of the SHI = pharmacy sales price times quantities sold - total copayments,
total expenses = expenses of the SHI + copayments

very similar across drug types, on average. In our analysis, we control for time invariant differences across packages and active agents by using package specific fixed effects.

Table 3 shows the descriptive statistics of the aggregated outcomes of interest for the five active agents with reference prices and copayment exemption levels where the latter two agents comprise the control group.

5.2 Effects of a change in the reference price at package level

Table 4 shows the results of the 2SLS estimation where we control for potential endogeneity of the reference price with package fixed effects. The package level effects of reference price reductions differ by brand status. Brand-name drugs' prices decrease by around .6 (retail price) to .9 percent (sales price) while generic prices decrease by .3 percent, if the reference price is reduced by 1 percent. Furthermore, co-payments increase

Table 4: Effect of decreases in the reference price at package level, 2SLS

$\ln(y)$	(1) Ex-factory p/ddd	(2) Retail p/ddd	(3) Copay/ddd	(4) Pr(Exempt=1)
Total				
ln(ref. price)	0.501***	0.316***	-0.592***	0.788***
	(7.85)	(12.10)	(-2.76)	(6.74)
F	40.82	165.7	15.13	76.01
N	15314	15314	8758	15314
F-value excl rest	22.84	22.84	8.091	22.84
Generics				
ln(ref. price)	0.462***	0.287***	-0.331	0.879***
	(7.05)	(9.75)	(-1.32)	(6.99)
F	38.05	184.5	11.58	80.09
N	12980	12980	6604	12980
F-value excl rest	18.42	18.42	5.376	18.42
Brand-name				
ln(ref. price)	0.883***	0.608***	-1.477***	-0.456**
	(6.00)	(7.87)	(-5.09)	(-2.09)
F	338.9	444.2	15.64	3.284
N	2334	2334	2154	2334
F-value excl rest	108.1	108.1	111.0	108.1

Data: Pharmascope, IMS Health, 2007-2010. Own calculations. t statistics in parentheses

* $p < .1$, ** $p < .05$, *** $p < .01$

ln(ref. price) instrumented with predicted ln(av. reference price in other active agents), using ln(av. # products in other active agents)

In (4) we drop exempt packages, since $\ln(0)$ is not defined.

for consumers of brand-name drugs by 1.5 percent and do not change for non-exempt generic drugs. Finally, the probability that a drug package is actually exempt (price below CEL) decreases for generics by .9 percentage points but increases for brand-name drugs by 0.5 percentage points due to price decreases (at a low level of 16 percent).

The linear regression results presented in Table 8 in the Appendix are very similar except that the probability that brand-name drugs are exempt does not significantly change.

Table 5: Effect of decreases in the reference price at active agent level, 2SLS

$\ln(y)$	(1) Firm revenues	(2) Quantities	(3) Copay	(4) Expenses SHI	(5) Total expenses
Total					
ln(ref. price)	0.157*	-0.403***	-2.281***	0.265***	0.0578
	(1.68)	(-4.75)	(-5.42)	(3.62)	(0.67)
F	863.5	630.5	16.52	1299.4	843.9
N	72	72	72	72	72
F-value excl rest	37.30	37.30	37.30	37.30	37.30
Generics					
ln(ref. price)	0.0197	-0.458***	-3.106***	0.168*	-0.0632
	(0.16)	(-4.35)	(-6.34)	(1.65)	(-0.56)
F	507.4	375.8	10.21	660.8	478.2
N	72	72	72	72	72
F-value excl rest	47.90	47.90	47.90	47.90	47.90
Brand-name					
ln(ref. price)	2.424***	1.125***	0.947	2.532***	2.236***
	(6.52)	(2.68)	(1.49)	(5.86)	(5.74)
F	11.70	30.61	4.098	9.795	11.09
N	56	56	56	56	56
F-value excl rest	25.74	25.74	25.74	25.74	25.74

Data: Pharmascope, IMS Health, 2007-2010. Aggregated at active agent level.

Own calculations. *t* statistics in parentheses

ln(ref. price) instrumented with predicted ln(av. reference price in other active agents), using ln(av. # products in other active agents)

5.3 Effects of change in reference price at active agent level

At the aggregate level, Table 5 shows the results of the instrumental variable regression.[9] While generic drugs mainly explain the increase in the aggregate co-payments when the reference price is decreased, brand-name drugs contribute most to the overall decrease in expenses of the health insurances, the firms' revenues and the sales. This is due to the fact that the brand-name drugs' co-payments increase if prices are not sufficiently much adjusted downwards, especially, if after the decrease, the price exceeds the new reference price. This, in turn, incentivizes substitution to cheaper generic drugs, decreasing quantities sold and revenues of brand-name firms. Since we also show that generic drugs' aggregate sales increase significantly while brand-name drugs' sales decrease, some patients, probably the new consumers of the respective active agents, may prefer to start with these generic drugs (overall sales increase by .4 percent if the reference price is reduced by 1 percent). Although expenses for brand-name drugs decrease by 2.2 percent, overall expenses in this subsample of anti-epileptics do not change. Thus, the lower expenses of the SHI are driven by lower revenues of the brand-name firms and higher sales and total copayments for generics. From the package level analysis we know that prices decrease and, at the same time, the probability for prices to lie below the co-payment exemption level decrease. The former explains the gains by the SHI where the letter, combined with the increase in sales of generics, explain the higher copayments.

To conclude, we know that decreasing reference prices indeed reduces prices and expenses of the SHI. However, this may have countervailing effects on copayments which should be considered upfront. The effects on innovation incentives are not important in this setup since we only look at off-patent drugs.

5.4 Robustness

At aggregate level, we tried to bootstrap the standard errors also for the 2SLS estimation. However, the more replications we tried, the higher the standard errors. With 5000 replications, only one variable was significantly different from zero, although the coefficients are quite high. Since we believe that there is some mistake, we do not present these results. That is to be done.

We also weigh the aggregate observations with the underlying number of packages per

[9] Table 9 presents the linear regression in the Appendix with bootstrapped standard errors based on 5,000 replications.

active agents. Results of the 2SLS estimation differ only slightly and are presented in Table 10 in the Appendix.

Furthermore, we realized today that primidone is just a reserve drug due to severe side effects. That is why we will exclude this small active agent (144 observations) in the future. A first run shows that the estimates and their precision only change slightly (second digit after comma, not presented).

Dropping the control group (simple before-after) works well in both regressions (coefficients show same signs and similar magnitude, if significant) but leads to low F-values in the first stage in the sample with generics only for both, the package level and the active agent level (not presented).

6 Conclusion

We explore the effects of reference price adjustments on competition and welfare in the German market for anti-epileptics for the years 2007 to 2010. We separate effects at the package level and at the aggregate level. At package level, we find that prices of both brand-name and generic drugs decrease, but only mildly, if the reference price is reduced. Furthermore, copayments for brand-name drugs increase. For generics, the probability that the drug is exempt from copayments decreases which increases overall copayments.

At the aggregate active agent level, revenues decrease for both firm types, where the decrease is most pronounced for brand-name drugs because here, both the price and quantity decreases. For generics the effect is weaker, because our data indicate significant substitution to cheaper generic drugs, so the total consumption for generic drugs increases, partly offsetting the negative price effect. The most interesting result from a policy perspective is the shift from expenses of the Statuary Health Insurance to aggregate consumer copayments, especially for generics where total expenses remain constant, although expenses for brand-name drugs shrink.

We can draw several policy conclusions from our analysis. First, as already confirmed in the existing literature, reference pricing helps to reduce health care expenditures by reducing prices. However, the effectiveness of this measure seems limited as a reference price reduction of 1 percent leads on average to a price reduction of around 0.5 percent. Second, policy makers should be aware that reference pricing may not only lead

to lower health care expenditures, but also has an effect on how costs are divided among the health care insurances and the consumers. On the one hand, this larger cost-sharing may lead to lower expenditures for the paying public and to a more price-elastic, and thus more efficient, behavior by the insureds. On the other hand, sufficiently high cost-sharing amounts can lead individuals to avoid medical care which is actually necessary to their health, substitute drug use by more costly doctor visits and/or impose a substantial financial burden. For Germany, the latter issue is solved by income-related out-of-pocket-limits as Gruber (2006) suggests when summarizing the results of the RAND Health Insurance Experiment. However, since in Germany reference price groups may comprise different active agents which are chemically similar or which even only have similar therapeutic outcomes, the consumers may perceive sufficiently high differences in quality or difficulties to substitute from one (more expensive) drug to the other.

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Table 6: Test on parallel trends of treatment and control group, OLS

	ln(retail price)		ln(sales price)	
	(1)	(2)	(3)	(4)
	Q1 2007- Q2 2008	Q3 2008- Q1 2010	Q1 2007- Q2 2008	Q3 2008- Q1 2010
quarter	-0.012***	0.004	-0.011***	0.009***
	(0.002)	(0.005)	(0.001)	(0.003)
$quarter^2$	-0.001**	-0.000	-0.000	-0.001***
	(0.000)	(0.000)	(0.000)	(0.000)
quarter×treat	-0.005	-0.007	-0.004**	-0.004
	(0.004)	(0.011)	(0.002)	(0.006)
$(quarter \times treat)^2$	0.000	-0.000	0.000	-0.000
	(0.001)	(0.001)	(0.000)	(0.000)
Constant	-0.131***	-0.271***	0.574***	0.460***
	(0.004)	(0.037)	(0.002)	(0.016)
N	4687	6732	4687	6732
R^2	0.337	0.103	0.504	0.158

Test on differences in price trends (quarter) between general trend and trend of the treatment group (quarter × treat) for the two treatments in Q3-2008 and Q2-2010 separately.
Standard errors in parentheses. * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

A Appendix

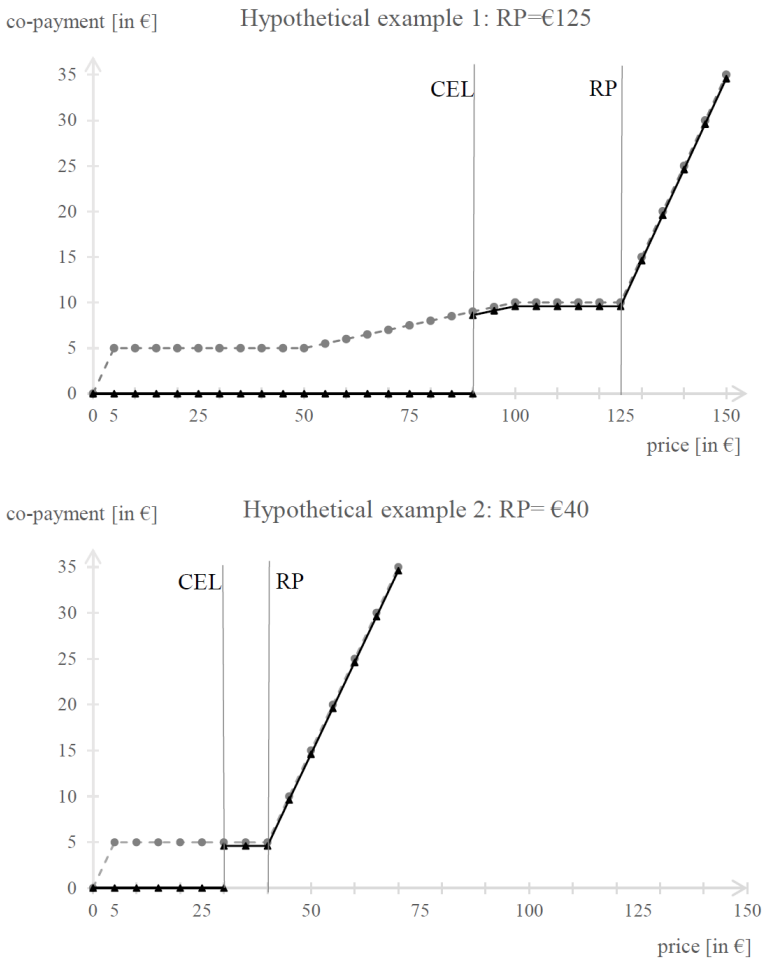

Figure 2: Copayments per product by price before (dashed line) and after (solid line) the introduction of a CEL (at $\approx$ 70% of RP). Source: Figure 1, (Herr and Suppliet, 2017). Two hypothetical examples with different levels of reference prices (€125 and €40). In general, drug copayments in Germany are defined as 10 percent of the pharmacy's selling price (or the reference price (RP) if the price lies above RP) with a minimum of €5 and a maximum of €10 plus the absolute difference to the RP, if applicable. If $p \leq CEL$, the copayment is 0.

Table 7: Test on parallel trends of treatment and control group, OLS

	(1) Q1 2007- Q2 2008 log(copay per ddd)	(2) Q3 2008- Q1 2010 log(copay per ddd)	(3) Q1 2007- Q2 2008 Prob(Exempt)	(4) Q3 2008- Q1 2010 Prob(Exempt)
quarter	-0.006***	0.017	-0.005**	0.139***
	(0.002)	(0.012)	(0.002)	(0.023)
$quarter^2$	-0.002***	-0.001	0.001**	-0.008***
	(0.000)	(0.001)	(0.001)	(0.001)
quarter×treat	0.001	-0.010	-0.007*	0.514***
	(0.004)	(0.012)	(0.004)	(0.042)
$(quarter \times treat)^2$	-0.000	0.000	0.001	-0.025***
	(0.001)	(0.001)	(0.001)	(0.002)
Constant	-1.384***	-1.381***	0.789***	-1.697***
	(0.004)	(0.021)	(0.002)	(0.124)
N	2847	3247	4687	6732
R^2	0.306	0.025	0.018	0.198

Standard errors in parentheses

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table 8: Effect of decreases in the reference price at package level, OLS

	(1)	(2)	(3)	(4)
$\ln(y)$	Ex-factory p/ddd	Retail p/ddd	Copay/ddd	Pr(Exempt=1)
Total				
ln(ref. price)	0.428***	0.344***	-0.184**	0.720***
	(8.75)	(17.84)	(-2.14)	(7.68)
R^2	0.437	0.563	0.0507	0.428
F	38.46	192.3	14.15	72.86
N	15314	15314	8827	15314
Generics				
ln(ref. price)	0.408***	0.322***	-0.0205	0.767***
	(7.82)	(13.98)	(-0.39)	(7.43)
R^2	0.441	0.576	0.0186	0.468
F	33.36	191.6	10.35	82.94
N	12980	12980	6672	12980
Brand-name				
ln(ref. price)	0.664***	0.602***	-0.934***	0.0743
	(6.34)	(7.49)	(-3.62)	(0.70)
R^2	0.453	0.585	0.240	0.150
F	293.9	393.3	11.32	3.038
N	2334	2334	2155	2334

Data: Pharmascope, IMS Health, 2007-2010. Own calculations. *t* statistics in parentheses

* $p < .1$, ** $p < .05$, *** $p < .01$

Table 9: Effect of decreases in the reference price at active agent level, OLS

	(1)	(2)	(3)	(4)	(5)
$\ln(y)$	Firm revenues	Quantities	Copay	Expenses SHI	Total expenses
Total					
ln(ref. price)	0.284**	-0.290***	-1.920***	0.371***	0.173
	(2.08)	(-3.85)	(-2.61)	(4.33)	(1.50)
r2	0.997	0.996	0.874	0.998	0.997
N	72	72	72	72	72
Generics					
ln(ref. price)	0.103	-0.409***	-2.845***	0.238**	0.00592
	(0.61)	(-4.16)	(-3.24)	(2.02)	(0.04)
r2	0.995	0.993	0.816	0.996	0.995
N	72	72	72	72	72
Brand-name					
ln(ref. price)	1.646***	0.303	-0.0213	1.639***	1.422***
	(3.42)	(0.52)	(-0.03)	(2.85)	(2.93)
r2	0.885	0.951	0.702	0.864	0.878
N	56	56	56	56	56

Data: Pharmascope, IMS Health, 2007-2010. Aggregated at active agent level.

Own calculations. t statistics in parentheses

* $p < .1$, ** $p < .05$, *** $p < .01$

Bootstrapped standard errors with 5,000 replications.

Table 10: Effect of decreases in the reference price at active agent level, 2SLS, weighted with no of packages

$\ln(y)$	(1) Firm revenues	(2) Quantities	(3) Copay	(4) Expenses SHI	(5) Total expenses
Total					
ln(ref. price)	0.105	-0.462***	-2.389***	0.201**	0.00834
	(0.99)	(-4.97)	(-4.82)	(2.57)	(0.09)
F	147.9	80.94	4.492	232.9	129.1
N	72	72	72	72	72
F-value excl rest	37.60	37.60	37.60	37.60	37.60
Generics					
ln(ref. price)	-0.0154	-0.490***	-3.270***	0.121	-0.0947
	(-0.13)	(-5.12)	(-5.82)	(1.35)	(-0.88)
F	143.1	72.19	4.289	211.7	128.3
N	72	72	72	72	72
F-value excl rest	55.95	55.95	55.95	55.95	55.95
Brand-name					
ln(ref. price)	3.065***	1.933***	1.402	3.344***	2.930***
	(5.72)	(3.32)	(1.46)	(5.49)	(5.25)
F	10.82	33.78	3.594	9.451	10.28
N	56	56	56	56	56
F-value excl rest	17.38	17.38	17.38	17.38	17.38
		Quarter and active agent fixed effects included			

Data: Pharmascope, IMS Health, 2007-2010. Aggregated at active agent level.

Own calculations. *t* statistics in parentheses

ln(ref. price) instrumented with predicted ln(av. reference price in other active agents),

using ln(av. # products in other active agents)

Weighted with no. of observations per active agent