Received: 20 May 2021 | Revised: 18 July 2022 | Accepted: 21 September 2022

DOI: 10.1002/hec.4627

RESEARCH ARTICLE

Health Economics WILEY

More cost-sharing, less cost? Evidence on reference price drugs

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Funding information
Deutsche Forschungsgemeinschaft, Grant/Award Number: HE 6825/2-1
Open Access funding enabled and organized by Projekt DEAL.

Abstract

This paper evaluates the causal effects of changes in reference prices (RP) on prices, copayments, and overall expenditures for off-patent pharmaceuticals. With reference pricing, firms set prices freely and the health plan covers the expenses only up to a certain threshold. We use quarterly data of the German market for anti-epileptics at the package level and at the active substance level and exploit that the RP has been adjusted in some of the active substances but not in others in a difference-in-differences framework. At the product level, we find that a lower RP reduces prices for both brand-name drugs and generics, but leads to higher copayments, especially for brand-name drugs. At the aggregate level, we find that a lower RP leads to savings for the public health insurer since revenues decrease substantially for brand-name firms and, to a lesser extent, also for generic firms. Overall expenditures (payments by the health insurer and the patients) for brand-name drugs decrease in proportion to the decrease in the RP, while the adjustment does not significantly influence overall expenditures for generics.

KEYWORDS
brand-name, cost-sharing, generics, pharmaceuticals, reference pricing

JEL CLASSIFICATION
I11, I18, L65, L15

1 | INTRODUCTION

Reference pricing has become an established tool for controlling pharmaceutical expenditures for off-patent drugs (Kanavos, 2001). With reference pricing, firms set prices freely and the health plan covers the expenses only up to a certain threshold. When choosing a high-price drug, the patient has to cover the positive difference between the price and the reference price (RP) out-of-pocket, in addition to other possible copayments.

Reference pricing aims at promoting more price-sensitive behavior of insured individuals, fostering substitution with cheaper drugs and, finally, reducing drug prices.[1] Our study of the German market for anti-epileptic drugs empirically analyzes whether a reduction of the RP contributes to these goals. The focus is, in particular, on whether lowering the RP reduces drug prices and whether it helps to contain the costs incurred by the public health insurers. One key objective is also to explore the extent to which a reduction in reference prices shifts the costs between health insurances and patients and to what extent it leads to overall cost savings for the health care system.

The extent to which patients are affected by reduced reference prices (possibly in the form of higher total copayments) depends on two effects. First, it depends on how much firms reduce prices following a RP adjustment. Existing research reports only modest price effects of RP *reductions*. For example, for the German market, Augurzky et al. (2009) report that a downward adjustment of the RP by 1% leads, on average, to a price decrease of about 0.3%. Consumer copayments may increase if the price reduction falls short of the RP reduction. Second, for total copayments at market level, it also depends on the degree to which lower reference prices induce substitution by cheaper generic drugs.

In addition to reference pricing, German patients also face a tiered copayment system. Patients face zero copayments for drugs with prices below an exemption level, while there is a positive copayment rate applied to drugs priced above the exemption level. This exemption level is set and adjusted relative to the RP. This tiered copayment system can contribute to more costs being shifted to consumers: If a decrease in the RP only induces a small change in the price, consumers may start paying copayments following the intervention.

We use quarterly data for anti-epileptic drugs for the years 2009–2010. Epilepsy is one of the most common chronic diseases affecting 0.5%–1% of the German population (Hamer et al., 2012), where annual sales of around €740 million in 2009 ranged among the top 10 drug classes (Schwabe, 2010). We observe prices and the total quantities of each single product sold to patients covered by the Statutory Health Insurance (SHI) (comprising around 73 million of the 83 million inhabitants in 2019) (GKV Spitzenverband, 2022). Our identification strategy relies on a difference-in-differences analysis where we exploit the fact that there was a change in the reference prices of three out of four active substances[2] under consideration. Our empirical analysis comes in two parts. First, we analyze the effects on prices, copayments, and the probability of being exempt from copayments (when the price lies below a certain exemption level) at the product level. In a second step, we aggregate our data at the active substance level. This allows us to estimate the overall effects of reduced reference prices on spending by the health insurance funds and on firm revenues. All estimations are conducted for all drugs and then separately for generic and brand-name drugs. We expect differentiated strategies by the firms based on the previous literature (see below). Importantly, this analysis also allows us to investigate how the total copayments by patients are affected.

In response to increasing health care costs, there is a growing interest in exploring the impact of cost-containment policies on outcomes in health care markets. The empirical literature on the effects of copayments for pharmaceuticals in general and reference pricing in particular looks at a number of indicators, such as choice and use (e.g., Whaley et al., 2017), drug adherence, costs for ambulatory or stationary services, as well as their effects on health outcomes (see, for instance, the surveys by Gemmill et al. (2008) and Doshi et al. (2016)). However, these studies mainly look at individual behavior and neither analyze the effects on market outcomes, such as prices or copayments, nor do they study aggregate effects.

There are also a number of studies that explore the effects on prices when reference pricing for pharmaceuticals is introduced. On average, prices decrease after the introduction for pharmaceuticals, for example, for Germany (Pavcnik, 2002), Denmark (Kaiser et al., 2014), Norway (Brekke et al., 2009, 2011) or a selection of private US employers (Robinson, Whaley et al., 2017). In contrast, the evidence with respect to individual copayments is mixed (see, for instance, the survey of Robinson, Brown et al. (2017)).

Closest to our analysis are the studies by Brekke et al. (2011) for Norway and Augurzky et al. (2009) and Herr and Suppliet (2017) for Germany. Brekke et al. (2011) evaluate 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 drug market shares, suggesting cost-savings for the health care system. They estimate a significant average copayment reduction that stems from both price reductions for generics and brand-name drugs and from substitution with cheaper generic drugs. In contrast, we evaluate the effects of RP reductions in a system where reference prices have been in place for 30 years and continually adjusted. Therefore, this paper analyzes the effects of one such RP adjustment (instead of introducing reference pricing, as in Brekke et al. (2011)). Our results suggest that the effects of decreasing reference prices can be quite different from the mere introduction of a RP. Additionally, we comment on the effects of copayment exemption levels (CEL) whereas there is no such instrument in the Norwegian market. Augurzky et al. (2009) analyze the effects of repeated adjustments of the RP in the German market at the product level. However, they do not consider different firm types and do not examine the effects on copayments or health care spending. Our study complements Herr and Suppliet (2017), who examine the effects of introducing a tiered copayment system in the German market for anti-epileptics. Copayment exemption levels, which are defined and adjusted relative to the RP, were introduced in RP markets after 2006 and affect prices and demand. While generic drug prices decreased due to this new incentive, brand-name drug prices increased significantly pointing to differentiated pricing strategies by drug type. In this paper, we analyze firms' responses and the implications for consumers if reference prices are reduced when CEL have already been implemented.

At the product level, we report ex-factory price reductions of, on average, 0.43% for a RP reduction of 1%. This result reflects earlier findings. In particular, prices for brand-name drugs decrease by 0.65% and for generic drugs by 0.41%. This is in line with the results by Brekke et al. (2011), who similarly report price reductions for both brand-name and generic drugs following a switch

from a price cap to an internal RP regulation. However, this finding runs counter to the price convergence theory by Danzon and Lui (1996) and Danzon and Ketcham (2004), who predict an increase in the generic drug price since demand becomes less elastic below the RP.[3] Copayments for brand-name drugs increase by about 0.58% and for generic drugs by 0.21% per package. Moreover, for generic drugs the probability of being exempt from copayments shrinks by about 0.92 percentage points.

At the aggregate level, we show that a 1% RP reduction leads to significant savings for the health insurers of around 0.42%. In particular, expenditures by the SHI for brand-name drugs decrease substantially by around 1.31%. Total payments for generic drugs also decrease, but to a lesser extent (0.33%). While the generic market share only increases slightly, the small savings can be explained by lower relative and absolute price reductions compared to brand-name drugs. Our analysis also allows us to investigate the sources of these cost savings for public health insurance funds. While firm revenues decrease, our results suggest that a part of the plans' cost savings comes from higher consumer payments. We note, however, that this estimate, while relatively large, is imprecisely estimated. We attribute this mainly to our small sample size when analyzing the aggregate effects. Importantly, the total expenditures (private copayments plus the expenditure of the health insurers) decrease a great deal for brand-name drugs (1.16%), but only modestly overall (0.28%) due to the insignificant and small decrease for generics, which represent the majority of purchased drugs. This small effect for generics may be due to an increase in generic quantities accompanied by a decrease in brand-name drug usage. However, both effects are imprecisely measured, small, and the change in the generic market share by 4% is also not statistically significant. Thus, our analysis suggests that a large part of the savings are not only based on price reductions but may partly be attributed to shifting costs to patients.

Our paper contributes to the literature in several ways. First, in contrast to almost all the cited studies above, which evaluate the introduction of reference prices, we analyze RP adjustments in a system where reference pricing has been in place for a long time. Second, we analyze the effects in a tiered copayment system, where patients only make copayments for prices above a threshold level. Third, we do this separately for brand-name and generic drugs and indeed find differentiated effects. Fourth, we observe all anti-epileptic drugs covered by the German SHI and can thus estimate marginal and aggregate effects based on around 90% of the German population. Lastly, we exploit the fact that not all anti-epileptics faced RP reductions at the same time in a difference-in-differences framework to identify causal effects. We also provide robustness checks using instrumental variables. Overall, our results are a bit more cautious as we show that reductions in reference prices may also lead to undesirable effects. In our study, total cost savings are only modest, but patients may end up footing a larger share of the bill.

2 | INSTITUTIONAL BACKGROUND

SHI coverage for prescription drugs includes a copayment scheme, in which patients need to copay for each drug package at the pharmacy. Patients pay 10% of the retail price within the minimum of €5 and the maximum of €10 to the SHI.[4] If the drug belongs to a RP market and the price lies above the RP, patients need to copay 10% of the RP (again within the minimum of €5 and the maximum of €10) plus the absolute difference between the drug's price and the RP. Firms are free to choose any price below or above the RP.

Reference pricing for off-patent drugs has been in place since 1989. Drugs are divided into RP groups based on the active substance. They typically include original drugs and their generics.[5] The RP is set by the Federal Association of Statutory Health Insurance Funds (FASHI) for each group of drugs. After the normalization of prices according to package size, dosage form, and concentration, the RP has to lie within the smallest 30% of the price distribution within the RP group. In addition, at least 20% of all packages and of all prescriptions must be available for prices equal to or below the RP at the time of implementation. Products with a market share of less than 1% are not considered when defining the price distribution. The FASHI reviews reference prices irregularly and adjusts them, if seen as necessary, for example, because of generic entry, based on the prices around 12 months before the date of the revision, more specifically, between 2007 and 2010, eight to 16 months before the revision (Herr & Suppliet, 2017). The timing of these reviews and the adjustments cannot be foreseen by firms and are announced in the quarter before the adjustment. Note that the pharmaceutical companies can influence neither the assignment of their drugs to a specific RP group nor the reference prices themselves. The whole procedure is exogenous to the producers but the timing may depend on the observed prices within the group and changes in the market structure. Since we only measure the short-term effects we argue that a single firm cannot strategically influence the RP in a group with around 30 other firms, on average. To confirm this conclusion, we show below that accounting for potential endogeneity does not alter the results significantly.

Since 2006, the FASHI has also been able to introduce CEL in selected groups of RP drugs. As a general rule according to German law (Social Security Code [SGB] V, section 31), the exemption level is set at 30% below the respective RP. In particular, it states in section 31, para. 3, sentence 4 (our translation) that the FASHI "may exempt from co-payment medicinal products whose sales price of the pharmaceutical entrepreneur *excluding value added tax* is at least 30% lower than the respectively valid RP on which this price is based." If firms decrease the price below this exemption level, consumers do not need

to copay for the drug. In our data, we observe retail prices and exemption levels including value added tax, which reduces the difference to 20%. Pricing strategies in groups with CELs are very different, and the introduction of such a CEL constitutes a structural break (Herr & Suppliet, 2017). Basically, this policy resembles the introduction of a tiered copayment system where firms can strategically decide on the copayment (either 0, general, or above RP). In our analysis, we focus on drugs where both reference pricing and CEL are in place.

Figure A1 in the appendix provides an illustrative example of the copayment scheme. It can be seen from the figure that reductions in the RP have two effects. If firms do not reduce the price by a sufficient amount, copayments are likely to increase. The price will then be either above the new RP or above the new exemption level when it was previously below one or both thresholds. In the latter case, the copayment will increase, in the former it is likely to increase depending on the difference to the new RP. By how much prices are reduced relative to the reduction in the RP, and whether consumers substitute with cheaper drugs to circumvent higher copayments, is an empirical question. Thus, the overall effects on copayments are not clear a priori and are rigorously analyzed in this study.

The physician payment for prescribing does not depend on the drug prescribed (fixed fee for writing a prescription). Furthermore, physicians face a drug budget based on their patient list and previous prescribing. Physicians need to give reasons for exceeding the budget if they want to avoid a fine (which is only rarely applied in practice). Thus, there are no financial incentives to deviate from prescribing the drug that is the most appropriate for the patient. In RP markets (with generic options), physicians have two options: they can prescribe either a substance or a specific brand. When prescribing a substance, the pharmacist has some options regarding substitution, for example, based on the lowest price. However, if adherence to a specific brand is essential for the therapeutic success, physicians may exclude the option to switch to brands other than the one prescribed.[6]

3 | DATA AND DESCRIPTIVE STATISTICS

We observe quarterly data for all anti-epileptic products reimbursed by the public health insurance (SHI) in Germany between 2009 and 2010.[7] The data contain information on prices (ex-factory and retail[8]) per defined daily dose (DDD), quantities sold in DDD in German pharmacies aggregated at the national level, and package characteristics (size, strength, dosage form). The active substance of a drug is defined following the Anatomical Therapeutic Chemical classification system by the WHO at the level of the chemical substance (fifth level).

3.1 | The German market for anti-epileptics

Epilepsy is one of the most common chronic neurological disorders. In 2016, 0.5%–1% of the German population suffered from epilepsy. Anti-epileptics help to control and reduce seizures and are the preferred form of treatment.

Defining a relevant market is simple since switching across active substances in the market for anti-epileptics only occurs if medically necessary. Herr and Suppliet (2017) estimate a classical nested logit demand function to analyze the price elasticity of demand for anti-epileptic drugs. The reported mean semi-elasticities suggest that there is a small but positive substitution of drug packages within substances, but cross-price elasticities are almost zero (Herr & Suppliet, 2017). However, even within some of the active substances in anti-epileptics, switching from one brand to another may have adverse health effects for some of the patients (Straka et al., 2017). That is why physicians may exclude the option to switch to a brand other than the one prescribed. However, physicians may prescribe (cheaper) generics to newly diagnosed patients, if available and suitable, which can increase the generic market share.

There are 22 active substances in the market for anti-epileptics, where seven face reference pricing. In our analysis, we focus on those molecules that have also faced CEL since 2008 at the latest (carbamazepine, gabapentin, lamotrigine, [primidone], valproate).[9] We drop those observations without a CEL in our main analysis to avoid confounding the effects of reference pricing and copayment exemptions (clonazepam and phenytoin). Overall, our sample accounts for 20% of the expenditures and 55% of the total quantity sold in the German market for anti-epileptics.

The data have been augmented with public information on reference prices (DIMDI, 2011) and product-specific CEL (GKV-Spitzenverband, 2011; Herr & Suppliet, 2017). We match the RP by grouping four variables: active substance, strength, package size, and dosage form. Copayments are calculated according to the above explained rules, which hold for all members of the SHI, if applicable (compare endnote 4).

In our empirical analysis, we exploit the fact that the RP was adjusted in only three of the four active substances between Q1-2009 and Q4-2010. Table 1 shows that RP adjustments took place in quarter Q2-2010 when, to our knowledge, there was no other change in regulation. There has been no RP adjustment for carbamazepine which will act as a control group in our

TABLE 1 Treatment and control group and timing of the reference price adjustments

Active substance	Adjusted in	Market share	# Obs.	# Firms
Treatment group				
Gabapentin	Q2-2010	0.12	2554	33
Lamotrigine	Q2-2010	0.09	2033	38
Valproate	Q2-2010	0.15	1305	24
Control group				
Carbamazepine	-	0.19	1886	27

Note: Market share measured as defined daily dose sold per active substance relative to all anti-epileptics per quarter. The number of observations refer to the number of different packages (the combination of manufacturer, active substance, package size, strength, and dosage form) for each active substance in the final sample.

Source: Pharmascope, IMS Health (2012), 2009–2010.

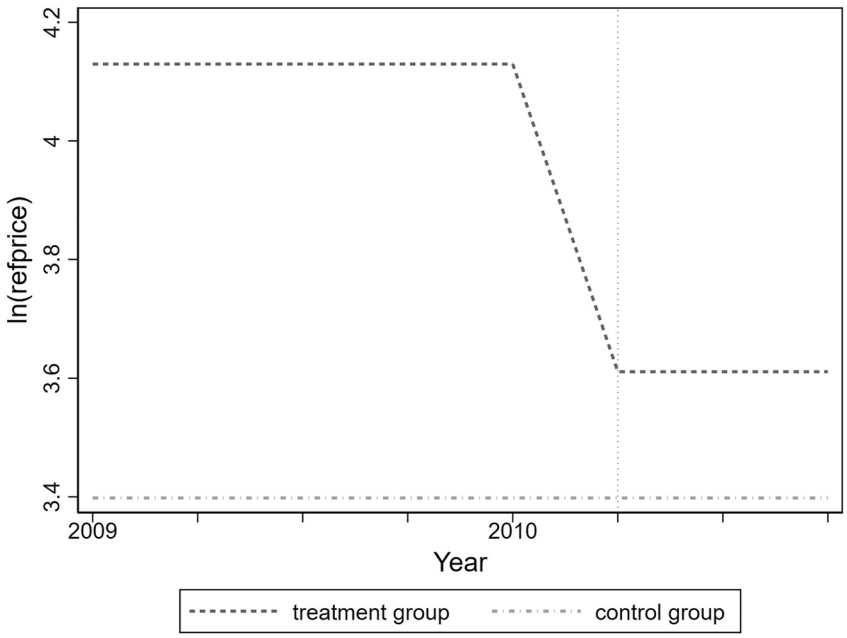

FIGURE 1 Mean logged reference prices by quarter for the treatment and the control group. 4 anti-epileptic substances, 2009–2010. *Source*: FASHI and Pharmascope, IMS Health (2012). Own calculations

difference-in-differences approach. The unit of observation is at the package-quarter level, where a package (also called a product) is defined as the combination of manufacturer, active substance, package size, strength, and dosage form. The markets we analyze are quite competitive with 24–38 firms per substance over time, offering brand-name drugs and generics.

3.2 | Descriptive statistics

Figure 1 provides some more information and displays the evolution of the (average) RP over the period 2009–2010, separately for the treatment and the control group. The figure shows the large reduction of the RP for the drugs in our treatment group.

Table 2 presents the descriptive statistics at the product level for the final sample. We split the sample by treatment and control group, brand-name and generic drugs, and before and after the reductions in the RP in the Q2-2010. Since pricing strategies differ between brand-name drugs and their generic counterparts (Herr & Suppliet, 2017), we differentiate by drug type. In our analysis, we exclude the pre-treatment quarter Q1-2010 in which the new RP is announced.[10]

If a RP adjustment takes place (the first two panels present the treatment group), the RP is decreased by around €41 on average (i.e., by around 45% given an average RP of €91 before the adjustment took place). However, the distribution is very skewed across different packages. Fifty percent of the 850 decreases lie below €22 and 25% below €8.60.

The exemption levels decrease accordingly when the RP decreases and lie, as the law indicates, 20% (note that our data include value added tax) below the RP before and after the reduction. There is one exception: in one of the treatment-substances (lamotrigine), where a RP had been newly introduced in the year before the sample period, the exemption level was 38% lower than the RP before the change for political reasons (to incentivize firms to decrease prices quickly). Since the exemption level

TABLE 2 Descriptive statistics at product level, by treatment and control group before and after the reference price (RP) reduction

Treatment group						
	Total		**Generic**		**Brand-name**	
	Mean	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**
1) Before						
Ref. price	91	84	92	84	90	84
Retail price	60	54	56	48	83	80
Ex-factory price	38	42	35	37	56	62
Copay	3.1	4.6	2.3	3.2	7.6	8
Exempt	0.57	0.49	0.65	0.48	0.092	0.29
CEL $\leq p \leq$ RP	0.42	0.49	0.35	0.48	0.88	0.32
$p >$ RP	0.0062	0.078	0.0027	0.052	0.027	0.16
N	3414		2924		490	
2) After						
Ref. price	50	44	50	43	53	46
Retail price	49	43	47	39	63	62
Ex-factory price	30	33	29	30	41	48
Copay	6.9	11	5.6	4.8	18	28
Exempt	0.14	0.35	0.16	0.37	0.0072	0.085
CEL $\leq p \leq$ RP	0.79	0.41	0.8	0.4	0.73	0.45
$p >$ RP	0.069	0.25	0.044	0.2	0.27	0.44
N	2478		2199		279	
Control group						
	Total		**Generic**		**Brand-name**	
	Mean	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**
3) Before						
Ref. price	33	16	34	16	32	15
Retail price	27	13	26	12	32	15
Ex-factory price	13	9.8	13	9.4	17	11
Copay	2.9	2.6	2.4	2.6	5.3	0.59
Exempt	0.46	0.5	0.53	0.5	0	0
CEL $\leq p \leq$ RP	0.54	0.5	0.47	0.5	1	0
$p >$ RP	0	0	0	0	0	0
N	1039		889		150	
4) After						
Ref. price	33	16	34	16	31	15
Retail price	27	13	27	13	31	15
Ex-factory price	13	10	13	9.7	16	12
Copay	2.1	2.6	1.6	2.5	5.2	0.47
Exempt	0.61	0.49	0.69	0.46	0	0
CEL $\leq p \leq$ RP	0.36	0.48	0.28	0.45	1	0
$p >$ RP	0.021	0.14	0.024	0.15	0	0
N	847		749		98	

Note: We calculate the upper bound as RP × 1.05 to ensure that small deviations from the reference price do not lead to large changes in the binary indicators.

Source: Pharmascope 2012, IMS Health. Quarterly, 2009–2010 (Q1-2010 dropped).

was relatively higher in the other substances than for lamotrigine, the change in the RP (and the respective exemption level) has larger effects for the other active ingredients. Thus, including lamotrigine, we estimate a lower bound of the copayment and price effects of a decreasing RP.

When looking at drug types in Table 2, it is clear that brand-name drugs are more expensive, come with higher copayments, and are less often exempt (from any copayment) than generic drugs. The average copayment lies below the minimum of €5 since 55% of the packages are exempt, on average. The RP is very similar across drug types.

Comparing outcomes before versus after the change in the RP (panels 1 and 2 in Table 2), we can see the changes in the outcomes in the treatment group, for instance, the drop in prices and in the share of exempt packages (from 65 [9]% to 16 [1]% for generics [brand-name drugs]). Furthermore, the table presents changes in the price distribution (below exemption level = "Exempt", in between CEL and RP = "CEL $\leq p \leq$ RP" and above RP = "$p >$ RP"). The share of generics priced in between the CEL and the RP more than doubles (from 35% to 80%) driven by the drop in exempt drugs (from 57% to 14%) despite a small increase in drugs priced above the RP (from 1% to 7%). For brand-name drugs, the story is different. 27% or 10 times more brand-name drugs are priced above the RP after the decrease than before. The share with intermediate prices decreases from 88% to 73%, now capturing the 10% of brand-name drugs that had been priced below the CEL before. There is almost no exempt brand-name drug after the decrease in the RP.

In the control group (panels 3 and 4), averages are stable except for copayments and the share of exempt drugs for generics, despite constant average prices. This is due to the fact that for 58 drug packages producers lower the prices below the exemption level in quarters 14 or 15 but, on average, by only 0.18 euro. This does not affect average prices but has an impact on average copayments and exemption status thereafter, where the changes are still much smaller than for generics in the treatment group (+143% in copayments per DDD and −75% lower share of exempt drugs).

Figure A2 in the appendix provides some more details on the price distributions and visualizes the different pricing strategies of brand-name and generic drugs by providing a histogram of the drugs' prices relative to the RP and the exemption level before and after the decrease in the RP. As can be seen, brand-name drugs are priced at or slightly below the RP and several even below the exemption level before the change. After the reduction, a larger number of brand-name drugs are priced above both thresholds, where almost none is exempt any more. In the right column, we can see that, while generic drugs move closer to the new RP from below, more packages are priced above the exemption level from Q2-2010 onwards.

Figure 2 presents the means of the four outcome variables (in logs) under analysis over time for the three treated active substances (treatment group) and for the control group. It becomes clear that the outcomes adjust quickly after the new RP is applied. Copayments and the share of exempt drugs change in the control group due to minimal price adjustments (see above).

Table 3 shows the descriptive statistics of the aggregated outcomes of interest for the four active substances, where carbamazepine forms the control group. We deal with relatively large groups of drugs with 30 firms, on average. Gabapentin generates the highest revenues while the aggregate copayments are similar across substances. Furthermore, the share of copayments relative to total expenditures is between 4% and 13%, reflecting that many products are exempt and copayments are small in Germany compared to other countries. The more detailed Table A1 in the appendix shows the descriptive statistics of the aggregated outcomes of interest for the four active substances by brand status before versus after the change in the RP analogously to Table 2. Summing across brand-status or substances yields total market outcomes. From the descriptive statistics it becomes clear that, over time, quantities move parallel in two of the four substances such that the generic market share does not change. There are small increases in the generic market share for valproate and gabapentin, though, which leads to an overall increase from 81% to 85%, on average, where the difference in means is not significant. Note that in these descriptive statistics, we do not control for general changes in supply and demand over time, which we do in the regression analysis.

4 | ESTIMATION STRATEGY

4.1 | Effects at product level

To analyze the effect of RP adjustments, we exploit the fact that the RP has been adjusted in all but one of the four active substances in a difference-in-differences framework (see Table 1 and Figure 1). The idea behind this method is that the non-treated group serves as a control group, capturing all other market-driven influences on the variables of interest except the change in the RP.[11]

In the linear regressions, we focus on changes in the RP while controlling for time fixed effects and all time-independent unobserved effects, such as quality, that are captured by product fixed effects. Our main estimation equation is given as

$$\ln(y)_{it} = \ln(\text{refprice})_{it} + \tau_t + \alpha_i + \epsilon_{it}, \quad (1)$$

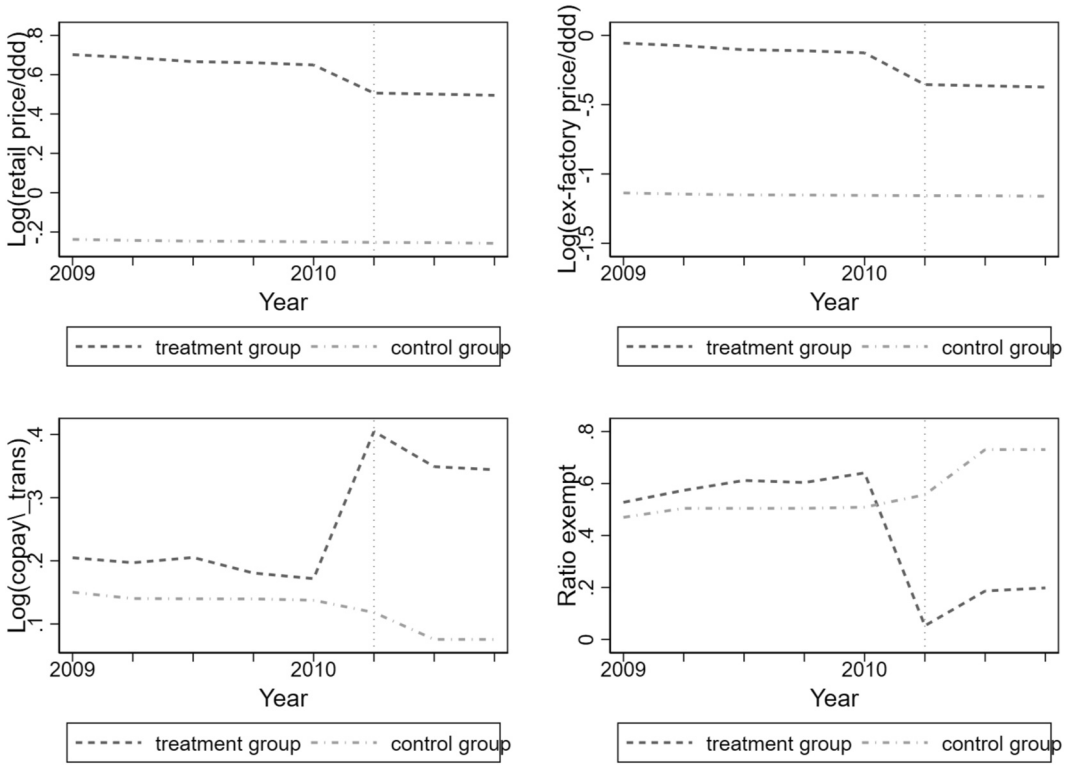

FIGURE 2 Mean logged prices, copayments, and exempt-ratio by quarter for the treatment and the control group. *Source*: FASHI and Pharmascope, IMS Health. Own calculations

TABLE 3 Descriptive statistics aggregated at substance level by active substance

Substance	Gabapentin		Lamotrigine		Valproate		Carbamazepine	
Variable	**Mean**	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**
Firm revenues [€1000]	14,399	781	5411	1216	5529	296	4755	191
Quantities [1000 ddd]	9107	533	6772	574	11,028	376	14,304	532
Copayments [€1000]	1169	899	808	172	1417	152	738	226
Expenditures SHI [€1000]	21,175	1772	7988	1671	8585	564	8455	198
Total expenditures [€1000]	22,344	963	8796	1504	10,002	428	9193	368
Firms	31	1	35	2	23	1	26	1
N	7		7		7		7	

Note: Firm revenues = ex-factory price times quantities sold measured in defined daily dose (ddd), Expenditures SHI = pharmacy sales price times quantities sold − total copayments, Total expenditures = Expenditures SHI + Copayments.

Source: Pharmascope, IMS Health, quarterly, 2009–2010 (Q1-2010 dropped). Aggregated at active substance level. Own calculations.

where the logged[12] dependent variable y varies: (1) ex-factory price per DDD, (2) pharmacy retail price per DDD (including taxes and pharmacists' reimbursement), (3) copayments per DDD, and (4) the probability of being exempt (linear probability model).[13] Variables are indexed by package i at quarter t. We include time fixed effects (τ_t) and fixed effects at the package level (α_i). Standard errors (ϵ_{it}) are clustered at the *RP group level* (which means here and in the following very narrowly having the same active substance, form of administration, package size, and concentration).

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

For the validity of the difference-in-differences approach, we need to verify that the control group behaved similarly to the treatment group prior to the change in the RP. We test for parallel trends in the treatment and the control group using event studies (see Figure 3 for all drugs here and Figure A3 by drug type in the appendix, which present very similar results), where we interact the quarters before and after treatment in Q2-2010 individually with a treatment dummy (drug belongs to one of the three treated drug

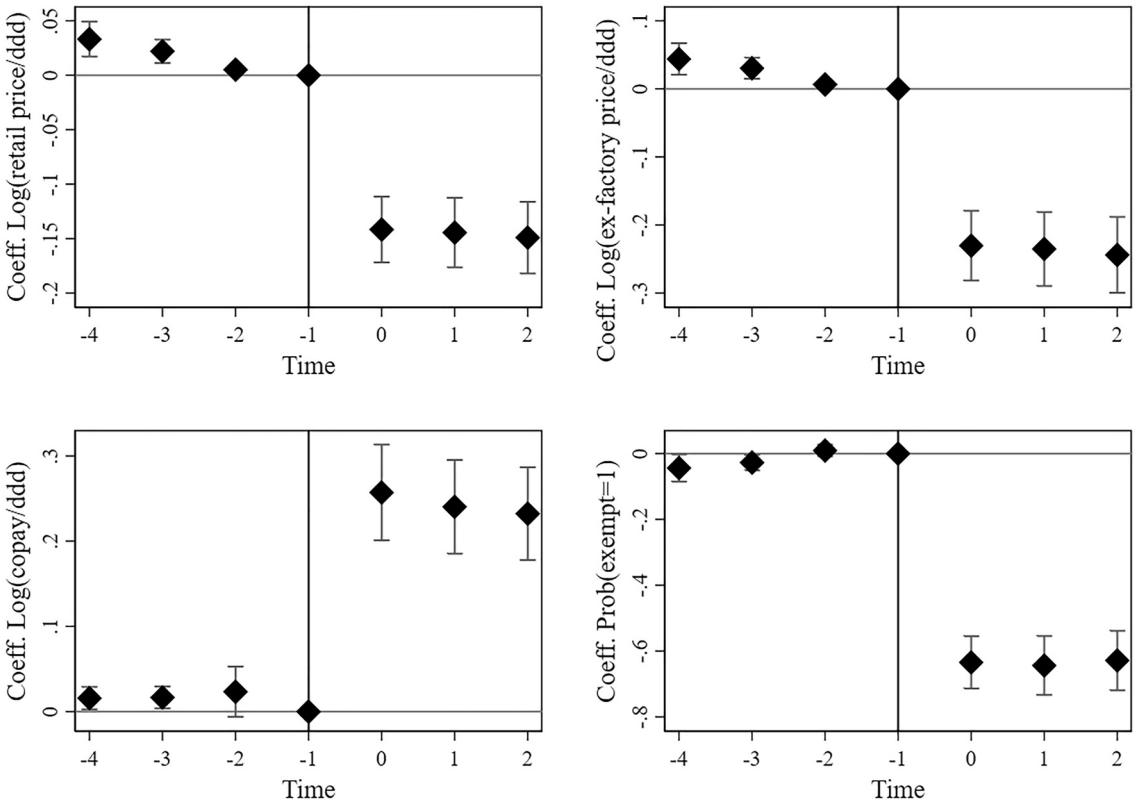

FIGURE 3 Event study of the four outcomes at package level, treatment versus control group. All drugs. The treatment dummy equals one for three of the four substances and is interacted with quarter dummies, where Q4-2009 serves as the base category (−1) and Q1-2010 is dropped. We include package and quarter fixed effects and cluster the standard errors at reference price group level. *Source*: FASHI and Pharmascope, IMS Health (2012). Quarterly, 2009–2010. Four anti-epileptic substances, 7778 observations. Own calculations

classes), where Q4-2009 serves as the base category. We include package and quarter fixed effects and cluster the standard errors at the RP group level. The three coefficients before 2010 are close to zero and most are not statistically different from zero.[14] After the change, we see a big jump across all four outcome variables and the two drug types. Since all outcomes are adjusted immediately in the first quarter after the change and remain stable afterward, in our final regressions, we estimate the average post-policy effects.

We argued earlier that changes in the RP are exogenous to the short-term decisions of the firms after controlling for time and package fixed effects. Nevertheless, as a robustness check, we also control for the fact that the treatment itself may be endogenous, which would invalidate the difference-in-differences analysis. Since reference prices are set based on past prices there may be both omitted variables and simultaneity biases with respect to the price and price-related variables. The regulation hinders strategic price increases, which excludes one possible bias. However, as the prices and reference prices move in the same direction and are negatively influenced by, for example, entry from (cheaper) competitors, this would bias our coefficients downwards and we would underestimate the true effects of the changes in the RP.

To address these potential biases, which we argue are small in the German setting, we use an instrumental variable approach and only exploit the variation in the RP that can be explained by an exogenous factor.[15] As the instrument, we use the average number of products in all other RP groups (Herr & Suppliet, 2017). We hypothesize that the instrument correlates negatively with the RP. The intuition is the following: An increase in the number of products in one RP group is likely to lead to a review by the FASHI, probably followed by a decrease in the group's RP. To use resources more efficiently, the regulator simultaneously checks the need for an adjustment in the RP of the six other anti-epileptics (see Table 1). Additionally, cost shocks that are independent of unobservable demand shocks may induce entry. Thus, when a RP in other active substances is adjusted downwards, for example, because of generic entry, the RP in the group of interest is also likely to be adjusted downwards. We provide evidence of this correlation below.

The strategic introduction of new substances following a reduction in the reference prices of older ones might pose another threat to the validity of our empirical approach. However, as argued above, substitution across different active substances of anti-epileptics is difficult and mostly depends on medical conditions as opposed to prices or copayments. Thus, the entry of drugs in other active substances is not directly correlated with the pricing of the own substance (Herr & Suppliet, 2017).

4.2 | Effects at aggregate level

In the second part of the analysis, we aggregate the package level data at the active substance level overall and by drug type.

We estimate the following model for the three samples separately:

$$\ln(y)_{jnt} = \ln(\text{refprice})_{jnt} + \tau_t + \alpha_j + \epsilon_{jnt}, \quad (2)$$

where $n \in \{\text{all, generic, brand-name}\}$, substance j, and quarter t, and the dependent variable y varies: (1) total firms' revenues (ex-factory price times quantity sold measured in DDD), (2) quantities sold, (3) total copayments, (4) total expenditures of the SHI, and (5) overall expenses (i.e., (3)+(4)). As above, we include active ingredient fixed effects. Since the number of observations is small (only $4 \times 7 = 28$) in the aggregate analysis, we bootstrap the standard errors (5000 replications).

In the appendix, we also present results using the instrumental variable approach and linear regressions, where both the change in the RP and the outcome variables are measured in units.

5 | RESULTS

5.1 | Effects of a change in the reference price at the product level

We first present our empirical results at the package level, which allows to explore how drug prices react to changes in the RP and the effects this has on consumer copayments. In Section 5.2, we show the effects on SHI expenditures, sales and copayments at the active substance level.

The linear regression results are presented in Table 4. The first row presents the average marginal effects for generic and brand-name products combined. We find (ex-factory) price effects of around 0.43% for a 1% reduction in the RP, which are in line with earlier studies (e.g., Augurzky et al., 2009). Copayments per DDD increase slightly by 0.24%. The probability of being exempt (with a price below the CEL) decreases by 0.88 percentage points or 1.54% at the mean if the RP is reduced by 1%.

TABLE 4 Effect of change in the reference price at the product level, OLS regressions

	(1)	(2)	(3)	(4)
ln(*y*)	Ex-factory *p*/ddd	Retail *p*/ddd	Copay/ddd	Pr(Exempt = 1)
Total				
ln(ref. price)	0.427***	0.356***	−0.237***	0.877***
	(0.0553)	(0.0229)	(0.0732)	(0.112)
R^2	0.443	0.558	0.154	0.363
F	24.41	92.84	13.70	55.54
N	7778	7778	7778	7778
Generic				
ln(ref. price)	0.411***	0.337***	−0.207***	0.923***
	(0.0589)	(0.0273)	(0.0717)	(0.126)
R^2	0.457	0.575	0.155	0.389
F	21.77	78.26	17.33	55.27
N	6761	6761	6761	6761
Brand-name				
ln(ref. price)	0.647***	0.615***	−0.582***	0.169**
	(0.127)	(0.0957)	(0.154)	(0.0711)
R^2	0.398	0.564	0.197	0.0695
F	12.49	16.79	8.741	2.594
N	1017	1017	1017	1017

Note: Standard errors in parentheses, $^*p < 0.1$, $^{**}p < 0.05$, $^{***}p < 0.01$. Time and product fixed effects included. Standard errors clustered at the reference price group level. For the list of analyzed substances compare Table 1.

Abbreviations: ddd, defined daily dose; OLS, ordinary least squares.

Source: Pharmascope, IMS Health, Quarterly, 2009–2010 (Q1-2010 dropped).

Table 4 also shows that the product level effects of RP reductions differ by brand status. Brand-name drug prices decrease by around 0.62% (retail price) to 0.65% (ex-factory price) while generic prices decrease by 0.34%–0.41% if the RP is reduced by 1%. Furthermore, copayments increase for consumers of brand-name drugs by 0.58% and by 0.21% for generic drugs. Finally, the probability that a product is actually exempt (its price lies below the CEL) decreases for generics by 0.92 percentage points or 1.42%. The effect for brand-name drugs is much smaller, which is intuitive as branded products are typically priced above the CEL prior to the RP reduction. Taken together, our results suggest two ways how RP reductions affect consumer copayments. First, copayments increase as price reductions fall short of the decrease of the RP. Second, in this tiered copayment system, fewer drugs (in particular, generics) are exempt from copayments so that patients need to start paying copayments after a RP reduction. Both effects result from price reductions falling short of the RP reduction.

Table 5 shows the results of the 2SLS estimation, where we instrument the RP with product and time fixed effects and the average number of products in other active substances. First-stage results can be found in Table A2 in the appendix. They confirm our predictions and the *F*-test statistics of excluded instruments lie between 147 and 189. Overall, the results of the 2SLS estimation are very similar to our baseline regression in Table 4. In line with our prior of a downward bias, they mostly show larger coefficients and standard errors. Only in column (2) for generics and overall, and columns (3) and (4) for brand-name drugs, are the 2SLS-coefficients slightly lower in absolute terms, but in these cases the differences are very small. To test for endogeneity, we applied the robust score test (Wooldridge, 1995) for each outcome and sample (12 tests). It fails to reject the null hypothesis of exogeneity for four of them (using pooled cross-sections with clustering and fixed effects for the RP group and quarter). In the aggregate sample, exogeneity is not rejected in any case (not bootstrapped). We therefore put more weight on the more conservative and more efficient ordinary least squares estimates.

In Table A4 in the appendix, we present regression results in levels, where a on-euro decrease in the RP leads to a decrease in the ex-factory price per DDD (which is, on average, €0.97 before the change) by €0.0015 (approx. 6.3% for an average decrease of €41). The coefficients for the retail price (on average, €2.2 per DDD) are only slightly larger. The only difference to the model in logs lies in column (3). Copayments per DDD (on average, €0.28 before the change) increase steeply for brand-name drugs (82% per DDD for a €41 decrease) and remain close to zero (and insignificant) for generics. Since the majority of drugs

TABLE 5 Effect of change in the reference price at the product level, 2SLS

	(1)	(2)	(3)	(4)
ln(*y*)	**Ex-factory *p*/ddd**	**Retail *p*/ddd**	**Copay/ddd**	**Pr(Exempt = 1)**
Total				
ln(ref. price)	0.564***	0.348***	−0.398***	1.057***
	(0.0680)	(0.0233)	(0.0800)	(0.114)
F	33.35	93.43	13.71	59.45
F weak instr.	228.9	228.9	228.9	228.9
N	7778	7778	7778	7778
Generic				
ln(ref. price)	0.528***	0.325***	−0.389***	1.135***
	(0.0677)	(0.0267)	(0.0802)	(0.130)
F	34.55	86.12	17.71	62.13
F weak instr.	198.8	198.8	198.8	198.8
N	6761	6761	6761	6761
Brand-name				
ln(ref. price)	0.969***	0.624***	−0.549***	0.0936
	(0.178)	(0.0853)	(0.156)	(0.0842)
F	7.589	17.40	7.624	2.492
F weak instr.	189.3	189.3	189.3	189.3
N	1017	1017	1017	1017

Note: Standard errors in parentheses, $^{*}p < 0.1$, $^{**}p < 0.05$, $^{***}p < 0.01$. Reference price instrumented with average number of products across all other active substances. Product fixed effects and time fixed effects included. Kleibergen-Paap Wald rk *F* statistic to test for weak instruments with instrumental variables and cluster-robust s.e. For first-stage regressions compare Table A2 in the appendix.

Abbreviation: ddd, defined daily dose.

are generic, the insignificant and small overall effect is mainly driven by this type of drug. Note that for copayments, the explanatory power of the model is very low. Finally, the probability of being exempt decreases significantly across both drug types.

Lastly, if we exclude lamotrigine, which faced a relatively lower exemption level before the change, the absolute coefficients' sizes increase throughout, as expected.

5.2 | Effects of a change in the reference price at the active substance level

We now present the empirical results at the active substance level, which show how our aggregate variables—firm revenues, overall consumer copayments and expenditures by the SHI—are affected by the RP reduction.

Table 6 presents the linear regression results at the aggregate active substance level by drug type. Standard errors are bootstrapped based on 5000 replications. The regressions show how the participants in the market (i.e., firms, patients, and public health insurance funds) are affected differently by reductions in reference prices.

On average, the expenditures of the SHI and firm revenues decrease while aggregate quantities sold increase across the three active substances when the reference price is decreased. The results also suggest that consumer copayments might increase following a reference price reduction. The coefficient is highly negative (−1.43), but not significant.

Differentiating by firm type, we see that the producers of both types are negatively affected. They see their revenues reduced, but the effect is much stronger for branded drug producers (1.38) than for generic drug producers (0.29). The total quantity sold by branded drug producers remains quite stable (−0.04%), while the overall quantity sold by the generic firms increases by only 0.22% if the RP is reduced by 1% (though not significantly). In Section 5.1, we showed that, at the product level, the brand-name drug copayments increase if prices are not adjusted downward by a sufficient amount, especially if after the decrease the price exceeds the new RP. This, in turn, should incentivize a substitution with cheaper generic drugs and lead to an increase in their market shares. However, the overall increase in quantities is again imprecisely measured. This confirms the descriptive evidence, where the increase in the generic market share is small. These two findings indicate that brand-name drug producers are hurt by lower reference prices more (their revenues decrease by 1.38%) and at a higher level, mostly due to price decreases. The revenues of generic firms decrease to a lesser extent, starting from a lower price level and facing rather increases in demand, if anything.

Expenditures by the Statutory Health Insurance (SHI) funds follow a similar pattern. They decrease by around 0.42%, which mainly results from a decrease in payments to branded drug producers (−1.31%). SHI plan payments for generics decrease modestly (0.33%). This confirms that another aim of reference pricing is reached, that is, a cost reduction for the health insurer.

TABLE 6 Effect of a change in the reference price at active substance level, OLS, bootstrapped standard errors

	(1)	(2)	(3)	(4)	(5)
ln(*y*)	Firm revenues	Quantities	Copay	Expend. SHI	Total expend.
Total					
ln(ref. price)	0.407***	−0.223	−1.425	0.419***	0.284**
	(0.156)	(0.200)	(2.555)	(0.150)	(0.140)
R^2 adj.	0.986	0.995	0.331	0.994	0.987
Generics					
ln(ref. price)	0.285*	−0.224	−1.868	0.326**	0.186
	(0.154)	(0.160)	(1.285)	(0.163)	(0.144)
R^2 adj.	0.990	0.989	0.302	0.995	0.990
Brand-name					
ln(ref. price)	1.382***	0.0380	0.144	1.306**	1.158***
	(0.405)	(0.510)	(0.298)	(0.557)	(0.436)
R^2 adj.	0.859	0.950	0.919	0.806	0.857

Note: Standard errors in parentheses. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. *N*: 28 observations. Bootstrapped standard errors with 5000 replications. R^2 from OLS regressions without bootstrapping with clustered standard errors. Time and active substance fixed effects included.

Abbreviation: OLS, ordinary least squares.

Source: Pharmascope, IMS Health, 2009–2010 (Q1-2010 dropped). Aggregated at active substance level. Own calculations.

We observe an element of cost-shifting when reference prices are reduced with aggregate copayments by patients. This increase in aggregate copayments stems primarily from the generic drugs where total copayments increase by 1.87% (though again imprecisely estimated) if the RP is reduced by 1%. From the product-level analysis, we know that prices slightly decrease but, at the same time, the probability that prices will lie below the copayment exemption level decreases for generics so that copayments increase more for those drugs that are priced close to the exemption level.

Interestingly, the coefficient on total expenditures (SHI expenditures plus consumer copayments) is slightly positive with a value of 0.28, suggesting that overall expenditures only decrease to a small extent following a reduction in the RP. Our analysis suggests that overall cost savings can be mostly attributed to savings from brand-name drugs. The coefficient on total expenditures for brand-name drugs is positive (around 1.16%) and significant while the coefficient for generic drugs is insignificant.

In the appendix, we provide further robustness checks. First, Table A3 presents the corresponding 2SLS results using the average RP in other groups as instrument. Again, the results are very similar. Second, Table A5 presents regressions where both the RP and the outcomes are measured in euros or absolute quantities as opposed to log values. This enables us to split the overall effect across the two samples. Several of the estimates are imprecisely estimated, particularly for generics, while overall the results present a similar picture. For each euro reduction in the RP, the SHI saves 52k euros, while the effect on total expenditures is much smaller (+32k) due to larger patient copayments (−21k, not statistically significant). Overall, quantities increase due to the change mostly driven by generics, but the effect is not significant in the two subsamples individually, which reflects the previous results in terms of elasticities. Third, we provide a decomposition of the aggregate effects by keeping either quantities and prices or only prices constant at the pre-treatment level (Q4-2008) for the quarters following the adjustment and compare the coefficients to the observed effects. The main insight from this decomposition is that, overall, changes induced on the supply side (i.e., changes in prices) are the main driver of our findings at the aggregate level, while changes in quantities are of minor importance. The details are relegated to Appendix B.

Finally, as previously emphasized, the results of the analysis at the aggregate level should be taken with some caution due to a relatively small number of observations.

To conclude, we show that RP decreases indeed reduce the prices and expenditures of public health insurance plans. Furthermore, they only lead to a small substitution of brand-name drugs with generics, if any. However, it should be emphasized that, overall, expenditures decrease only modestly if reference prices are continually reduced, particularly for generics, which start from a low price level. Regulators should be careful not to shift the burden to the patients instead.

6 | CONCLUSION

We explore the causal effects of RP adjustments on prices, copayments, and aggregate expenditures and sales by drug type and quarter in the German market for anti-epileptics between 2009 and 2010 using a difference-in-differences approach. We separate the effects at the product level and at the aggregate level. At the product level, we find that the prices of both brand-name and generic drugs decrease mildly if the RP is reduced. Furthermore, copayments increase and the probability of the drug being exempt from copayments also decreases for both types of drugs.

At the aggregate, active substance level, revenues decrease significantly for brand-name firms mostly because the prices decrease. For generics, the revenue effect is weaker. An interesting result from a policy perspective is the shift from the expenditures of the SHI plans to aggregate consumer copayments, especially for generics. Our estimated coefficient on consumer copayments is highly positive but not significant, possibly due to a relatively small number of observations in the aggregate analysis. Other studies also find increasing copayments when reference pricing is introduced, but on a smaller scale relative to the payer's savings (Robinson, Whaley et al., 2017, e.g.,). Thus, future research would be welcome to explore the effects of cost-shifting due to changes in reference pricing in more detail. Finally, we find that total expenditures decrease only mildly. Since the characteristics of the anti-epileptic drug market (low cross-price elasticity, medical dependence on specific substances, no outside option) can be found in many drug markets, particularly for chronic diseases, it is an important question whether this research is generalizable to other prescription drug classes.

In a recent comment, Scanlon (2020) argued that administrative burden may hinder the roll-out of, in his view, successful reference pricing with a high potential for savings in many areas in health care (e.g., areas other than pharmaceuticals, compare the literature therein). This is different in Germany, where reference pricing for drugs is not part of a specific health plan but has been embedded in the law (German Social Code V) since 1989. Furthermore, the SHI, to which these rules apply, covers almost 90% of the German population. The RP is monitored and adjusted by one regulatory body and fixed across all health plans and pharmacies, which simplifies the administration.

We can draw several policy conclusions from our analysis. First, as already shown in the existing literature, reference pricing can help to lower health care expenditures by reducing prices. In our analysis of the German antiepileptics market, we find that a RP reduction of 1% leads, on average, to a price reduction of 0.43%. The reduction in price is stronger for brand-name

products than for generics (0.65% vs. 0.41%). Second, policymakers should be aware that further RP reductions may lead to only modest reductions of total health care expenditures, but may rather have an effect on how costs are split between the health insurance plans and the patients. On the one hand, more 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, a sufficient level of drug cost-sharing can lead to individuals avoiding necessary medical care or substituting drug use with more costly visits to a physician and imposing a substantial financial burden. For Germany, the latter issue is approached by income-related copayment limits. The so-called overcharge clause exempts families or individuals for whom the total annual copayments for drugs, dressings, and remedies exceed 2% of the gross annual family income (§62 SGB V). Such an income-based cap on copayments was suggested by Newhouse and the Insurance Experiment Group (1993) and later by Gruber (2006) when summarizing the results of the RAND Health Insurance Experiment. Finally, since in Germany RP groups may comprise different active substances that are only chemically similar or that have similar therapeutic outcomes, patients may perceive major differences in quality or may face difficulties with substituting one (more expensive) drug with another.

ACKNOWLEDGMENTS

We would like to thank Kurt Brekke, Nils Gutacker, Ulrich Heimeshoff, Olena Izhak, Arndt Reichert, Martin Salm, Hendrik Schmitz, Moritz Suppliet, Stephan L. Thomsen, and Sebastian Wichert for helpful comments. We are grateful for comments and discussions with the seminar audiences at the University of Augsburg, at the KOF seminar at the ETH Zürich, LUH, and at the Center for Health Economics in York. We also thank the participants of the Empirical Health Economics Workshop in Wuppertal 2017, the Vereinstagung in Freiburg 2018, the Euhea conference in Maastricht 2018 and the annual conference of the dggö in Nürnberg (online) 2021 for helpful discussions. We are grateful to IQVIA (former IMS Health) for providing the data. The research has been started while we worked at the Düsseldorf Institute for Competition Economics (DICE) at Heinrich Heine University. Annika Herr acknowledges financial support by the German Research Foundation (DFG) (grant HE 6825/2-1).

Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST

The authors do not have any conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from IMS Health (now IQVIA). Restrictions apply to the availability of these data, which were used under license for this study.

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ENDNOTES

[1] The famous RAND Health Insurance Experiment (HIE) with 2000 US families conducted between 1971 and 1986 showed that demand for pharmaceuticals behaves price-elastic: individuals reduce health care expenditure when co-insurance rates increase (see Leibowitz et al. (1985), Manning et al. (1987) as well as Gruber (2006)).

[2] In the following, we use the terms active substance, active ingredient, and molecule synonymously.

[3] Note that, as pointed out by Brekke et al. (2011), the price convergence prediction only holds if the reference price is exogenously set, but not if the adjustment depends on the firms' pricing decisions. In their analysis of the Norwegian market, Brekke et al. (2011) also find no evidence supporting price convergence.

[4] Low-income insureds with health care costs exceeding a household-income related threshold (1%–2%) and minors are exempt for social reasons. Because of the pharmacist's reimbursement, the price for prescription drugs always exceeds €8.

[5] It is possible that drugs with similar (but not the same) chemical compounds are grouped in one category (level 2) or with similar therapeutic effects or combinations of active substances (level 3). Since 2011, on-patent drugs may also be grouped into reference price groups if they cannot prove significant additional benefits to a pre-defined comparator.

[6] In a pharmacy, different rules apply if no brand has been specified. The two most important are, first, that pharmacists are supposed to hand out the drug for which the patient's health insurance has negotiated a rebate (if available in short notice) or, second, one of the three cheapest alternatives (whichever is available). In urgent cases, they can dispense another drug that is in stock.

[7] The data were provided by IMS Health (2012) and are also used in Herr and Suppliet (2017).

[8] Note that there is a mechanical relationship between the ex-factory price and the retail price paid by patients. The retail price is calculated by adding regulated compensation for pharmacies and wholesalers and value-added tax to the ex-factory price.

[9] We further drop primidone since the market share of this group is small with only three firms serving the market. This active ingredient is used as a reserve drug because of severe side effects.

[10] Some prices change early during this period. However, including that quarter alters the coefficient sizes only slightly, while the precision remains. Tables upon request.

[11] It has been shown that the difference-in-differences approach gives robust estimates of the introduction of reference pricing compared to several matching methods (Brown & Atal, 2019).

[12] In the appendix, we also present regression results in levels, where both change in the reference price and the outcome variable are measured in euros.

[13] Note that 70% of the generic drugs would be dropped for this outcome because they are exempt from copayments and log(0) is undefined. For the estimation in logs, we transpose zero copayments by using $\log(copay\_ddd) \approx \log\left(copay\_ddd + \sqrt{(copay\_ddd + 1)}\right)$ (Helmdag, 2017).

[14] If they are, the difference is still close to zero and opposed to the treatment effect (compare quarters −3 and −4 for retail and ex-factory prices overall and for generics).

[15] We use STATA 15 and apply *xtivreg2* by Schaffer (2010) with clustered standard errors at reference price group level and *ivregress 2sls* with bootstrapping at the aggregate level.

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How to cite this article: Herr, A., Stühmeier, T., & Wenzel, T. (2023). More cost-sharing, less cost? Evidence on reference price drugs. *Health Economics*, *32*(2), 413–435. https://doi.org/10.1002/hec.4627

APPENDICES

A | Tables and figures

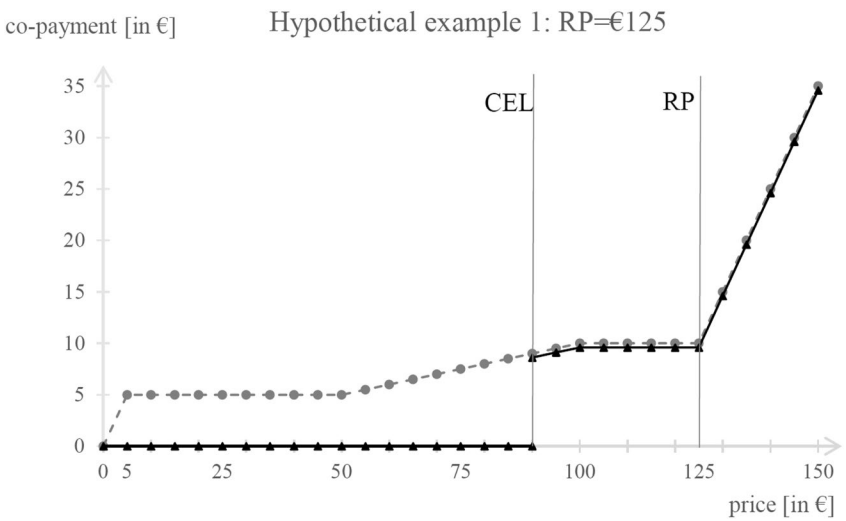

FIGURE A1 Copayments per product by price before (dashed line) and after (solid line) the introduction of a copayment exemption levels (CEL) (at ≈ 70% of reference price [RP]). Hypothetical example with rp = €125. In general, drug copayments in Germany are defined as 10% of the pharmacy's selling price (or the RP if the price lies above the 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. *Source*: Figure 1 from Herr and Suppliet (2017)

TABLE A1 Descriptive statistics at substance level, by substance before and after the reference price (RP) reduction

	Before				After			
	Generics		Brand-name		Generics		Brand-name	
Substance	**Mean**	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**
Carbamazepin (control)								
Firm revenues	4105	66	792	16	3808	56	757	17
Quantities	12,985	248	1706	35	12,140	159	1649	39
Copayments	705	38	195	6	341	157	179	4
Expenditures Statutory Health Insurance (SHI)	7395	133	1176	23	7168	150	1133	25
Total expenditures	8100	122	1371	27	7509	88	1312	28
Number of firms	20	1	6	0	21	0	5	1
Generic market share	0.88				0.88			
Gabapentin								
Firm revenues	13,855	414	1098	66	13,292	421	366	50
Quantities	8401	447	394	25	9332	359	191	22
Copayments	342	181	116	9	1978	74	140	28
Expenditures SHI	21,057	766	1439	87	19,019	707	396	46
Total expenditures	21,399	699	1555	96	20,997	661	535	74
Number of firms	24	1	8	0	25	0	6	1
Generic market share	0.96				0.98			
Lamotrigin								
Firm revenues	5124	101	1254	64	3642	167	480	34
Quantities	5678	289	717	38	6508	353	766	60
Copayments	513	17	158	4	864	25	125	13
Expenditures SHI	7649	180	1662	87	5516	273	707	55
Total expenditures	8162	183	1820	90	6380	266	833	68
Number of firms	29	1	8	1	30	0	4	1
Generic market share	0.89				0.89			
Valproate								
Firm revenues	4250	178	1489	43	3954	110	1294	24
Quantities	7891	432	3044	84	8444	342	2708	50
Copayments	936	70	375	11	1227	81	331	6
Expenditures SHI	6662	397	2304	67	6081	271	1996	35
Total expenditures	7598	338	2679	78	7308	208	2327	41
Number of firms	17	1	6	0	18	1	6	1
Generic market share	0.72				0.76			

Note: 7778 observations. RP × 1.05 ensures that small deviations from the reference price do not lead to large changes.

Source: Pharmascope 2012, IMS Health (2012). Quarterly, 2009–2010 (Q1-2010 dropped).

TABLE A2 First-stage estimates with fixed effects, at the product level

	(1)	(2)	(3)
ln(ref. price)	**Total**	**Generic**	**Brand-name**
ln(# products in other ATC5)	−4.702***	−4.757***	−4.191***
	(0.377)	(0.392)	(0.316)
N	7778	6761	1017
F	108.6	96.85	120.1
F excl. rest.	189.349	147.53	175.83

Note: Standard errors in parentheses *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. First-stage estimates compare to 2SLS-regressions presented in Table 5. Regressions include quarter and product fixed effects and standard errors are clustered at reference price group level.

Source: FASHI and Pharmascope, IMS Health (2012). Quarterly, 2009–2010.

TABLE A3 Effect of a change in the reference price at active substance level, 2SLS, bootstrapped standard errors

	(1)	(2)	(3)	(4)	(5)
ln(*y*)	**Firm revenues**	**Quantities**	**Copay**	**Expend. SHI**	**Total expend.**
Total					
0.368**	−0.224	−1.679	0.399	0.255**	
	(0.157)	(0.157)	(2.066)	(0.253)	(0.130)
R^2 adj.	0.986	0.995	0.322	0.994	0.987
Generics					
ln(ref. price)	0.248	−0.221	−2.122	0.304*	0.160
	(0.169)	(0.201)	(1.559)	(0.174)	(0.150)
R^2 adj.	0.989	0.989	0.296	0.995	0.990
Brand-name					
ln(ref. price)	1.715**	0.350	0.0208	1.738**	1.502**
	(0.670)	(0.674)	(0.428)	(0.817)	(0.682)
R^2 adj.	0.842	0.946	0.916	0.784	0.841

Note: Aggregated at active substance level. Standard errors in parentheses. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. *N*: 28 observations. Bootstrapped standard errors with 5000 replications. Time and active substance fixed effects included.

Source: Pharmascope, IMS Health, 2009–2010 (Q1-2010 dropped).

TABLE A4 Effect of a change in the reference price at the product level, Regression with reference price and outcomes in units, OLS

	(1)	(2)	(3)	(4)
	Ex-factory *p*/ddd	**Retail *p*/ddd**	**Copay/ddd**	**Pr(Exempt = 1)**
Ref. price	0.00149***	0.00179***	−0.000451	0.00495***
	(0.000398)	(0.000513)	(0.000979)	(0.00151)
R^2	0.338	0.342	0.0144	0.305
F	25.25	30.77	8.005	50.91
N	7778	7778	7778	7778
Generic				
Ref. price	0.00107***	0.00124**	0.000164	0.00533***
	(0.000365)	(0.000475)	(0.000836)	(0.00169)
R^2	0.362	0.368	0.0196	0.333
F	27.54	29.62	12.04	46.48
N	6761	6761	6761	6761

TABLE A4 (Continued)

	(1) Ex-factory *p*/ddd	(2) Retail *p*/ddd	(3) Copay/ddd	(4) Pr(Exempt = 1)
Brand-name				
Ref. price	0.00540***	0.00681***	−0.00565*	0.000991**
	(0.00103)	(0.00134)	(0.00293)	(0.000491)
R^2	0.403	0.396	0.0190	0.0649
F	23.91	22.73	5.276	2.670
N	1017	1017	1017	1017

Note: At product level. Standard errors in parentheses. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. Time and product fixed effects included. All outcomes and the reference price are used in absolute terms.

Abbreviations: ddd, defined daily dose; OLS, ordinary least squares.

Source: Pharmascope, IMS Health (2012), 2009–2010 (Q1-2010 dropped).

TABLE A5 Effect of a change in the reference price at active substance level, Regression in levels, OLS, bootstrapped standard errors

	(1) Firm revenues	(2) Quantities	(3) Copay	(4) Expend. SHI	(5) Total expend.
Ref. price	30.12***	−25.86**	−20.74	52.98***	32.25*
	(10.12)	(11.51)	(15.70)	(14.28)	(16.93)
R^2 adj.	0.998	0.995	0.703	0.999	0.998
Generics					
Ref. price	16.42	−23.61	−20.83	35.82***	14.99
	(15.15)	(21.32)	(19.37)	(13.76)	(22.49)
R^2 adj.	0.998	0.990	0.698	0.999	0.997
Brand-name					
Ref. price	13.39***	−2.655	−0.277	16.97***	16.69***
	(1.766)	(2.787)	(0.585)	(3.022)	(2.866)
R^2 adj.	0.983	0.995	0.974	0.981	0.986

Note: Standard errors in parentheses. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. *N*: 28 observations. Bootstrapped standard errors with 5000 replications. Time and active substance fixed effects included. Aggregate values in 1000 Euro or drug packages.

Abbreviation: OLS, ordinary least squares.

Source: Pharmascope, IMS Health, 2009–2010 (Q1-2010 dropped). Aggregated at active substance level. Own calculations.

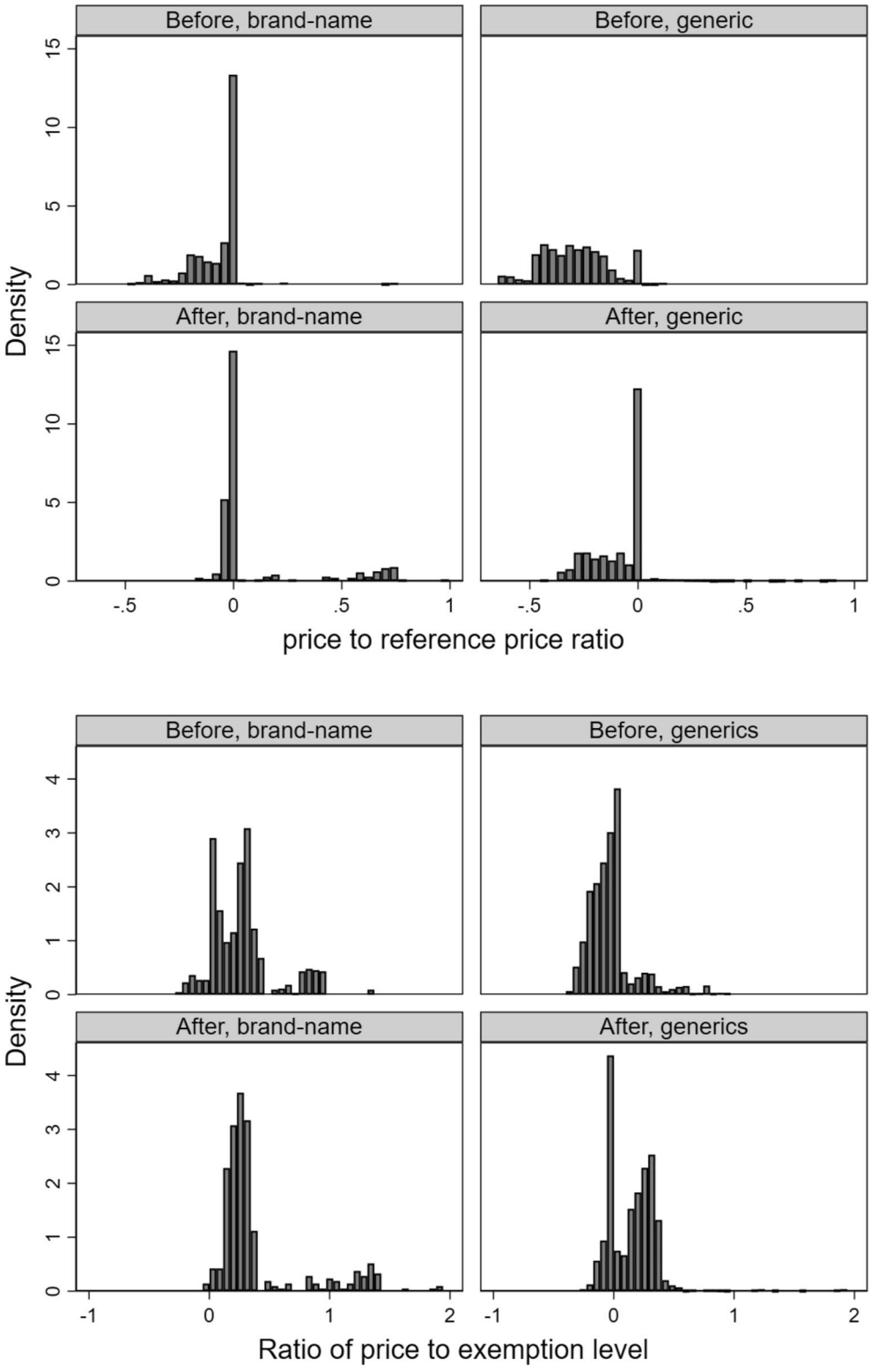

FIGURE A2 Histogram of price to reference price ratio and price to exemption level ratio before versus after Q2-2010 (all drugs). 4 anti-epileptic substances, 2009–2010. *Source*: FASHI and Pharmascope, IMS Health (2012). Own calculations

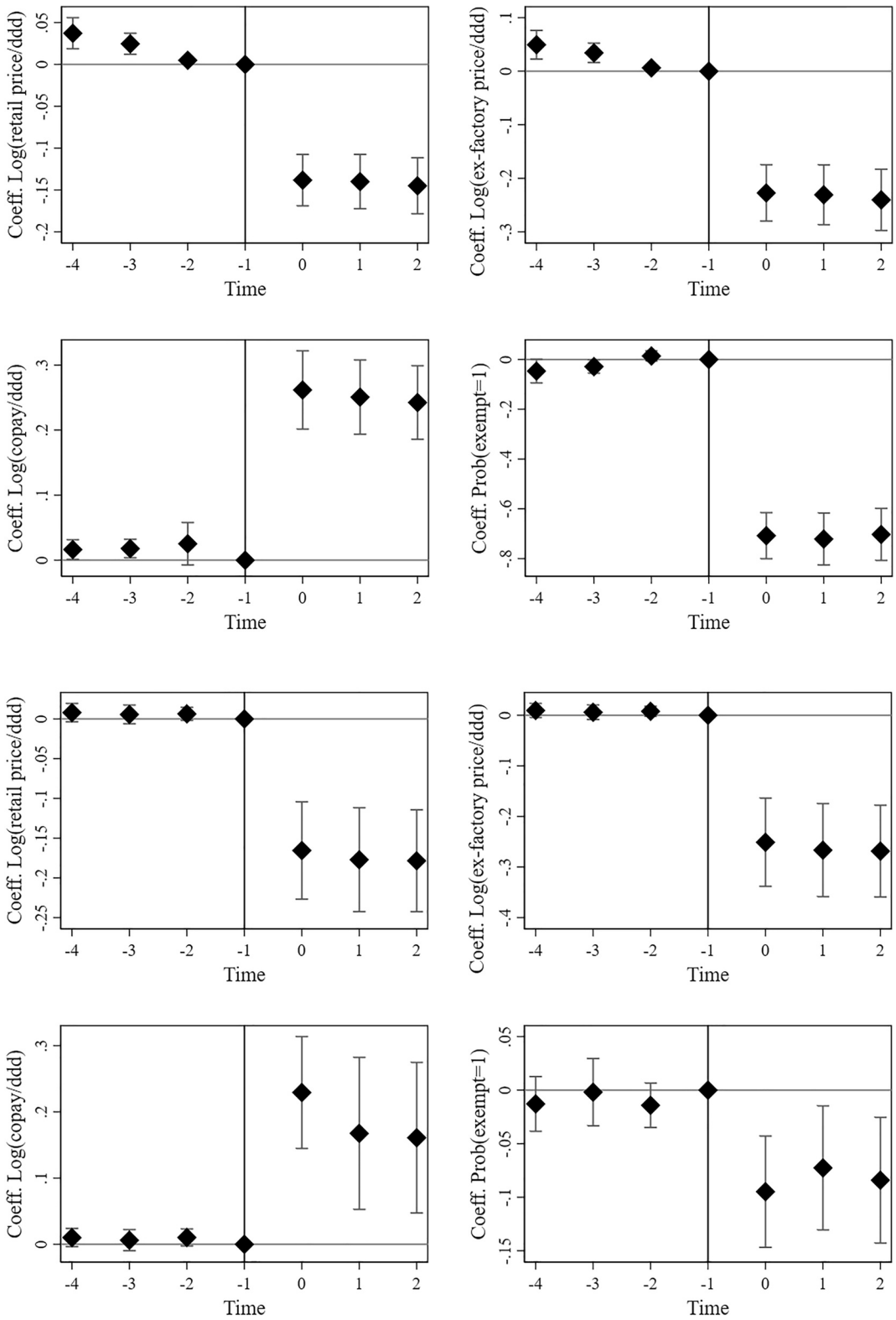

FIGURE A3 Event study (estimation coefficients by quarter) of the treatment versus the control group. Top: Generic drugs; bottom: Brand-name drugs. The treatment dummy equals one for three of the four substances and is interacted with quarter dummies, where Q4-2009 serves as the base category (−1) and Q1-2010 is dropped. We include package and quarter fixed effects and cluster the standard errors at reference price group level. *Source*: FASHI and Pharmascope, IMS Health (2012). Quarterly, 2009–2010 (Q1-2010 dropped). 7778 observations. Own calculations

B | Decomposition analysis: Hypothetical changes in aggregate measures holding prices and/or quantities fixed at pre-treatment level

To better understand the drivers of the changes in aggregate revenues, expenditures and copayments, we created hypothetical aggregates, where we kept (i) both quantities and prices fixed and (ii) only prices fixed from quarters six to eight at the level of quarter 4 (Q4-2009). This decomposition allows us to explore whether the overall effects are induced by changes on the supply side of the market (changes in prices) or by changes on the demand side (changes in consumed quantities) (Nevo & Hatzitaskos, 2006) compared to the pure mechanical effect of changing copayments (i). Tables A6–A8 present the analyses for three of the five outcomes (firm revenues, copayments and SHI expenditures). The first column of each table presents the estimation results when both quantities and prices are fixed, that is, these estimations represent the purely mechanical effects of a reduction in the RP and the corresponding changes in the copayments. The second column of each table shows the results when prices are kept fixed so that only changes on the demand side are considered (observed changes in the quantities). The final column repeats the overall effect from the main analysis taking both changes on the supply and demand side into account.

We start by looking at firm revenues in more detail. In column (1), if both prices and quantities are fixed (only the RP and the copayments vary, while the firms and the demand do not react), there is no significant effect on revenues and the coefficients are close to zero. Column (2) is the most interesting column. If prices are hypothetically fixed at the pre-treatment level and quantities are adjusted, revenues for generics would increase, while the decrease for brand-name drugs is not significant as is the total (negative) effect. The final column (3) shows the results if also prices are adjusted. It can be seen that changes in prices play a large role and that brand-name drugs' revenues are negatively affected. Thus, the overall effect is driven by both, increasing quantities and decreasing prices for generics, while decreasing prices drive the effects for brand-name drugs.

For aggregate copayments (Table A7), we note that copayments for both generics and brand-name drugs are increasing when prices and quantities are kept fixed at the level of Q4-2009. This is the mechanical effect of a reduction in the RP and leads, by definition, to larger copayments since prices do not adjust accordingly. The overall effects in column (3) are not statistically significant, but large. Hence, we can conclude from this analysis, that due to the price decreases following the RP decrease, total copayments increase less than they would without.

Lastly, the decrease in aggregate expenditures of the statutory health insurances (column 3) would not occur for generics and would be much larger for brand-name drugs if prices did not react (column 2). Interestingly, the pure mechanical copayment effect is similar to the overall effect. This is due to the fact that, on the one hand, price reductions reduce the mechanical copayment effect and lower savings while, on the other hand, changes in drug type composition help to remain changes in savings at a similar level.

Overall and confirming our analysis of the main results, price changes (supply side) drive the results more than changes in quantities.

TABLE A6 Effect of a change in the reference price on firm revenues at active substance level, OLS, bootstrapped standard errors

	Aggregate firm revenues		
	(1)	(2)	(3)
	***p* and *q* fixed**	***p* fixed**	**Overall**
Total			
ln(ref. price)	−0.0082	−0.146	0.407***
	−0.0445	−0.218	−0.156
R^2 adj.	1	0.989	0.986
Generics			
ln(ref. price)	0.00185	−0.303**	0.285*
	−0.0977	−0.15	−0.154
R^2 adj.	0.999	0.992	0.99
Brand-name			
ln(ref. price)	−0.0404	1.506	1.382***
	−0.0893	−1.28	−0.405
R^2 adj.	0.971	0.347	0.859

Note: Standard errors in parentheses. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. *N*: 28 observations. Bootstrapped standard errors with 5000 replications. Time and active substance fixed effects included. Column (3) reproduces the main results, Columns (1)–(2) present estimations with hypothetical quantities and prices.

Abbreviation: OLS, ordinary least squares.

Source: Pharmascope, IMS Health, 2009–2010 (Q1-2010 dropped). Aggregated at active substance level. Own calculations.

TABLE A7 Effect of a change in the reference price on aggregate copayments at active substance level, OLS, bootstrapped standard errors

	Aggregate copayments		
	(1)	(2)	(3)
	***p* and *q* fixed**	***p* fixed**	**Overall**
Total			
ln(ref. price)	−2.598	−2.682	−1.425
	−2.447	−2.472	−2.555
R^2 adj.	0.824	0.812	0.331
Generics			
ln(ref. price)	−2.573***	−2.898***	−1.868
	−0.952	−0.973	−1.285
R^2 adj.	0.772	0.774	0.302
Brand-name			
ln(ref. price)	−2.941***	−2.007***	0.144
	−0.595	−0.516	−0.298
R^2 adj.	0.879	0.825	0.919

Note: Standard errors in parentheses. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. *N*: 28 observations. Bootstrapped standard errors with 5000 replications. Time and active substance fixed effects included. Column (3) reproduces the main results, Columns (1)–(2) present estimations with hypothetical quantities and prices.

Abbreviation: OLS, ordinary least squares.

Source: Pharmascope, IMS Health, 2009–2010 (Q1-2010 dropped). Aggregated at active substance level. Own calculations.

TABLE A8 Effect of a change in the reference price on aggregate expenditures by Statutory Health Insurance (SHI) at active substance level, OLS, bootstrapped standard errors

	Aggregate expenditures by SHI		
	(1)	(2)	(3)
	***p* and *q* fixed**	***p* fixed**	**Overall**
Total			
ln(ref. price)	0.554***	0.336	0.419***
	−0.147	−0.205	−0.15
R^2 adj.	0.993	0.978	0.994
Generics			
ln(ref. price)	0.460***	0.147	0.326**
	−0.163	−0.208	−0.163
R^2 adj.	0.995	0.985	0.995
Brand-name			
ln(ref. price)	1.225***	2.730**	1.306**
	−0.21	−1.331	−0.557
R^2 adj.	0.942	0.616	0.806

Note: Standard errors in parentheses. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. *N*: 28 observations. Bootstrapped standard errors with 5000 replications. Time and active substance fixed effects included. Column (3) reproduces the main results, Columns (1)–(2) present estimations with hypothetical quantities and prices.

Abbreviation: OLS, ordinary least squares.

Source: Pharmascope, IMS Health, 2009–2010 (Q1-2010 dropped). Aggregated at active substance level. Own calculations.