International Journal of Clinical Pharmacology and Therapeutics, Vol. 49 – No. 6/2011 (397-402)

ISSN 0946-1965

DOI 10.5414/CP201552

The negative impact of rebate contracts on the health care of patients with depression in Germany

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Key words
antidepressants – rebate contract – compliance – hospitalization – data base

Abstract. Background: Aim of this study was to show the negative consequences of rebate contracts on health care of patients with depression. Negative consequences were defined as therapy withdrawal, increased resource utilization and the frequency of switch-back to initial pharmaceutical product in patients with conversion to a rebate pharmaceutical. Methods: This retrospective analysis was performed combining the information of 3 databases including information about 20 millions patients and 80% of all prescriptions in Germany. The time period of observation started 1 year before the initiation of rebate contracts. Observation time was 2 years. This study included adults (> 18 years) with an antidepressive drug therapy and who had a statutory health insurance with rebate contracts on antidepressive pharmaceuticals. Results: The mean persistence was 329 days for patients, who were switched to a rebate product compared to 365 days for patients who stayed on the initial drug therapy ($p < 0.0001$). 29.9% of the patients who were converted to a rebate product switched back to the initial antidepressive drug therapy within 1 year. 1,871 additional patients would be hospitalized due to the conversion to a rebate pharmaceutical that caused direct inpatient costs amounting to 19.9 million EUR per year in Germany. Conclusions: Despite the above limitations this analysis presents a clear association between the initiation of rebate contracts and a negative impact on health care of patients with an antidepressive drug therapy.

Received
January 26, 2011;
accepted
March 2, 2011

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Introduction

The Act on the Stabilizing of Contributions to Statutory Health Insurers ("Beitragssicherungsgesetz") came into force in January 2003 and set the compulsory conditions for the conclusion of rebate contracts. The options of the statutory health insurance companies for the composition of rebate contracts were enhanced by the Economic Optimization of Pharmaceutical Care Act ("Arzneimittelversorgungs-Wirtschaftlichkeitsgesetz"), which came into force in May 2006 and the health system reform bill ("GKV-Wettbewerbsstärkungsgesetz"). The health system reform bill became operative in April 2007 and allowed the realization and the initiation of rebate contracts, which have been used by many statutory health insurance companies. The Federal Government aims to lower costs of pharmaceutical products for the statutory health insurance companies by the rebate contracts.

The great amount of rebate contracts, the non-availability and the frequent switches of pharmaceutical products unsettle many patients [1]. According to an interview of the Allensbach Institute every third German receives a different pharmaceutical product as prescribed by their physician or as the patient was familiar with before the initiation of rebate contracts [2]. Anyway, 7% of the affected patients and 11% in the age group over 60 years stated to have problems, especially with tolerance and side effects of their pharmaceutical product due to the rebate contract switch. Moreover, impairments of the therapeutic effect were mentioned by the patients. However, for some of the pharmaceuticals, i.e. antidepressive drugs, a substitution referred to be critical by the German Pharmaceutical Society (Deutsche Pharmazeutische Gesellschaft), as the accurate adjustment of therapy is essential for the therapeutic success and the avoidance of side effects [3]. An analysis of the KV Nordrhein (Regional Association of Statutory Health Insurance Physicians) documented that the majority of general practitioners perceive an association of rebate con-

tracts and severe problems with substitution and compliance [4].

Non-compliance is fundamental in pharmaceutical therapy. Different studies reveal, that every fifth prescription is refused at pharmacy (primary non-compliance) and that non-compliance is existent in 50% of the prescribed pharmaceutical products. Even life-saving drugs are not excluded, as the compliance rates for statins in secondary prevention of myocardial infarction and stroke prove [5].

Non-compliance is often followed by therapeutic failure and significant costs of the health system and the society. In case of antibiotics non-compliance lead to therapeutic failure, increase of relapse, development of resistance and enhanced rates of complications. The extension of disease duration is followed by significant economic costs [6]. Therapy failure and the associated consequences including the aggravation of disease can lead to excessive physician visits and additional examinations, prescriptions, hospitalizations and associated direct and indirect costs [7]. The costs of non-compliance for the German health care system are estimated to amount to 10 billion EUR per year according to health economic publications [8]. A recent expert estimation assumes costs to amount to 15 billion EUR [9]. The costs of non-compliance induced by rebate contracts are unknown.

Aim of this study was to show the negative consequences of rebate contracts on health care of patients with depression. Negative consequences were defined as therapy withdrawal, increased resource utilization and the frequency of switch-back to the initial pharmaceutical product in patients with conversion to a rebate pharmaceutical.

Methods

Databases

This retrospective analysis was performed combining the information of 3 databases including IMS Contract Monitor®, IMS® LRx and IMS® Disease Analyzer.

The IMS Contract Monitor® database contains information regarding the volume of drug delivery of public pharmacies in the SHI market at a national level or AHIP regions. It is differentiated according to the seven individual state health insurance types and analyses the five largest substitute sickness insurance societies in the SHI market. The designation is compliant with § 305a SGB V (Social Security Code Book V) and takes into account discount agreements according to § 130a para. 8 SGB V. The data contain an identification of the rebate to regulated commercial forms. Based on the IMS Contract Monitor® information concerning the drug manufacturer, the health insurances involved in the discount contracts and the introduction date of a discount contract (= index date in the group of patients who were not switched to a discount drug) can be determined.

The IMS® LRx database allows continuous long-term analyses of patients with SHI prescriptions. IMS® LRx can be used to represent different treatment courses between physicians. The database records all prescription information for SHI patients nationwide with coverage of about 80%.

IMS® Disease Analyzer is a database whose data originates from more than 2,000 practices of various specialist groups in Germany, which continually provide anonymized consultation data via standardized interfaces. Available data include diagnoses (according to ICD-10 or original reports of the physician), prescriptions, reception orders and referrals, disability certificates, as well as demographic data about physician and patient, and other resource consumption. The practices are selected by drawing a stratified random sample of all practices in Germany that use computerized accounting [10].

Observation time

The time period of observation started 1 year before the initiation of rebate contracts (i.e. 04/2007) or with the first prescription of a rebate pharmaceutical (index date). Observation time was two years.

Study population

This study included adults (> 18 years) with an antidepressive drug therapy who had

Table 1. Baseline characteristics of the study patients.

Variable	Switch (n = 464,116)	No switch (n = 703,069)
Mean age (standard deviation)	61.1 (16.7)	62.2 (16.4)
Female patients in %	71.8%	72.3%
Treatment with antihypertensives	60.7%	59.9%
Treatment with lipid regulators	21.7%	19.5%
Treatment with oral antidiabetics	13.5%	13.8%
Treatment with thrombo-inhibitors	21.2%	17.8%
Treatment with cardiac drugs	12.9%	11.7%
Treatment with blood clotting agents	0.1%	0.1%
Number of different additional therapies (standard deviation)	1.3 (1.2)	1.2 (1.2)
Treatment with antipsychotics	40.7%	34.6%

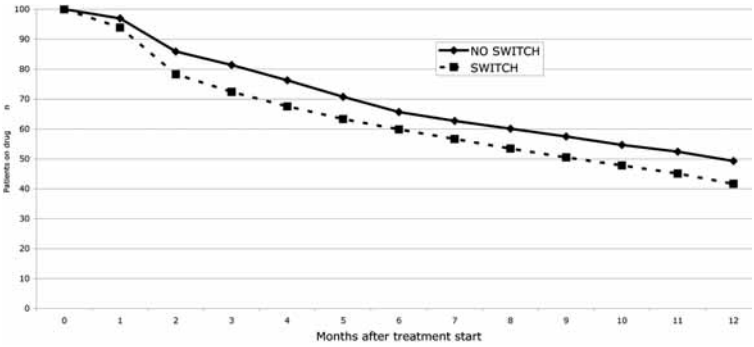

Figure 1. Persistence curves 12 months after switch to a rebate product for patients on antidepressive therapy with a switch versus patients without.

a statutory health insurance with rebate contracts on antidepressive pharmaceuticals.

Outcome parameters

Three outcome parameters were defined:

1. Rate of therapy withdrawal: defined as the number of patients, who did not continue therapy with the initial pharmaceutical product or a product of the same ATC class. Persistence ranged from index date unitil the day, on which the last package was used up, maximum 1 year. The persistence rate was calculated as percentage of patients with a prescription of the initial drug in a defined time horizon. Persistence curves served as illustration. Furthermore, the rate of therapy withdrawal was evaluated identifying the number of patients, who did not receive the initial pharmaceutical product after the conversion to a rebate product in comparison to patients without conversion to a rebate product. The differences of the rates of therapy withdrawal were tested on significance using the χ^2-test.

2. Switch-back rates were defined as percentage of patients, who switched back to the initial pharmaceutical product within one year after conversion to a rebate product. The focus of the switch-back analyses was descriptive; subgroup analyses regarding age and gender were performed.

3. Hospitalization rates due to a depression within 1 year after index date were compared to hospitalization rates before index date. The association of hospitalization rates and conversion to a rebate product was analyzed by using multivariate regression including potential confounders (age, gender, insurance status, region, co-diagnoses and co-therapies).

4. Direct and indirect costs due to additional hospitalization of patients who were switched to a rebate product were estimated based on official sources [11, 12, 13].

Results

Study population

1,167,185 patients with an antidepressive drug therapy were included in the persistence analysis using the LRx database. 464,116 patients were converted to a rebate product whereas 703.069 patients continued with the initial pharmaceutical product.

Persistence and rates of therapy withdrawal

The persistence analyses revealed that patients, who were converted to a rebate product had a higher rate of therapy withdrawal compared to patients without conversion (Figure 1). The proportion of the converted antidepressant patients who withdrawn therapy within 3 months after the switch is 48.1% higher than the proportion of patients who discontinued treatment within the same period and receiving the initial drug therapy (27.7% versus 18.7%, $p < 0.0001$). The mean persistence was 329 days for patients, who

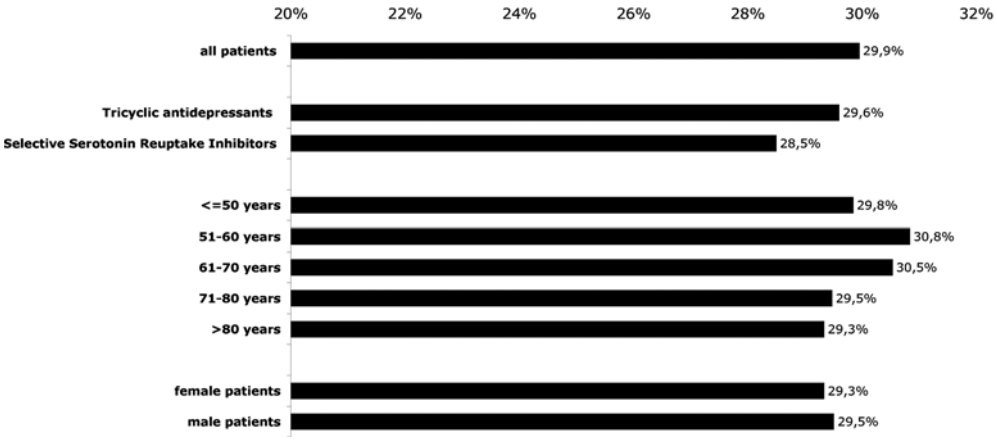

Figure 2. Frequency of switch-back to the initial therapy in patients who were switched to a rebate product.

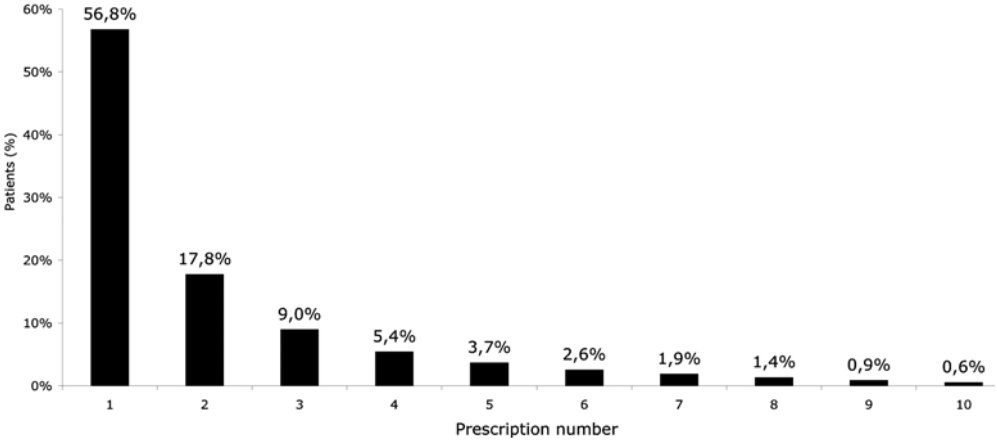

Figure 3. Time points of switch-back to the initial therapy in patients with depression.

were switched to a rebate product compared to 365 days for patients who stayed on the initial drug therapy ($p < 0.0001$).

Switch-back

29.9% of the patients who were converted to a rebate product switched back to the initial antidepressive drug therapy within 1 year. A high rate of switch-back was found in all age groups, especially younger patients showed high switch-back rates in contrast to elderly patients (> 80 years) who tend to stay on the rebate product. The proportion of switch-back is independent on age and gender of the patients (Figure 2). 56.8% of switch-back patients switch to the initial drug therapy after the first prescription of the rebate product. 83.6% of the switch-back patients perform their switch-back within the time period until their 3. prescription (Figure 3).

Ressource utilization and costs

35,073 patients were included in this study, of which 4,589 patients were converted to a rebate pharmaceutical. The descriptive analysis shows that patients with conversion to a rebate product require enhanced resource utilization (physician visits, hospitalizations, assignments to specialized physicians) whereas resource utilization in patients, who stay on initial therapy is stable or even decreasing. The major difference is seen in hospitalization rates. The probability of hospitalization due to a depressive episode in antidepressant patients is unadjusted 27% higher after a switch to a rebate pharmaceutical compared to patients on initial therapy ($p = 0.0001$). After adjusting for the majority of demographic and clinical variables the risk of hospitalization is 18% higher in patients with a switch to a rebate pharmaceutical in comparison to patients without change of drug therapy. Moreover, in patients over 65 years this risk is 22% higher (Table 2).

Table 2. Probability of hospitalization of for antidepressant patients after switching to a rebate product.

Logistic regression model	Odds ratio (95% CI)	p value
Without covariates	1.27 (1.13 – 1.43)	0.0001
Adjusted for hospitalization prior to index date	1.26 (1.12 – 1,42)	0.0002
Adjusted for hospitalization prior to index date, age, gender, region	1.25 (1.10 – 1.42)	0.0004
Adjusted for hospitalization prior to index date, age, gender, region, comorbidity (heart, metabolism, kidney, liver, oncology)	1.18 (1.04 – 1.34)	0.0088
Patients 65 years and up; adjusted for hospitalization prior to index date, age, gender, region, comorbidity (heart, metabolism, kidney, liver, oncology)	1.22 (1.02 – 1.46)	0.0274

Especially due to frequent hospitalizations high costs for the health care system arise. The costs of additional hospitalizations in patients with conversion to a rebate pharmaceutical were estimated by the percentage of antidepressant patients, who were switched to a rebate pharmaceutical and hospitalized (12,106 patients according to the present study and extrapolated regarding the German population based on IMS disease analyzer database). In contrast only 10,235 patients without conversion would be hospitalized within 1 year. As a consequence, 1,871 additional patients would be hospitalized due to conversion to a rebate pharmaceutical. Assuming a mean duration of stay of 50 days and mean costs of 10.650 EUR per hospitalization period direct inpatient costs amount to 19.9 million EUR per year in Germany [11]. Indirect costs were calculated based on employer rates, days of hospitalization and failure in productivity and amounted to 3.5 Mio. EUR per year [11, 12, 13]. Additional non-productive days due to illness were not considered.

Conclusion

There are examples of other diseases in literature concerning this problem.

Several studies indicate non-compliance due to switch to another pharmaceutical product [14, 15, 16]. Often, patients feel irritated towards their medication and failure in drug application and dosing is seen [15]. The majority of patients with a conversion to a rebate product experience adverse events due to the new drugs or have serious problems regarding intake of medication [16]. Additionally, Schmidt analyzed the massive pressure on physicians due to rebate contracts [17]. In different areas of therapy (Diabetes, Migraine, Parkinson) patients who were switched to a rebate product switch back to their original product [18].

The patients switched to a rebate simvastatin product discontinue their lipid-lowering treatment more often than patients who had not been switched to another drug. The proportion of the switched simvastatin patients who discontinue treatment within 12 months after the switch is 10% higher than the proportion of not switched patients who discontinue treatment within the same period. Both the number of physicians visits and referrals is significantly higher in patients who were switched to a rebate simvastatin product than in not switched patients [18].

To our knowledge the present analysis is the first one to evaluate consequences of rebate contracts on persistence, resource utilization and costs of antidepressant patients based on real-life health care data.

The results of this database analysis reveal that rebate contracts are associated with a worse persistence and enhanced therapy withdrawal rates in patients with an antidepressive drug therapy. This may be interpreted as patients' irritation due to the rebate pharmaceutical or may be a consequence of problems with the medication, like adverse events or decreased effectiveness. The switch-back analyses confirm the difficulties with rebate products as many patients were converted to their initial therapy.

Resource utilization was increased in patients with a switch to a rebate product, especially due to higher rates of hospitalization. Direct and indirect costs were estimated to amount to 23 Mio. € due to additional hospitalization rates within the first year after therapy conversion. However, the limitations of this cost analysis should be noticed. The mean residence time and the mean costs of a hospital stay were drawn from a study including 10 hospitals in Bavaria, Baden-Wuerttemberg and Nordrhein-Westfalen between 2001 and 2003. The actual costs may vary. However, this was the study with best available evidence.

Further fundamental limitations should be kept in mind, when interpreting the results of this study. This analysis was conducted to evaluate the impact of rebate contracts on the health care of patients with an antidepressive drug therapy and should not be interpreted beyond that. Furthermore, the effectiveness of therapy could not be analyzed given that relevant outcome parameters were not documented in the database (i.e. suicides).

Despite the above limitations this analysis presents a clear association between the initiation of rebate contracts and a negative impact on health care of patients with an antidepressive drug therapy. The impact of rebate contracts on health care should be evaluated for further therapeutic fields in additional research projects.

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