

Trends in Outpatient Prescription Drug Costs in Diabetic Patients in Germany, 1994–2004

WOLFGANG RATHMANN, MD, MSPH
BURKHARD HAASSTERT, PHD

ANDREA ICKS, MD, MPH, DRPH
GUIDO GIANI, PHD

OBJECTIVE — New antidiabetic medications have been introduced during the last decade, but their impact on health care cost is largely unknown. Prescription costs in diabetic patients in primary care in Germany were evaluated (1994–2004).

RESEARCH DESIGN AND METHODS — A total of 46,017 diabetic patients and 46,017 age- and sex-matched control subjects in 400 nationwide practices (2004) were compared with 29,956 diabetic patients and 13,226 control subjects (361 practices) in 1994 (data from IMS HEALTH). Inflation-adjusted age- and sex-standardized costs (ex-manufacturer prices) were calculated.

RESULTS — Mean annual total prescription costs per diabetic patient were €559 in 2004 (€372 in 1994), equaling a 60% (standardized) increase ($P < 0.01$). Average costs for antidiabetic medication were €172 in 2004, a 100% increase ($P < 0.01$). The major antidiabetic cost factor was insulin and analogs, which accounted for 22% of total drug costs in diabetic patients in 2004 (17% in 1994). All oral antidiabetic drugs together accounted for 8% of total costs (6% in 1994). New drugs (glitazones, glinides, and insulins) accounted for 15% of total costs (40% of antidiabetic drugs) in 2004. A 40% increase (€387 vs. 286) in all non-diabetes-related drugs was due mainly to cardiovascular and lipid-lowering drugs. In nondiabetic patients, only a 30% cost increase was found (€210 vs. 147; $P < 0.01$).

CONCLUSIONS — Prescription drug costs among diabetic patients increased 60% during the last decade, which was twofold higher than the increase in nondiabetic patients. New types of antidiabetic drugs accounted for a substantial cost share of the overproportional increase for diabetes treatment. Progress in pharmacological therapy is a key driver of drug expenditure growth in diabetes treatment.

Diabetes Care 30:848–853, 2007

During the last decade, antidiabetic prescription patterns have become increasingly complex (1–3). This complexity is the result of both the expanding evidence obtained from major clinical trials on intensified treatment of type 2 diabetic patients (e.g., the U.K. Prospective Diabetes Study) and the launch of new medications such as human insulin analogs (4). In particular, continuously increasing prescription use

of insulin was observed during the last decade in European countries (5,6). Since 1995, the number of insulin prescriptions has almost doubled in Germany (5). Currently, 27% of diabetic patients receive insulin prescriptions, based on German health insurance data (7). Among oral antidiabetic drugs, prescription use of biguanides increased fourfold during the last decade, whereas use of sulfonylureas has steadily declined (5).

From the Institute of Biometrics and Epidemiology, German Diabetes Center, Leibniz Institute at the Heinrich-Heine-University, Düsseldorf, Germany.

Address correspondence and reprint requests to Dr. Wolfgang Rathmann, MSPH (USA), Institute of Biometrics and Epidemiology, German Diabetes Center, Aufm Hennekamp 65, D-40225 Düsseldorf, Germany. E-mail: rathmann@ddz.uni-duesseldorf.de.

Received for publication 25 July 2006 and accepted in revised form 29 December 2006.

Abbreviations: ATC, anatomical therapeutic chemical classification system; SMBG, self-monitoring blood glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc06-2000

© 2007 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

In most countries including Germany, the majority of diabetic patients are treated predominantly by general practitioners and internists. There has been no evaluation of current trends in prescription use and costs among diabetic patients in the German primary health care system. To our knowledge, there also has been no longitudinal cost analysis from other European countries. In 1994, we found that diabetes was associated with threefold increased prescription costs in German primary care practices, due mainly to antidiabetic treatment and cardiovascular drugs (8). We have used a database of a nationwide sample of general and internal medicine practices (Disease Analyzer, IMS HEALTH) (9). We now expand this prior analysis by a second cross-sectional economic evaluation in 2004 using a similar nationwide pharmaceutical database to study 10-year changes in prescription drug costs in diabetic patients and nondiabetic control subjects.

RESEARCH DESIGN AND METHODS

Disease Analyzer database

The Disease Analyzer database (IMS HEALTH) has been described in detail elsewhere (8–10). Briefly, all drug prescriptions, diagnoses, and basic demographic data are prospectively assembled from the practice computer system of 400 practices (about 1% of primary health care practices) throughout Germany, which largely resemble the characteristics of all general and internal medicine practices with respect to geographic distribution, age and sex of physicians, and the ratio of primary care internists to general practitioners (8,9). Diagnoses (International Statistical Classification of Diseases, 10th Revision [ICD-10] and prescriptions (anatomical therapeutic chemical classification system [ATC]) are coded, and the quality of practice reports is continuously monitored by IMS HEALTH on the basis of a number of criteria (e.g., completeness of records and linkage of diagnoses and prescriptions).

Diabetic patients were identified on the basis of prescription of antidiabetic

drugs or specific diagnoses. In 1994, diabetes-related diagnoses were used for selecting diabetic patients only when confirmed by a diabetologist referring to the complete original physician text. In 2004, the panel physicians were asked to classify all diabetes diagnoses into confirmed or suspected cases. Only patients with a "confirmed diagnosis" of diabetes were selected for the study.

In Germany, migrations of patients from one physician to another are seen frequently. Therefore, to obtain a more valid estimate of patients treated by the same practitioner and their corresponding prescription costs, the analyses were limited to subjects who had at least one consultation per year over a 3-year period (1993–1995 and 2003–2005). Because there were few diabetic patients in young age-groups and to restrict the analysis mainly to patients with type 2 diabetes, a minimum age of 30 years was chosen. The vast majority of patients aged <30 years have type 1 diabetes. In Germany, this cost-intensive patient population is predominately treated by diabetologists having their own practice or in outpatient clinics. Thus, the database does not cover the antidiabetic treatment costs for this age-group. In 1994, all diabetic patients ($n = 29,956$) in 361 panel practices were compared with a 5% random sample ($n = 13,226$) of the nondiabetic population. In 2004, all 46,017 diabetic patients and 46,017 randomly selected nondiabetic control subjects were included. The two practice panels were independent samples with little overlap.

Prescriptions and related costs

Prescription costs were assessed in euros as ex-manufacturer prices, which are ~50% of pharmacy sales prices in Germany. The 1994 costs were inflation-adjusted to 2004 euros based on the German Consumer Price Index by the German Federal Statistical Office (inflation factor 1.15; <http://www.destatis.de>, as of August 2006).

First, the proportions of patients with specific prescriptions, the mean number of prescriptions, and mean costs per treated patient were calculated for all ATC groups. In addition, the mean prescription costs referring to the whole patient group including both subjects with and without a specific prescription (costs per patient) were also calculated. Relative cost ratios (2004/1994) were estimated by direct standardization of age (seven strata)- and sex-specific values in the basis of the

total patient population in 2004; 99% CIs were estimated for the age- and sex-standardized ratios, which were considered to be significantly increased or decreased at a level of $P < 0.01$ if the CIs did not include 1.0. We also compared diabetic and nondiabetic patients by applying age- and sex-standardized ratios (99% CI) using the whole population as standard. Thus, all prescription prevalences and costs are crude (nonstandardized) values, whereas all ratios (2004/1994; diabetic versus control subjects) are standardized with respect to age and sex (standard: whole patient population). All analyses were performed using SAS for Windows (version 9.1; SAS Institute, Cary, NC).

RESULTS— The age (mean \pm SD) of diabetic patients was >10 years higher than that of nondiabetic control subjects (1994: 68 ± 13 vs. 55 ± 16 years; 2004: 68 ± 12 vs. 57 ± 15 years; $P < 0.01$). No significant difference was found for sex in 1994, whereas in 2004, a lower percentage of women was found among diabetic patients (58 vs. 51%, $P < 0.01$). Treatment in internal medicine practices was only slightly more frequent among diabetic patients (1994: 27 vs. 25%, 2004: 25 vs. 24%; $P < 0.01$).

Prescription prevalences and costs

Table 1 shows the prescription prevalences of various treatments, and the mean annual number of prescriptions per patient for five major cost-intensive ATC groups. The prevalence of diabetic patients with prescriptions for antidiabetic agents or diabetes care products increased from 1994 to 2004, whereas no significant difference was found for all non-diabetes-related prescriptions. An increasing prevalence was also found for cardiovascular and hematological (including antithrombotic agents) drugs, whereas prescriptions of neurological agents, gastrointestinal drugs, and anti-inflammatory agents declined both in diabetic and nondiabetic patients over the 10-year period. Substantial differences between diabetic patients and control subjects (ratio) were found only for use of cardiovascular and hematological drugs ($P < 0.01$) (Table 1).

The mean annual number of prescriptions per drug-treated patient was also higher among diabetic subjects compared with control subjects, with little change over time. Overall, diabetic patients re-

ceived more than twice the number of prescriptions per year than control subjects in 2004, which was still higher after excluding all diabetes-related agents and adjusting for age and sex (ratios) ($P < 0.01$) (Table 1).

The mean annual costs per treated patient for all prescriptions combined increased by 50% (2004 vs. 1994) in diabetic patients and were still 40% higher after excluding all diabetes-related agents ($P < 0.01$) (Table 1). A 30% increase was found in nondiabetic patients ($P < 0.01$). Prescription costs were about 30–50% higher for most ATC groups both in diabetic and nondiabetic patients in 2004 compared with 1994 ($P < 0.01$). As expected, substantial cost differences between diabetic patients and control subjects were found for cardiovascular drugs at both time periods ($P < 0.01$). Overall, the age- and sex-adjusted costs per treated patient were about twofold higher in 1994 and 2004 among diabetic patients.

The average annual prescription costs per patient in the diabetic population were €559 in 2004, equaling a 60% increase ($P < 0.01$) (Table 1). Average costs for antidiabetic medications increased 100% ($P < 0.01$). With respect to all non-diabetes-related drugs, 40% higher costs were found over the 10-year period. In nondiabetic patients, a 30% increase for total prescription costs was observed from 1994 to 2004 ($P < 0.01$). The average 10-year cost increase in the various ATC groups ranged between 10 and 50%, except for neurological agents, for which 110–120% higher drug costs were found in both diabetic and nondiabetic patients ($P < 0.01$). In 1994, the average prescription costs among diabetic patients were increased twofold compared with control subjects after age and sex differences were taken into account, with a slight increase in 2004 (ratio 2.4; $P < 0.01$). Among the different ATC groups, a widening difference in costs between diabetic and nondiabetic patients was found for cardiovascular drugs only.

Prevalence and costs of antidiabetic drugs and agents

A 50% prevalence increase for insulin prescriptions, an almost fourfold increase for biguanide use, and a threefold higher prevalence of self-monitoring blood glucose (SMBG) tests was observed over the 10 years (all $P < 0.01$) (Table 2). A substantial decline was found for sulfonylureas (–37%) and acarbose (–50%).

Table 1—Prevalence of various treatments, mean number of prescriptions per year, mean costs (ex-manufacturer prices) per treated patient, and mean costs per patient/year (all subjects) among diabetic subjects and nondiabetic control subjects in general and internal medicine practices in Germany in 1994 and 2004 (Disease Analyzer, IMS HEALTH)

ATC codes	Prevalence 1994 (%)	Prevalence 2004 (%)	Prescriptions per treated 1994 (mean)	Prescriptions per treated 2004 (mean)	Costs per treated 1994 (€)	Costs per treated 2004 (€)	Ratio (2004/1994)	Costs per patient (all) 1994 (€)	Costs per patient (all) 2004 (€)	Ratio (2004/1994)
Diabetes treatment and care products										
Diabetic	60.5*	70.4*	7.2*	8.3*	143.4*	244.4*	1.5*	86.7*	172.1*	2.0*
Non-diabetes-related drugs and products										
Diabetic	96.0	96.6	22.2*	19.9*	297.7*	401.7*	1.4*	285.8*	387.1*	1.4*
Total prescriptions										
Diabetic	98.0*	99.2*	26.2*	25.2*	380.0*	564.1*	1.5*	372.5*	559.2*	1.6*
Control	93.4*	92.8*	13.1*	11.4*	157.0*	227.7*	1.3*	146.7*	210.0*	1.3*
Ratio	1.0*	1.1*	1.6*	1.9*	2.0*	2.2*		2.0*	2.4*	
Major cost factors										
Cardiovascular										
Diabetic	76.5*	83.7*	10.8	10.2	190.7*	227.6*	1.3*	145.8*	190.5*	1.4*
Control	47.2	51.2	6.7	6.6	117.1*	150.7*	1.3*	55.3*	77.1*	1.2*
Ratio	1.2*	1.4*	1.4*	1.5*	1.5*	1.5*		1.7*	1.9*	
Neurological										
Diabetic	49.7*	38.4*	6.0*	6.4*	46.7*	131.1*	2.8*	23.2*	50.4*	2.2*
Control	38.7*	31.8*	4.5	4.8	34.8*	94.4*	2.7*	13.5*	30.0*	2.1*
Ratio	1.1*	1.1*	1.2*	1.2*	1.2*	1.2*		1.3*	1.3*	
Gastrointestinal										
Diabetic	48.0*	36.8*	5.0*	4.3*	76.9*	113.0*	1.5*	36.9*	41.5*	1.1*
Control	39.0*	30.9*	3.9*	3.5*	54.4*	88.5*	1.6*	21.2*	27.4*	1.2*
Ratio	1.1*	1.1*	1.2*	1.1*	1.3*	1.2*		1.4*	1.3*	
Hematological										
Diabetic	18.4*	34.2*	3.2*	3.0*	82.1*	69.4*	0.8*	15.1*	23.7*	1.3*
Control	9.5	15.5*	2.8*	2.7*	73.7	68.5	1.0	7.0*	10.6*	1.4*
Ratio	1.5*	1.6*	1.1*	1.1*	1.2*	1.0		1.7*	1.5*	
Anti-inflammatory										
Diabetic	47.0*	45.0*	3.9*	3.5*	27.3*	40.7*	1.5*	12.8*	18.3*	1.5*
Control	38.1*	36.2*	3.0*	2.7*	22.5*	35.0*	1.5*	8.6*	12.7*	1.4*
Ratio	1.1*	1.1*	1.1*	1.2*	1.0	1.1		1.1	1.2	

In 1994: 29,956 diabetic patients and 13,226 nondiabetic control subjects; in 2004: 46,017 diabetic subjects and 46,017 nondiabetic control subjects. "Per treated" refers to patients with at least one prescription (of interest) per year. Ratio indicates the age- and sex-standardized ratio (diabetic patients vs. control subjects). * $P < 0.01$: differences 2004 vs. 1994; ratio (2004/1994) after direct age and sex standardization of age- and sex-specific values. Costs from 1994 were adjusted for inflation on the basis of the German Consumer Price Index.

Overall, the major cost factors among antidiabetic agents in both periods were insulins and analogs, followed by oral antidiabetic drugs and BGSM tests. In 2004, insulin accounted for 22% of total drug costs among diabetic patients (17% in 1994), whereas all oral antidiabetic drugs combined accounted for only 8.4% (6.2% in 1994, $P < 0.01$). BGSM tests accounted for 6.5% (4.4% in 1994).

Overall, annual insulin costs per *insulin-treated* patient increased by 30% (Table 2) ($P < 0.01$). Whereas costs for traditional insulins declined (−10%), the highest annual costs per treated patient were seen for newly launched rapid-acting insulin analogs.

An 80% treatment cost increase was observed for all oral agents combined. Prescription costs per treated patient were

70% higher for sulfonylureas in 2004 than in 1994 ($P < 0.01$). On the other hand, a 20% treatment cost decline was found for biguanides ($P < 0.01$). Annual expenses for the newly launched glitazones were >10-fold higher than for biguanides in 2004. Furthermore, glinide prescriptions were more than threefold more expensive than prescriptions for classic sulfonylureas.

Finally, the average annual prescription costs in the total diabetic population for insulins were 90% higher than in 1994 ($P < 0.01$) (Table 2). Average costs for all traditional insulins combined only increased by 10%. Thus, although both short- and long-acting insulin analogs were only prescribed in 6% of diabetic patients, respectively, they represented

the major drivers for the total insulin cost increase (Table 2).

With respect to all oral antidiabetic drugs, more than twofold higher standardized costs per diabetic subject were found over the 10-year period. Although the cost-intensive glitazones were only prescribed in 3.6% of patients in 2004, average expenses in the total diabetic population were already similar to those of biguanides, which have a 10-fold higher prescription prevalence. It is noteworthy that average costs for BGSM tests in the diabetic population in 2004 were almost threefold higher than those for sulfonylureas or biguanides. Because of their high annual expenses and the threefold increased prescription use, BGSM tests became a major cost factor in 2004 among antidiabetic agents.

Table 2—Prevalence of various treatments, mean number of prescriptions per year, mean costs (ex-manufacturer prices) per treated patient, and mean costs per patient/year (all subjects) for antidiabetic agents in general medicine practices in Germany in 1994 and 2004 (Disease Analyzer, IMS HEALTH)

Agents	Prevalence 1994 (%)	Prevalence 2004 (%)	Prescriptions per treated 1994 (mean)	Prescriptions per treated 2004 (mean)	Costs per treated 1994 (€)	Costs per treated 2004 (€)	Ratio (2004/1994)	Costs per patient (all) 1994 (€)	Costs per patient (all) 2004 (€)	Ratio (2004/1994)
Insulin	18.1*	26.1*	7.3*	6.7*	282.5*	372.6*	1.3*	51.0*	97.2*	1.9*
Analog (rapid)	—	6.0	—	4.6	—	346.1	—	—	20.9	—
Analog (long)	—	6.0	—	3.1	—	235.5	—	—	14.2	—
Traditional insulins	18.1*	22.5*	7.3*	5.7*	282.5*	276.8*	0.9*	51.0*	62.0*	1.1*
Oral antidiabetics	48.1*	52.4*	5.4*	5.5*	50.7*	87.0	1.8*	24.4*	45.6*	2.1*
Sulfonylureas	42.1*	26.5*	4.4*	3.6*	28.5*	44.3*	1.7*	12.0	11.7	1.0
Biguanides	9.7*	34.8*	3.3*	4.1*	41.5*	31.7*	0.8*	4.0*	11.0*	2.8*
Glucosidase inhibitors	9.7*	4.7*	4.2	4.6	86.5*	98.3	1.1*	8.4*	4.6*	0.6*
Glitazones	—	3.3	—	3.0	—	341.0	—	—	11.3	—
Glinides	—	3.6	—	5.1	—	153.4	—	—	5.5	—
BGSM strips	8.2*	26.3*	3.9	4.3	123.4*	110.4*	0.8*	10.1*	29.0*	2.3*
UGSM strips	3.2*	2.7*	2.2*	1.6*	15.9*	8.5*	0.5*	0.5*	0.2*	0.4*

In 1994: 29,956 diabetic patients; in 2004: 13,226 diabetic subjects. "Per treated" refers to patients with at least one prescription (of interest) per year. * $P < 0.01$, differences in 2004 vs. 1994; ratios (2004/1994) after direct age and sex standardization of age- and sex-specific values. Costs for 1994 were adjusted for inflation on the basis of the German Consumer Price Index. UGSM, urine glucose self-monitoring test.

New types of antidiabetic drugs accounted for a substantial share of the cost increase in 2004. Antidiabetic agents launched in the market since 1994 accounted for 14.6% of total drug costs in diabetic patients (new insulins 9.3%) and accounted for 39.8% of all antidiabetic drug costs in 2004.

Costs of cardiovascular and lipid-modifying drugs

ACE inhibitors, β -blockers, diuretics, and calcium antagonists were the most frequently prescribed cardiovascular drugs among diabetic patients in 2004 (Table 3). Prescription prevalences of ACE inhibitors and β -blockers roughly

doubled over the 10-year period, whereas a large decline (approximately -50%) was found for glycosides and nitrates.

Overall, the highest mean annual costs per treated patient were observed for the newly launched angiotensin II antagonists in 2004, which were used by 16% of diabetic patients. On the other hand, average treatment costs for ACE inhibitors and nitrates substantially declined over the study period ($P < 0.01$). Furthermore, a reduction in treatment cost was found for calcium-channel blockers and β -blockers ($P < 0.01$).

ACE inhibitors showed the highest mean costs per patient-year for the whole diabetic population, which was similar to

that in 1994 (Table 3). Because of their high treatment costs, the newly launched angiotensin II antagonists became the second major cost factor in 2004. The third ranking drugs were β -blockers, which showed a cost increase mainly through higher prescription use in the diabetic population. They surpassed calcium-channel antagonists, which had been the second major cost factor in 1994.

Among lipid-modifying drugs, almost eightfold higher prescription prevalence was found for statins in 2004. Over the same period, utilization of fibrates showed an almost 50% reduction (Table 3). For statins, costs per treated patient in 2004 were substantially higher as for all

Table 3—Prevalence of various treatments, mean number of prescriptions per year, mean costs (ex-manufacturer prices) per treated patient, and mean costs per patient/year (all subjects) for cardiovascular drugs in diabetic patients in primary care in 1994 and 2004 (Disease Analyzer, IMS HEALTH)

Agents	Prevalence 1994 (%)	Prevalence 2004 (%)	Prescriptions per treated 1994 (mean)	Prescriptions per treated 2004 (mean)	Costs per treated 1994 (€)	Costs per treated 2004 (€)	Ratio (2004/1994)	Costs per patient (all) 1994 (€)	Costs per patient (all) 2004 (€)	Ratio (2004/1994)
Glycosides	25.7*	12.0*	3.3	3.1	13.4*	9.8*	0.7*	3.4*	1.2*	0.3*
Nitrates	21.7*	13.1*	4.7*	3.8*	69.7*	40.4*	0.5*	15.1*	5.3*	0.3*
Diuretics	29.4*	32.6*	4.0	4.0	46.7	41.3	0.8	13.7	13.4	1.0
β -Blockers	15.6*	39.1*	3.7	3.6	88.1*	57.3*	0.7*	13.7*	22.4*	1.5*
Calcium channel blockers	27.8*	25.0*	5.0*	4.1*	90.1*	76.0*	0.8*	25.0*	19.0*	0.7*
ACE inhibitors	24.5*	45.8*	4.1*	3.8*	149.9*	75.1*	0.5*	36.7	34.4	1.0
Angiotensin II antagonists	—	15.8	—	3.4	—	208.8	—	—	32.9	—
Lipid-modifying										
Statins	3.3*	25.2*	2.9	2.9	186.0	165.4	0.9	6.1*	41.7*	6.3*
Fibrates	6.1*	3.7*	3.2*	3.0*	90.2*	64.7*	0.7*	5.5*	2.4*	0.4*

In 1994: 29,956 diabetic patients; in 2004: 13,226 diabetic subjects. "Per treated" refers to patients with at least one prescription (of interest) per year. * $P < 0.01$, differences 2004 vs. 1994; ratios (2004/1994) after direct age and sex standardization of age- and sex-specific values. Costs in 1994 were adjusted for inflation on the basis of the German Consumer Price Index.

other cardiovascular drug groups. Thus, statins were the major cost factor in 2004 in the ATC-C (cardiovascular and lipid-modifying drugs) group, with higher costs than the frequently prescribed ACE inhibitors.

The ATC-C group accounted for 30% of total prescription costs among diabetic patients in 2004 (34% in 1994). The five most cost-intensive groups were statins (6.8% of total drug costs), followed by angiotensin II antagonists (5.6%), ACE inhibitors (5.5%), β -blockers (3.8%), and calcium channel blockers (2.8%). Compared with 1994, statins showed the largest increase (1.7% of total costs in 1994), whereas calcium channel blockers (5.8% in 1994) and ACE inhibitors declined (8.9% in 1994) and the proportion of total costs for β -blockers remained stable (3.8% in 1994).

Finally, it is noteworthy that although cardiovascular and lipid-lowering drugs were still a major prescription cost sector in 2004 (30%), they dropped from the first rank, which is now held by antidiabetic prescriptions (37%). In 1994, cardiovascular drugs were a more important factor (34%) than antidiabetic treatment (28%).

CONCLUSIONS— The present study provides for the first time estimates for longitudinal changes in prescription use and related costs for diabetic patients in Germany. The average total annual medication costs among diabetic patients increased ~60% over 10 years in our study. An even higher amount was found for antidiabetic agents, insulin, and BGSM tests, which showed a twofold cost increase. Major cost factors among antidiabetic agents were insulin, in particular, newly launched analogs, BGSM tests, and biguanides, the latter due mainly to a more than threefold prescription prevalence. Among non-diabetes-related drugs, ACE inhibitors, angiotensin II antagonists, and statins were major cost factors in the diabetic population.

There are only a few other studies on medication costs among diabetic patients in Germany (11–13). A comparison of these studies is difficult because of different study designs and populations. However, the main results resemble the cost estimates of the present investigation. Based on regional health insurance data in 2001, annual medication costs (primary care and other prescribers) of €1,006 per diabetic patients (pharmacy prices) were calculated (13). We have estimated aver-

age primary care prescription costs of €559 in 2004, based on ex-manufacturer prices, which are about 50% of pharmacy prices. Furthermore, the present antidiabetic prescription prevalence fitted well in the current epidemiological picture, e.g., we have observed a prevalence of 26% insulin-treated primary care patients in 2004, which was comparable to another practice-based study (28%) and data from a regional health insurance (27%) (7,14).

Prescription drug costs are the most rapidly growing component of total health expenditures in most Western countries (15). Our data underline the fact that antidiabetic treatment accounts for a substantial share of this rapid growth. This is not only related to an increasing prevalence of type 2 diabetes, but also is due to the approval of new cost-intensive types of antidiabetic drugs (3). Advances in technology and medication have been recognized as key drivers of health expenditure growth (16). Furthermore, there has been a trend toward more aggressive medical treatment of diabetes, i.e., increased use of various oral hypoglycemic agents, alone or in combination with insulin (17).

There is an ubiquitous increase in utilization of antidiabetic agents (6). However, the increase differs greatly in neighboring countries in Europe, despite similar guidelines (6). Thus, these between-country differences may reflect different therapeutic traditions. An important issue in future studies would be to evaluate whether these between-country variations have consequences for diabetes control and complications (6). There is an urgent need to investigate the most cost-effective therapeutic regimen for management of type 2 diabetes. The present study contributes at this point by the evaluation of current antidiabetic prescription trends in Germany.

Another reason for high prescription costs is the fact that diabetes is closely related to other cost-intensive conditions, in particular, cardiovascular disease and its risk factors (hypertension and lipid disorders) (8). Cardiovascular and lipid-modifying drugs were the second major cost factor in the present longitudinal study. The data suggest that there have been different developments within this drug category. On the one hand, similar to antidiabetic agents, there has been an introduction of new cost-intensive agents into the market (e.g., angiotensin II antagonists). Furthermore, because of higher prescription prevalences, some groups

such as β -blockers became a more important cost factor. The most impressive increase was observed for statins: prescription use was eightfold higher in 2004 than 1994. However, only 25% of diabetic patients were treated with statins in 2004 on the basis of data from the present study, although they are highly recommended as preventive agents. A similar prevalence of diabetic patients treated with lipid-lowering agents was observed in another recent study in primary care practices (18). Compared with other European countries, the prescription prevalences of statins in Germany remained below the average (19). Thus, changes in prescription use of lipid-lowering agents in primary care practices in Germany were consistent with the evolving evidence base but were still inadequate.

The present study also indicated that there were longitudinal changes in prescription use and costs for a variety of other drug groups, e.g., neurological, gastrointestinal, and anti-inflammatory agents, among diabetic patients. As a general pattern, prescription use for these agents declined slightly over the 10-year period. However, because of higher treatment costs (prices), the overall costs increased. Again this finding was partly related to the launch of new medications, e.g., the almost threefold higher treatment costs for neurological agents can be explained by the introduction of the cost-intensive triptans in migraine therapy (5,20). It is noteworthy that in addition to developments in other therapeutic areas, antidiabetic agents have become the most important cost factor in diabetic patients in primary care in Germany. Thus, it will be necessary to monitor, in particular, cost development of diabetes treatment products and agents in the future.

The present study has a number of limitations. We were not able to evaluate diabetes type. However, it is conceivable that the majority of patients have type 2 diabetes owing to our age limit. Because of a change in coding practices in primary care, the methods of case ascertainment were slightly different in 1994 and 2004. The diabetes diagnoses were made by general practitioners in both periods. In general, the validity of diabetes diagnoses in primary care practices is high (80–90% correct diagnoses) (21). In 1994, the original text of the general practitioner diagnosis was available. These documents were reviewed by a diabetologist because, in a few patients (<10% of all documented diabetes diagnoses), a “suspicion

of diabetes” was noted. These patients were excluded, and only patients with a definitive diagnosis of diabetes were included in the analysis. In 2004, the database contains ICD-10 codes only. This documentation system allows the possibility of coding if a diagnosis is definitive or only a suspicion. Thus, no further confirmation was required. As an external reference, we have compared the antidiabetic prescription prevalences (insulin or oral antidiabetic agents) with other studies and found good agreement (7,13,14).

Furthermore, the selection criterion (at least one visit per year) may have introduced selection bias (more chronically ill patients); however, it was necessary because of the high fluctuation of patients. Finally, although our economic perspective was that of the health insurance companies, our cost estimates were only based on actual ex-manufacturer prices, which were ~50% of pharmacy sales prices. However, the emphasis was to study longitudinal changes in costs.

In summary, prescription drug costs among diabetic patients in primary care practices in Germany increased ~60% during the last decade. An overproportional increase (100%) was observed for costs of diabetes treatment (insulin, antidiabetic agents, and BGSM tests). New types of antidiabetic agents accounted for a substantial cost share of this increase. Pharmacological advance is a key driver of drug expenditure growth in antidiabetic treatment, indicating the need for cost-effectiveness analyses of new medications.

References

- Grant RW, Pirraglia PA, Meigs JB, Singer DE: Trends in the complexity of diabetes care in the United States from 1991 to 2000. *Arch Intern Med* 164:1134–1139, 2004
- Cohen FJ, Neslusan CA, Conklin JE, Song X: Recent antihyperglycemic prescribing trends for U.S. privately insured patients with type 2 diabetes. *Diabetes Care* 26:1847–1851, 2003
- Wysowski DK, Armstrong G, Governale L: Rapid increase in the use of oral antidiabetic drugs in the United States, 1990–2001. *Diabetes Care* 26:1852–1855, 2003
- UK Prospective Diabetes Study (UKPDS) Group: Intensive blood-glucose control with sulfonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 35). *Lancet* 352:837–853, 1998
- Schwabe U, Paffrath D, Eds.: *Arzneiverordnungen—Report 2005*. Berlin, Springer-Verlag, 2006
- Melander A, Folino-Gallo P, Walley T, Schwabe U, Groop PH, Klaukka T, Vallano A, Laporte J-R, Gallego MR, Schiapa M, Røder M, Kampmann JP, De Swaef A, Åberg M, Mansson O: Utilisation of antihyperglycaemic drugs in ten European countries: different developments and different levels. *Diabetologia* 49:2024–2029, 2006
- Hauner H, Köster I, von Ferber L: Prevalence of diabetes mellitus in Germany 1998–2001: secondary data analysis of a health insurance sample of the AOK in Hesse/KV in Hesse [in German]. *Dtsch Med Wochenschr* 128:2632–2638, 2003
- Rathmann W, Haastert B, Roseman JM, Gries FA, Giani G: Prescription drug use and costs among diabetic patients in primary health care practices in Germany. *Diabetes Care* 21:389–397, 1998
- Dietlein G, Schröder-Bernhardi D: Use of Mediplus patient database in healthcare research. *Int J Pharmacol Ther* 40:130–133, 2002
- Krobot KJ, Miller WC, Kaufman JS, Christensen DB, Preisser JS, Ibrahim MA: Quantifying delay in access to new medical treatment: an application of risk advancement period methodology. *Epidemiology* 15:202–207, 2004
- Liebl A, Neiß A, Spannheimer A, Reitberger U, Wagner T, Görtz A: Costs of type 2 diabetes in Germany: results of the CODE-2 Study [in German]. *Dtsch Med Wochenschr* 126:585–589, 2001
- Stock SAK, Redaelli M, Wendland G, Civello D, Lauterbach KW: Diabetes-prevalence and cost of illness in Germany: a study evaluating data from the statutory health insurance in Germany. *Diabet Med* 23:299–305, 2005
- Köster I, von Ferber L, Ihle P, Schubert I, Hauner H: The cost burden of diabetes mellitus: the evidence from Germany: the CoDiM Study. *Diabetologia* 49:1498–1504, 2006
- Rothenbacher D, Ruter G, Saam S, Brenner H: Management of patients with type 2 diabetes: results in 12 practices of general practitioners [in German]. *Dtsch Med Wochenschr* 127:1183–1187, 2002
- Bodenheimer T: High and rising health care costs. Part 1: seeking an explanation. *Ann Intern Med* 142:847–854, 2005
- Bodenheimer T: High and rising health care costs. Part 2: technologic innovation. *Ann Intern Med* 142:932–937, 2005
- Walley T, Hughes D, Kendall H: Trends and influences on use of antidiabetic drugs in England, 1992–2003. *Pharmacoepidemiol Drug Saf* 14:769–773, 2005
- Böhler S, Scharnagl H, Freisinger F, Stojakovic T, Glaesmer H, Klotsche J, Pieper L, Pittrow D, Kirch W, Schneider H: Unmet needs in the diagnosis and treatment of dyslipidemia in the primary care setting in Germany. *Atherosclerosis* 190:397–407, 2007
- Bischoff B, Silber S, Richartz BM, Pieper L, Klotsche J, Wittchen HU, DETECT Study Group: Inadequate medical treatment of patients with coronary artery disease by primary care physicians in Germany. *Clin Res Cardiol* 95:405–412, 2006
- Goldberg LD: The cost of migraine and its treatment. *Am J Manag Care* 11:S62–S67, 2005
- Deckers JG, Schellevis FG, Fleming DM: WHO diagnostic criteria as a validation tool for the diagnosis of diabetes mellitus: a study in five European countries. *Eur J Gen Pract* 12:108–113, 2006