Patterns of antihypertensive drug utilization in primary care

D. Pittrow, W. Kirch, P. Bramlage, H. Lehnert, M. Höfler, T. Unger, A. M. Sharma, H.-U. Wittchen

Abstract

Background: In the treatment of hypertension, physicians' attitudes and practice patterns are receiving increased attention as contributors to poor blood pressure (BP) control. Thus, current use of antihypertensive drugs in primary care was analyzed and the association with selected physician and patient characteristics was assessed.

Methods: The Hypertension and Diabetes Risk Screening and Awareness (HYDRA) study is a cross-sectional point prevalence study of 45,125 primary care attendees recruited from a representative nationwide sample of 1912 primary care practices in Germany. Prescription frequencies of the various antihypertensive drugs in the individual patients were recorded by the physicians using standardized questionnaires. We assessed the association of patient variables [age, gender; co-morbidities such as diabetes, nephropathy or coronary heart disease (CHD)] and physician variables (general practitioner vs internist, guideline adherence, etc.) with drug treatment intensity and prescription patterns.

Results: Of all 43,549 patients for whom a physician diagnosis on hypertension or diabetes was available, 17,485 (40.1%) had hypertension. Of these hypertensive patients, 1647 (9.4%) received no treatment at all, 1191 (6.8%) received non-pharmacological measures only, and 14,647 (83.8%) were given one or more antihypertensive drugs. Drug treatment rates were lower in young patients (16–40 years: 57.4%). BP control was poor: 70.6% of all patients were not normalized, i.e., had BP $\geq$ 140/90 mmHg. Antihypertensive treatment was generally intensified with increasing age, or if complications or comorbidities were present. The use of the different drug classes was rather uniform across the various patient subgroups (e.g., by age and gender). Individualized treatment with regard to co-morbidities as recommended in guidelines was not the rule. Adherence to guidelines as self-reported by physicians as well as other physician characteristics (region, training etc.) did not result in more differentiated prescription pattern.

Conclusions: Despite the broad armamentarium of drug treatment options, physicians in primary care did not treat hypertension aggressively enough. Treatment was only intensified at a late stage, after complications had occurred. Treatment should be more differentiated in terms of coexisting morbidities such as diabetes, nephropathy, or CHD.

Keywords Antihypertensive drugs, Drug utilization, Prevalence

Introduction

Hypertension is among the leading reasons for office visits in primary care [1, 2] and its treatment is sometimes even regarded as a barometer for the general quality of healthcare systems [3]. Despite the undisputed importance to treat hypertension aggressively, control rates are still unsatisfactory [4, 5]. This holds especially true for the general population in Europe compared with the US, with Germany having the least favourable outcome [6]. At the same time, the new JNC-VII guidelines propose even lower BP targets, defining patients with BP values of 120–139/80–89 mmHg as pre-hypertensive requiring lifestyle modification [5]. Along with such data, there is growing evidence now that uncontrolled hypertension also occurs in populations with good access to health care [7, 8].

Efforts to effectively improve the extent of control of hypertension should ideally be based on a thorough understanding of the characteristics of patients, the dynamics of the health care system and, most importantly, on the work and function of the primary care physician as the gatekeeper [9]. Therefore, the role of physicians' attitudes and practice patterns (recognition,

treatment, and management) has received increased attention as a contributor to poor control of hypertension [3, 10, 11]. Within this search, an important, but obviously largely neglected, aspect is the choice and intensity of antihypertensive medication treatments in routine care. To our knowledge, there are no major drug utilization studies that directly link the patient's diagnoses to actual treatment patterns in unselected primary care samples.

In an attempt to provide such data, we analyzed recent cross-sectional data from the Hypertension and Diabetes Risk Screening and Awareness Study (HYDRA) to address the following questions: (1) Which antihypertensive drug classes and combinations, respectively, are applied by general physicians in patients with hypertension? (2) Do drug treatments differ with respect to certain patient characteristics such as age, gender, and frequent concomitant diseases such as diabetes mellitus, nephropathy, or coronary heart disease (CHD), since these patients are considered to be at particularly high cardiovascular risk? (3) Are certain physician variables, such as type of medical training, regional setting or others, associated with differences in drug treatment?

Methods

Study design

HYDRA was a cross-sectional point prevalence study. It was based on a two-step observational epidemiological design (Fig. 1). A nationwide sample of doctors with primary care functions (medical practitioners, generalists, general internists) was drawn on the basis of 1060 regional segments [according to the criteria of the Institute for Medical Statistics (IMS), Frankfurt am Main, Germany], clustered into geographical areas for which primary care doctor addresses were available [12]. In step 1, $n=2416$ of these physicians were asked to complete a prestudy questionnaire [response rate $n=1912$ (79.1%)] to describe personal and structural characteristics of each practice and to assess self-perceived qualifications and attitudes related to recognition, diagnosis, and care of patients. Step 2 was an assessment (half day on 18 or 20 September 2001) of all patients attending doctors' offices on this day. Patients were informed by posters and leaflets about participation of the respective practices in the study and they were free to decline participation. The following exclusion criteria applied: age below 16 years, acute medical condition making the screening procedure unacceptable on ethical grounds, dementia or other cognitive or sensory deficits that would make it unlikely that the self-reported measures could be completed or would provide meaningful information. Oral informed consent was obtained from all patients. Importantly, physicians were instructed not to change their routine-practice behaviors nor to selectively invite patients for participation. Patients completed a self-report patient questionnaire, followed by a structured doctor's clinical appraisal, including documentation of lab-test findings from the charts, BP measurements, and assessment of albuminuria and urine glucose in spot samples (Fig. 1).

Sample and study participation

An estimated total of 66,920 patients attended the participating practices (mean number of patients per doctor: 35). Because of logistical problems resulting from high patient load, 53% of participating doctors were unable to successfully screen all eligible patients. Thus, only a total of 51,905 questionnaires were distributed to patients attending the practice, of which 46,129 were evaluable for further analyses (reasons for non-inclusion: refusal or withdrawal of consent, only sketchy information, etc.). In 1004 cases (2.2%), patient and physician questionnaires could not be matched. A set of analyses was run, using all available

information, comparing the complete with the incomplete cases and the completers with the patients refusing participation. We found that the results did not vary across the number of valid questionnaires per primary care setting, and thus there was no evidence for bias. In 1576 (3.5%) cases, physicians failed to provide sufficient clinical information on hypertension or diabetes, and the present analysis was based on those 43,549 cases for which a valid clinical diagnosis for hypertension and diabetes was provided (either yes or no). In this sample, 17,485 (40.1%) were rated as hypertensive: 2702 (6.2%) as borderline cases, 12,286 (28.2%) as having mild to moderate, and 2497 (5.7%) as having severe to extremely severe hypertension.

Instruments

The prestudy questionnaires served to collect information on participating physicians' profiles (education and specialization), practice setting, and physicians' attitudes and perceptions toward guidelines and programs for diabetes and hypertension management. The patients' questionnaires were used to collect data on a variety of variables including biosocial characteristics, quality of life measures, life-style and behavioral risk factors, health status, and details on hypertension and diabetes history – and treatment, if applicable. The doctor's clinical assessment of each individual patient by a standardized doctor's questionnaire included rating of the current presence of hypertension and diabetes using the Clinical Global Impression Scale (CGI: not present, borderline, mild/ moderate, severe/extreme) [13] and indicating the presence or absence of 22 predefined somatic and mental disorders. Apart from hypertension, particular focus in the study was on diagnosis and treatment of diabetes.

Diagnostic conventions

The present analysis was exclusively based on the physicians' clinical diagnoses of hypertension, diabetes, nephropathy and CHD. A comparison between the clinical hypertension diagnoses and the measured blood pressure values was the subject of another analysis [14]. Physician-rated borderline cases were included in accordance with the JNC-VI [15] and ICH-WHO [16] criteria, which also subsume these cases under mild hypertension. In diabetes, the situation is similar, since at diagnosis the disease has been present for several years, and already in early stages complications may occur [17].

For the detection of albuminuria in a spot urine sample, the semi-quantitative dipstick Micral-Test II (Boehringer Mannheim, Germany) was used [18], as it has proven useful in a primary care setting [19]. However, the diagnosis "nephropathy" was again a clinical one assigned by the treating physician. Body weight and height information were taken from the patient questionnaire. Body mass index (kg/m²) was calculated from these self-reported data and classified according to international conventions [20].

The prescription information on antihypertensive drug classes for each patient was obtained from the physician questionnaire, using the following categories: none; ACE inhibitor, alpha blocker, AT1 receptor antagonist, b-blocker, calcium channel blocker, diuretic, other (such as centrally acting drug: reserpine, hydralazine, etc.). No information on non-proprietary names, brand names or dosages was collected.

Statistical analyses

Cross tables, frequency distributions and descriptive statistics were used to compare the distributions of variables among all categories. Differences in hypertension prevalence were quantified with odds ratios (ORs) estimated from logistic regressions [21] while adjusted for age group, sex and gender * age group and calculating robust confidence intervals for

observations clustered within primary care settings [22]. Significance was assessed at the $P=0.05$ level. All analyses were conducted using the Stata 8 software package (Stata Corporation, College Station, TX USA 2003).

Results

Sample characteristics and drug treatment rates

Table 1 summarizes selected sociodemographic and clinical baseline characteristics of the total of hypertensive patients, and – in order to display variability of characteristics of an important subgroup – of hypertensive patients with concomitant diabetes compared with hypertensive patients without diabetes. Typically, for primary care settings, a large proportion of these patients were of older age (mean 63.2 years; proportion aged 60 years or above: 42%). Consistent with high age, the mean time since first diagnosis of hypertension was about 4 years. Among diabetics with hypertension, males and older patients were overrepresented, had a slightly higher weight, and a higher number of additional diagnoses. In terms of mean systolic and diastolic BP, the groups were similar, i.e., had the same control status. Of all hypertensive patients ($n=17,485$), 1647 (9.4%) received no treatment at all, 1191 (6.8%) received non-pharmacological measures only, 5791 (33.1%) antihypertensive drug therapy only and 8856 (50.7%) both antihypertensive drug therapy and non-pharmacological measures.

The drug classes most frequently prescribed were in declining order, ACE inhibitors in 7126 patients (40.8%), b-blockers in 6304 (36.1%), diuretics in 5546 (31.7%), calcium channel blockers in 3903 (22.3%), AT 1 receptor antagonists in 2470 (14.1%), „other“ antihypertensives in 763 (4.4%) and alpha-receptor blockers in 494 (2.8%) (Fig. 2).

Prescription frequencies by age and gender

Hypertensive patients aged 16–40 years received antihypertensive drug therapy only in 57.4%, patients aged 41–60 years in 79.6% and those aged over 60 years in 87.7%. For all drug classes, a clear and significant association between age and the rate of prescriptions was found, with the exception of b-blockers or „other antihypertensives“, respectively.

Figure 2 displays the prescription frequency of the various drug classes in males and females by age group. While there were no differences between genders in the overall probability of receiving drug treatment, certain gender specific differences in treatment patterns were evident. The figure indicates the following major differences: females in all age groups received ACE inhibitors, those in the 41- to 60-year-old group received alpha blockers and calcium channel blockers, and those in the above 60-year-old group received b-blockers less frequently. Conversely, females aged 16–40 years received b-blockers much more frequently than males in the same age group. After adjustment for age, these differences remained significant at the $P<0.05$ level for ACE inhibitors in all age groups [16–40 years: OR 0.5, (95% CI: 0.4;0.8); 41–60 years: OR: 0.8 (95% CI: 0.7;0.8); >60 years: 0.9 (95% CI: 0.8;0.9)], for alpha blockers only in the >60-year-old group [OR: 0.6 (95% CI: 0.5;0.7)], for calcium channel blockers in the 41- to 60-year olds: [OR: 0.8 (95% CI: 0.7;0.9)], and for b-blockers only in the 16- to 40-year olds [OR: 1.6 (95% CI: 1.2;2.1)].

Concerning the use of combination therapy, there were no relevant differences between genders, with the exception of treatment with four or more drugs, which was less frequent in women than in men [OR: 0.8 (95% CI:0.6; 0.9)].

Prescription frequencies according to concomitant disease

Table 2 displays the number of antihypertensive drugs and the prescription rates of the individual classes by concomitant disease. Among patients with the diagnosis hypertension alone, the proportion of treated patients was 79.3%, among those with hypertension and diabetes it was 87.8%, among those with hypertension and nephropathy 88.3%, and among those with hypertension and CHD 93.1%.

In comparison with hypertension „alone“ (i.e., without concomitant diabetes, nephropathy or CHD), patients with these co-morbidities had (1) a higher probability of receiving any drug treatment, (2) a higher probability of receiving, in particular, ACE inhibitors, diuretics, and calcium channel blockers, and (3) as indicated in the lower part of the table, a higher likelihood of receiving multiple drug prescriptions at the same time; thus, an increased treatment intensity. As can be derived from the ORs, these differences remain largely significant even after adjustment for age and gender.

Prescription frequencies by physician characteristics and factors

In addition to patient factors above, we also investigated certain physician characteristics that might have influence on drug treatment patterns. For example, in Germany, in certain settings or states (e.g., in Saxony) local guidelines exist that have particularly stringent treatment goals. Therefore, we investigated regional effects. There were no significant and pronounced differences in prescription patterns (defined as $0.66 \leq \text{ORs} \leq 1.5$, $P < 0.05$) in different settings (e.g., rural area vs major city; federal states).

Among the participating physicians, 77% were GPs and 23% physicians for internal medicine in general practice. They prescribed anti-hypertensive drugs in a similar frequency (83.6% and 84.9%). No differences were found between their use of combination therapy and the individual drug classes, respectively.

Of physicians, 31.7% reported following guidelines (German Hypertension League) when treating antihypertensive patients. However, the prescription pattern between these physicians and those not reporting following guidelines was marginal (differences in proportions in the various drug classes was about 2%).

Discussion

Data on drug utilization linked to routine diagnoses in primary care are scarce. These data, however, are of importance in view of the fact that the prevalence of hypertension in this setting was very high (40.1% of all patients in this study). The large majority of all hypertensive patients received drug treatment, and, despite these efforts, control rates were poor. In our sample, 70.6% of all hypertensive patients were not controlled and mean BP levels were 144.5/84.5 mmHg. This was considerably higher than mean BP values sampled from general population registries in Germany (136/ 83 mmHg in individuals aged 18–79 years) [6, 23].

The main outcomes of our study were: (1) Treatment rates depended on age: young hypertensive patients (16–40 years) compared with the older age groups were substantially less aggressively treated (low rate of drug treatment; if treated, mostly with monotherapy). (2) There were only limited gender differences. (3) Treatment intensity increased when concomitant diseases were present, while there were only minor changes in preferences of the various drug classes. (4) Selected physician variables did not influence drug prescribing. When interpreting the results of our study, certain limitations have to be taken into account. First, because of the cross-sectional design, there was no assessment whether the present

therapy was the initial one (first line) or whether it replaced (switch) or amended (add-on) the original one. Therefore, no information about the treatment strategies over time can be provided. The design also did not allow determination of causal relationships. Third, as the study was performed on two half days (morning), selection bias with underrepresentation of employed patients cannot be excluded. Fourth, the results apply for typical primary care patients. Cases with severe forms of morbidity that were treated by specialists (e.g., certain hypertensive patients with CHD treated by a cardiologist) were not covered. Having these limitations in mind, treatment pattern with antihypertensive drugs appeared relatively uniform. Treatment intensity (as indicated by number of prescriptions) increased with age, and there were no major differences between genders, with few exceptions which are hard to explain. For example it is unclear why younger women received substantially more b-blockers than their male peers, and why this difference disappeared in the higher age groups. Did physicians make use of the additional psychotropic effects of b-blockers here or was it a precaution in women of childbearing age? In addition, a lower proportion of women received ACE inhibitors, while there were no major differences in the concomitant diseases. Importantly, treatment was intensified only (regarding proportion of treated patients, and/or number of drugs per patient) after complications had occurred. The broad armamentarium of drug treatment options seemed to be applied preferably at a later age and in patients with comorbidities. Secondary prevention rather than primary prevention of complications seemed to prevail in primary care.

The 1999 ISH/WHO guidelines, which were widely disseminated during the time of the study, recommended „all available drug classes for the initiation and maintenance for antihypertensive therapy“ (i.e., diuretics, b-blockers, calcium channel blockers, ACE inhibitors, alpha blockers and AT1 receptor antagonists), but indicated that the choice of drugs is influenced by many factors such as socio-economic, cardiovascular risk factors, co-existing diseases, patient responses, interactions, and strength of evidence. According to our data, it is likely that those differential considerations are applied in a limited manner. For example, age was a compelling indication for the selection of diuretics [16], and indeed it was prescribed more frequently in elders; however, to a smaller extent than calcium channel blockers, for example.

The uniform use of antihypertensive drugs is striking when analyzing subgroups of patients with certain concomitant diseases, which should, according to acknowledged guidelines, trigger the selection of certain drug classes. For example, in nephropathy, ACE inhibitors or AT1 receptor antagonists should be preferred, but physicians used ACE inhibitors only in 47.5% and AT1 receptor antagonists in 15.3%. In CHD patients with hypertension, which have a compelling indication for b-blockers and calcium channel blockers [16] the greatest increase in drug use compared to hypertension alone was for ACE inhibitors and diuretics. In this respect, it has been highlighted that the co-existence of diabetes and hypertension is important, as they are multiplicative risk factors for macrovascular and microvascular disease, resulting in increased rates of cardiac deaths, CHD, congestive heart failure and peripheral vascular disease [24, 25]. A hypertensive diabetic carries an approximately fourfold risk of mortality and morbidity in comparison with a non-hypertensive, non-diabetic individual. According to the ISH/WHO guidelines, the concomitant presence of hypertension – of any grade – and diabetes renders an individual to be a „high risk“ patient with a probability of experiencing a cardiovascular event of 20–30% in the next 10 years [16]. By the same token, several studies have impressively shown that BP lowering in diabetic patients leads to a considerably stronger risk reduction than in non-diabetics (HOT [26], STOP-2 [27], UKPDS [28]). This high risk is only partly considered when it comes to drug treatment. The treatment rates of hypertensive diabetics were somewhat higher than in patients with hypertension alone (87.8% vs 79.3%), and they were treated more often with combination therapy. Physicians in our study preferred ACE inhibitors and diuretics, which is according to current knowledge

[29], however, did not apply b-blockers (which would address the high cardiac risk of diabetics) or AT1 receptor antagonists (effective in diabetic nephropathy) more frequently. Control rates in this group were astonishingly poor, and the need for aggressive therapy to reach the low target pressure of <130/85 mmHg was certainly not met [30].

Interestingly, also „old“ drugs (such as reserpine, hydralazine, etc. categorized as „other anti-hypertensive drugs“ in our study) were still in frequent use, despite the fact they were not recommended in clinical guidelines. The same was true for alpha blockers. The alpha blocker arm of the ALLHAT study was stopped because of an increase in cases of new-onset heart failure in patients assigned to the alpha blocker [31]. While this could merely represent unmasking of heart failure in patients previously treated with an ACE inhibitor or a diuretic, still the benefit of such treatment is questionable.

A broad range of physician characteristics was investigated and was found to have only marginal effects on antihypertensive drug prescription behavior. For example, it was interesting to note that no important differences in prescribing occurred between general practitioners and internists. If one would have expected differences, e.g., due to differences in training, they might have vanished due to comparable work setting in daily practice, or common continuous medical education activities. Indeed hypertension treatment is one of those medical areas in which generalists and specialists provide care of equivalent quality [32]. It was surprising at first glance that no differences, too, were found when comparing physicians reporting adhering to guidelines compared with those who did not. However, the limited impact of guidelines is well known in a variety of medical fields, and has also been acknowledged in the WHO/ ISH 1999 hypertension guidelines („words without action“) [16]. What might be the underlying reasons for the reluctance of physicians to treat hypertension aggressively enough? A variety of factors might explain this; for example the expectation in the management of younger patients that life style change or other non-pharmacological treatment may be sufficient [33], and in elderly the fear of doing harm by applying too-intensive treatment [10, 34].

Reasons for the relative uniformity of drug treatment – particularly evident when looking at the prescription patterns in subsets of patients with diabetes, nephropathy, or CHD – however, include the aspect that recommendations for optimal pharmacological treatment of hypertensive patients have been subject of debate, thus often not being perceived to be a real guidance for clinicians. Three examples may illustrate this: the controversy about potential harm of calcium channel blockers in increasing myocardial infarction [35], the one about usefulness of diuretics and b-blockers in hypertensive diabetics due to their potentially untoward effects [36], and the current one about the implications of the ALLHAT study [37]. Clinical inertia [38] on the side of physicians might well result from these experiences.

Fig. 1 Study design

Fig. 2 Prescriptions of antihypertensive drugs by gender and age group. Prescriptions on the study day according to physician report. Men: 16–40 years: $n = 506$, 41–60 years: $n = 2287$, > 60 years: $n = 4653$. Women: 16–40 years: $n = 469$, 41–60 years: $n = 2849$, > 60 years: $n = 6721$. [%] Proportions within all patients with the clinical diagnosis hypertension

Table 1 Characteristics of hypertensive patients (total and grouped according to hypertension without diabetes, and hypertension with concomitant diabetes). Data are means (SD) unless specified otherwise. *CHD* coronary heart disease, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein. Blood pressure was measured on the study day, microalbuminuria with semi-quantitative Micral-II urine dip sticks on the study day. All diagnoses are according to physician's assessment. The *n* value for each variable varies due to missing values

	Hypertension total <i>n</i> = 17,485	Hypertension/no diabetes diagnosis <i>n</i> = 12,281	Hypertension + diabetes diagnosis <i>n</i> = 5,204
Gender, %			
Male	42.6	41.1	46.1
Female	57.4	58.9	53.9
Age, years	63.2 (12.4)	62.0 (13.0)	66.1 (10.6)
Months since first diagnosis	47.1 (16.3)	46.9 (16.3)	47.8 (16.3)
Body mass index (kg/m ²)	28.4 (5.7)	28.0 (5.6)	29.5 (5.8)
Normal weight, %	24.0	26.7	17.5
Overweight/obesity, %	76.0	73.3	82.5
Blood pressure ≥140/90 mmHg, %	70.6	69.9	72.3
Systolic blood pressure, mmHg	144.5 (18.2)	143.9 (18.2)	145.8 (18.2)
Diastolic blood pressure, mmHg	84.5 (10.3)	84.9 (10.3)	83.3 (10.1)
Microalbuminuria, %	25.0	20.4	35.6
Number of additional diagnoses, %			
None	17.2	20.1	10.3
One	24.2	26.7	18.3
Two	36.2	36.6	35.2
Three	14.9	12.2	21.3
Four	4.9	3.2	8.9
Five or more	2.6	1.1	6
CHD, %	23.9	19.5	34.3
Heart disease other than CHD, %	29.2	24.8	39.4
Cerebral infarction, %	3.6	3.1	4.9

Table 2 Prescription rates of various antihypertensive drug classes in hypertensive patients by concomitant disease. Odds ratios (OR) from logistic regression (controlled for age and gender) indicate strengths of association between the respective disease status and prescription of drug classes, or number of different drug classes, respectively. *HYP* hypertension, *CHD* coronary heart disease. All diagnoses as reported by the treating physician on the study day. Borderline cases are included. Decimals were rounded; thus, totals may deviate slightly from 100%. For further explanations, see text

Patients with Hypertension							
	Total <i>n</i> = 17,485	HYP alone* <i>n</i> = 9,146	HYP + Diabetes <i>n</i> = 5,204		HYP + Nephropathy <i>n</i> = 1,589		HYP + CAD <i>n</i> = 4,179
	(%)	(%)	(%)	vs HYP alone OR [95% CI]	(%)	vs HYP alone OR [95% CI]	(%)
Any	83.8	79.3	87.8	1.6 [1.4;1.8]	88.3	1.8 [1.5;2.1]	93.1
Alpha blockers	2.8	2.4	3.6	1.3 [1.1;1.6]	4.0	1.6 [1.2;2.1]	3.9
Other antihypertensives	4.4	3.7	4.6	1.2 [1.0;1.4]	5.2	1.4 [1.0;1.9]	5.8
AT1 receptor antagonists	14.1	14.0	14.4	1.0 [0.9;1.1]	15.3	1.1 [0.9;1.3]	14.8
Calcium-channel blockers	22.3	17.4	28.6	1.6 [1.5;1.8]	29.8	1.8 [1.5;2.2]	31.2
Diuretics	31.7	23.6	41.8	2.0 [1.9;2.2]	42.9	2.2 [1.9;2.6]	45.9
Beta blockers	36.1	34.7	34.6	1.1 [1.0;1.1]	39.5	1.3 [1.1;1.5]	43.9
ACE inhibitors	40.8	31.4	52.4	2.1 [1.9;2.3]	47.5	1.8 [1.6;2.0]	57.0
Number of different classes				vs 0 drug classes OR [95% CI]		vs 0 drug classes OR [95% CI]	
None*	16.2	20.7	12.2	—	11.7	—	6.9
One	37.6	44.0	29.7	1.0 [0.9;1.2]	30.3	1.2 [1.0;1.4]	26.0
Two	28.3	24.7	32.0	1.8 [1.6;2.0]	29.6	1.9 [1.6;2.3]	34.7
Three	13.6	8.6	19.3	3.0 [2.6;3.5]	20.1	3.7 [2.9;4.6]	23.6
Four or more	4.2	2.1	6.9	4.4 [3.5;5.5]	8.2	6.1 [4.3;8.6]	8.7

[] 95% confidence interval (CI)

*Indicates reference (1.0)

Acknowledgements

The study was supported by an unrestricted educational grant of Sanofi-Synthelabo, Berlin, Germany.

References

- Schappert SM, Nelson C (1999) National ambulatory medical care survey: 1995–96 summary. Vital and health statistics, series 13, no. 142. DHHS Government Printing Office, Washington
- Pittrow D, Wittchen H, Kirch W (2003) Hypertension and diabetes care among primary care doctors in Germany: results from an epidemiological cross-sectional study. In: Kirch W (ed) Public health in Europe. Springer, Berlin Heidelberg New York, pp 203–218
- Hyman DJ, Pavlik VN (2000) Self-reported hypertension treatment practices among primary care physicians: blood pressure thresholds, drug choices, and the role of guidelines and evidence-based medicine. Arch Intern Med 160:2281–2286

4. Guidelines committee (2003) European society of hypertension – European society of cardiology guidelines for the management of arterial hypertension. *J Hypertens* 21:1011–1053
5. Chobanian AV, Bakris GL, Black HR et al (2003) The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 289:2560–2572
6. Wolf-Maier K, Cooper RS, Banegas JR et al (2003) Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *JAMA* 289:2363–2369
7. Alexander M, Tekawa I, Hunkeler E et al (1999) Evaluating hypertension control in a managed care setting. *Arch Intern Med* 159:2673–2677
8. Stockwell D, Madhavan S, Cohen H, Gibson G, Alderman M (1994) The determinants of hypertension awareness, treatment, and control in an insured population. *Am J Public Health* 84:1768–1774
9. Hyman DJ, Pavlik VN (2001) Characteristics of patients with uncontrolled hypertension in the United States. *N Engl J Med* 345:479–486
10. Berlowitz DR, Ash AS, Hickey EC et al (1998) Inadequate management of blood pressure in a hypertensive population. *N Engl J Med* 339:1957–1963
11. Hyman DJ, Pavlik VN, Vallbona C (2000) Physician role in lack of awareness and control of hypertension. *J Clin Hypertens* 2:324–330
12. Wittchen H, Krause P, Höfler M et al (2003) Objective, design and methodology of the hypertension and diabetes risk screening and awareness (HYDRA) study. *Fortschr Med* 121[Suppl 1]:2–11
13. National Institute of Mental Health (1976) Clinical global impressions. In: Guy W (ed) ECDEU assessment for psychopharmacology. National Institute of Mental Health, Rockville, pp 221–227
14. Sharma A, Wittchen H, Kirch W et al (2004) High prevalence and poor control of hypertension in primary care – cross sectional study. *J Hypertens* 22:1–9
15. Joint national committee on prevention, detection, evaluation, and treatment of high blood pressure (1997) The sixth report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med* 157:2413–2446
16. Guidelines subcommittee (1999) 1999 World health organization – international society of hypertension guidelines for the management of hypertension. *J Hypertens* 17:151–183
17. Harris MI, Flegal KM, Cowie CC et al (1998) Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The third national health and nutrition examination survey, 1988–1994. *Diabetes Care* 21:518–524
18. Gerber L, Johnston K, Alderman M (1998) Assessment of a new dipstick test in screening for microalbuminuria in patients with hypertension. *Am J Hypertens* 11:1321–1327
19. Piehlmeier W, Renner R, Schramm W et al (1999) Screening of diabetic patients for microalbuminuria in primary care – the PROSIT project. Proteinuria screening and intervention. *Exp Clin Endocrinol Diabetes* 107:244–251
20. Anonymous (2000) Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 894:i–xii, pp 1–253
21. McCullagh P, Nelder JA (1989) Generalized linear models. Chapman and Hall, London
22. Royall RM (1986) Model robust confidence intervals using maximum likelihood estimators. *Int Stat Rev* 54:221–226
23. Thamm M (1999) Blood pressure in Germany – current status and trends. *Gesundheitswesen* 61[Suppl]:S90–S93
24. Epstein M, Sowers J (1992) Diabetes mellitus and hypertension. *Hypertension* 19:403–418
25. Grossman E, Messerli FH, Goldbourt U (2000) High blood pressure and diabetes mellitus: are all antihypertensive drugs created equal? *Arch Intern Med* 160:2447–2452
26. Hansson L, Zanchetti A, Carruthers S et al (1998) Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the hypertension optimal treatment (HOT) randomised trial. HOT study group. *Lancet* 351:1755–1762
27. Hansson L, Lindholm L, Ekblom T, et al (1999) Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish trial in old patients with hypertension-2 study. *Lancet* 354:1751–1756
28. UK prospective diabetes study group (1998) Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* 317:703–713

29. Sowers JR, Epstein M, Frohlich ED (2001) Diabetes, hypertension, and cardiovascular disease: an update. *Hypertension* 37:1053–1059
30. Berlowitz DR, Ash AS, Hickey EC, Glickman M, Friedman R, Kader B (2003) Hypertension management in patients with diabetes: the need for more aggressive therapy. *Diabetes Care* 26:355–359
31. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group (2000) Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 283:1967–1975
32. Greenfield S, Rogers W, Mangotich M, Carney MF, Tarlov AR (1995) Outcomes of patients with hypertension and noninsulin dependent diabetes mellitus treated by different systems and specialties. Results from the medical outcomes study. *JAMA* 274:1436–1444
33. Pickering TG (2003) Lifestyle modification and blood pressure control: is the glass half full or half empty? *JAMA* 289:2131–2132
34. Chobanian AV (2001) Control of hypertension – an important national priority. *N Engl J Med* 45:534–535
35. Kizer JR, Kimmel SE (2001) Epidemiologic review of the calcium channel blocker drugs: an up-to-date perspective on the proposed hazards. *Arch Intern Med* 161:1145–1158
36. Gress TW, Nieto FJ, Shahar E, Wofford MR, Brancati FL (2000) Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus. Atherosclerosis risk in communities study. *N Engl J Med* 342:905–912
37. Williams B (2003) Drug treatment of hypertension. *BMJ* 326:61–62
38. Phillips L, Branch W, Cook C et al (2001) Clinical inertia. *Ann Intern Med* 135:825–834