



## Drug Therapy of Cardiovascular Risk Factors: Guidelines versus Reality in Primary Health Care Service

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- Aim** To determine the monthly costs of prescription drugs for the treatment of hypertension, hypercholesterolemia, and diabetes mellitus and their share in the total prescription drugs expenditures allowed by the Croatian Institute for Health Insurance.
- Methodology** Hypertension, hypercholesterolemia, and diabetes mellitus were diagnosed in 4,916 patients in three general practitioner (GP) offices in the Zagreb area in January 2005. The monthly cost of medications prescribed by the GPs for the treatment of these three diseases was obtained by summarizing the prices of all antihypertensive, lipid-lowering, and antidiabetic drugs prescribed in one month. The monthly medication costs for each disease separately and all three diseases together were compared with the total prescription drug expenditures approved by the Croatian Institute for Health Insurance.
- Results** Hypertension was diagnosed in 1,112 (22.6%), hypercholesterolemia in 324 (6.5%), and diabetes mellitus in 359 (7.3%) patients. Monthly cost of all medications prescribed for these three diseases accounted for 81.2% of the total amount approved for medications by the Croatian Institute for Health Insurance. Antihypertensive drugs accounted for 51.1%, antidiabetic drugs for 11.7% for, and lipid-lowering treatment for 18.4%. The medications were prescribed most often to patients older than 65 years (93.6%).
- Conclusion** GPs are strongly obligated by the annual contract with the Croatian Institute for Health Insurance to keep the medication expenses within the approved amount. However, the approved amount is spent mostly on the drug treatment of hypertension, hypercholesterolemia, and diabetes mellitus as the main cardiovascular risk factors.

Cardiovascular diseases, in particular coronary heart disease and myocardial infarction, are the leading cause of death in Croatia, responsible for 53% of all deaths in 2003 (1). Therefore, one of the basic tasks of general practitioners (GPs) in Croatia is to work on the prevention and treatment of these diseases. In the developed European countries, the number of deaths caused by cardiovascular diseases has decreased by 39% in the last

decade (2), whereas it remained the same or increased in low- and middle-income countries (2). The death rate from cardiovascular diseases is 250/100,000 population in UK, compared with 290/100,000 in Slovenia and 412/100,000 in Poland (2). Unfortunately, Croatia is among the countries where this number has been increasing, from 610/100,000 population in 2000 to 628/100,000 in 2003 (1). The World Health Organiza-

tion (WHO) and the European Society of Hypertension recognize that the early death and disability caused by cardiovascular diseases are a big economic burden for any country, but could be solved by preventive measures, particularly good control of hypertension (2,3). However, one of the major limitations in the effective hypertension control are the constraints imposed on health care resources, particularly in low- and middle-income countries, which contribute to 80% of the global burden of cardiovascular diseases (4). Since the benefits and cost-effectiveness of managing hypertension are determined by the overall risk of cardiovascular diseases, there should be a paradigm shift from a "single risk" reduction to an "absolute risk" reduction (4). A third of patients with hypertension have also diabetes mellitus and/or hyperlipidemia, which further increase their cardiovascular risk (5). According to the guidelines of professional societies, these patients should receive an adequate drug therapy.

Given these facts, the increase in the consumption of medications for the treatment and prevention of cardiovascular diseases in the last 20 years is not surprising. In the last five years, the spending on medications for the prevention and treatment of cardiovascular diseases increased by over 50% in Great Britain (6). In the USA, it increased by 173% from 1990 to 2000 (7), with the annual increase of 22.8% in the total amount spent on medications until 2004 and only 8.7% afterwards (8). In 2003, 21.3% of the Croatian health budget was spent on medications, which was 17.4% more than in 2002 (9). Some of the leading causes for this increase were irrational prescribing practice by both GPs and specialists, inadequate prices of some medications, and decreased financial contribution of patients to health insurance (10). In 2002, 15-18% of health budget was allocated for medications in European Union (EU) countries (2). In 2003, the percentage of the drug budget spent on cardiovascular drugs was 69.3% in Sweden, 52.1% in Finland, and 49% in UK (2), whereas in Croatia it was 30% (9). In EU countries, hospital treatment of cardiovascular diseases accounted for 53% of the total health expenditures, while 34% was spent on drug therapy (3).

When it comes to antihypertensive, lipid-lowering, and antidiabetic drugs, there are large variations in prescription habits of by GPs not only in Croatia (11) but also in other countries

(6,7). Implementation of guidelines for the prevention and treatment of cardiovascular diseases, especially the drug therapy, by GPs and specialists could improve prevention, diminish the differences in the prescription habits of GPs and specialists, and lower the expenditures (12).

Every year, the Croatian Institute for Health Insurance, a national compulsory health insurance system, determines the amount of money that GPs are allowed to spend on prescription drugs, and that amount depends on the finances from the health budget for primary health care. GPs in Croatia, as independent contractors with the Croatian Institute for Health Insurance, sign an annual contract that stipulates the approved amount (13) and obligates them to keep the expenses on prescription drugs within its limits. Neither specialists of family medicine nor GPs are allowed to prescribe statins and angiotensin II receptor antagonists without consulting a cardiologist. Although GPs could prescribe some other drug independently or following the recommendations of specialists, the financial responsibility is only theirs (14). If they overspend without a justification, the Croatian Institute for Health Insurance first sends an official warning, then imposes a financial penalty, and eventually cancels the contract (14).

Our aim was to calculate monthly costs of prescription drugs for the treatment of hypertension, hypercholesterolemia, and diabetes mellitus and to determine their share in the total prescription drug expenditures annually approved by the Croatian Institute for Health Insurance.

### Participants and Methods

The study was performed in three GP offices in Zagreb, serving 4,916 patients, in January 2005. All three offices were equipped with PCs and kept medical records in an electronic form.

#### Participants

A total of 4,916 patients were divided into 5 age groups, according to which the Croatian Institute for Health Insurance allocates the budget for prescription drugs. The patients with hypertension, hyperlipidemia, and diabetes mellitus were identified, and the amount of money spent on the prescription drugs for the treatment of these three diseases was recorded. Patients with blood pressure above  $\geq 140/90$  mm Hg at two consecutive measurements and patients who had normal

blood pressure but were taking antihypertensive medications were considered to have hypertension (15). Patients were diagnosed with hypercholesterolemia if they had either cholesterol concentration above 5.2 mmol/L or normal cholesterol concentration but were taking lipid-lowering drugs (16). Diabetes mellitus was diagnosed in patients whose fasting blood glucose concentration was above 6.4 mmol/L or in patients with normal blood glucose concentration who were receiving antidiabetic treatment (17).

### Cost-analysis

The monthly expenditures for antihypertensive drugs, statins, and antidiabetic medications were obtained by the summation of monthly expenses on these drugs for each patient and then compared with the total monthly prescription drug expenditures approved by the Croatian Institute for Health Insurance, according to the following formula: number of patients x approved drug budget per one insured person in 2005/12 months.

### Statistical Analysis

Differences between patient age groups and Croatian population were tested by  $\chi^2$  test. The significance level was set at  $P < 0.05$ . The statistical analysis was performed with SPSS 9.0 software (SPSS Inc., Chicago, IL, USA, 1999).

### Results

The age distribution of the patients included in the study corresponds with the age distribution of the whole Croatian population (Table 1). The prescription drug expenses per insured person allowed by the Croatian Institute for Health Insurance in 2005 increased with age (Table 2). Out of 4,916 patients, 1,112 (22.62%) had hyper-

**Table 1.** Comparison of age groups of patients in his study (n=4,916) and total Croatian population (N=4.418,155)

Age groups	Percentage of age group*	
	Croatian population	patients
0-9	11.0	1.4
10-19	12.8	5.5
20-29	13.6	7.9
30-39	13.9	16.2
40-49	15.1	19.6
50-59	12.0	18.6
60-69	11.7	15.6
70-79	7.7	10.4
80-89	2.0	4.1
90-99	0.3	0.7
≥100	0.002	0.0

\*There were no significant differences in the age distribution between the Croatian population and patients included in the study ( $\chi^2$  test,  $P > 0.05$ ,  $df = 10$ ).

**Table 2.** Approved drug expenditures per insured person in 2005 covered by the Croatian Institute for Health Insurance (13)

Age group (years)	Drug expenditure per patient (HRK*)	
	per year	per month
0-34	130.79	10.89
35-44	229.08	19.09
45-54	434.49	36.20
55-64	825.54	68.79
≥65	1,141.36	95.11

\*HRK – Croatian Kuna; €1 = HRK 7.44.

**Table 3.** The distribution of hypertension, hypercholesterolemia, and diabetes according to age in studied patient population

Age groups (years)	No. of patients	No. (%) of patients with		
		hypertension	hypercholesterolemia	diabetes
0-34	1,047	0	0	0
35-44	959	55 (5.7)	18 (1.9)	24 (2.5)
45-54	962	148 (15.4)	54 (5.6)	59 (6.1)
55-64	837	280 (33.5)	99 (11.8)	101 (12.1)
≥65	1,111	625 (56.4)	153 (13.8)	175 (15.6)
Total	4,916	1,112 (22.6)	324 (6.6)	359 (7.3)

tension, 324 (6.6%) had hypercholesterolemia, and 359 (7.3%) had diabetes mellitus (Table 3). All three diseases, which are the risk factors for the development of cardiovascular disease, were most frequently diagnosed in the oldest group of patients, ie, those aged over 65 years. Hypertension was found in 626 (56.4%), hypercholesterolemia in 153 (13.8%), and diabetes mellitus in 175 (15.8%) patients aged over 65 years. The incidence of these risk factors was lowest in patients between 35 and 44 years of age, and increased with age.

The Croatian Institute for Health Insurance approved the GPs included in this study a monthly amount of HRK218,771,95 for prescription drugs. The monthly amount that the three GPs spent on the investigated prescription drugs – antihypertensive drugs, statins, and antidiabetic drugs – for the patients included in this study was HRK177,609.25 (€23,872.21), or 81.2% of the total amount approved by the Institute. Most of it was spent on antihypertensive drugs (51.1%), whereas less was spent on statins (18.4%) and antidiabetic drugs (11.7%). The cost of antihypertensive drugs was HRK111,678.47 (€15,010.55), the cost of statins was HRK40,294.54 (€5,415.93), and the cost of antidiabetic drugs was HRK 25,636.24 (€3,445.73). Out of HRK177,609.25 of monthly expenditures on the prescription drugs for the prevention and treatment of cardiovascular diseases, 62.8% was spent on antihypertensive

drugs, 22.6% on statins, and 14.4% on antidiabetic drugs.

The highest expenditures for the investigated drugs were found in the oldest group of patients, ie, those aged  $\geq 65$  years (Table 4). The monthly amount spent on antihypertensive drugs, statins, and antidiabetic drugs for these patients was HRK98,937.16 (€13,298.01), ie, 93.6% of the total monthly amount approved for prescription drugs in this age group (HRK105.667.21; Table 4).

**Table 4.** Expenditures for antihypertensive drugs, statins, and antidiabetic drugs according to patient age groups in comparison with total prescription drugs expenditures approved by Croatian Institute for Health Insurance in 2005\*

Age groups (years)	No. of patients	Monthly prescription drugs expenditures (HRK)	
		total approved by CIHI	spent on CVD prevention drugs (%)
0-34	1,047	2,395.80	0.00
35-44	959	18,307.31	7,793.82 (42.6)
45-54	962	34,824.40	23,158.52 (66.5)
55-64	837	57,577.23	47,719.75 (82.9)
$\geq 65$	1,111	105,667.21	98,937.16 (93.6)
Total	4,916	218,771.95	177,609.25 (81.2)

\*Abbreviations: HRK – Croatian kuna (€1 = HRK 7.44); CIHI – Croatian Institute for Health Insurance; CVD – cardiovascular diseases.

## Discussion

We found that the expenditures for antihypertensive drugs, statins, and antidiabetic drugs for all age groups of patients amounted to 81.2% of the total amount allocated by the Croatian Institute for Health Insurance to the GPs for prescription drugs in 2005.

Antihypertensive drugs accounted for more than a half of the prescription drug expenditures, although only 22.6% patients had hypertension. In the US, antihypertensive drugs for 27.8% of all patients with hypertension accounted for 45% of drug expenditures (6). The cost of antihypertensive drugs was on the second place of all prescribed drugs in Great Britain in 2002, following closely after statins (4). The Croatian Institute of Public Health reported in 2003 that 10.5% of patients had a diagnosis of increased blood pressure recorded in medical files in GP offices in Croatia (1). To obtain reliable data on the prevalence of hypertension in Croatia, a project called Epidemiology of Hypertension in Croatia (EH-UH Study) was started in 2000 (18). By 2004, the project had included 1,458 participants aged  $\geq 18$  years in whom the prevalence of hypertension was 44% (<http://ipehuh.irb.hr/~ipehuh/portal/reports/>

*reports.php*). The average percentage of people diagnosed with hypertension in EU countries is 44% (Germany 55%, Italy 38%, and Finland 49%) (19). The number of patients diagnosed with high blood pressure in our study was almost half the number of patients with hypertension in EU countries and total Croatian population (18), but also twice higher than the number of patients diagnosed with hypertension in general practice in Croatia according to the Croatian Institute for Public Health (1). Nevertheless, more than a half of the amount approved to GPs for prescription drugs was spent on the patients with hypertension.

Hypercholesterolemia was diagnosed in only 6.6% of the patients included in this study. The data on prevalence of hypercholesterolemia in Croatia do not exist. Recent research by the WHO highlights the increased blood cholesterol as a risk factor for cardiovascular diseases. The World Health Report 2002 estimates are that around 8% of the total disease burden in developed countries is caused by increased blood cholesterol, and that over 50% of cardiovascular diseases in developed countries are due to blood cholesterol concentrations exceeding the theoretical minimum of 3.8 mmol/L (2). According to WHO, 8% of people with hypercholesterolemia remain undiscovered in developed countries, while in developing countries, this proportion is estimated to be 50% (2). Rapid increase in the diagnosis of hypercholesterolemia has been noticed in EU countries during the last 10 years (20). It has been shown that the risk of the development of coronary heart disease could be lowered by 60% by adequate regulation of blood cholesterol (3). The GPs in our study, following the specialist recommendations, spent 18.4% of the total budget allocated for drugs on the treatment of 6.6% patients with hypercholesterolemia. In Great Britain, statins are more frequently prescribed than antihypertensives (4). In EUROASPIRE study, the share of statins prescriptions was 68% for 60% diagnosed hypercholesterolemia patients in France, 60% for 57% in Italy, and 69% for 54% patients diagnosed with hypercholesterolemia in UK (21). These differences between European countries in the number of statins prescriptions were one of the reasons why the experts agreed that the guidelines were necessary (21). However, despite the high prescription rate for statins in EU countries, some reports show it is still not enough (22). The results

of our study showed that, with respect to the number of patients with hypercholesterolemia, statins were prescribed three times more often than in France, Italy, or UK.

Diabetes mellitus was diagnosed in 7.3% of the patients in this study. The prevalence of diabetes mellitus in Croatia is 2.4% (1), similar to that in Europe (3%) but twice lower than that in the US (6%) (2). We found that 11.7% of total drug expenditures approved by the Croatian Institute for Health Insurance were spent on antidiabetic drugs for 7.3% patients with diabetes mellitus. In France, 34.4% of drug expenditures were spent on the treatment of diabetes mellitus in 3% of the patients diagnosed with that disease (23), 29% was spent in Italy (24), and 27% in Germany (25). In Spain, 5-6% of patients with diabetes mellitus spent 7.4% of total National Health System expenditures (26) for their treatment, whereas in Germany, patients with diabetes mellitus spent 7.1% of health insurance expenditures (25).

In our study, drug expenditures and drug prescription rate increased with patient age, with the patients in the oldest age group accounting for 93.6% of the expenditures on antihypertensive, lipid-lowering, and antidiabetic drugs. It is to be expected because the oldest population suffers from more chronic diseases and takes more medications, but it also means that only 6.4% of the amount approved to GPs for prescription drugs is left for the treatment of other health conditions. Due to aging of population, the number of cardiovascular diseases is expected to increase by 60% by 2025 (2). The implementation of guidelines for prevention of cardiovascular diseases means an increase in drug prescription rate for patients at higher risk, as well as expenditures. However, these expenditures are still lower than the expenditures for the treatment of the consequences of cardiovascular diseases (hospitalization, rehabilitation, and disability) (4).

In the last two years in Croatia, the total drugs expenditures covered by the Croatian Institute for Health Insurance increased from HRK29,386,844.46 (€3,949,844.69) to HRK 31,304,471.63 (€4,207,590.27), or 17.4% (7). All EU countries have a similar problem, and programs to lower expenditures and to standardize drug prescription by GPs are being developed in Europe (27). The most acceptable and effective approach to decreasing expenditures for drug pre-

scription is to increase prescription rate of cheaper generic drugs (28). Better education of GPs, computerization (29), specific guidelines for drug prescription (3) and – as considered in USA (30) – a reform of health insurance might be necessary.

The main limitation of our study was that it included only urban population, so the conclusions could not be made generally for total drug expenditures of all GPs in the whole Croatia, although there were no significant differences in the distribution by age between our sample and the Croatian population. This study may be considered a pilot study for further investigations in prevalence, benefits, and cost effectiveness of prevention and treatment of these diseases. Prevalence of diabetes in Croatia is similar to other EU countries. Prevalence of hypertension in Croatia is less well understood and varies in different surveys (1,18), whereas no data exist for the prevalence of hyperlipidemia. Drug expenditures for registered patients with hyperlipidemia are much higher in Croatia than in other EU countries, they are quite similar for hypertension and about 60% lower for diabetes mellitus. As total drug expenditures allowed by the Croatian Institute for Health Insurance are hardly sufficient for the treatment these three diseases, maybe part of the solution lies in the prevention and treatment of other diseases.

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