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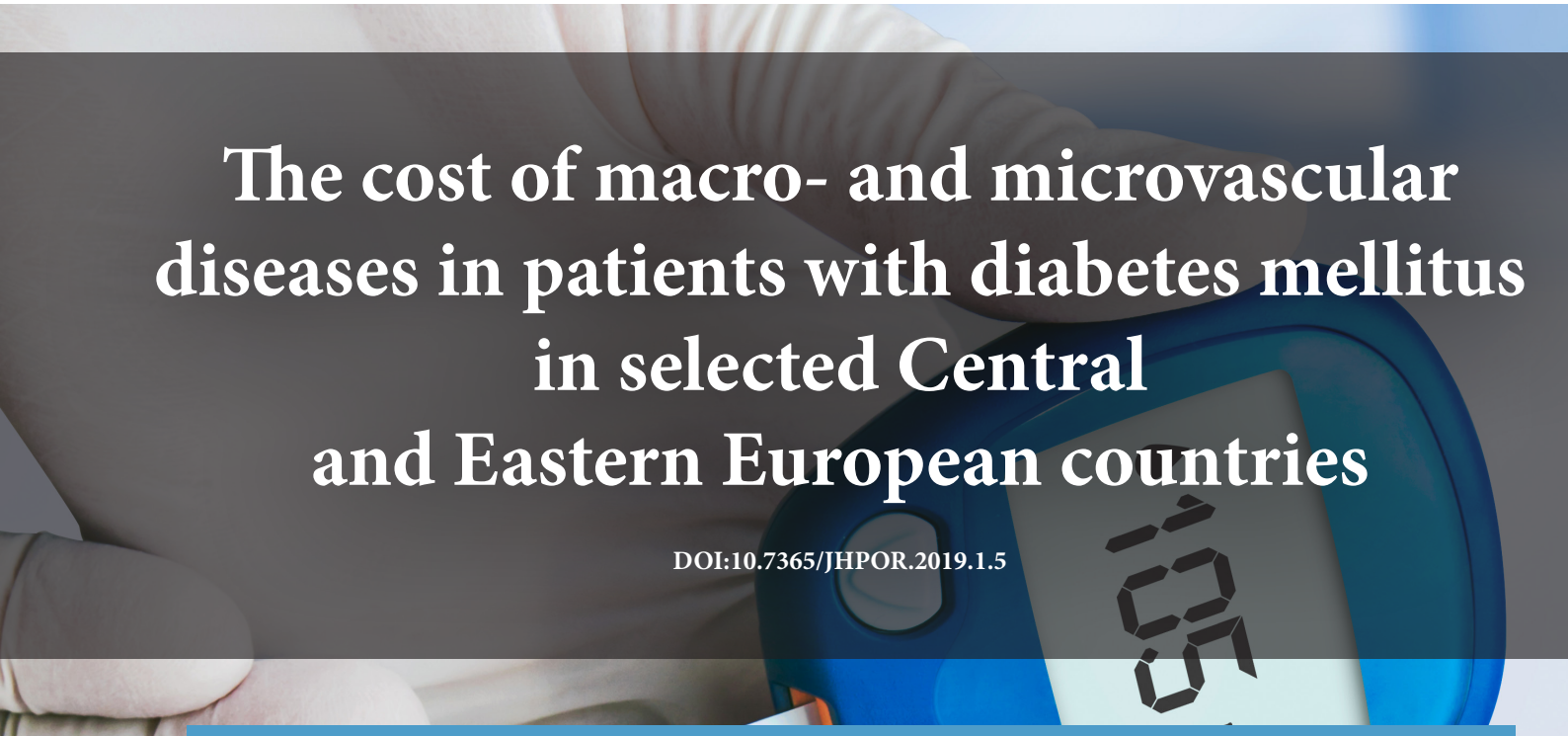

The cost of macro- and microvascular diseases in patients with diabetes mellitus in selected Central and Eastern European countries

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Abstract

Background

Macro- and microvascular diseases (MMVDs) in diabetes mellitus (DM) are important clinical and economic burdens. Reimbursement decisions require substantiated information; however, for Central and Eastern European (CEE) countries cost data are lacking. Our aim was to estimate the direct public-payer medical costs of MMVDs in adult DM (regardless of the type of DM) patients in Bulgaria, Lithuania, Poland, Republic of Srpska/Bosnia and Herzegovina, Romania, and Slovenia.

Methods

The MMVDs considered were diabetic foot, end-stage renal disease (ESRD), heart failure (HF), painful neuropathy, peripheral vascular disease, retinopathy, stable angina pectoris, myocardial infarction (MI), stroke, transient ischemic attack, and unstable angina (UA). They were split into complications (the first seven) and events; prevalence and incidence-based approaches, respectively, were used. Experts in participating countries provided information via a unified questionnaire.

Results

The total cost of DM-related MMVDs (EUR per annum) amounted to 1,165 million (m) in Poland, 581m in Romania, 103m in Bulgaria, 76m in Slovenia, 47m in Republic of Srpska/Bosnia and Herzegovina, and 29m in Lithuania (some categories omitted). The cost per DM patient was similar for most included countries (range 586–759), and lower in Lithuania (301) and Bulgaria (219). The largest individual contributor was HF (20.9%), followed by 13% for MI, UA, stroke, and ESRD.

Conclusions

DM-related MMVDs impose a significant financial burden in CEE countries; our results can aid economic assessments of treatments for DM. Collecting data for several countries is challenging as available information differs; however, a unified methodology allow quality checks. The results are consistent between the countries, which supports the credibility.

Introduction

Diabetes mellitus (DM) is a chronic disease that results in elevated blood glucose levels, leading to damage in many tissues in the body. According to the International Diabetes Federation (IDF), there were about 425 million (m) people worldwide with DM in 2017, including 58m in Europe. The number of patients with DM is expected to increase to 67m in Europe and to 629m worldwide by 2045.[1] The reasons for a high prevalence of DM are an ageing population, reduced physical activity, increased sugar intake, low fruit and vegetable intake, an increasing number of people with obesity, and increasing urbanisation.[2] According to the IDF, the age-adjusted comparative prevalence of DM is 8.7% worldwide and 6.8% in Europe.[1] The cost of DM in European Union (EU) countries varies between 10% and 18.5% of total healthcare expenditure.[3] According to the European Commission, DM-related expenditure accounted for 10.2% of the total healthcare costs in Bulgaria, 8.0% in the Czech Republic, 8.6% in Germany, 8.3% in France and Italy, 11.2% in Lithuania, 12.4% in Poland (EUR 591 million in total), 10.8% in Romania, and 11.0% in Serbia.[4] In 2017, the healthcare expenditure on treatment for DM amounted to USD 166 billion in Europe and USD 727 billion worldwide, and these expenditures are expected to grow.[1]

Macro- and microvascular diseases (MMVDs), such as stroke, heart failure, myocardial infarction, nephropathy, retinopathy, or diabetic foot, are of particular importance, and are a leading cause of death amongst patients with DM.[5] According to the 2015 IDF Diabetes Atlas, cardiovascular diseases (CVDs), a large subset of MMVDs, account for >50% of deaths due to DM [5], and other sources provide estimates as high as 75–80%.[7] Type 2 DM increases the risk of CVDs by 2–4 times.[6]

CVDs shorten life expectancy by 5–10 years in patients with DM.[8] At the same time, treatment of CVDs generates substantial costs.[7] It was estimated that CVDs (all, not only DM-related) accounted for costs of EUR 210 billion annually in the EU.[9] Einarson et al conducted a systematic search for publications on CVD costs and found 10 studies for different countries (inter alia: India, Korea, Spain, the United Kingdom, and the United States); it was

estimated that the average treatment cost annually was USD 8,310 in patients without CVDs and USD 15,505 in patients with CVDs [10]. In developed countries, about 75% of costs for CVDs are related to hospital treatment; in developing countries, the bulk of costs is borne by the patients.[3] The CVD-related costs are often several times higher than expenditures on the prevention and treatment of DM itself.[7]

Understanding the sources and magnitude of the MMVD-related costs might help payers and decision makers to optimise healthcare spending and to allocate the scarce resources in the most efficient way. In health technology assessment (HTA), the evaluation of treatment cost-effectiveness is based on cost estimates. Different treatments for DM may have different risk profiles for MMVDs; therefore, assigning costs to specific complications enables HTA bodies to assess the benefits of different treatments based on risk reductions of MMVDs. At the same time, given the large number and variability of MMVDs, estimating their costs is not an easy task. Costs may vary across countries due to differences in prices, clinical practice and available treatment methods, or how the healthcare systems are organised and financed.

A pragmatic search of the literature (not reported here) demonstrated a lack of data regarding the costs of DM-related MMVDs in Central and Eastern European (CEE) countries, a clear obstacle to making the HTA process informative and effective. To fill the gap, the current study aimed to estimate the direct medical costs of selected MMVDs in adult patients with DM (regardless of the type) in Bulgaria, Lithuania, Poland, Republic of Srpska/Bosnia and Herzegovina, Romania, and Slovenia from the public payer perspective. The selection of countries was pragmatic, i.e. based on the willingness to participate in the study.

Methods

MMVDs were selected for consideration in the current study based on the CORE Diabetes Model,[11] LEADER trial,[12] and clinical experts' opinions as to which MMVDs are clinically most significant and prevalent. The included MMVDs have potentially the biggest impact on healthcare budgets and therefore are of most interest to public decision makers. The following MMVDs were selected: diabetic foot; end-stage renal disease (ESRD); heart failure (HF); myocardial infarction (MI); painful neuropathy; peripheral vascular disease (PVD); retinopathy; stable angina; stroke; transient ischemic attack (TIA); and unstable angina (UA). The selected MMVDs were divided into two groups based on different clinical characteristics, as described below: one group consisted of events and had cost calculated as such (MI, stroke, TIA, and UA), and the other group were chronic complication conditions and had cost calculated as such (diabetic foot, ESRD, HF, painful neuropathy, PVD, retinopathy, and stable angina).

Cost calculations for events

Events have a well-defined moment of occurrence, are not long-lasting , and the associated costs are expected to decrease over time. The incidence-based approach was used for MMVDs classified as events. The total cost was calculated as a sum of costs generated during three sub-periods: at the event (i.e. during the initial hospitalisation); within the remaining part of the first year after the event; and in the second year after the event. Risk of death was accounted for in the calculations; only survivors generated costs in subsequent sub-periods. However, we did not account for deaths occurring during the event-driven hospitalisation, as the bulk of the cost is incurred regardless of whether the patient survived the event or died during the event.

The incidence-based results are straightforward to interpret as costs generated in subsequent years by a cohort of patients having the event at a single, given moment. Alternatively, the results can be interpreted as the sum of the costs incurred in a single year generated by different patient cohorts suffering from the consequences of a given event experienced in different years in the past. Under the latter interpretation, the total cost consists of: costs for a cohort of patients that experienced the event (cost at the event); costs for a cohort of patients that survived the event, but had the event over the preceding year (first year cost); and costs for a cohort of patients that had the event two years earlier (the second year cost). The costs of subsequent years (years 2+) were not included, due to a lack of credible and precise mortality data. This approach to cost calculation requires several assumptions to give correct estimates, which are included in this analysis: a stable incidence rate; population size; treatment process; and prices.

Some events might occur in a single patient twice in their lifetime or different events may occur in a single patient over time. In the questionnaire described below, the cost path following a single event was assessed, and the recurrence of a given event was assumed to be reflected in the epidemiology (i.e. the incidence data).

Cost calculations for complications

Complications are long-lasting health conditions, with no specific starting point. Patients are typically diagnosed after already having the condition for some time. Moreover, the condition of the patient who developed a given

complication might deteriorate over time. Hence, calculating the total cost of a given complication from the time of diagnosis onwards would require accurate, long-term survival data, which is often difficult to obtain. Therefore, the prevalence-based approach was used in the present study, with prevalence data and the annual average cost for a typical patient as a base for cost calculations. Data for an average patient (i.e. not newly diagnosed or with the complication in an advanced stage) were used to avoid under or overestimating the annual cost. The estimates of costs obtained with the prevalence-based approach should be interpreted as the total annual cost per given complication.

Questionnaire

Data were collected in the participating countries via a single questionnaire. The invitation to participate in the study was extended to a range of experts (incl. physicians) in the fields of cardiology, neurology, diabetes and epidemiology, to health economists, and to policy makers. The questionnaire comprised questions related to the epidemiology of DM, the annual rate of DM-related MMVD events, the prevalence of DM-related MMVD complications, the risk of death among patients with DM due to specific events (at the event and within a year), and the costs. The costs were divided into hospitalisations, other procedures, and drugs.

The experts were asked to provide costs of procedures and drugs only if these were financed separately and not included in a wider cost category, e.g. overall hospitalisation cost or diagnosis-related group (DRG) category, to avoid double counting.

Some events might occur twice in a patient's lifetime (or different events may occur in a single patient over time). In the questionnaire, the cost path following a single event was assessed, and the reoccurrence of a given event was assumed to be reflected in the epidemiology (i.e. the incidence data).

In case of missing non-cost-related values (e.g. rate, prevalence, or mortality), the average values from the other participating countries were used. A public payer perspective was assumed, and the costs were converted to Euros (EUR), if necessary, using the exchange rate from the European Central Bank between April and May 2017.
The data collected were verified (e.g. by juxtaposing against other countries). In order to use the most reliable data, all the doubts were discussed with the respondents and the data were amended, if needed.

Total cost estimation

The hospitalisation cost was calculated by multiplying the percentage of patients using a given type of hospitalisation by the average number of units used and by the unit cost; the results were then summed over all types of hospitalisation. The costs of other medical procedures and drugs were calculated in a similar way, with calculations of drugs costs accounting for different possible dosing patterns.

The sum of the three cost categories (hospitalisations, procedures and drugs) yields the annual average treatment cost of a complication per patient. The total annual average cost for each country was calculated using the number of adult patients with DM and the prevalence of the complication in question. Finally, to provide a total cost of DM-related MMVD complications in a country, the results for all considered complications were aggregated.

For the events, the cost for each of the three sub-periods (at the event, the first year, and the second year) were calculated for the cost of hospitalisations, procedures, and drugs in the same way as described above. The three cost components (hospitalisations, procedures and drugs) were then added and the survival rates were applied to derive the costs for each of the three sub-periods. Finally, the total cost per patient was multiplied by the number of adult patients with DM and by the annual incidence rate. The methodology of cost calculations is illustrated in Fig. 1.

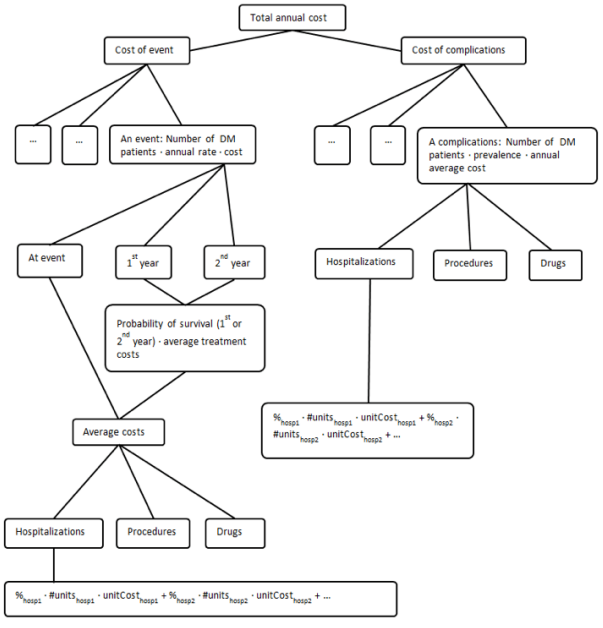

Figure 1. Methodology of total annual cost calculations for events and complications.

Methodology used for Slovenia and Lithuania

A different approach to cost calculation was used in Slovenia and Lithuania due to a different format of available data. For Slovenia, the average event cost per patient (split

into sub-periods) was calculated as described above. To calculate the number of patients, the annual number of DRG cases was used (instead of the number of patients with DM and the annual incidence rate). The percentage of patients using a given resource in subsequent sub-periods was applied to the starting cohort. Hence, the mortality rate was not used. The cost of complications was estimated using the same formula as used for Bulgaria, Poland, Romania, and Republic of Srpska/Bosnia and Herzegovina.

For Lithuania, we used information on the total annual costs of DM-related complications from the National Health Insurance Fund (NHIF), data received from the Department and Institute of Endocrinology, Medical Academy, University of Health Sciences Kaunas Clinics (HSU Kaunas Clinics), and the cost study of DM complications in Lithuania by Domeikienė et al.[13] Based on data from the NHIF, the total annual cost of hospitalisations related to DM complications was calculated. Costs were split into MMVDs[1] (not distinguishing specific diseases), stroke, renal failure, and foot amputation. HSU Kaunas Clinics provided detailed data on the costs of hospitalisations of patients with diabetic foot, neuropathy and retinopathy. The costs of cardiologist, foot care, nephrologist, neurologist and ophthalmologist consultations were estimated based on the study by Domeikienė et al.[13] Due to different methodology, the split into specific events and complications is not presented; hence, the results for Lithuania are omitted in some tables and figures.

Results

The highest annual incidence rates of MI are reported for Slovenia (0.0980) and Romania (0.0805). Romania also has a substantially higher annual rate of stroke (0.2315), TIA (0.0307) and UA (0.0695) compared with the other countries in the study (Tab. 1). Across all events, the highest average annual rate is for stroke (0.0693) and the lowest is for TIA (0.0151) (Fig. 2).

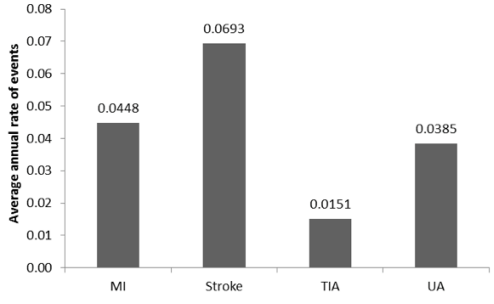

Figure 2. Annual rate of DM-related events among patients with DM (average across participating countries).

Stable angina is most prevalent (among DM patients) in Poland (32.25%), HF in Bulgaria (18.30%) and Poland (16.00%), and painful neuropathy in Bulgaria (31.90%). The prevalence of PVD is similar in Poland, Romania, and Slovenia (range 10.00–13.16%) and very low in Republic of Srpska/Bosnia and Herzegovina and Bulgaria (0.27% and 0.50%, respectively). Romania and Republic of Srpska/Bosnia and Herzegovina have a similar low prevalence of retinopathy (0.51% and 0.56%, respectively), while the highest prevalence is in Poland (10.40%). The prevalence of diabetic foot is highest in Poland (8.00%) and lowest in Romania (0.06%) (Tab. 2). On average amongst the DM-related complications, the most often observed were stable angina (13.70%), painful neuropathy (11.68%), and HF (10.26%). The lowest average prevalence is for ESRD (0.96%) and diabetic foot (2.84%) (Fig. 3).

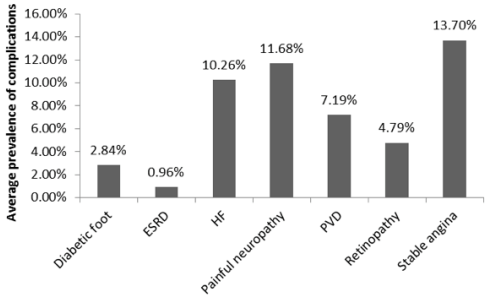

Figure 3. Prevalence of DM-related complications among patients with DM (average across participating countries).

The cost of events decreases over time in all countries (Tab. 3), as expected (and constituted a reason to use an incidence-based approach).[14, 15]

For MI treatment, the highest cost was calculated for Slovenia and the lowest for Romania. At the time of event, costs are similar in Republic of Srpska/Bosnia and Herzegovina (EUR 3,614) and Bulgaria (EUR 3,016). The highest cost of stroke at the time of the event is in Slovenia (EUR 4,820) and the lowest in Romania (EUR 582). The cost of TIA at the time of the event is the highest in Slovenia (EUR 1,417) and the lowest in Bulgaria (EUR 210) and Romania (EUR 233). Furthermore, the TIA treatment costs at the event are related only to hospitalisations in all countries. The highest cost of UA at the event is in Slovenia (EUR 2,430) and Poland (EUR 2,086) and the lowest in Romania (EUR 502). The largest share of cost at the time of the event is due to hospitalisations. With time, drug costs tend to increase (Supplementary File).

The cost of diabetic foot treatment was similar in all countries except for Republic of Srpska/Bosnia and Herzegovina, where it was higher (Tab. 4). The cost of HF treatment is similar in Slovenia (EUR 1,891), Poland (EUR 1,830) and Republic of Srpska/Bosnia and Herzegovina (EUR 1,267).

Table 1 Annual rate of events among patients with DM.				
	MI	Stroke	TIA	UA
Bulgaria	0.0069	0.0143	0.0174	0.0186
Poland	0.0111	0.0065	0.0028	0.0042
Republic of Srpska/Bosnia and Herzegovina	0.0274	0.0284	0.0094	0.0615
Romania	0.0805	0.2315	0.0307	0.0695
Slovenia	0.0980	0.0660	0.0151*	0.0385*
Average	0.0448	0.0693	0.0151	0.0385

*average value from the other participating countries

Table 2 Prevalence of DM-related complications among patients with DM.							
	Diabetic foot (%)	ESRD (%)	HF (%)	Painful neuropathy (%)	PVD (%)	Retinopathy (%)	Stable angina (%)
Bulgaria	2.80*	0.11*	18.30	31.90	0.50	7.70*	8.90
Poland	8.00*	0.30*	16.00	15.00	10.00	10.40*	32.25
Republic of Srpska/Bosnia and Herzegovina	0.48*	0.05*	4.40	3.42	0.27	0.56*	6.15
Romania	0.06*	3.39*	4.70	2.10	13.16	0.51*	11.70
Slovenia	2.84*	0.96*	7.90	6.00	12.00	4.79*	9.50
Average	2.84*	0.96*	10.26	11.68	7.19	4.79*	13.70

*average value from the other participating countries

Table 3 Summary of annual costs of events (per event).			
Country	Costs of MI, EUR		
	At the event	The 1st year	The 2nd year
Bulgaria	3 016.47*	815.38	213.07
Poland	2 267.63*	1 588.43	437.95
Republic of Srpska/Bosnia and Herzegovina	3 613.52*	1 344.27	1 171.40
Romania	774.42*	147.39	107.03
Slovenia	5 361.47*	2 388.50	404.23
Country	Costs of stroke, EUR		
	At the event	The 1st year	The 2nd year
Bulgaria	874.21*	680.18	162.98
Poland	1 791.53*	1 076.08	78.38
Republic of Srpska/Bosnia and Herzegovina	1 929.92*	1 198.70	1 254.71
Romania	582.19*	168.11	157.80
Slovenia	4 820.08*	1 722.75	500.28
Country	Costs of TIA, EUR		
	At the event	The 1st year	The 2nd year
Bulgaria	210.24*	675.18	124.18
Poland	774.62*	148.76	22.51
Republic of Srpska/Bosnia and Herzegovina	342.86*	1 043.20	916.23
Romania	232.71*	1 713.19	93.10
Slovenia	1 416.99*	453.62	194.49
Country	Costs of UA, EUR		
	At the event	The 1st year	The 2nd year
Bulgaria	1 261.75*	824.03*	261.73*
Poland	2 085.81*	1 079.88*	297.73*
Republic of Srpska/Bosnia and Herzegovina	1 806.53*	1 538.85*	1 224.17*
Romania	501.83*	146.07*	139.97*
Slovenia	2 430.36*	761.93*	386.31*

*Hospitalisation costs

Table 4 Summary of annual costs of complications (per complication).	
Country	Average annual costs of diabetic foot, EUR
Bulgaria	381.57
Poland	259.94
Republic of Srpska/Bosnia and Herzegovina	4 727.73
Romania	707.29
Slovenia	693.21
Country	Average annual costs of ESRD, EUR
Bulgaria	11 830.77
Poland	12 804.27
Republic of Srpska/Bosnia and Herzegovina	696.56
Romania	5 373.87
Slovenia	8 971.51
	Average annual costs of HF, EUR
Bulgaria	318.20
Poland	1 830.53
Republic of Srpska/Bosnia and Herzegovina	1 268.80
Romania	173.51
Slovenia	1 891.11
Country	Average annual costs of painful neuropathy, EUR
Bulgaria	33.78
Poland	401.55
Republic of Srpska/Bosnia and Herzegovina	366.74
Romania	281.18
Slovenia	2 235.45
Country	Average annual costs of PVD, EUR
Bulgaria	777.12
Poland	135.91
Republic of Srpska/Bosnia and Herzegovina	2 535.18
Romania	96.24
Slovenia	433.54
Country	Average annual costs of retinopathy, EUR
Bulgaria	67.60
Poland	477.49
Republic of Srpska/Bosnia and Herzegovina	287.76
Romania	130.34
Slovenia	180.75
Country	Average annual costs of stable angina, EUR
Bulgaria	116.05
Poland	199.76*
Republic of Srpska/Bosnia and Herzegovina	1 629.01
Romania	62.11
Slovenia	552.66

*hospitalisation costs

Table 5 Total annual costs of treatment of specific MMVDs (EUR), percentage share of the costs of individual MMVDs in the total annual cost of MMVD-treatment in the specific country, and average percentage share across countries.

	Bulgaria, EUR (%)	Poland, EUR (%)	Republic of Srpska/Bosnia and Herzegovina, EUR (%)	Romania, EUR (%)	Slovenia, EUR (%)	Average percentage share of MMVDs
MI	12 381 039 (12.0%)	84 865 494 (7.3%)	9 805 785 (20.7%)	76 448 107 (13.2%)	5 381 780 (7.1%)	12.06%
Stroke	10 422 479 (10.0%)	33 139 140 (2.8%)	6 670 569 (14.1%)	185 003 020 (31.8%)	4 468 852 (5.9%)	12.92%
TIA	8 181 683 (8.0%)	4 974 749 (0.4%)	1 323 291 (2.8%)	59 927 035 (10.3%)	217 866 (0.3%)	4.36%
UA	20 123 508 (19.0%)	26 974 525 (2.3%)	17 024 601 (36.0%)	51 321 959 (8.8%)	1 329 455 (1.8%)	13.58%
Diabetic foot	4 998 283 (5.0%)	39 089 244 (3.4%)	1 413 236 (3.0%)	406 972 (0.1%)	2 462 856 (3.2%)	2.94%
ESRD	5 927 894 (6.0%)	72 204 173 (6.2%)	21 689 (0.0%1)	174 703 968 (30.1%)	12 345 697 (16.3%)	11.72%
HF	27 241 749 (26.0%)	550 533 281 (47.3%)	3 476 698 (7.4%)	7 820 752 (1.3%)	18 689 708 (24.6%)	21.32%
Painful neuropathy	5 042 255 (5.0%)	113 219 201 (9.7%)	781 086 (1.7%)	5 662 646 (1.0%)	16 779 293 (22.1%)	7.90%
PVD	1 817 788 (2.0%)	25 546 090 (2.2%)	426 279 (0.9%)	12 144 743 (2.1%)	6 508 215 (8.6%)	3.16%
Retinopathy	2 435 139 (2.0%)	93 342 539 (8.0%)	100 353 (0.2%)	637 492 (0.1%)	1 083 119 (1.4%)	2.34%
Stable angina	4 831 733 (5.0%)	121 093 760 (10.4%)	6 239 072 (13.2%)	6 968 481 (1.2%)	6 568 045 (8.7%)	7.70%

Table 6 Number of patients with DM and total annual costs of all selected MMVDs and per single patient with DM.

	Number of diagnosed adults, all DM types	Total annual cost of all MMVDs, EUR	Total annual cost of all MMVDs per patient with DM, EUR
Bulgaria	473 1921	103 403 550	218.5
Lithuania	98 8251	29 787 238	301.4
Poland	1 879 690[1]	1 164 982 196	619.8
Republic of Srpska/Bosnia and Herzegovina[2]	62 3011	47 282 659	758.9
Romania	991 5371	581 045 175	586.0
Slovenia	125 1001	75 834 886	606.2

[1] - Type 1 and 2 DM
[2] - Data for Republic of Srpska only

The cost of painful neuropathy treatment is similar in Poland (EUR 402), Republic of Srpska/Bosnia and Herzegovina (EUR 367), and Romania (EUR 281); the highest cost is in Slovenia (EUR 2,235). Stable angina treatment costs are highest in Republic of Srpska/Bosnia and Herzegovina (EUR 1,629) and lowest in Romania (EUR 62).

The total costs of each MMVD were calculated as described in the methods section. The percentage share of an individual MMVD in the total treatment costs of MMVDs in a given country was calculated as the annual cost of a single event or complication in the country divided by the total annual cost of all MMVDs in that country (Tab. 5). The highest total annual costs of UA, stroke, TIA, and ESRD are reported for Romania. In Poland, the highest costs are related to the treatment of diabetic foot, HF, painful neuropathy, and stable angina. The single MMVD with the largest share of costs in Poland, Bulgaria and Slovenia is HF (47%, 26% and 25%, respectively). In Romania, stroke and ESRD (approximately 30%) contribute the highest percentage share in the total treatment costs of MMVDs. In Republic of Srpska/Bosnia and Herzegovina, treatment of UA has the highest percentage share in the total treatment cost of MMVDs (36%). The average share (for all countries, except Lithuania) of individual MMVDs in the total treatment costs is highest for HF (21.3%), followed by UA (13.6%), stroke (12.9%) and MI (12.1%). The lowest average percentage share of costs is for retinopathy (2.3%), diabetic foot (2.9 %), PVD (3.2%), and TIA (4.4%). The average percentage share of costs in the total cost of treatment of MMVDs was similar for stable angina (7.7 %) and painful neuropathy (7.9 %).

The data on the number of patients with DM presented for Republic of Srpska/Bosnia and Herzegovina are representative of patients in the Republic of Srpska only. The number of patients with DM in each country is an aggregate, i.e. data are presented without specific numbers for different types of DM: type 1, type 2, gestational, maturity onset diabetes of young (MODY), and latent autoimmune

diabetes of adults (LADA). These aggregate numbers were used in the cost calculations, as it was assumed that the treatment of a given MMVD is not dependent on diabetes type, e.g. the treatment of stroke would use the same resources for a patient with type 1 DM as a patient with type 2 DM.

In absolute terms, the total annual cost of all selected MMVDs is highest in Poland (EUR 1,165m), the country with most inhabitants amongst all countries participating in the study (Tab. 6). The second highest total annual cost of all MMVDs is reported for Romania (EUR 581m). The lowest treatment costs of MMVDs are in Republic of Srpska/Bosnia and Herzegovina (EUR 47m) and Lithuania (EUR 29m). It is worth noting that the results for Lithuania are likely to be underestimated since only some cost categories were included in the total cost calculations.

The cost per patient was calculated as the total annual treatment costs of all selected MMVDs divided by the number of DM adult patients in a given country (Tab. 6). The total average annual cost of treatment of DM-related MMVDs per patient with DM is similar across the participating countries, ranging from EUR 586 in Romania to EUR 759 in Republic of Srpska/Bosnia and Herzegovina, with the exception of Lithuania (EUR 301) and Bulgaria (EUR 218).

Discussion

Patients with DM, when not well controlled, tend to develop numerous macro- and microvascular complications throughout their lifetime. The current study focused only on selected MMVDs that are deemed most important from a clinical and economical point of view. Drug-induced hypoglycaemia and other DM-related complications such as hyperosmolar hyperglycaemic non-ketotic syndrome and diabetic ketoacidosis — which are important both from a clinical and economic perspective — were not considered in the current study. Therefore, the cost estimates presented here are conservative.

Collecting data for several countries with different healthcare organisations is challenging since the availability, structure, quality, and timeliness of data differ. Despite sharing common political and economic backgrounds, the countries participating in this study differ in terms of economic development, price levels, clinical practice, available treatment methods, and the scope of public payer healthcare coverage. Hence, the comparability of the results between countries is limited. Using a single questionnaire allowed for keeping a consistent methodological approach to data collection (with the exception of Lithuania and Slovenia, where a modified approach was applied due to different formats of available data). To ensure the best quality of the results, all inputs were checked for inconsistencies. In case the input values for one country were substantially different from those reported by other countries, the data were double checked for reporting errors. A unified framework also allowed for inputting mean values of data reported by other participating countries as a proxy for any missing clinical data. The data for each country were provided by more than one person to ensure the validity of the input values. Any doubts and inconsistencies were discussed with the respondents and the input data were amended, if needed.

The differences in methodology of collection of cost data for Slovenia do not impede the comparability of results. In the case of Lithuania, only some cost categories were included. In addition, all costs used in the current study represented average annual costs. Therefore, the methodology for cost calculations for events and complications used for the other countries was not applied (e.g. the breakdown into sub-periods for events). The cost calculations did not account for the cost of drugs used for the treatment of MMVDs (although it should be acknowledged that some of this cost might have been included in the tariffs covering hospitalisation costs). Therefore, the total treatment cost of MMVDs in Lithuania presented in this study is likely to be underestimated.

This study was conducted from a public payer perspective. The reasons for assuming a narrow perspective in the cost calculations are two-fold. Data on patients' expenditures are scarce and rarely available in CEE countries. Therefore, assessing the indirect cost would likely be extremely challenging and require arbitrary methodological decisions and assumptions (e.g. whether to use a human capital approach or a friction cost method). The second reason for restricting the cost assessment to a public payer perspective only is that this perspective is used most often in HTA applications in CEE countries. This means that the results presented in this study do not include any societal costs of MMVDs that patients with DM, their families, or society as a whole may bear. It is also worth noting that the study focused only on the costs attributable to MMVDs and not to DM in general.

The calculations for the total cost of the treatment of MMVDs did not account for the treatment costs incurred in the years 2+. However, we believe this approach resulted in only minor underestimation of the total costs. The total cost calculations did not account for the probability of a patient dying during the event and not generating the full cost. This could lead to the overestimation of the total treatment cost; however, this overestimation is likely to be negligible since the hospitalisation cost will also be incurred for dying patients in most cases and therefore also reimbursed by public payers. Moreover, as reported in the literature, fatal events are often

associated with higher costs than non-fatal ones.[16,17] The death of a patient during the sub-period may lead to a reduction in overall drug costs, but this component of the total treatment cost is negligible compared with the cost of hospitalisations and procedures performed before the patient's death.

Another possible reason for cost underestimation is that when a patient is hospitalised due to DM-related complications, DM itself may not be listed in the medical record as the main diagnosis.[18] This might result in not including all the data in cost calculations.

According to the IDF Diabetes Atlas 2017, the number of adult patients with DM was 424,300 in Bulgaria, 366,900[2] in Bosnia and Herzegovina, 108,700 in Lithuania, 2,235,800 in Poland, 1,785,300 in Romania, and 161,600 in Slovenia.[1] These values are somewhat higher than the estimates presented in this study (Tab. 6), with the exception of Bulgaria (473,192). The number of people with diabetes is constantly increasing all over the world,[1] but despite this fact reliable and high-quality data on DM epidemiology are still insufficient in Europe[19] and in the CEE region in particular. The main reason for this may be that non-communicable diseases are not required to be closely monitored and reported, in contrast to, for example, infectious diseases.[19]

There were some differences in the input values provided by participating countries, for example, the stroke incidence rate ranged from 0.0065 in Poland to 0.2315 in Romania. This difference may be partially explained by different sources used for parameters. In Poland, this particular value was based on experts' opinion, while in Romania, the value was retrieved from a hospital morbidity database and may be overestimated due to including non-DM-related strokes or other events reported as a stroke. However, consistently higher rates were reported for Romania for other considered events, suggesting the risk of the events might indeed be greater in comparison with other countries.

The prevalence of complications varies between complications and between countries (Tab. 2). ESRD and diabetic foot are least prevalent (0.96% and 2.84% on average, respectively). In a study by Rodriguez-Poncelas et al, the estimated prevalence of ESRD for patients with type 2 DM in Spain was 1.2%, including patients with stage 4 and 5 chronic kidney disease.[20] A study by Zhang et al estimated the global prevalence of diabetic foot to be 6.3%, and 5.1% in Europe.[21]

In this study, the highest average prevalence rates were observed for stable angina (13.7%), painful neuropathy (11.68%), and HF (10.26%). In a study by Deedwania, it was estimated that approximately 25–45% of patients with type 2 DM and coronary artery disease have stable angina.[22] According to the IDF Diabetes Atlas 2017, the worldwide prevalence of neuropathy among patients with DM varied from 16% to 66% between countries.[1] In a study by Boonman-de Winter et al, the prevalence of HF was 30.6% among patients with type 2 DM.[23] The prevalence values for MMVDs used in this study were in most cases lower than the values presented in the literature, which may indicate that the estimates of the total treatment costs of MMVDs could potentially be underestimated.

The treatment costs of MI, stroke, TIA, and UA at the time of the event were mostly related to hospitalisation (Tab. 3 and Supplementary File); only a small portion of the total cost at the event was associated with other procedures (5%), and no drug costs were reported (possibly due to the drug cost being included in the hospitalisation fee). For all events, the share of costs attributed to other procedures and drugs tended to increase over time: for drugs to 48% in the first year and to 57% in the second year; for procedures to 19% in the first year and to 24% in the second year. The share of hospitalisation costs concurrently decreased (to 33% in the first year and to 19% in the second year). A similar tendency was observed by Fattore et al; in the first six months after a stroke (including treatment during the event), the majority of the treatment costs were due to hospitalisations and inpatient rehabilitation, and over the following six months the main component of costs were drugs costs.[24] The same study also showed that the total cost of stroke tends to decrease after the event, as was observed in our study. For all events, most of the costs were incurred during the event and these tended to decrease with time (Tab. 3).

The complications diabetic foot, HF, neuropathy, and PVD see hospitalisation costs contributing the highest average share in the total treatment costs, while for retinopathy and ESRD the highest shares of average costs are due to procedures. For individual complications, the share of costs incurred by hospitalisations, other procedures, and drugs in total treatment costs varied between countries more than in the case of the events (Tab. 3 and Supplementary File). For example, costs of HF in Poland and in Republic of Srpska/Bosnia and Herzegovina were mostly incurred due to hospitalisations, whereas in Bulgaria and Slovenia these costs were mostly related to the use of drugs. These differences may result from different clinical practice and treatment methods in participating countries.

The total annual treatment costs of MMVDs vary between countries (Tab. 5) and were highest in Poland (due to the high number of patients with diabetes mellitus) and Romania (most probably due to the high incidence and prev-

alence of MMVDs) and lowest in Bulgaria and Republic of Srpska/Bosnia and Herzegovina. The cost of HF was significantly higher in Poland (EUR 550,533,281) compared with all other MMVDs. In Republic of Srpska/Bosnia and Herzegovina, the total annual cost of ESRD treatment was considerably lower (EUR 21,689) than in all other countries, likely due in part to the low prevalence of this complication (0.05%).

The percentage contribution of individual MMVDs in the total annual treatment cost of MMVDs differs largely between participating countries (Tab. 5). These differences are mainly due to differences in cost data available for individual MMVDs. However, the largest expenses on average are incurred due to HF (21%), followed by UA, stroke, and MI (in the range of 13%). In a study by Leśniowska et al, the largest share of costs of DM complications treatment in Poland was for heart disease.[25] This was also confirmed in the current study; the percentage share of total costs for HF, MI, stable angina, UA and PVD amounted to 70% of the total cost of treatment of all MMVDs in Poland.

The average annual cost of MMVD per adult patient with DM varies between EUR 218.5 in Bulgaria and EUR 758.9 in Republic of Srpska/Bosnia and Herzegovina. For the majority of participating countries, it is in the range of EUR 586–620. The consistency of the results is reassuring and suggests that any biases related to individual MMVDs may average out in the study overall.

Degli Esposti et al estimated the total annual hospitalisation cost of CVDs (ischemic heart disease, HF, cerebrovascular disease, arterial disease) in Italy to be EUR 347.07 per patient with DM.[26] The hospitalisation cost per patient with DM estimated in this study was higher than reported by Degli Esposti et al in Poland (EUR 521, 84% of the total costs per patient with DM), similar in Republic of Srpska/Bosnia and Herzegovina (EUR 405, 53% of the total cost per patient with DM), and lower in Romania (EUR 249, 43% of the total cost per patient with DM), Slovenia[3] (EUR 180, 30% of the total cost per patient with DM) and Bulgaria (EUR 81, 37% of the total cost per patient with DM). The data reported in this study should not be directly compared with the results reported by Degli Esposti et al, as the current study included more DM-related complications. However, a broad conclusion can be drawn that hospitalisation costs are lower in CEE countries compared with Western Europe (e.g. Italy).

The total annual cost of MMVDs varied between countries, ranging from EUR 47m in Republic of Srpska/Bosnia and Herzegovina to EUR 1,165m in Poland. These values depend on the estimated number of patients in a given country and should be interpreted with caution, due to difficulties in assessing the DM prevalence.

A study by Nerat et al[27] estimated the annual costs of DM-related complications in Slovenia for patients with type 2 DM (118,750 patients). The total cost of nephropathy equalled EUR 13,032,321,[27] which is comparable to the value reported in the current study for ESRD (EUR 12,345,697). The reported cost of retinopathy treatment was also similar to that calculated in this study (EUR 670,694[27] vs EUR 1,083,119, respectively), as was the cost of stroke treatment in the first year after the event, including costs incurred during the event (EUR 4,951,306[27] vs EUR 4,151,426, respectively). However, in the current study, costs in the following years decreased significantly to EUR 317,427.66, whereas in the study by Nerat et al they are substantially more (EUR 1,885,681.00)[27]. The lower costs calculated for the following years in this study may have resulted from accounting for mortality rate in cost estimations for this event. The cost of foot ulcers was reported as EUR 5,108,738, of which EUR 4,249,724 were due to amputations.[27] In the current study, the cost of diabetic foot treatment was estimated as EUR 2,462,856; however, the cost of amputations was not included. Neuropathy costs were reported as EUR 1,054,500[27], whereas in the current study these costs were substantially higher (EUR 16,779,293). The main component of these costs in the current study was drugs, with 100% of patients with neuropathy assumed to be treated with drugs, whereas in the study by Nerat et al only some patients were treated with drugs — 1 in 6 patients with sensory neuropathy.[27] The largest cost difference between the two studies was for HF; Nerat et al[27] reported these costs as EUR 4,879,533 in the first year and EUR 3,273,440 in subsequent years, whereas the current study estimated the annual average costs of HF in Slovenia as EUR 18,689,708. However, in the Nerat et al study, the cost of HF was calculated for patients who were hospitalised according to the DRG codes F62A and F62B.[27] In the current study, the cost of HF was estimated using a higher number of DRG codes, and also included the costs of other procedures and drug costs (which accounted for the main part of these costs, approximately 70%). In conclusion, the results for Slovenia estimated in this study seem credible, which is further supported by the fact that the per patient MMVD cost in Slovenia resembles the costs estimated for the other participating countries.

Dimitrova et al estimated the cost of microvascular (neuropathy, nephropathy, retinopathy and diabetic angiopathy) and macrovascular (hypertension, stroke, myocardial infarction, heart failure, and coronary artery disease) complications leading to hospitalisation in Bulgaria for patients with type 1 and type 2 DM. For patients with type 2 DM, the hospitalisation costs relating to microvascular and macrovascular complications accounted for 16% and 41% of the total hospitalisation cost, respectively (the remaining 43% of the total hospitalisation costs was associ-

ated with diabetes costs in general). For patients with type 1 DM, 19% of the total hospitalisation costs was related to microvascular complications and 18% to macrovascular complications (the remaining 63% was associated with diabetes costs in general). The cost per patient with type 2 DM and type 1 DM for complications (micro– and macrovascular) was reported as EUR 157.53 and EUR 81.21, respectively.[28] In the current study, the cost estimated for DM complications per patient in Bulgaria was EUR 218.5 (for both DM types). The slight differences between the per patient costs reported by Dimitrova et al and those calculated in this study may result from including different complications; for example, in the study by Dimitrova et al[28], hypertension and diabetic angiopathy costs were included and this was not the case in the current study, but diabetic foot, PVD and TIA are included in the current study but not included in the Dimitrova et al study.[28]

A study by Domeikienė et al estimated the direct cost of type 2 DM and related complications in Lithuania using the prevalence-based, top-down approach.[4] The following prevalence rates of MMVDs in the study group were reported: 65.1% of patients had one or more DM-related chronic complications; 31.5% of patients with DM had neuropathy; 26.9% had angina pectoris; 26.2% had HF; 18% had stroke; 4.6% had retinopathy (including proliferative retinopathy, macular oedema, and blindness); 4.2% had PVD; 3.0% had nephropathy; 1.7% had renal failure; 1.0% had diabetic foot; and 0.9% had MI. The direct annual costs of ambulatory care per patient were: EUR 32.93 for nephrologist consultations; EUR 26.39 for cardiologist consultations; EUR 19.49 for ophthalmologist consultations; EUR 15.65 for neurologist consultations; and EUR 8.03 for foot care consultations. The direct annual costs of hospital inpatient care per patient were: EUR 1,632.31 for haemodialysis; EUR 788.19 for cardiology; EUR 503.40 for nephrology; EUR 434.74 for neurology; and EUR 331.4 for ophthalmology.[13]

Conclusions

To the best of our knowledge, the current study is the first attempt to assess the cost of DM-related MMVDs in several CEE countries. MMVDs generate a cost of ca. EUR 600 annually per adult patient with DM. Even though multi-country studies are difficult to conduct due to the heterogeneity of the data sources, the consistency of the results is reassuring. In absolute terms, the DM-related MMVD cost ranges between EUR 47 million in Republic of Srpska/Bosnia and Herzegovina and EUR 1,164 million in Poland (as much as 6% of annual public healthcare expenditure in Poland[29]). Of all the MMVDs analysed in this study, those consuming the most resources are HF (21% average share of the total treatment cost of MMVDs in all countries), UA (14%), and MI (12%). The presented estimates show the overall economic burden of DM-related MMVDs for public payers in CEE countries, and can be used in cost-effectiveness modelling in DM by providing cost estimates for individual MMVDs.

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This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors. Hence, no ethical approval was needed.

Additional data on which the results are based can be found in the Supplementary File. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Abbreviations

CEE Central and Eastern Europe
CVDs Cardiovascular diseases
DM Diabetes mellitus
DRG Diagnosis-related group
ESRD End-stage renal disease
EUR Euro
HF Heart failure
HTA Health technology assessment
IDF International Diabetes Federation
LADA Latent autoimmune diabetes of adults
LHSU Kaunas Clinics
Lithuanian University of Health Sciences Kaunas Clinics
MI Myocardial infarction
MMVDs Macro- and microvascular diseases
MODY Maturity onset diabetes of the young
NHIF National Hospital Insurance Fund
PVD Peripheral vascular disease
TIA Transient ischemic attack
UA Unstable angina
USD United States dollar

Supplementary material

"Supplementary Information File.docx", containing the following elements:

- Risk of death related to the events
- Annual cost of MI treatment
- Annual cost of stroke treatment
- Annual cost of TIA treatment
- Annual cost of UA treatment
- Annual costs of treatment of complications

Risk of death related to the events

Tab. 1 Risks of death related to the events.					
Risk of death[1] — at the event (%)					
	Bulgaria	Poland	Romania	RS/BiH	Slovenia
MI	16.00	8.44	10.95	11.80	11.80
Stroke	13.35	18.00	9.62	13.66	13.66
UA	1.82	1.26	2.37	1.82	1.82
Risk of death — within a year (%)					
	Bulgaria	Poland	Romania	RS/BiH	Slovenia
MI	10.01	12.68	10.01	7.33	10.01
Stroke	27.53	33.00	27.53	22.05	27.53
TIA	3.78	3.00	3.78	4.56	3.78
UA	7.90	9.73	7.90	6.07	7.90

[1] - *The risk of death at the event related to TIA was not considered, due to the definition of this event (non-fatal)*

Annual cost of MI treatment

Tab. 2 Annual costs of MI treatment split into hospitalizations, procedures and drugs.				
Country	Costs during the event (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	3 016.47	—	—	3 016.47
Poland	2 267.63	—	—	2 267.63
Romania	570.88	203.54	—	774.42
RS/BiH	3 613.52	—	—	3 613.52
Slovenia	4 135.91	1 225.56	—	5 361.47
Country	After the event (after the hospitalization), the 1st year (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	4.93	140.52	669.93	815.38
Poland	1 470.49	—	117.94	1 588.43
Romania	53.32	21.69	72.38	147.39
RS/BiH	85.71	—	1 258.56	1 344.27
Slovenia	1 161.23	998.63	228.64	2 388.50
Country	The 2nd year (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	—	50.59	162.48	213.07
Poland	385.89	—	52.06	437.95
Romania	13.08	21.57	72.38	107.03
RS/BiH	66.12	—	1 105.28	1 171.40
Slovenia	66.21	109.38	228.64	404.23

Annual cost of stroke treatment

Tab. 3 Annual costs of stroke treatment split into hospitalizations, procedures and drugs.

Country	Costs during the event (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	874.21	—	—	874.21
Poland	1 791.53	—	—	1 791.53
Romania	582.19	—	—	582.19
RS/BiH	1 929.92	—	—	1 929.92
Slovenia	3 594.52	1 225.56	—	4 820.08
Country	After the event (after the hospitalization), the 1st year (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	—	91.48	588.70	680.18
Poland	994.59	80.71	0.78	1 076.08
Romania	44.26	27.99	95.86	168.11
RS/BiH	96.98	—	1 101.72	1 198.70
Slovenia	428.65	939.14	354.96	1 722.75
Country	The 2nd year (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	—	81.49	81.49	162.98
Poland	—	77.61	0.78	78.38
Romania	36.80	25.14	95.86	157.80
RS/BiH	172.71	—	1 082.00	1 254.71
Slovenia	145.32	—	354.96	500.28

Annual cost of TIA treatment

Tab. 4 Annual costs of TIA treatment split into hospitalizations, procedures and drugs.

Country	Costs during the event (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	210.24	—	—	210.24
Poland	774.62	—	—	774.62
Romania	232.71	—	—	232.71
RS/BiH	342.86	—	—	342.86
Slovenia	1 416.99	—	—	1 416.99
Country	After the event (after the hospitalization), the 1st year (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	—	86.48	588.70	675.18
Poland	120.04	27.94	0.78	148.76
Romania	6.85	1 648.78	57.56	1 713.19
RS/BiH	89.27	—	953.93	1 043.20
Slovenia	138.52	184.08	131.02	453.62
	The 2nd year (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	—	42.69	81.49	124.18
Poland	—	21.73	0.78	22.51
Romania	16.40	19.14	57.56	93.10
RS/BiH	17.14	—	899.09	916.23
Slovenia	13.57	49.90	131.02	194.49

Annual cost of UA treatment

Tab. 5 Annual costs of UA treatment split into hospitalizations, procedures and drugs.

Country	Costs during the event (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	1 261.75	—	—	1 261.75
Poland	2 085.51	—	—	2 085.51
Romania	405.84	95.99	—	501.83
RS/BiH	1 806.53	—	—	1 806.53
Slovenia	2 430.36	—	—	2 430.36
Country	After the event (after the hospitalization), the 1st year (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	16.19	137.94	669.90	824.03
Poland	1 079.88	—	—	1 079.88
Romania	54.23	17.22	74.62	146.07
RS/BiH	267.14	—	1 271.71	1 538.85
Slovenia	423.91	109.38	228.64	761.93
Country	The 2nd year (EUR)			
	Hospitalization	Any other procedure	Drugs	Cost total
Bulgaria	16.19	82.85	162.69	261.73
Poland	297.73	—	—	297.73
Romania	48.13	17.22	74.62	139.97
RS/BiH	88.16	—	1 136.01	1 224.17
Slovenia	48.29	109.38	228.64	386.31

Annual costs of treatment of complications

Tab. 6 Annual costs of treatment of diabetic foot, ESRD, HF, painful neuropathy, PVD, retinopathy, and stable angina.

Country	Cost of diabetic foot (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	335.72	40.90	4.95	381.57
Poland	259.94	—	—	259.94
Romania	707.29	—	—	707.29
RS/BiH	1 328.57	3 399.16	—	4 727.73
Slovenia	181.33	438.60	73.28	693.21
Country	Cost of ESRD (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	—	11 830.77	—	11 830.77
Poland	69.07	12 735.20	—	12 804.27
Romania	79.82	5 219.26	74.79	5 373.87
RS/BiH	597.55	—	99.01	696.56
Slovenia	330.45	6 052.99	2 588.07	8 971.51
Country	Costs of HF (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	47.38	134.14	136.68	318.20
Poland	1 830.53	—	—	1 830.53
Romania	109.79	25.18	38.54	173.51
RS/BiH	1 206.73	—	62.07	1 268.80
Slovenia	632.55	260.02	998.54	1 891.11
Country	Cost of painful neuropathy (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	—	26.33	7.45	33.78
Poland	338.22	14.90	48.43	401.55
Romania	218.67	21.23	41.28	281.18
RS/BiH	342.86	—	23.88	366.74
Slovenia	4.19	266.85	1 964.41	2 235.45
Country	Cost of PVD (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	612.03	86.75	78.34	777.12
Poland	135.91	—	—	135.91
Romania	9.50	16.75	69.99	96.24
RS/BiH	2 081.63	152.11	301.44	2 535.18
Slovenia	310.36	49.90	73.28	433.54
Country	Cost of retinopathy (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	—	47.43	20.17	67.60
Poland	6.20	471.29	—	477.49
Romania	58.49	15.21	56.64	130.34
RS/BiH	287.76	—	—	287.76
Slovenia	47.46	133.29	—	180.75
Country	Costs of stable angina (EUR)			
	Hospitalization	Any other procedure	Drugs	Costs total
Bulgaria	—	70.21	45.84	116.05
Poland	199.76	—	—	199.76
Romania	4.65	18.92	38.54	62.11
RS/BiH	446.02	—	1 182.99	1 629.01
Slovenia	234.79	109.38	208.48	552.66

[1]Definition of CVDs different than assumed in the current study.
[2]The main difference between the number of patients with DM in our study (Tab. 6) compared with the IDF data is due to the fact that data in Tab. 6 represent number of patients in the Republic of Srpska only.
[3]In this case, the costs of procedures for complications often exceeded the hospitalisation cost itself
[4]In the top-down approach, the costs are calculated by multiplying the total healthcare expenditure by the percentage of health resources used for the treatment of a specific condition.

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