



## Economic burden of cardiovascular diseases in Serbia

### Kardiovaskularne bolesti u Srbiji – ekonomski teret

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#### Abstract

**Background/Aim.** Cardiovascular disease imposes a burden to society in terms of mortality, morbidity and economic losses. The aim of this study was to estimate the economic burden of cardiovascular disease in Serbia in 2009 from the perspective of the society. **Methods.** For the purpose of the study cardiovascular disease was defined by the International Classification of Diseases, 10th revision, as the following diagnosis: hypertension, coronary heart disease, cardiomyopathy, heart failure and cerebrovascular disease. The prevalence, top-down method was used to quantify the annual cardiovascular costs. Productivity losses were estimated using the human capital approach and the friction cost method. A discount rate of 5% was used to convert all future lifetime earnings into the present value. **Results.** The total direct costs of cardiovascular disease in 2009 were € 400 million. The results showed that more than half a million working days were lost due to incapacity resulting from cardiovascular diseases, yielding the € 113.9 million. The majority of total costs (€ 514.3 million) were for: medication (29.94%), hospital days (28.97%) and hospital inpatient care – surgical and diagnostic interventions (17.84%). The results were robust to a change in 20% of volume or the unit price of all direct and indirect cost and to discount rate 2% and 10%. **Conclusions.** The total cardiovascular disease costs in 2009 represented approximately 1.8% of the Serbian gross domestic product. The results of the study would be valuable to health policy makers to bridge the gap between invested resources and needs, in order to improve cardiovascular disease outcomes.

#### Key words:

cardiovascular diseases; health care costs; serbia.

#### Apstrakt

**Uvod/Cilj.** Kardiovaskularne bolesti predstavljaju teret za društvo u smislu mortaliteta, morbiditeta i ekonomskih gubitaka. Cilj ove studije bio je procena ekonomskog značaja kardiovaskularnih bolesti u Srbiji u 2009. godini iz perspektive društva. **Metode.** Za potrebe istraživanja, kardiovaskularne bolesti su definisane pomoću Međunarodne klasifikacije bolesti, 10. revizija, kao sledeće dijagnoze: hipertenzija, koronarne bolesti, kardiomiopatija, srčana insuficijencija i cerebrovaskularne bolesti. Korišćen je *top-down* metod, baziran na prevalenciji, kako bi se kvantifikovali godišnji kardiovaskularni troškovi. Troškovi smanjene produktivnosti su procenjeni korišćenjem dva pristupa: pristup ljudskom kapitalu (*human capital approach*) i metod frikcionih troškova (*friction cost method*). Za obračunavanje troškova u sadašnju vrednost korišćena je diskontna stopa od 5%. **Rezultati.** Ukupni direktni troškovi kardiovaskularnih bolesti u 2009. godini iznosili su 400 miliona evra. Rezultati pokazuju da je više od pola miliona radnih dana izgubljeno zbog nesposobnosti usled kardiovaskularnih bolesti, dajući ukupno 113,9 miliona evra indirektno troškove. Većina ukupnih troškova (514,3 miliona evra) bili su za: lekove (29,94%), hospitalizaciju (28,97%) i bolničko lečenje – hirurške intervencije i dijagnostiku (17,84%). Rezultati su bili robusni na promene od 20% u volumenu ili ceni pojedinih kategorija troškova, kao i na primenjenu diskontnu stopu od 2% i od 10%. **Zaključak.** Ukupni troškovi kardiovaskularnih bolesti u 2009. godini su predstavljali oko 1,8% bruto domaćeg proizvoda. Rezultati studije su značajni za kreiranje zdravstvene politike i premošćavanja jaza između uloženi sredstava i potreba, a u cilju poboljšanja ishoda kardiovaskularnih bolesti.

#### Ključne reči:

kardiovaskularne bolesti; zdravstvena zaštita, troškovi; srbija.

## Introduction

Cardiovascular disease (CVD) imposes a burden to society in terms of mortality and morbidity, as well as an economic impact. Management of CVD consumes a large amount of healthcare resources. In America nearly 2,400 Americans die of CVD each day, an average of one death every 37 seconds<sup>1</sup>. CVD mortality in Eastern European countries is much higher than the European average as it reaches a value of 650 deaths per 100,000 in some countries<sup>2</sup> CVD dominated the burden of premature mortality in Serbia (48%) with almost 400,000 years of life lost<sup>3</sup>.

Cost of illness (or burden of disease) analysis involves identification, measurement and valuation of resources related to the illness, in this case CVD. The economic burden of CVD consists of direct and indirect costs. Direct costs are associated with hospitalisations, physician visits, rehabilitation services and medications. Indirect costs represent losses to the economy due to premature mortality and morbidity, resulting in lost economic production and consumption and the associated effect on the functioning of the economy. The total costs of CVD in the European Union were over 168 billion Euros in 2003, of which direct healthcare costs represented 62%<sup>4</sup>.

National health authorities have postulated in their report<sup>5</sup> that intensive research work is needed in the field of CVD, particularly the impact of hypertension and its major complications. Therefore, the purpose of this study was to estimate the economic burden of cardiovascular disease in Serbia in 2009 from the perspective of the society.

## Methods

For the purpose of the study CVD was defined by the International Classification of Diseases, 10th revision as the following diagnosis: hypertension (I10–I15), coronary heart disease (I20–I25), cardiomyopathy (I42), heart failure (I50) and cerebrovascular disease (I60–I69). The method of prevalence was used to quantify the annual CVD costs for the total Serbian population in 2009<sup>6</sup>. The analysis was performed from the societal perspective including direct healthcare costs, as well as indirect costs associated with productivity loss due to morbidity or premature death which were estimated.

We employed a top-down approach, using aggregate data on morbidity, doctor visits at primary care, hospitalisations, medications utilisation, rehabilitations and mortality. This approach was previously developed by Liu et al.<sup>7</sup> to estimate economic burden of coronary heart disease. Productivity losses were estimated using the human capital approach and the friction cost method<sup>8</sup>. All costs were expressed in Euros (€), using the 2009 average exchange rate to convert Serbian dinar (RSD) to the € (€1 = 94.12 RSD)<sup>9</sup>.

### *Healthcare direct costs*

Direct costs include the value of medical care resources used to treat a disease. Healthcare costs were calculated by assessing the value of resources used by patients for detection, treatment and rehabilitation of CVD.

The following items of healthcare service were included: primary care provided by general practice; emergency care; hospital care; diagnostic and surgical procedures; rehabilitation services and medication treatment.

The number of patients visits to general practice regarding CVD was obtained from the Republic Institute for Health Insurance (RIHI). The total number of hospital emergency visits and hospitalisations were provided by the RIHI; the average length of stay in hospital due to CVD was eight days. The number of surgical interventions: percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG) and coronography was also obtained from RIHI, due to their complete coverage by the RIHI. The number of diagnostic procedures was estimated based on the prevalence of the given CVD and the current clinical practice and guidelines in Serbia<sup>10–13</sup>. The number of rehabilitations was obtained from the Republic Institute for Public Health; the average length of stay at the rehabilitation unit was 20.5 days. Utilisation of the medications in hospital and ambulatory settings aimed at prevention and treatment of CVD was provided from the RIHI. Data regarding the utilisation were considered for the following Anatomical Therapeutic Chemical (ATC) classification system medicines groups: B01 (antithrombotic agents), C01 (cardiac therapy), C02 (antihypertensives), C03 (diuretics), C07 (beta blocking agents), C08 (calcium channel blockers), C09 (agents acting on renin-angiotensin system) and C10 (serum lipid reducing agents).

The values of resources used were calculated by multiplying the resource quantities used in healthcare services for management of CVD with their unit costs. All costs are derived from the RIHI price list. The RIHI is a leading health care payer, responsible for the health care of almost the entire Serbian population (7.3 million). Hospitalisation daily costs are calculated as the average value of days spent in cardiovascular, neurological and neurosurgical unit, due to the fact that the RIHI charges hospitalisation cost *per diem*. Costs for a diagnostic procedures, both cerebrovascular disease and coronary heart disease, were calculated as the number of units consumed multiplied by the sum of different diagnostic procedures applied for given disease (e.g. neurological exam, computed tomography scan, magnetic resonance imaging of the head, basic analysis of blood, biochemical analysis of C-reactive protein, creatine kinase, electrocardiogram, etc.). The costs of rehabilitation were calculated as the average cost per day spent in rehabilitation centres, multiplied with the average length of stay (20.5) and the number of rehabilitation procedures. For ambulatory prescribed medicines we included the pharmacy mark-up and value added tax.

### *Healthcare indirect costs*

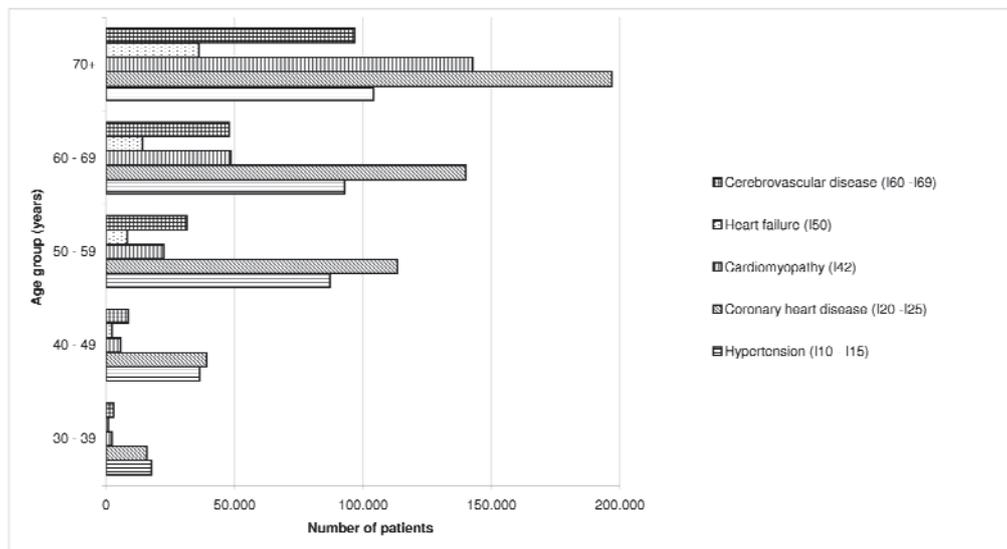
Indirect costs included forgone earning related to mortality and morbidity due to CVD which were estimated using the human capital approach. The indirect cost from mortality was estimated considering the following: the number of premature deaths due to CVD<sup>14</sup>, the number of working years left till retirement (65 years of age for men, 60 for women)<sup>15</sup>, unem-

ployment rate and the 2009 average earnings<sup>16</sup>. We also calculated the productivity loss in retirement based on predicted years spent in retirement, life expectancy, and 2009 average pension earnings.

The value of indirect cost from morbidity was estimated as total number of days lost from work obtained from the RIHI multiplied by the average daily earnings<sup>16</sup>. According to the current legislation<sup>17</sup>, the first 30 sick days are paid by the employer, additional sick days are charged to RIHI. Thus

## Results

In 2009 women were diagnosed more often with CVD than men (54% vs 46%). There were 338,279 patients diagnosed with hypertension; 505,358 patients with coronary heart diseases; 221,663 patients with cardiomyopathy; 61,713 patient diagnosed with heart failure and 187,564 patient with cerebrovascular disease. Most of the diagnosed diseases occurred in patients aged over 70 (Figure 1).



**Fig. 1 – Number of patients diagnosed with cardiovascular diseases according to age. In brackets are the diagnoses defined by the International Classification of Disease, 10th revision.**

we estimated the number of employers' paid sick days as the total number of persons for which the RIHI paid sick allowances multiplied by 30 days. The authors did not find any way of estimate the number of days lost due to morbidity paid by employers not followed by the RIHI coverage.

Due to the fact that an estimate of lost production using the human capital approach tends to be overestimated, we also apply the friction cost method. In this case, production losses are calculated during "the friction period" (time between the start of absence from work and replacement). This is estimated to be about 90 days<sup>18, 19</sup>. The friction period adjusted productivity loss was calculated by multiplying the unadjusted productivity loss, obtained as described above, by the friction period (90 days) and then dividing this product by the average duration of work incapacity (calculated in this study, for CVD patient). A discount rate of 5% was used to convert all future lifetime earnings into the present value<sup>20</sup>.

### Sensitivity analysis

To examine the robustness of the results we performed one-way sensitivity analyses. We assessed the change in the estimated total cost of CVD resulting from a 20% change in the volume or the unit price of all direct and indirect costs; the 20% change was based on the cost of illness study conducted in EU<sup>4</sup>. The effect of discounting on indirect costs was assessed using the rates of 2% and 10%. All analyses were performed using the Microsoft Excel.

### Direct costs

The total direct costs of CVD in 2009 were €400 million (Table 1). Hospitalisation and surgical and diagnostic procedures applied to hospitalised patients accounted for €240.7 million, or 60.13% of the direct costs. The majority of costs attributable to surgical and diagnostic procedures were allocated on diagnostic of cerebrovascular sequel (25.48% of costs allocated on surgical and diagnostic procedures) and PTCA (30.77% of costs allocated on surgical and diagnostic procedures). Medication treatment accounted for 38.46% of total direct costs (€154 million). Of these costs, 87.2% was for prescription medicine covered by the RIHI used by outpatients. Physician visits at primary care and rehabilitation accounted just for 0.83% and 0.58%, respectively, of total direct costs.

### Indirect costs

The results showed that more than a half million working days were lost due to incapacity resulting from CVD (Table 2). Cerebrovascular and coronary heart diseases caused the longest absence from work, on average, 112.8 days and 100.7 days, respectively. The average length of incapacity for all CVD patients was 95 days. The production losses due to CVD morbidity estimated using the human capital approach were €11.6 million; with the friction cost method the estimate was lower at €11 million. According to

Table 1

The direct costs of cardiovascular disease (CVD)				
Direct costs	Number of units	Average cost per unit (€)	Average stay (days)	Total cost (€)
Doctor (GP) visit at clinic	1 596 638	2.07		3 312 193
Hospitalisations due to CV complications	521 514	35.71	8	149 000 960
Interventions due to CV complications				
PTCA (without stent)	13 500	1 455.79		19 653 171
drug eluting stent (DES)	6 750	1 058.23		7 143 042
bare metal stent (BMS)	6 750	211.65		1 428 638
Coronography	18 300	494.96		9 057 839
By-pass revascularisation; graft (CABG)	4 800	3 083.54		14 801 003
Diagnostic procedures for cerebrovascular disease*	146 024	160.04		23 369 984
Diagnostic procedures for coronary heart disease†	521 514	31.22		16 280 080
Rehabilitation due to CV complications	9 695	11.69	20.5	2 322 803
Medication treatment				
antitrombolytic medicine (utilised in hospital)	1 821 787.45			4 330 162
outpatient reimbursed medicine (covered by RIHI)	36 630 948.55			130 490 385
outpatient medicine (patient participation)	36 630 948.55			19 160 657
Total direct cost (€)				400 350 917

\*Diagnostic procedures for cerebrovascular disease include: neurological exam, computed tomography (CT) scan, and magnetic resonance imaging (MRI) of the head; †diagnostic procedures for coronary heart disease include: basic analysis of blood, additional analysis of C-reactive protein (CRP), creatine kinase (CK), myoglobin, and troponin-I, echocardiogram, electrocardiogram, and ergometry; GP – general practitioner; CV – cardiovascular; PTCA – percutaneous transluminal coronary angioplasty; CABG – coronary artery bypass grafting; RIHI – Republic Institute for Health Insurance.

Table 2

The indirect costs of cardiovascular disease			
Indirect costs	Number of units	Average cost per unit (€)	Total cost (€)
Mortality			
working years lost (men)	5 270.3	5 628.6*	19 738 507
working years lost (women)	1 857.7	5 628.6*	7 279 430
years lost in retirement (men)	8 693	2 523.6†	20 246 645
years lost in retirement (women)	26 080	2 523.6†	55 617 209
Morbidity (number of days lost from work)			
RIHI paid	353 130	22.3	7 472 293
employer paid	168 720	22.3	3 570 145
Total indirect cost (€)			113 924 229

\*Average annual earnings in 2009. For all future years the values of annual earning were discounted at 5% depending on the age of death; †Average annual pension in 2009. For all future years the values of annual pension were discounted at 5% depending on the age at which death occurred.

the results, more than 7100 working years were lost from CVD; 74% of these years lost were from deaths in men. Of all working years lost in men 83.05% were in the 40–59 year age range; in women 74.92% of the working years lost were from deaths in the 40–59 year age range. The mortality costs due to CVD were estimated to be €104.4 million. However, after adjustment for friction period estimate fell to €102.9 million.

#### Total costs

Table 3 shows the total costs of CVD for Serbia in 2009. The total costs resulted in €514.3 million; most of these costs were used for medication (29.94%), hospital days (28.97%) and hospital inpatient care – surgical and diagnostic interventions (17.84%). Indirect costs (mortality and morbidity) accounted for 22.15% of total costs.

Table 3

The total costs of cardiovascular disease		
Type of costs	Value (€)	Percentage of total cost (%)
Direct costs		
doctor (GP) visit at clinic	3 312 193	0.64
hospitalisation	149 000 960	28.97
surgical and diagnostic procedures	91 733 757	17.84
rehabilitation	2 322 803	0.45
medication treatment	153 981 203	29.94
Total direct cost	400 350 917	77.85
Indirect costs		
mortality	102 881 791	20.00
morbidity	11 042 438	2.15
Total indirect cost	113 924 229	22.15
Total costs (€)	514 275 146	100

### Sensitivity analysis

The baseline estimate of total cost related to CVD was not sensitive to changes in the input variables (Figure 2).

A change of 20% in volume or cost of hospitalisation and prescription medicine produced the largest variation in the baseline estimate of total cost of  $\pm 5.79\%$  and  $\pm 5.07\%$ , respectively. Regarding the variables included in indirect costs, the largest impact on total cost had 20% change in the number of years lost in retirement for women ( $\pm 2.16\%$ ) and change in discount rate. When a discount rate of 2% was applied, the baseline estimate changed for 2.31%; with the rate 10%, the total cost decline for -2.80%. Changes in all other variables produced very small effects on the total cost estimate (between 0.06% and 1.03%).

to mortality. The cost of CVD in EU revealed that almost 70% of indirect costs are attributable to mortality; in some EU countries, like Latvia, mortality represented 90.63%<sup>4</sup>.

The total cost of CVD in Serbia was estimated to be over €514 million. Only a quarter (22.15%) of total cost was estimated to be indirect cost (Table 3). In contrast, studies conducted in UK, Canada, Finland and Mexico<sup>7, 21, 22, 24</sup> noted that much higher percent (in some cases over 50%) of total cost is attributable to indirect costs. Such difference could be explained by much lower average earning than in the above mentioned, Western market economics. Bloom et al.<sup>25</sup>, in the review article of published cost-of-illness studies on US populations, estimated that more than 48% of total cost was attributable to indirect costs. A study by Leal et al.<sup>4</sup>, showed that daily and annual earnings in newer EU

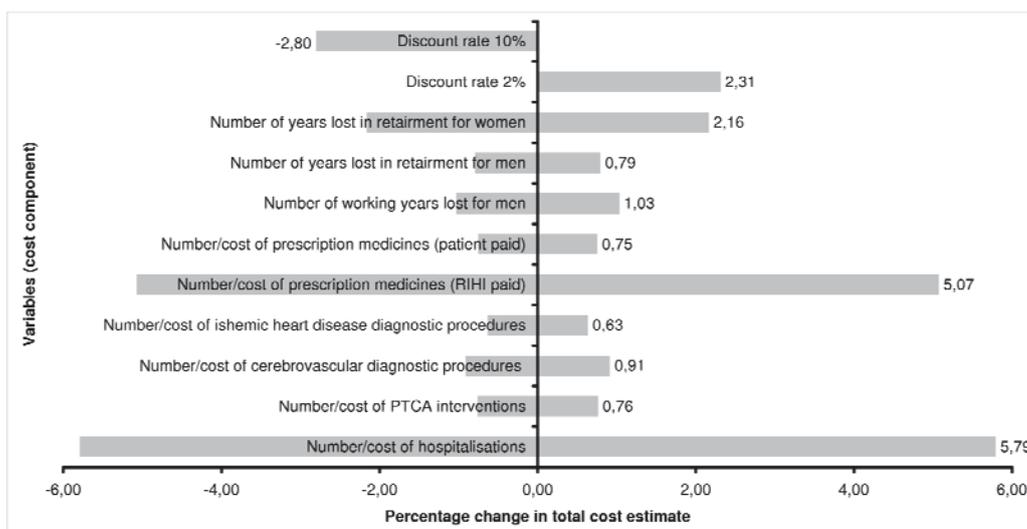


Fig. 2 – One-way sensitivity analyses of direct and indirect costs resulting from a  $\pm 20\%$  change in the volume or the unit price of all factors, and discount rates of 2% and 10%. The sensitivity analyses of the factors that resulted with an change in total cost estimate below  $\pm 0.5\%$  are not shown.

### Discussion

CVDs are a costly group of diseases to the health care system. In 2009, the average CVD direct costs per patient were over €300. The results of the direct costs of CVD show that more than 60% of the costs are attributable to hospitalisation and surgical/diagnostic procedures, while medication treatment represented over 38% of the direct costs. Primary care, which to some extent can be considered as preventive medicine, accounts only for 0.83% of direct costs. In the majority of studies on evaluation of economic burden of CVD, hospital costs were the most expensive direct category, with the values of 50–66% of total direct cost, followed by pharmaceutical expenditures<sup>4, 7, 21, 22</sup>. On the other hand, Maetzel et al.<sup>23</sup> showed that 51.2% of direct costs in hypertension were attributable to drugs, and only 20% to hospitalisation. Primary care accounted for only 8.8% in direct costs in EU, with significant variation between countries, from 0.7% in Greece to 15.9% in Germany<sup>4</sup>.

The estimated total indirect costs of CVD in Serbia were almost €114 million, with more than 90% attributable

countries (like Estonia, Latvia or Lithuania) in 2003, were more than eight times lower than in older EU countries. Similar results were observed in other transition countries, after conducting the different cost of illness studies<sup>26, 27</sup>. The magnitude of the total costs devoted to CVD prevention and treatment can be best represented as a % of gross domestic product (GDP). According to our results, total cost of CVD comprises approximately 1.78% of the total Serbian GDP<sup>15</sup>. In 2009 the total CVD cost was 3.37% of the total American GDP<sup>1</sup>. On the other hand, results of study conducted in China in 2003, showed that 0.62% of the China GDP was attributable to direct costs only<sup>28</sup>.

In Serbia, women were diagnosed more often with CVD, primarily coronary heart disease. Similar results were shown in other studies<sup>1, 23</sup> where the prevalence of CVD was higher in women. As it would be expected the majority of diagnosed patients were older than 70 years. The prevalence of CVD increases with age, from 38.2% in the age group 40–59 to 82.6% among those aged 80 years or older<sup>1</sup>.

A sensitivity analysis indicates that volume or cost of hospitalisations and medicines are components which are

most likely to affect estimated total cost but the overall impact is small, less than 6% on total cost estimate (Figure 2).

This study has limitations because estimates of costs are likely to be underestimated. The authors did not include preventive actions like anti-smoking campaigns in the analysis, because of unavailability of the quantity of promotion activities and the amount of money devoted to them in Serbia. A study on coronary heart disease costs in UK<sup>7</sup> estimated that less than 0.002% of total cost was attributable to prevention, so the authors believe that this omission would not affect our results substantially.

The authors analysis also did not consider the cost of patient travel expenses. However these costs make up only a small percentage of CVD costs<sup>29</sup>. The out-of-pocket expenditures for different Over the Counter (OTC) medicines or dietary supplements for CVD were not considered in the analysis due to no published data regarding the consumption. As the authors postulated in the Methods section the sick leave less than 30 days was not included in the study due to the absence of the data. Also, since we used the prevalence, top-down approach, productivity losses were estimated as average earning and pension. The cost estimate would probably be different if patient population was divided into subgroups according to the education level and socioeconomic status. However, due to the absence of these data, a more accurate estimate was impossible.

Authors did not focus on the clinical guidelines and protocols. It would be interesting for further research to evaluate compliance of the prescribers with the clinical guidelines, especially with the recommendations regarding antihypertensive medications, since our study showed that almost 30% of a total cost is attributable to medications cost.

In spite of its limitations, this is the first cost of illness study that estimated direct and indirect costs associated with CVD in Serbia. Cost of illness studies cannot determine whether healthcare system is spending too much in a particular area, in this case CVD, but it has the potential to identify main cost drivers of the disease. This helps in allocating scant health care resources efficiently, and consequently leads to improved clinical and economic outcomes, reducing the morbidity and mortality of CVD, resulting with the substantial financial savings. Also, the magnitude and pattern of expenditure can guide research priorities and decision makers in the development of better action plan in order to decrease the burden of CVD.

## Conclusion

CVD is a high costly group of diseases with the heavy burden to society. The total costs in 2009 represented approximately 1.8% of the Serbian GDP. The authors believe that the results of this study would be of special interest for national health policy makers to bridge the gap between invested resources and needs, in order to improve CVD outcomes. High efforts should be made and taken to prevent CVD in order to reduce medical costs and productivity losses to society.

## Acknowledgments

The work was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia (Project No. 175035). The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report.

## R E F E R E N C E S

1. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, Flegal K, et al. Heart disease and stroke statistics-2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2009; 119(3): e21–e181.
2. European health for all database. Available from: <http://data.euro.who.int/hfad/> [accessed 2011 May 26].
3. Vljajinac H, Marinkovic J, Kocov N, Sipetic S, Bjegovic V, Jankovic S. Years of life lost due to premature death in Serbia (excluding Kosovo and Metohia). *Public Health* 2008; 122(3): 277–84.
4. Leal J, Luengo-Fernandez R, Gray A, Petersen S, Rayner M. Economic burden of cardiovascular diseases in the enlarged European Union. *Eur Heart J* 2006; 27(3): 1610–9.
5. Ministry of Health. Final report of population health research in 2006. Available from: <http://www.zdravlje.gov.rs/showpage.php?id=142> [accessed 2011 May 26].
6. Rice D. Cost-of-illness studies: fact or fiction? *Lancet* 1994; 344(8936): 1519–20.
7. Liu JY, Manadakis N, Gray A, Rayner M. The economic burden of coronary heart disease in the UK. *Heart* 2002; 88(6): 597–603.
8. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the economic evaluation of health care programmes*. 3rd ed. New York: Oxford University Press; 2005.
9. National Bank of Serbia. Exchange rates. Available from: <http://www.nbs.rs/export/internet/english/80/index.html> [accessed 2011 May 26].
10. Ministry of Health. National Guideline of Clinical Practice: Prevention of ischemic heart disease Belgrade: Faculty of Medicine University of Belgrade; 2005. (Serbian)
11. Ministry of Health. National Guideline of Clinical Practice: Acute ischemic cerebral infraction. Belgrade: Faculty of Medicine University of Belgrade; 2004. (Serbian)
12. Ministry of Health. Guidelines for prevention, diagnosis and treatment of patients with chest pain. Belgrade: Faculty of Medicine University of Belgrade; 2002. (Serbian)
13. Ministry of Health. National Guideline of Clinical Practice: Arterial hypertension. Belgrade: Faculty of Medicine University of Belgrade; 2005. (Serbian)
14. Institute of Public Health of Serbia. Health Statistical Yearbook of Republic Serbia 2009. Available from: <http://www.batut.org.rs/download/publikacije/pub2009.pdf> [accessed 2011 February 06].
15. Law on Pension and Social Security. ("Official Gazette of the Republic of Serbia" 101/2010). (Serbian)
16. Statistical Office of the Republic of Serbia. Statistical Database. Available from: <http://webzrzs.stat.gov.rs/WebSite/public/ReportView.aspx> [accessed 2011 February 6].

17. Law on healthcare insurance. ("Official Gazette of the Republic of Serbia" 109/2010). (Serbian)
18. *Koopmanschap MA, Rutten FF, van Ineveld BM, van Roijen L*. The friction cost method for measuring indirect costs of disease. *J Health Econ* 1995; 14(2): 171–89.
19. *Koopmanschap MA, van Ineveld BM*. Towards a new approach for estimating indirect costs of disease. *Soc Sci Med* 1992; 34(9): 1005–10.
20. *Shaffer PA, Haddix AC*. Time Preference. In: *Haddix AC, Teutsch SM, Shaffer PA, Dunnet DO*, editors. *Prevention Effectiveness: A Guide to Decision Analysis and Economic Evaluation*. New York: Oxford University Press; 1996. p. 76–84.
21. *Chan B, Coyte P, Heick C*. Economic impact of cardiovascular disease in Canada. *Can J Cardiol* 1996; 12(10): 1000–6.
22. *Kiiskinen U, Vartiainen E, Pekurinen M, Puska P*. Does prevention of cardiovascular diseases lead to decreased cost of illness? Twenty years of experience from Finland. *Prev Med* 1997; 26(2): 220–6.
23. *Maetzel A, Li LC, Pencharz J, Tomlinson G, Bombardier C*. The economic burden associated with osteoarthritis, rheumatoid arthritis, and hypertension: a comparative study. *Ann Rheum Dis* 2004; 63(4): 395–401.
24. *Arredondo A, Zuniga A*. Epidemiological changes and economic burden of hypertension in Latin America. *Am J Hypertens* 2006; 19(6): 553–9.
25. *Bloom BS, Bruno DJ, Maman DY, Jayadevappa R*. Usefulness of US cost-of-illness studies in healthcare decision making. *Pharmacoeconomics* 2001; 19(2): 207–13.
26. *Grover S, Avasthi A, Bhansali S, Chokrabarti S, Kulhara P*. Cost of ambulatory care of diabetes mellitus: a study from north India. *Postgrad Med J* 2005; 81(956): 391–5.
27. *Poulos C, Rienpaiboon A, Stewart JF, Clemens J, Gub S, Agtini M*, et al. Cost of illness due to typhoid fever in five Asian countries. *Trop Med Int Health* 2011; 16(3): 314–23.
28. *Yang L, Wu M, Cui B, Xu J*. Economic burden of cardiovascular diseases in China. *Expert Rev Pharmacoecon Outcomes Res* 2008; 8(4): 349–56.
29. *Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ*, et al. Cost of stroke in Australia from a societal perspective: results from the North East Melbourne Stroke Incidence study (NEMESIS). *Stroke* 2001; 32(10): 2409–16.

Received on October 4, 2011.

Revised on January 15, 2013.

Accepted on June 6, 2013.