Simulation analysis of economic burden in hypertension and myocardial infarction treatment with beta blockers

Simulacijsko vrednotenje ekonomskega bremena zdravljenja hipertenzije in miokardnega infarkta z uporabo beta blokatorjev

Maja Atanasijević-Kunc,[1] Jože Drinovec,[2] Barbara Guštin,[3] Aleš Mrhar[3]

[1] *University of Ljubljana, Faculty of Electrical Engineering, Tržaška 25, 1000 Ljubljana*

[2] *University of Maribor, Faculty of Medicine, Slomškov trg 15, 2000 Maribor*

[3] *University of Ljubljana, Faculty of Pharmacy, Aškerčeva 7, 1000 Ljubljana*

Korespondenca/ Correspondence:
Maja Atanasijević-Kunc, Fakulteta za elektrotehniko, UL, Tržaška 25, 1000 Ljubljana; maja.atanasijevic@fe.uni-lj.si

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Abstract

Background: Hypertension has become a very frequent chronic disease worldwide and Slovenia is no exception. It is defined as a serious risk factor for developing different cardiovascular diseases. Several important studies proved that cardiovascular diseases are the main reason of deaths in more than 50 % of cases in the developed countries. All mentioned facts are indicating that treatment costs in patients with hypertension and cardiovascular diseases represent an important economic burden, which cannot be neglected. It may also be expected that in the next few decades the situation will become even worse. The reasons are the expected earlier disease development due to unhealthy life style and the fact that people live longer and populations are growing older. The mentioned facts have motivated the study, which would enable the estimation of patients' number in the observed population and the evaluation of economic burden when using beta blockers, drugs which have become an important choice in antihypertensive treatment and are also used in patients with different cardiovascular complications. The projections indicating the expected trends of mentioned problems in the forthcoming decades would also be of interest.

Methods: To answer some of the indicated questions, a simulation model was developed, which enabled the prediction of patients with hypertension and the influence of this disease to the development of myocardial infarction. Modeling was performed using the available statistical data and published studies. Main attention was devoted to the circumstances in Slovenia, but the results were also verified using the available data for some other countries. Combination of simulation results with demographic data enabled the estimation of the number of patients observed. In addition, expenses for the observed groups of patients were evaluated and, based on that, the economic burden was estimated. The mentioned expenses include hospitalizations, drugs required and the estimated mortality-related expenses. The developed model was accomplished with dynamical mathematical structure predicting the development of population number in Slovenia in the forthcoming decades, taking into account that the demographic properties remain unchanged. Also the observation of potential scenario regarding patients' number and thus expected economic burden distribution among younger and older population is made possible.

Results: In the paper simulation results are presented which enable the estimation of patients with hypertension and their connection with those who have experienced myocardial infarction. It is possible to observe the prevalence and the number of patients in Slovenia by age. In addition, economic burden associated with the observed groups of patients is calculated taking into account needed drugs, hospitalizations and patient mortality. In such circumstances it is possible to expect that in the group of one million people approximately 264,000 are patients with hypertension for whom, when healed optimally with beta blockers, over EUR 13 million is needed per year. In the same group of one million people are also patients with myocardial infarction. Among them 11 % experienced infarction within the current year. This amounts to more than 22,000 such patients and over EUR 22 million needed for them each year. In the case of unchanged statistical demographic characteristics in the future, it can be expected that in 50 years relative economic burden for active population would become twice as high as it is now.

Conclusions: For optimal treatment, hospitalization and due to mortality more than EUR 35 million per year would be needed for patients with hypertension (around 260,000 patients)

and for those who have experienced myocardial infarction (around 22,000) if observing the population of one million people. As the population is growing older, it can be expected that the relative economic burden will become significantly greater for active population in the forthcoming decades.

Izvleček

Izhodišča: Hipertenzija je kronična bolezen, ki je dosegla že zelo zaskrbljujoče razsežnosti, pri čemer tudi Slovenija ni izjema. Opredeljena je kot pomemben dejavnik tveganja za razvoj različnih srčno-žilnih bolezni. Analize kažejo, da so srčno-žilne bolezni vzrok smrtnosti že v več kot 50 % v državah razvitega sveta. Vse to opozarja na dejstvo, da je zdravljenje bolnikov z visokim krvnim tlakom in srčno-žilnimi boleznimi za družbo postalo nezanemarljivo ekonomsko breme. Pričakujemo, da se bo v naslednjih desetletjih stanje še slabšalo. Razloge za takšno napoved pripisujejo vse zgodnejšemu razvoju bolezni zaradi nezdravega načina življenja pa tudi staranju prebivalstva. Omenjena dejstva so spodbudila študij možnosti določanja števila teh bolnikov v opazovani populaciji in vrednotenja stroškov ustreznega zdravljenja pri uporabi blokatorjev beta, ki so postali zdravilo izbire pri antihipertenzivnem zdravljenju, uporabljajo pa se tudi pri zdravljenju bolnikov z različnimi srčno-žilnimi zapleti. Zelo zanimive bi bile tudi projekcije, ki bi nakazale trende te problematike v prihodnjih letih oz. desetletjih.

Metode: Da bi odgovorili na zastavljena vprašanja, smo zgradili simulacijski model, ki napoveduje razvoj prevalence bolnikov s hipertenzijo ter vpliv te bolezni na razvoj miokardnega infarkta. Modeliranje smo temeljili na razpoložljivih statističnih podatkih in objavljenih študijah. Osrednjo pozornost smo namenili razmeram v Sloveniji, rezultate modeliranja pa smo vrednotili tudi glede na dosegljive podatke v nekaterih drugih državah. Kombinacija rezultatov modeliranja z demografskimi podatki je omogočila tudi izračun števila opazovanih bolnikov. Nadalje smo ovrednotili tudi stroške, povezane z opazovanima skupinama bolnikov, in na takšen način omogočili tudi oceno ekonomskega družbenega bremena. V prikazanem izračunu smo upoštevali stroške zdravil pri optimalnem zdravljenju, hospitalizaciji in smrtnosti. Razviti model smo dopolnili še z dinamičnim matematičnim modelom razvoja prebivalstva v Sloveniji ob upoštevanju predpostavke, da demografske značilnosti ostajajo nespremenjene. S tem smo omogočili opazovanje nekaterih možnih scenarijev razvoja številčnosti opazovanih bolnikov v prihodnosti in prerazporejanja bremena stroškov zdravljenja med mlajšimi in starejšimi v naslednjih desetletjih.

Rezultati: V prispevku smo predstavili simulacijske rezultate, ki omogočajo oceno števila bolnikov s hipertenzijo in njihovo povezavo z bolniki, ki so doživeli miokardni infarkt. Predstavljena je prevalenca teh bolnikov in njihova številčnost v Sloveniji glede na njihovo starost. Ovrednotili smo tudi ekonomsko breme, povezano z opazovanimi bolniki in sicer tako, da smo določili stroške, povezane s potrebnimi zdravili, hospitalizacijo in smrtnostjo. Ugotovitve je mogoče tudi ekstrapolirati na države s primerljivim ekonomskim, socialnim in demografskim stanjem. V takšnih razmerah pričakujemo, da bo v milijonski skupini ljudi približno 264 000 oseb s hipertenzijo, za katere bi ob optimalnem zdravljenju z blokatorji beta potrebovali letno prek 13 milijonov evrov. V isti skupini se nahajajo seveda tudi bolniki, ki so doživeli miokardni infarkt, med katerimi je kar 11 % takšnih, ki so infarkt doživeli v obdobju, ki je krajše od enega leta. Na milijon prebivalcev se pričakuje, da jih je prek 22 000 takšnih, ki so že doživeli miokardni infarkt. V povezavi z njimi je letno potrebno preko 22 milijonov evrov. V primeru, da se statistične demografske značilnosti v prihajajočih letih ne bodo bistveno spreminjale, pričakujemo izrazito staranje populacije, ekonomsko breme aktivne populacije v zvezi s hipertenzijo in miokardnim infarktom pa bo čez 50 let vsaj dvakrat višje.

Zaključki: Glede na predstavljene rezultate pričakujemo, da bi letno potrebovali prek 35 milijonov evrov na milijon prebivalcev za bolnike s hipertenzijo (okrog 260 000 oseb) in za tiste, ki so doživeli miokardni infarkt (okrog 22 000 oseb). Ker se prebivalstvo stara, se je potrebno zavedati, da postaja za aktivno populacijo to ekonomsko breme sorazmerno vse večje.

1. Introduction

A century ago, cardiovascular (CV) diseases were not very frequent. At the beginning of the 20th century they represented the cause of mortality in less than 10 % of cases. But throughout the century this number increased to over 50 % in developed countries.[1,2]

Regarding current forecasts, it can be expected that numerous factors can further increase the number of patients with CV diseases in the future. One reason is the fact that people live longer and consequently the population is becoming older. In addition, also the number of overweight population is increasing and thus giving rise to the occurrence of diabetes and hypertension. These chronic diseases further represent a significant risk factors for developing CV diseases. It is also important to take into account longer working time with a lot of stress and not enough physical activity. A very important risk factor is also smoking.[2-7]

Analyses show that hypertension is the most frequent chronic disease and the most important reason among adults to visit a physician.[8] For example, approximately 31 % of American population has hypertension. Blood pressure volumes increase with age. The lifetime risk of developing hypertension among people 55 years of age and older is 90 %. The population prevalence of hypertension in the population aged 60 years and older is 65.4 %.[9] It is important to point out that significant differences are detected in the epidemiology of observed diseases between different countries. The main reasons are due to environmental, economic and social status, which influence the adopted life style, but the sensitivity to salt among the black population cannot in general be neglected either. Some differences were also detected when smaller areas were investigated. Very interesting results are for example presented by Accetto et al. [10,11] for the regions of Slovenia. Hypertension can represent a risk for developing different health complications. The risk of cardiovascular morbidity and mortality is directly correlated with blood pressure.[12,13]

Several important studies prove that optimal antihypertensive treatment (optimal treatment is the treatment which follows the evaluated and adopted treatment directions [14,15]) decreases the risk of developing CV diseases and a number of serious health complications and consequently also necessary hospitalizations or even mortality.[11,16] Among the mentioned serious complications is myocardial infarction (MI), which is also subject to investigation in the present study. Myocardial infarction is the most evident form of acute coronary syndromes, such as unstable angina, MI and the forms of coronary heart disease that constitute the most common causes of cardiovascular death.[17]

Each year more than 1.5 million Americans experience an acute coronary syndrome, and 220,000 die of an MI. More than 7.6 million living persons have survived an MI. Coronary heart disease is the leading cause of premature chronic disability in the United States. The cost of coronary heart disease is high, with direct and indirect costs estimated at $ 151.6 billion for 2007.[17]

Beta–adrenergic receptor blockers (or in short beta blockers – BB) came to the market in 1950's. Through the following decades their usage was extended to the treatment of different CV diseases. They do not form a homogenous group of cardiovascular drugs. Most control clinical studies have been performed with old BB having rather frequent side effects. Probably, clinical results with BB are even more favorable when more selective or vasodilatory new BB are used.[18] Several important studies prove the importance of BB in the treatment of MI, angina pectoris, congestive heart failure in addition to hypertension, etc. Clinical studies also pointed out the fact that BB decrease mortality and risk for developing a new CV complication. They have become a drug of choice in the treatment of hypertension[19-22] where they importantly reduce coronary events and death.[23] Following MI, all patients should receive indefinite therapy with BB in addition to acetylsalicylic acid and an angiotensin-corverting enzyme inhibitor for the prevention of death, stroke, and recurrent infarction.[24] It is proven that they slow

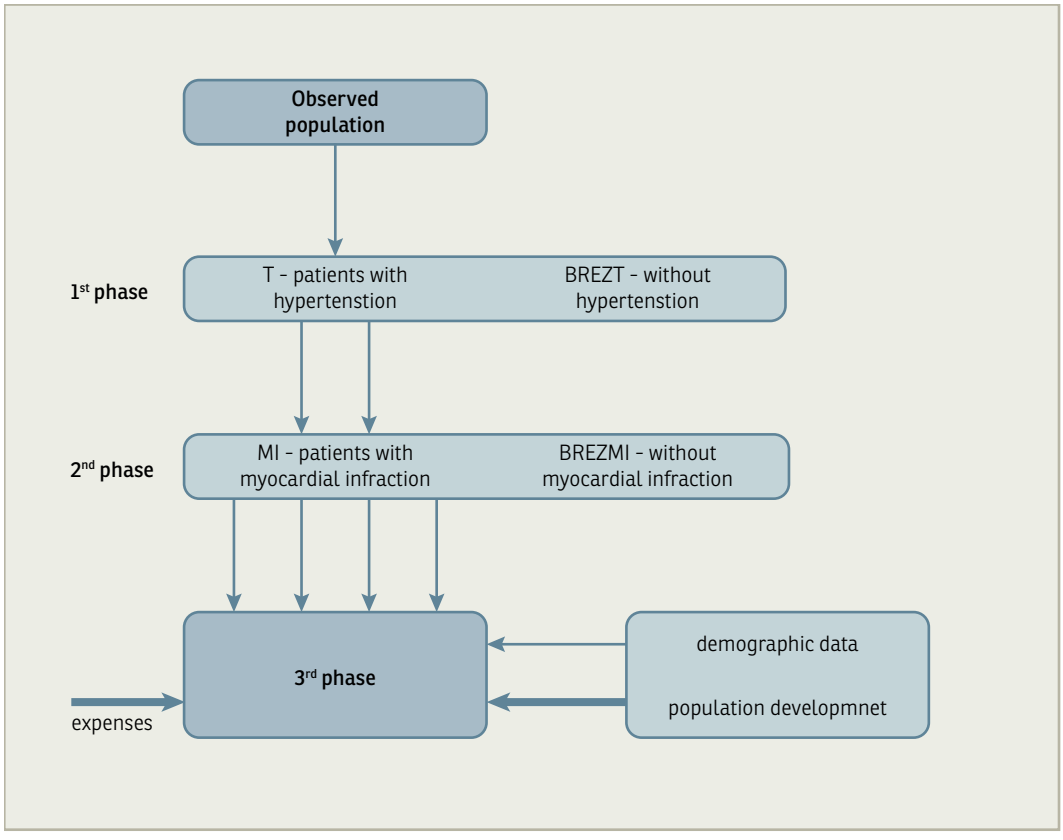


Figure 1: Modeling structure.

down disease development and thus increase life quality.

It is interesting that despite the fact that BB have been present in the treatment of different CV diseases for several decades, their actual usage varies from country to country and also from disease to disease. For example, in treatment of CV diseases their usage ranges from 25 % to 78 % of all patients.[25,26] In European guidelines on hypertension BB are preferred in hypertensive patients with previous MI, angina pectoris, heart failure, permanent arterial fibrillation and during pregnancy.[27]

The paper is organized as follows: in the next section the structure of the model developed for the estimation of patients under study is described. Further on, simulation results are presented, which enable the estimation of economic burden of patients under study. In the fourth section predictions are given and discused regarding the fact that the population of Slovenia is growing older. In the Conclusion the presented results are summarized and extrapolation is suggested, which can be used for the countries with similar economic, social and demographic situation. At the same time some future possibilities in model development are discussed.

2. Methodology

When observing disease development, its state, consequences or treatment efficacy, modeling approaches can be described using very different model structures and tools, but also the level of problem description must be chosen in a corresponding manner.[28-30] Crucial for the suitable decision is the purpose of model usage and data available through modeling procedure.

Disease development can be observed, for example, at metabolic level or at the level of individual patient,[31,32] but in some cases the response of the group observed or even the whole population can be of great importance.[4,5,33] Furthermore, the problem can be associated with one disease only, or with a combination of diseases, where different processes can be under investigation. These processes can be interpreted as continuous or developing gradually, but sometimes their appearance is more important.

Table 1: Prevalence of hypertension.

Age (years)	Men (%)	Women (%)	Average (%)
20–34	11.1	5.8	8.45
35–44	21.3	18.1	19.7
45–54	34.1	34.0	34.05
55–64	46.6	55.5	51.05
65–74	60.9	74.0	67.45
75 and more	69.2	83.4	76.3

Table 2: Prevalence of myocardial infarction.

Age (years)	Men (%)	Women (%)	Average (%)
35–44	0.8	0.3	0.55
45–54	2.2	0.8	1.5
55–64	6.7	2.1	4.4
65–74	12.1	4.2	8.15
75 and more	15.7	8.1	11.9

In the first case usually differential equations and continuous simulation are used for their interpretation,[34,35] while in the second case discrete or statistical interpretation[36,37] can be more appropriate. Due to the fast development of hardware and software a combination of mentioned approaches (hybrid solutions) are also frequently used.

Of course, additional moments or dimensions of observation appear when economical aspects become important in problem investigation.[5,38] So, the harmonization of the desired presentation, which should efficiently illuminate all relevant aspects of the problem, is of crucial importance.

As already mentioned, in the course of the present study several objectives were under consideration. This study should enable the observation of patients with high blood pressure and their influence on those who have experienced MI or reinfarction. In some countries or regions such data or registers are not available while for very small populations the value of statistical data may be questionable. The appearance of mentioned diseases is in a high correlation with patient age, therefore this variable was chosen as the main independent variable.

In our case, modeling results should also enable the evaluation of economic burden of treatment expenses for mentioned patients, this being important not only for governments, health insurance companies and hospitals, but actually for everyone in terms of education, thus reducing the probability of developing such diseases. To fulfill all mentioned goals, the model structure presented in Figure 1 was developed.

Modeling was realized through three main design phases. In the first one, a dynamical structure with two output signals was identified, presenting percentage distribution of patients with hypertension (T) and those who are healthy as regards this disease (BREZT). Hypertension is defined as a chronic disease when patients have blood pressure higher than 140/90 mm Hg, or are using corresponding antihypertensive drugs.[14,15,39] Input signal into the first phase is unity step indicating the start of problem observation, namely at birth, and indicating the observation of the whole population. Observation time is 95 years regarding patients' age.

Modeling has started using data as presented in Table 1.[39] For the sake of simplici-

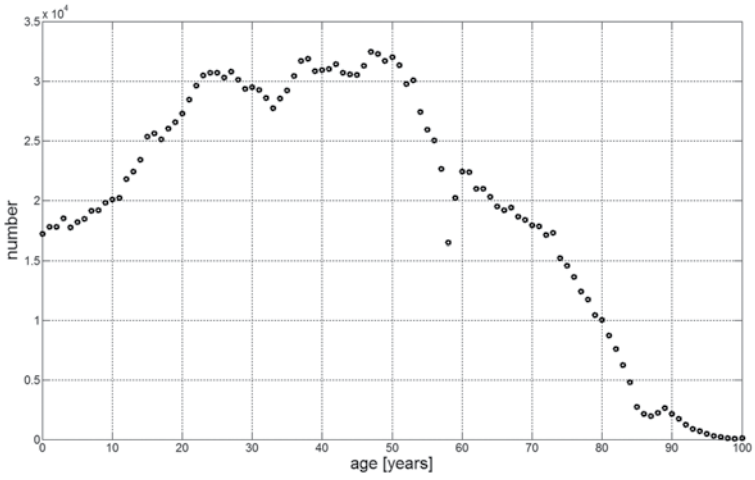


Figure 2: Population of Slovenia.

ty, the average between both sexes was taken into account. The resulting identified model of hypertension prevalence is of high order, nonlinear, with different time constants and with time delays, as hypertension can be neglected in the youth (before the age of 20).

In the second phase, modeling structure was extended with a dynamical model describing the prevalence development of the patients who have experienced MI. The dynamical properties of this phase also depend on whether patients are from the group with hypertension or they belong to those without this chronic disease. Output signals from this phase are four, representing all possible combinations of patients under study.

The data used for modeling in the second phase are given in Table 2. At the same time the information describing the correlation between both observed diseases[18,40,41] was also taken into account.

In the third modeling phase demographic data for Slovenia was added.[42] In Figure 2 the distribution of people by their age in 2003 is presented. Combination of disease prevalence with the number of people enables the estimation of the patients, as presented through simulation results in the next section.

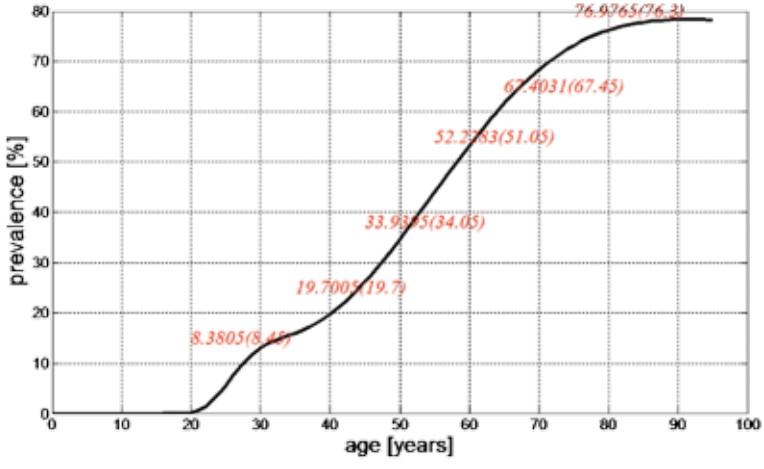
In the third phase, the estimated expenses were taken into account with reference to the patients under study. The expenses included the necessary drugs and hospitalizations as well as patients' mortality-related expenses.[18] In this way annual economic burden was calculated for each observed disease.

Similar results as for Slovenia can be expected also for other countries with comparable demographic, social and economic situations, which mean the great majority of EU countries.[43] Simple result extrapolation is suggested, which can be used for the mentioned purpose.

Finally, the mathematical model was supplemented with a dynamical structure, predicting population development in Slovenia throughout the next few decades. It was developed under the assumption that all main demographic properties (fertility, mortality and migrations) remain unchanged.

All calculations were realized using Matlab and Simulink.[44,45]

Figure 3: Prevalence of patients with hypertension.



3. Simulation results and economic burden evaluation

As already mentioned, in the first modeling phase patients with hypertension were observed. Simulation results are presented in Figure 3, where also good matching with statistical data is indicated within given age groups. The obtained average simulation results are presented for different age groups, while the reference values are indicated in parentheses.

In the third phase this result was combined with the number of people and so the distribution of patients by age was obtained for Slovenia, as presented in Figure 4. This model prediction indicates that there are

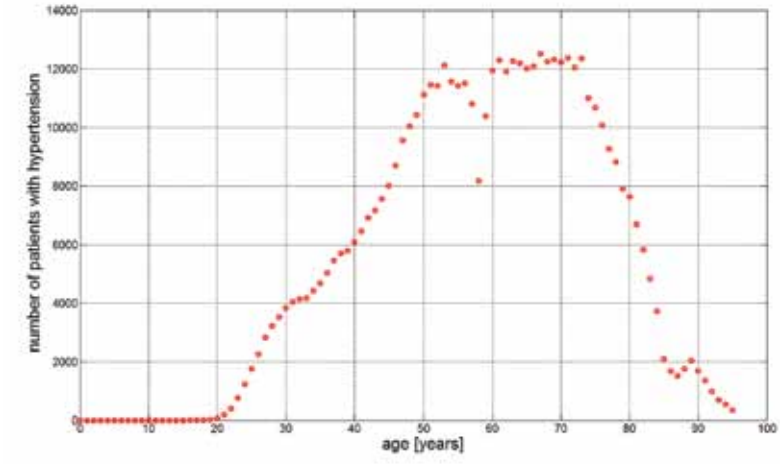


Figure 4: Number of patients with hypertension.

over 526,000 patients with hypertension in Slovenia, which represents 26.4 % of the whole population.

It is important to point out, that sometimes very different and therefore also misleading data are interpreted regarding the prevalence of hypertension (and also some other diseases). The reason lies mainly in the fact that the age window for which the result was calculated or presented has not been clearly defined. For example, in Figure 5 it can be observed how the onset of patients' observation is influencing the patients' average, which starts from 26.4 %, as already mentioned, when the whole population is taken into account, but can also reach the value of 78 % when only elderly population is observed. In the age window from 50 to 95 years almost 60 % of people are also patients with hypertension, which is more than twice as much as in the case, when the whole population is taken into account.

Figure 5: Average prevalence of hypertension –by onset of observation.

For model validation the presented hypertension prevalence was also combined with demographic data for Germany and Great Britain, and good matching was obtained for all three countries.[10,11,46-48] Of course, regional differences[11] cannot be covered by the proposed modeling approach where only average characteristics are taken into account.

As patients' number is known, it is also possible to evaluate their treatment-related expenses. When treated optimally with BB, it would represent an economic burden of over EUR 27 million per year for Slovenia, because it was estimated that annual expenses for drugs needed for each patient are EUR 51.49.[18] The shape of the expenses curve by patient age is of course the same as the one in Figure 4, which means that the highest expenditures are needed for the patients at an age between 50 and 73 years, as their number is the highest.

As already mentioned, it can be expected that in the next decades the number of patients with chronic diseases will increase due to unhealthy life style. Let us presume, for example, that hypertension delay time would become a bit shorter (for example for 5 years), while the range of prevalence can also become higher. The mentioned possibilities are indicated in Figure 6 with curves 2 and 3. If the number of people and treatment prices would remain unchanged, such changes would represent the increase in the number of patients with hypertension to 31.5 % or even to 36.5 % with respect to the whole population, while the treatment expenses would be over EUR 32 or 36.5 million. Investments into healthier life style, which would consequently lead to slower and less intensive development of this chronic disease would therefore be of great importance.

Patients with MI were introduced in the second design phase. Here dynamic modeling structure was developed, where it is important to distinguish from which group of the first phase people are entering the second phase, i.e. either from the group with hypertension or the group without it. The study presented by Allender S. et al.[41] in-

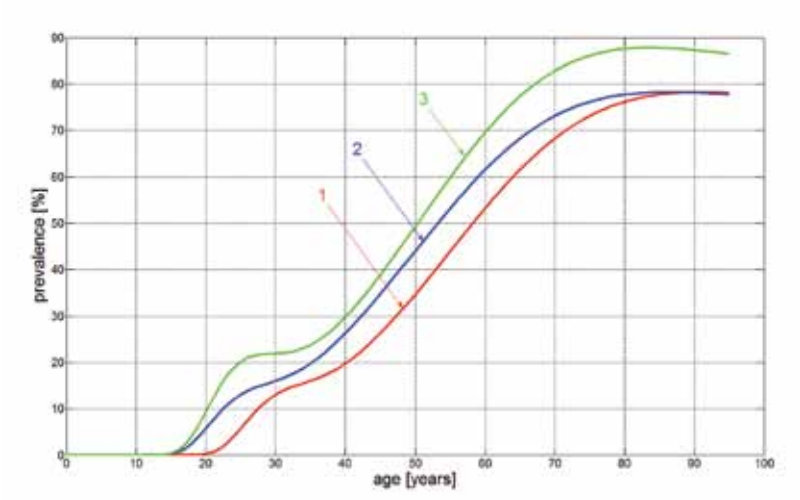


Figure 6: Hypertension prevalence increase (1-starting situation, 2-shorter delay time, 3-shorter delay time with increased gain).

dicates that from 22 % (in West Europe) to 25 % (in Central and East Europe) patients with MI also have hypertension (23.5 % in average). The second phase model responses (prevalence by patient age) are presented in Figure 7.

Combination of the presented results with the information from Figure 2 (population of Slovenia) enables the estimation of the number of patients with MI, which is illustrated in Figure 8. Here it is possible to differ those who have both diseases (curve 2) at the same time from those who experienced only MI (curve 1) but are not hypertonics. The model predicts that in Slovenia there are 43,500 patients who have experienced MI, representing 2.2 % of the whole population. Among these patients 24 % are also hypertonics, which is in good agreemant with the previously mentioned data.

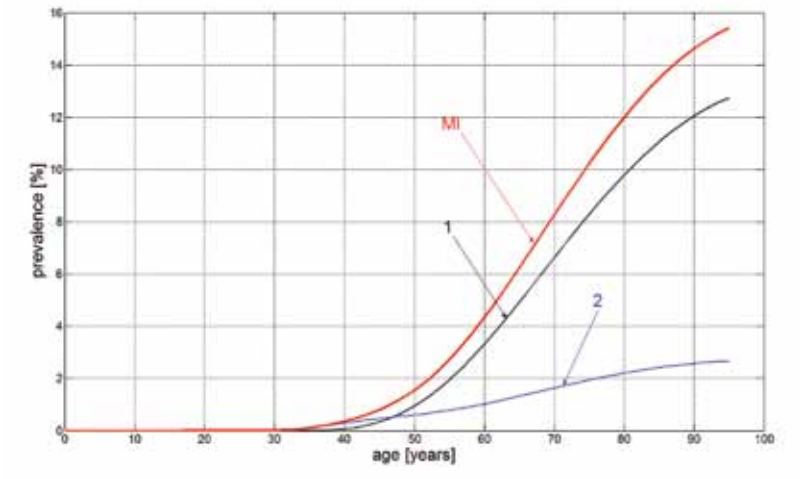


Figure 7: Prevalence of patients with MI (MI-all patients with MI, 1-patients with MI and without T, 2-patients with MI and T).

Table 4: Annual drug expenses for one patient with MI in one year after MI.

ACEI	€ 180.18
ASA	€ 12.57
clopidogrel	€ 469.81
statins	€ 234.10
Total	**€ 896,66**

Table 5: Annual drug expenses for one patient with MI more than one year after MI.

ACEI	€ 180.18
ASA	€ 12.57
statins	€ 234.10
Total	**€ 426.85**

For the observed patients different expenses can be estimated. In the present study, necessary drugs (BB and other needed for optimal treatment), hospitalizations and patient mortality-related expenses are taken into account.

It was estimated[12] that in Slovenia for one MI–patient EUR 80.01 is needed for BB per year, which represents annual economic burden of almost EUR 3.5 million.

In addition to BB, guidelines also suggest the use of:

- ACEI (angiotensin-converting enzyme inhibitors) – to slow down heart remodeling and to decrease recurrence of complications and patient mortality;
- ASA (acetylsalicylic acid) – prevents sticking of thrombocytes and blood coagulation and consequently also recurrence of CV complication;
- clopidogrel (needed only in the first year after MI) – prevents sticking of thrombocytes and blood coagulation and consequently also recurrence of CV complication;
- statins – decrease blood cholesterol and in this way prevent recurrence of CV complication.

Evidently, it is important to differ among the patients one year after MI and those whose period after MI is longer. Prices, which were taken into account, are given in Tables 4 and 5.

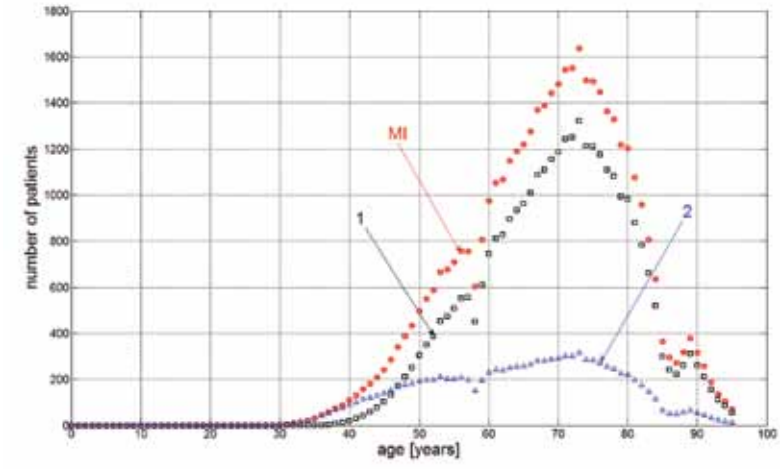


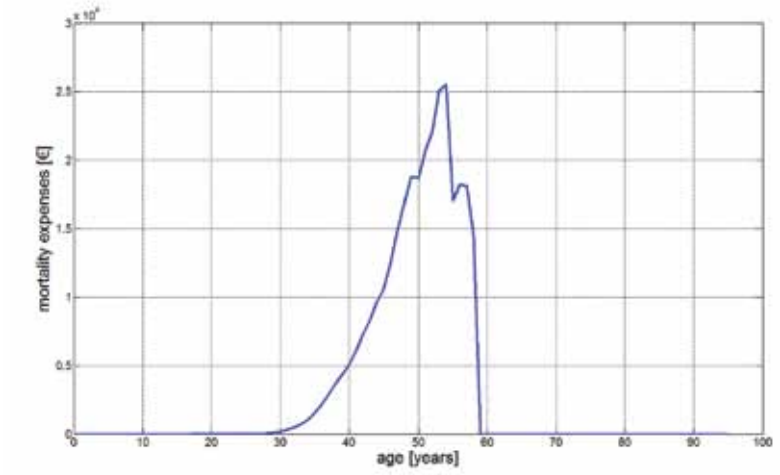
Figure 8: Number of patients with MI in Slovenia (MI-all patients, 1-patients with MI but without T, 2-patients with MI and T).

The number of MI patients is varying from year to year, but in average it can be taken into account that 11 % of MI patients are from the group for which the time elapsed from MI is shorter than one year.

From the presented data and simulation results the following can be concluded: for optimal treatment of MI patients almost EUR 3.5 million is needed for BB each year in Slovenia and additionally EUR 20.8 million for other drugs needed. In other words, in Slovenia the annual burden due to drugs needed for MI patients is approximately EUR 24.3 million.

Expenses for hospitalizations were evaluated with respect to their number per year (because of the settling of insurance accounts in Slovenia). Each hospitalization of a patient after MI costs EUR 4157,79.[18] It was also taken into account that each patient is hospitalized once after MI or reinfarction.

Figure 9: Annual expenses due to mortality among MI patients in Slovenia.



As mentioned, 11 % of all MI patients on average contribute to this group each year. Annual economic burden for hospitalizations therefore represents almost EUR 20 million.

Annual mortality was estimated to be 4 % on average, which represents for Slovenia around 1700 people who die because of MI each year. Such expenses are mostly influenced by the status of the patient (active or retired). On average, people are retired at the age of 59 (57 for women and 60 for men) in Slovenia.[18] Expenses are calculated using the following equation:

$$N(i) = N_m(i) * as * dwa * (1 - du) * f_x$$

where indexes i indicate patients' age (i=0, 1, ..., 95), $N(i)$ mortality expenses at age i, $N_m(i)$ is the number of patients who die at age i, as represents an average salary, dwa is the so called degree of working activity, which mainly depends on the patients' age, du is a degree of unemployment, and f_x is a parameter, which is 1 if the observed patient was from the group of active people, otherwise it is 0.

The estimated expenses are shown in Figure 9. It means that over EUR 300,000 is needed per year due to mortality among MI patients.

Therefore, the total estimated annual expenses regarding MI patients in Slovenia are: EUR 24.3 million (drugs) + EUR 19.9 million (hospitalizatin) + EUR 0.3 million (mortality) = EUR 44.5 million. It is obvious that the expenses for necessary drugs and hospitalizations are essentially higher than those incurred by mortality. The reason lies in the fact that the number of patients who die at their active age is not very high. The number of patients who experience MI is the highest at the age of 73, when they are already retired and, regarding the adopted methodology, they do not contribute anymore to the estimated expenses.

Simulation results for Slovenia indicate that there are approximately 10,000 patients who have at the same time hypertension and MI. During the first calculation we have taken into account that they also contribute to the expenses of antihypertensive treatment.

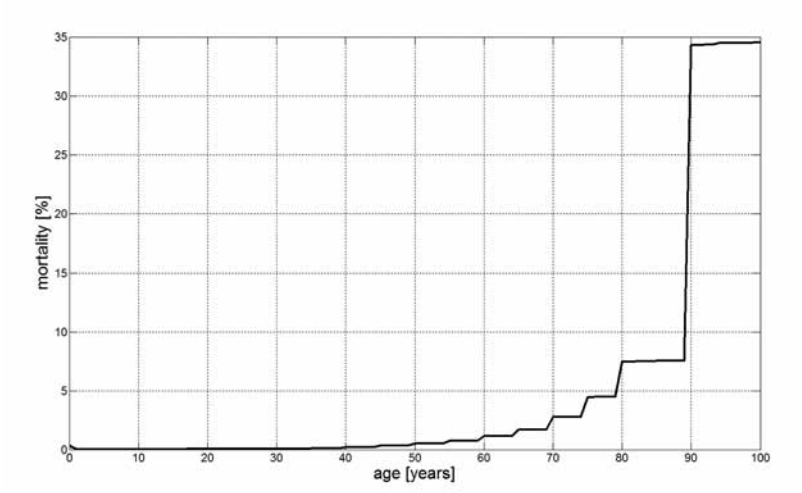


Figure 10: Average mortality rate by population age.

These expenses are approximately EUR 0.5 million. However, as these patients are treated more intensively due to MI, the previously presented expenses attributable to high blood pressure alone have to be subtracted. Therefore, the estimated annual price for antihypertensive treatment is EUR 26.5 million and the total estimated economic burden is EUR 71 million.

4. Demographic expectations

In Slovenia, there are good healthcare network and living conditions while at the same time fertility is still very low. The expectations predict that in the future the population will grow older. In this section, simulation estimations are presented, predicting population number in Slovenia in the future decades and its influence on the distribution of patients with T and MI. The predictions are based on the presumption that demographical statistics, namely fertility, mortality and migration, will remain unchanged. Average statistical parameters were calculated using data from 2004 to 2007 as presented by Statistical Office of the Republic of Slovenia.[42] In Figure 10 average mortality from 2004 to 2007 is presented in percentage according to population age. Data are available for the groups of people and therefore the curve is segmented.

Fertility was calculated from the number of people in the age window from 18 to 45 years. It was estimated that each year 2.2715 % newborns can be expected in the mentioned group of people.

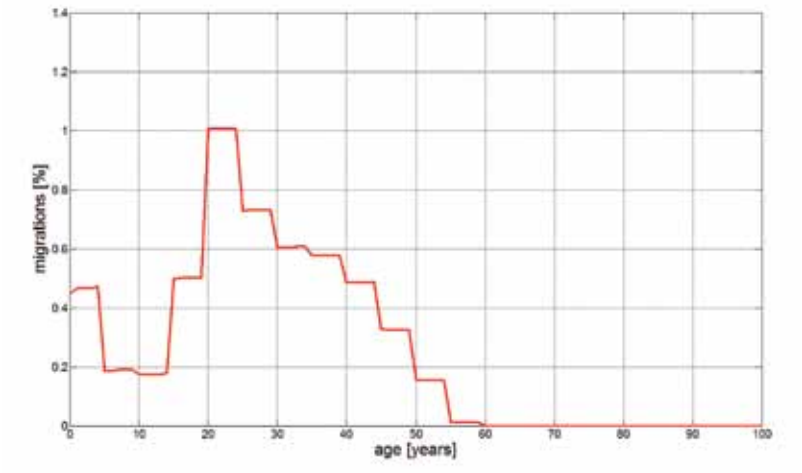
Average percentage of migrations is presented in Figure 11. For Slovenia, relative low migration flows are characteristic, these being generally under 1 % and for the population older than 60 years, they can be neglected.

The realized prediction starts in 2003 and illustrates the expectations till the year 2052. The situation is shown in Figures 12 and 13. In Figure 12 distribution of population in Slovenia is presented for each year of fifty--year window, while in Figure 13 only starting distribution in 2003 and the final one for 2052 can be observed.

These two figures clearly show that a decrease in younger population can be expected in the next decades and, which is even more important, the ratio between the younger and the older people is changing dramatically. For example, in 2003 in Slovenia 1,191,502 people were in age window between 20 and 60, while in the window of elderly people (between 61 and 95) there were only 384,017 people. The ratio between these two groups was 3.1.

Prediction for 50 years later expects only 840,642 people in the mentioned group of younger population, but the number of people in the group of the elderly is expected to increase to 583,462 people. This means that the ratio between the observed groups will decrease to 1.44. In other words, this means that the ratio between younger and older people will probably change to 2.15. This of course means that considerably higher economic burden regarding treatment (and other

Figure 11: Average migration rate by population age.



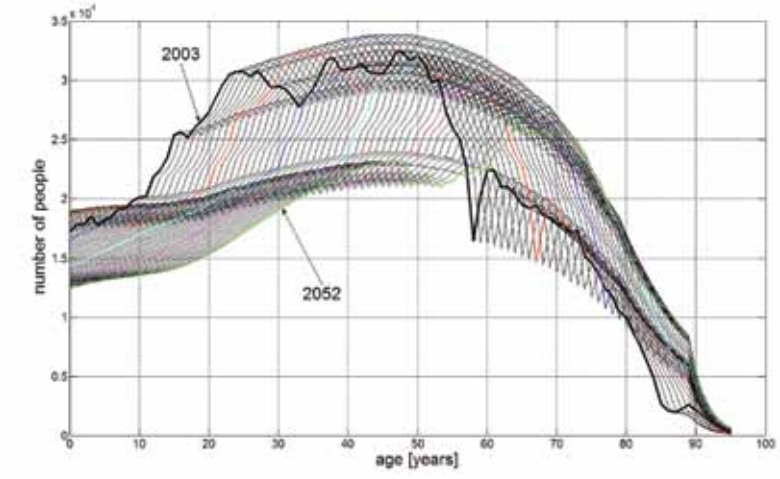


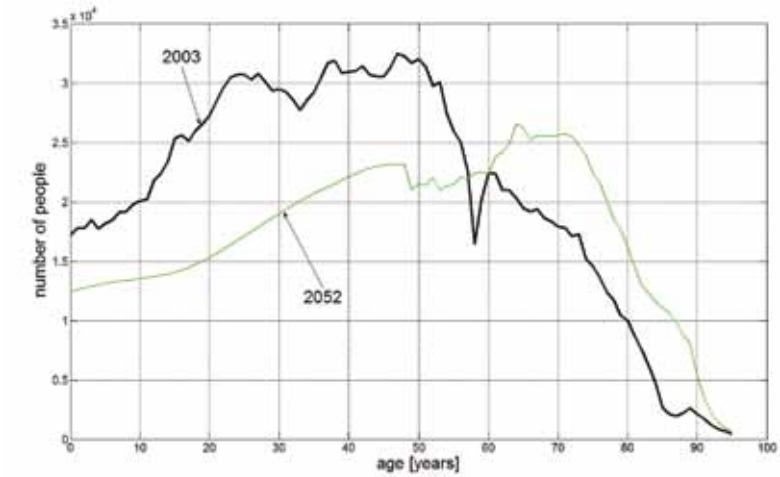
Figure 12: Population prediction for the years 2003–2052 in Slovenia.

social) expenses can be expected in the next decades, provided that the fertility or input migration flows of younger population remain unchanged.

The mentioned population changes also influence the distribution of patients with T and MI, taking into account that the prevalence of the observed diseases remains unchanged. These estimations are presented in Figure 14 for the patients with T and in Figure 15 for the patients with MI. In both cases it can be expected that their number will decrease for the patients up to 60 years of age. The reason for this lies in the fact that the number of these people is lowering (see Figure 13). After the age of 60 the number of people is increasing and at the same time also the disease prevalence is increasing (see Figures 3 and 7).

Number of patients and expectations together with their trends are also presented in Table 6.

Figure 13: Population number in 2003 and prediction for 2052 in Slovenia.



5. Conclusions

The presented three-design-phase model structure was developed for estimating the number of patients with hypertension, myocardial infarction and all possible combinations with respect to their age from the perspective of a larger society, e.g. at the level of the whole country. From this perspective it is also possible to evaluate the corresponding social and economic burden. Regarding patients with myocardial infarction, the estimated annual expenses include the costs needed for hospitalizations and drugs and mortality-related costs, while for patients with high blood pressure only the expenses for drugs, i.e. the cheapest beta blockers available in the Slovenian market, were taken into account.

In the modeling studies such as this one, data are the most important and at the same time the most problematic part; this is true of both the phase of model development as well as of the validation phase. Further model development always requires the introduction of carefully chosen simplifications and harmonization of information obtained from different sources. Combining the information from different sources is also important from the validation point of view, but this has to be realized with respect to the aim of model usage. In our case it was taken into account that the influence of globalization can be observed in a great majority of countries worldwide, where EU countries are no exception. That means that adopted life style is also becoming more and more similar. As a result, the epidemiological characteristics of diseases in countries with similar social, economic and demographic conditions are becoming comparable. Therefore, the proposed model is tuned to the average circumstances in Europe, and was evaluated with respect to the available data for Slovenia, Great Britain and Germany. It is important to point out that it is not in

Table 6: Number of patients in Slovenia in 2003 and the expectations for 2052.

	2003	2052	Trend
Number of people aged 20–60 yrs	x1a=1191502	x1b=840640	decrease: x1b/x1a=0.71
Number of people aged 61–95 yrs	x2a=384017	x2b=583455	increase: x2b/x2a=1.52
Number of patients with T aged 20–60 yrs	x3a=266270	x3b=206359	decrease: x3b/x3a=0.78
Number of patients with T aged 61–95 yrs	x4a=259990	x4b=403515	increase: x4b/x4a=1.55
Number of patients with MI aged 20–60 yrs	x5a=10434	x5b=8854	decrease: x5b/x5a=0.85
Number of patients with MI aged 61–95 yrs	x6a=33097	x6b=53968	increase: x6b/x6a=1.63

contradiction with the specific regional situations, which cannot be taken into account through the proposed structure. Hoever, due to its flexibility, the model facilitates further adaptations with respect to the proposed phases, where an increase (or decrease) in specific disease prevalence, demographic variations and also the price changes can be tuned separately, taking into account any specific region, country or changed epidemiology of the disease observed.

On the basis of modeling results the following can be expected in a group of one million people:

- over 260,000 patients with hypertension,
- if they are treated optimally with beta blockers, over EUR 13 million is needed per year,
- around 22,000 patients experience infarction or reinfarction each year,
- for the corresponding drugs (with BB and other necessary medicaments) around EUR 12 million is needed each year,
- additionally, hospitalizations contribute almost EUR 10 million,
- the expenses were also estimated with respect to patient mortality, namely EUR 0.15 million per year in the group of one million people, where around 900 patients die because of MI.

To summarize, from the economic point of view in the group of one million people more than EUR 35 million would be needed for patients with hypertension and for those who have experienced myocardial infarction, covering their optimal treatment and hospitalization as well as mortality-related costs.

Difficulty, which can be expected in the future, is that population is growing older. As a consequence, this will significantly increase the economic burden for the active population. Simulation projections show that relative burden may double in the next few decades if fertility and migration remain low. If in the same time an increase in chronic diseases is expected, the situation may become even more alarming.

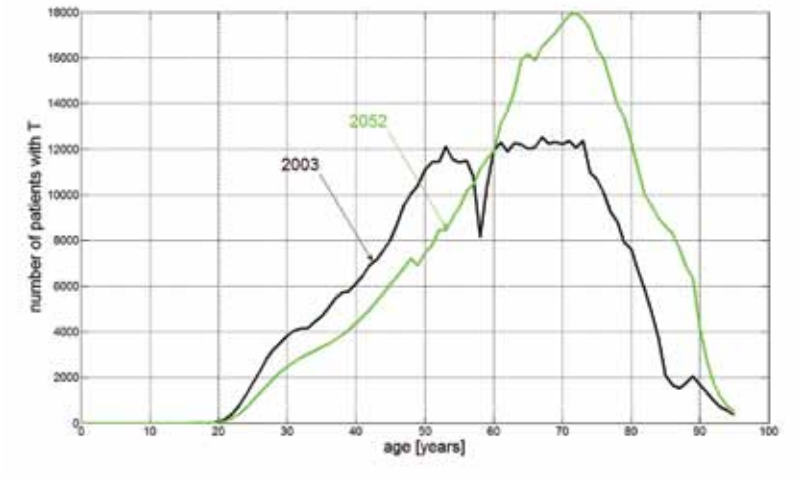


Figure 14: Number of patients with hypertension in Slovenia in 2003 and prediction for 2052.

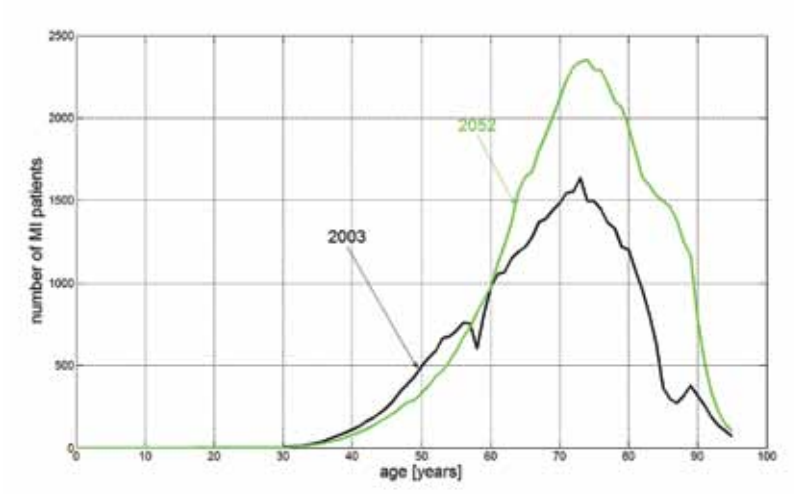


Figure 15: Number of MI patients in Slovenia in 2003 and prediction for 2052.

The developed model structure facilitates further extensions. In the future it is expected that the patients with other CV diseases (such as stroke, chronic heart failure, etc.) would be included. Attention would be paid also to the evaluation of treatment efficacy in comparison with placebo results.

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