Research article/Raziskovalni prispevek

MODELLING OF THE RISK FACTORS AND CHRONIC DISEASES THAT INFLUENCE THE DEVELOPMENT OF SERIOUS HEALTH COMPLICATIONS

MODELIRANJE DEJAVNIKOV TVEGANJA IN KRONIČNIH BOLEZNI, KI VPLIVAJO NA RAZVOJ HUJŠIH ZDRAVSTVENIH ZAPLETOV

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Abstract

Background *Some chronic diseases, like diabetes type 2 and hypertension, and risk factors, such as obesity, hypercholesterolemia, and smoking, are strongly correlated with the potential development of serious health complications that can threaten a patient's life or significantly influence the quality of life, while at the same time representing an enormous economic burden. Such complications include, for example, stroke, coronary heart disease, peripheral arterial vascular disease, end-stage renal disease and congestive heart failure.*

Methods *For a quantitative evaluation of the mentioned patient groups, the age distribution and an estimation of the treatment expenses a dynamic mathematical model was developed, where special attention was devoted to its structure, as it should enable the sequential construction and representation of different forms of data information. The model was realized in the Matlab program package with the Simulink Toolbox.*

Conclusions *A dynamic mathematical model is described that enables the observation of patients (in percentage terms) with diabetes type 2 and obesity, as well as those who smoke, have hypercholesterolemia and hypertension and all possible combinations of these problems, related to their age. Taking into account the Slovenian demographic data and annual treatment expenses, we were able to quantitatively evaluate these factors, not only in Slovenia, but also in other developed regions where the demographic and economic situations are similar. It is also possible to extend the model to patients with serious complications, also taking into account the population dynamics, which is the goal of the next steps in our investigation.*

Regarding the presented results, it is estimated that from a group of a million people, those requiring treatment for diabetes type 2 cost as much as € 19.5 millions per year, since the treatment of one patient for one year is € 355. If all the sufferers requiring such treatment were located, as a consequence of more systematic medical examinations, an additional € 16 millions would be needed.

In this group of one million people, as many as 40 % are expected to develop hypercholesterolemia, of which 26 % are diagnosed and treated adequately. The annual cost for the treatment of one patient is € 313, which means that for a group of a million people the costs would be € 82 millions per year. An additional € 43.5 millions would be needed if all the sufferers with hypercholesterolemia were treated.

Another chronic disease is hypertension. The annual cost for treating one patient is estimated to be € 271, and so for a group of a million people the treatment costs would be € 69.5 millions. If this were extended to include so far undiscovered sufferers with this chronic disease an additional € 14.5 millions would be needed.

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The treatment expenses for all mentioned chronic diseases in Slovenia amount to over € 340 millions per year, with an additional € 148 millions needed for those sufferers who remain undiagnosed. Furthermore, it is well known that serious health complications are significantly reduced if these chronic diseases are adequately treated. From this point of view diagnosing and treating these chronic sufferers is, of course, efficient. But with a further development of the model we can also have an economic evaluation, indicating the potential savings, resulting from an early treatment and the consequently decreasing serious health problems.

Key words *modelling; simulation; diabetes type 2; obesity; smoking; hypercholesterolemia; hypertension*

Izvleček

Izhodišča *Nekatere kronične bolezni, kot so diabetes tipa 2 in hipertenzija ter dejavniki tveganja, kamor uvrščamo debelost, dislipidemijo in kajenje, so tesno povezani z razvojem hudih zdravstvenih zapletov, ki lahko ogrozijo pacientovo življenje oz. bistveno vplivajo na kvaliteto življenja, hkrati pa pomenijo izjemno veliko ekonomsko breme. Med tovrstne zaplete sodijo npr. možganska kap, koronarna srčna bolezen, srčno popuščanje, periferna arterijska žilna bolezen pa tudi končna odpoved ledvic.*

Metode *Da bi lahko tudi kvantitativno ovrednotili razširjenost in starostno porazdelitev posameznih skupin pacientov ter stroškov zdravljenja, smo razvili dinamični matematični model, pri čemer je bila posebna pozornost posvečena njegovi strukturi, ki omogoča postopen razvoj ter upoštevanje in prikaz informacij različnih oblik. Model je realiziran v programskem paketu Matlab z orodjem Simulink.*

Zaključki *Opisani dinamični matematični model razvoja diabetesa tipa 2, debelosti, kajenja, dislipidemije in hipertenzije omogoča opazovanje opisanih bolezni in dejavnikov tveganja relativno, v procentih, glede na starost pacientov, pri čemer smo pri modeliranju upoštevali tudi vse možne kombinacije omenjenih skupin pacientov. Dodajanje informacij, povezanih z demografskimi razmerami v Sloveniji ter letno ceno zdravljenja posameznih bolezni, je omogočilo tudi kvantitativno vrednotenje razmer, in sicer tako v Sloveniji kot tudi v razvitih deželah, kjer sta demografska struktura prebivalstva in ekonomski razvoj primerljiva. Možno pa je tudi dopolnjevanje modela z vključitvijo hujših zdravstvenih zapletov in napovedmi spreminjanja števila prebivalstva, kar bo predmet naših nadaljnjih raziskav.*
Na osnovi predstavljenih rezultatov modeliranja je mogoče pričakovati, da je v populaciji z milijon prebivalci za letno zdravljenje diabetesa 2 namenjeno 19,5 milijona €, oz. 355 € na pacienta, še dodatnih 16 milijonov € pa bi potrebovali, če bi s sistematskimi pregledi odkrili vse paciente.
V isti skupini prebivalcev lahko pričakujemo kar 40 % pacientov z dislipedimijo, med katerimi je odkritih in ustrezno zdravljenih 26 %. Ker znaša letna cena zdravljenja te kronične bolezni na pacienta 313 €, je na milijon prebivalcev za zdravljenje dislipidemije potrebnih 82 milijonov €, še dodatnih 43,5 pa bi potrebovali, če bi bili zdravljeni vsi pacienti.
Zelo razširjena kronična bolezen je tudi hipertenzija. Letno zdravljenje enega pacienta znaša 271 €, kar pomeni 69,5 milijona € na milijon prebivalcev, še dodatnih 14,5 milijona pa bi jih potrebovali, če bi bili z bolj sistematičnimi pregledi odkriti vsi pacienti.
Za zdravljenje omenjenih kroničnih bolezni je torej potrebnih v Sloveniji preko 340 milijonov €, še dodatnih 148 pa bi jih morali nameniti zaenkrat neodkritim pacientom. Poznano je, da so hudi zdravstveni zapleti med ustrezno zdravljenimi kroničnimi bolniki izrazito redkejši, tako da je z etičnega stališča odkrivanje tovrstnih pacientov seveda upravičeno. Z nadaljnjim razvojem modela pa bomo skušali ovrednotiti tudi ekonomske prihranke, ki bi nastopili z zdravljenjem vseh obravnavanih kroničnih bolnikov zaradi zmanjšanja hudih obolenj.

Ključne besede *modeliranje; simulacija; diabetes tipa 2; debelost; kajenje; dislipidemija; hipertenzija*

Introduction

It is well known that chronic diseases like, for example, diabetes type 2, hypercholesterolemia and hypertension are frequent in large numbers in countries all over the world, and Slovenia is no exception. Some reports suggest that these diseases have already reached epidemic proportions.[1–3] In developed regions regular examinations discover many sufferers who are afterwards advised to undertake a particular diet and, if necessary, also treatment with drugs. Due to the range of these diseases the costs of treatment cannot be ignored, as they represent a serious economic burden, not only for governments, hospitals and medical insurance companies, but also for individuals, especially when taking into account the important influence of these diseases, and risk factors like obesity and smoking, on serious health complications that can threaten a person's life or dramatically lower the quality of life. This is true without taking into account the additional treatment expenses, which are usually a few times higher than those for the treatment of chronic diseases.

The goal of this study was to develop a dynamic model that would make it possible to:

- identify the main dynamic properties of the observed diseases and risk factors,
- estimate the number of sufferers in terms of age,
- identify any possible overlapping of the observed groups of sufferers,
- estimate the healing effects and treatment costs for each of the observed diseases,
- predict the social burden of the treatment,
- model extensions that would enable an estimation of the influence of chronic diseases and risk factors on serious health complications, estimate and evaluate possible savings, and study the ageing population's influence on the distribution of diseases and the economic burden.

Such types of modelling results are not directly available in the literature. They often cover some of the mentioned aspects, but are usually connected with a specific region or country.[4] In this paper the results are evaluated for Slovenia, and then an extrapolation is suggested, which can be applied to countries with a similar demographic and social situation.[5] It is, we believe, reasonable to assume that the circumstances are similar in practically all of the countries of the EU.

The study is organized as follows. First, the main modelling steps are described, where special attention is given to the model's structure. This enables the sequential building of a dynamic system, taking into account all the observed risk factors, diseases, the population distribution and the treatment costs. In the next step, the simulation results and the model predictions are presented and discussed. The paper ends with concluding remarks and some suggestions for future work.

Methodology

When developing a model it is very important to take into account the purpose of the model's usage, the reliability of the data on which it is constructed, the mathematical correctness of its interpretation, its suitability for manipulation and the possibility to evaluate the results.[6] Therefore, the structure of our model was developed in such a manner that it allows the sequential adding of each phenomenon in the whole observed population, while the evaluation of the model's results are compared with different data forms and sources.

The concept used regarding the development of the model is illustrated in Figure 1, where all three modelling phases are also indicated.

The first phase of the modelling, which is described in detail, enables the observation of the mentioned diseases and the percentage risk factors in terms of the age of the sufferers, the relations between the observed groups of sufferers, and their possible overlapping. These results can be further used for the prediction of more serious complications (which are still under investigation) but they can also represent the input data for an estimation of the size of the observed groups of people, taking into account the chosen geographical area. In our case the results are evaluated for Slovenia and developed regions where the age distribution and the distribution of diseases is similar. This part of results was calculated inside the third design phase, where the cost evaluation of a suitable disease treatment was also realised.

The presented modelling results were obtained with the Matlab program package.[7, 8]

The concept of the first phase is presented in more detail in Figure 2. It is separated into five main design steps. The result of the first step gives the information about the distribution of the sufferers with diabetes type 2 (D2) in the observed population. In the next

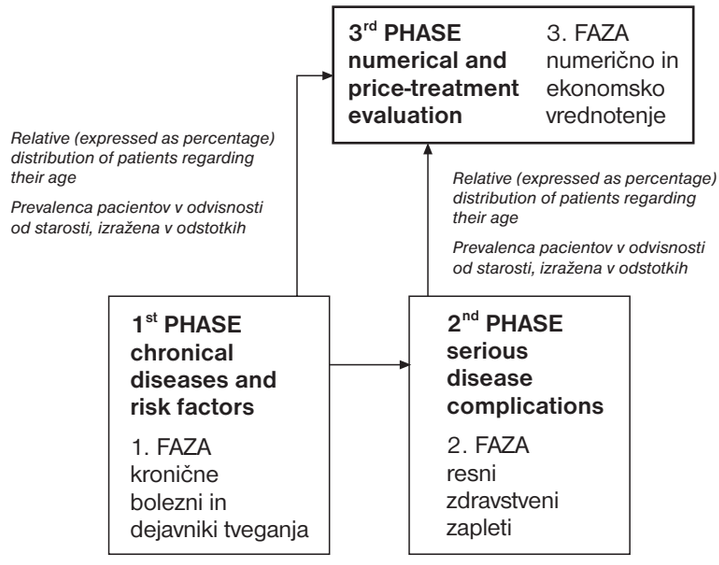

Figure 1. *The concept of the model's construction.*

Sl. 1. *Koncept izgradnje modela.*

Figure 2. *The structure of the first modelling phase.*

Sl. 2. *Struktura prve faze modeliranja.*

step the set of obese people is introduced. In the third step it is taken into account that in the observed population there is also a group of people who are smokers, while in the fourth and fifth steps the model is additionally extended to describe people with hypercholesterolemia and hypertension.

Results and discussion

The development of diabetes type 2 in the population

The distribution of diabetes type 2 (D2) has been reported by different data sources.[9,10] In,[9] for example, it is possible to find the information, presented in the third column of Table 1, where the simplifying assumption that between the ages of 0 and 24 the number of people with D2 can be neglected is introduced.

Table 1. *Data comparison from[9] and[10] regarding the prevalence of people with D2.*

Razpr. 1. *Primerjava prevalenčnih podatkov iz[9] in[10] pacientov z D2.*

Age group Starostna skupina	Age in years Starost v letih	% D2 (due to [9]) % D2 (glede na [9])	% D2 (due to [10]) % D2 (glede na [10])
1.	0–24	0	0
2.	25–29	0.8	3.5
3.	30–34	0.3	3.5
4.	35–39	1.4	4.2
5.	40–44	2.6	4.2
6.	45–49	5.4	8.9
7.	50–54	5.6	8.9
8.	55–59	10	15.5
9.	60–64	9.3	15.5
10.	65–69		19
11.	70–74		19
12.	75–79		19
13.	80–84		19
14.	85–89		20
15.	90–94		20
16.	95 and over 95 in več		20

It is evident that the data from[9] differ a good deal from those in.[10] The reason can probably be explained by the relatively small number of people investigated in.[9] This was also the reason why the data from[10] were used for modelling purposes. Regarding the last column of Table 1, it is again taken into account that the number of people with D2 up to the age of 24 is negligible, while the number between the ages of 75 and 84 is 19 % of people, and for the older population this number can be increased to 20 %.

These data indicate, of course, the people who were diagnosed with the disease. However, based on some estimations[11] there are approximately two times as many people who are not diagnosed and therefore not adequately treated. The number of people in this group is not the same for all age groups. It is probably that their number decreases with age, due to the fact that different health problems stimulate detailed analyses and the discovery of D2.

Taking into account all the data and the assumptions, a mathematical model for diabetes type 2 was developed, where the independent variable is not the group of people from the chosen time interval but the age in years, as the changes inside each group can be significant. Of course, the mean values of the percentage function from the model and the data should be as similar as possible. The prediction of the model is illustrated in Figure 3, where the curve D2NEZDRA represents the undiagnosed and, therefore, untreated sufferers, D2ZDRA is the treated sufferers, while D2 indicates all the people with diabetes type 2.

The demographic data are illustrated in Figure 4, where the population for Slovenia in 2003 for males and females is shown. By combining the two it is possible to quantify the number of observed sufferers, as presented in Figure 5, where, again, the treated (D2ZDRA) and untreated (D2NEZDRA) sufferers are shown.

In the study[12] it was estimated that the annual cost for the D2 treatment for one patient is on average € 355. This price includes all the expenses for the examinations and drug treatments (general practitioner, 4 times/year; laboratory, 2 times/year; drugs). From this the annual cost of D2 treatment in Slovenia was estimated, as shown in Figure 6, for the different ages of patients. The lower curve indicates the costs for the treated patients, while the upper line is an estimation of the increase in costs if all sufferers with D2 were to be diagnosed and, therefore, also treated.

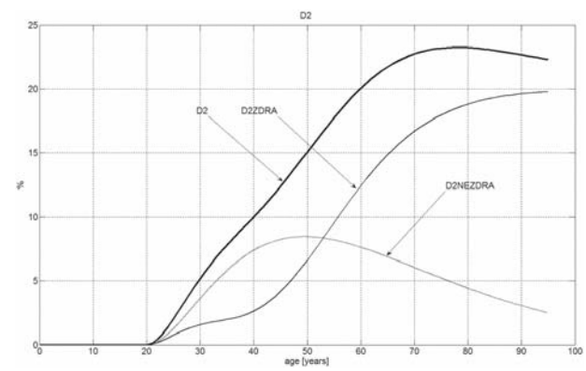

Figure 3. *Percentage distribution of D2 (D2ZDRA – diagnosed patients, D2NEZDRA – undiagnosed sufferers, D2 – all with diabetes type 2).*

Sl. 3. *Procentualna porazdelitev D2 (D2ZDRA – odkriti pacienti, D2NEZDRA – neodkriti pacienti, D2 – vsi pacienti z diabetesom tipa 2).*

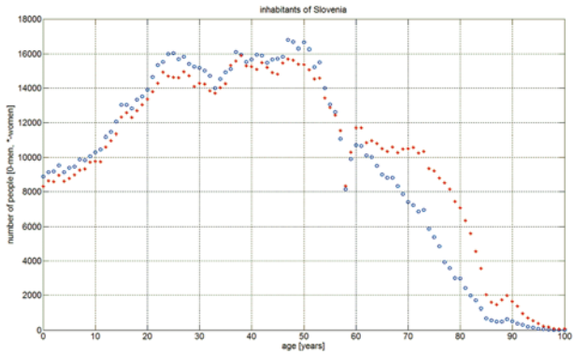

Figure 4. *Population of Slovenia in 2003 sex and age.*

Sl. 4. *Prebivalci Slovenije leta 2003, porazdeljeni po spolu in starosti.*

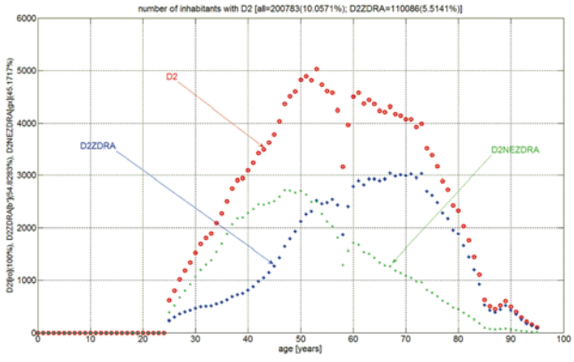

Figure 5. *Number of inhabitants in Slovenia with D2 (all) (D2ZDRA – treated and D2NEZDRA – untreated) by age.*

Sl. 5. *Število sladkornih bolnikov v Sloveniji v odvisnosti od starosti (D2 – vsi, D2ZDRA – zdravljeni, D2NEZDRA – nezdravljeni).*

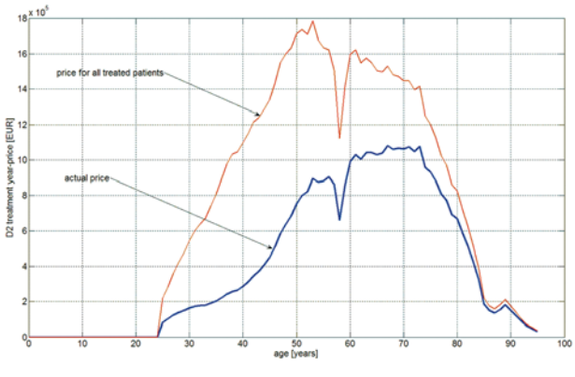

Figure 6. *D2 treatment costs in euros.*

Sl. 6. *Cena zdravljenja pacientov z D2 v €.*

On the basis of the presented results the following can be concluded:

1. In Slovenia there are around 100,000 people, or 5.5 % of the population, with diabetes type 2 (the model predicts 110,086) who are being treated.
2. Approximately 90,000 people (the model predicts 90,697), or 4.5 % of the population, are undiagnosed.
3. Approximately 200,000 people (the model predicts 200,783) or 10 % of the population have diabetes type 2.
4. Of all the D2 sufferers there are 54.83 % being treated and 45.17 % not being treated.
5. The annual cost for D2 treatment is around € 39 millions (the model predicts € 39,080,530).
6. If all the sufferers were to be diagnosed and treated, the annual cost of treatment would increase to approximately € 71 millions, which represents a cost increase of € 32 millions (the model predicts € 32,197,435).

As Slovenia can be regarded as a developed country in terms of lifestyle and nutrition,[5] it can be concluded that in similar countries the following can be expected:

1. For every 1 million people there are 5.5 % with diagnosed diabetes D2 and 4.5 % who are not diagnosed and therefore not treated.
2. The annual cost for D2 treatment is approximately € 19.5 millions per million people.
3. If all sufferers of D2 were diagnosed the annual cost would increase by € 16 millions.

Obesity

The outputs from the first step are three signals representing the following: the patients being treated for D2 (D2ZDRA); the sufferers who have not been diagnosed (D2NEZDRA); and the people without D2. These three signals are then entered into the second subsystem (Figure 2), where the observed population is further transformed into the group of people with a healthy weight and the group of people who are overweight. The outputs from this block are six signals, representing all the groups of people.

Several studies[13–15] show a significant correlation between obesity and diabetes type 2. As a measure of obesity the body mass index (BMI) is normally used.[15] In order to keep the situation simple and because the vast majority of obese people belong to that group with a BMI between 25 and 30, all the people with a BMI > 25 are regarded as a single group.

Table 2[13] shows the distribution of overweight people. It is, therefore, to be expected that 22.2 % (between the ages of 20 and 39) to 29.2 % (between the ages of 40 and 59) of the population is overweight, while over the age of 60 it is to be expected that the number decreases to an average of 24.4 % of people being described as obese. Looking at the whole population, the ratio of those classed as overweight to those with a healthy weight equals 25.3 %/74.7 % = 0.3387.

The modelling results for this design step are illustrated in Figures 7 and 8. Regarding the situation in Figure 7, it can be concluded that the group of young, obese people (PTT) is made up mainly of those without D2 (BREZD2inPTT). This situation is to be expected as D2 starts later in life than obesity. Over time the size of this group of people decreases as they begin to join the group with D2 (D2VSIinPTT). Over the age

Table 2. *Percentage distribution of the overweight and obese population and the population with a healthy weight, by age and on average.*

Razpr. 2. *Procentualna razporejenost ljudi s prekomerno in primerno telesno maso glede na starost in v povprečju.*

Age Starost	% of overweight % ljudi s prekomerno telesno maso	% of healthy weight % ljudi z zdravo telesno maso
20–39	22.2	77.8
40–59	29.2	70.8
60 and over 60 in več	24.4	75.6
Over 20 on average by age Nad 20 povprečno, glede na starost	25.3	74.7

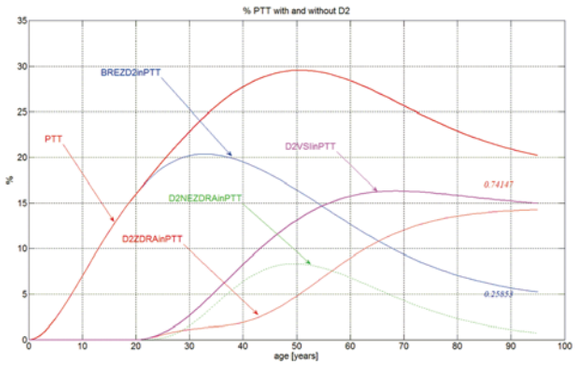

Figure 7. *Percentage distribution of obese people (PTT) with and without D2 (PTT – obese, BREZD2inPTT – obese without D2, D2VSIinPTT – obese with D2, D2ZDRAinPTT – obese with treatment for D2, D2NEZDRAinPTT – obese with untreated D2).*

Sl. 7. *Procentualna porazdelitev ljudi s prekomerno telesno težo (PTT), ki imajo oz. nimajo D2 (PTT – vsi s prekomerno telesno težo, BREZD2inPTT – brez D2 in s PTT, D2VSIinPTT – z D2 in PTT, D2ZDRAinPTT – D2 zdravljeni in s PTT, D2NEZDRAinPTT – D2 nezdravljeni in s PTT).*

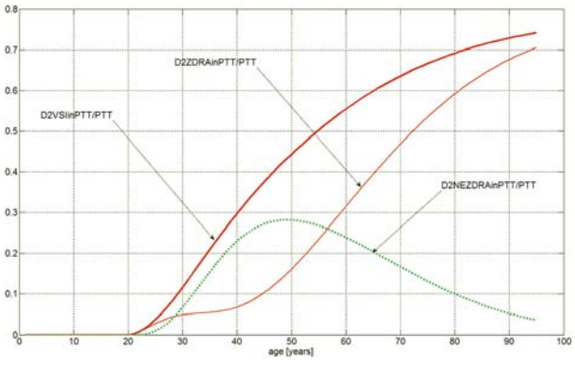

Figure 8. *The ratio of people with and without D2 for the obese population.*

Sl. 8. *Zastopanost ljudi z diabetesom 2 v skupini ljudi s prekomerno telesno maso.*

of 60 the size of group decreases due to the normalization of body weight. Between the ages of 30 and 60 the group of obese people begin to join those with diagnosed and undiagnosed D2, while later on this is true mainly for the diagnosed and, therefore, treated patients (D2ZDRAinPTT).

In Figure 8 the following ratios are illustrated: D2ZDRAinPTT/PTT represents the ratio between obese patients with treated D2 and all obese people, D2NEZDRAinPTT/PTT represents the ratio between obese people with untreated D2 and all obese people, while D2VSIinPTT/PTT represents the ratio between all the obese people with D2 and all the obese people.

Taking into account counting data (Figure 4) and the obesity-modelling results (Figure 7) the number of overweight people in Slovenia can be estimated. The results suggest that more than 400,000 people in Slovenia are overweight (the model predicts 434,681) or almost 22 % of the population.

Smoking

The model's structure is further extended with the division into the groups of smokers and non-smokers, using the data presented in Table 3.[16]

Table 3. *Percentage distribution of smokers by age and on average.*

Razpr. 3. *Procentualna porazdelitev kadilcev glede na starost in povprečno.*

Age (irrespective of sex) Starost (ne glede na spol)	% of smokers % kadilcev
18–44	24.1
45–64	21.9
65 and over 65 in več	8.6
Over 20 – balanced regarding age Nad 20 – uravnoteženo glede na starost	20.8

The structure and parameters were defined with respect to the data, while at the same time the fact that D2 is more frequently detected in the population of smokers than among people who are not smoking was taken into account.

Figures 9 and 10 show the results predicted by this modelling phase. From Figure 9 it is obvious that the group of young smokers is mainly made up of those people without D2. Later on, however, the share of D2 sufferers becomes significant. After the age of 60 the group of smokers with D2 begins to decrease due to the fact that a large number of people give up smoking when they get older. When the situation with regard to smokers is defined, the circumstances relating to non-smokers are also known.

Figure 10 shows the ratios that are informative with regard to the occurrence of D2 sufferers among the smokers and non-smokers. It is obvious that the curve r1 = smokers with D2 / smokers is, over time (in other words, age), significantly higher than r2 = non-smokers with D2 / non-smokers. The average value of the ratio r1/r2 is 1.68 between the ages of 25 and 95. The

model's responses are, therefore, a very good match for the data in,[16] where the results indicate that the risk factor among smokers is, on average, 1.68 times higher than among non-smokers (1.42 for women and 1.94 for men).

Regarding the modelling results (Figure 9) and the counting data (Figure 4) the distribution of the smoking population in Slovenia was defined. According to the modelling results there are over 340,000 people who smoke in Slovenia (the model predicts 342,941) or the group of smokers represents 17.18 % of population. In the interval between the ages of 25 and 70 the model predicts more than 23 % of smokers.

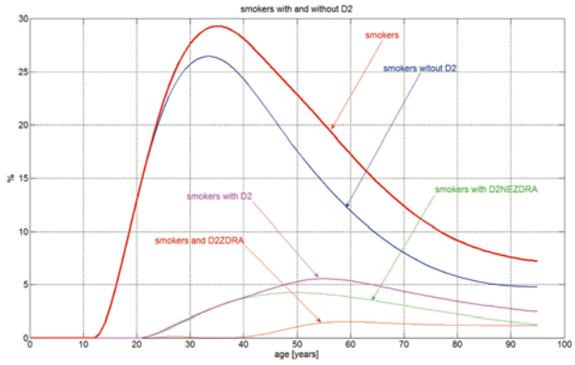

Figure 9. *Smokers with and without D2 (D2NEZDRA – untreated D2, D2ZDRA – treated D2).*

Sl. 9. *Kadilci z in brez D2 (D2NEZDRA – nezdravljen D2, D2ZDRA – zdravljen D2).*

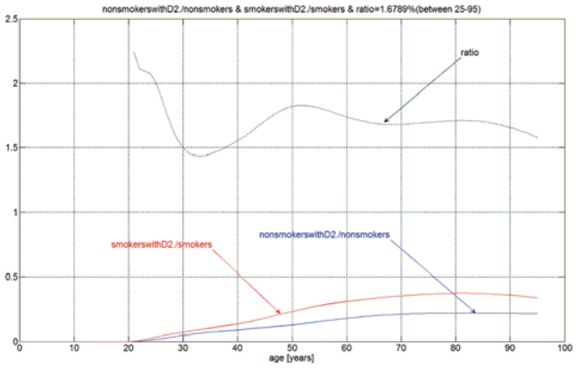

Figure 10. *Ratios: r1 = smokers with D2 / smokers, r2 = non-smokers with D2 / non-smokers, ratio = r1/r2.*

Sl. 10. *Razmerji: r1 = kadilci z D2 / kadilci, r2 = nekadilci z D2 / nekadilci, razmerje = r1 / r2.*

Hypercholesterolemia

The model was then expanded to also incorporate the people with hypercholesterolemia (H). This means that the whole population (in all its subgroups) is further divided into three groups: to those without hypercholesterolemia (BREZH), to the group with the treated disease (HZDRA) and to those sufferers who are not diagnosed and are therefore untreated (HNEZDRA). This step of the model was constructed on the basis of the data presented in Table 4.[17, 18]

Table 4. *Percentage of people with hypercholesterolemia with regard to age and concomitant D2.*

Razpr. 4. *Procentualna razporeditev pacientov z dislipidemijo glede na starost in procentualna razporeditev pacientov, ki imajo hkrati H in D2.*

Age (men and women in average)	% of people with hypercholesterolemia	% of people with hypercholesterolemia and D2
Starost (moški in ženske povprečno)	% ljudi z dislipidemijo	% ljudi, ki imajo hkrati dislipidemijo in D2
18–24	9.3	44.1
25–34	17.2	44.1
35–44	26.5	44.1
45–54	37.7	59.7
55–64	50.3	59.7
65–74	50.6	58.7
75 and over 75 in več	50.6	53.5

During modelling the following simplifying assumptions were taken into account:

- when one of the observed diseases is discovered, this stimulates a more detailed examination of the patient and, consequently, other diseases are also diagnosed and are therefore treated,
- all the people with D2 who are not treated also develop hypercholesterolemia.

The modelling results are illustrated in Figures 11 and 12. Figure 11 shows the patients with hypercholesterolemia (H) as well as the sufferers (HNEZDRA) and treated patients (HZDRA). In Figure 12 it is possible to observe those who also have D2 and hypercholesterolemia (D2andH), with the distinction among those who are treated (D2andHZDRA) and those who are not (D2andHNEZDRA).

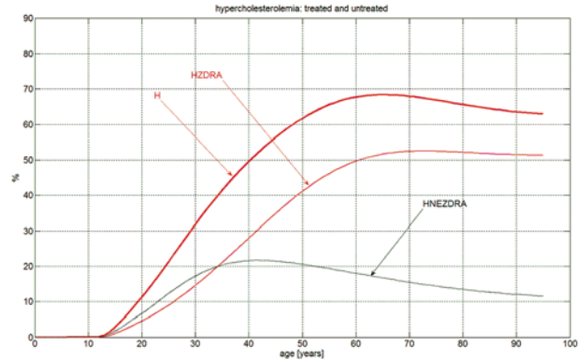

Figure 11. *Hypercholesterolemia (H), diagnosed and, consequently, treated (HZDRA), untreated (HNEZDRA).*

Sl. 11. *Dislipidemija (H), odkriti in zdravljeni (HZDRA), neodkriti in nezdravljeni (HNEZDRA).*

Taking into account the situation in Figures 11 and 4 the number of treated and untreated sufferers with hypercholesterolemia can be calculated as presented in Figure 13. The annual cost for treating this disease

is € 313[12] (general practitioner, 4 times/year; laboratory, 2 times/year; drugs). Figure 14 shows the annual cost for treating this disease with regard to the age of the sufferer.

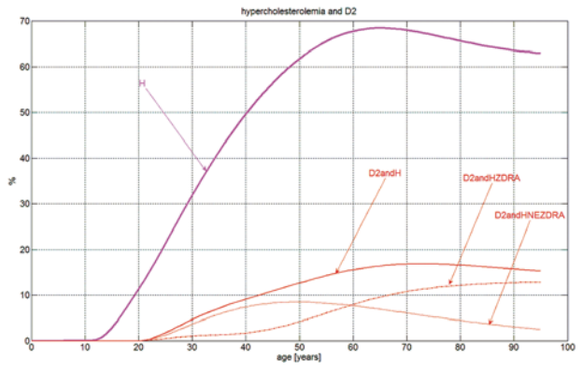

Figure 12. *D2 in combination with hypercholesterolemia (D2andH) (D2andHZDRA – treated, D2andHNEZDRA – untreated).*

Sl. 12. *Pacienti, ki imajo hkrati D2 in dislipidemijo (D2andH) (D2andHZDRA – zdravljeni, D2andHNEZDRA – nezdravljeni).*

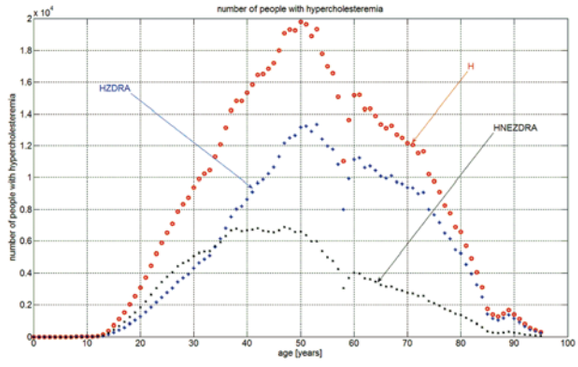

Figure 13. *Number of people with hypercholesterolemia (H) in Slovenia (treated – HZDRA, undiagnosed and untreated – HNEZDRA, and all – H).*

Sl. 13. *Število pacientov z dislipidemijo (H)v Sloveniji (zdravljeni – HZDRA, neodkriti in nezdravljeni – HNEZDRA, vsi – H).*

On the basis of the presented results the following can be concluded:

1. In Slovenia there are over 500,000 treated sufferers (the model predicts 525,632) with hypercholesterolemia, which means 26.33 % of the population.
2. The number of undiagnosed sufferers exceeds 280,000 (the model predicts 280,168 prediction), which means 14.03 % of the population of Slovenia.
3. Over 40 % of the population, or over 800,000 people, are, therefore, suffering with hypercholesterolemia.
4. The annual cost for treating this disease in Slovenia is over € 160 m (the model predicts € 164,522,816).

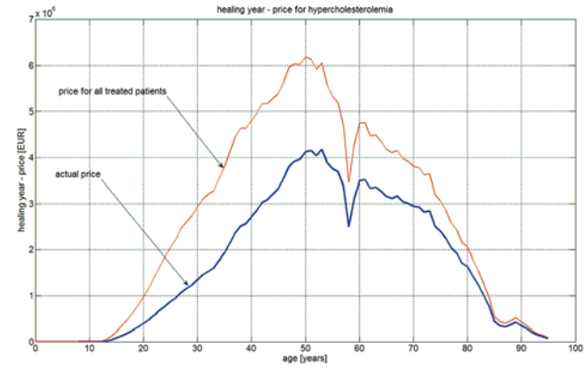

Figure 14. *Annual treatment costs for sufferers of hypercholesterolemia (diagnosed – lower curve, all – upper curve).*

Sl. 14. *Letna cena zdravljenja pacientov z dislipidemijo (odkritih pacientov – spodnja krivulja, vseh – zgornja krivulja).*

5. For the case of all the sufferers being diagnosed and treated the cost would increase by 53.3 % (the model predicts a total of € 252,215,400).

Therefore, in developed regions the following can be expected:

1. 40 % of the population are suffering from hypercholesterolemia,
2. 26 % are diagnosed and are receiving treatment,
3. an annual cost of € 82 m per one million people can be anticipated,
4. for the case of all the sufferers being diagnosed and treated, the treatment cost would increase by € 44 m per one million people.

Hypertension

The first modelling phase was completed by a further separation of the observed population, taking into account hypertension. Again, a distinction was made between people who are diagnosed and treated (TZDRA) and those who are not being treated (TNEZDRA). These two groups form the group of people with hypertension (T), while the others are not suffering from hypertension (BREZT).

The assumption was made that when one of the observed diseases is diagnosed, so are the others, and that smoking and an increased body mass are not treated and are taken into account.

For modelling purposes the data as presented in Table 5[19] were used. These data report the percentage of diagnosed sufferers with hypertension. It is estimated that in Slovenia there is an additional, approximately 20 % of people with undiagnosed hypertension. Taking into account this assumption and the fact that their number is decreasing with the sufferers' age, this group was included in the model.

The results of this modelling step are illustrated in Figures 15 to 19. In Figure 15 the people with hypertension (T) are presented with regard to their age. This group consists of those patients who are discovered and are therefore treated (TZDRA) and of those who are not treated because they are not diagnosed

Table 5. *Percentage of people with hypertension with regard to age.*

Razpr. 5. *Procentualna razporeditev ljudi s hipertenzijo glede na starost.*

Age Starost	% of men % moških	% of women % žensk	% in average % povprečno
16–24	10.6	1.5	6.05
25–34	13.6	4.9	9.25
35–44	21.3	10.4	15.85
45–54	36.7	24.3	30.5
55–64	53.2	48.2	50.7
65–74	66.6	67.3	66.95
75 and more 75 in več	66.7	76.6	71.65

(TNEZDRA). The presented curves match the source data very well. Figure 15 also shows the situation with regard to diabetes type 2. All the patients with D2 (D2), the set of patients with D2 and hypertension (D2andT) and those who have hypertension but not diabetes type 2 (BREZD2inT) are shown. In Figure 16 the following ratios are illustrated:

r1=D2inT/D2VSI [solid line]
r2=(D2inT/D2VSI)/(BREZD2inT) [dotted line]

It is evident that among patients with diabetes, hypertension is approximately two times more frequent than among the healthy population.
Finally, also the time-varying ratios of treated hypertension patients / all with hypertension and untreated sufferers / all with hypertension were defined as shown in Figure 17. It is evident that at the beginning the group of undiagnosed and untreated sufferers is greater, but with time the sufferers are discovered directly or indirectly because of other health problems.

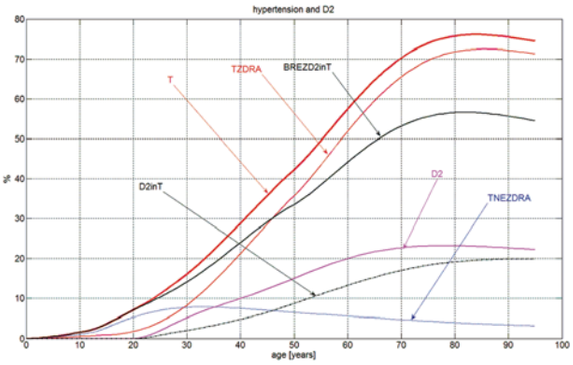

Figure 15. *Percentage of patients with hypertension and with combination of T and D2 regard to age (T – all with hypertension, TZDRA – treated patients with hypertension, TNEZDRA – untreated sufferers with hypertension, BREZT – people without hypertension, BREZD2inT – people without D2 and with T, D2inT – people with D2 and T).*

Sl. 15. *Prevalenca pacientov s hipertenzijo in kombinacijo T in D2 glede na starost (T – vsi hipertoniki, TZDRA – zdravljeni hipertoniki, TNEZDRA – nezdravljeni hipertoniki, BREZT – ljudje brez hipertenzije, BREZD2inT – ljudje brez D2 in s T, D2inT – ljudje z D2 in s T).*

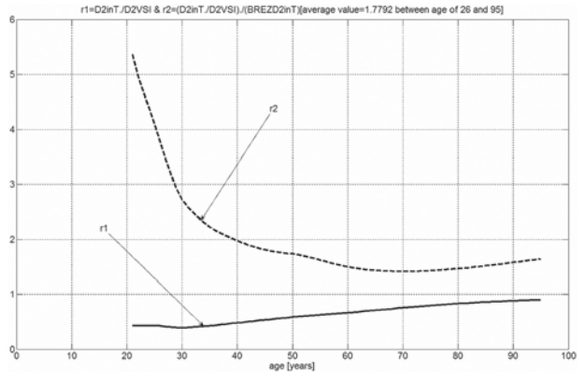

Figure 16. *Hypertension and D2 – ratios: r1=D2inT/D2VSI and r2=D2inT/D2VSI)/(BREZD2inT).*

Sl. 16. *Hipertenzija in D2 – razmerja: r1=D2inT/D2VSI in r2=D2inT/D2VSI)/(BREZD2inT).*

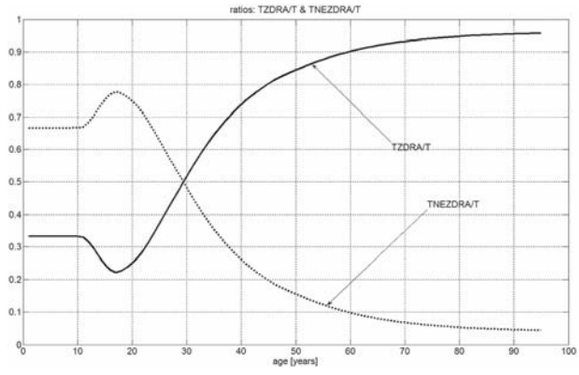

Figure 17. *The ratios of treated and untreated sufferers with hypertension, for all sufferers of hypertension.*

Sl. 17. *Razmerji zdravljenih in nezdravljenih pacientov s hipertenzijo glede na vse hipertonike.*

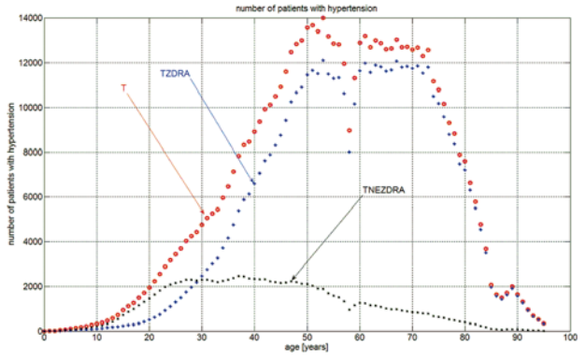

Figure 18. *Number of sufferers with hypertension in Slovenia (treated – TZDRA, undiagnosed and untreated – TNEZDRA, all – T).*

Sl. 18. *Število pacientov s hipertenzijo v Sloveniji (zdravljeni – TZDRA, neodkriti in nezdravljeni – TNEZDRA, vsi – T).*

The mean value of the population with hypertension is 31.14 %, according to the model forecast.

Using the information as presented in Figures 15 and 4, the number of treated and untreated sufferers with hypertension can be calculated, as illustrated in Figure 18.

The estimated average annual cost for hypertension treatment is € 271 per person[12] (general practitioner, 4 times/year; laboratory, once/year; drugs). On the basis of this data it is possible to calculate of the annual cost of hypertension treatment in Slovenia, as illustrated in Figure 19.

On the basis of presented results the following can be concluded:

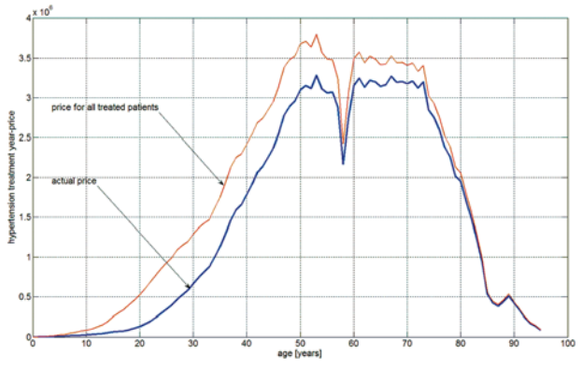

Figure 19. *Annual cost for hypertension treatment with regard to age (actual cost – lower curve, total cost for the case of treating all sufferers – upper curve).*

Sl. 19. *Letna cena zdravljenja hipertenzije glede na starost pacientov (dejanska cena – spodnja krivulja, cena zdravljenja vseh pacientov – zgornja krivulja).*

1. In Slovenia there are over 500,000 patients with hypertension (the model predicts 513,561) being treated; the mean value in therefore 25.7 %.
2. Over 108,000 sufferers, or 5.4 % of the population are undiagnosed, and are therefore untreated.
3. A total of 31 % of the population of Slovenia is hypertonic, which means over 600,000 sufferers (the model predicts 621,695).
4. The annual cost of hypertension treatment in Slovenia is over € 139 millions (the model predicts € 139,175,031).
5. For the case of all the sufferers being diagnosed the cost would increase to € 168 m (the model predicts € 168,479,345), which means a 21 % increase.

In developed countries the following can be expected:

1. over 30 % of the population have hypertension,
2. the diagnosed and treated are 25 to 26 %,
3. an annual cost of € 69.5 m for a population of million people can be expected,
4. for the case of all sufferers being diagnosed the annual cost for hypertension treatment would increase by € 14.5 m per million people.

Conclusions

Recent estimates suggest that 195 million people throughout the world have diabetes and that this number will increase to 330, maybe even to 500 million, by 2030.[20] The prevalence of type 2 diabetes increases with age, especially in Europe.[21] The most common cause of death in European adults with diabetes is coronary artery disease. Several studies have demonstrated that D2 increases a risk for two to three times in comparison with people without diabetes.[22] In combination with other chronic diseases, like hypertension and hypercholesterolemia, and risk factors, like obesity and smoking, the development of other serious health complication can also be expected (stroke, coronary heart disease, end-stage renal disease and congestive heart failure). Such a range of epidemic chronic diseases indicates that they have become (in a direct and indirect manner) significant social and economic burdens, important for governments, hospitals, health-insurance companies and, regarding educational programs, for the whole population. In many countries (especially smaller) national registers for such health problems do not exist (or are available only for some diseases). So expectations have to be estimated with regard to epidemiological statistical data.

In this paper the results of nonlinear, dynamic, mathematical modelling are presented, which make it possible to track sufferers with diabetes type 2, hypercholesterolemia, hypertension, overweight people and smokers. Also, all possible combinations were taken into account, which means that the output of the last block of the first design phase consists of 108 time signals for each observed group. A complete mathematical description is given in Appendix.[23]

These groups are presented with regard to age and percentage. The obtained information was used as a direct input to the third modelling phase, where it was combined with demographic data and with the estimated treatment costs. From this the number of sufferers and patients the economic burden were also derived for Slovenia and other developed countries. The modelling results are summarized in Tables 8 and 9.

From the presented results it is obvious that the number of patients with chronic diseases and risk factors is very large. The situation should in fact be treated as an epidemic, especially when we realise that the trends suggest an even worse situation in the future. In spite of the fact that obesity and smoking were, in this study, not evaluated as an economic burden (the potential treatment costs for these two risk factors were not included) the treatment cost per year for the observed chronic diseases is estimated to be € 491 m. In the case where all sufferers were to be diagnosed (i.e., a more systematic examination) and therefore also correspondingly treated, this economic burden would initially increase by an additional € 148 m. But as mentioned, diseases and risk factors are strongly correlated with the potential development of a stroke, coronary heart disease, peripheral arterial-vascular disease, end-stage renal disease and congestive heart failure, and so such an investment could be justified from the economic point of view. The treatment costs for these complications are significantly higher than the treatment costs of initial diseases.

Table 8. *Number of sufferers, patients and the annual treatment cost in Slovenia.*

Razpr. 8. *Število bolnikov (neodkritih in odkritih) in letna cena zdravljenja v Sloveniji.*

Disease or risk factor and annual treatment cost for one patient	Number of diagnosed sufferers in SLO	Treatment annual cost (€) for diagnosed patients in SLO	Number of undiagnosed sufferers in SLO	Treatment annual cost in SLO for all patients (€)	Cost increase in the case that all sufferers were to be treated (€)
Letna cena zdravljenja za enega pacienta za posamezno bolezen ali dejavnik tveganja	Število diagnosticiranih bolnikov v SLO	Letna cena zdravljenja (€) odkritih bolnikov v SLO	Število nediagnosticiranih bolnikov v SLO	Letna cena zdravljenja v SLO za vse bolnike (€)	Povečanje letne cene zdravljenja za primer, če bi bili odkriti vsi bolniki (€)
D2 (€ 355)	over / preko 110,000	over / preko 39 m	over / preko 90,000	over / preko 71 m	over / preko 32 m
Obese population Populacija s prekomerno telesno maso	over / preko 430,000	/	/	/	/
Smokers Kadilci	over / preko 342,000	/	/	/	/
Hypercholesterolemia Dislipidemija (€ 313)	over / preko 525,000	over / preko 164 m	over / preko 280,000	over / preko 252 m	over / preko 87 m
Hypertension Hipertenzija (€ 271)	over / preko 513,561	over / preko 139 m	over / preko 108,000	over / preko 168 m	over / preko 29 m

Table 9. *Percentage of sufferers, patients and treatment cost in a population of a million people in developed regions.*

Razpr. 9. *Procentualna zastopanost opazovanih pacientov in cena zdravljenja na milijon prebivalcev v razvitih območjih.*

Disease or risk factor and annual treatment cost for one patient	% of diagnosed sufferers	Treatment annual cost (€) for diagnosed patients	% of undiagnosed sufferers	Treatment annual cost for all sufferers (€)	Cost increase in the case that all sufferers were to be treated (€)
Letna cena zdravljenja za enega pacienta za posamezno bolezen ali dejavnik tveganja	% diagnosticiranih bolnikov	Letna cena zdravljenja (€) odkritih bolnikov	% neodkritih bolnikov	Letna cena zdravljenja za vse bolnike (€)	Povečanje letne cene zdravljenja za primer, če bi bili odkriti vsi bolniki (€)
D2 (€ 355)	5.5 %	19.5 m	4.5 %	35.5 m	16 m
Obese population Populacija s prekomerno telesno maso	22 %	/	/	/	/
Smokers Kadilci	17.2 % (23 % between the age of 25 and 70) (23 % v starosti med 25 in 70)	/	/	/	/
Hypercholesterolemia Dislipidemija (€ 313)	26.33 %	82 m	14 %	126 m	44 m
Hypertension Hipertenzija (€ 271)	25.7 %	69.5 m	5.4 %	8.4 m	14.5 m

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