DISEASES AND FACTORS OF RISK MODELLING REGARDING THE DEVELOPMENT OF STROKE

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Abstract

In the paper simulation results of developed dynamical mathematical model are presented enabling the observation of different diseases and risk factors which are strongly correlated with a potential development of serious disease complications. Proposed model structure enables sequential model construction, relative observation of risk factors and diseases development (independent of the number of people in the concrete country) but can also be applied to specific data (population) taking into account age-distribution at the observed area. The first modelling phase includes the development of five different groups of patients with diabetes type 2, obesity, smoking, hypercholesterolemia and hypertension where also all possible combinations were taken into account. In the second design phase serious complications are observed between which stroke is presented in the paper while the influence to coronary heart disease, peripheral arterial-vascular disease, end-stage renal disease and congestive heart failure are still under investigation. Modelling results of the first and second phase were transferred to the third design phase where they were used for quantitative evaluation of circumstances in Slovenia and developed regions. In this stage we have added also the information of treatment prices regarding each observed disease to enable the observation of healing effect to overall treatment outgoings. From presented results it can be concluded that efficient treatment of the first phase diseases can prevent a great number of serious complications which in addition means also lower overall treatment price.

Keywords: Diabetes type 2, Hypercholesterolemia, Hypertension, Risk factors, Stroke.

Presenting Author's biography

Maja Atanasijević-Kunc. She received B.Sc., M. Sc. and Ph. D. degrees from the Faculty of Electrical Engineering, University of Ljubljana, Slovenia where she is currently assistant professor. Her research interests include modelling and simulation of dynamical systems and control systems analysis and design, specially of MIMO-systems.

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1 Introduction

When developing model it is very important to take into account the purpose of model usage, data reliability on the basis of which it is constructed, mathematical correctness of its interpretation, manipulation suitability and possibility of results evaluation. These were the reasons which motivated us to develop the model structure in such manner that it would enable sequential adding of each phenomena in the whole observed population while the evaluation of model results were compared with different data sources.

The concept used regarding model development is illustrated in Fig. 1 where also all three modelling phases are indicated.

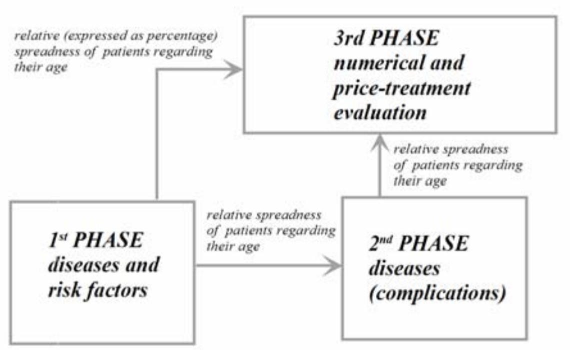

Fig. 1 The concept of model building

The first phase of modelling enables the observation of mentioned diseases and risk factors in percentage by age of the patients, the relations between the observed groups of patients and their possible overlapping. These results can further be used for prediction of more serious complications. In the paper the influence to stroke is presented and evaluated in details. Outputs from the first and the second modelling phase can also present an input data for estimation of extensiveness of observed groups of people taking into account the chosen geographical area. In our case the results are evaluated for Slovenia and developed regions where age distribution and percentage disease-distribution is similar [23]. This part of results was calculated inside the third design-phase, where also the price-evaluation of suitable disease treatment was realized.

We have to point out that all modelling and simulation was realized inside programme package Matlab [1] and Simulink [2].

2 First modelling phase

In the first modelling phase the development of diabetes type 2, obesity, smoking, hypercholesterolemia and hypertension are included. They were designed as cascaded dynamical subsystems where the first one represents the group of patients with diabetes type 2 (D2).

The spreadness of D2 is reported by different data sources (like [4-6]), where the information is presented in percentage regarding age groups, typically aggregated for five to 10 years. This data indicates of course the people where disease was discovered. But due to some estimations [6] there is approximately two times as much patients who are not discovered and therefore also not adequately treated. The number of this group of patients is not equal in all age sets. It can be expected that their number decreases with age due to the fact that different health-problems stimulates detailed analysis and discovers also D2. It can be taken into account that the number of undiscovered D2 patients after the age of 50 begins to decrease distinctly.

Taking into account all mentioned data and presumptions the mathematical model of diabetes type 2 was developed where independent variable is not the group of people from the chosen time interval but time in years as also the changes inside each group can be significant. Of course mean values of percentage function from the model and data should be as similar as possible. Model prediction is illustrated in Fig.2 where the curve D2NEZDRA represents undiscovered and therefore untreated patients, D2ZDRA treated patients, while D2 indicates all patients with diabetes type 2.

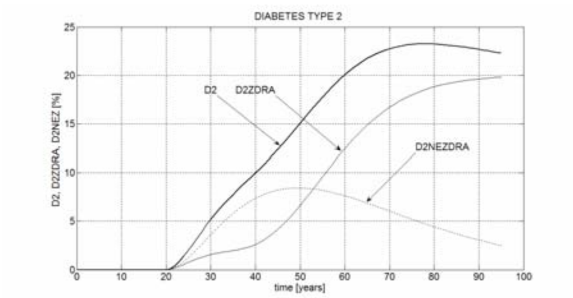

Fig. 2 Percentage distribution of diabetes type 2 (D2ZDRA – discovered patients, D2NEZDRA – undiscovered patients, D2 – all with diabetes type 2)

In the second subsystem the observed population is further divided into the group of people with healthy weight and overweighed one. Several studies [7-9] show a significant correlation between obesity and D2. As a measure of obesity the body mass index (BMI) is usually used [10]. For simplification purposes all with BMI>25 are regarded as a single set. Modelling results of this design step are illustrated in Fig. 3.

Regarding the situation in Fig. 3 it is possible to conclude that to the group of obese people (PTT) in youth contribute mainly those without D2 (BREZD2andPTT). This situation could be expected as D2 starts later as obesity. Through the time this group of people is decreasing as they partly passing to the group with D2 (D2andPTT). After the age of 60 the group is decreasing mainly due to the normalization of body weight.

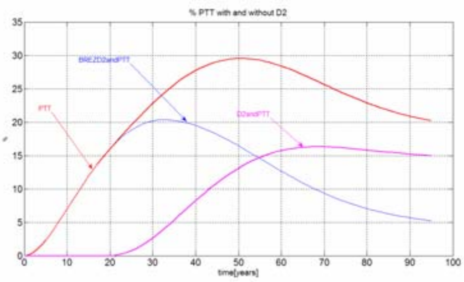

Fig. 3 Percentage distribution of obese people with and without diabetes type 2

In the next modelling step observed groups were further divided into the set of smokers and unsmokers by using the data presented in [11]. The structure and parameters were defined regarding mentioned data while in the same time we have taken into account the fact that diabetes type 2 is more frequently detected between smokers as between people who are not smoking.

In Fig. 4 it is possible to observe the results which are predicted by this modelling step. It is obvious that to the group of smokers in youth mainly contribute those without D2. Later on also the contribution of D2-patients becomes significant. After the age of 60 the group of smokers with D2 is decreasing due to the fact that a great number of people is giving up smoking when they are older. When the situation regarding smokers is defined also the circumstances between unsmokers are known.

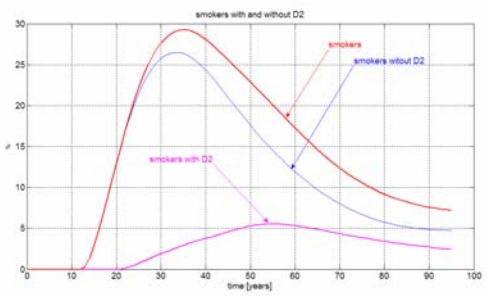

Fig. 4 Percentage distribution of smokers with and without diabetes type 2

In the fourth step of the first modelling phase the patients with hypercholesterolemia were incorporated. That means that entire population (all its subsets) is further divided into three groups, to those without hypercholesterolemia (BREZH), to the group with healed disease (HZDRA) and to those patients who are not discovered and are therefore unhealed (HNEZDRA). This model step was constructed on the basis of data presented in [13] and [14]. During modelling the following simplification assumptions were taken into account:

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

Modelling results are illustrated in Fig. 5 where we distinguish between healed (HZDRA) and undiscovered (HNEZDRA) patients.

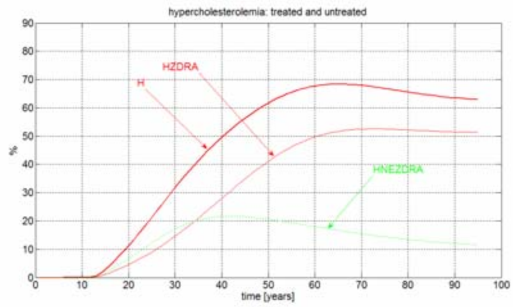

Fig. 5 Percentage distribution of the patients with hypercholesterolemia

The first modelling phase was completed by further separation taking into account also the hypertension. Again we are distinguishing the patients where disease is discovered and treated (TZDRA) and those who are unhealed (TNEZDRA). These two groups form the set of patients with hypertension (T), while others are without hypertension.

Again we have taken into account the assumption that when one of the observed diseases is discovered also the others are. We are also supposing that smoking and unhealthy body mass are not healed. For modelling purposes the data in [15] were taken into account. These data report of course percentage of discovered patients with hypertension. We have estimated that in Slovenia there is in addition approximately 30% of undiscovered patients. Taking into account this estimation and the fact that their number is decreasing regarding the patients' age, also this group was added to modeling results as are illustrated in Fig. 6 where the patients with hypertension (T) are presented regarding the age. This group consists of those patients who are discovered and therefore treated (TZDRA) and of those who are not treated because they are not discovered (TNEZDRA). It is possible to find out, that presented curves match very good with source data. On the basis of modelling results it is evident that between the patients with diabetes the hypertension is approximately two times more frequent as between the healthy population.

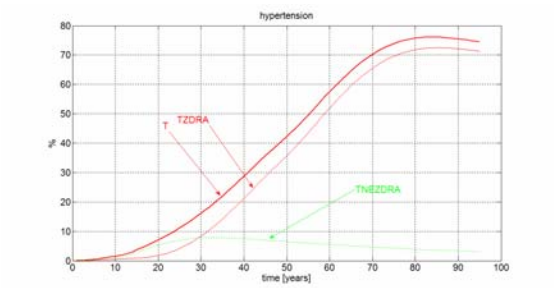

Fig. 6 Percentage distribution of the patients with hypertension

3 Second modelling phase

The second modelling phase is devoted to serious health complications. In the paper simulation results regarding stroke are presented while a development of coronary heart disease, peripheral arterial-vascular disease, end-stage renal disease and congestive heart failure are still under investigation.

Modelling procedure based on data as are presented in Tab. 1 [16]. In addition we have taken into account that regarding described risk factors and diseases the most important is hypertension as 77% of patients with stroke have also high blood presure [17]. It is also reported [18,19] that stroke is 2 to 6 times more frequent among the patients with hypertension. Efficient hypertension treatment during longer period can decrease the risk up to 33%.

For development of stroke also diabetes type 2 is important. It was reported [20] that the risk factor for stroke is 2.5 times higher between the people with D2 as between healthy population. Also hypercholesterolemia has important influence to development of described complicatin but efficiant treatment can decrease the probability to sicken up to 22% [21]. The risk is also 2-4 times higher among the smokers and 2 times higher between obese populatin.

Taken into account all mentioned data the dynamical, nonlinear, time-varying model was developed where inputs consist of 108 signals from previous design phase. Percentage distribution of patients with stroke is illustrated in Fig. 7 which prooves very good matching with reported data.

As this group of patients was constructed from the whole observed population also the combination regarding mentioned risk factors can be observed.

In Figs. 8 and 9 relations between stroke and D2 are illustrated.

Tab. 1 Percentage of population with stroke regarding the oldness

oldness	stroke [%]
20-34	0.35
35-44	0.95
45-54	1.65
55-64	3.0
65-69	6.4
70-74	6.4
75-79	12.0
80-85	12.0
85 and more	12.0

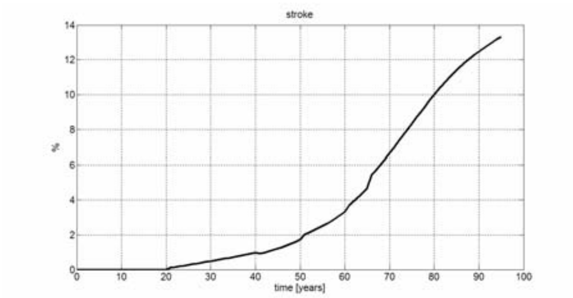

Fig. 7 Percentage distribution of the patients with stroke due to model prediction

In Fig. 8 the population with stroke (MK) is presented in comparison with the people with D2, where it is possible to differ between treated (D2ZDRA) and untreated (D2NEZDRA) patients. In the same figure also the groups of patients are presented who have in the same time both diseases (D2andMK), where again we differ between those where D2 is discovered (D2ZDRAandMK) and those where it isn't (D2NEZDRAandMK).

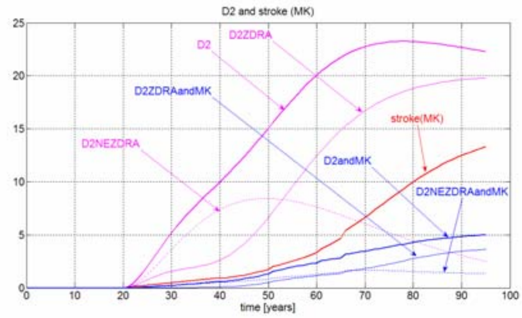

Fig. 8 Percentage distribution of the patients with D2 and stroke and the combination of both diseases

In Fig. 9 two time-varying ratios are presented which are illustrating the fact that between healthy population (r1=BREZD2inMK/BREZD2) the stroke is significantly less frequent while in the group of patients with D2 (r2=D2inMK/D2). Here of course treated and untreated D2-patiens are taken into consideration.

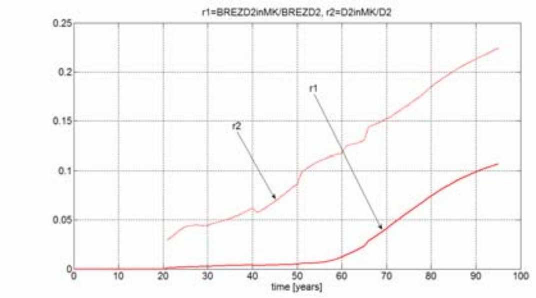

Fig. 9 The ratios: r1=BREZD2inMK/BREZD2,

r2=D2inMK/D2

In the time range between the age of 70 and 95 the average value of r2/r1 is 2.6 which is in a good agreement regarding statistical data.

The influence of the next observed risk, that is obesity, is presented in Figs. 10 and 11. In Fig. 10 percentage value of population with stroke regarding the oldness is presented where we differ those who are obese (PTTandMK) and those with healty weight (NTTandMK). After the age of 65 the obese group becomes smaller. The reason lies in the fact that the number of people with healthy weight is significanly greater.

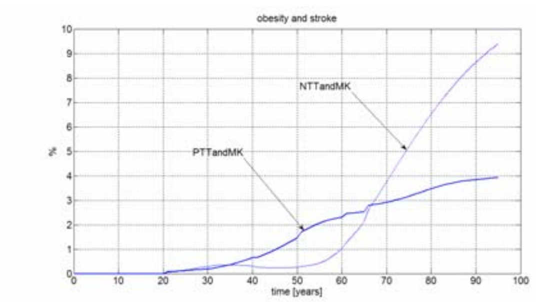

Fig. 10 Obesity and stroke (PTTandMK – obese and stroke; NTTandMK – healthy weight and stroke)

Observing the situation in Fig. 11 it is possible to conclude that in the whole life the frequency of stroke is much higher between the obese population (r1=PTTandMK/PTT) in comparison with the healthy weighted population (r2=NTTandMK/NTT).

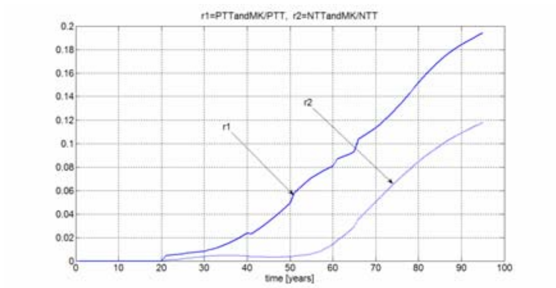

Fig. 11 The ratios: r1 = PTTandMK / PTT, r2 = NTTandMK / NTT

The next risk factor – smoking is illustrated in Figs. 12 and 13. In Fig. 12 it is possible to observe two curves representing smokers with stroke an unsmokers with stroke.

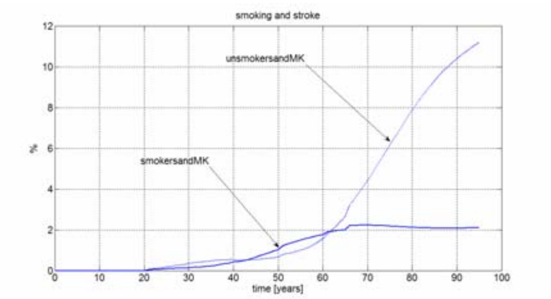

Fig. 12 Smokers and unsmokers with stroke

Again the group of unsmokers with stroke is after the age of 60 greater due to the fact that the number of smokers is significantly smaller in comparison with the people who are not smoking. But if we observe the ratios presented in Fig. 13 it is evident that between smokers the frequency of stroke is much higher.

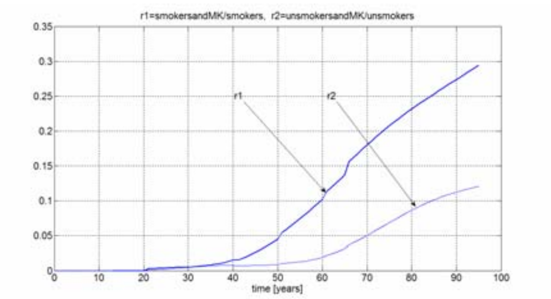

Fig. 13 The ratios: r1 = smokersandMK / smokers,

r2=unsmokersandMK / unsmokers

Important influence to development of stroke has also hypercholesterolemia. Combination of both diseases is presented in Fig. 14, where the curve HZDRAandMK indicates the patients with treated hypercholesterolemia and stroke, while the curve

HNEZDRAandMK represents the patients with stroke where hypercholesterolemia was not discovered. The sum of both functiones is marked with HandMK.

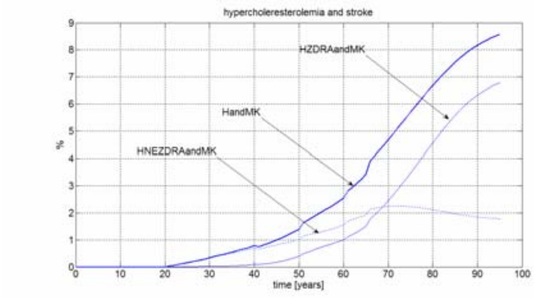

Fig. 14 Hypercholesterolemia and stroke (HandMK)

Finally we are presenting also the combination of stroke and hypertension which is illustrated in Figs. 15 and 16. In Fig. 15 we again differ between the patients with treated hypertension (TZDRAandMK) and those with undiscovered disease (TNEZDRAandMK), while TandMK indicates the sum of both groups.

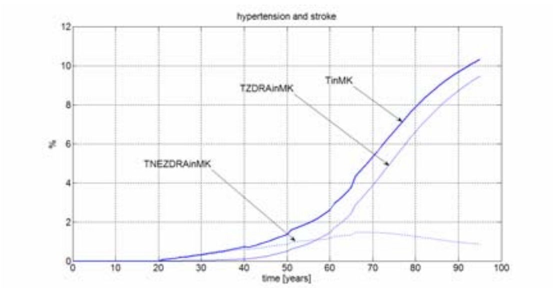

Fig. 15 Hypertension and stroke (TandMK)

(TZDRAandMK - treated hypertension and stroke, TNEZDRAandMK – undiscovered hypertension and stroke)

In Fig. 16 the following ratio is presented: TandMK/MK, that is the group of people with hypertension and stroke against all with stroke. From this it is also obvious that model predicts the average value of this ratio to be 78% between the age of 35 to 95, which is practicaly identical to statistical data.

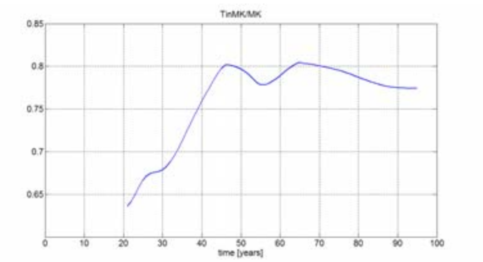

Fig. 16 The ratio TandMK /MK

4 Third modelling phase

The goal of the last design phase was to evaluate quantitatively the distribution of observed patients. For this we have used the last counting data in Slovenia (from 2003) as are presented in Fig. 17.

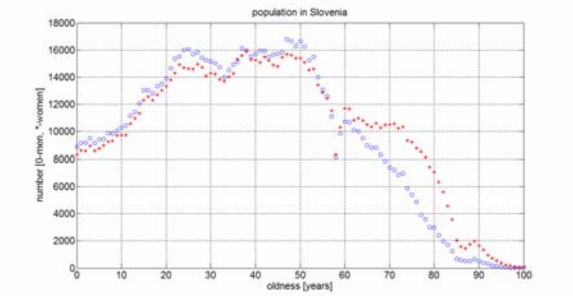

Fig. 17 Population counting results in Slovenia in 2003

Taking into account these data and modelling results presented in Fig. 2 the distribution of D2 patients in Slovenia was calculated as is illustrated in Fig. 18, where it is possible to observe the distribution of treated patients (D2ZDRA), undiscovered patients (D2NEZDRA) and the sum of both functions (D2).

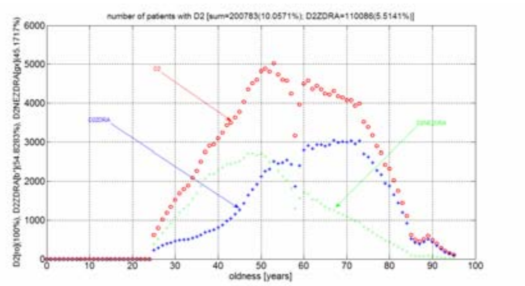

Fig. 18 Number of patients with D2 in Slovenia regarding their oldness

We have also estimated that an average treatment year price for one patient is 355 euro [22]. So the year treatment price for the whole country can be presented as is illustrated in Fig. 19, where the lower curve represents the actual treatment price, while the upper represents the situation where all D2 patients would be discovered and therefore also suitable healed. From this it can be concluded that in Slovnia we have approximately 110 000 D2 patients who are discovered. The treatment year price is approximately 39 millions euro. If all patients with D2 would be discovered this would represent an increase of 32 millions euro.

Fig. 19 Year price for D2/healing in Slovenia

Slovenia can be, regarding [23] classified as developed country. This means that on the basis of modelling results for such regions can be expected, that:

1. in 1 million population group there are 5.5% patients with treated D2 and 4.5% who are undiscovered and unhealed,

2. year-price of D2-treatment inside this population is approximately 19.5 millions euro;

3. if all patients with D2 would be discovered the year-price would be increased for 16 millions euro.

In the similar manner also the number of the patients with hypercholesterolemia and hypertension can be evaluated [3] for whom we have estimated [3,22] that year treatment prices for one patient are 313 euro (for hypercholesterolemia) and 271 euro (for hypertension).

From this it can be concluded that in Slovenia we have over 525 000 patients with discovered hypercholesterolemia and over 280 000 undiscovered patients. Year treatment price for this disease is over 164 millions euro. If all patients would be discovered and healed the price would be increased to over 252 millions euro. In developed regions therefore the following can be expected:

1. 40% of population belongs to the patients with hypercholesterolemia;

2. 26% are discovered and therefore treated patients,

3. which means the year-price of 82 millions euro per one millon of patients;

4. if all patients would be discovered and treated healing year-price would be increased for 44 millions euro per one million people.

Regarding hypertension it is expected that in Slovenia we have over 513 000 discovered and arround 108000 undiscovered patients, which means year price for healing around 139 millions euro. In the case of all discovered patiens this price would be increased to over 168 millions euro. In developed countries the following can be expected:

1. there are over 30% of patients with hypertension,

2. discovered and treated are 25 to 26%,

3. which means year-price of 69.5 millions euro for the population of million people;

4. if all the patients would be discovered year-price for hypertension treatment would be increased for 14.5 millions euro per million people.

Let us present now also the situation regarding observed complication, that is stroke. Taking into account Slovene population as is presented in Fig. 17 and modelling prediction in Fig. 7 the spreadness of the patients with stroke regarding their age can be presented as is illustrated in Fig. 20.

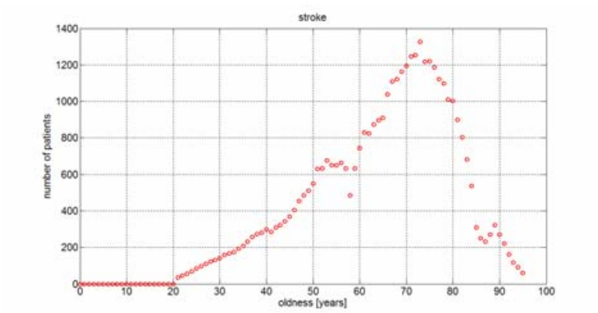

Fig. 20 Number of patients with stroke in Slovenia

As year price for treatment of stroke is in average for one patient 12.341 euro [22], price distribution can be defined as is presented in Fig. 21.

Fig. 21 Price of stroke treatment

From these results it is clear that in Slovenia we have over 40 000 patients with stroke. The consequence is that year price for treatment of these patients is almost 499 millions euro.

For developed regions it can be therefore expected that arround 2% of population has experienced stroke which means the year price of almost 249.5 millions euro per one million population.

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5 Individual disease healing influence

In this section we would like to estimate the individual disease healing influence to the frequency of observed diseases and complication and to overall treatment price.

5.1 Healing influence of diabetes type 2

As mentioned we have in Slovenia arround 90 000 patients with D2 who are not discovered and are therefore not treated. If they would be discovered (by more systematic examination) the year price of treatment would be increased for over 32 millions euro. Lets try to estimate the influence of such treatment to development of hypercholesterolemia, hypertension and stroke.

We have assumed that in the group of unhealed patients the treatment would cause that till the age of 50 after such treatment 50% of patients with hypercholesterolemia would not suffer any more from this disease, while between older population the treatment efficacy is linearly decreasing toward 25%. That means that the number of patients with hypercholesterolemia is decreased for over 25 000 people. These patients all belong to the group where hypercholesterolemia is not treated due to the modelling assumptions.

Direct influence of D2 treatment to development of hypertension have been neglected.

Also direct influence of D2 treatment to stroke can be neglected but can not be neglected regarding indirect influence because of improved situation between the patients with hypercholesterolemia. It can be assumed that suitable healing of hypercholesterolemia can prevent 25 to 30% of stroke development. But as we have assumed that due to D2 treatment the patients would not developed hypercholesterolemia this number can be increased to 50%. Regarding model prediction we have 2653 such patients which means the saving of 32 740 673 euro. That means that it can be expected that such investition would repay already at this stage not only from ethical point of view but also economicaly. Expeted financial saving at this point is arround 540 000 euro. As efficiant D2 healing has also important influence to other health complications expected savings are actually much higher.

5.2 Healing influence of hypercholesterolemia

As mentioned we have in Slovenia arround 280 000 patients with undiscovered hypercholesterolemia. If they would be discovered the healing price of this disease would be increased for 87 692 000 euro.

It can be assumed that hypercholesterolemia treatment has practicaly no influence on development of D2 and very low influence on development of hypertension. As also the price for hypercholesterolemia healing is higher than for hypertension this type of savings can be neglected.

But it can be expected significant improvment regarding stroke development. We have taken into account that efficient treatment of hypercholesterolemia can decrease 22% of strokes. That means that in Slovenia the number of such patients would be decreased for 3512. From economical point of view the investition would be decreased for over 43 millions euro. Again we have to point out that here only the number of patients with stroke were taken into account, while other serious complications are still under investigation.

5.3 Healing influence of hypertension

On the basis of model prediction it can be expected that in Slovenia we have over 12 000 patients with untreated hypertension who experienced stroke per year. Good treatment can decrease this number up to 35%. For prediction purposes we have assumed 30% which indicates that it woud be possible to prevent over 3600 strokes by uncovering and healing all the patients with hypertension. The investment would be approximatelly 29 300 000 euro but it would decrease stroke healing price for 44 760 000 per year. Expected savings regarding only this complication are therefore over 15 400 000 euro.

6 Conclusions

In the paper three-phase modelling results are presented. First the spreadness of the patients regarding diabetes type 2, obesity, smoking, hypercholesterolemia and hypertension are presented. Through the second phase the influence of these factors of risk and diseases to stroke was added. All results are presented in percentage regarding the oldness of observed population in years.

In the last modelling step the results were connected with the counting data for Slovenia which enabled also quantitave results evaluation.

Finally the year price treatment of each disease was estimated. As sitation is regarding age distribution, disease distribution and price of treatment simillar for developed regions in all such countries also simillar situation can be expected.

In the end it is possible to conclude that investment to uncovering all the patients with diabetes type 2, hypercholesterolemia and hypertension would prevent important number of health complications like stroke and it can be expected that this would be important also from economical point of view.

In the paper we have presented only the influence to stroke, while the influence to coronary heart disease, peripheral arterial-vascular disease, end-stage renal disease and congestive heart failure are still under investigation.

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