MODELLING OF END-STAGE RENAL DISEASE ECONOMICS

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Abstract. Risky lifestyle, several chronic diseases and very often also the combination of mentioned factors have become a considerable social burden in many countries around the world, a problem which should not be underestimated. The situation is even more worrying when taking into account their influence on serious health complications that can threaten patients' lives or significantly reduce life quality. The presented modelling study enables to estimate the number of patients with chronic diseases like type-2 diabetes, hypercholesterolemia and hypertension, and risky factors like obesity and smoking and the influence of these conditions on the development of serious health complications where special attention is in the paper devoted to end-stage renal disease. In addition, an estimate of treatment costs makes it possible to evaluate the social burden and provide information about the potential savings resulting from intensive chronic diseases treating.

1 Introduction

Influence of globalization can be observed practically everywhere, also in an everyday life of each individual, where long working time, unhealthy nutrition habits, stress and lack of recreation have significant influence to health condition all over the world. Such unhealthy lifestyle in combination with population ageing and, partly at least, also because of more intensive and systemized medical examinations in developed countries, revealed that the number of patients with chronic diseases like type-2 diabetes (D2), hypertension (T) and hypercholesterolemia (H) has reached epidemiological proportions. For example, the International Diabetes Foundation (IDF) has reported [1] that 194 million people suffered from D2 in 2003. In 2007, it was estimated that 7.3% of adults aged 20–79 in 172 countries, covering 90% of the world's population, have diabetes. The highest prevalence of diabetes is in North America (9.2%), followed by Europe (8.4%). Based on information from the IDF it can be expected that the number of patients with D2 will double by 2030. Regarding some predictions [2] the number of D2-patiens will reach even 500 million in the next 20 years. The consequence of such situation is a non-negligible economic burden for treatment, which is important not only for governments, hospitals and medical insurance companies, but also for individuals, especially when taking into account also the significant influence of these diseases, and risk factors like obesity (PTT) and smoking, on serious health complications among which it is important to mention the strokes (MK), peripheral arterial-vascular disease (PAVD), coronary heart disease (CHD), congestive heart failure (CHF) and end-stage renal disease (ESRD) [3, 4, 5].

The aim of this modelling and simulation study is to develop a mathematical model with which it would be possible to identify the main dynamic properties of the observed diseases and risk factors, to estimate the number of patients in terms of their age, to identify any possible overlapping of the observed groups of patients, to estimate the healing effects and treatment costs for each of the observed diseases, to predict the social burden of treatment, to estimate and evaluate possible savings, and to enable model extensions, with which a study of an ageing population's influence on the distribution of diseases as well as the economic burden would be possible.

Such types of modelling results are not directly available in the literature. They often cover some of the mentioned aspects, but are frequently connected with a specific region or country, like, for example, in [6]. In this paper the results are evaluated for Slovenia, and then an extrapolation is suggested, which can be applied to the countries with a similar demographic and social situation [7]. We can expect that the circumstances are similar in practically all the EU countries.

To cover all the mentioned goals, and taking into account also the available data, the modelling structure was developed as is presented in Fig. 1. That means that the work was realized in three main phases. In the first phase mentioned risk factors and chronic diseases were described taking into account also all possible combinations of observed patients. In the next phase the influence to serious health complications is studied, while in the third phase the information of population distribution was applied and accomplished by price-treatment evaluation.

The modelling and simulations were realized with Matlab [8] and Simulink [9].

The work is organized as follows. First, model development is described, where special attention is given to its structure, which enables the sequential building of a dynamic system, taking into account all the observed risk factors, diseases, population distribution and treatment costs. In the next section, the model predictions regarding the influence of additional chronic diseases treatment to development of end-stage renal disease are discussed

from the medical and economical point of view. The paper ends with concluding remarks and some suggestions for future work.

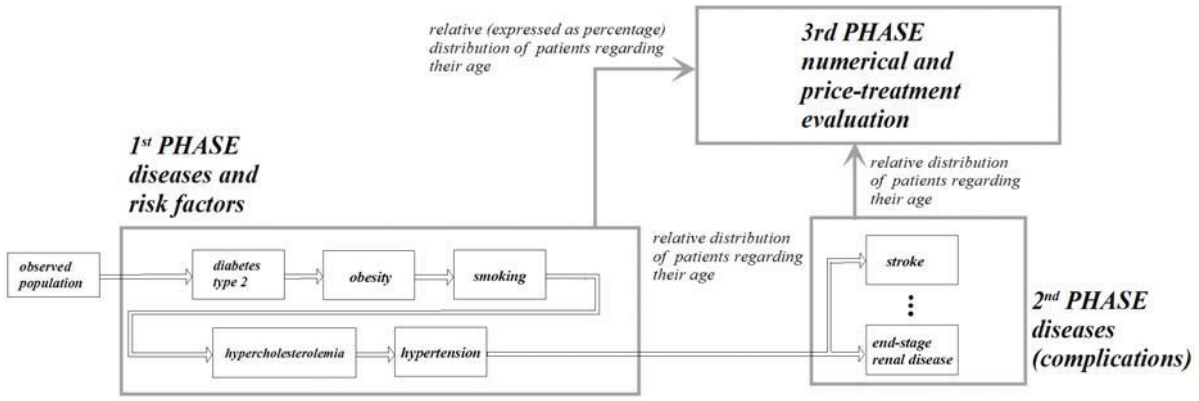

Figure 1. Modelling structure.

2 Model development

Regarding the complexity of design goals the work was organized in such manner that it enabled sequential adding of each important phenomena in the whole observed population. In the studies as the present one, data are always the most problematic part in the process of model development and its validation. Part of them were used in the form of statistical tables averaging number of people for each age class and served for curve fitting. The other part, however, were obtained from area experts. The mentioned estimates were taken into account in the process of model development, such including also expert knowledge in the modelling procedure. Additional model validation was realized regarding estimated numbers of patients when demographic data were taken into account.

The first modelling phase includes the development of diabetes type-2 (D2), obesity, smoking, hypercholesterolemia (H) and hypertension (T). They were designed as cascaded, dynamic subsystems, as indicated in Fig. 1, where the properties of each block were described by ordinary differential equations, which for obesity and smoking are nonlinear. It is important to notice that in each block of the structure in Fig. 1 the whole observed population is taken into account. The second-phase diseases were presented in a similar way, but time-varying parameters were also introduced to achieve suitable matching of model responses regarding reference data. Finally in the third phase, results from the first an second phases were combined with demographic data and estimated treatment prices to evaluate the economical burden and potential savings in the case of more intensive chronic disease treatment.

2.1 Chronic diseases and risk factors

Distribution of D2 is reported by different data sources (like [2, 10-12]), where the information is usually presented in percentage in terms of age groups, typically aggregated for five to 10 years, as illustrated in Table 1. It is important to mention that the statistical data for smaller countries are often not sufficiently reliable. This data indicates of course the people where disease was discovered. But due to some estimations [2, 12] 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.

age group	1.	2.	3.	4.	5.	6.
age [years]	0–24	25–34	35–44	45–54	55–64	65 and over
% D2	0	3.5	4.2	8.9	15.5	19

Table 1. Prevalence of D2 [10].

With regard to the last row of Table 1, it was taken into account that the number of patients with D2 is negligible up until the age of 24, while between the ages of 65 and 84 there are an average of 19% of patients with D2, but within the older population this number can increase to 20%.

Taking into account all mentioned data and presumptions the mathematical model of D2 was developed, where independent variable is not the group of people from the chosen time interval but age in years, as also the changes inside each group can be significant. Of course mean values of percentage function from the model

(equations (1) - (4)) and data should be as similar as possible. Input signal into this block is unity step indicating the beginning of the life. 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. When patients with D2 in observed population are defined also those without D2 can be calculated.

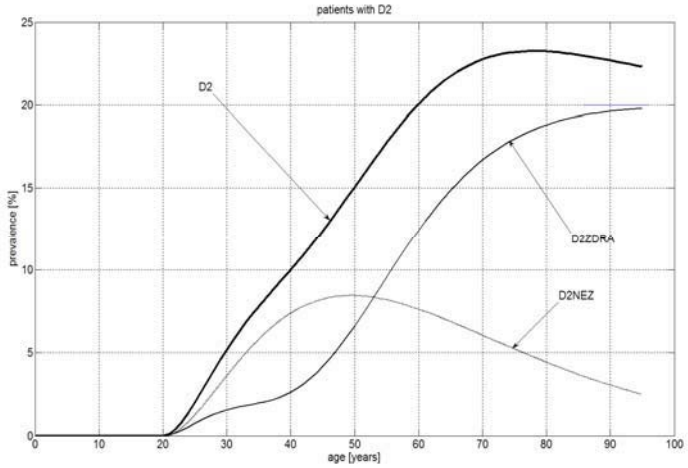

Figure 2. Percentage distribution of diabetes type-2 (D2ZDRA – discovered patients, D2NEZDRA – undiscovered patients, D2 – all with diabetes type 2).

$$D2ZDRA = \left[\frac{K_{sD2}}{(T_{D2} * s + 1)^7} * e^{-s*TmD2ZDRA} + \frac{s * K_{sD2a}}{(T_{D2a} * s + 1)^3} e^{-s*TmD2ZDRA} \right] * u \quad (1)$$

$$D2NEZDRA = \left[\frac{s * KsD2NEZDRA}{(s * TD2NEZDRA + 1)^7} e^{-s*TmD2NEZDRA} \right] * u \quad (2)$$

$$D2 = D2ZDRA + D2NEZDRA \quad (3)$$

$$BREZD2 = 100 - D2 \quad (4)$$

The parameters in eqns. (1) to (4) are the following: K_{sD2}=20, T_{D2}=4.9, *TmD2ZDRA*=24, K_{sD2a}=50, T_{D2a}=7.5, *KsD2NEZDRA*=460, *TD2NEZDRA*=14.75, *TmD2NEZDRA*=20. The units of time constants are years. It can be observed that the given data requires subsystems of higher order and with delay time, representing the time of the beginning of *D2* development in the population.

The information from this first modelling step can immediately be combined with the information of the age distribution of the population (the third phase), as the development of disease is closely related to a patient's age. Here, the data for Slovenia from 2003, as presented in Fig. 3, were used to obtain the information of D2-patients' number, which is illustrated in Fig. 4.

From the information in Fig. 4 the following can be derived. In Slovenia we have over 200 000 D2-patients, where 110 086 are correspondingly treated. Taking into account that average annual treatment costs for one D2-patient [3, 4] are 355 € (costs include: general practitioner: 4 times / year, laboratory: 2 times / year and drugs), €39 million per year are needed for all discovered patients.

On the basis of these results it can be expected that in the countries with similar demographic situation in a population group of 1 million there are 5.5% of patients with treated D2 and 4.5% who are undiagnosed and not treated. The annual costs for D2 treatment for this population are approximately €19.5 million. If all patients with D2 would be diagnosed the annual costs would be increased by €16 million.

Three signals from the first step (D2ZDRA, D2NEZDRA, BREZD2) entering the second block in Fig. 1, where the set of obese people [3, 4, 13, 14] are introduced, in the sense of additional transformations. Therefore the block "obesity" has six output signals describing all combinations of obese patients with D2 (diagnosed or undiscovered), obese people without D2, and with that also the whole population is defined. In the similar way each disease or risk factor [15-19] was taken into account and so the output from the first modelling phase consists of 108 signals describing percentage distribution of all observed patients and their combinations in the population.

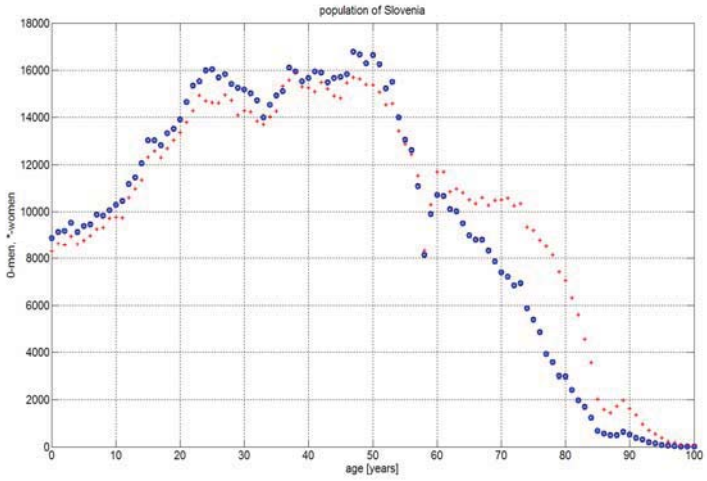

Figure 3. Population of Slovenia.

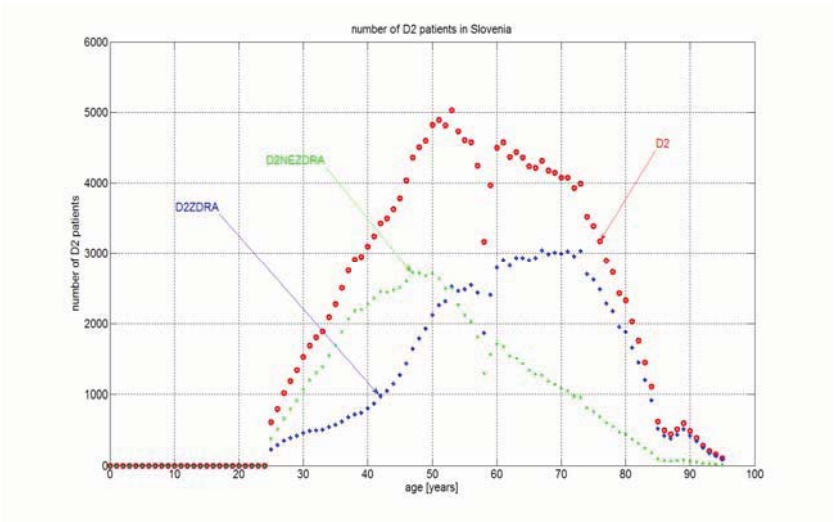

Figure 4. Number of patients with D2 in Slovenia (D2ZDRA-treated, D2NEZDRA-undiscovered, D2-all).

In Fig. 5 also the patients with hypertension are presented [3, 4, 19]. Similar as with D2 and H it was taken into account the fact that some of the patients are not discovered and are therefore not treated. When people are older the number of undiscovered patients decreases due to the fact that they are more frequently ill and when one of the mentioned chronic disease is discovered more intensive examinations usually discover also other diseases.

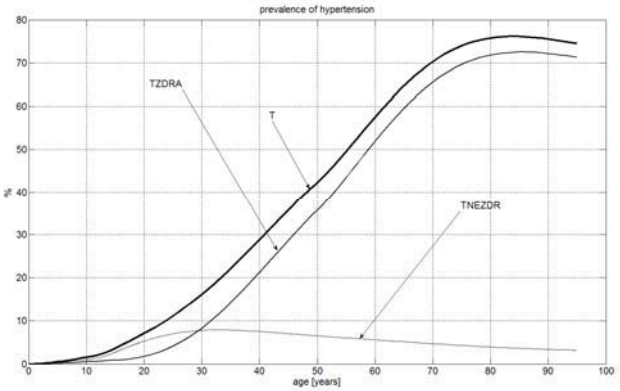

Figure 5. Percentage distribution of hypertension (TZDRA – discovered patients, TNEZDRA – undiscovered patients, T – all with hypertension).

These results (108 output signals from the first phase) can further be used to predict serious health problems in the second modelling phase. In the next subsection the influence on the end-stage renal disease (ESRD) is presented and evaluated in detail.

As the first phase of the model offers the summation of 108 situations combining different risk factors and chronic diseases it is obvious that due to the lack of space it can not be described in details in its complete version. Therefore only one combination influencing ESRD will illustrate the mathematical background used in the model.

In the sequel, the following situation is described: the patients who are healed regarding hypertension (TZDRA), hypercholesterolemia (HZDRA) and diabetes (D2ZDRA) and are at the same time obese smokers. One part of patients with treated D2 is obese (D2ZDRAandPTT) as shown in eqn. (5), where K_{12}=0.72.

$$D2ZDRAandPTT = K_{12} * D2ZDRA \tag{5}$$

The further target group are obese people with D2 who are smokers (D2ZDRAandPTTandKAD):

$$D2ZDRAandPTTandKAD = K_{25} * \left[\frac{\left(T_{kaj3} * s + 1\right)^3}{\left(T_{kaj2} * s + 1\right)^4} \right]^2 * D2ZDRAandPTT \tag{6}$$

Parameters of eqn. (6) are the following: K_{25}=0.005, T_{kaj2}=2.55, T_{kaj3}=9.384. This group can further be transformed into the group with treated hypercholesterolemia (*D2ZDRAandPTTandKADandHZDRA*):

$$D2ZDRAandPTTandKADandHZDRA = K_{315} * D2ZDRAandPTTandKAD \tag{7}$$

with K_{315}=*0.49*. The observed group of patients can develop also hypertension and if they are discovered (D2ZDRAandPTTandKADandHZDRAandTZDRA) they can be described with:

$$\begin{aligned} y_T(95) &= D2ZDRAandPTTandKADandHZDRAandTZDRA = \\ &= K_{442} * D2ZDRAandPTTandKADandHZDRA \end{aligned} \tag{8}$$

where K_{442}=*0.97*. Percentage distribution of this group of patients is presented in Fig. 6.

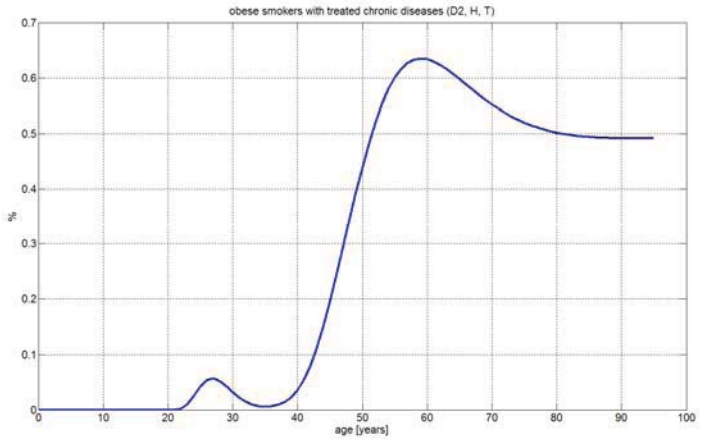

Figure 6. Percentage distribution of obese smokers with treated chronic diseases (diabetes type 2 –D2ZDRA, hypercholesterolemia–HZDRA, hypertension–TZDRA).

In table 2 modelling results of the first phase in combination with the information collected in the third phase are summarized.

disease or risk factor	annual treatment costs for one patient [€]	costs include	annual treatment costs for the population of one million people [€]	additional healing costs for the population of one million people [€] if all patients are discovered
diabetes type-2	355	general practitioner: 4 times / year, laboratory: 2 times / year, drugs	$19.5*10^6$	$16*10^6$
obesity	/	/	/	/
smoking	/	/	/	/
hypercholesterolemia	313	general practitioner: 4 times / year, laboratory: 2 times / year, drugs	$82*10^6$	$43.8*10^6$
hypertension	271	general practitioner: 4 times / year, laboratory: once / year, drugs	$69*10^6$	$14.6*10^6$

Table 2. Number of the patients regarding observed chronic diseases and risk factors and estimated year treatment costs.

2.2 End-stage renal disease

The signal, described with eqn. (8), is one of 108, which are participating to the groups of the patients with serious health problems, among which one is end-stage renal disease (*ESRD*). It can in general be expressed as:

$$ESRD = \sum_{i=1}^{108} AT_i(t) * g_i(s) * y_T(i) \tag{9}$$

where $AT_i(t)$ are age dependent parameters. For $i=29$ AT(t) is presented in Fig. 7, and $g_{29}(s)$ is:

$$g_{29}(s) = 5.5*10^{-4} * \left(\frac{1}{T_{29}*s+1}\right)^2 * e^{-T_{m29}*s} \tag{10}$$

where T_{29}=3 and T_{m29}=5.

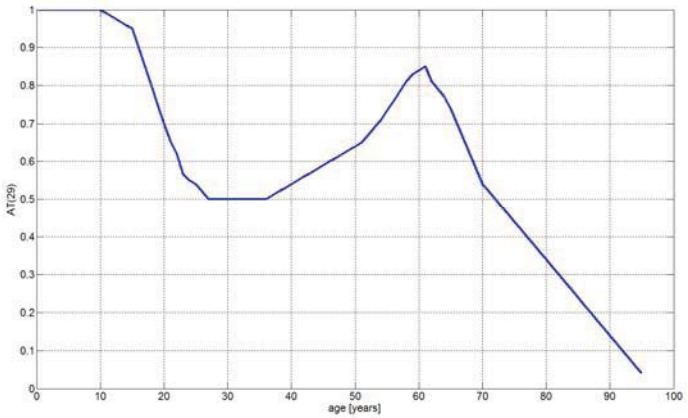

Figure 7. Age – dependent parameter *AT*.

Model adjustment was realized according to the prevalence presented in table 3 [20-22].

age group	1.	2.	3.	4.	5.
age [years]	0–19	20–44	45–64	65–44	75 and over
% ESRD	0.00121	0.01753	0.02410	0.01740	0.01203

Table 3. Prevalence of ESRD.

Among the risk factors which most significantly influence the development of end-stage renal disease is diabetes [20-22]. Primary diagnosis of patients who have started with dialysis indicate that among them 50% have also D2. The second most important factor is hypertension as 27% of ESRD patients have also high blood pressure. Other mentioned risk factor and chronic diseases are also significant but with lower importance.

The percentage distribution of patients with ESRD is shown in Fig. 8. As this group of patients was constructed from the whole observed population, the combinations regarding the mentioned chronic diseases and risk factors can also be observed.

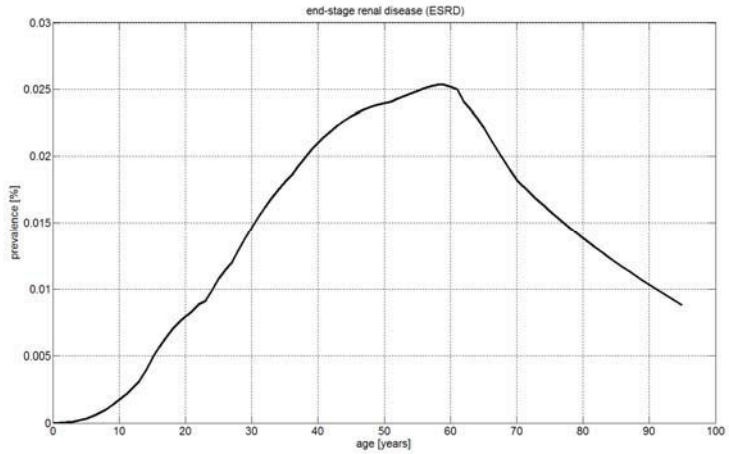

Figure 8. Percentage prevalence of end-stage renal disease.

In Figs. 9, 10 and 11 the relations between D2 and ESRD are illustrated. In Fig. 9 the population with ESRD is shown in comparison to the patients with treated and untreated D2, who have in the same time also ESRD. In spite of the fact that the group of patients with treated D2 and ESRD can not be neglected it is important to point out that the frequency of ESRD between the healed D2-patients is significantly lower as is presented in Fig. 10. In Fig. 11 the ratio is presented which illustrates the frequency of D2 patients among ESRD population. The average value in the time range between the age of 15 to 95 is 50% which is in good agreement with mentioned data.

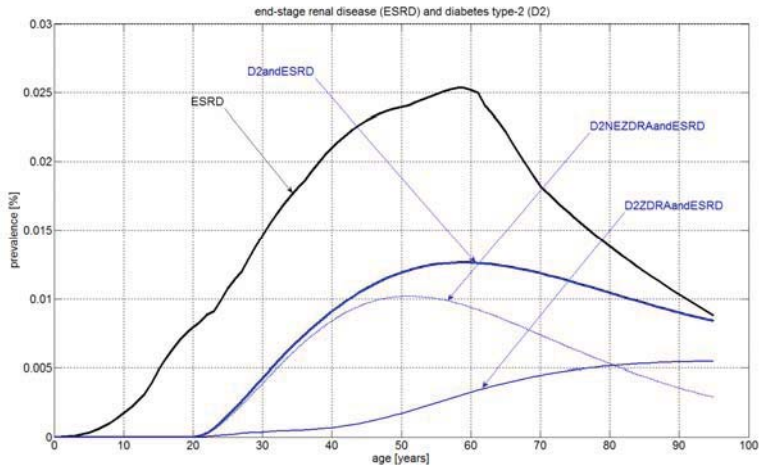

Figure 9. Patients with D2 and ESRD in comparison with ESRD
(D2ZDRAandESRD-patients with treated D2 and ESRD, D2NEZDRAandESRD-patients with unhealed D2 and ESRD).

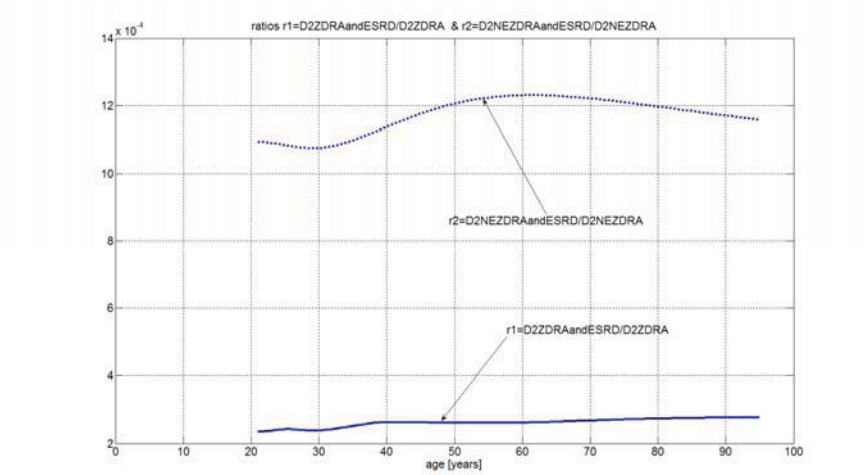

Figure 10. Ratios: r1=D2ZDRAand ESRD/D2ZDRA and r2=D2NEZDRAandESRD/D2NEZDRA.

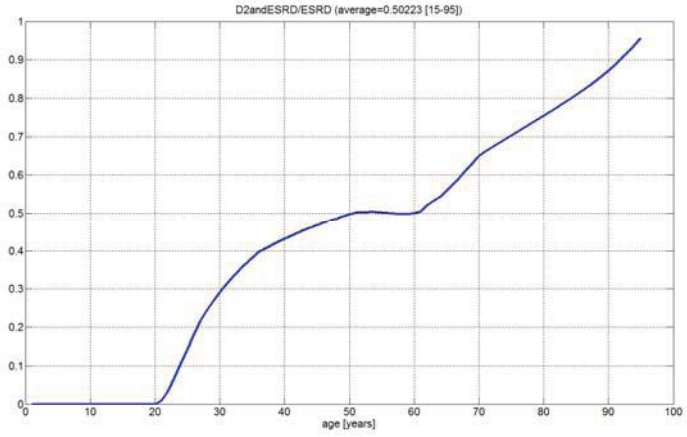

Figure 11. Ratio: D2and ESRD/ESRD.

The second most important influence to development of ESRD has hypertension and therefore in Fig. 12 the ratio between the patients who have in the same time ESRD and high blood pressure against the whole group of ESRD patients is presented. The average value of this ratio in the interval of 70 years is 28%.

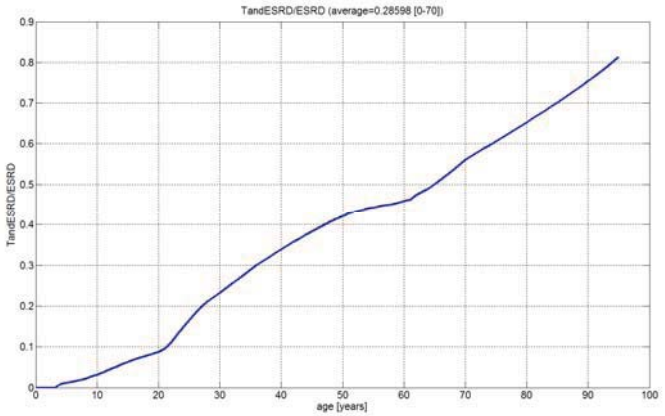

Figure 12. Ratio: Tand ESRD/ESRD.

Taking into account the information from Fig. 3 and model prediction of ESRD percentage prevalence from Fig. 8, the number of ESRD patients in Slovenia was calculated regarding their age, as presented in Fig. 13.

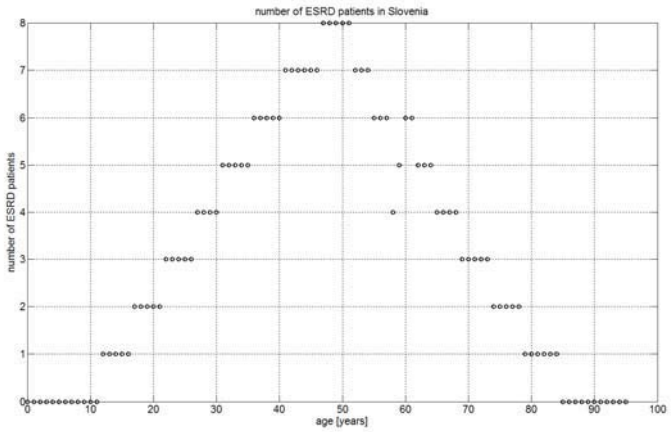

Figure 13. Number of patients with ESRD in Slovenia.

From this also their number – 305 patients, was derived which is in very good agreement regarding the information obtained from hospitals. As year healing price in average for one patient is estimated to be €72 208,8 (general practitioner: 4 times / year, drugs, hemodialysis: 3 times / week, travelling expenses, absence from the work: 2 months, hospitalization: 2 weeks, invalid retirenment: 2 years) [5] in one million population €11 million is needed per year for this group of patients.

3 Additional healing influence

As already mentioned a significant number of patients with chronic diseases is not discovered. In the case of more systematic examination of population these patients would also be discovered and correspondingly treated, what would, of course increase year healing costs as indicated in table 2. But such an investment would of course decrease the number of serious health complications (several, not only ESRD) and in this way increase quality of life and very often also save patients' lifes. In the following we are trying to estimate some consequences of such situations.

3.1 Influence of additional D2 treatment

If also undiscovered D2 patients would be optimally treated it would increase year costs for this disease for €16 million in the population of million people.

This would decrease the group of patients with H up to 50% if they are younger than 50, after this age healing efficacy linearly decreases to the value of 25%. As in the group of untreated D2-patients also the patients with H

are not healed (modelling presumption) this would not influence the price of H-treatment, but would only decrease the number of H-patients for approximately 13 000 in one million population.

As year hypertension treatment costs for one patient are lower (€271) as those for D2 (€355), from economical point of view no advantages are expected regarding this disease. Also from medical point of view direct influence of D2-treatment to hypertension is not important and can be neglected.

Regarding the patients with ESRD the effects of additional D2-treatment are direct and indirect, through the influence on hypercholesterolemia (H). Direct improvements are in average estimated to reach 25%, while indirect are around 20%. But in the cases where H is due to D2-treatment not developed the improvements are twice as good, and ESRD is decreased up to 40%. For the circumstances in Slovenia that would be 20 ESRD patients less due to indirect influence (€1.5 million saving), and 22 patients less (€1.6 million saving) due to direct influence of D2-treatment. In the population of million people 21 ESRD patients per year less is of course important number, but in addition also the investment in D2-healing would be decreased for €1.5 million.

3.2 Influence of additional H treatment

If also undiscovered patients with H would be optimally treated it would increase year costs for this disease for €43.8 million in the population of million people. H-treatment does not have significant influence to D2 or hypertension, but is important, as already mentioned, for the development of ESRD. Optimal treatment of hypercholesterolemia (H) can improve the situation among the ESRD patients up to 20%, which would decrease the number of these patients for 11-12 per year in one million population. From economical point this represent the saving of €830 000 per year.

3.3 Influence of additional T treatment

If also undiscovered patients with hypertension (T) would be optimally treated it would increase year costs for this disease for €14.6 million in the population of million people.

T-treatment is not important regarding D2 and H, but has the influence to ESRD. Regarding model predictions in Slovenia is 74 patients with ESRD and undiagnosed hypertension. Treatment of hypertension would improve the situation up to 50%. In such case we would have 37 ESRD patients per year less, and healing costs would be reduced for €2.7 million. In one million population group savings are therefore estimated to be €1.35 million per year due to 18-19 ESRD patients less.

4 Conclusions

In this paper three-phase modelling results are presented illustrating the distribution and influence of chronic diseases (diabetes type-2, hypercholesterolemia, hypertension) and risk factors (obesity, smoking) to serious health complications. Due to a changed lifestyle and an aging population they have become 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 of the mentioned diseases). So the expectations have to be estimated regarding epidemiological statistical data.

In the paper only the influence on end-stage renal disease is presented, while the influence on other complications is still under investigation. But, it can be expected, that also regarding other mentioned complications the number of patients can be significantly decreased by efficient treatment of chronic diseases and so also additional economical savings are expected.

In addition to the existing model structure, a dynamic interpretation of the demographic situation will also be added as population aging is becoming an increasingly important factor for health.

5 References

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