INTRODUCTION

Diabetes mellitus /DM/ is a widespread socially significant disease whose frequency continuously increases. It is a chronic disease that occurs either when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces [1, 2]. High blood glucose, a common effect of uncontrolled diabetes, may, over time, leads to serious damages of the heart, blood vessels, eyes, kidneys and nerves. DM is recognized as an important cause of premature death and disability. It is one of the four non-communicable diseases (NCDs) that should be set up as a priority in all countries according to the 2011 Political Declaration on the Prevention and Control of NCDs and the Global Action Plan for the Prevention and Control of NCDs 2013-2020 [3, 4].

The data provided by the International Diabetes Federation (IDF) in the 7th edition of Diabetes Atlas pointed out that one in eleven adults has diabetes, in one of two adults diabetes has not been diagnosed, 12% of the global health expenditure are spent on diabetes, one in seven births is affected by gestational diabetes, 542,000 children globally have type 1 diabetes with the highest prevalence in Europe [5].

DM is one of the leading health challenges to the global health in the 21st century. The World Health Organization (WHO) estimates that globally, high blood glucose is the third highest risk factor for premature mortality, after high blood pressure and tobacco use. Approximately 5.6 million people aged 20 to 79 years died from DM in 2015, which is equivalent to one death every six seconds. DM accounted for 14.5% of the global all-cause mortality among people in this age group [6].

According to IDF, the global cost of diabetes for health systems was about 548 billion US$ in 2013, and it is expected to increase to 627 billion by 2035. In addition to the enormous financial burden on individuals and their families due to the cost of insulin and other essential medicines, DM also has a substantial economic impact on countries and their national health systems. It is related to an increased use of health services, loss of productivity and long-term care and treatment of diabetes related complications, such as kidney failure, blindness or cardiac problems. The majority of countries spend between 5% and 20% of their total health expenditure on DM [6, 7]. With such high expenditures, the disease is a significant challenge for health care systems and an obstacle to sustainable economic development [4].

Health technology assessment /HTA/ has been increasingly applied in the reimbursement policy and costs and benefits assessment of the new drugs compared to existing therapeutic alternatives.

The evaluation of health technology involves not only economic assessment but also assessment of efficacy, effectiveness and accessibility of new technology. The aim of this paper is to analyse the burden of diabetes in Bulgaria and the necessity of applying Health Technology Assessment.
RESULTS and DISCUSSIONS

Incidence and prevalence of diabetes mellitus in Bulgaria

There is no accurate statistics on the number of diabetics in Bulgaria. The national diabetes registry is still not implemented.

During the review of available literature sources we found only a few publications and study results. Some authors provide approximate estimates for the number of diabetics about 600 000, which accounts for nearly 9% of the total population. Almost 40% of them do not know that they have diabetes before the complications arise [8].

In 2003 the National Centre for Health Information published data about the prevalence of diabetes in Bulgaria and according to these data diabetics in Bulgaria counted to 164 818 people. Highest prevalence rates were registered in Ploeven, Turnovo and Varna, and the lowest in Montana, Sliven and Silistra. During the 10-year period (1993-2003) the prevalence of diabetes has increased by 1.5 times with the largest proportion of diabetics in the age groups 30-45 and 45-60 years. Over 50% of patients were in working age. By the year 2007 the prevalence of DM in the age group 20-70 years was 9% and the total number of patients was estimated to be around 519 500 [9].

In 2012, the results from a multicentre study for assessment of prevalence of DM were published. The study used the methodology of IDF and encompassed a sample of 2032 persons visiting endocrinologists in different health care institutions from 12 Bulgarian regions. The sample consisted of men and women aged 20-79 years (mean age = 49,30 ± 14,75). The main results showed the frequency of DM in the country 9.6% (7.1% - diagnosed and 2.5% - undiagnosed); the frequency of pre-diabetes 3.7% (1.6% - impaired glucose tolerance and 2.1% - impaired fasting blood glucose). The incidence of DM is significantly higher among males as compared to females - 56.7% and 43.3% respectively. The age distribution of DM showed that 83% of all diabetics were over 50 years old. Therefore, the age of 50 years should be a signal for the necessity to perform a test for DM and especially in risk groups [9].

In 2013, the Bulgarian Society of Endocrinology assessed that the number of diabetics over 20 years of age has increased and accounted to 9.6% of the population. About 75% of diagnosed diabetics have poor metabolic control, resulting in complications such as myocardial infarction, stroke, blindness, limb amputations and chronic renal failure. The incidence of DM type 2 is three times higher among overweight people than among those with normal weight. Usually its victims are people over 40 years of age. But as the rate of obesity increases among children and adolescents, DM is also common at these age groups [10].

In 2015, the Minister of Health has set up a工作组 to analyse the morbidity and mortality due to DM as well to assess the validity of criteria for the effect of diagnostic and therapeutic activities in patients with DM, cardiovascular diseases and other diseases. According to the report of this工作组 and the data provided by the NHIF [11], the total number of officially registered and treated patients with DM in the outpatients’ lists by years was as follows:

<table>
<thead>
<tr>
<th>Year</th>
<th>Total number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>431 197</td>
</tr>
<tr>
<td>2013</td>
<td>446 881</td>
</tr>
<tr>
<td>2014</td>
<td>461 644</td>
</tr>
<tr>
<td>2015</td>
<td>473 192</td>
</tr>
</tbody>
</table>


Mortality from diabetes in Bulgaria

To estimate the mortality of diabetes in Bulgaria we can rely on data provided by National Statistical Institute for mortality by causes using the specific death rates due to diabetes. Unfortunately, the official complete information on this indicator is available for the last 7 years (2010-2016), as it can be seen in table 1 [12]. European Health for All Database, using the information from national statistics, provided data for standardised death rate due to diabetes for more than 40 years period (1970-2015).
As it can be seen in figure 1, the standardized death rates (SDR) of diabetes in Bulgaria were significantly higher than the average level for EU members before 2004 and since 2004, as well as compared to Romania. The most unfavourable trends can be seen after 1980s [13].

The difference between Bulgaria and Romania can be seen also in the country profiles developed by the Institute for health metrics and evaluation in the Global Burden of Disease studies. Diabetes as one of the leading causes of Disability-adjusted life years (DALYs) in Bulgaria shifts from 8th position in 1990 to 7th position in 2010, for Romania the change is from 14th position in 1990 to 12th position in 2010 [14].

In order to fight against the global epidemic of diabetes and non-communicable diseases, WHO states that it is imperative to create a basis for monitoring trends and assessing the progress of countries. For this purpose, WHO published diabetes profiles for all countries in 2016, the goal of which is to synthesise the national status of diabetes prevention and control in a single reference document. Each profile includes data on prevalence and trends in diabetes, mortality, risk factors, availability of diabetes plans, monitoring and surveillance, primary prevention and treatment policies, availability of medicines, basic technologies, and procedures. Data from the diabetic profile of Bulgaria are as follows:

- 390 deaths of males in age group 30–69;
- 270 deaths of females in age group 30–69;
- 510 deaths of males in age group 70+;
- 860 deaths of females in age group 70+;
- 1490 deaths of males attributable to high blood glucose in age group 30–69;
- 730 deaths of females attributable to high blood glucose in age group 30–69;
- 2350 deaths of males attributable to high blood glucose in age group 70+;
- 3530 deaths of females attributable to high blood glucose in age group 70+;
- 1490 deaths of males attributable to high blood glucose in age group 30–69;
- 730 deaths of females attributable to high blood glucose in age group 30–69;
- 3530 deaths of males attributable to high blood glucose in age group 70+;
- 3530 deaths of females attributable to high blood glucose in age group 70+;
- Prevalence of diabetes – males 10.7%; females 10.0%; total population 10.3%;
- Prevalence of overweight – males 67.8%; females 59.7%; total population 63.6%;
- Prevalence of obesity – males 23.6%; females 27.5%; total population 25.6%;
- Prevalence of physical inactivity – males 19.0%; females 26.7%; total population 23.0%.

Health expenditure on treatment of Diabetes mellitus

According to WHO Global Report on Diabetes, public expenditures on healthcare in Bulgaria were the lowest among EU Member States. For the period 2006-2012 they range from 3.98% to 4.30% of GDP as compared to the average of 7.3% for EU countries. In most countries the second largest source of funds is direct payment by patients. In 2010, the proportion of direct payment by patients was highest in Cyprus (49%), Bulgaria (43%) and Greece (38%). In nearly half of the EU Member States, this share has risen over the last ten years, and especially in Bulgaria, Cyprus, Malta and Slovak Republic [6]. IDF estimate that mean diabetes-related expenditure per person with diabetes in Bulgaria for 2015 is 647.2 US$ [5].

Bulgarian National Health Insurance Fund has paid 31 272 443 Bg leva for the second quarter of 2016 on treatment of diabetes. This means that the NHIF spends more than 125 million leva per year only on DM [11].
What is the National response to diabetes?

Availability of policies, guidelines and monitoring:

Bulgaria declares that there is an operational action plan for diabetes and strategy to reduce physical inactivity. Available and fully implemented are Evidence-based national diabetes standards and Standard criteria for referral of patients from primary care to higher level of care. But there is no strategy to reduce overweight and obesity, diabetes registry and recent national risk factor survey in which blood glucose was measured. Availability of medicines, basic technologies and procedures in the public health sector All medicines in primary care facilities – Insulin, Metformin and Sulphonylurea are available in Bulgarian health services. All procedures - Retinal photocoagulation, Renal replacement therapy by dialysis and Renal replacement therapy by transplantation are accessible to Bulgarian citizens.

The same is the situation with Basic technologies in primary care facilities - blood glucose measurement, oral glucose tolerance test, HbA1c test, dilated fundus examination, foot vibration perception by tuning fork, foot vascular status by Doppler and urine strips for glucose and ketone measurement.

Nevertheless, the Euro Diabetes Index (EDI) performed in 2014 by the Health Consumer powerhouse shows very poor position of Bulgaria between 30 European countries. The aim of EDI was to select a limited number of indicators, grouped in sub-disciplines, which in combination can present a tale of how healthcare is being provided by the respective national systems. The underlying idea was that good diabetes care requires an integrated healthcare system, making many professionals and functions work together. Bulgaria had gathered total score of 473 points and was ranked on 30th position. Romania as the country that joined EU together with was ranked on 27th rank with the total score 551 points. Almost all indicators in sub-discipline “Prevention” are assessed as “not -so-good”: exercise in compulsory school, bicycle usage, fruit/vegetable consumption and raised blood pressure among adults. “Case-findings” (diabetes registry and screening for gestational diabetes) are also not-so-good. For the sub-disciplines “Range and reach of services” and “Access to treatment” two out of four and four out of five show not-so-good results. For almost the whole sub-disciplines “Procedures” and “Outcomes” data for Bulgaria are not available for [15].

Health Technology Assessment

The cost of medicines is one of the components of health care costs that can be most easily established. Therefore, governments are implementing a variety of regulatory measures addressing the cost of medicines in order to control the overall costs of healthcare. DM is one of the most appropriate examples because the cost of diabetes is very high not only for a particular patient and his family but for the health systems and societies.

The reimbursement policy in a country usually is mainly based on the efficacy, safety and quality of medicines. Additional criteria, such as budget impact, severity of the disease, are included. The medicinal products are then included in Positive or Negative Drug Lists respectively.

Health Technology Assessment (HTA) is a very useful tool by which the researchers are trying to determine the relationship between the quality and price of new products compared to existing ones depending on whether the costs can be reimbursed.

More and more countries are introducing HTA to assess the value of therapeutic alternatives in relation to specific indications from a medical, economic and social point of view. Organizations performing HTA may be the regulatory bodies responsible for reimbursement decisions or advisory bodies that give recommendations for reimbursement to decision-makers. HTA is increasingly been taken into account in the pricing and determination of reimbursement.

Pharmacoeconomic Analysis is used to determine the profitability of medicinal products in comparison with other existing therapies. In addition, HTA can analyse social, ethical, medical-legal, forensic, and organizational issues related to the use of different technologies, including spending of public resources, implications of budget costs and budget impact.
The first document, which regulates the legal basis for the assessment of health technologies in Bulgaria, is the Ordinance on the conditions of the rules and order for the regulation and registration of the prices of the medicinal products, introduced in 2013. It is in force until December 2015, when another Ordinance No 9 on the conditions and procedure for carrying out health technology assessment, issued on the basis of the Law on Medicinal Products in Human Medicine, was promulgated. This Ordinance regulates the requirements, the conditions and the order for carrying out health technology assessment in Bulgaria, as well as the structure and functions of the Health Technology Assessment Commission at the Ministry of Health.

The implementation of this document still meets a lot of obstacles related to the:

- lack of experts capacity for HTA working committees;
- lack of reliable and accessible data on epidemiology of diseases;
- lack of reliable data on health care prices and different therapeutic alternatives;
- necessity of standardisation for assessments of the HTA reports.

CONCLUSION

The information on diabetes from different national and international sources outlines its high prevalence and its great burden on the national health system in Bulgaria. These trends are particularly alarming as they occur on the background of the steadily decreasing total number of population. It is therefore necessary to introduce effective preventive measures against risk factors and to create conditions for early diagnosis.

The diabetes registry is of utmost importance for gathering reliable data and has to be introduced instantly together with effective prevention programmes on diabetes in different age groups.

HTA allows implementation of better and more cost-effective technologies and will be an effective approach and the right instrument to manage public expenditures for the treatment of DM. The implementation of HTA will contribute to better use of scarce financial resources.

Improved collaboration between healthcare professionals and pharmaceutical structures can contribute to better understanding of public health technologies concerning diabetes.

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