Improved quality of diabetes control reduces complication costs in Bulgaria

Konstantin Tachkov, Konstantin Mitova, Zornitsa Mitkova, Maria Kamusheva, Maria Dimitrova, Valentina Petkova, Alexandra Savova, Miglena Doneva, Dimitar Tcarkciev, Vasil Valov, Galia Angelova, Manoela Manova and Guenka Petrova

Department of Organisation and Economy of Pharmacy, Faculty of Pharmacy, Medical University of Sofia, Sofia, Bulgaria; University Endocrinology Hospital “Ivan Penchev”, Medical University of Sofia, Sofia, Bulgaria; NovoNordisk Pharma, Sofia, Bulgaria; Linguistic Modelling and Knowledge Processing Department, Institute of Information and Communication Technologies, Bulgarian Academy of Sciences, Sofia, Bulgaria

ABSTRACT
The study investigates the quality of diabetes control and its economic implications in Bulgaria for the years 2012–2016. It is a retrospective study of the national diabetes register. Patients were categorized according to type of diabetes, gender, newly diagnosed cases per year, body-mass index (BMI) and achieved disease control. The relative risks for reducing the diabetes-related complications achieved through a 1% reduction of HbA1c were taken from literature data, and macrocosting was used to calculate the saved cost for diabetes complications. The new cases of type 1 diabetes decreased (10% lower in 2016 than in 2012) but the number of new cases with type 2 diabetes increased (12%). In 2012, the average percentage of glycosylated hemoglobin in the second recording at the end of the year was 7.59% (SD 1.85), whereas the second recording of values for 2016 revealed an average value of 7.3% (SD 1.32). The mean yearly reduction in 2012 was 0.05% (SD 1.1) with a slow increase to 0.07% (SD 0.46) in 2016. The absolute risk reduction for all diabetes-related complications was 20.6. The total prevented costs for all complications in the entire population were 20 million BGN. The results for the period 2012–2016 showed improved control of diabetes. The proportion of patients who achieved control increased over the period, reaching over 40% of the afflicted population. The achieved adequate control led to a reduced risk of developing diabetes-related complications, thereby saving costs of 20 million BGN associated with them, and decreasing the burden on the healthcare system.

ARTICLE HISTORY
Received 19 January 2019
Accepted 2 April 2019

KEYWORDS
Diabetes control; diabetes complications; diabetes registry; glycosylated hemoglobin; saved costs; macroeconomic analysis

Introduction
Diabetes mellitus (DM) is a serious debilitating disease which poses an increasing socio-medical challenge to all countries worldwide. Diabetes-related deaths in 2017 reached 4.0 (3.2–5.0) million people [1]. During the last two decades, the number of new diabetes cases has increased twofold, which has led to higher healthcare costs and a serious economic burden on healthcare systems [2, 3]. DM affects more than 32 million citizens of the European Union [4]. In Bulgaria, the number of diabetics has grown and is estimated to affect 9.6% of the population, with a mortality rate of 23.3 per 100,000 individuals [5]. Around 75% of diagnosed diabetics in Bulgaria also have poor metabolic control, which is a factor in developing diabetes-related complications: myocardial infarction, stroke, retinopathy and blindness, limb amputations and chronic kidney failure. The number of deaths due to DM is far greater if deaths due to complications and bad disease control are included in the mortality estimates [6]. Estimates of the long-term quality of life of patients are largely influenced by the development of comorbidities, as well as their severity—such as diabetic retinopathy, diabetic nephropathy, macroangiopathy, brain and cardiovascular diseases and ischemic heart disease. The association between DM, hypertension, increased serum cholesterol levels and smoking greatly increases the risk of health [7]. Major studies have found that DM type 1 decreases the life expectancy with 15 years, whereas type 2DM, with 5–10 years [8]. Ultimately DM complications lead to lower health-related quality of life, with studies estimating 50–80% increased risk of disability compared

CONTACT Guenka Petrova, gpetrova@pharmfac.mu-sofia.bg Department of Organisation and Economy of Pharmacy, Faculty of Pharmacy, Medical University of Sofia, 2 Dunav Str., Sofia 1000, Bulgaria. © 2019 The Author(s). Published by Taylor & Francis Group on behalf of the Academy of Forensic Science. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
to the healthy population [9, 10]. At the same time, a substantial body of literature shows that good disease control is associated with higher life expectancy and reduced risk of developing diabetes-related complications [11, 12].

This study aims to investigate the quality of diabetes control and its economic implications in Bulgaria for the years 2012–2016.

**Materials and methods**

This is a retrospective study of the national diabetes register. It was conducted for the Bulgarian population of patients with DM.

**Analysing diabetes control**

We extracted data from the national diabetes register concerning the total number of patients with DM for the years 2012–2016. Patients were categorized according to type of diabetes, gender, newly diagnosed cases per year, body-mass index (BMI) and achieved disease control. Patients with glycosylated hemoglobin (HgA1c) values of less than 7% were considered to have good disease control.

The subgroup analysis was performed for all patients for whom there were at least two HgA1c values recorded per year. These values were determined at the beginning and end of each year and were documented. Based on this, we calculated the change in the recorded levels (higher, no change, lower).

The reduction in the relative risks (RRs) of development of diabetes-related complications achieved through a 1% reduction in HbA1c (Table 1) were taken from published literature [11, 12]. The RR of reducing these diabetes-related incidents in the population observed by us was calculated by multiplying the average reduction of HbA1c by the expected RR according to Table 1. This was done only for the group of patients for whom data were available and who showed reduction in the HbA1c levels for all 5 years. Thus, we evaluated the reduction in RR of diabetes-related complications occurring through the reduction of glycosylated hemoglobin.

The mean duration of follow-up varies in the literature from ca. 10.4 years for all-cause mortality to 10 years for all diabetes-related endpoints; therefore we assumed the median duration of follow-up of RR to be 10 years.

**Table 1. Reduction of relative risk of diabetes-related complications upon achieving 1% reduction in HbA1c, according to UKPDS35 [11, 12].**

| Diabetes-related complications | Relative risk (RR) reduction for 1% reduction in HbA1c level | 95% CI for RR |
|-------------------------------|-------------------------------------------------------------|---------------|
| Any diabetes-related endpoint | 21                                                          | 17            |
| Diabetes-related death        | 21                                                          | 15            |
| All-cause mortality           | 14                                                          | 8             |
| Fatal or non-fatal myocardial infarction | 200                      | 51.22         |
| Fatal or non-fatal stroke     | 12                                                          | 8             |
| Microvascular endpoints       | 37                                                          | 33            |
| Cataracts extraction          | 19                                                          |               |
| Amputation or death due to peripheral vascular disease | 43                      |               |
| Heart failure                 | 16                                                          |               |

**Analysis of costs of diabetes-related complications**

The calculated reduction in the RR of diabetes-related incidents was expressed as prevented complications and the corresponding prevented costs were calculated. A macro-costing approach was used. The costs were calculated by multiplying the number of prevented incidents by the respective costs as illustrated in Table 2. Total costs were calculated as a sum of ambulatory costs and the cost of in-hospital treatment. Data on the costs of ambulatory treatment were taken from Ostrowska et al. [13], an international study that includes data for Bulgaria. The costs of hospitalization were taken from the published tariffs of the National Health Insurance Fund of Bulgaria [14].

Several assumptions were made. First, we assumed that before occurrence of death by any cause, patients had been hospitalized as being “comatose and admitted for intensive care”. The other two assumptions made were in the calculation of the average weighed costs of stroke hospitalizations and microvascular complications. A further assumption was that the deaths...
by any cause fell under the intensive care clinical tariff, while the deaths due to diabetes hospitalizations were under the tariff of diabetes complications. The costs of ambulatory therapy of complications were calculated for the period of 10 years, which was the mean duration of follow-up in literature, after which mean yearly costs were multiplied by 5 to obtain the total costs for a 5-year period of follow-up [12].

The number of prevented diabetes-related complications was multiplied by the costs of hospitalizations plus the costs of ambulatory treatment, so as to give a final estimate of the total prevented costs. We also assumed that every patient indicated for hospitalization had only one type of diabetes-related complication.

The costs are presented in national currency at the exchange rate of 1 BGN $0.51 Euro.

Results and discussion

Patients’ demographics

For the duration of the observed period, there was a reduction of new cases of type 1 diabetes (10% lower in 2016 than in 2012) and an increase in the number of new cases of type 2 diabetes (12% more cases in 2016 than in 2012)—Table 3. Over a period of 5 years, the number of patients with type-2 diabetes increased by 52,639 people. The yearly mean incidence rate for type 1 diabetes was 1500 people, whereas it was ~73,000 for type 2 diabetes (Table 3).

Obesity, as a major risk factor for the development of type 2 diabetes, was prevalent in the observed population and probably a leading cause of developing the disease. The data showed that 30–35% of the registered patients had a BMI over 30 (Table 4).

Regarding the percentage of patients with levels of glycosylated hemoglobin under 7%, we observed a lower proportion among the patients with type 1 diabetes (average 30% had ‘good’ control), with the highest proportion of patients achieving good control gradually increasing through the years to 32% (in 2016). In contrast, on average 42% of patients with type 2 diabetes achieved good control, this trend increasing over the years (Table 5).

Diabetes control in a subgroup analysis

Approximately a third of the patients had at least two changes in the HbA1c levels recorded per year. The number of closely monitored and recorded patients increased during the period (Table 6). The mean age of the patients with recorded values was 63, with data predominantly available for type 2 diabetics. The average recorded value of glycosylated hemoglobin at the beginning of the period was 7.6% (SD 1.88) in 2012, which decreased to 7.4% (SD 1.35) at the end of the period in 2016. The data showed a reduction in HbA1c level and a trend towards improvement in the control: in 2012 the average percent of glycosylated hemoglobin in the second recording at the end of the year was 7.59% (SD 1.85), whereas the second recording of values for 2016 revealed an average value of 7.3% (SD 1.32). The mean yearly reduction in 2012 was 0.05% (SD 1.1) with a slow trend towards reaching 0.07% (SD 0.46) in 2016. The number of patients who achieved a reduction in the levels of glycosylated hemoglobin increased from 18,000 to 26,000 in 2016, which indicates a positive trend towards improvement of glycosylated hemoglobin checks and records. However, the number of patients who showed no change was also significant: it increased from 59,000 to 93,000 people in 2016.

Prevented complications

Reduction in the values of glycosylated hemoglobin has been proved to reduce the risk of developing many diabetes-related complications, whereby the absolute risk reduction for all events was 20.6. The most significant risk reduction in risk was for amputations, followed by microvascular complications (Table 7).

For the whole observed population with at least two cases of recorded HbA1c (approx. 25%), the reduction in the RR of developing a diabetes-related

---

**Table 3. Prevalence and incidence of diabetes recorded in the national diabetes register.**

| Description                  | 2012    | 2013    | 2014    | 2015    | 2016    |
|-----------------------------|---------|---------|---------|---------|---------|
| Total number of DM cases    | 431,197 | 446,881 | 461,645 | 473,192 | 483,836 |
| Patients with type-1 DM     | 28,108  | 27,886  | 27,193  | 26,259  | 25,426  |
| Patients with type-2 DM     | 397,154 | 413,331 | 428,972 | 441,199 | 452,490 |
| New cases of type-1 DM      | 1474    | 1982    | 1722    | 1613    | 1538    |
| New Cases of type-2 DM      | 72,973  | 75,120  | 75,447  | 71,948  | 713,31  |

**Table 4. Percentage of patients with body mass index above 30.**

| BMI (as per available data) | 2013 | 2014 | 2015 | 2016 | 2017 |
|-----------------------------|------|------|------|------|------|
| >30                         | 23.79| 24.01| 24.06| 23.76| 24.05|
| >35                         | 11.22| 11.32| 11.58| 11.85| 12.39|
A complication would lead to the prevention of 5065 incidents (Table 8). Since the sample is representative of the total diabetic population, we can calculate that the total number of prevented incidents would be ca. 20,000.

### Costs of prevented complications

The total costs that would have been incurred for treatment of the 5056 incidents, which were prevented due to reduction of glycosylated hemoglobin, are ca. 5 million BGN (Table 9). The total saved costs for all...
predicted diabetes-related complications in the entire population are 20 million BGN for the whole period. These results from this study are representative of the population of diabetic patients in Bulgaria. For the period, the observed reduction in the incidence of type 1 diabetes by 10% and increase in the cases of type 2 by 12% could be interpreted as good detection of new cases of diabetes, but also as a high incidence rate. The newly diagnosed cases of type 1 diabetes yearly are around 1500, which demonstrates a stable type 1 diabetic population, since this trend did not change over the years. The fact that the prevalence of type 1 diabetes has remained relatively constant in Bulgaria, but the prevalence of type 2 diabetes is continuously increasing at a growing rate, is indicative of the country’s aging population and people living a sedentary life. This observation is in agreement with other reports [15, 16].

The average age of patients with type 2 diabetes did not change in our study and remained at ~65 years, which could be considered a positive trend. Despite this, the standard deviation in the age of the patients (8 and 11 years) indicates that many of the diabetics in Bulgaria are diagnosed at an early age.

The percentage of patients with values of glycosylated hemoglobin under 7% was approx. 30% in type 1 diabetes and 32% in type 2. Among the type 2 diabetics, the level of control was overall better, with 42% experiencing a slight increase over the studied period. However, it is still important that these values are far lower than the desired targets and it could be argued that there is room for improvement [17]. Data indicate that the control of the disease is gradually improving, with the number of undiagnosed or late-diagnosed cases decreasing, as well as an observed improvement in the healthcare services provided to the affected population. Therefore we might expect an improvement in the diabetes related complications [18–20].

The analysis showed a definite observable improvement in the control of glycosylated hemoglobin. The average difference was 0.05% for the observed period. The number of patients who showed a reduction in the levels of glycosylated hemoglobin increased from 18,000 to 26,000 from 2012 to 2016, which is also a positive trend. The most significant proportion of the population was the one with no change in glycosylated hemoglobin percentages, increasing from 59,000 people in 2012 to 97,000 people in 2016. The average reduction in the HbA1c values was 1%, while the average increase in the HbA1c level was 1.1%. No significant differences were observed between genders [21].

The control of DM is much less satisfactory in Bulgaria than in other countries. The PANORAMA study, for instance, documented that 37.4% of patients do not achieve adequate glycemic control, which they consider a serious issue, since the main factors influencing the poor control were: patient characteristics, inadequately targeted levels of glycosylated hemoglobin by physicians, duration of disease and treatment [22]. Another study of 1853 diabetic patients from Bulgaria and other countries, with an average age of 63.5 ± 10.7 years, and average disease duration of 8.9 ± 7.1 years, showed that 40% of the patients had HbA1c measurements every 6 months and 34% had at least one measurement every 12 months [23], which is in accordance with our data. The average levels of HbA1c were 7.3 ± 1.5, and 35% of patients had levels of <6.5% HbA1 [23], which also agrees with our dataset.

The recorded reduction in glycosylated hemoglobin is expected to lead to a 20-fold reduction in the risk of developing diabetes-related complications, which in turn would lead to saving costs amounting to 20 million BGN for the entire diabetic population for the period. These costs do not take into account hypertension; thus, we could speculate that the real-life benefits would be higher.

This study, however, has some limitations. We took the risk reduction from UKPDS study, which concerns type-2 diabetes. To account for this, we compared the UKPDS risk reduction results with similar studies on the control of type 1 diabetes [24–28] by using chi-square
analysis to compare the difference in risk reduction between all studies. We did not find a statistically significant difference among the related risks between type 2 and type 1 studies and therefore we used the UKPDS results due to similar reporting of the risks in the Bulgarian practice. Another limitation is that the control was not correlated with the type of diabetes therapy. This will be the next step in our study, i.e. to combine the control and type of medications.

Conclusions

For the period 2012–2016, the control of diabetes has improved in Bulgaria. The levels of glycosylated hemoglobin measured at different instances within a year, as well as throughout the years, point towards overall better treatment. The proportion of patients that achieved good control also increased throughout the years, reaching over 40% of the afflicted population. Among this population, the achieved adequate control leads to a reduced risk of developing diabetes-related complications, thereby saving costs associated with them, and decreasing the burden on the healthcare system.

Acknowledgement

This study is part of the national science program "Electronic health in Bulgaria" (e-health).

Authors’ contribution

Study design, data processing, analysis and writing (KT, GP and VV), statistical analysis, data extraction and processing (KM, GA, MDoneva and DT), data collection, systematization, calculations, referencing (ZM, MK, MDimitrova, VP, AS and MM).

Disclosure statement

V.V. works at NovoNordisk Bulgaria.

ORCID

Konstantin Tachkov  http://orcid.org/0000-0002-3961-7556
Maria Kamusheva  http://orcid.org/0000-0002-4379-5283
Guenka Petrova  http://orcid.org/0000-0001-8116-5138

References

[1] Ministry of Health. Guidelines for good clinical practice in Diabetes Mellitus. Sofia (Bulgaria): Bulgarian Endocrinology Society; 2016 [cited 2018 Dec 20]. Available from: http://endo-bg.com/wp-content/uploads/2016/04/DIABET-2016-new.pdf

[2] Zimmet PZ, Magliano DJ, Herman WH, et al. Diabetes: a 21st century challenge. Lancet Diabetes Endocrinol. 2014;2:56–64.

[3] WHO. Global status report on noncommunicable diseases. 2014. Available from: http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf?ua=1

[4] European parliament resolution from 14 March 2012 regarding countermeasures against the diabetes epidemic in the EU [cited 2018 Dec 20]. Available from: http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+TA+P7-TA-2012-0082+0+DOC+PDF+V0/BG

[5] Bulgarian Diabetes Association. Memorandum on limiting the incidence of Diabetes Mellitus in Bulgaria; 2008. Available from: http://www.badiabet.com/index.php?option=com_content&view=article&id=3-63

[6] Tancredi M, Rosengren A, Svensson AM, et al. Excess mortality among persons with type 2 diabetes. N Engl J Med. 2015;373:1720–1732.

[7] Gaede P, Lund-Andersen H, Parving H-H, et al. Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med. 2003;348:580–591.

[8] Miller RG, Secrest AM, Sharma RK, et al. Improvements in the life expectancy of Type 1 diabetes: the Pittsburgh Epidemiology of Diabetes Complications study cohort. Diabetes. 2012;61:2987–2992.

[9] Gregg EW, Beckles GL, Williamson DF, et al. Diabetes and physical disability among older U.S. adults. Diabetes Care. 2000;23:1272–1277.

[10] Wong E, Backholer K, Gearon E, et al. Diabetes and risk of physical disability in adults: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2013;1:106–114.

[11] Gale EAM. The United Kingdom Prospective Diabetes Study [UKPDS] [Internet]. [cited 2014 Oct 20]; Diapedia 1104085197. Available from: https://doi.org/10.14496/dia.1104085197.20

[12] Stratton IM, Adler AI, Neil AHW, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321:405.

[13] Ostrowska J, Jakubczyk M, Niewada M, et al. Estimating the cost of diabetes related cardiovascular complications in selected Central and Eastern European countries. Value Health. 2017;20:4A76.

[14] Ministry of Health of Bulgaria. Decision № RD-NS-04-24-1 from March 29th 2016 г. under section 54, paragraphs 9 and 59a, sub-paragraph 6 of the Health Insurance law by the Council of oversight to the National Health Insurance Fund (NHIF), State Gazette 25/31.03.2016. Bulgarian.

[15] Lee IM, Shiroma EJ, Lobelo F, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet. 2012;380:219–229.

[16] Guariguata L, Whiting DR, Hambleton I, et al. Global estimates of diabetes prevalence for 2035. Diabetes Res Clin Pract. 2014;103:137–149.

[17] Stolar MW. Defining and achieving treatment success in patients with type 2 diabetes mellitus. Mayo Clin Proc. 2010;85:550–559.
Herman WH, Ye W, Griffin SJ, et al. Early detection and treatment of type 2 diabetes reduce cardiovascular morbidity and mortality: a simulation of the results of the Anglo-Danish-Dutch Study of Intensive Treatment in People With Screen-Detected Diabetes in Primary Care (ADDITION-Europe). Diabetes Care. 2015;38:1449–1455.

Norhammar A, Bodegard J, Nyström T, et al. Incidence, prevalence and mortality of type 2 diabetes requiring glucose-lowering treatment, and associated risks of cardiovascular complications: a nationwide study in Sweden, 2006–2013. Diabetologia. 2016;59:1692–1701.

Chawla A, Chawla R, Jaggi S. Microvascular and macrovascular complications in diabetes mellitus: distinct or continuum? Indian J Endocrinol Metab. 2016;20:546–551.

Kautzky-Willer A, Harreiter J, Pacini G. Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. Endocr Rev. 2016;37:278–316.

de Pablos-Velasco P, Parhofer K, et al. Current level of glycaemic control and its associated factors in patients with type 2 diabetes across Europe: data from the PANORAMA study. Clin Endocrinol. 2014;80:47–56.

Cokolic M, Lalic N, Micic D, et al. Patterns of diabetes care in Slovenia, Croatia, Serbia, Bulgaria and Romania. Wien Klin Wochenschr. 2017;129:192–200.

Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin dependent diabetes mellitus. New Engl J Med. 1993;329:977–986.

Nathan DM, Cleary PA, Backlund JY, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. New Engl J Med. 2005;353:2643–2653.

Martin CL, Albers GW, Pop-Busui R. DCCT/EDIC Research Group. Neuropathy and related findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. Diabetes Care. 2014;37:31–38.

The DCCT/EDIC Research Group, Aiello LP, Sun W, et al. Intensive diabetes therapy and ocular surgery in type 1 diabetes. New Engl J Med. 2015;372:1722–1733.

Klein R, Klein BE, Moss SE, et al. The Wisconsin epidemiologic study of diabetes retinopathy: XVII, The 14 years incidence and progression of diabetic retinopathy and associated risk factors in type 1 diabetes. Ophthamology. 1998;105:1801–1815.