

# Regional differences in diabetic patients' pharmacotherapy in Bulgaria

V. VALOV<sup>2</sup>, M. DONEVA<sup>1</sup>, A.M. BORISOVA<sup>3</sup>, T. TANKOVA<sup>3</sup>, M. CZECH<sup>4</sup>,  
M. MANOVA, A. SAVOVA<sup>1</sup>, L. PEIKOVA<sup>1</sup>, G. PETROVA<sup>1</sup>

<sup>1</sup>Faculty of Pharmacy, Medical University of Sofia, Sofia, Bulgaria

<sup>2</sup>Novo Nordisk Pharma EAD, Sofia, Bulgaria

<sup>3</sup>Clinical Center of Endocrinology, Sofia, Bulgaria

<sup>4</sup>Novo Nordisk Pharma, Warsaw, Poland; and Department of Pharmacoeconomics, Medical University of Warsaw, Warsaw, Poland

**Abstract. – BACKGROUND:** The regional analyses play an important role in understanding a state of diabetes mellitus management and to support informed policy options. They need to be explored in more details in order to ensure an equal patients' access to health care services of the same value and quality.

**AIM:** The aim of this study is to analyze regional differences in a cost of diabetes therapy for insulin users in Bulgaria.

**MATERIALS AND METHODS:** It is a combined prospective and retrospective observational study with duration of 6 months. Diabetic patients on insulin therapy were recruited by 35 endocrinologists. Information about the health care resources used was collected within 3-prospective and 3 retrospective months in 2010 and 2011. The regional cost of illness analysis was performed by calculating the average cost attributable to each individual patient despite the fact that some might not use a particular health care resource. Subgroup analysis was performed for hospitalized patients.

**RESULTS:** A detailed analysis revealed cost differences in the regions, especially with more vulnerable population like Burgas and Pleven regions. Another reason for the cost differences is the type of insulin or type of therapy. Our study confirms the fact that the hospitalizations are the major cost driver. Rising diabetes prevalence and associated costs, including hospitalizations and management of diabetes complications, are a growing concern. The last possible reason for regional differences is the patients' characteristics and therapy differences. We add evidence demonstrating that the patients on insulin and OAD consume more resources including hospitalizations and suffer from more complications of diabetes.

**CONCLUSIONS:** Reasons for regional differences might have different origin as there are various population characteristics, type of therapy, socio economic status and others.

## Key Words

Insulin therapy, Cost of illness analysis, Diabetes, Pharmacoeconomics, Cost of diabetes.

## Introduction

Diabetes mellitus is recognized as a huge burden for the health care systems. It affects people in productive age and in the recent years affects younger generations<sup>1</sup>. The diabetes pathology is well established and its therapy is harmonized even at the international level, the fact that is unique for not so many diseases<sup>2</sup>. Medicinal products developed for the diabetes therapy are well known; especially for the patients with lack of insulin secretion for which the only one choice is the external injection of insulin. After the development of the insulin analogues they became a new promising therapy for patients with diabetes due to their better efficacy and safety profile, but their cost remains concern for health authorities<sup>3</sup>.

The cost of diabetes therapy is widely studied from different perspectives and in many health care systems<sup>4-8</sup>. Profound differences in the cost of therapy exist among countries in spite of internationally accepted therapeutic guidelines<sup>9</sup>. The differences are reported also at the national level and depend on many factors, as a type of diabetes, time of onset, proper management, complications, patients' characteristics, type of insulin or oral anti diabetics, etc.<sup>10-15</sup>.

The goal of this study is to analyze the regional differences in the cost of diabetes therapy for insulin users in Bulgaria.

## Materials and Methods

It is a combined prospective and retrospective observational study with duration of 6 months. Diabetic patients on insulin therapy were recruited by 35 endocrinologists from different country regions. The later were then grouped in the analysis according to the main town nearby, as follows: Sofia as capital (N 20 on the map), Sofia region (covers areas N7; N11; N21), Varna (covers areas N3; N14; N16; N23; N24), Burgas (covers N2; N5; N18; N28), Plovdiv (N6; N10; N13; N22), and Pleven (N8; N12; N25; N27) (Figure 1). Every region, except Sofia covers in fact patients from surrounding areas, thus, including almost all country areas.

Information about the health care resources used was collected within 3-prospective and 3 retrospective months in 2010 and 2011.

There was a random selection of patients. Within a one-month period, five consecutive insulin-treated diabetic patients who agree to participate were included in the observation. A sample size of 433 patients was created and was divided in 3 subgroups: 153 patients on insulin analogues, 115 on human insulin, and 165 on a combination of insulin and oral antidiabetic drugs (OAD).

Information about the health care resources, namely type of insulin and therapeutic regimen, medications for outpatient therapy of complications, hospitalizations due to diabetes and complications, physician visits (GP and specialists; endocrinologist, ophthalmologists, neurologists, nephrologists, and cardiologists), and medical devices (test-strips and glucometers) was collected.

The regional cost of illness analysis was performed by calculating the average cost attributable to each individual patient despite the fact that some might not use a particular health care resource. The subgroup analysis was performed for hospitalized patients.

These patients were extracted from the same three therapeutic subgroups – on analogues (n=45), human insulin (n=46) and OAD (n=69) therapy, and their average cost of therapy was calculated on a regional basis.

The prices of drugs and medical devices for outpatient treatment were taken from the official web site of the pricing and reimbursement committee at the Ministry of Health<sup>16</sup>. The cost of physicians' visits and hospitalizations were taken from the National Health Insurance Fund tariffs (NHIF)<sup>17</sup>.

All costs were calculated from payer perspective, and no patients' or indirect costs were considered. All the costs are presented for a six-month period in the national currency – Bulgarian Lev (BGN). The exchange rate in 2010 and 2011 is 1 Euro = 1.95 BGN.

Descriptive statistical methods were applied for the analysis of patients' characteristics and cost. *t*-test analysis was applied to test the cost differences.

## Results

### Cost of Illness Analysis

Patients' characteristics in the main sample are shown on Table I.



Figure 1. Country map with regions.

**Table 1.** Patients' characteristics.

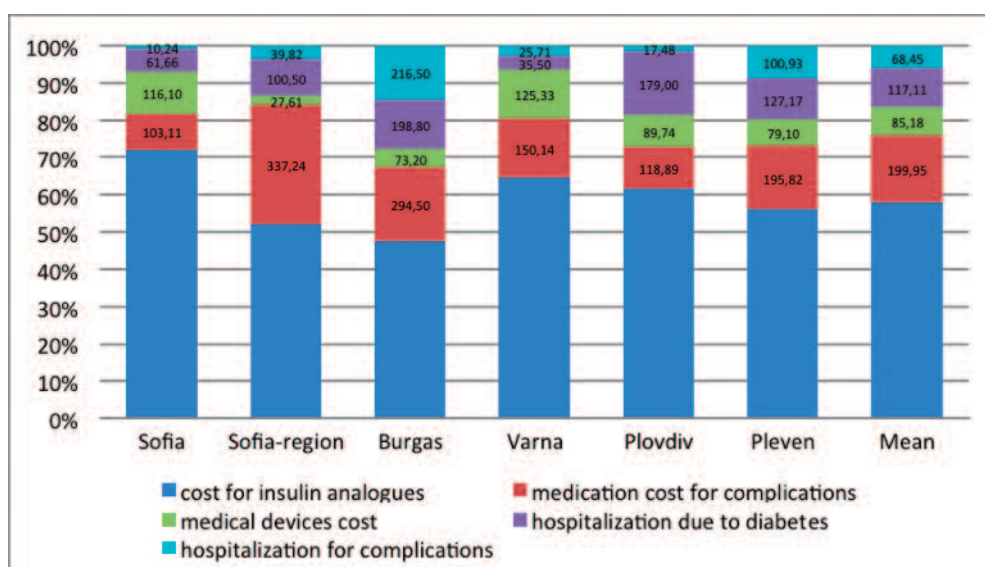
	Insulin analogues	Human insulin	Insulin and OAD
Average age in years (SD)	43.12 (16.02)	58.54 (16.44)	58.94 (9.9)
Male (n)	83	56	68
Female (n)	70	59	97
Duration of diabetes in years (SD)	15.46 (9.94)	12.97 (10.55)	12.53 (6.57)
Number of patients with complications due to diabetes (other complications)	63 (70)	58 (79)	78 (137)
Stroke	3	9	7
MI	0	2	2
Polyneuropathy	60	59	76
Retinopathy	13	8	13
Hypertension	44	60	121
Nephropathy	4	3	3

The general sample characteristics revealed that the group of patients on insulin and OAD is older and with more complications than the other two groups. This might be explained with the fact that those are mainly type 2 diabetes patients with inefficient control with only OAD. Some of the patients have more than one complication, especially in the group on insulin and OAD. The duration of diabetes in the group on insulin analogue is higher and those are younger patients all of them with type 1 diabetes.

For the group of patients treated with insulin analogues the main cost drivers were the cost of analogues therapy that accounts for 43%, cost of medicines for complication therapy (27%) and cost of hospitalization due to diabetes (14%). The highest total cost of therapy

(1596.52 BGN; SD = 152.99) was observed in Varna (Figure 2). The differences in the cost of Varna region are mostly due to the highest medication cost for hospitalization and cost of hospitalization due to complications. The total cost of therapy is almost equal in the rest of the regions. A variety of differences are observed among the medication cost for complications. The cost of insulin analogues therapy in Sofia differs statistically significant compared to the other regions ( $p < 0.05$ ), as well as the cost of hospitalization due to diabetes in Burgas region in comparison with the rest of the regions ( $p < 0.05$ ).

Total cost for patients on human insulin therapy is 925.28 BGN on average (SD95.93) (Figure 3). In this group again Burgas region



**Figure 2.** Regional differences in cost structure (BGN) for patients on insulin analogues.

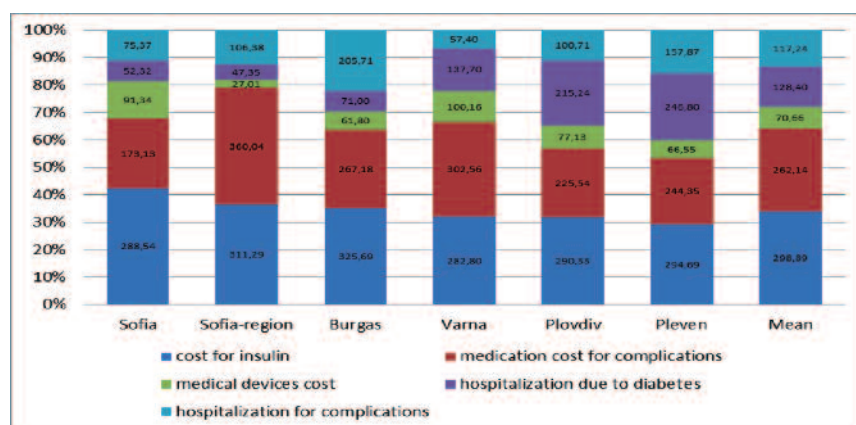


Figure 3. Regional differences in cost structure (BGN) for patients on human insulin.

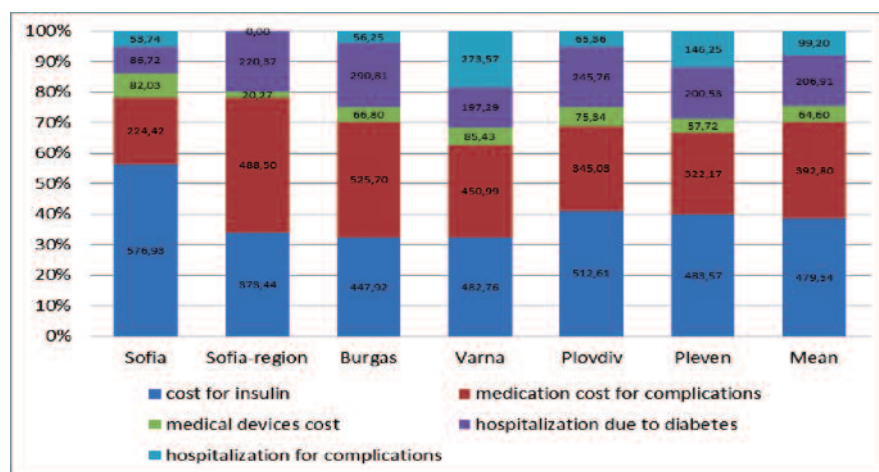


Figure 4. Regional differences in cost structure (BGN) for patients on insulin analogues and OAD.

and Pleven region are with highest total cost of therapy accounting for 980.97 and 1060.91 BGN respectively. The total cost of therapy in the other regions is varying between 717 and 969 BGN. In this group of patients mainly hospitalization due to diabetes (15%), insulin cost (34%), and medication cost for complications (30%) are the main cost drivers, thus accounting for 79% of total cost for all regions.

In the group of patients on insulin and OAD Varna region is with highest cost of therapy (1596.52 BGN), followed by Burgas (1492.10 BGN) (Figure 4). Differences in cost with the other regions are statistically significant ( $p < 0.05$ ). In this group the high relative share of the hospitalization cost due to diabetes (16%), insulin plus OAD (39%) and medications due to complications cost (31%) is observed thus accounting for 88% of total cost of health care resources use in the group.

### Subgroup Cost of Illness Analysis

The subgroup analysis focused only on the patients with hospitalizations due to diabetes during the observed period. Their demographic characteristics are shown on Table II.

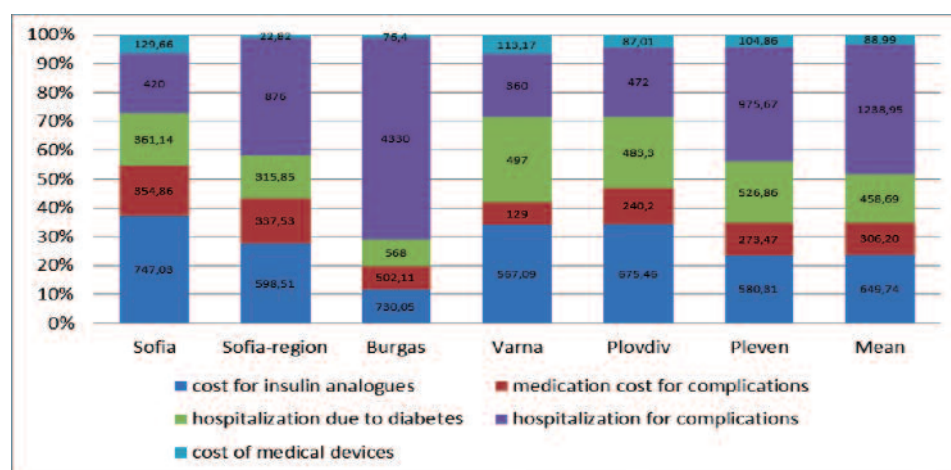
In this sample subgroup again the patients on insulin analogues are the youngest while those on combination therapy are with more complication (Table II).

The subgroup analysis revealed that the relative share of the cost of insulin therapy decreases while the hospitalization cost and complications cost increases. A variety of differences in cost structure exist. The highest is the cost of hospitalizations due to complications in Burgas (502.11 BGN) that might be due to the insufficient diabetes control. Also the hospitalization cost due to diabetes in Varna, Plovdiv and Pleven region is higher than that in Sofia and Burgas (Figure 5). Total cost of therapy for this subgroup is varying

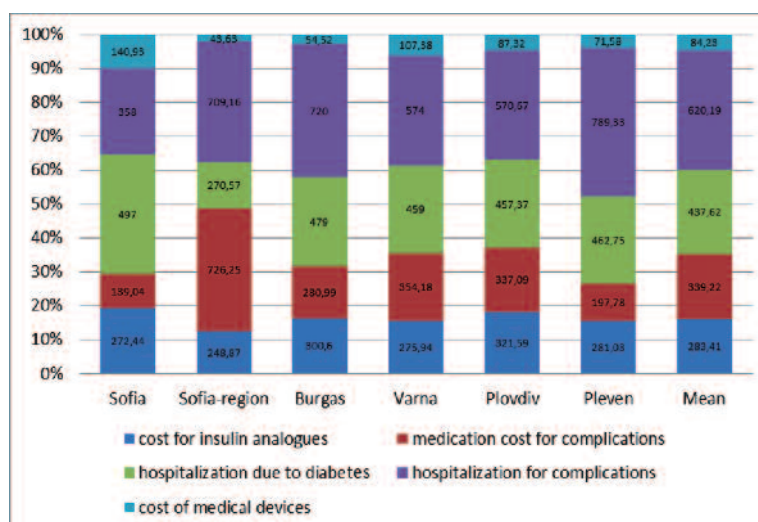
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**Table II.** Patients' characteristics for the subgroup analysis.

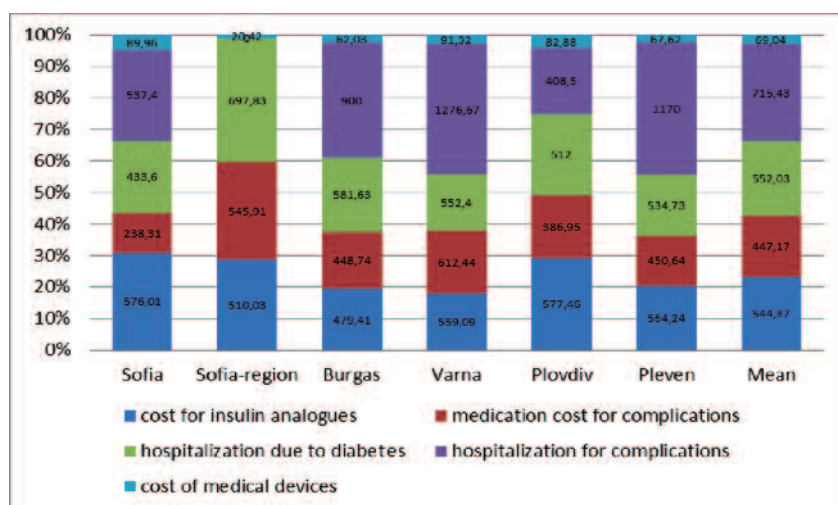
	Insulin analogues	Human insulin	Insulin and OAD
Average age in years (SD)	43.5 (14.6)	58.67 (16.7)	58.5 (9.58)
Male (n)	21	21	28
Female (n)	24	25	41
Duration of diabetes in years (SD)	16.24 (10.24)	12.98 (11.26)	13.27 (6.98)
Number of patients with complications due to diabetes (other complications)	32 (27)	26 (35)	36 (60)
Stroke	2	3	2
MI	0	2	1
Polyneuropathy	31	26	36
Retinopathy	6	4	11
Hypertension	18	28	55
Nephropathy	2	3	2



**Figure 5.** Regional cost differences (BGN) for patients on insulin analogues with hospitalizations.



**Figure 6.** Regional cost differences (BGN) for patients on human insulin with hospitalizations.



**Figure 7.** Regional cost differences (BGN) for patients on insulin and OAD with hospitalizations.

between 1700 and 2500 BGN with great variances observed in the hospitalization cost due to complications (from 360 to 876 BGN).

When comparing the patients on insulin analogues with these on human insulins, one can observe the smaller relative share of the cost of insulin and relatively similar proportions of cost for hospitalization due to diabetes and diabetes complications accounting for near 60% of all costs (Figure 6).

For the group of patients on insulin and OAD the relative share of the cost of hospitalizations both due to diabetes and due to complications is even higher and differs significantly among the regions (60%-68%) (Figure 7). This is the group of patients with lots of variations in their personal characteristics as duration of diabetes, ages etc. Also in this last subgroup usually the introduction of insulin is mainly the result of inefficient control of the diabetes only with OAD thus supposing more severe complications. The weak control leads to the increase in the total cost of diabetes therapy in this last subgroup (from 1800 to 3200 BGN).

The fact that in Sofia-region the hospitalization due to diabetes and medication cost for complications are with highest relative share and together with the insulin and OAD they account almost to 96% of the total cost might be explained by the transfer of their therapy to Sofia (the highest reference level centers) in the case of complications because of a the lack of appropriate facilities nearby.

## Discussion

Our report is the second Bulgarian study focusing on the regional differences in the cost of

diabetes therapy<sup>18</sup>, but in contrast with the previous one it includes modern anti diabetes medicines, as human insulin and insulin analogues, and is focusing on many cost components.

The analysis of the cost differences revealed the regions with high and low expenditures that might influence the diabetes control, especially in regions with more vulnerable population like Burgas and Pleven regions. Similar results are achieved in Italy and USA<sup>15,19</sup>. Both studies consider that the high spending regions consume more and are with better controlled patients. We did not evaluate the diabetes control but we can consider that regions with vulnerable groups consume more hospitalization costs probably because of a poor diabetes control. For such regions more prevention efforts are needed to reduce the cost burden because of the very low expenditures per capita in poor countries indicating that more resources are required to provide basic diabetes care in such settings<sup>4,20</sup>.

Another reason for the cost differences might be the type of insulin or type of therapy. Some authors found that the insulin might increase the cost with 10% when added to OAD<sup>21</sup>. This is the case and in our study where the medication cost of patients on insulin and OAD is with the highest value in comparison with the medication cost of patients on human insulin. The insulin analogues also add significant cost burden but their utilization decreases the cost of complications and hospitalizations, the fact that is also discussed in another studies<sup>22</sup>.

Our study confirms the fact that the hospitalizations are the major cost driver. Rising diabetes prevalence and associated costs, including hospitalizations and management of diabetes compli-

cations, are a growing concern. Authors from lots of studies consider that there is a lack of contemporary and on time data for such components even in countries like France, Germany, and Spain. This limits the ability to accurately gauge the health of the diabetes population or make any appropriate impacts on quality of care. As a result, the true impact of diabetes and its associated complications is likely to be underestimated or altogether unmeasured in EU<sup>23</sup>.

The last possible reason for regional differences is the patients' characteristics and therapy differences. We add some evidence that the patients on insulin and OAD are consuming more resources and are with more complications and hospitalizations<sup>24</sup>.

## Conclusions

Reasons for regional differences might have different origin as there are various population characteristics, type of therapy, socio economic status and others.

The regional analyses seem to play an important role in understanding a state of diabetes management and to support informed policy options. They need to be explored in more details in order to ensure an equal patients' access to health care services of the same value and quality.

## Conflict of Interest

Vasil Valov is regularly employed by Novo Nordisk Pharma EAD, Sofia, Bulgaria. Marcin Czech is employed by Novo Nordisk Pharma, Warsaw, Poland and part time employed by the Medical University of Warsaw, Department of Pharmacoeconomics, Warsaw, Poland.

## Financial Disclosure

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