

Hypolipidemic and antihypertensive therapy in diabetic patients in the Czech Republic: Notes on the VZP (General Health Insurance Company) Data

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Summary

Diabetes mellitus and in particular type 2 diabetes mellitus is one of the most important risk factors of cardiovascular disease. To influence cardiovascular risk there is enormous important not only positive influence of glycaemia, but also the treatment of diabetic dyslipidemia and hypertension. The present work provides an analysis of lipid-lowering and antihypertensive therapy for all diabetics registered with General Health Insurance Company in the period 2010–2013. In this time 866 570 patients with diabetes mellitus registered with General Health Insurance Company were treated, the majority of them were diabetics independent on insulin. Approximately half of the patients were observed by diabetologists and half of them by the doctors of other specialization. Out of antihypertensive medication, patients were most often treated by drugs that affect the renin-angiotensin system, as well as beta-blockers and diuretics. Prescription of the lipid-lowering therapy, especially prescription of statins, in accordance with the guidelines, is increasing, but remains insufficient (at 2013 43.6% diabetics treated by diabetologists and 51.3% diabetics treated by GP's did not have lipid lowering therapy). Inadequate use of combination lipid-lowering therapy was recorded too, still was represented mainly by combination of statin and fibrate, but in the coming years we expect (based on the positive results of the subanalysis IMPROVE-IT study), an increase in the combination therapy of statin and ezetimibe.

Keywords: diabetes mellitus type 2 – diabetic dyslipidemia – ezetimibe – cardiovascular risk – statins

Introduction

Diabetes mellitus type 2 (DM2T) represents one of the most important risk factors of cardiovascular diseases (CVDs). For DM2T patients, the risk of CVD development is 5 times higher [1,2] and the risk of stroke is 2 to 4 times higher [3]. Cardiovascular diseases are the cause of death of 2/3 of patients affected by DM2T. Moreover, taking into account that patients with diabetes constitute almost 1/10 of the population, it is obvious that the issues related to comprehensive influencing of the CV risk in diabetics are critical, from the medical as well as economic point of view.

Cardiovascular risk of type 2 diabetics and the possibilities of its influencing depend in particular on diabetes duration and presence of other CVD risk factors.

At the time of diagnosis or within 10 years after its establishing, diabetes does not represent the same CV risk as the presence of ischemic heart disease does in

a nondiabetic patient [4]; on the other hand, the CV risk for a diabetic patient with the disease duration 10 and more years is the same as in patients in secondary prevention, i.e. with an already manifest CVD.

Thus the lowest risk exists for patients with newly diagnosed diabetes, the highest then for diabetics whose disease lasts longer than 10 years and who also have the already manifest CVD. To influence cardiovascular risk in such patients, not only positive influencing of glucose levels, but also the treatment of diabetic dyslipidemia and arterial hypertension is of enormous significance [5–7].

Czech physicians have at their disposal a huge amount of information on innovations and new recommendations in diabetes, arterial hypertension and dyslipidemia treatment, not only in the form of original works [8–10], but also contained in numerous comments and summary articles

in the Czech journals. We also have at our disposal relatively large portfolio of both original and generic preparations for treatment of the above diseases. What we are still somewhat missing in the Czech Republic are studies evaluating the efficiency of our treatment of type 2 diabetics, or rather not only of the glycemia levels, but also other CVD risk factors (up to now, only the studies post-MONICA, VARO, and VATARO that were however not focused primarily on the diabetic population) [11–13].

Methodology

The work constitutes a part of the detailed analysis of hypolipidemic therapy in all diabetics registered with VZP (General Health Insurance Company). The basic set of persons was identified in the database of all persons insured with VZP for whom a prescription of an antidiabetic medicine was recorded or a diagnosis of any type of diabetes mellitus was established within the monitored period of 2010 – 2013. For this analysis, both the whole set described above and also subsets of persons who are monitored only by a diabetologist or only by a general practitioner according to the procedures reported were selected. Hypolipidemic treatment was identified according to the records of paid prescriptions for the given patient in each year, as when the prescription was paid, it was also collected.

Results

Within 2010 – 2013, 866 570 patients with a diabetes mellitus diagnosis registered with VZP were treated, the majority of them (57.6 %) being diabetics not depending on insulin.

The absolute numbers of VZP insured patients with diabetes mellitus slightly decreased between 2010 and 2013 (from 794 785 patients in 2010 to 728 717 patients in 2013), which is related to the decrease of persons insured with VZP (Chart 1).

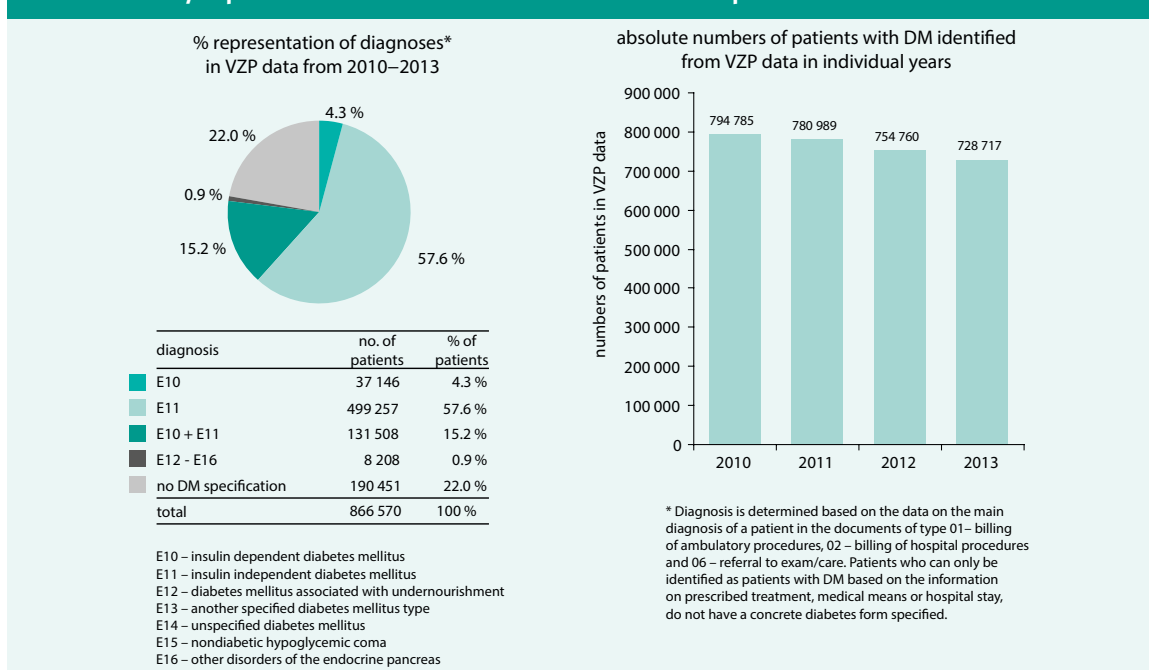
Almost 50 % of the registered diabetics were monitored by a diabetologist only. Others were cared for either by a general practitioner only (2.1 % in 2010, 7.2 % in 2013), a negligible amount (0.4 %) of was monitored by both a general practitioner and diabetologist at the same time, the remaining patients (52.2 % in 2010 and 44.1 % in 2013) by other specialists, or without a monitoring record from either a diabetologist or a general practitioner (Tab. 1).

Treatment of arterial hypertension and dyslipidemia in patients with diabetes mellitus

It can be stated based on the available data that, in accordance with the applicable recommendations, both diabetologists and general practitioners choose for the treatment of arterial hypertension primarily drugs affecting the renin-angiotensin system – i.e. ACE inhibitors and sartans (a moderate increase was recorded for both diabetologists and general practitioners between 2010 and 2013), followed by medicines from the beta-blocker group (again for both professions) and by diuretics placing third (very closely ahead of calcium blockers); see Chart 2 and Chart 3.

It can be further stated based on the data in Chart 2 that slightly over half of the monitored diabetics in diabetologists' ambulances took hypolipidemic treatment, whose prescription moderately increased in the given period

Chart 1. Summary of patients with diabetes mellitus in VZP data in the period 2010–2013



(from 52.7 % patients in 2010 to 56.4 % patients in 2013). Prescription of hypolipidemics by general practitioners was somewhat lower, however, it also moderately increased in the given period (from 44.6 % in 2010 to 48.7 % in 2013); see [Chart 3](#).

It is gratifying that most the hypolipidemics prescribed are statins. In 2013, statins were used by 50.3 % of diabetic patients (insured with VZP) monitored in diabetologist outpatient clinics ([Chart 4](#)) and 42.6 % diabetic patients visiting their general practitioners ([Chart 5](#))

If you take a closer look at the prescriptions of the individual statins ([Chart 6](#), [Chart 7](#)), you will find that the most often prescribed statin, both by general practitioners and diabetologists, is still atorvastatin. The increase in prescriptions of newer and more efficient statins, like rosuvastatin, is also pleasing. The increase recorded for diabetologists was from 2.2 % in 2010 to 8.9 % in 2013; for general practitioners, it was from 1.6 % in 2010 to 8.8 % in 2013. On the other hand, prescriptions of older statins, like pravastatin, lovastatin and fluvastatin, already represents a negligible proportion of the overall prescription of statins; the number of patients taking simvastatin also decreases.

It follows from the above data that although the prescription of statins in the group of diabetics increases, it is still unsatisfactory and we cannot but hope that this trend will continue to grow in the coming years. Likewise, considerable reserves were recorded in the combination hypolipidemic treatment which makes up a very small proportion, both in the group of patients treated only by diabetologists (of the total of 50.3 % of diabetics treated with statins in 2013, only 4.6 % were taking combination treatment, 45.7 % were taking statin in monotherapy; see [Chart 8](#)), and in the group treated by general practitioners (of the total percentage of 42.6 % of diabetic patients treated with statins in 2013, only 2.2 % were using combination treatment, and 40.4 % were taking statin in monotherapy, see [Chart 9](#)).

Within the monitored period, the prescription of fibrates moderately decreased both in diabetologists' outpatient clinics (7.7 % of patients in 2013 compared to 8.6 % of patients in 2010) and in general practitioner's surgeries (5.6 % of patients in 2013 compared to 7.1 % in 2010). In both cases, the amount of fenofibrate was predominant. In the future, in particular after

Table 1. Overall summary of patients in VZP data from 2010 to 2013. Numbers of patients in VZP data based on monitoring by a specialist physician in the individual years of the period of 2010–2013

Specialty of the physician monitoring the patient	2010	2011	2012	2013
All patients recorded in VZP data	794 785 (100 %)	780 989 (100 %)	754 760 (100 %)	728 717 (100 %)
Diabetologist or general practitioner	380 147 (47.8 %)	398 895 (51.1 %)	404 109 (53.5 %)	407 241 (55.9 %)
Only diabetologist	360 357 (45.3 %)	360 644 (46.2 %)	356 267 (47.2 %)	351 930 (48.3 %)
Only general practitioner	16 853 (2.1 %)	35 595 (4.6 %)	44 880 (5.9 %)	52 312 (7.2 %)
Diabetologist and general practitioner	2 937 (0.4 %)	2 656 (0.3 %)	2 962 (0.4 %)	2 999 (0.4 %)
Patients without a record of monitoring by a diabetologist or general practitioner	414 638 (52.2 %)	382 094 (48.9 %)	350 651 (46.5 %)	321 476 (44.1 %)

Chart 2. Patients monitored only by a diabetologist: Overall summary of treatment of patients with drugs influencing cardiovascular system

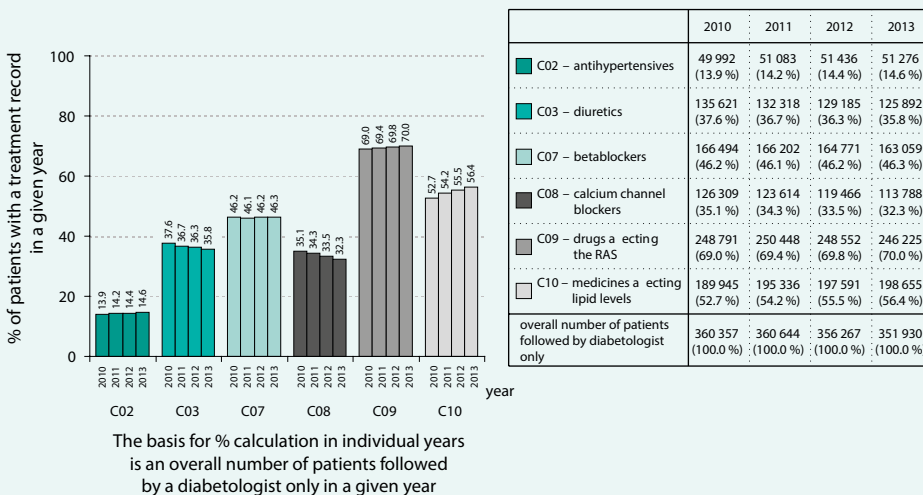


Chart 3. Patients monitored only by a general practitioner: Overall summary of treatment of patients with drugs influencing cardiovascular system

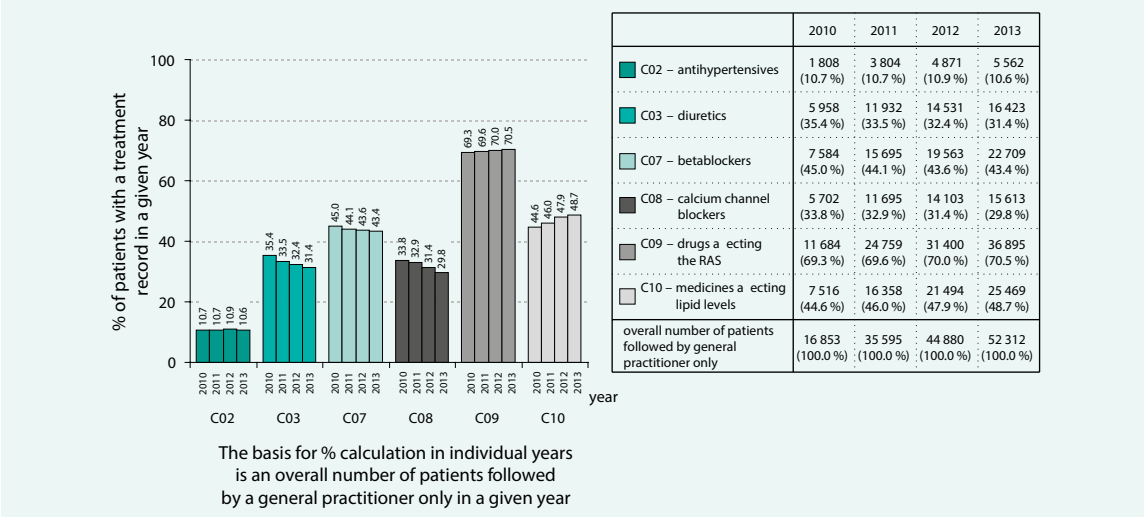
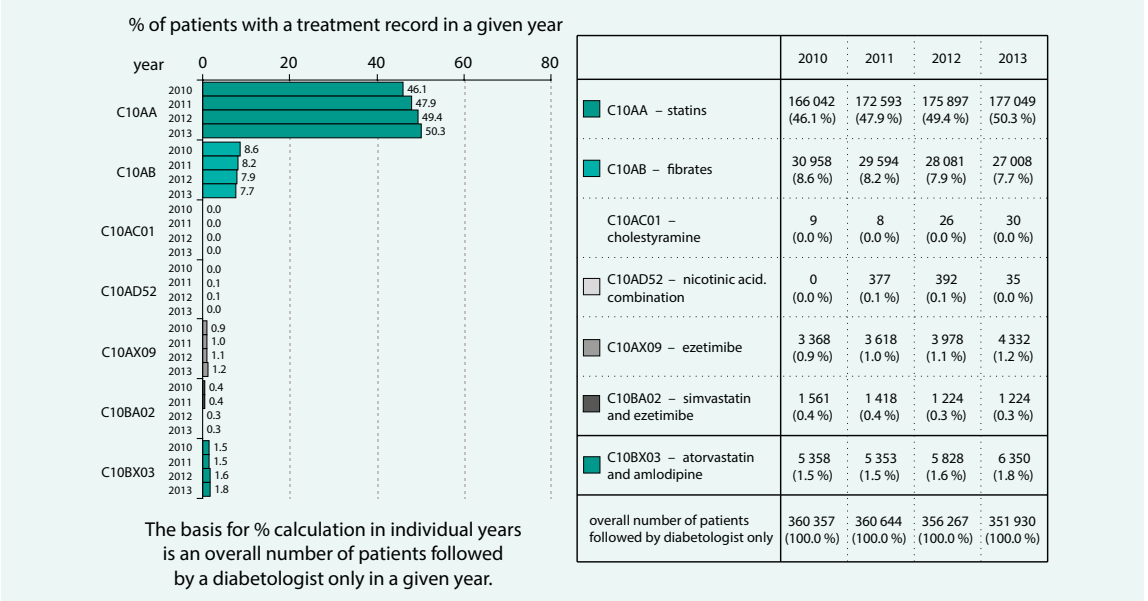


Chart 4. Patients monitored only by a diabetologist: Analysis of medicines influencing the level of lipids (C10)



the publication of the long awaited results of the IM-PROVE-IT [14] study, the trend in the combination treatment will certainly move toward the combination of statin and ezetimibe, especially when it comes to the population of diabetic patients.

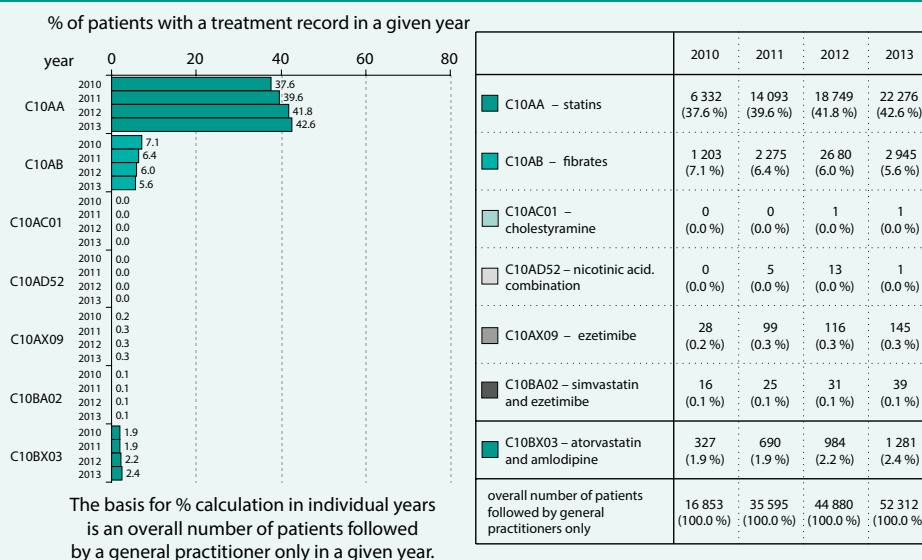
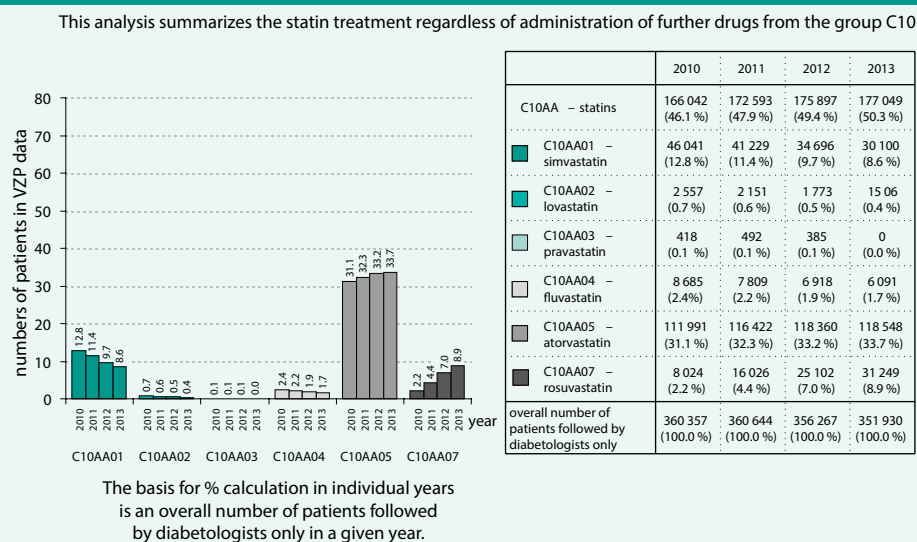
According to the data available, the use of ezetimibe in hypolipidemic treatment of patients with diabetes has so far been marginal – in 2013, 1.2 % of them receiving care in diabetologist clinics and 0.3 % in general practitioners’ surgeries were taking ezetimibe.

Recently, the analysis was complemented by the 2014 results. The analysis was performed in a subcohort of

those patients who had any antidiabetic medication prescribed in the given year, which information clearly identifies patients with diabetes in a non-pharmacological therapy with antidiabetic medication which is also burdened with higher risk. In 2014, 57.3 % of persons with pharmacological treatment of diabetes were treated with some hypolipidemic medicine; see Chart 10.

Discussion

The risk of cardiovascular disease development is about 5 times higher for diabetic patients, and in particular those with type 2 diabetes, compared to the non-diabetic

Chart 5. Patients monitored only by a general practitioner: Analysis of medicines influencing the level of lipids (C10)**Chart 6. Patients monitored only by a diabetologist: Analysis of medicines influencing the level of lipids – statins (C10AA) I**

population, with 70 to 75 % of diabetics dying of CVD. Consistent intervention in all atherosclerosis risk factors in type 2 diabetics is therefore the method to reduce cardiovascular morbidity and mortality of this population. In the Czech Republic, there are very few cross-sectional studies that would evaluate efficiency of our treatment in the diabetic population; however, thanks to the databases of health insurance companies, the necessary data on therapeutic care, i.e. on the use of the individual groups of pharmaceuticals, can be at least partly gained.

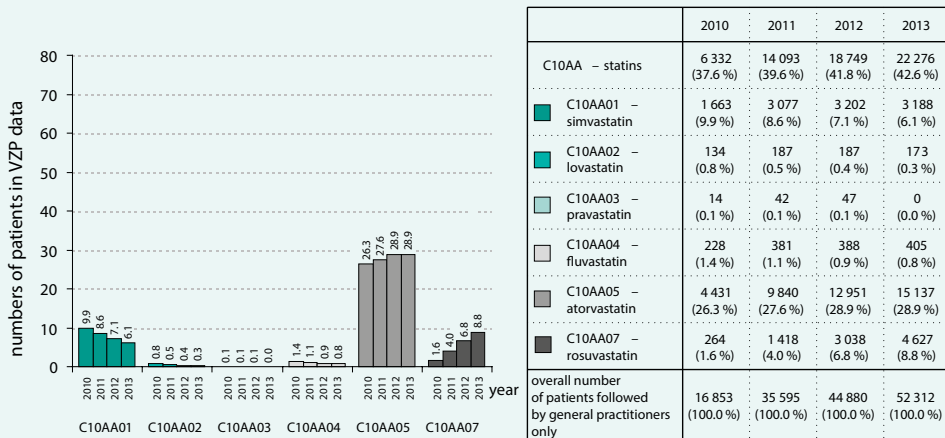
Within 2010 – 2013, 866 570 patients with diabetes mellitus diagnosis registered with VZP were treated, the majority of them (57.6 %) being insulin independent. It

can be assumed that a much higher percentage of patients could be included in this group – in particular a part of the 15.2 % of patients who were assessed as “E10 + E11”, i.e. most probably patients dependent on insulin only temporarily, and also a part of the 22 % of patients without specification of diabetes type. 4.3 % of patients were assessed as definitely insulin dependent.

Despite the constantly increasing incidence and prevalence of diabetes in the Czech population, the absolute numbers of VZP insured patients with diabetes mellitus slightly decreased between 2010 and 2013 (from 794 785 patients in 2010 to 728 717 patients in 2013). This decrease was most probably caused by an increase in the

Chart 7. Patients monitored only by a general practitioner: Analysis of medicines influencing the level of lipids – statins (C10AA) I

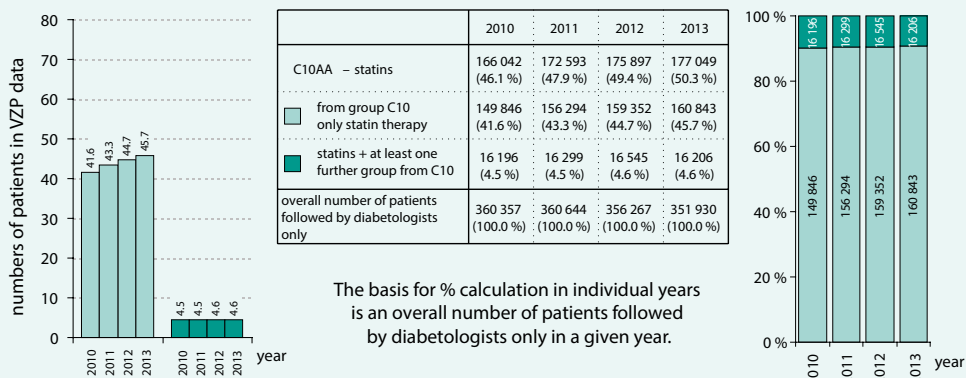
This analysis summarizes the statin treatment regardless of administration of further drugs from the group C10



The basis for % calculation in individual years is an overall number of patients followed by a general practitioner only in a given year.

Chart 8. Patients monitored only by a diabetologist: Analysis of medicines influencing the level of lipids – statins (C10AA) II

This analysis summarizes the statin treatment regardless of administration of further drugs from the group C10



The basis for % calculation in individual years is an overall number of patients followed by diabetologists only in a given year.

percentage of patients insured with smaller health insurance companies having left VZP.

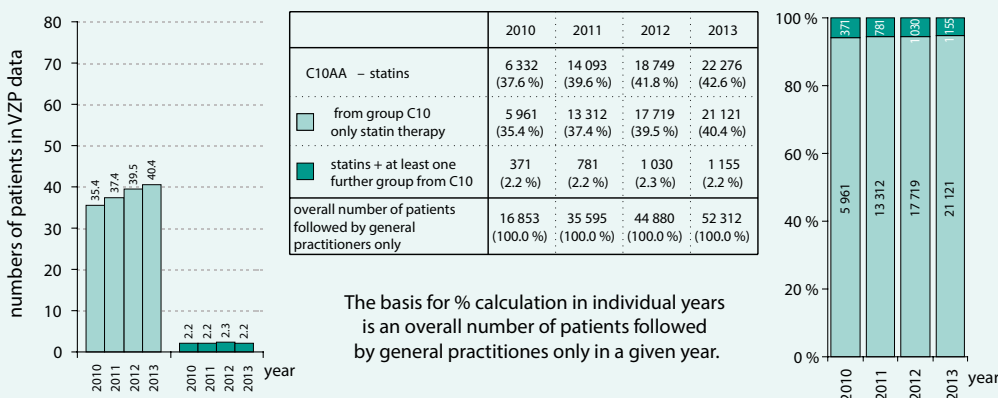
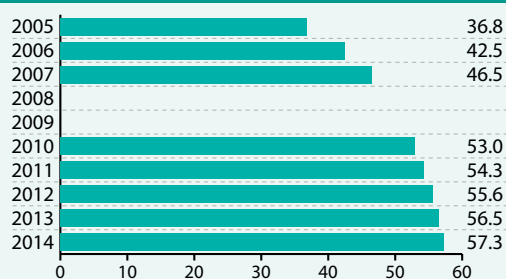
Almost 50 % of registered diabetics were monitored by a diabetologist (whether only by a diabetologist or by a diabetologist and a general practitioner at the same time). The other half was monitored by other specialists (not further specified). The stated data is a summary; it does not detail the level of diabetes compensation and diabetic complications. There is no way to specify whether really all “complicated” diabetic patients are monitored in diabetes outpatient clinics, by internists, endocrinologists and other specialists who can provide the patient with the most modern and effective available treatment within the prescription limitations.

ACE inhibitors and sartans are leading in the arterial hypertension treatment; a relatively high amount of beta-blockers was a little surprising. It is not clear from the data obtained which beta-blockers and for what indication were introduced; on account of that a more specific evaluation is very difficult.

Very gratifying is the increasing prescription of hypolipidemic treatment, both in diabetologist clinics (56.4 % of patients in 2013) and in general practitioners’ surgeries (48.7 % in 2013), still with a predominant proportion of statins among hypolipidemics. It is just the statins that are responsible for the increase in the prescriptions of hypolipidemics, notwithstanding the alarming information about their diabetogenic effects.

Chart 9. Patients monitored only by a general practitioner: Analysis of medicines influencing the level of lipids – statins (C10AA) II

This analysis summarizes the statin treatment regardless of administration of further drugs from the group C10

**Chart 10. The proportion of patients with DM treated by any hypolipidemics of all patients with DM treated with antidiabetic medication**

The risk of development of diabetes mellitus following the statin treatment is low compared with the degree of influencing the CV risk for a patient with DM [15].

Evidently, when taking into account the risk profile of a diabetic population, it can be inferred that, despite the increasing trend of statin prescription, there still remains a high percentage of those who should be taking statins and they do not, or rather it cannot be assumed that patients not treated with hypolipidemics were only uncomplicated, low risk, recently diagnosed diabetics. On the other hand, we must also consider the possibility of statin intolerance or a mere refusal of hypolipidemic treatment by patients. Also nonadherence of a patient may play an important role. Only the hypolipidemic drugs prescribed and picked up from a pharmacy (i.e. prescriptions paid by a health insurance company) are evaluated, which means that patients may not have picked up all prescribed drugs. Neither can it be evaluated what amount of the picked-up drugs the patients have actually taken.

When examining in detail the prescription of the individual statins, you will find that the most often prescribed

statin, both by general practitioners and by diabetologists, is still atorvastatin in line with the results of the STEP (Statin Therapy Results in the Real World Practice in the Czech Republic of 2010) study [16], according to which the generally most often prescribed statin in the Czech Republic is atorvastatin in a dose of 20 mg. An increase in the prescription of newer and more efficient statins, such as rosuvastatin, is also gratifying. The increase recorded for diabetologists was 4 times higher, for general practitioners more than 5 times higher. On the other hand, the prescription of older statins, such as pravastatin, lovastatin and fluvastatin, already make up a negligible percentage of the overall prescription of statins; the number of patients taking simvastatin also decreases.

Similarly, the prescription of fibrates, concerning the predominant proportion of fenofibrate, moderately decreased within the monitored period.

Big reserves were recorded in the combination hypolipidemic treatment which only represents a small proportion both in the group of patients treated only by diabetologists (of the total of 50.3 % of diabetics treated with statins in 2013 only 4.6 % was taking combination treatment) and in the group treated by general practitioners (of the total of 42.6 % of diabetics treated with statins in 2013, only 2.2 % was taking combination treatment). In most cases, statin was combined with fibrate, the use of ezetimibe (even as an only drug) was very low within the monitored period (in 2013, it amounted to 1.2 % in diabetologist outpatient clinics and 0.3 % in general practitioners' surgeries).

After the publication of the long awaited results of the IMPROVE-IT (Improved Reduction of Outcomes: Vytorin Efficacy International Trial) study and its comments [14,15], increase in patients with combination hypolipidemic therapy, or rather a combination of statin and ezetimibe, can be expected, particularly as far as the diabetic population is concerned.

The subanalysis of the diabetic population (4 933 patients) in the IMPROVE-IT study has proven that, although patients with DM are at a higher CV risk, they had a higher relative and absolute benefit from the hypolipidemic therapy with simvastatin being reinforced with ezetimibe, as compared to the non-diabetic population, which mainly consists in the reduction of the number of myocardial infarctions and ischaemic strokes.

Conclusion

With regard to cardiovascular diseases, individuals with type 2 diabetes belong to a high risk population. Positive influencing of both cardiovascular morbidity and mortality involves a comprehensive approach to the patient and consistent intervention in all influenceable risk factors – among those pharmacologically influenceable they include, apart from hyperglycemia, in particular diabetic dyslipidemia and arterial hypertension.

According to the available VZP data, the pharmacological treatment of Czech patients exhibits a constantly improving trend, still it must be admitted that there are further means available to be put to good use.

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