

Chapter 3

Changes in prescribed medication in patients with type 2 diabetes in a diabetes management system: an observational 7-years follow-up study

L.M.C. Welschen

M.C. van Veen

S.D.M. Bot

J.M. Dekker

G. Nijpels

Submitted for publication

Abstract

Objective

To describe the changes in prescribed medication in patients with type 2 diabetes after entry into a Diabetes Management System (DMS).

Research design and methods

Patients with type 2 diabetes who were included in a DMS were followed for up to seven years. From 1998 till 2005 data on prescribed medication was collected annually. The proportion of patients who were prescribed diabetes related medication as well as the number of medicines was calculated. Furthermore, variation in prescription of medication at entry between calendar years was investigated.

Results

A total of 4782 patients entered the DMS between 1998 and 2005 (mean age 62 ± 12 years; 51% men). There were 440 patients with a follow-up of seven years. The proportion of patients who were prescribed insulin increased from 11.7% at entry to 40.9% at seven years follow up; oral antihyperglycemic drugs increased from 65.9% to 80.7%; antihypertensive medication increased from 49.5% to 68.2%; and lipid modifying medication increased from 23.9% to 51.6%. Prescribed medication at entry varied between calendar years: in 1998 sulfonylureas were prescribed the most and in 2005 metformin. During later years, prescription of antihypertensive medication doubled and of lipid modifying medication increased with 20%.

Conclusions

The proportion of patients with type 2 diabetes included into a DMS who were prescribed diabetes related medication and the number of diabetes related medicines increased every year during 7 years of follow-up. In addition, prescription of medication became more intense during later calendar years. It appears that with increasing diabetes duration intensified prescription of medication is needed in order to maintain management goals.

Introduction

Type 2 diabetes is a progressive disease which requires intensive chronic care in order to optimize metabolic control and prevent diabetes related complications and cardiovascular disease (1). Patients with type 2 diabetes have a highly increased risk for cardiovascular morbidity and mortality (2-5). To prevent cardiovascular disease or early death, intensive medication therapy is needed. Management of type 2 diabetes requires a multifactorial approach aimed at treating multiple risk factors (6,7). Strict glycaemic and blood pressure control with glucose lowering and antihypertensive medication can reduce the risk of micro- and macrovascular complications (8-11) and lipid modifying medication treatment can also decrease the cardiovascular risk for patients with type 2 diabetes (12). As type 2 diabetes is characterized by a progressive deterioration when diabetes duration increases, the need for medicines usually increases in order to maintain management goals (13,14).

During the last few decades, the role of chronic care models became acknowledged, because it was believed that the 'classical' healthcare system might be inadequate to provide chronic care according to standard guidelines (15-17). It has been suggested that implementation of multifaceted interventions in primary care can improve the quality of chronic care processes (18,19) and metabolic control for patients with type 2 diabetes (20-22). In 1997, a multifaceted Diabetes Management System (DMS) was implemented in the region West-Friesland, The Netherlands. General practitioners (GPs) in the region were invited to refer their patients with diabetes to the DMS. The DMS provides coordination of care between different caregivers, including feedback to the GPs. Patients are invited every year for an annual medical assessment, followed by an education session by a diabetes nurse and a dietician, in order to stimulate patient empowerment.

Longitudinal data of annual cardiovascular risk factor assessments and prescription of medication, with a follow-up of 7 years, are now available. We have already shown that the clinical characteristics of the patients included in the DMS improved and stabilized during follow-up (23). In the present study, we will focus on the prescription of medication that was required to maintain risk factor control, during up to 7 years of follow-up.

Research design and methods

Diabetes Management System

This study was an observational study conducted in a DMS, which was set up in 1997 in the region West-Friesland, the Netherlands. General Practitioners (GPs) in the region were requested to refer all patients with type 2 diabetes to the DMS, except for immobile patients and patients with a short life expectation. Each patient visited the DMS annually, in addition to the care of the GP. The annual assessments consisted of two separate visits within a period of approximately three weeks. Details concerning these visits and the objective of the DMS have been described previously (23). Briefly, at the first annual visit, patients had a physical examination, and patients brought packages of prescribed medications. Name, dose and frequency of every medicine were noted by a research assistant into a central computer system. If the information of the prescribed medicine was unclear, a pharmacist was consulted for clarification. The second visit consisted of a consult with a diabetes nurse and with a dietician, 30 minutes each. Patients were informed about the results of the physical examination and received information and education on the control of their diabetes, including information on how to use the prescribed medication. This advice was also sent to the GPs. According to the advice and the outcomes of the physical examination, GPs were requested to change current medication therapy according to the guidelines of the Dutch College of General Practitioners (24) .

Study population

Measurements of patients who visited the DMS in 1997 were not included, because this study year was primarily used to implement the system. In 1998, 803 patients were included in the DMS. With an average of about 400 new patients per year, 3777 patients had been included in the DMS in 2005. In addition, with a mean dropout of about 3% per year, 597 patients dropped out during the study period. The main cause was death ($n=293$); 72 patients moved to another region; 26 patients moved to a nursing home or a home for elderly people; 119 patients preferred the care from their GP or specialist only; and 87 patients dropped out for other reasons (e.g. non-compliance, dementia, severe illness).

For this study, patients with incomplete data regarding prescribed diabetes related medication were excluded from the study ($n=151$). Clinical characteristics of these patients did not differ with those of the study population. However, excluded patients were older at entry into the DMS (64.3 ± 11.1 years) and had a longer diabetes duration (5.2 ± 6.5 years).

Statistical analyses

In order to evaluate medication trends following entry into the DMS, a study population was defined. Measurements of every patient at entry into the DMS were set at T=1. Measurements during the follow-up period were defined as T=2 to T=8.

Prescribed medicines were categorized and recoded according to the ATC codes of the WHO Collaborating Centre for Drugs Statistics Methodology (25). Medications were categorized into the following medication groups: insulin (A10A), oral antihyperglycaemic drug (OAD) (A10B), antihypertensive medication (C02-C09DA), lipid modifying medication (C10), platelet aggregation inhibitors (B01AC) and coumarin derivatives (B01AA-B01AB). The OADs were further classified into metformin (A10BA), sulfonylureas (A10BB), acarbose (A10BF), thiazolidinediones (A10BG) and repaglinide (A10BX).

For each year of follow-up the proportion of patients, who were prescribed diabetes related medication was determined for each group. Glucose lowering medication was divided into three groups: insulin only, OAD only, or a combination of these two medication groups. In addition, the number of different prescribed medicines per medication group and for all medication groups together were calculated.

Patients entered the DMS between 1998 and 2005, which means that the study population at entry (T1) consisted of patients who were included in different calendar years. In order to evaluate time trends, the proportion of patients who were described different diabetes related medication at entry was compared for the different calendar years.

All statistical analyses were performed using SPSS for Windows (version 12.0.1, SPSS Inc., Chicago, IL).

Results

The remaining study population consisted of 4782 patients at T=1. Mean age of the patients was 62 ± 12 years and 51% were male. 440 patients were followed for 7 years. Mean diabetes duration of patients increased from 4.6 years at entry into the system to 13.3 years at T=8.

The changes in clinical characteristics of patients are shown in Table 1. The levels of HbA1c, fasting glucose levels, diastolic blood pressure and total cholesterol decreased during the study period, whereas systolic blood pressure showed an increase.

Table 1. Clinical characteristics of patients with type 2 diabetes in a Diabetes Management System during 7 years of follow-up

	T1	T2	T3	T4	T5	T6	T7	T8
Number of patients	4782	3580	3052	2425	1884	1451	1000	440
Men (%)	50.9	51.5	50.5	50.7	51.3	50.9	49.1	47.3
Age (years)	62.4 (12.2)	62.8 (11.7)	63.7 (11.4)	64.6 (11.3)	65.6 (10.7)	66.7 (10.6)	67.7 (10.4)	69.2 (10.1)
BMI (kg/m²)	29.8 (5.4)	29.8 (5.4)	29.9 (5.3)	29.9 (5.2)	30.0 (5.3)	30.2 (5.5)	30.3 (5.5)	30.2 (5.5)
Diabetes duration (yrs)	4.6 (6.0)	5.4 (5.6)	6.6 (5.6)	7.7 (5.6)	8.7 (5.4)	10.0 (5.7)	11.4 (5.7)	13.3 (5.7)
HbA1c (%)	7.7 (1.8)	7.0 (1.2)	7.1 (1.2)	7.1 (1.2)	7.1 (1.2)	7.2 (1.2)	7.2 (1.1)	7.1 (1.1)
Fasting glucose (mmol/l)	8.9 (3.5)	8.2 (2.2)	8.2 (2.5)	8.3 (2.5)	8.2 (2.9)	8.3 (2.2)	8.2 (2.1)	8.2 (2.2)
Systolic BP (mm HG)	143.3 (21.8)	141.5 (21.5)	142.5 (21.3)	144.1 (21.7)	147.3 (21.6)	149.3 (22.3)	151.2 (21.8)	151.2 (21.2)
Diastolic BP (mm HG)	82.5 (11.2)	81.3 (11.2)	80.9 (11.2)	80.5 (10.7)	79.8 (10.9)	78.6 (10.5)	77.9 (10.0)	76.4 (10.3)
Total cholesterol (mmol/l)	5.5 (1.1)	5.3 (1.1)	5.2 (1.1)	5.1 (1.1)	5.1 (1.0)	5.0 (1.1)	4.9 (1.0)	4.8 (1.0)

T1 = time of study entry, T2, T3 etc. = follow-up years. Data are percentages or means (\pm standard deviation). BMI = body mass index, BP = blood pressure.

Glucose lowering medication

Prescription of glucose lowering medication is shown in Table 2. The proportion of patients who were prescribed OAD as only glucose lowering medication decreased from 61.5% at T=1 to 53.2% at T=8. The proportion of patients who

were prescribed insulin as glucose lowering monotherapy increased from 7.3% at T1 to 13.4% at T8. At T=1, 4.4% and at T=8 27.5% of the patients were prescribed a combination of OAD and insulin. In total, the proportion of patients who were prescribed glucose lowering medication increased from 73.2% at T1 to 94.1% at T8. The increased prescription of OAD consisted of an increased prescription of metformin, sulfonylureas and thiazolidinediones.

Table 3 shows the number of prescribed medicines. The proportion of patients who were prescribed none or one OAD decreased from 34.1% at T1 to 19.3% at T8 and from 48.9% to 40.2% respectively, while the proportion of patients who were prescribed two OADs increased from 16.8% at T= 1 to 39.8% at T=8.

Antihypertensive and lipid modifying medication

The proportion of patients who were prescribed antihypertensive and lipid modifying medication during the study period is shown in Table 2. At T=1 49.5% of the patients were prescribed antihypertensive medication, compared to 68.2% at T=8. The proportion of patients that were prescribed lipid modifying medication showed an increase from 23.9% at T=1 to 51.6% at T=8.

The number of antihypertensive and lipid modifying medicines prescribed for patients is shown in Table 3. The proportion of patients who were prescribed no antihypertensive medicines decreased from 50.5% to 31.8%. The proportion of patients who used one antihypertensive medicine remained nearly stable during the entire follow-up period, while the proportion of patient who were prescribed two, three or even four or more antihypertensive medicines increased. The proportion of patients with no prescription of lipid modifying medicines decreased from 76.1% at T=1 to 48.4% at T=8. This was accompanied by an increase in the proportion of patients who were prescribed one lipid modifying medicine to 22.5% of the patients at T=1 and to 49.5% of the patients at T=8. Less than 1.8% of the patients were prescribed two or three lipid modifying medicines during the study period.

Platelet aggregation inhibitors and coumarin derivatives

The proportion of patients who were prescribed platelet aggregation inhibitors increased from 18.9% at T=1 to 33.0% at T=8 (Table 2). Coumarin derivatives were prescribed to 4.3% of the patients at T=1 and to 7.3% of the patients at T=8. Prescription of more than one platelet aggregation inhibitor or coumarin derivative rarely occurred.

Table 2. Prescribed medication in patients with type 2 diabetes in a Diabetes Management System during 7 years of follow-up

	T1	T2	T3	T4	T5	T6	T7	T8
Number of patients	4782	3580	3052	2425	1884	1451	1000	440
Glucose lowering medication								
Only OAD	61.5	63.1	62.2	61.7	59.0	55.4	54.5	53.2
Only Insulin	7.3	9.1	8.9	9.9	10.7	11.5	11.7	13.4
Combination	4.4	8.2	11.2	13.8	17.0	20.9	23.1	27.5
Total	73.2	80.4	82.3	85.4	86.7	87.8	89.3	94.1
Oral antihyperglycaemic drugs								
Metformin	42.2	48.7	51.9	56.3	57.8	60.0	64.0	67.7
Sulfonylureas	39.3	44.4	47.7	49.6	49.7	48.6	49.2	47.7
TZDs	0.7	1.3	1.4	2.0	2.9	3.1	4.3	6.4
Acarbose	0.8	0.4	0.4	0.3	0.3	0.3	-	-
Repaglinide	-	0.1	0.1	0.1	0.1	0.2	0.1	-
Antihyper-tensive medication	49.5	54.7	57.7	59.5	61.8	65.1	66.8	68.2
Lipid modifying medication	23.9	31.4	35.0	37.6	40.3	43.6	47.8	51.6
Platelet aggregation inhibitors	18.9	21.1	22.1	22.2	23.5	25.2	26.8	33.0
Coumarin derivatives	4.3	4.7	5.4	5.7	5.9	6.4	6.9	7.3

T1 = time of study entry, T2, T3 etc. = follow-up years. Data are percentages or means (\pm standard deviation). BP = blood pressure, OAD = oral antihyperglycaemic drugs, BMI = body mass index. Total glucose lowering medication includes OAD and insulin. TZDs = thiazolidinediones

Table 3. Number of medicines prescribed for patients with type 2 diabetes in a Diabetes Management System during 7 years of follow-up

	T1	T2	T3	T4	T5	T6	T7	T8
Number of patients	4782	3580	3052	2425	1884	1451	1000	440
Oral antihyperglycaemic drugs								
0	34.1	28.7	26.6	24.5	24.0	23.7	22.4	19.3
1	48.9	48.0	45.4	43.0	41.3	40.8	38.2	40.2
2	16.8	22.9	27.9	32.4	34.0	34.9	38.3	39.8
≥ 3	0.2	0.4	0.1	0.1	0.7	0.6	1.1	0.7
Glucose lowering medicines (combination of OAD and insulin)								
0	26.8	19.6	17.7	14.6	13.3	12.2	10.7	5.9
1	52.4	50.8	45.9	42.4	39.7	37.1	33.4	32.3
2	19.8	27.4	33.5	33.5	41.9	44.5	48.3	55.0
3	1.0	2.1	2.9	2.9	5.0	6.1	7.5	6.8
≥ 4	-	0.1	-	-	0.1	0.1	0.1	0.1
Antihypertensive drugs								
0	50.5	45.3	42.3	40.5	38.2	34.9	33.2	31.8
1	25.1	27.2	27.0	28.0	27.7	26.6	25.0	25.7
2	16.2	18.2	19.3	19.6	21.3	22.7	24.4	22.5
3	6.4	7.3	8.7	8.6	9.7	11.9	14.3	16.4
≥ 4	1.8	2.0	2.7	3.3	3.1	3.9	3.1	3.6
Lipid modifying drugs								
0	76.1	68.6	65.0	62.4	59.7	56.4	52.2	48.4
1	22.5	29.9	33.7	36.0	39.2	42.0	46.2	49.5
2	1.4	1.4	1.2	1.5	1.1	1.5	1.5	1.8
≥ 3	-	0.1	0.1	0.1	-	0.1	0.1	0.3
Total drugs								
0	13.0	8.0	7.2	5.7	4.9	3.7	3.5	1.8
1	25.2	20.7	17.2	14.9	13.2	10.5	9.3	6.4
2	23.2	23.6	22.2	22.1	20.8	20.8	18.0	15.7
3	15.6	18.6	19.0	20.2	19.4	19.7	17.8	19.3
4	11.5	13.4	14.4	15.2	16.9	16.1	17.8	20.5
≥ 5	11.5	15.7	20.0	21.9	24.8	29.2	33.6	36.3

Data are proportions of patients (%). Total number of prescribed medicines includes all medication groups (insulin, oral hyperglycaemic drugs, antihypertensive medication, lipid modifying medication, platelet aggregation inhibitors and coumarin derivatives), OAD = oral antihyperglycaemic drugs.

Total prescribed medication

The overall prescription of medication is shown in Figure 1. The proportion of patients who were prescribed diabetes related medication increased every year for each medication group during the study period. The proportion of patients who were not prescribed any diabetes related medication decreased from 13.0% of the patients at T=1 to 1.8% at T=8 (Table 3). The proportion of patients who were prescribed five or more medicines increased from 11.5% at T=1 to 36.3% at T=8.

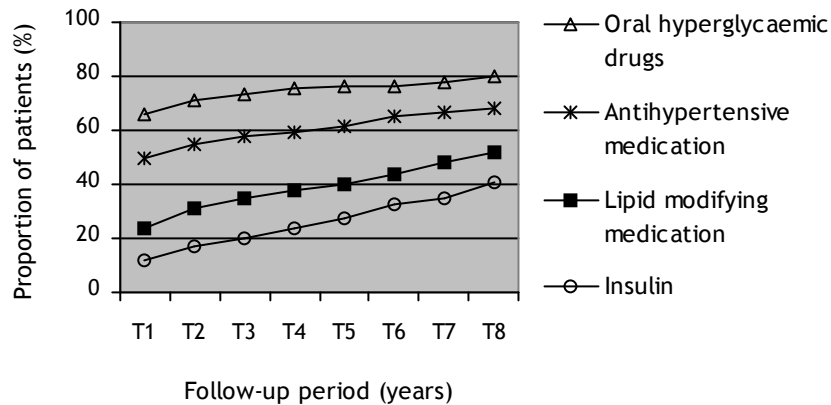


Figure 1. Proportion of patients with type 2 diabetes who were prescribed diabetes related medication during seven years of follow-up.

Prescription of medication at entry, specified by calendar year

The number of patients who entered the DMS during the subsequent calendar years of the study, their characteristics and prescribed diabetes related medication at entry (T=1) in proportion of patients is shown in Table 4.

In 1998, 28.8% of the patients were prescribed metformin, whereas 60.1% of the patients were prescribed metformin at entry in 2005. Sulfonylureas were prescribed to 50.2% of the patients in 1998, compared to 25.2% of the patients at entry in 2005. Thiazolidine-diones were not prescribed until 2001. In that year, 0.2% of the patients included into the DMS were prescribed thiazolidinediones at entry, compared with 3.7% in 2005

In 1998, 41.2% of the patients were prescribed antihypertensive medication at entry, compared to 57.9% of the patients in 2005. The proportion of patients who were prescribed lipid modifying medication was 15.0% at entry in 1998 compared to 42.1% at entry in 2005.

Table 4. Characteristics and proportion of patients who were prescribed diabetes related medication at entry of the Diabetes Management System for the subsequent calendar years of the study.

	1998	1999	2000	2001	2002	2003	2004	2005
Number of patients	775	745	607	521	540	551	554	489
Men (%)	45.9	49.7	52.9	52.2	51.1	51.7	52.7	54.0
Body Mass Index (kg/m²)	29.2 (5.1)	29.7 (5.2)	30.0 (5.6)	29.8 (5.0)	29.8 (5.5)	29.7 (5.3)	30.1 (5.8)	29.9 (5.4)
Age (years)	65.1 (11.1)	62.9 (11.5)	62.3 (11.9)	61.1 (12.4)	60.8 (13.0)	61.9 (12.3)	60.6 (12.8)	63.0 (12.5)
Diabetes duration (years)	7.2 (7.0)	5.1 (5.8)	4.3 (5.6)	4.0 (5.1)	3.9 (5.4)	3.3 (4.8)	4.1 (6.9)	4.6 (6.0)
Proportion of patients who were prescribed:								
Glucose lowering medication								
Only insulin	7.4	7.7	7.4	4.8	5.4	6.7	10.3	8.2
Only OAD	55.4	58.4	56.0	67.6	64.8	63.2	64.8	66.9
Combination	8.6	3.1	2.3	2.3	4.1	4.7	4.9	4.5
Total	71.4	69.2	65.7	74.7	74.3	74.6	80.0	79.6
Oral antihyperglycaemic drugs								
Metformin	28.8	29.0	32.5	42.6	47.2	53.2	57.6	60.1
Sulfonylureas	50.2	49.0	40.7	44.3	38.3	30.5	26.9	25.2
TZDs	0	0	0	0.2	1.1	0.5	1.3	3.7
Antihypertensive medication	41.2	47.9	47.3	47.2	49.4	55.9	52.5	57.9
Lipid modifying medication	15.0	15.3	19.8	21.5	24.6	29.0	32.5	42.1
Platelet aggregation inhibitors	16.9	16.9	18.3	17.1	20.6	21.4	20.9	21.3
Coumarin derivatives	5.2	3.4	3.1	3.6	4.6	5.8	3.4	5.7

Data are percentages or means (\pm standard deviation). OAD = oral hyperglycaemic drugs, TZDs = thiazolidinediones. Total glucose lowering medication includes OAD and insulin.

Discussion

In this study, we described changes in the prescription of diabetes related medication in patients with type 2 diabetes after entry into a DMS in a region in the Netherlands during seven years of follow up. We found that the proportion of patients who were prescribed diabetes related medication increased every year. 73.2% of the patients were prescribed glucose lowering medication (i.e. insulin and OAD), which increased to 94.1% after 7 years of follow-up. Simultaneously, HbA1c decreased from 7.7% to 7.0% in the first year after entry into the system, followed by a stabilization during follow-up. Also, fasting glucose levels decreased and reached a stable level of 8.2 mmol/l.

The proportion of patients who were prescribed antihypertensive or lipid modifying medication also showed a considerable increase. After seven years, 51.6% used lipid modifying medication and 68.2% of the patients used antihypertensive medication. As a result, cholesterol levels decreased every year, but systolic blood pressure increased, indicating that the prescription of antihypertensive medication should even be further intensified. Only 1.8% of all patients (n = 6) were not prescribed any medication at the end of the study period.

The prescription of medication for patients at entry of the DMS varied between the subsequent calendar years of the study. Patients who were included in 1998 were prescribed sulfonylureas above metformin as OAD, whereas in 2005, a considerable greater proportion was prescribed metformin in advantage of sulfonylureas. In addition, during later calendar years, a greater proportion of patients was prescribed antihypertensive and lipid modifying medication at entry. The differences between the calendar years are to a large extent explained by the changes in the guidelines of the Dutch College of General Practitioners for diabetes. Starting in 1999, revised guidelines recommended to prescribe obese patients metformin instead of sulfonylureas and emphasized a multifactorial treatment of type 2 diabetes (24). At later calendar years patients had a shorter diabetes duration at entry. This could be an explanation for the fact that at entry in 2005, a smaller proportion of patients used insulin or a combination of insulin and OAD than patients who were included in 1998. The diabetes duration was longer in 1998 because that was one of the first years that the DMS existed. During that time, GPs referred all known diabetic patients to the DMS, whereas during later years, more newly diagnosed patients were referred.

To our knowledge, this is the first study describing changes in prescribed medication for patients who were included in a DMS. The strengths of the study are the long follow-up period and the fact that it was performed in a real-life

setting. Other studies that included data on medication were performed in an experimental setting (7,22), had a short follow-up duration (26), or were not able to achieve good glycaemic control (27). These results of these studies were in agreement with our results. Gaede et al. (7) investigated differences in the prescription of medication between patients who received conventional treatment (n = 80) and patients who received an intensive treatment (n = 80) which consisted of a behavioral modification and pharmacological treatment. They found that more patients in the intensive treatment than in the conventional treatment group received antihypertensive and lipid lowering treatment at the end of the study (mean follow-up 7.8 years). No differences were found for glucose lowering medicines. This was accompanied by statistically significant differences between the groups on clinical outcomes resulting in a reduction in cardiovascular events and other diabetes related complications (28), in favor of the intensive treatment group. Hansen et al. (27) performed a 6-year observational study of newly diagnosed patients (n = 729) who received a multifaceted intervention from their GPs. A large increase in the use of antidiabetic medicines and a reduction in diet therapy alone was reported. The percentage of patients treated with lipid-lowering and antihypertensive medication showed a more gradual increase. Blood pressure and cholesterol stabilized, but HbA1c increased somewhat after the first 2 years of treatment. Olivarius et al. (22) assessed the effect of a multifaceted intervention directed at general practitioners in newly diagnosed patients (n = 874) compared to usual care. After 6 years, they found lower levels of risk factors in the intervention group than in the control group. However, the only difference in prescriptions was found for metformin. Karter et al. (26) performed a cohort study of poorly controlled patients (n = 4775) who initiated new glucose lowering therapies with a follow-up of 1 year. They found that a good glycaemic control was accompanied by a dramatic shift from monotherapy towards polypharmacy, in particular with an increase in use of insulin.

The increase in prescribed medication is probably due to the structured care of the DMS. It seems that the multifaceted character of the DMS is beneficial for the patients. The DMS provides feedback to the GP, who is responsible for the prescription of the required medication. The continuing feedback by means of yearly assessments is important to provide optimal medication therapy in order to maintain management goals.

This study had some limitations. Since data were primarily collected to provide adequate care for patients with type 2 diabetes, there was no control group. Therefore, we cannot confirm whether the patients who were included in the DMS were prescribed more or less medication than type 2 diabetes patients

receiving conventional treatment by their GP or specialist. However, 88% of the GPs in the region West-Friesland participated in referring all patients with type 2 diabetes to the DMS (23). Therefore, we believe that this study gives a good insight in how prescribed diabetes related medication of a real-life type 2 diabetes population changes in a DMS. Despite the fact that patients had to bring medication packages to the DMS and pharmacists were consulted when prescription of medication was unclear, 151 patients had to be excluded because of incomplete or inaccurate registration of prescribed medication. An inaccurate medication registration might have occurred for more patients resulting in an underestimation of actual medication use of the patients included in the DMS.

In conclusion, this study showed an increase in prescribed medication for patients with type 2 diabetes, who were included in a DMS, during seven years of follow-up. This indicates that intensive prescription of medication seems inevitable. This study highlights the importance of strict medication treatment for type 2 diabetes patients, in order to achieve good metabolic control.

References

1. Langendam MW, Hooijkaas C, Piepenbrink JF: [The increase in the use of drug treatment for diabetes mellitus in the Netherlands, 1998-2003]. *Ned. Tijdschr. Geneeskd.* 150:1396-1401, 2006
2. Gu K, Cowie CC, Harris MI: Mortality in adults with and without diabetes in a national cohort of the U.S. population, 1971-1993. *Diabetes Care* 21:1138-1145, 1998
3. Booth GL, Kapral MK, Fung K, Tu JV: Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. *Lancet* 368:29-36, 2006
4. de Vegt F, Dekker JM, Ruhe HG, Stehouwer CD, Nijpels G, Bouter LM, Heine RJ: Hyperglycaemia is associated with all-cause and cardiovascular mortality in the Hoorn population: the Hoorn Study. *Diabetologia* 42:926-931, 1999
5. Lee WL, Cheung AM, Cape D, Zinman B: Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies. *Diabetes Care* 23:962-968, 2000
6. Gaede P, Vedel P, Parving HH, Pedersen O: Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study. *Lancet* 353:617-622, 1999
7. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O: Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N.Engl.J.Med.* 348:383-393, 2003
8. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 352:837-853, 1998
9. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 352:854-865, 1998
10. Shichiri M, Kishikawa H, Ohkubo Y, Wake N: Long-term results of the Kumamoto Study on optimal diabetes control in type 2 diabetic patients. *Diabetes Care* 23:B21-B29, 2000
11. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ* 317:703-713, 1998
12. Costa J, Borges M, David C, Vaz CA: Efficacy of lipid lowering drug treatment for diabetic and non-diabetic patients: meta-analysis of randomised controlled trials. *BMJ* 332:1115-1124, 2006
13. Turner RC, Cull CA, Frighi V, Holman RR: Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. *JAMA* 281:2005-2012, 1999
14. Nathan DM, Buse JB, Davidson MB, Heine RJ, Holman RR, Sherwin R, Zinman B: Management of hyperglycaemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. A consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia* 49:1711-1721, 2006
15. Bodenheimer T, Wagner EH, Grumbach K: Improving primary care for patients with chronic illness. *JAMA* 288:1775-1779, 2002
16. Renders CM, Valk GD, Griffin SJ, Wagner EH, Eijk VJ, Assendelft WJ: Interventions to improve the management of diabetes in primary care, outpatient, and community settings: a systematic review. *Diabetes Care* 24:1821-1833, 2001

17. Wagner EH, Austin BT, Davis C, Hindmarsh M, Schaefer J, Bonomi A: Improving chronic illness care: translating evidence into action. *Health Aff.(Millwood.)* 20:64-78, 2001
18. Majumdar SR, Guirguis LM, Toth EL, Lewanczuk RZ, Lee TK, Johnson JA: Controlled trial of a multifaceted intervention for improving quality of care for rural patients with type 2 diabetes. *Diabetes Care* 26:3061-3066, 2003
19. Renders CM, Valk GD, Franse LV, Schellevis FG, van Eijk JT, van der WG: Long-term effectiveness of a quality improvement program for patients with type 2 diabetes in general practice. *Diabetes Care* 24:1365-1370, 2001
20. Bodenheimer T, Lorig K, Holman H, Grumbach K: Patient self-management of chronic disease in primary care. *JAMA* 288:2469-2475, 2002
21. Bodenheimer T, Wagner EH, Grumbach K: Improving primary care for patients with chronic illness: the chronic care model, Part 2. *JAMA* 288:1909-1914, 2002
22. Olivarius NF, Beck-Nielsen H, Andreasen AH, Horder M, Pedersen PA: Randomised controlled trial of structured personal care of type 2 diabetes mellitus. *BMJ* 323:970-975, 2001
23. Welschen LM, Bot SD, Dekker JM, Stalman WA, Nijpels G: The implementation of a diabetes care system: a prospective observational 8-years follow-up study. *Diabetologia* 49; Suppl. 1:142, 2006
24. Bouma M, Rutten GE, de Grauw WJ, Wiersma T, Goudswaard AN: [Summary of the practice guideline 'Diabetes mellitus type 2' (second revision) from the Dutch College of General Practitioners]. *Ned.Tijdschr.Geneeskd.* 150:2251-2256, 2006
25. WHO Collaborating Centre for Drugs Statistics Methodology. www.whocc.no/atcddd. 2007.
26. Karter AJ, Moffet HH, Liu J, Parker MM, Ahmed AT, Ferrara A, Selby JV: Achieving good glycemic control: initiation of new antihyperglycemic therapies in patients with type 2 diabetes from the Kaiser Permanente Northern California Diabetes Registry. *Am.J.Manag.Care* 11:262-270, 2005
27. Hansen LJ, Olivarius NdF, Siersma V, Beck-Nielsen H, Pedersen PA: Encouraging structured personalised diabetes care in general practice. A 6-year follow-up study of process and patient outcomes in newly diagnosed patients. *Scand.J.Prim.Health Care* 21:89-95, 2003
28. Pedersen O, Gaede P: Intensified multifactorial intervention and cardiovascular outcome in type 2 diabetes: the Steno-2 study. *Metabolism* 52:19-23, 2003