

Chapter 2

Successful risk reduction using a diabetes management system: an observational 7-year follow-up study

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Abstract

Aims

The 'classical' healthcare system may be inadequate to provide the required care for diabetes patients; structured disease management programs may offer an improvement. The aim of this study was to describe the changes in patients' clinical characteristics after their entry into a structured diabetes management system.

Methods

Patients with type 2 diabetes who entered a diabetes management system in the Netherlands between 1998 and 2005 were followed for up to 7 years. HbA1c, weight, blood pressure, fasting blood glucose, cholesterol, triglycerides, medication use, and smoking status were measured annually. The 10-year risk of a coronary heart disease (CHD) event was calculated using the UKPDS risk engine. Multilevel regression models were used to account for calendar year of follow-up. Analyses were repeated on a data set that was created by multiple imputation.

Results

A total of 4933 patients (mean age 62 ± 12 years; 51% men) entered the system. Body-mass index was 29.8 kg/m^2 and did not change during follow-up. HbA1c showed an initial sharp decrease from $7.7 \pm 1.8\%$ to $7.0 \pm 1.2\%$, and then stabilized during follow-up. Total cholesterol and triglycerides decreased, whereas HDL cholesterol increased. Systolic blood pressure increased, and diastolic blood pressure decreased. The risk of a CHD event decreased from $19.6 \pm 15.5\%$ to $12.3 \pm 9.4\%$.

Conclusions

The diabetes management system was successful in reducing HbA1c and in improving and stabilizing patients' clinical characteristics and CHD risk. This implies that a disease management system may be a major step in the improvement of care for patients with type 2 diabetes.

Introduction

Diabetes mellitus is a major health problem, and its prevalence and incidence are on the rise (1). Strict glycaemic control reduces the risk of developing severe micro- and macrovascular complications (2-4), and tight control of blood pressure and cholesterol levels is also very important (5,6). However, it has been shown that the 'classical' healthcare system is inadequate to provide the required care and support to attain such control (7). The main limitations are: coordination between different caregivers is lacking; the patient is not centralized in the care; standard guidelines are often not implemented; care is more targeted to acute problems than the control of chronic diseases; and the patient's role is passive, indicated by a low perception of risk and a low responsibility for their own disease (8).

It is believed that care for patients with a chronic disease can be improved by implementing a chronic care model (9,10). In this model, a central organization coordinates the care, self-management support, and continuing education and feedback, and uses a clinical information system to make patient outcomes available to the various caregivers (8-11). Based on the chronic care model, a structured diabetes management system (DMS) was implemented in 1997 in the West-Friesland region, the Netherlands. General practitioners (GPs) were invited to refer all their patients with type 2 diabetes to the DMS, in addition to the GPs' own care. The DMS provides coordination of the regional care, including benchmarking of main treatment outcomes and feedback to the GPs. Patients receive annual medical examinations and extensive education given by diabetes nurses and dieticians in order to improve patient empowerment.

In the present study, we evaluated the changes in clinical characteristics, with a focus on glycosylated hemoglobin (HbA1c levels, and changes in the 10-year risk of a coronary heart disease (CHD) event, of the enrolled patients in order to gain insight into the long-term benefits of a structured DMS.

Patients and Methods

This was an observational study of a DMS in the West-Friesland region, the Netherlands. Patients who entered the DMS between 1998 and 2005 were followed annually for up to 7 years.

The Diabetes Management System

The DMS coordinates regional diabetes care using a centrally organized database that is available to all involved caregivers. Diabetes nurses and dieticians

perform an annual follow-up examination of individual patients to assess glucose control, cardiovascular disease risk profile, and the presence of complications, and coordinate the care among different healthcare providers, including GPs, specialists, and podotherapists. The diabetes nurses visit the GPs every 6 months to compare mean risk factor levels of the patients in that GP's practice with mean levels from all GPs, and to discuss results for individual patients. The diabetes nurses also provide specific therapeutic advice for the GPs to implement. Patient empowerment in the DMS consists of 3 elements in order to improve patient self-management: providing education, both individual and in groups; supplying information; and promoting self-monitoring of blood glucose.

Measurements

A physical examination was performed according to a standardized protocol during each annual visit.

Weight and height were measured while patients were barefoot and wearing light clothes. HbA1c was measured with high-performance liquid chromatography. Fasting plasma glucose was measured by means of a hexokinase method (Roche Diagnostics GmbH, Mannheim, Germany). Levels of total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were measured using enzymatic techniques (Boehringer-Mannheim, Mannheim, Germany). Systolic and diastolic blood pressure were measured on the right arm after 5 minutes of rest in a seated position using a random-zero sphygmomanometer (Hawksley-Gelman, Lancing, Sussex, UK); from 2003 on, an oscillometric device was used (Colin Press-Mate BP-8800, Komaki City, Japan). Patients' self-reported information on current medication use and smoking (yes/no) was obtained. Patients' characteristics were entered into a database.

Three weeks after each annual physical examination, patients visited a diabetes nurse and a dietician, 30 minutes each, to discuss the results of the physical examination and obtain information and advice on diabetes complications, cardiovascular risk factors, dietary intake, physical activity, and medication use. Further visits to the diabetes nurse and dietician, in between annual visits, were optional. Information and advice were based on a standardized protocol. The diabetes nurses and dieticians sent their given advice to the GPs. According to risk factor levels and the advice, GPs were requested to change medication as appropriate, according to the guidelines of the Dutch College of General Practitioners (12).

Statistical analysis

Data from the central database were used for analyses. The database was checked and if outliers were found, original data were searched in patient records. A study population was defined in which the measurements in a patient's first year of entry into the system were set at T1. Follow-up measurements were defined as T2 up to T8.

Descriptive statistics are presented as mean \pm SD of all patients, or percentage of patients with a given characteristic, for T1 through T8. The 10-year risk of a CHD event was calculated using the UK Prospective Diabetes Study (UKPDS) risk engine (13). A multilevel linear regression analysis (14) was performed on HbA1c values to investigate whether there were statistically significant changes during follow-up, taking into consideration the calendar year (1998-2005) in which patients entered the DMS. Models were adjusted for age, sex, and diabetes duration.

Selection bias may have occurred in our study since the number of patients in the cohort decreased every year due to drop-outs. In addition, 'newer' patients, incorporated in the system during the last few calendar years of the study, had a shorter follow-up. To evaluate possible selection bias due to missing data, we repeated the analyses on a data set that was developed using a multiple imputation method. We generated 5 multiple imputed data sets (15,16). For this purpose, an imputation model was developed that used available data as predictor variables to calculate missing data (17). We used the following variables in our imputation model: age, diabetes duration, HbA1c, fasting glucose, total cholesterol, HDL and low-density lipoprotein (LDL) cholesterol, triglycerides, body-mass index, systolic and diastolic blood pressure. Analyses were performed on each of the 5 data sets, and simple pooling rules were used to obtain the final result. Missing data until 2005 were calculated. For example, for a patient that entered the DMS in 2005, no data were imputed, because we considered it unreasonable to calculate 'future' data. For a patient who started in 1999 and died in 2003, data for 2 follow-up years were imputed (2004 and 2005).

P-values below 0.05 were considered statistically significant. Statistical analyses were performed using SPSS for Windows (version 12.0.1, SPSS Inc., Chicago, IL) and multiple imputations were performed by using R (2000, MathSoft Inc.).

Results

At the start-up of the DMS in 1997, 65 patients were included. After a sharp increase of patients added during the first 2 years of our study (803 in 1998 and

1330 in 1999), the average number of new patients added per year was between 300 and 400. By 2005, 3770 patients were in the DMS.

When combining all data from 1998 to 2005, the study population consisted of 4933 patients at entry (T1) (Table 1). The year 1997 was not included, because this year was mainly used to initiate the DMS. There were 461 patients with a follow-up of 7 years (T8). There were 614 drop-outs during follow-up, including 299 (49%) because of death.

Table 1. Number of patients in the study population and reasons for drop-out

	T1	T2	T3	T4	T5	T6	T7	T8	Total
Number of patients	4933	3709	3179	2539	1974	1526	1049	461	n/a
Reason for dropping out:									
Died	82	62	47	38	37	18	13	2	299
Moved to other region	24	18	14	9	5	0	2	1	73
Care in hospital/specialist	30	12	15	17	5	8	7	2	96
Care at general practitioner	9	5	4	5	2	3	0	0	28
Moved to nursing home/rest home	9	3	8	5	3	1	0	0	29
Dementia	2	1	0	0	0	0	0	0	3
Severe illness/cancer	4	1	1	3	2	1	0	0	12
Voluntary drop-out	9	6	6	7	2	2	2	0	34
Unknown reason	11	5	8	6	3	4	3	0	40
Total number of drop-outs	180	113	103	90	59	37	27	5	614

T1 = time of study entry, T2, T3, etc = follow-up years; n/a = not applicable.

Patient characteristics

The patients' mean age was 62 ± 12 years at T1 and 51% were men. Body-mass index was 29.8 kg/m^2 and did not change during follow-up. Diabetes duration was 4.6 ± 6.1 years at study entry and increased to 13.4 ± 5.7 years at T8 (Table 2).

HbA1c showed a considerable decrease from 7.7 ± 1.8 to $7.0 \pm 1.2\%$ after 1 year, and stabilized during subsequent follow-up. Fasting glucose levels showed the same course and decreased from 8.9 ± 3.5 to $8.2 \pm 2.2 \text{ mmol/l}$ after 1 year, and also stabilized during follow-up. Total cholesterol and triglycerides both

decreased during the 7 years of follow-up, and HDL cholesterol increased slightly. Systolic blood pressure increased and diastolic blood pressure decreased. The 10-year estimated mean risk of a CHD event decreased from 19.6 ± 15.5 to $15.9 \pm 12.3\%$ after 1 year of care in the DMS and decreased further during follow-up; at T8, it was $12.3 \pm 9.4\%$.

When repeating the analyses using the imputed data sets, we found similar results, except for CHD risk. The estimated mean risk of a CHD event decreased from $19.9 \pm 15.7\%$ at T1 to $16.3 \pm 12.9\%$ at T2; it continued to decrease during follow-up and was $14.8 \pm 12.0\%$ at T8.

Table 3 shows the results of the multilevel analysis for HbA1c values. Both follow-up and calendar year showed a statistically significant change during follow-up ($P < 0.001$, F for follow-up = 114.1 with degrees of freedom (df) = 5345, F for year = 5.7 with df = 4111); however, the effect of calendar year lost significance after adjusting for diabetes duration. Sex did not influence the results ($P = 0.184$, $\beta = 0.04$). Age and diabetes duration both contributed significantly to the results ($P < 0.001$, $\beta = -0.13$ for a 10-year increase in age, and $\beta = 2.65$ for a 10-year increase in diabetes duration), showing that a higher age and/or a shorter diabetes duration resulted in a lower HbA1c.

The use of medication increased substantially during the study (Table 2). The proportion of patients using insulin increased from 11.7 to 40.9% from T1 to T8. At T8, 80.3% of patients were using oral glucose-lowering medication, 68.2% antihypertensive medication, and 51.6% lipid-modifying drugs, each of which was much higher than at study entry.

Table 2. Clinical characteristics of patients

	T1	T2	T3	T4	T5	T6	T7	T8
Number of patients	4933	3709	3179	2539	1974	1526	1049	461
Diabetes duration (yr)	4.6±6.1	5.5±5.7	6.7±5.7	7.7±5.6	8.8±5.5	10.1±5.8	11.5±5.8	13.4±5.7
HbA1c (%)	7.7±1.8	7.0±1.2	7.1±1.2	7.2±1.2	7.1±1.2	7.2±1.2	7.1±1.1	7.1±1.1
Fasting glucose (mmol/l)	8.9±3.5	8.2±2.2	8.3±3.0	8.3±2.5	8.2±2.9	8.3±2.2	8.2±2.1	8.2±2.3
Systolic BP (mmHg)	143.3±21.8	141.6±21.7	142.4±21.6	144.1±21.7	147.3±21.5	149.4±22.2	151.3±21.7	151.6±21.3
Diastolic BP (mmHg)	82.6±11.3	81.3±11.1	80.9±11.3	80.5±10.8	79.7±10.9	78.6±10.5	77.9±10.0	76.4±10.3
Total cholesterol (mmol/l)	5.4±1.1	5.3±1.1	5.2±1.1	5.2±1.1	5.1±1.0	5.1±1.1	4.9±1.0	4.8±1.0
HDL cholesterol (mmol/l)	1.2±0.4	1.3±0.4	1.3±0.3	1.3±0.4	1.3±0.4	1.3±0.4	1.3±0.4	1.4±0.4
Triglycerides (mmol/l)	2.1±2.0	1.9±1.2	1.9±1.2	1.9±1.1	1.8±1.0	1.8±1.1	1.8±1.1	1.8±1.0
CHD risk (% in next 10 yr)	19.6±15.5	15.9±12.3	15.6±12.2	15.2±11.5	14.9±11.2	14.6±11.0	13.4±10.2	12.3±9.4
Patients who smoke (%)	21.3	20.8	19.7	18.9	17.4	16.3	13.3	14.5
Patients on insulin (%)	11.7	17.3	20.1	23.7	27.7	32.4	34.8	40.9
Patients on oral glucose-lowering medication (%)	65.9	71.3	73.4	75.5	76.0	76.3	77.6	80.3
Patients on antihypertensive medication (%)	49.5	54.7	57.7	59.5	61.8	65.1	66.8	68.2
Patients on lipid-modifying medication (%)	23.9	31.4	35.0	37.6	40.3	43.6	47.8	51.6

T1 = time of study entry, T2, T3, etc = follow-up years. Data are mean ± SD, or % of patients.

Table 3. Change in HbA1c during 7 yr of follow-up according to calendar year of entry to the DMS.

Patients included in the later years had a higher level of HbA1c at entry than patients from 1998 and 1999, indicating that patients entering in the later years were 'newer' patients who had not received treatment yet, which was also shown by their shorter diabetes duration (7.2 yr at T1 vs. 4.1 yr at T8, data not shown). From 2000, levels of HbA1c reached lower levels after the first year of entry and then stabilized. In 1998 and 1999, levels remained >7.0% and stabilization was not yet achieved. The difference in HbA1c levels at T1 between 1998-1999 and 2000-2005 was statistically significant (data not shown).

	1998	1999	2000	2001	2002	2003	2004	2005
T1	7.4	7.4	7.9	7.9	7.8	7.7	7.9	7.6
T2	7.1	7.3	7	7	6.9	6.9	6.8	
T3	7.5	7.1	7.2	7	7.1	6.8		
T4	7.4	7.3	7.1	7.2	7			
T5	7.5	7.1	7.2	6.8				
T6	7.4	7.4	7.1					
T7	7.4	7.1						
T8	7.2							

Discussion

In the present study, we evaluated the implementation of a DMS in the West-Friesland region, the Netherlands, during a follow-up of up to 7 years. To our knowledge, this is the first study evaluating the long-term success of a structured chronic care system for patients with type 2 diabetes in a normal real-life setting in a large population. We found that this structured DMS was successful in improving and stabilizing patients' clinical characteristics. In particular, HbA1c showed a decline from 7.7 to 7.0% during the first study year, followed by stabilization during follow-up, despite an increase in diabetes duration. Total

cholesterol level decreased every year, and was 4.8 mmol/l in the seventh year of follow-up. Consequently, the 10-year risk of a CHD event decreased by 7.3 percentage points (from 19.6 to 12.3%) during follow-up. This implies that the improvement in clinical characteristics was not only statistically but also clinically relevant. The increased use of medication during the subsequent years, likely a result of the structured care of the DMS, most likely explained a major part of the improvement. However, blood pressure control still remains a challenge, since systolic blood pressure increased while diastolic blood pressure decreased. The increased systolic blood pressure might be explained by an increase in arterial stiffness, which has previously been shown in patients with diabetes (18). When the analyses were repeated using multiple imputation, the results for CHD risk changed, but not those for individual risk factors. This reflects that the possibility that selective mortality in those with high CHD risk affected the estimated CHD risk during follow-up. However, results of imputation of individual risk factors showed this did not explain the entire risk reduction.

The success of this DMS is of clinical importance. Many large studies have shown that strict control of risk factors reduces diabetes-related morbidity and mortality (2-4,19). The stabilization of HbA_{1c} values in our study is noteworthy, since other large studies were not able to maintain low levels of HbA_{1c} with intensive treatment. In the UKPDS, the design of the intervention may have contributed to the general increase of HbA_{1c} (20). However, a 6-year follow-up study evaluating structured diabetes care in general practices in Denmark was not able to stabilize HbA_{1c}, but showed an increase after the second year of follow-up (21). A cohort study in New Zealand of the relationship between baseline and subsequent clinical parameters after 6 years also found that HbA_{1c} increased, in this case from 6.3 to 7.2% (22). The Steno-2 study, a target-driven intensified intervention focused on reducing risk factor parameters, did show a stabilization of HbA_{1c} during 8 years of follow-up, but their study population was much smaller (n=160) than ours (23). Several randomized controlled trials (24-28) and observational studies (29,30) based on the chronic care model have been performed and also found that risk factor parameters decreased. Although randomized controlled trials provide the best available evidence, follow-up of patients is usually only possible for a short period and study populations tend to be small. We were able to include almost 5000 patients and to provide long-term follow-up data.

We think that the success of the DMS lies in its multifaceted character, as has been suggested earlier (24). The Steno-2 study also concluded that the multifactorial design of the study was very effective (6,23). The combination of

good coordination, feedback to patients and GPs, and the role of diabetes nurses and dieticians in patient empowerment seems effective.

This study had some limitations. First, we did not have a control group in order to compare results. We cannot state that diabetes care improved as a result of a general trend. The National Health and Nutrition Examination Survey (NHANES) showed that diabetes care has improved over time in the United States (31), but data in the Netherlands are not available. Second, data on diabetes duration was often unknown and this resulted in many missing values for this variable. However, multiple imputation has been shown to remain precise with as much as up to 80% missings (15). Third, we did not collect data on quality of life or patient satisfaction. Such data would have provided more insight into the success of this care system.

In conclusion, this study shows that a DMS can help to improve and stabilize patients' clinical characteristics and to reduce CHD risk. Further research is needed before we can definitively conclude that chronic care systems are effective in improving diabetes care or that they lead to a decrease in diabetes-related morbidity and mortality.

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