Randomised controlled trial of structured personal care of type 2 diabetes mellitus

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Abstract

Objective To assess the effect of a multifaceted intervention directed at general practitioners on six year mortality, morbidity, and risk factors of patients with newly diagnosed type 2 diabetes.
Design Pragmatic, open, controlled trial with randomisation of practices to structured personal care or routine care; analysis after 6 years.
Setting 311 Danish practices with 474 general practitioners (243 in intervention group and 231 in comparison group).
Participants 874 (90.1%) of 970 patients aged ⩾40 years who had diabetes diagnosed in 1989-91 and survived until six year follow up.
Intervention Regular follow up and individualised goal setting supported by prompting of doctors, clinical guidelines, feedback, and continuing medical education.
Main outcome measures Predefined clinical non-fatal outcomes, overall mortality, risk factors, and weight.
Results Predefined non-fatal outcomes and mortality were the same in both groups. The following risk factor levels were lower for intervention patients than for comparison patients (median values): fasting plasma glucose concentration (7.9 *v* 8.7 mmol/l, P = 0.0007), glycated haemoglobin (8.5% *v* 9.0%, P < 0.0001; reference range 5.4-7.4%), systolic blood pressure (145 *v* 150 mm Hg, P = 0.0004), and cholesterol concentration (6.0 *v* 6.1 mmol/l, P = 0.029, adjusted for baseline concentration). Both groups had lost weight since diagnosis (2.6 *v* 2.0 kg). Metformin was the only drug used more frequently in the intervention group (24% (110/459) v 15% (61/415)).Intervention doctors arranged more follow up consultations, referred fewer patients to diabetes clinics, and set more optimistic goals.
Conclusions In primary care, individualised goals with educational and surveillance support may for at least six years bring risk factors of patients with type 2 diabetes to a level that has been shown to reduce diabetic complications but without weight gain.

Introduction

Efforts to control hyperglycaemia,[1] hypertension,[2 3] and dyslipidaemia[4] may postpone the development of complications in patients with type 2 diabetes.[5] However, it is not known whether these results can be implemented over a long period in general practice. General practitioners often do not follow international recommendations,[6 7] and the quality of care is not satisfactory even when clinical guidelines are provided.[8 9] A combination of interventions, including prompting, may be needed to change general practitioners' behaviour and improve quality of care.[10–13]

We report the final results of a six year study from general practice examining the effect of structured personal care compared with routine care on overall mortality and on risk factors for and incidence of clinical complications in newly diagnosed diabetic patients aged 40 years or older. Structured care included regular follow up and setting of individualised goals for important risk factors, supported by prompting of doctors, feedback on individual patients, short clinical guidelines, and a brief training programme for general practitioners.

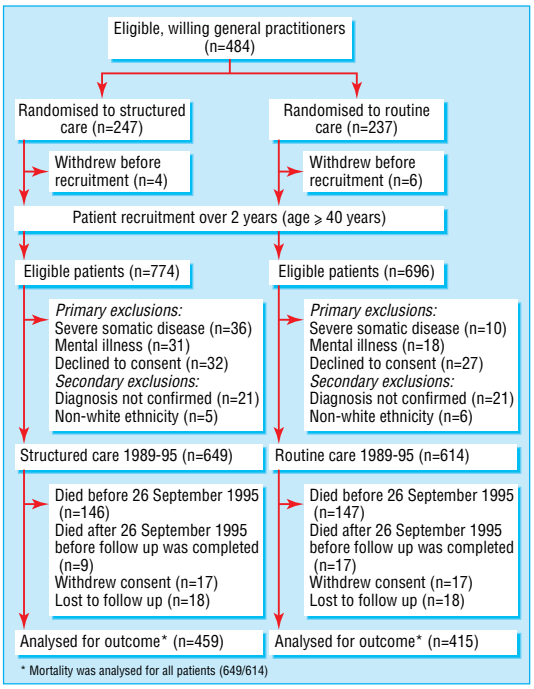
Participants and methods

Recruitment of general practitioners

The study was a pragmatic, open, multicentre, cluster randomised controlled trial. In 1988, we sent a random sample of two thirds of Danish general practices, excluding singlehanded practices with a doctor aged ⩾60 years, a written invitation to participate in the study. Of 1902 doctors, 484 (25.4%) volunteered. Their practices were allocated by random numbers to two groups: structured care and routine care. Before randomisation, practices were stratified according to number of partners and spelling of practice address. Immediately after randomisation, 10 doctors dropped out, leaving 474 doctors in 187 single handed practices and 124 group practices (figure). After this no doctors who had study patients withdrew, but 80 and 67 new doctors joined the intervention and comparison group, respectively, when patients moved or new doctors joined or took over a practice. Only one doctor refused to examine a patient who had moved to the practice.

Recruitment of patients

We included all patients aged 40 or older with newly diagnosed diabetes between 1 March 1989 and 28 February 1991 based on hyperglycaemic symptoms or raised blood glucose values measured in general prac-



Flow of participants through trial

tice, or both, and who were registered with a participating general practitioner. In all, 1470 patients were eligible (figure). The diagnosis was subsequently established by a single fasting whole blood or plasma glucose concentration ⩾7.0/8.0 mmol/l measured at a major laboratory. The doctors were repeatedly instructed not to alter diagnostic practice during the inclusion period and to include all newly diagnosed patients. Patients who were in hospital at the time of diagnosis were also considered for inclusion.

The protocol based exclusion criteria were life threatening somatic disease, severe mental illness, or unwillingness to participate. For this analysis, we also excluded non-white patients and patients whose diagnosis was not established by a blood glucose measurement at a major laboratory within 500 days after diagnosis.

After the recruitment period ended, doctors were asked how many patients they had not included. Intervention and comparison doctors reported 39 and 51 patients, respectively, of whom they considered that 16 and 24 would eventually have been included if they had remembered or managed to do so. Eighteen of the 649 patients in the intervention group started insulin within 180 days after diagnosis. Insulin was discontinued for two of these patients during the observation period. Thus, at least 633 (97.5%) patients were considered to have type 2 diabetes.

Informed consent was obtained from all participants. The protocol was in accordance with the Helsinki declaration and was approved by the ethics committee of Copenhagen and Frederiksberg.

Comparison group: routine care

In the comparison group, doctors were free to choose any treatment and change it over time. From 1988 to 1996, all Danish general practitioners received diabetes guidelines on five occasions.[14–16] These differed only slightly from the study guidelines. The study coordinating centre did not contact comparison practices after the end of recruitment (late 1991) until the final follow up examinations started in 1995. During the study period, the study coordinator (NdFO) sent 51 personal letters to doctors in the intervention group and 32 to doctors in the comparison group about study progress and preliminary results. In Denmark, routine care of patients with type 2 diabetes is usually given by general practitioners in ordinary consultations and not in disease management sessions run by nurses.

Intervention group: structured care

In the intervention group, follow up every three months and annual screening for diabetic complications were supported by sending a questionnaire to the general practitioner one month before the next expected consultation. The general practitioner was also requested to define, together with the patient, the best possible goals for blood glucose concentration, glycated haemoglobin, diastolic blood pressure, and lipids within three predefined categories (table 1). At each quarterly consultation, the general practitioner was asked to compare the achievements with the goal and consider changing either goal or treatment accordingly. In overweight patients, the general practitioner was prompted to get agreement on a small, realistic weight reduction and to follow up on this. However, a specific relative body weight was not strived for.

The doctors received annual descriptive feedback reports on individual patients. They comprised the last six measurements of risk factors, complications, current treatment goal, and pharmacological treatment. No specific advice on treatment was given, but the role of microalbuminuria as a risk marker for cardiovascular disease was underlined.

The general practitioners were introduced to possible solutions to therapeutic problems through clinical guidelines supported by an annual half day seminar. The patients were never approached by the study centre, but four patient leaflets were produced for the doctor to hand out. The doctors were not obliged to follow the guidelines concerning diet and drug treatment (box). Generally, the importance of diet was stressed, and doctors were recommended to postpone, if possible, the start of antidiabetic drugs until at least three months after diagnosis to observe the effect of a possible weight loss.

Table 1 Treatment goals for intervention group

	Good control	Acceptable control	Poor control
Fasting blood glucose (mmol/l)*	⩽7.0	⩽8.0	>8.0
Non-fasting blood glucose (mmol/l)*	⩽9.0	⩽11.0	>11.0
Glycated haemoglobin (%)†	⩽7.0	⩽8.5	>8.5
Diastolic blood pressure (mm Hg)	⩽90	⩽100	>100
Total cholesterol (mmol/l)	⩽6.0	⩽7.0	>7.0
Fasting triglyceride (mmol/l)	⩽2.0	⩽5.0	>5.0

*Capillary whole blood glucose.
†Reference range 5.4-7.4%.
Instructions for general practitioners: The aim is normalisation of blood glucose, blood pressure, lipids, and possibly weight. For some patients, it will be impossible or even inappropriate to try to achieve the ideal goal, but prolonged symptoms of hyperglycaemia or hypoglycaemia must not be accepted for any patient. From an overall therapeutic point of view, the general practitioner chooses to aim at the treatment goals in one of the three categories. The choice of category is primarily based on glycated haemoglobin. Good control (normalisation of metabolism) is particularly relevant in young and middle aged patients and in well motivated older patients. Acceptable control applies to some older patients and patients who are difficult to treat or motivate. Poor control (freedom from symptoms) is intended for use when treatment has shown that any other goal is beyond reach.

Summary of treatment guidelines for general practitioners

Diet
Increase complex carbohydrate to at least 50% of the diet, and in particular increase water soluble fibre
Reduce fat content to maximum of 30%
Reduce alcohol intake
Eat 5-6 meals a day
Increase physical exercise

Smoking
Advise patients to cut down or stop

Persistent hyperglycaemia
Metformin for overweight patients
Glipizide or glibenclamide for patients with normal weight
Tolbutamide for patients >70 years
If goal for blood glucose is not met, metformin should be combined with a sulphonylurea before starting insulin

Hypertension
Angiotensin converting enzyme inhibitors or β blockers for most patients
Furosemide (frusemide) for patients with heart failure
Thiazides for patients >70 years

Hyperlipidaemia
Lipid lowering drugs for diet resistant hyperlipidaemia

Assessments

On 26 September 1995, the protocol based final follow up examinations were initiated in both groups and the intervention was terminated. The last examination was made in January 1998. Predefined primary outcomes were overall mortality and incidences of diabetic retinopathy, urinary albumin concentration ≥15 mg/l, myocardial infarction, and stroke in patients without these outcomes at baseline. Secondary outcomes were new peripheral neuropathy, angina pectoris, intermittent claudication, and amputation. Tertiary outcomes were levels of risk factors included in patients' goals. We did not intend to do subgroup analyses.

The doctors recorded the following information on patients: body height and weight without shoes and outer garments; blood pressure and heart rate by routine methods after a 10 minutes' rest in a sitting position; sense of touch of cotton wool and pin prick on both feet; presence of patellar reflexes; drug treatment; history of myocardial infarction and stroke causing hospital admission; amputation of leg or part before or at the time of diagnosis of diabetes; familiarity with the patient; severe hypoglycaemic events that impaired consciousness and required help from another person during the preceding year; and doctors' background variables.

In questionnaires, patients gave information about whether they lived alone, education, (former) occupation, smoking habits,[17] leisure time physical activity, angina pectoris,[17] intermittent claudication,[17] global self rated health, change of habits, food habits, symptoms of diabetes, and home glucose monitoring.

Eye backgrounds were evaluated by primary care ophthalmologists, who recorded the results of funduscopy in a multiple choice question that listed microaneurysms as the least severe lesions. Hypertension was defined as systolic/diastolic blood pressure ≥160/90 mm Hg or the use of antihypertensive or diuretic drugs, or any combination of these. Peripheral neuropathy was defined as lack of a sense of touch of cotton wool or pin prick on at least one foot or absent patellar reflex on at least one knee, or any combination of these.

The day of death was taken from the death certificate. We obtained information on hospital admissions for relevant conditions (myocardial infarction, stroke, amputation, etc) since diagnosis from the national hospital discharge registry.

Assays

Fasting blood samples were analysed at Odense University Hospital. Plasma glucose concentration was measured by a glucose dehydrogenase method. Fraction of glycated haemoglobin was determined by ion exchange, high performance liquid chromatography (reference interval: 5.4-7.4%). Serum creatinine concentration was determined by the Jaffe reaction. Serum total cholesterol concentration was measured enzymatically with cholesterol esterase-cholesterol oxidase-peroxidase reagent. Serum triglyceride concentrations were determined enzymatically with a lipase-glycerolkinase-glycerol-3-phosphate oxidase-peroxidase reagent. Urinary albumin concentration was measured in a freshly voided morning urine sample at Århus University Hospital by a polyethyleneglycol radioimmunoassay.[18]

Statistical analysis and sample size

From the available unpublished clinical experience in 1987, we estimated that we needed between 100 and 1200 patients in each group to detect a 40% difference over 10 years between the groups in the four non-fatal outcomes with 80% power and 95% confidence. On the basis of published estimates of incidence,[19] we needed 400 general practitioners to include 1600 patients over two years.

Analysis was by intention to treat. Quoted P values are not adjusted for multiple comparisons. Since there are five primary outcome variables we used the Bonferroni method and accepted $P<0.01$ as significant. All other outcomes were interpreted at the 5% level, but only to show tendencies. We compared intervention and comparison groups at follow up using a Wald test for binary and continuous variables. We did the analyses with the software PROC GENMOD, SAS version 6.12, using generalised estimating equations (GEE) methods to account for clustering at doctor level. Similarly, we used logistic regression analysis with non-fatal outcomes as responses to adjust for allocation of treatment group, age, sex, occupation, smoking habits, and time from diagnosis to measurement of outcome. We used a generalised linear mixed model (restricted maximum likelihood methods) with the predefined outcomes and explanatory variables as fixed effects and doctor identification as random effect to model the clustering. The time from diabetes diagnosis to death was taken into account by using a Cox regression model with no random effects.

Results

Doctors

When the study started, the general practitioners in the intervention and comparison groups had similar char-

acteristics. There were no differences in sex (P = 0.46) or median age (44 *v* 44 years, P = 0.56), years of practice experience (10 v 10, P = 0.95), years of hospital experience (6 *v* 6 years, P = 0.40), number of doctors in the practice (2 *v* 2, P = 0.10), number of patients per doctor (1158 *v* 1151, P = 0.51), and weekly hours of work (43 *v* 43, P = 0.69).

Patients

In all, 1316 (85.9%, range 0-12 per doctor) of 1470 eligible newly diagnosed diabetic patients were considered for this analysis. More patients in the intervention group than the comparison were excluded (P = 0.002, χ^2 test), mainly because of severe somatic disease (figure). The two groups did not differ in total number of patients included (P = 0.33, χ^2 test), inclusion activity over time (P = 0.32, log rank test), and number of patients per doctor (P = 0.51, χ^2 test). Of 39 baseline variables, only occupation (P = 0.01, χ^2 test) and smoking habits (P = 0.039) differed between the two groups (table 2).

The numbers completing the final follow up examination were similar in the two groups (459 *v* 415, P = 0.21, χ^2 test). A generalised linear mixed model was constructed with treatment group allocation, age, sex, whether living alone, education, and self rated health as fixed effects and doctor identification as random effect, but none of these variables predicted whether follow up was done or not for surviving patients. At the final follow up examination, the median (interquartile range) duration of diabetes was 5.75 (5.25-6.32) years for the intervention group and 5.86 (5.30-6.47) years for the comparison group (P = 0.023).

Process of treatment

In the comparison group, no information was collected about the treatment process from diagnosis until the final examination. In the intervention group, the proportion of patients who had an annual clinical examination fell to 79% (327/412) over four years, and attendance at three monthly consultations was even less, despite prompting. The proportion of patients aiming at "good control" fell from 68% (401/587) to 63% (218/348) over four years. Of 459 intervention patients, 44 had a doctor who did not attend any of the six annual half day seminars, 104 had doctors who attended 1-2 seminars, 155 had doctors who attended 3-4 seminars, and 156 patients had doctors who attended 5-6 seminars.

Table 3 shows the drugs prescribed at the end of the study. Metformin was more widely used in the intervention group, the only group difference observed. Of those given oral antidiabetic drugs, 55% (58/105) of those with body mass ≥30 in the intervention group and 32% (28/87) in the comparison group had metformin, P = 0.001, χ^2 test); for patients with a body mass index <30, the proportions were 31% (52/169) and 23% (33/142), respectively (P = 0.14). The dose of the drugs was similar in both groups, except for in the eight intervention patients and 12 comparison patients receiving a combination of insulins, where the dose in the intervention group was lower. Insulin and lipid lowering drugs were recommended increasingly explicitly at the seminars, but doctors or patients were reluctant to comply.

Intervention doctors used their patients' participation in the study during consultations with patients more than comparison doctors (table 4). Intervention doctors set more optimistic goals for blood glucose concentration (P = 0.0003, Wilcoxon test) and were less likely to regard their patients' motivation as very good than comparison doctors, but the doctors in the two groups were equally satisfied with their achievements (table 4).

Table 2 Baseline characteristics of patients. Values are medians (interquartile ranges) unless stated otherwise

Characteristic	No of respondents (structured/routine care)	Structured care	Routine care
Sociodemographic			
No (%) men	649/614	340 (52.4)	326 (53.1)
Age (years)	649/614	65.5 (55.3-74.0)	65.3 (56.3-73.5)
No (%) live alone	634/600	211 (33.3)	197 (32.8)
No (%) basic school education only	621/583	491 (79.1)	453 (77.7)
(Former) occupation (No (%))	631/596		
Self employed		153 (24.2)	95 (15.9)
Salaried employee		158 (25.0)	186 (31.2)
Worker		246 (39.0)	231 (38.8)
Housewife and other		74 (11.7)	84 (14.1)
Doctor's familiarity with patient (No (%))	648/614		
Thorough		306 (47.2)	311 (50.7)
Moderate		251 (38.7)	229 (37.3)
Poor		91 (14.0)	74 (12.0)
Clinical			
Body mass index (kg/m^2)	647/614	29.4 (26.2-33.0)	28.8 (26.0-32.3)
Body weight (kg)	647/614	81.5 (71.3-94.3)	82.1 (72.0-92.2)
No (%) with hypertension	649/614	487 (75.0)	456 (74.3)
Systolic blood pressure (mm Hg)	649/614	150 (130-164)	148 (130-160)
Diastolic blood pressure (mm Hg)	649/614	85 (80-90)	85 (80-90)
No (%) with diabetic retinopathy	577/559	29 (5.0)	25 (4.5)
No (%) with peripheral neuropathy	645/610	121 (18.8)	120 (19.7)
Resting heart rate (beats/min)	647/613	76 (68-84)	76 (68-84)
No (%) with known cardiovascular disorders:			
History of myocardial infarction	649/613	43 (6.6)	47 (7.7)
Angina pectoris	633/596	74 (11.7)	71 (11.9)
History of stroke	649/614	23 (3.5)	26 (4.2)
Intermittent claudication	634/598	25 (3.9)	20 (3.3)
Amputation	649/614	2 (0.3)	4 (0.7)
Biochemical			
Diagnostic fasting glucose (mmol/l)	649/614	13.8 (10.7-17.0)	13.7 (10.7-17.0)
Glycated haemoglobin (%)*	534/506	10.2 (8.6-11.6)	10.2 (8.7-11.9)
Total cholesterol (mmol/l)	628/604	6.2 (5.4-7.1)	6.2 (5.5-7.2)
Fasting triglyceride (mmol/l)	625/604	2.03 (1.44-2.91)	1.98 (1.39-2.95)
Urinary albumin (mg/l)	615/589	11.7 (6.0-32.5)	11.8 (5.7-27.5)
Serum creatinine (μmol/l)	628/605	90 (81-101)	88 (79-100)
Behavioural			
No (%) of smokers	633/598		
Never		210 (33.2)	167 (27.9)
Former		198 (31.3)	225 (37.6)
Current		225 (35.5)	206 (34.5)
Tobacco consumption (g/day)†	394/400	17.7 (10.0-23.0)	15.7 (10.0-22.0)
Activity (No (%))	632/598		
Low		182 (28.8)	159 (26.6)
Moderate		405 (64.1)	403 (67.4)
High		45 (7.1)	36 (6.0)
Self rated health (No (%))	635/600		
Very good		71 (11.2)	75 (12.5)
Good		219 (34.5)	195 (32.5)
Average		286 (45.0)	267 (44.5)
Poor or very poor		59 (9.3)	63 (10.5)

*Measured within 45 days of diabetes diagnosis. With a time limit of 365 days, glycated haemoglobin is 9.6% (8.1-11.5%) / 9.7%(8.2-11.5%), n=634/604, P=0.40. Reference range 5.4-7.4%.
†Former and current smokers together.

Table 3 Numbers (percentages) of patients receiving drug treatment at end of study

	Age 40-69 years			Age ⩾70 years		
	Structured care (n=325)	Routine care (n=298)	P value*	Structured care (n=134)	Routine care (n=117)	P value*
Treatments to lower blood glucose						
Diet only	92 (28)	92 (31)	0.53	42 (31)	39 (33)	0.74
Oral antidiabetic drugs, total	196 (60)	165 (55)	0.22	79 (59)	64 (55)	0.52
Sulphonylureas (SU) only	101 (31)	111 (37)	0.11	61 (46)	54 (46)	0.92
Metformin only	32 (10)	14 (5)	0.013	7 (5)	2 (2)	—
Sulphonylurea and metformin	61 (19)	39 (13)	0.073	10 (7)	6 (5)	0.46
Other (combinations of) oral antidiabetics	2 (1)	1 (0)	—	1 (1)	2 (2)	—
Insulin†	39 (12)	42 (14)	0.42	14 (10)	15 (13)	0.55
No of different oral antidiabetic drugs						
1	132 (41)	125 (42)	0.74	67 (50)	56 (48)	0.74
2	64 (20)	40 (13)	0.05	12 (9)	8 (7)	0.54
Drugs to lower blood pressure						
Total	170 (52)	144 (48)	0.35	86 (64)	77 (66)	0.80
Angiotensin converting enzyme inhibitor‡	72 (22)	73 (25)	0.50	17 (13)	15 (13)	0.98
β blocker‡	28 (9)	22 (7)	0.59	10 (7)	6 (5)	0.44
Calcium channel blocker‡	47 (14)	44 (15)	0.92	17 (13)	17 (15)	0.68
Diuretic‡	107 (33)	90 (30)	0.46	74 (55)	63 (54)	0.84
Other antihypertensive drugs‡	6 (2)	5 (2)	0.88	0	5 (4)	—
No of different drugs to lower blood pressure:						
1	93 (29)	71 (24)	0.18	50 (37)	45 (38)	0.86
2	55 (17)	53 (18)	0.78	31 (23)	28 (24)	0.88
⩾3	22 (7)	20 (7)	0.98	5 (4)	4 (3)	—
Lipid lowering drugs						
Total	20 (6)	14 (5)	0.45	0	0	—

*Wald test. Not shown when cells have expected counts less than five.
†In five cases in combination with an oral drug
‡Alone or in combination with other antihypertensive drugs.

Primary and secondary outcomes

When multiple outcomes were taken into account with Bonferroni's adjustment, we found no differences in the predefined outcomes (table 5). The treatment group allocation was not a significant predictor of death in a Cox regression model adjusted for age, sex, body mass index, glycated haemoglobin, diastolic and systolic blood pressure, cholesterol concentration, triglyceride concentration, smoking habits, and physical activity (hazard ratio 0.91, 95% confidence interval 0.72 to 1.14; P = 0.41). In logistic regression analyses taking in account clustering at doctor level and adjusted for age, sex, occupation, smoking habits, and duration of diabetes, there was no difference between groups in diabetic retinopathy (odds ratio 0.90, 95% confidence interval 0.53 to 1.52; P = 0.69), microalbuminuria (0.63, 0.41 to 0.98; P = 0.042), non-fatal myocardial infarction (0.65, 0.31 to 1.35; P = 0.25), non-fatal stroke (0.89, 0.39 to 2.01; P = 0.77), peripheral neuropathy (0.86, 0.57 to 1.28; P = 0.45), angina pectoris (0.90, 0.49 to 1.66; P = 0.74), or intermittent claudication (0.81, 0.35 to 1.88; P = 0.63).

Table 4 Attitudes and opinions of general practitioners. Values are numbers (percentages) of respondents

For patient in question, doctor's indication of:	Structured care	Routine care	P value*
Realistic goal for fasting whole blood glucose (mmol/l)			
⩽7.0	158 (35)	107 (27)	0.025
>7.0-8.0	108 (24)	88 (22)	0.56
>8.0-9.0	70 (15)	61 (15)	0.94
>9.0	120 (26)	146 (36)	0.010
Satisfaction with own efforts to obtain best possible diabetes control			
Completely satisfied	132 (29)	128 (31)	0.51
Fairly satisfied	256 (56)	213 (52)	0.29
Not satisfied	70 (15)	69 (17)	0.55
Patient's attitude to study participation			
Happy with the attention	219 (48)	91 (22)	<0.0001
No special importance	184 (40)	287 (69)	<0.0001
Irritated or bothered	44 (10)	18 (4)	0.006
Other	12 (3)	18 (4)	0.16
Use of fact that patient was participating in a study during consultations			
Used vigorously	60 (13)	6 (1)	<0.0001
Used moderately	206 (45)	34 (8)	<0.0001
Only mentioned when necessary	189 (42)	368 (90)	<0.0001
Patient's motivation for best possible control and treatment over past year			
Very good	86 (19)	118 (29)	0.002
Good	169 (37)	128 (31)	0.062
Fair	124 (27)	96 (23)	0.24
Poor	78 (17)	71 (17)	0.96

*Wald test.

Other outcomes

Median fraction of glycated haemoglobin was 8.5% in the intervention group, which is 1.1% higher than the upper limit of the reference range(5.4-7.4%) and 0.5% lower than in the comparison group (table 6). The difference of 0.5% corresponds to about 0.8 mmol/l in fasting plasma glucose concentration (table 6). The group differences for median systolic and diastolic blood pressures were 5 mm Hg and 4 mm Hg. Adjustment for baseline level of the outcome, duration of diabetes, age, sex, occupation, and smoking habits in linear regression analyses confirmed the treatment group difference for the logarithm of glycated haemoglobin (difference (log %) −0.056, 95% confidence interval −0.081 to −0.031; P < 0.0001), systolic blood pressure (−5.0 mm Hg, −7.6 to −2.4 mm Hg; P = 0.0002), and cholesterol concentration (−0.15 mmol/l, −0.29 to −0.02 mmol/l; P = 0.029), but not for weight (−0.83 kg, −1.75 to 0.09 kg; P = 0.076), diastolic blood pressure (−0.6 mm Hg, −1.9 to 0.7

mm Hg; P = 0.35), logarithm of triglyceride concentration (−0.05 log mmol/l, −0.12 to 0.02 log mmol/l; P = 0.19), or logarithm of serum creatinine concentration (−0.004 log μmol/l, −0.033 to 0.025 log μmol/l; P = 0.79). Intracluster correlation coefficients varied from −0.021 to 0.054. Compared with weight at diagnosis, the weight at follow up was on average 2.6 kg lower in the intervention group and 2.0 kg lower in the comparison group.

The patients give similar behavioural reports in both groups, but the intervention seems to have decreased referrals to diabetes clinics and increased the number of consultations (table 6). The main difference was that more intervention patients than control patients had four consultations a year (28% (129/459) *v* 19% (77/414) of control patients) and fewer had 0-1 consultations a year (10% (44/459) *v* 23% (95/414)). Hospital admission, severe hypoglycaemia, and experience of symptoms were similar in both groups. Hypoglycaemic episodes were suspected in 23%

Table 5 Outcomes at end of study.* Values are numbers (%) of group (mortality) or numbers (%) who completed follow up examination and did not have the outcome at baseline (all other outcomes)

	No (%) in structured care group	No (%) in routine care group	P value†
Primary outcomes:			
Overall mortality	216/649 (33.3)	208/614 (33.9)	0.82
Diabetic retinopathy	43/359 (12.0)	45/330 (13.6)	0.55
Urinary albumin ⩾15 mg/l	56/249 (22.5)	72/234 (30.8)	0.04
Myocardial infarction	15/437 (3.4)	18/393 (4.6)	0.40
Stroke	18/446 (4.0)	16/405 (4.0)	0.95
Secondary outcomes:			
Peripheral neuropathy	69/375 (18.4)	69/329 (21.0)	0.41
Angina pectoris	22/371 (5.9)	23/346 (6.7)	0.68
Intermittent claudication	13/382 (3.4)	13/374 (3.5)	0.96
Amputation	2/459 (0.44)	4/414 (0.97)	0.35

*Median follow up period for structured care group was 7.41 years for mortality and 5.75 years for other outcomes; median follow up for routine care group was 7.32 years and 5.86 years, respectively.
†Wald test. As there are five outcomes we accepted P<0.01 as significant.

Table 6 Clinical, biochemical, behavioural, and process variables at end of study. Values are medians (interquartile ranges) unless stated otherwise

Clinical	No of patients (structured/routine care)	Structured care	Routine care	P value*
Body weight (kg)	448/404	79.9 (69.5-90.4)	80.5 (70.0-92.0)	0.72
No (%) with hypertension	455/409	333 (73)	307 (75)	0.56
Systolic blood pressure (mm Hg)	455/409	145 (130-160)	150 (140-165)	0.0004
Diastolic blood pressure (mm Hg)	455/409	80 (78-90)	84 (78-90)	0.40
Resting heart rate (beats/min)	452/404	72 (68-80)	76 (68-80)	0.43
Biochemical				
Fasting plasma glucose (mmol/l)†	350/296	7.9 (6.5-10.6)	8.7 (7.2-11.6)	0.0007
Glycated haemoglobin (%)‡	450/408	8.5 (7.7-9.5)	9.0 (8.0-10.4)	<0.0001
Total cholesterol (mmol/l)	449/408	6.0 (5.2-6.8)	6.1 (5.4-6.9)	0.12
Fasting triglyceride (mmol/l)	418/350	1.78 (1.25-2.52)	1.89 (1.27-2.75)	0.32
Serum creatinine (μmol/l)	449/408	89 (81-103)	91 (80-105)	0.84
No (%) with glycosuria	445/400	100 (22)	148 (37)	<0.0001
Behavioural (No (%) of patients)				
Has altered habits	417/391	344 (82)	315 (81)	0.48
Smoking	419/390			
Never		147 (35)	124 (32)	0.32
Former		138 (33)	151 (39)	0.10
Current		134 (32)	115 (29)	0.45
Activity	415/392			
Low		122 (29)	122 (31)	0.62
Moderate		258 (62)	239 (61)	0.75
High		35 (8)	31 (8)	0.78
Food habits	416/393			
Diet with certain amounts of selected foodstuffs		140 (34)	121 (31)	0.59
Full diet without sugar		213 (51)	207 (53)	0.67
Diet as non-diabetic subjects		63 (15)	65 (17)	0.36
Performs home blood or urine glucose monitoring	416/388	117 (28)	114 (29)	0.73
Self rated health	421/394			
Very good		68 (16)	83 (21)	0.087
Good		176 (42)	150 (38)	0.29
Average		153 (36)	147 (37)	0.77
Poor or very poor		24 (6)	14 (4)	0.15
Process of care				
No of consultations/year	459/414	6 (5-10)	6 (4-9)	0.002
No of diabetes related consultations/year	459/414	4 (3-6)	4 (2-6)	<0.0001
No (%) ever treated at diabetes clinic	459/415	79 (17)	106 (26)	0.009
No of hospital admissions since diagnosis	459/415	1 (0-3)	1 (0-3)	0.79
Total length of stay in hospital (days)	281/256	16 (7-39)	19 (8-45)	0.066
No (%) with severe hypoglycaemia since diagnosis	457/413	17 (4)	15 (4)	0.94
No (%) with symptoms of diabetes in past two weeks	419/393	194 (46)	193 (49)	0.42

*Wald test.
†Including only results from samples analysed one day after sampling, or less.
‡Reference range 5.4-7.4%.

(12/53) of intervention and 11% (6/57) of comparison patients receiving insulin.

Discussion

This long term randomised trial in primary care shows that a multifaceted intervention directed at general practitioners moderates risk factors of patients with newly diagnosed type 2 diabetes. The interventions included regular follow up and individualised goals for patients supported by prompting of doctors, clinical guidelines, feedback, and continuing medical education. We achieved the same level of risk factors as recent large intervention studies from secondary care without the expected adverse weight gain.[1 2 5]

The randomisation of practices was successful both on doctor and patient level, and follow up was completed for 90% of surviving patients, which may be because of our simple, precisely defined eligibility criteria and measures.[20] The list system with a well defined background population in each practice, the few exclusions, the unchanged inclusion activity over time irrespective of treatment allocation, and doctors' self reports suggest that our patients are likely to be representative of the general population of newly diagnosed diabetic people. This is an advantage over intervention studies in secondary care, which often use selected study populations.[1]

Predefined outcomes

Modern diabetes care is founded on the results from the UK prospective diabetes study[1 2] and Steno type 2 study[5] and post hoc analyses of hypertension and lipid trials.[3 4] In retrospect, our study was underpowered to detect differences in the primary outcomes in an intention to treat analysis after only six years.[1 2] Furthermore, some outcome measures lacked precision because we kept the demands on practitioners and patients to a minimum to prevent attrition.[20] Comparison doctors may also have managed their patients more effectively than the average practitioner,[21] decreasing the size of any effect.

Risk factors

After almost six years of intervention, the glycaemic control in the intervention group was similar to that achieved in the intervention arms of the Steno type 2 study[5] and UK prospective diabetes study at the same point.[1] The result is put into perspective by the relatively high median plasma glucose concentration at presentation in our study (13.8 mmol/l) compared with the UK prospective diabetes study (11.3 mmol/l), primarily reflecting the low diagnostic limit in that study.

The glycated haemoglobin fraction in our routine care group, however, was only 0.5% higher than in the structured care group. This reflects the fact that comparison doctors were supposed to "do their best," and were not under the constraints imposed on doctors treating the comparison group in the UK prospective diabetes study.[1] The doctors' reports on their use of study participation and their patients' attitude to it indicate a beneficial effect of study participation in itself. This is highest in the intervention group but also present in the comparison group. The many initiatives taken in Denmark to improve diabetes treatment in primary care may also have contributed.[14–16]

The favourable weight course, especially in the intervention group, might be ascribed to doctors being taught to await the effect of diet, exercise, and weight loss before starting antidiabetic drugs. This contrast with the strategy in UK prospective diabetes study[1] and Steno type 2 study,[5] which used stepwise increase of drugs to reach predefined treatment goals. Our individually agreed small, realistic weight losses may have prevented doctors and patients from losing focus on the individual goals for risk factors, in contrast to other approaches to personal care.[22]

At entry, the average blood pressures in our study (148-150/85 mm Hg) were similar to those in the Steno type 2 study (146-149/85-86 mm Hg)[5] but higher than in the UK prospective diabetes study glucose trial(135/82 mm Hg)[1] and lower than in its hypertension trial (159-160/94 mm Hg).[2] The variation reflects differences in patient age and selection. The average difference between treatment groups in blood pressures was larger than in Steno type 2 study, but smaller than in the UK prospective diabetes study subgroup of hypertensive patients.

Despite reduced glycosuria, the symptom burden as well as a simple measure of self rated health was the same in both groups as in the UK prospective diabetes study.[23] Our focus on individualised treatment therefore did not affect wellbeing measurably, although wellbeing has been reported to improve in patient centred diabetes care.[22] Our failure to show a clinically important improvement in dyslipidaemia may be connected to our adoption of the relatively lax targets for lipid concentrations that were in use in 1988-95.[14–16]

What caused the reduction in risk factors?

Our flexible approach to the intervention may have maximised not only doctors' ability to participate but also the ultimate generalisability of results. The approach is feasible to implement within the health service[24] and the patient sample was non-selective. In complex interventions the effect cannot be ascribed to single elements, although the continuing medical education is probably a core element.[12 13] The fact that we used many ways to change doctors' behaviour may be the reason for success.[10 11]

The intervention apparently did not affect patient behaviour, except that more followed a three monthly follow up scheme, but this could be because of limitations in our measures. Intervention doctors, however, became more focused on lowering risk factors through setting goals, which perhaps prevented doctors from losing professional autonomy[20 25] and involved patients in decision making.[22 26] The psychological effect of the labelling of care explicitly as good, acceptable, and poor must not be underestimated either.[27] Although normoglycaemia was rarely achieved in any of the groups, this was the goal for most intervention patients throughout the study. As a possibly negative side effect of this, intervention doctors tended to regard their patients' motivation as relatively low. Contrary to study recommendations, the referral rate of intervention patients to diabetes clinics was low. This could be because doctors were empowered by structuring care[28] or because of patients' improved diabetes status.[29]

The only major difference in drug treatment between groups was that metformin was used more in

What is already known on this topic

Evidence is increasing that control of hyperglycaemia, hypertension, and dyslipidaemia may postpone the development of diabetic complications in patients with type 2 diabetes

Maintaining good control over a long period can be difficult

What this study adds

Structured individualised personal care with educational and surveillance support for general practitioners reduced levels of risk factors in type 2 diabetic patients after six years

Risk factors were reduced to a level that has been shown to have a beneficial effect on diabetic complications

Participants also showed modest weight loss

the intervention group, especially among obese patients, and this may have contributed to the lower glycated haemoglobin fraction.[30] Doctors' reports on their patients' antihypertensive treatment were similar in both groups. Therefore, the effect of the intervention on risk factors may also be partly explained by better compliance with treatment,[31] which has been shown to be poor in type 2 diabetic patients.[32] The prevalence of severe hypoglycaemia did not differ between groups and was similar to that in other trials.[1 5] The tendency among those receiving insulin towards more hypoglycaemic episodes in the intervention group, unrelated to dose, supports the compliance hypothesis mentioned above.

Conclusion

We have shown that even in a group of motivated, volunteering general practitioners that were already supplying acceptable basic patient care, a multifaceted, individualised disease management strategy can provide extra benefit for patients with type 2 diabetes patients for at least six years. The flexible approach to the intervention and the population based patient sample suggest that our model for structured personal care could be applied at population level. Use of the model may reduce risk factors to a level that has been shown to have a beneficial effect on the development of diabetic complications without adverse weight gain.

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