

Effects of Protocol-Driven Care Versus Usual Outpatient Clinic Care on Survival Rates in Patients With Type 2 Diabetes

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Objective: To determine whether clinical outcomes in patients with type 2 diabetes were improved by protocol-driven care in a Diabetes Centre compared with usual outpatient care.

Study Design: Descriptive analysis of a prospective cohort.

Patients and Methods: During a median 7-year observational period, 91 patients with type 2 diabetes and no cardiovascular or renal complications were monitored by a nurse and a diabetologist in a clinical trial setting according to a structured protocol. Another 81 patients with comparable clinical characteristics were monitored by generalists at the medical clinic in the same hospital. Clinical end points, defined as death and cardiovascular and renal events, were evaluated in 1997 by review of case records.

Results: Patients receiving structured care had lower mortality (relative risk [RR] = 0.21; 95% confidence interval [CI] = 0.07, 0.65; $P = .006$) than the usual-care group, as well as a lower incidence of combined clinical end points (RR = 0.43; 95% CI = 0.22, 0.84; $P = .01$). In the usual-care group, patients who had no monitoring of glycosylated hemoglobin or plasma lipid levels during the entire observational period (8.6%) had a 14.6-fold ($P < .01$) and 15.7-fold ($P < .01$) increased risk of death and combined clinical end points, respectively, compared with those who had at least one measurement (60.5%).

Conclusion: Management by protocol-driven care model improved survival and clinical outcomes in patients with type 2 diabetes. Definitive studies are required to confirm these findings and compare the cost effectiveness of these care models.

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tance of periodic assessments, patient empowerment, and treatment to target.¹² However, in most healthcare settings, organization of care for patients with chronic diseases such as diabetes often is suboptimal because of a lack of resources or personnel with the appropriate expertise.

This descriptive analysis is based on a clinical trial conducted in 1989 that compared the renal protective effects of nifedipine (slow release) and enalapril in 102 hypertensive patients with type 2 diabetes over a 5-year period.^{13,14} Enalapril was confirmed to be more effective in reducing albuminuria and the rate of decline of renal function, especially in macroalbuminuric patients. In this long-term study, we noted that only 4 patients had died, for an annual mortality rate of 0.8%.^{13,14} This is in marked contrast to the conventionally reported mortality rate of 2% to 4% in unselected cohorts of patients with type 2 diabetes.^{1,15-17} Until recently, most studies of protocol-driven diabetes care only examined relatively short-term clinical effects.^{18,19} However, results of the Steno type 2 diabetes study showed that, compared with usual care, a multidisciplinary and "treat-to-target" approach to optimize risk factors reduced by 70% the risk of developing all microvascular complications after 3.5 years of follow up.²⁰ These beneficial effects were fur-

Type 2 diabetes is a massive public health problem associated with diminished quality of life, increased health care utilization, decreased societal productivity, and early mortality, mainly because of cardiovascular and/or renal diseases.¹⁻³ Optimal control of risk factors in patients with diabetes has been confirmed to reduce the risk of diabetes-related complications by 20% to 70%.⁴⁻⁸ Appropriate use of medications like angiotensin-converting enzyme (ACE) inhibitors by patients with type 2 diabetes has been associated with renal and cardiac protection independent of blood pressure reduction.⁹⁻¹¹ As a result, American Diabetes Association treatment guidelines emphasize the impor-

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ther translated to a reduction in cardiovascular events at 7.8 years. However, there was no difference in mortality between the 2 groups.²¹ Against this background, we hypothesized that the provision of structured care to patients with type 2 diabetes would reduce mortality and morbidity through several processes, including risk stratification, treatment to target, patient empowerment, and improved control of metabolic risk factors (Figure 1). We selected a cohort of patients who had similar baseline clinical characteristics in 1989 but who did not receive protocol-driven care (usual-care group) for comparison with the structured-care group.^{13,14}

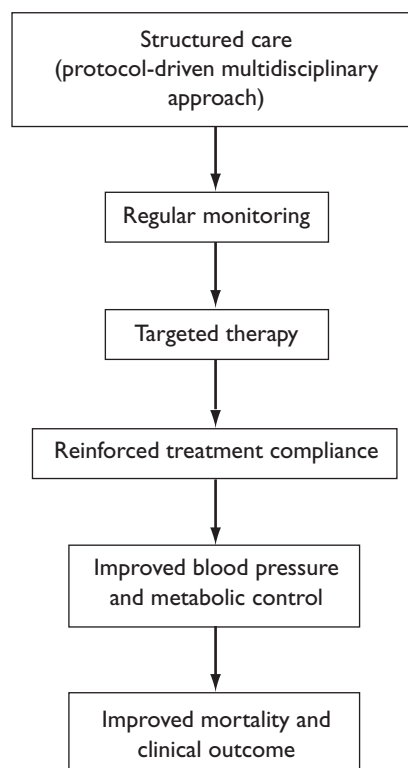
RESEARCH DESIGN AND METHODS

The study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong. The structured-care cohort came from the original cohort of 102 Chinese patients with type 2 diabetes (age 30-70 years) who were recruited in 1989 from the outpatient medical clinic.¹³ They were randomized in a double-blind manner to receive either enalapril (10-40 mg daily) or nifedipine (slow release 40-80 mg daily) for the treatment of hypertension after detailed assessments. The study design has been previously described.^{13,14} At the time of recruitment, none of the patients were being treated with insulin or lipid-lowering drugs. None of the patients had cardiovascular disease or significant renal impairment, defined as a plasma creatinine concentration of $\geq 150 \mu\text{mol/L}$.

A research nurse and a diabetologist monitored these patients between early 1989 and late 1997 according to a prespecified protocol.¹³ Once blood pressure control was attained after the initial 12-week titration period, all patients had medical consultations every 4 months that lasted for 15-20 minutes. They also were monitored at 2-month intervals by a research nurse for treatment compliance by direct questioning and tablet counting, as well as measurement of body weight and blood pressure. An annual assessment was performed, which included fundus and foot examination, and measurement of renal function and 24-hour urinary albumin excretion. Glycosylated hemoglobin (HbA_{1c}) was measured every 4 months; and a complete lipid profile (total cholesterol, triglycerides, high-density lipoprotein [HDL] cholesterol, calculated low-density [LDL] cholesterol) was done every 6 months.

Between 1989 and 1990, as part of our recruitment process for the clinical trial, we kept a record of all patients with diabetes attending the medical clinic who did not have cardiovascular complications or renal impairment at the time. The usual-care group was

Figure 1. Improved Clinical Outcomes in Patients With Type 2 Diabetes Attributable to Use of Structured Care. Structured Care Included Risk Stratification, Targeted Therapy, Reinforced Compliance, and Improved Metabolic Risk Factor Control.



selected from those patients not recruited into the clinical trial because their blood pressure was lower than that mandated by the protocol criteria ($\geq 160/90$ mm Hg). Otherwise, usual-care and structured-care patients were matched for age, sex, duration of disease, and clinical characteristics. The usual-care patients were monitored at 4- to 6-month intervals by generalists or various specialists with an average consultation time of 8-12 minutes. Blood pressure, fasting plasma glucose, and fructosamine were measured at each clinic visit. All doctors had unrestricted access to laboratory tests. It was recommended that they perform an annual exam to assess complications, using a protocol similar to that used for patients in the structured-care group. However, there was no mechanism to ensure the compliance of patients and medical staff.

In late 1997, we examined the clinical progress of these patients by review of their medical records. Blood pressure and metabolic indices at each visit, drug treatment, and yearly renal function, if available, were docu-

mented. Clinical end points were defined as death, cardiovascular events (heart failure or angina requiring hospitalization, myocardial infarction, lower limb amputation, revascularization procedures, cerebrovascular accidents), and end-stage renal disease (doubling of baseline plasma creatinine level or need for renal dialysis). The rate of decline of renal function was estimated by the regression coefficient of the yearly plasma creatinine (Cr) reciprocal ($\beta[1/\text{Cr}]$). In Hong Kong, due to the lack of a comprehensive health insurance policy and primary healthcare system, the majority of patients, especially those with chronic diseases like diabetes, are managed in public hospitals where they need to pay only a nominal fee to cover medical consultations, medications, and investigations. As a result, the default rate was very low.

This prospective cohort consisted of 91 patients in the structured-care group and 81 patients in the usual-care group. Eleven older patients from the structured-care group were excluded from the present analysis because we could not find matched subjects in the medical clinic setting. None of these excluded patients died or experienced clinical end points during the observational period. In the survival analysis, those who survived fewer than 6 months after recruitment were excluded.

Laboratory Assays

Plasma glucose was measured by a glucose oxidase method (Diagnostic Chemicals reagents kit, Diagnostic Chemicals, Los Angeles, Calif). Plasma creatinine was measured by using the Jaffe method on a Beckman Astra-8 Chemistry Analyzer (Beckman, Brea, Calif). Plasma fructosamine was measured on a centrifugal analyzer (Cobas Bio, Hoffman-La Roche, Basel, Switzerland).²² HbA_{1c} was measured by an automated ion-exchange chromatographic method (Bio-Rad Laboratories, Hercules, Calif) (reference range: 5.1% to 6.4%). Total cholesterol, HDL cholesterol, and triglyceride concentrations were measured enzymatically with commercial reagents automated on a centrifugal analyzer (Boehringer Mannheim, Mannheim, Germany). Low-density lipoprotein cholesterol was calculated by the Friedewald equation.²³

STATISTICAL ANALYSIS

The analysis was performed with version 9.0 of the Statistical Package for Social Sciences (SPSS Inc, Chicago, Ill). All data are expressed as the mean \pm SD or the geometric mean \times/\div antilog SD. The yearly values for blood pressure, fasting plasma glucose, HbA_{1c}, total cho-

lesterol, triglycerides, HDL cholesterol, and LDL cholesterol were used to estimate the mean values during the follow-up period. The student *t* test or analysis of variance was used for between-group comparisons for continuous variables after adjustment for covariates. The chi-square test was used for comparison of categorical variables. For some of the variables, only results at the end of the study period are shown because of missing baseline values in the usual-care group. The Cox proportional hazard model was used for the analysis of survival and other clinical end points; relative risk (RR) was expressed with 95% confidence intervals (CIs). A two-tailed *P* value of $<.05$ was considered to be significant.

RESULTS

Table 1 summarizes the clinical and biochemical characteristics of both groups of patients in 1989 and 1997 after a median follow-up period of 88 months (range: 6.1-119.4 months). In 1989, patients receiving structured care had higher blood pressure than those receiving usual care due to the nature of the clinical trial.¹³ They also had a higher prevalence of sensory neuropathy and retinopathy. Despite having lower blood pressure in 1989, patients in the usual-care group ended up having higher blood pressure and fasting plasma glucose values than the structured-care group in 1997.

In the structured-care group, 8.8% of patients died during the 6-year follow-up period compared with 24.7% in the usual-care group. The deceased were older, had a longer duration of diabetes, had worse glycemic control, and tended toward a more rapid rate of decline in renal function than the survivors during the follow-up period. A lower proportion of them were treated with an ACE inhibitor or were monitored according to the structured-care protocol (**Table 2**).

Figure 2 and **Figure 3** show the survival rates and the percentage of patients free of clinical end points, respectively, in the 2 groups. Compared with the usual-care group, the RR for mortality was 0.21 (95% CI = 0.07, 0.65; *P* = .006) and the RR for combined clinical end points was 0.43 (95% CI = 0.01, 0.84; *P* = .01) in the structured-care group. The absolute risk reduction for mortality was 0.16 in the structured-care group and the number needed to treat to prevent 1 death was 6.3 (95% CI = 3.9, 15.9; *P* < .0001). For the combined death, renal, and cardiovascular end points, the absolute risk reduction in the structured-care group was 0.15 and the number needed to treat was 6.7 (95% CI = 3.5, 55.6; *P* < .0001) to prevent 1 combined clinical end point.

Table 1. Clinical and Biochemical Characteristics in 1989 and 1997 of a Cohort of Patients With Type 2 Diabetes Receiving Either Structured or Usual Care*

Variable	Structured-Care Group (n = 91)	Usual-Care Group (n = 81)	P
Age, y	60.2 ± 7.9	61.1 ± 7.5	.472
Ratio of men to women	38:53	27:54	.255
Duration of diabetes, y	5.7 ± 4.9	5.9 ± 4.7	.795
No. of medical follow-up visits	18.4 ± 8.7	18.5 ± 6.8	.878
Follow up, y	6.1 ± 2.9	5.6 ± 2.5	.217
Use of ACE inhibitors, %	50.5	21.0	<.001
Retinopathy, %	41.8	22.2	.009
Neuropathy, %	31.9	12.5	.004
Body weight, kg, 1989			
Male	66.7 ± 9.2	67.7 ± 10.3	.175 [†]
Female	56.5 ± 8.0	56.9 ± 8.7	.14 [†]
Body weight, kg, 1997			
Male	65.2 ± 7.7	67.7 ± 10.4	.04 [†]
Female	54.9 ± 7.3	56.1 ± 8.6	.181 [†]
Systolic blood pressure, mm Hg			
1989	154.4 ± 24.7	142.7 ± 20.4	.001
1997	126.2 ± 16.3	155.0 ± 27.2	<.0001 [†]
Diastolic blood pressure, mm Hg			
1989	88.5 ± 11.4	83.7 ± 11.8	.007
1997	70.6 ± 15.1	76.7 ± 14.9	.004 [†]
Fasting plasma glucose, mmol/L			
1989	10.5 ± 3.7	10.8 ± 5.3	.740
1997	7.5 ± 2.6	9.8 ± 4.3	<.0001 [†]
Fructosamine, mmol/L [‡]	483.7 ± 64.6	475.7 ± 92.3	.536
HbA _{1c} , % [§]			
1989	7.2 ± 2.2	8.2 ± 1.6 (n = 9)	.189
1997	7.6 ± 1.3	7.4 ± 1.7 (n = 61)	.392 [†]
Total cholesterol, mmol/L [§]			
1989	5.9 ± 1.2	5.9 ± 1.4 (n = 15)	.958
1997	5.4 ± 1.1	5.5 ± 1.7 (n = 51)	.440 [†]
Total triglycerides, mmol/L [§]			
1989	1.7 ×/+ 1.9	2.1 ×/+ 1.7 (n = 15)	.280
1997	1.4 ×/+ 1.6	1.7 ×/+ 1.8 (n = 51)	.506 [†]
HDL cholesterol, mmol/L	1.4 ± 0.5	2.1 ± 5.3	.110 [†]
LDL cholesterol, mmol/L	3.7 ± 1.0	3.5 ± 1.0	.674 [†]
Plasma creatinine, mmol/L			
1989	83.5 ×/+ 1.3	86.0 ×/+ 1.4	.532
1997	104.8 ×/+ 1.6	122.2 ×/+ 2.3	.181 [†]
β(1/Cr)	-(3.2 ± 6.2) × 10 ⁻⁴	-(5.7 ± 15.7) × 10 ⁻⁴	.200 [†]
No. of deaths	8 (8.8%)	20 (24.7%)	.005
Combined death, cardiovascular, and renal end points	20 (22.0%)	30 (37.0%)	.043
Nonfatal cardiovascular and renal events, %	14.5	16.4	.817

*ACE indicates angiotensin-converting enzyme; HbA_{1c}, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein. Results are shown either as the mean ± SD or as the geometric mean ×/+ antilog SD.

[†]P value for comparison of results at the end of the observational period after adjustment for blood pressure differences at baseline.

[‡]Fructosamine assay was replaced by HbA_{1c} assay in 1995 as a hospital policy.

[§]n = Number of measurements available for analysis.

^{||}Because of missing baseline values in the usual-care group, only results at the end of study period are shown.

To identify the components of structured care that explain these marked differences in terms of clinical outcomes, we examined the levels of assessments and use of medications in these 2 groups of patients. None of these patients were treated with insulin or lipid-lowering drugs in 1989. In 1997, insulin use was similar in the structured-care and usual-care groups (17.6% vs 11.8%; $P = .25$). There was a tendency toward increased use of lipid-lowering drugs (22.5% vs 11.7%; $P = .054$) in the structured-care group, although such use did not result in a survival benefit (data not shown). Because of the nature of the clinical trial,¹⁴ more patients (50% vs 21%; $P < .001$) received an ACE inhibitor in the structured-care group. In the whole group analysis, patients treated with ACE inhibitors had higher blood pressure at baseline but a tendency toward lower mortality (RR = 0.41, 95% CI = 0.15, 1.10; $P = .08$) and combined clinical end points (RR = 0.60, 95% CI = 0.32, 1.15; $P = .1$). In the usual-care group, patients treated with an ACE inhibitor had a reduced risk of combined clinical end points (RR = 0.25, 95% CI = 0.06, 1.03; $P = .06$) compared with those who did not receive the drug.

The HbA_{1c} values and lipid profiles of all patients in the structured-care group were monitored regularly. In the usual-care group, fructosamine was the main glycemic index used until 1995, when the test was replaced by HbA_{1c} as a hospital policy. In the usual-care group, 18.5% of patients had no lipid profile, 11.1% had no measurement of HbA_{1c}, and 8.6% of patients had neither result available during the observation period. The latter group had a 14.6-fold (95% CI = 5.5, 38.5; $P < .01$) and 15.7-fold (95% CI = 6.46, 38.0; $P < .01$) increased risk of death and combined clinical end points, respectively, compared with those who had at least 1 measurement of either lipids or HbA_{1c} (60.5%) in the usual-care group.

In the Cox regression analysis, fewer medical follow-up visits, higher mean plasma glucose values, higher baseline plasma creatinine levels, and usual care were independent predictors of death. Higher plasma creatinine and fasting plasma glucose values at baseline, fewer medical follow-up visits, lack of monitoring of either HbA_{1c} or lipid indexes, and usual care were independent predictors of combined end points (Table 3 and Table 4). The use of ACE inhibitors was not an independent predictor for either survival or combined clinical end points in the Cox regression analysis.

DISCUSSION

Management of diabetes and chronic diseases often is fragmented and disorganized, with the main focus on treatment of complications. Recent results indicate that

an integrated approach can improve quality of care and metabolic control, although most of these studies had been relatively short term.¹⁹ In this study, we hypothesized that structured care in the setting of a clinical trial would improve clinical outcomes through a number of processes (Figure 1). Despite having higher blood pressure in 1989, patients in the structured-care group had an RR reduction of 79% in mortality and 57% in the combined clinical end points of death, renal events, and cardiovascular events compared with the usual-care group. The annual mortality rate of structured-care patients was estimated to be 1.5%, which was comparable to that of the general population of similar age. Looked at another way, one needs to treat only 6 patients in 6 years using a structured-care protocol to prevent 1 death or 1 combined clinical end point.

Improved Outcomes From Blood Pressure and Metabolic Control

In 1989, patients in the structured-care group had a higher mean systolic blood pressure than the usual-care group (154 mm Hg vs 143 mm Hg), but by 1997 they had lower blood pressure (126 mm Hg vs 155 mm Hg). This marked difference in blood pressure control must have contributed to the improved clinical outcomes. Although compliance was not formally documented in this observational study, one of the key roles of the nurse in the structured-care setting was to reinforce treatment compliance by direct questioning and tablet counting.

Because of the small number of patients in the usual-care group who had lipid profiles or measurements of HbA_{1c} during the follow-up period, we were unable to detect a difference in these metabolic indexes between the 2 groups. Nonetheless, there is epidemiologic evidence showing that glycemia was a strong predictor of clinical outcomes in both diabetic and nondiabetic populations.^{24,25} In our Cox regression analysis, fasting plasma glucose values (which were available for all patients) were found to be the most important independent predictors of death and clinical end points. Although the beneficial effects of lowering blood glucose were unimpressive in randomized clinical trials such as the UK Prospective Diabetes Study,²⁴ there is now a wealth of experimental evidence confirming the direct toxic effects of hyperglycemia through increased oxidative stress, formation of glycated end products, and alterations in intracellular metabolism,^{26,27} all of which can contribute to poor clinical outcomes.

Benefits of Angiotensin-Converting Enzyme Inhibitors

In 1989, the beneficial effects of ACE inhibitors on organ protection had yet to be proven. In our study,

Table 2. Clinical and Biochemical Characteristics in 1989 and 1997 of a Cohort of Patients With Type 2 Diabetes Categorized According to Their Survival Status*

Variable	Deceased (n = 28)	Survivors (n = 144)	P
Age, y	64.2 ± 9.0	60.0 ± 7.3	.008
Ratio of men to women	12:15	53:92	.437
Duration of diabetes, y	9.4 ± 6.2	5.1 ± 4.2	.001
Use of ACE inhibitors, %	18.5	40.0	.033
No. of medical follow-up visits	10.2 ± 6.2	20.1 ± 7.1	<.001
Follow up, y	2.3 ± 2.2	6.5 ± 2.2	<.001
Use of structured care, %	25.9	57.9	.002
Retinopathy, %	51.9	51.9	.024
Neuropathy, %	44.4	19.1	.004
Body weight, kg			
1989	61.3 ± 11.1	60.5 ± 10.0	.716
1997	60.9 ± 11.6	59.4 ± 10.8	.277
Systolic blood pressure, mm Hg			
1989	143.0 ± 22.4	150.0 ± 23.5	.153
1997	143.9 ± 25.4	140.1 ± 26.9	.514
Diastolic blood pressure, mm Hg			
1989	82.5 ± 13.6	87.0 ± 11.3	.070
1997	75.0 ± 16.5	73.2 ± 15.1	.560
Fasting plasma glucose, mmol/L			
1989	12.4 ± 5.8	10.3 ± 4.1	.084
1997	11.2 ± 5.4	8.1 ± 3.0	<.0001
Fructosamine, mmol/L [†]	484.5 ± 95.4	479.8 ± 71.9	.772
HbA _{1c} , % [‡]			
1989	8.0 ± 1.7 (n = 17)	7.2 ± 2.2 (n = 80)	.147
1997	7.8 ± 2.8 (n = 19)	7.5 ± 1.3 (n = 143)	.556
Total cholesterol, mmol/L [‡]			
1989	6.6 ± 2.0 (n = 9)	5.9 ± 1.2 (n = 90)	.347
1997	6.4 ± 2.2 (n = 14)	5.4 ± 1.2 (n = 128)	.007
Total triglyceride, mmol/L [‡]			
1989	2.8 ×/+ 1.8 (n = 9)	1.7 ×/+ 1.8 (n = 92)	.018
1997	1.8 ×/+ 2.0 (n = 4)	1.4 ×/+ 1.7 (n = 128)	.141
HDL cholesterol, mmol/L [‡]			
1989	1.03 ± 0.18 (n = 8)	1.19 ± 0.35 (n = 78)	.162
1997	1.06 ± 0.17 (n = 9)	1.28 ± 0.56 (n = 119)	.244
LDL cholesterol, mmol/L [‡]			
1989	3.87 ± 2.43 (n = 7)	3.82 ± 1.17 (n = 69)	.962
1997	3.93 ± 1.80 (n = 9)	3.41 ± 0.92 (n = 114)	.582
Plasma creatinine, mmol/L			
1989	114.7 ×/+ 1.5	80.0 ×/+ 1.3	<.001
1997	227.3 ×/+ 2.7	98.9 ×/+ 1.6	<.001
β(1/Cr)	-(1.6 ± 2.6) × 10 ⁻³	-(2.5 ± 5.8) × 10 ⁻⁴	.022

*ACE indicates angiotensin-converting enzyme; HbA_{1c}, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein. Results are shown either as the mean ± SD or as the geometric mean ×/+ antilog SD.

[†]Fructosamine assay was replaced by HbA_{1c} assay in 1995 as a hospital policy.

[‡]n = Number of measurements available for analysis.

Figure 2. Survival Rates in Patients With Type 2 Diabetes Receiving Either Structured or Usual Care

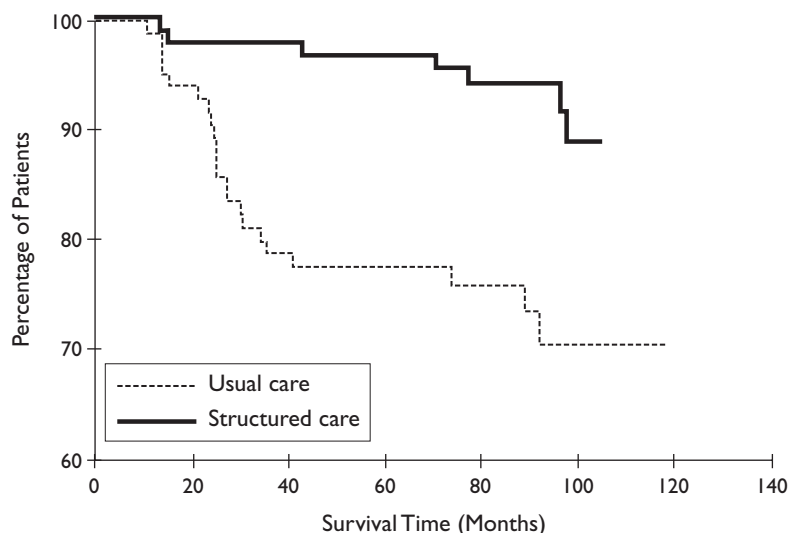
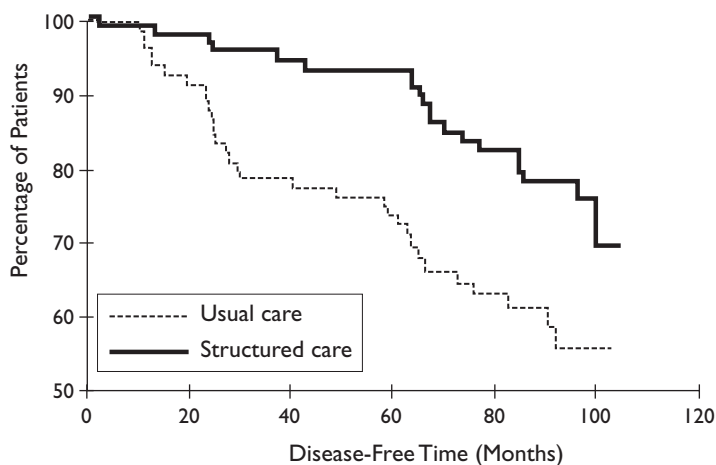


Figure 3. Percentage of Patients With Type 2 Diabetes Receiving Either Structured or Usual Care Who Were Free of Combined Death, Cardiovascular, and Renal End Points



only 21% of patients in the usual-care group received an ACE inhibitor compared with 50% in the structured-care group.¹⁴ Although patients receiving an ACE inhibitor had higher baseline blood pressure, by the end of the study they had a lower mortality rate than the nonusers. Given the accumulating evidence of the organ-protective effects of ACE inhibitors,⁹ the better clinical outcomes in the structured-care group were likely to be partly related to the increased use of ACE

inhibitors, even though the beneficial effect of these agents was observed only in the usual-care group. Optimal control of other risk factors in patients receiving structured care might have overwhelmed the effects of ACE inhibition. In our Cox regression analysis, structured care rather than use of ACE inhibitors was the main determinant of clinical outcomes. All these findings emphasize the importance of multifaceted care rather than reliance on 1 or 2 pharmacologic agents in the management of patients with multiple risk factors.

Importance of Periodic Monitoring

An important observation in this study was the impact of periodic assessments on mortality and clinical outcome. Our patients were monitored in the early 1990s, when results from randomized clinical trials on lipid and glycemic control were not available; hence, awareness of the need for periodic monitoring and intensive therapy was generally low. Given the silent nature of diabetes and its complications, proper management cannot be initiated unless metabolic indexes are measured periodically.²⁸ In the present study, omission of measurement of these indexes was associated with a 14.6-fold increased risk of death compared with the risk for those who had at least 1 measurement. These findings emphasize the importance of periodic measurements and intervention in these high-risk subjects.

Translation of Evidence-Based Medicine

To date, most of the evidence supporting the beneficial effects of optimal diabetes care on clinical outcomes has been collected under closely supervised clinical trial conditions.^{20,24,29} Indeed, a follow up epidemiological study of the recent Diabetes Control and Complications Trial showed a progressive deterioration in glycemic control once these intensively treated patients returned to their usual-care setting.³⁰ In the United States, the care processes received by many patients with diabetes do not meet the 5 standards recommended by the American Diabetes Association (self-monitoring of

blood glucose, physician visit for diabetes care, measurement of HbA_{1c}, and fundus examination through dilated pupils at least once a year).³¹⁻³³ Despite the proven benefits of many therapeutic agents, many patients were not prescribed insulin, ACE inhibitors, or lipid-lowering drugs even in the presence of indications.³⁴⁻³⁹ The drug compliance of patients receiving chronic medications can be less than 50% when there is inadequate education and periodic reinforcement.⁴⁰⁻⁴² In addition, despite the complexity of and rapid advances in diabetes management, generalists often did not perceive the need for further training in this disease area.^{32,33,43,44} All these psychological and cognitive factors are likely to determine the attitudes of both healthcare professionals and patients toward evidence-based treatment protocols, as well as their adherence to these protocols. These factors should be explored systematically to improve our understanding and management of chronic diseases.

Merit of Disease Management by a Nurse-Diabetes Specialist Team in a Diabetes Center

Disease management is being increasingly advocated to overcome barriers to the provision of quality care. It adopts an organized, proactive, multicomponent approach to deliver healthcare to patients with complex diseases such as diabetes.^{19,45} Review of the literature suggests that periodic attendance at a diabetes center⁴⁶ and frequent reminders to patients by paramedical staff could improve metabolic control, clinical outcomes, and survival.^{20,47-51} Apart from the Steno type 2 study, only a few research studies have examined the long-term effects of different care models on clinical outcomes in patients with diabetes.^{19,52}

In our study, the joint efforts of a nurse and a diabetologist in a clinical trial setting enabled patients in the structured-care group to receive protocol-driven care characterized by periodic assessments and appropriate therapy. The improvements in metabolic control and blood pressure were translated into major clinical benefits (Figure 1). This was apparent at approximately 24 months after the implementation of structured care.

Because of the nonrandomized nature of this study and the fact that patients in the structured-care group

Table 3. Results of the Relative Risk Analysis for Independent Predictors of Death in a Cohort of Patients With Type 2 Diabetes Receiving Either Structured or Usual Care*

Variable	Relative Risk (95% Confidence Interval)	P
Use of structured care	0.21 (0.07, 0.65)	.006
Mean plasma glucose level during follow up	1.21 (1.08, 1.36)	<.001
Total number of medical follow-up visits	0.81 (0.75, 0.87)	<.001
Logarithmically transformed plasma creatinine level in 1989	3.04 (1.30, 7.13)	.01

*Relative risk assessment was done by using the Cox proportional hazard model for death (death = 1, survival = 0). Independent variables in the model included age, sex, mean arterial blood pressure, and fasting blood glucose in 1989 and their mean values during the 7-year follow-up period; baseline logarithmically transformed plasma creatinine level in 1989; total number of medical follow-up visits; use of angiotensin-converting enzyme inhibitors; use of structured care (structured care = 1, usual care = 0); and availability of glycosylated hemoglobin values and lipid profile during the follow-up period.

volunteered to be in the clinical trial, these results—despite their encouraging nature—must be interpreted with caution. Despite similarities to usual-care patients in socioeconomic and health status, the patients who entered the clinical trial might have been more compliant, resulting in selection bias. They also might have differed in their attitudes toward their disease as well as knowledge and skill related to diabetes and self-management, all of which would not be easily detected by case-control matching. In addition, our sample size was relatively small; and we did not investigate the reasons for the noncompliance of the medical staff and patients in the usual-care group.

Our observations support the beneficial effects of provision of structured care. However, this is only a pilot study and the results need to be confirmed, preferably using a randomized methodology in a larger population. The cost effectiveness of this care model, involving a multidisciplinary specialist team and increased use of medications such as ACE inhibitors, also needs to be evaluated.

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CONCLUSION

This study demonstrates the dramatic effects of organization of care on clinical outcomes in patients with chronic diseases. Given the finite resources and rising prevalence of chronic diseases such as diabetes, our findings should provide a strong incentive for healthcare providers to develop specialized teams to

Table 4. Results of the Relative Risk Analysis for Predictors of Combined Death, Cardiovascular, and Renal End Points in a Cohort of Patients With Type 2 Diabetes Receiving Either Structured or Usual Care*

Variable	Relative Risk (95% Confidence Interval)	P
Use of structured care	0.47 (0.24, 0.92)	.03
Fasting plasma glucose	1.08 (1.01, 1.15)	.02
Total number of medical follow-up visits	0.91 (0.87, 0.95)	<.001
Availability of monitoring during follow up	0.14 (0.05, 0.44)	<.001
Logarithmically transformed plasma creatinine level in 1989	5.75 (2.55, 12.94)	<.001

*Relative risk assessment was done by using the Cox proportional hazard model for combined clinical end points. Clinical end points were defined as death, cardiovascular events (heart failure or angina requiring hospitalization, myocardial infarction, lower limb amputation, revascularization procedures, cerebrovascular accidents), and end-stage renal disease (doubling of baseline plasma creatinine level or need for renal dialysis) (end point = 1, no end point = 0). Independent variables included age, sex, mean arterial blood pressure, fasting blood glucose, and logarithmically transformed plasma creatinine in 1989; total number of medical follow-up visits; use of angiotensin-converting enzyme inhibitors; availability of monitoring during follow up; and use of structured care (structured care = 1, usual care = 0).

deliver protocol-driven care, with particular emphasis on adherence to guidelines and treatment to target. The normalization of the mortality rate of these high-risk patients with diabetes to that of the general population by using a structured-care approach can have major socioeconomic implications not only for the patients but also for their families and the society.

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