Glycemic and Risk Factor Control in Type 1 Diabetes

Results from 13,612 patients in a national diabetes register

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OBJECTIVE — This study was designed to investigate the clinical characteristics of a large type 1 diabetic population and to evaluate the degree of fulfillment of recently updated treatment goals.

RESEARCH DESIGN AND METHODS — The Swedish National Diabetes Register was initiated in 1996 as a tool for quality assurance in diabetes care. A1C levels, treatment, and risk factors were analyzed in two cross-sectional samples of 9,424 patients in 1997 and 13,612 patients in 2004 and in a smaller longitudinal sample from 1997 to 2004.

RESULTS — Mean A1C decreased from 8.2 ± 1.3% in 1997 to 8.0 ± 1.2% in 2004 ($P < 0.001$). The proportion of patients reaching A1C <7.0% increased from 17.4 to 21.2% in 2004. A slow but significant improvement in blood pressure levels was seen, but only 61.3% reached the blood pressure goal of <130/80 mmHg in 2004. Lipid control improved, and the use of lipid-lowering drugs increased. Among patients treated with lipid-lowering agents, 38% reached the goal of total cholesterol <4.5 mmol/l, and 48% reached the goal of LDL cholesterol <2.5 mmol/l. Successful long-term glycemic and blood pressure control were both independently predicted by low BMI and the absence of microalbuminuria in 1997.

CONCLUSIONS — In this large cohort of type 1 diabetic patients, there was a slow improvement in glycemic and risk factor control from 1997 to 2004, although the gap between the clinical results and current Swedish and American treatment goals is still unsatisfactory. It is crucial that additional measures be taken to improve risk factor control in type 1 diabetic patients.

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It has long been established that good glycemic control of diabetes prevents microvascular complications (1,2), and epidemiological studies have demonstrated that glycemic control reduces the risk of macrovascular disease (3,4). In the recently updated American Diabetes Association (ADA) clinical practice recommendations (2006), the general glycemic goal is A1C <7.0% with an individual goal for A1C as close to normal as possible (<6%) (5). Clinical guidelines in Sweden since 1998 have recommended an A1C <7.3% (Diabetes Control and Complications Trial [DCCT] standardized A1C). The importance of treating hyperlipidemia (6), hypertension, and microalbuminuria (7) has clearly been shown, and, thus, strict risk factor control is recommended (5). The blood pressure goal has been set at <130/80 mmHg, and the goals for blood lipid levels have also recently been updated (total cholesterol <4.5 mmol/l, LDL cholesterol <2.5 mmol/l, HDL cholesterol ≥1.0 mmol/l in men and ≥1.3 mmol/l in women, and triglycerides <1.7 mmol/l) in ADA and European guidelines (5,8).

The incidence of type 1 diabetes is high, ≥20/100,000 inhabitants per year, in Scandinavia (9,10). In 2004, 13,612 adult type 1 diabetic patients were reported to the Swedish National Diabetes Register (NDR). This cohort represents about 50% of the adult type 1 diabetic population in Sweden, and many of the subjects had been repeatedly reported to the NDR since 1996. The NDR therefore offers a unique possibility to survey the treatment and risk factor control of type 1 diabetic patients in everyday clinical practice. Thus, the aim of this study was to describe the clinical characteristics of this population and to see to what extent the recommended treatment goals were met, using cross-sectional and longitudinal analyses from 1996 to 2004. It has recently been shown that the gap between guidelines and reality was large in Swedish type 2 diabetic patients as well as in the U.S. (National Health and Nutrition Examination Survey [NHANES], both type 1 and type 2 diabetes) (11–13).

RESEARCH DESIGN AND METHODS

— The NDR was initiated in 1996 as a tool for quality assurance in diabetes care, with reports of patient data from hospital outpatient clinics and primary care centers nationwide (11,14). Physicians and nurses report patients annually to the NDR using paper forms, computer software, or the Internet. Clinical characteristics, A1C, treatments, and risk factors are registered. All reported patients were aged >18 years at the time of the study. The epidemiological definition

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Abbreviations: ADA, American Diabetes Association; CSII, continuous subcutaneous insulin infusion; DCCT, Diabetes Control and Complications Trial; EDC, Epidemiology of Diabetes Complications; NDR, Swedish National Diabetes Register; NHANES, National Health and Nutrition Examination Survey.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Clinical characteristics in type 1 diabetic patients in the cross-sectional surveys*

	1997	2004	*P*
Age (years)	38.6 ± 13.0 (9,424)	41.6 ± 13.5 (13,612)	<0.001
Women/men (%)	45.6/54.4 (9,424)	45.5/54.5 (13,612)	NS
Age of debut (years)	15.4 ± 7.6 (9,424)	15.5 ± 7.7 (13,612)	NS
Duration (years)	23.1 ± 13.4 (9,424)	26.1 ± 14.1 (13,612)	<0.01
A1C (%)	8.16 ± 1.27 (9,424)	7.96 ± 1.22 (13,612)	<0.001
A1C <7.0% (%)	17.4 (9,424)	21.2 (13,612)	<0.001
A1C <8.0% (%)	49.1 (9,424)	56.2 (13,612)	<0.001
A1C <9.0% (%)	76.7 (9,424)	82.0 (13,612)	<0.001
Systolic BP (mmHg)	130.0 ± 17.6 (9,424)	128.7 ± 16.8 (13,612)	<0.001
Diastolic BP (mmHg)	75.0 ± 9.0 (9,424)	73.6 ± 9.0 (13,612)	<0.001
BP <130/80 mmHg (%)	35.2 (9,424)	39.3 (13,612)	<0.001
BP <140/85 mmHg (%)	77.1 (9,424)	80.6 (13,612)	<0.001
Antihypertensive drugs (%)	23.0 (9,424)	33.9 (13,612)	<0.001
BP <130/80 mmHg (%)	17.4 (2,170)	20.0 (4,610)	<0.01
BP ≤140/85 mmHg (%)	56.1 (2,170)	62.6 (4,610)	<0.001
Hypertension (%)	42.4 (9,424)	45.5 (13,612)	<0.001
Antihypertensive drugs (%)	54.3 (3.997)	74.4 (6,193)	<0.001
BP <130/80 mmHg (%)	9.4 (3.997)	14.9 (6,193)	<0.001
BMI women (kg/m^2)	24.9 ± 3.9 (9,424)	25.2 ± 4.3 (13,612)	<0.001
BMI men (kg/m^2)	25.0 ± 3.2 (9,424)	25.4 ± 3.4 (13,612)	<0.001
BMI <25 kg/m^2 (%)	56.2 (9,424)	52.3 (13,612)	<0.001
BMI ≥30 kg/m^2 (%)	8.1 (9,424)	10.5 (13,612)	<0.001
Smokers, aged <30 years, women (%)	15.4 (9,424)	16.0 (13,612)	NS
Smokers, aged <30 years, men (%)	9.0 (9,424)	9.3 (13,612)	NS
Smokers, aged 30–59 years (%)	17.0 (9,424)	14.3 (13,612)	<0.001
Smokers, aged >60 years (%)	8.8 (9,424)	9.0 (13,612)	NS
	2002	2004	*P*
Total cholesterol (mmol/l)	4.93 ± 0.91 (6,804)	4.78 ± 0.89 (10,933)	<0.001
Triglycerides (mmol/l)	1.12 ± 0.58 (6,804)	1.08 ± 0.57 (10,933)	<0.01
HDL cholesterol (mmol/l)	1.61 ± 0.47 (6,804)	1.62 ± 0.50 (10,933)	NS
LDL cholesterol (mmol/l)	2.82 ± 0.80 (6,804)	2.67 ± 0.78 (10,933)	<0.001
Lipid-lowering drugs (%)	20.5 (10,114)	24.4 (13,091)	<0.001
Total cholesterol <5.0 (%)	49.9 (1,474)	58.8 (2,738)	<0.001
Total cholesterol <4.5 (%)	27.7 (1,474)	37.7 (2,738)	<0.001
Triglycerides <1.7 (%)	75.9 (1,474)	80.9 (2,738)	<0.001
HDL cholesterol ≥1.0 men/≥1.3 women (%)	87.5 (1,474)	87.8 (2,738)	NS
LDL cholesterol <2.5 (%)	38.3 (1,474)	48.1 (2,738)	<0.001
ASA, all patients (%)	11.9 (7,332)	16.8 (11,980)	<0.001
ASA, BP-treated patients (%)	29.7 (2,320)	39.1 (4,098)	<0.001
ASA, lipid-treated patients (%)	37.6 (1,445)	46.3 (2,949)	<0.001
Eye control last 2 years (%)	88.8 (9,716)	93.5 (12,713)	<0.001
Foot control last year (%)	89.7 (8,009)	92.5 (11,895)	<0.001

Data are means ± SD values (*n*) or frequencies (*n*). Significance levels were adjusted for age and sex. ASA, aspirin; BP, blood pressure.

of type 1 diabetes used was age <30 years at onset of diabetes in patients with insulin treatment only.

In 2004, almost 95% of all hospital diabetes outpatient clinics participated in the NDR, and 97% of all patients in this study were reported from these. The mean reported number of patients was 162 per participating unit. In this study we report results obtained from cross-sectional surveys on 9,424 type 1 diabetic patients in 1997 and 13,612 patients in 2004. Registered variables were age, sex, BMI, year of onset of diabetes, A1C, blood pressure, type of treatment (but not doses of insulin or other pharmaceutical agents), and smoking status. As blood lipids and the use of aspirin have been registered since 2002, a cross-sectional survey in 2002 of 10,114 patients was also included to compare these variables with those of patients in 2004. Furthermore, a longitudinal analysis was performed on a cohort of 4,296 type 1 diabetic patients who could be followed individually from 1997 to 2004.

Measurement of A1C has been quality assured since 1996 in Sweden. Both diabetes outpatient clinics and primary care centers use methods regularly calibrated to the high-performance liquid chromatography Mono-S method. In this report, all A1C values were converted to the DCCT standard levels using the formula: A1C (DCCT) = 0.923 × A1C (Mono-S) + 1.345 (R^2 = 0.998) (15). The Swedish

Table 2—*Clinical characteristics by duration of diabetes in 13,612 type 1 diabetic patients in the cross-sectional survey 2004*

	Total *n*	Duration of diabetes				
		0–9 years	10–19 years	20–29 years	30–39 years	>40 years
n		1,685	3,127	3,530	2,752	2,518
Age of debut (years)		21.6 ± 5.0	16.9 ± 7.2	14.9 ± 7.7	14.2 ± 7.7	12.2 ± 7.0*
Age (years)		26.9 ± 5.0	31.6 ± 7.2	39.1 ± 8.3	48.3 ± 8.2	60.0 ± 8.5*
Men (%)		58.9	55.2	55.4	53.5	50.8*
A1C (%)		7.66 ± 1.43	8.02 ± 1.27	8.05 ± 1.19	8.04 ± 1.14	7.88 ± 1.08*
A1C <7.0% (%)		35.9	20.6	18.5	17.0	20.7*
Systolic BP (mmHg)		119.7 ± 11.8	122.1 ± 13.3	127.2 ± 15.7	133.5 ± 16.9	139.8 ± 17.2*
Diastolic BP (mmHg)		72.0 ± 8.7	73.9 ± 8.7	75.0 ± 9.1	74.4 ± 8.8	71.5 ± 9.1*
Pulse pressure (mmHg)		47.6 ± 10.7	48.2 ± 10.9	52.1 ± 12.9	59.1 ± 15.1	68.3 ± 16.2*
BP <130/80 mmHg (%)		60.2	52.0	40.5	29.0	19.1*
Antihypertensives (%)		4.4	10.8	31.0	52.0	66.5*
Hypertension (%)		12.8	20.2	41.8	65.8	81.9*
BMI (kg/m^2)		24.8 ± 4.3	25.4 ± 3.8	25.5 ± 3.7	25.4 ± 3.9	25.0 ± 3.8*
Total cholesterol (mmol/l)	11,855	4.49 ± 0.89	4.67 ± 0.91	4.80 ± 0.91	4.93 ± 0.92	4.91 ± 0.88*
Triglycerides (mmol/l)	11,358	1.12 ± 1.01	1.12 ± 0.90	1.11 ± 0.71	1.15 ± 0.78	1.13 ± 0.66†
HDL cholesterol (mmol/l)	11,219	1.47 ± 0.46	1.53 ± 0.45	1.61 ± 0.47	1.68 ± 0.53	1.74 ± 0.53*
LDL cholesterol (mmol/l)	10,993	2.53 ± 0.76	2.64 ± 0.80	2.71 ± 0.78	2.74 ± 0.79	2.68 ± 0.76*
Lipid-lowering drugs (%)	13,091	3.0	8.5	20.9	36.2	50.8*
Smokers (%)	10,832	12.8	14.2	13.4	14.3	11.1‡
ASA (%)	11,980	0.7	2.6	10.0	25.4	44.4*

Data are mean values ± SD and frequencies. Significance levels for trend of mean values (ANOVA) or frequencies (χ^2 test): *$P < 0.001$; †$P > 0.05$ (NS); ‡$P < 0.05$. ASA, aspirin; BP, blood pressure.

standard recommendation for blood pressure recording is the mean value of two readings (Korotkoff 1–5) in the supine position with a cuff of appropriate size (14). With use of the current World Health Organization and ADA definition, hypertension was defined as blood pressure ≥140/90 mmHg or antihypertensive treatment (5,16). The target blood pressure was <130/80 mmHg, as recommended by the ADA (5). Microalbuminuria was defined as urine albumin excretion of 20–200 μg/min in two of three consecutive tests. A smoker was defined as a patient smoking ≥1 cigarettes/day or who had stopped smoking within the past 3 months. Ophthalmologists graded diabetic retinopathy.

Statistical methods

Results are presented as mean values ± 1 SD. Comparisons between means and frequencies in cross-sectional samples were adjusted for age and sex. Trends for mean values and proportions were calculated with ANOVA and the χ^2 test. Logistic regression was used to analyze long-term development of A1C and blood pressure as nominal dependent variables, with clinical characteristics at the baseline as continuous or nominal predictors. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using JMP (SAS Institute, Cary, NC).

RESULTS

Cross-sectional studies

Clinical characteristics in the cross-sectional surveys of type 1 diabetic patients in 1997 ($n = 9,424$) and 2004 ($n = 13,612$) are given in Table 1. Between 1997 and 2004, the mean age and diabetes duration increased slightly, but the mean age at onset of diabetes was virtually unchanged (~15 years). There was an increase in the mean BMI from 24.9 to 25.3 kg/m^2, but there was no significant difference between men and women.

Mean A1C levels decreased significantly from 8.16% in 1997 to 7.96% in 2004. The proportion of patients reaching A1C <8.0% increased from 49.1 to 56.2% ($P < 0.001$). However, the proportion of patients reaching A1C <7.0%, recommended by the ADA, only increased from 17.4 to 21.2% ($P < 0.001$). Information on types of insulin was available for 2,923 patients in 2004, of whom 88.2% used a short-acting insulin (regular, lispro, and aspart), 36.2% used a medium-acting insulin (NPH), 4.7% used a premixed insulin, and 46.7% used a long-acting insulin (glargine, detemir, and Ultratard). Patients treated with a combination of lispro/aspart and glargine ($n = 373$) had a slightly lower mean A1C (7.85%) than those treated with a combination of regular and NPH insulin ($n = 1,064$; 7.95%) ($P = 0.16$). Possibly because of the relatively small numbers of patients, no significant differences could be seen between treatment groups with different mean age or duration of diabetes. Continuous subcutaneous insulin infusions (CSIIs) were used by 14% of the patients in 2004. Their mean A1C value was somewhat, but significantly, lower than that for all other patients (7.8 and 8.0%, respectively; $P < 0.001$). The proportion of CSII patients reaching A1C <8% was 62% compared with 56% for non-CSII patients ($P < 0.001$), and 22% of the CSII patients reached A1C <7.0% compared with 21% of the non-CSII patients (NS).

Antihypertensive treatment was used to a larger extent in 2004 than in 1997. Slightly improved blood pressure control was seen in all patients and in the subjects treated with antihypertensive agents. Among hypertensive patients, the blood pressure target (<130/80 mmHg) was reached by only 9% of the patients in 1997 and by 15% in 2004.

Blood lipid levels, registered since 2002, are given in Table 1. From 2002 to 2004, the lipid profile improved with re-

gard to total cholesterol, triglyceride, and LDL cholesterol levels, whereas no change was seen in mean HDL cholesterol levels. The use of lipid-lowering drugs increased, and, among patients using lipid-lowering drugs, the present treatment goals were reached in 2004 by 38 and 48% for total and LDL cholesterol, respectively, and by > 80% for triglycerides and HDL cholesterol. There was also an increase in the use of aspirin, especially in the groups of patients who were also treated with antihypertensive and lipid-lowering agents. Only 7% of the type 1 diabetic patients reached the combined treatment goal for metabolic, blood pressure, and lipid control. Among the middle-aged type 1 diabetic patients, the rate of smoking decreased from 17 to 14%, but smoking habits were unchanged in young women (16%). Repeated assessments of eye and foot status were performed in almost all patients in 2004.

Clinical characteristics in relation to diabetes duration are given in Table 2. The lowest mean A1C was seen in patients with short diabetes duration (36% achieved A1C <7.0%). In patients with long diabetes duration, the success rate was lower (17–21%). In patients with <20 years duration of diabetes, there was no difference in mean A1C levels between CSII users and nonusers of CSII (*n* values 501 and 3,395, respectively), whereas in patients with longer duration of diabetes, glycemic control was clearly better in CSII users (A1C 7.8 ± 1.1 vs. 8.0 ± 1.2%, $P <$ 0.001; *n* values 1,060 and 6,175, respectively). With longer duration of diabetes, there was also a marked increase in mean systolic and pulse pressures, as well as in the use of antihypertensive medication, whereas the proportion of patients reaching a blood pressure <130/80 mmHg was lower. The mean total and LDL cholesterol levels also increased with longer duration of diabetes. Interestingly, the mean HDL cholesterol value increased with longer duration.

Longitudinal study

In the longitudinal study, i.e., 4,296 type 1 diabetic patients followed individually from 1997 to 2004, there was a significant decrease in the mean A1C from 8.10 ± 1.23 to 7.98 ± 1.14% ($P < 0.001$). Although there was a marginal increase in the mean systolic blood pressure from 129.1 ± 17 to 130.4 ± 17 mmHg, the mean diastolic blood pressure decreased from 74.5 ± 9 to 73.4 ± 9 mmHg ($P <$ 0.001). The mean BMI increased from

Table 3—*Logistic regression in 4,151 type 1 diabetic patients, followed from 1997 to 2004, with either long-term successful or deteriorating glycemic control or successful blood pressure (BP) control as dependent variables and with clinical characteristics in 1997 as predictors*

	A1C <7.3% 1997–2004 vs. A1C ≥7.3% 1997–2004		A1C 1997 < 2004 vs. A1C 1997 ≥ 2004		BP ≤130/80 1997–2004 vs. BP >130/80 1997–2004	
	Means ± SD	OR (95% CI), χ^2 value	Means ± SD	OR (95% CI), χ^2 value	Means ± SD	OR (95% CI), χ^2 value
n	620 vs. 3,531		1,837 vs. 2,314		1,763 vs. 2,388	
Continuous predictors*						
Age	37.9 ± 12.8 38.5 ± 11.9	1.23 (0.87–1.75), 1.4	37.9 ± 12.1† 38.9 ± 12.0	0.76 (0.59–0.98), 4.6‡	33.2 ± 9.8§ 42.3 ± 12.2	0.22 (0.17–0.29), 114§
Diabetes duration	21.5 ± 14.3§ 23.4 ± 12.5	0.66 (0.46–0.94), 5.2‡	22.4 ± 13.3† 23.7 ± 12,4	0.97 (0.75–1.26), 0.05	18.2 ± 10.8§ 26.7 ± 13.0	0.52 (0.40–0.69), 21.2§
BMI 1997	24.3 ± 3.2§ 24.9 ± 3.3	0.53 (0.42–0.68), 27.0§	24.9 ± 3.3 24.8 ± 3.3	1.15 (0.98–1.36), 2.8	24.3 ± 3.0§ 25.2 ± 3.4	0.49 (0.41–0.59), 56.4§
BMI 2004 − BMI 1997	0.52 ± 1.82 0.61 ± 2.10	0.81 (0.64–1.03), 2.8	0.46 ± 1.98§ 0.71 ± 2.12	0.62 (0.53–0.74), 30.1§	0.58 ± 1.90 0.61 ± 2.17	0.73 (0.61–0.88), 10.9§
	%	OR (95% CI), χ^2 value	%	OR (95% CI), χ^2 value	%	OR (95% CI), χ^2 value
Nominal predictors						
Male sex	58.2† 52.7	1.30 (1.08–1.55), 8.3†	54.5 52.8	1.09 (0.97–1.24), 2.0	47.4§ 58.0	0.62 (0.54–0.71), 45.6§
Smoker 1997	9.8§ 16.5	0.60 (0.44–0.79), 12.6§	15.2 15.8	1.03 (0.87–1.23), 0.11	14.5 16.3	1.12 (0.92–1.36), 1.3
Microalbuminuria 1997	8.1§ 17.2	0.47 (0.34–0.64), 21.9§	14.5‡ 16.9	0.85 (0.71–1.02), 3.1	8.6§ 21.2	0.45 (0.36–0.56), 53.7§

The odds ratio (OR) for each predictor was adjusted for all other predictors in the table and for use of antihypertensive drugs 1997–2004. *The OR for each continuous predictor was the result of an increase in quartiles of this predictor. Significance levels: †$P < 0.01$; ‡$P < 0.05$; §$P < 0.001$.

24.8 ± 3.3 to 25.4 ± 3.7 kg/m^2 ($P <$ 0.001).

A logistic regression analysis showed that long-term successful glycemic control (A1C <7.3% in 1997 and 2004) was strongly predicted by low BMI, nonsmoking, and absence of microalbuminuria at baseline, independent of age, sex, diabetes duration, and use of antihypertensive drugs (Table 3). Weight loss from 1997 to 2004 was significantly associated with deteriorating glycemic control during the period, and a subgroup analysis disclosed that this finding was significant among patients with A1C ≥8% at baseline (regression coefficient [95% CI] 0.093 [0.046–0.141], $P < 0.001$), whereas not in patients with A1C <8% (regression coefficient 0.017, NS). Successful long-term blood pressure control (blood pressure <130/80 mmHg in 1997 and 2004) was strongly predicted by low BMI and absence of microalbuminuria at baseline and also by weight loss during the period, independent of age, sex, diabetes duration, and use of antihypertensive drugs.

CONCLUSIONS — In this survey, representing approximately half of all Swedish type 1 diabetic patients treated in everyday clinical practice, glycemic and risk factor control improved slightly but significantly from 1997 to 2004. Thus, the proportion of patients achieving the treatment goals increased, although an A1C <7.0% (5) was reached by only 21.2% of the patients in 2004, demonstrating a gap between clinical practice and recent guidelines. These findings are, to some degree, consistent with the results of the few other, but smaller, studies addressing glycemic control in similar groups of patients. In the Epidemiology of Diabetes Interventions and Complications (EDIC) study, A1C decreased from 9.1 to 8.3% in the former conventional treatment group but increased from 7.3 to 8.1% in the former intensive treatment group (17). A Dutch study from 1997 showed that 37% of type 1 diabetic patients had good metabolic control, defined as <20% above the upper limit of normal A1C (18). In a study of 333 type 1 diabetic patients from New Zealand, there was a nonsignificant tendency toward improved A1C levels from 8.8 to 8.6% between 1998 and 2003 (19). The NHANES surveys from 1999 to 2002, including both type 1 and type 2 diabetic patients of whom approximately one-fourth were using insulin, showed that 37–49% reached the A1C goal of <7.0% (12,13,20).

The importance of multiple risk factor intervention in type 2 diabetic patients was shown in the Steno-2 study (21). Likewise, type 1 diabetic patients treated in centralized diabetes units in Hungary had lower A1C and fewer microvascular complications than type 1 diabetic patients in the U.S. treated in both primary care and by specialists (22), although modern care resulted in declining incidence for mortality and renal failure but not for nephropathy and retinopathy according to recent data from the Pittsburgh Epidemiology of Diabetes Complications (EDC) (23). The Linköping Diabetes Complication Study also showed, encouragingly, that modern treatment of type 1 diabetic patients could reduce the frequencies of severe retinopathy and nephropathy after 25 years, from 47 to 24% (24). The same pattern was seen in a study from Denmark, also showing lower A1C and blood pressure in recent years (25).

Insulin is mostly given by multiple daily injections in Sweden, and prefilled pens and direct-acting as well as long-acting insulin analogs are used to a large extent. Switching to newer insulin regimens might improve glycemic control, and we found a nonsignificant tendency of improved control using insulin analogs compared with other insulin regimens, although the reported numbers of patients receiving the various treatments were small. A recent meta-analysis showed a 0.12% decrease of A1C after a change from regular insulin to short-acting insulin analogs in combination with NPH insulin (26), but the combination of insulin glargine and insulin lispro has recently been reported to yield a 0.5% decrease compared with regular and NPH insulin in an open study with a cross-over design (27). In the current study, patients using CSII had a 0.2% lower mean A1C than the patients receiving other treatment regimens, and more patients reached A1C <8% but not A1C <7%. Interestingly, CSII was particularly efficient in patients with a long duration of diabetes. Generally, intensive insulin treatment leads to an increasing number of hypoglycemic events (22,28). Unfortunately, hypoglycemic events are not yet registered in the NDR, because recognition of this variable in clinical practice is very subjective.

The associations between weight, weight changes, and glycemic control are complex. In type 2 diabetic patients, this issue has been addressed in another study from the NDR (29). The current study showed that successful glycemic control was predicted by low BMI, nonsmoking, and the absence of microalbuminuria at baseline. This finding is supported in part by results from the Pittsburgh EDC study of 441 type 1 diabetic patients, which showed that a lower baseline BMI was associated with better glycemic control, although weight gain also correlated with improved A1C levels (30). A recent report from EURODIAB also showed that improved glycemic control was associated with weight gain (31). In our study, weight loss was significantly associated with deteriorating metabolic control between 1997 and 2004, regardless of BMI at baseline, diabetes duration, or smoking habits. A subgroup analysis showed that weight loss was associated with deteriorating metabolic control only for those with A1C levels >8%, possibly explained by an insulin-deficient catabolic state with hyperglycemia and weight loss.

Blood pressure control improved slightly from 1997 to 2004 in the type 1 diabetic patients. The current U.S. and European blood pressure goal of <130/80 mmHg (5,8) was achieved by only 39% of patients in 2004. NHANES 1999–2000 (type 1 and type 2 diabetes) showed that 36–40% achieved blood pressure of <130/80 mmHg (12,20). Increasing adherence to guidelines (which included use of ACE inhibitors) was suggested by the increased use of antihypertensive agents in the NDR from 1997 to 2004. The prevalence of hypertension was 46% in 2004 in our study, and 74% of the hypertensive patients were receiving blood pressure–lowering therapy, whereof 15% achieved the blood pressure goals of <130/80 mmHg. The corresponding figures among type 1 diabetic patients in the EURODIAB (32), Pittsburgh EDC (33), and Coronary Artery Calcification in Type 1 Diabetes (CACT1) (34) studies were 24, 43, and 35% for hypertension; 42, 62, and 87% for use of antihypertensive medication; and 11, 28, and 42 for blood pressure <130/80 mmHg (<130/85 in EURODIAB). Thus, the proportion of patients considered to be hypertensive in our study was relatively high. This situation is probably caused by antihypertensive treatment for albuminuria in normotensive patients (especially ACE inhibitors), an issue also previously addressed by others (32,34). Successful blood pressure control with blood pressure <130/80 mmHg in both 1997 and 2004 was predicted by young age, female sex, short diabetes duration, low BMI in 1997, weight loss during the

period, and absence of microalbuminuria in 1997. As has recently been reported in type 2 diabetic patients, lower BMI and absence of microalbuminuria at baseline were strong independent predictors of long-term successful blood pressure control (35).

Mean total cholesterol was 4.8 mmol/l in all patients, which is lower than 5.5–5.4 mmol/l as found in NHANES 1999–2000 (12,20). The mean HDL cholesterol level was surprisingly high (1.6 mmol/l), and it was even higher in patients with a longer duration of diabetes and could represent a survival factor. In 2004, among the patients given lipid-lowering drugs (almost always statins in a smaller subgroup with reported type of lipid-lowering medication, data not shown), 38% reached the present goal levels for total cholesterol and 48% reached the goal for LDL cholesterol. Interestingly, >80% reached the triglyceride and HDL cholesterol goals. The differences between patients with a short and long duration of diabetes, including treatments and their effects, need to be further addressed in future studies.

This is an observational study and data from the participating centers are collected according to local practices and, thus, may vary in accuracy. Guidelines are available to minimize errors, and direct transferal of data from patient record databases is being increasingly used. Some selection bias cannot be ruled out, however, as centers with special interests in diabetes care and quality assurance may participate to a higher degree. This is likely to be a smaller problem with type 1 diabetes than with type 2 diabetes, because hospital outpatient clinics most often participated from the start of the register, and in 2004 >95% of the clinics reported to the NDR. Another concern is that the patients with significant comorbidity, e.g., patients with cardiovascular disease or patients who are undergoing hemodialysis, may not be reported to the NDR if their diabetes is managed in other clinics. Work is in progress to address this confounding issue. Data concerning socioeconomic variables, which are additional possible confounding factors, were unfortunately not registered in the NDR.

The epidemiological definition of type 1 diabetes in this study (<30 years of age at the onset of diabetes in patients with insulin treatment only) reasonably well excludes all type 2 diabetic patients. Data concerning the need for insulin treatment within 1 year of diagnosis is currently not available in the NDR, and autoantibody measurements are currently not reported because they are generally not required for the diagnosis of type 1 diabetes in clinical practice. However, 95% of all hospitals reported to the NDR in 2004, and the type 1 diabetic patients constituted around 4% of all diabetic patients in every county council. Thus, the participants of this study amount to >50% of all type 1 diabetic patients in Sweden and should therefore be fairly representative of patients with type 1 diabetes.

Ninety-seven percent of the patients were managed in hospital outpatient clinics and were generally treated by specialists in diabetology, endocrinology, or internal medicine, as well as by specialist nurses and dietitians. The number of patient visits per year is usually individualized. Recent clinical treatment guidelines have been implemented, based on national and local educational meetings, and are well known by the diabetes teams. The high frequency of yearly foot examinations and fundus examinations every 2nd year (93%) suggests good adherence to such guidelines. Thus, the gap between guidelines and results for glycemic, blood pressure, and lipid control focuses on the difficulties in real life to adequately individualize the treatment of patients.

In this large cohort of type 1 diabetic patients, a slow improvement was seen in glycemic and risk factor control from 1997 to 2004. There is still, however, a big gap between clinical results and treatment goals, and only 7% of the type 1 diabetic patients reached the combined targets for A1C, blood pressure, and cholesterol as recommended by the ADA. A low BMI and absence of microalbuminuria predicted better long-term A1C and blood pressure results. Metabolic and risk factor control in type 1 diabetes is unsatisfactory, and it is crucial that additional and improved therapeutic alternatives be used to improve diabetes care.

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References

1. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus: the Diabetes Control and Complications Trial research group. *N Engl J Med* 329:977–986, 1993
2. Reichard P, Nilsson BY, Rosenqvist U: The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. *N Engl J Med* 329:304–309, 1993
3. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B, Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study Research Group: Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 353:2643–2653, 2005
4. Nathan DM, Lachin J, Cleary P, Orchard T, Brillon DJ, Backlund JY, O'Leary DH, Genuth S, Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group: Intensive diabetes therapy and carotid intima-media thickness in type 1 diabetes mellitus. *N Engl J Med* 348: 2294–2303, 2003
5. American Diabetes Association: Clinical Practice Recommendations 2006. *Diabetes Care* 29 (Suppl. 1):S1–S85, 2006
6. Collins R, Armitage J, Parish S, Sleigh P, Peto R: MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet* 361: 2005–2016, 2003
7. Mogensen CE: Microalbuminuria and hypertension with focus on type 1 and type 2 diabetes. *J Intern Med* 254:45–66, 2003
8. De Backer G, Ambrosioni E, Borch-Johnsen K, Brotons C, Cifkova R, Dallongeville J, Ebrahim S, Faergeman O, Graham I, Mancia G, Cats VM, Orth-Gomér K, Perk J, Pyöräl ä K, Rodicio JL, Sans S, Sansoy V, Sechtem U, Silber S, Thomsen T, Wood D: European guidelines on cardiovascular disease prevention in clinical practice: Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J* 24:1601–1610, 2003
9. Karvonen M, Viik-Kajander M, Moltchanova E, Libman I, LaPorte R, Tuomilehto J: Incidence of childhood type 1 diabetes worldwide: Diabetes Mondiale (DiaMond) Project Group. *Diabetes Care* 23: 1516–1526, 2000
10. Pundziute-Lyck A, Dahlquist G, Nystrom L, Arnqvist H, Björk E, Blohmé G, Bolinder J, Eriksson J, Sundkvist G, Ostman J, Swedish Childhood Diabetes

Study Group: The incidence of type I diabetes has not increased but shifted to a younger age at diagnosis in the 0–34 years group in Sweden 1983–1998. *Diabetologia* 45:783–791, 2002
11. Eliasson B, Cederholm J, Nilsson P, Gudbjornsdottir S: The gap between guidelines and reality: type 2 diabetes in a National Diabetes Register 1996–2003. *Diabet Med* 22:1420–1426, 2005
12. Resnick HE, Foster GL, Bardsley J, Ratner RE: Achievement of American Diabetes Association clinical practice recommendations among U.S. adults with diabetes, 1999–2002: the National Health and Nutrition Examination Survey. *Diabetes Care* 29:531–537, 2006
13. Saaddine JB, Cadwell B, Gregg EW, Engelgau MM, Vinicor F, Imperatore G, Venkat Narayan KM: Improvements in diabetes processes of care and intermediate outcomes: United States, 1988–2002. *Ann Intern Med* 144:465–474, 2006
14. Gudbjornsdottir S, Cederholm J, Nilsson PM, Eliasson B: The National Diabetes Register in Sweden: an implementation of the St. Vincent Declaration for Quality Improvement in Diabetes Care. *Diabetes Care* 26:1270–1276, 2003
15. Hoelzel W, Weykamp C, Jeppsson JO, Miedema K, Barr JR, Goodall I, Hoshino T, John WG, Kobold U, Little R, Mosca A, Mauri P, Paroni R, Susanto F, Takei I, Thienpont L, Umemoto, M, Wiedmeyer H-M, IFCC Working Group on HbA_{1c} Standardization: IFCC reference system for measurement of hemoglobin A1c in human blood and the national standardization schemes in the United States, Japan, and Sweden: a method-comparison study. *Clin Chem* 50:166–174, 2004
16. Alberti KG, Zimmet PZ: Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1. Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 15:539–553, 1998
17. Effect of intensive therapy on the microvascular complications of type 1 diabetes mellitus. *JAMA* 287:2563–2569, 2006
18. Jacobs ML, Elte JW, van Ouwerkerk BM, Janssens EN, Schop C, Knoop JA, Hoogma RP, Groenendijk R, Weber RF: Effect of BMI, insulin dose and number of injections on glycaemic control in insulin-using diabetic patients. Studygroup Diabetes Rijnmond (SDR). *Neth J Med* 50:153–159, 1997
19. Coppell KJ, Anderson K, Williams S, Manning P, Mann J: Evaluation of diabetes care in the Otago region using a diabetes register, 1998–2003. *Diabetes Res Clin Pract* 71:345–352, 2005
20. Saydah SH, Fradkin J, Cowie CC: Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA* 291:335–342, 2004
21. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O: Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 348:383–393, 2003
22. Tabak AG, Tamas G, Zgibor J, Wilson R, Becker D, Kerenyi Z, Orchard TJ: Targets and reality: a comparison of health care indicators in the U.S. (Pittsburgh Epidemiology of Diabetes Complications Study) and Hungary (Diabetes Care Hungary). *Diabetes Care* 23:1284–1289, 2000
23. Pambianco G, Costacou T, Ellis D, Becker DJ, Klein R, Orchard TJ: The 30-year natural history of type 1 diabetes complications: the Pittsburgh Epidemiology of Diabetes Complications study experience. *Diabetes* 55:1463–1469, 2006
24. Nordwall M, Bojestig M, Arnqvist HJ, Ludvigsson J: Declining incidence of severe retinopathy and persisting decrease of nephropathy in an unselected population of type 1 diabetes—the Linkoping Diabetes Complications Study. *Diabetologia* 47:1266–1272, 2004
25. Hovind P, Tarnow L, Rossing K, Rossing P, Eising S, Larsen N, Binder C, Parving HH: Decreasing incidence of severe diabetic microangiopathy in type 1 diabetes. *Diabetes Care* 26:1258–1264, 2003
26. Plank J, Blaha J, Cordingley J, Wilinska ME, Chassin LJ, Morgan C, Squire S, Haluzik M, Kremen J, Svacina S, Toller W, Plasnik A, Ellmerer M, Hovorka R, Pieber TR: Multicentric, randomized, controlled trial to evaluate blood glucose control by the model predictive control algorithm versus routine glucose management protocols in intensive care unit patients. *Diabetes Care* 29:271–276, 2006
27. Ashwell SG, Amiel SA, Bilous RW, Dashora U, Heller SR, Hepburn DA, Shutler SD, Stephens JW, Home PH: Improved glycaemic control with insulin glargine plus insulin lispro: a multicentre, randomized, cross-over trial in people with type 1 diabetes. *Diabet Med* 23:285–292, 2006
28. Hypoglycemia in the Diabetes Control and Complications Trial: the Diabetes Control and Complications Trial Research Group. *Diabetes* 46:271–286, 1997
29. Ridderstrale M, Gudbjornsdottir S, Eliasson B, Nilsson PM, Cederholm J: Obesity and cardiovascular risk factors in type 2 diabetes: results from the Swedish National Diabetes Register. *J Intern Med* 259: 314–322, 2006
30. Williams KV, Erbey JR, Becker D, Orchard TJ: Improved glycemic control reduces the impact of weight gain on cardiovascular risk factors in type 1 diabetes: the Epidemiology of Diabetes Complications Study. *Diabetes Care* 22:1084–1091, 1999
31. Ferriss JB, Webb D, Chaturvedi N, Fuller JH, Idzior-Walus B: Weight gain is associated with improved glycaemic control but with adverse changes in plasma lipids and blood pressure in type 1 diabetes. *Diabet Med* 23:557–564, 2006
32. Collado-Mesa F, Colhoun HM, Stevens LK, Boavida J, Ferriss JB, Karamanos B, Kempler P, Michel G, Roglic G, Fuller JH: Prevalence and management of hypertension in type 1 diabetes mellitus in Europe: the EURODIAB IDDM Complications Study. *Diabet Med* 16:41–48, 1999
33. Zgibor JC, Wilson RR, Orchard TJ: Has control of hypercholesterolemia and hypertension in type 1 diabetes improved over time? *Diabetes Care* 28:521–526, 2005
34. Maahs DM, Kinney GL, Wadwa P, Snell-Bergeon JK, Dabelea D, Hokanson J, Ehrlich J, Garg S, Eckel RH, Rewers MJ: Hypertension prevalence, awareness, treatment, and control in an adult type 1 diabetes population and a comparable general population. *Diabetes Care* 28: 301–306, 2005
35. Nilsson PM, Cederholm J, Gudbjornsdottir S, Eliasson B: Predictors of successful long-term blood pressure control in type 2 diabetic patients: data from the Swedish National Diabetes Register (NDR). *J Hypertens* 23:2305–2311, 2005