

ORIGINAL ARTICLE

Treatment of Type 2 Diabetes Mellitus in a Primary Care Setting in Taiwan: Comparison with Secondary/Tertiary Care

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Background: This study investigated the status of diabetes control and management in patients treated in a primary healthcare setting and compared the results with data previously obtained for secondary/tertiary care patients in Taiwan.

Methods: This study was conducted at 51 primary healthcare stations randomly selected island-wide in Taiwan in 2001. A total of 1302 type 2 diabetes patients who had been followed-up for more than 1 year were included. Blood was collected for centralized HbA_{1c} assay. The remaining data and information were collected by review of medical records and patient interview.

Results: Compared with the results of a previous study on patients treated in a secondary/tertiary care setting, a significantly smaller percentage of primary care patients were receiving insulin therapy. Primary care patients also had a shorter duration of diabetes, a higher HbA_{1c} level, better blood pressure control and a lower prevalence of complications. The proportion of patients achieving optimal control of glycemia and blood pressure was low. Patients aged < 65 years had a significantly shorter duration of diabetes, poorer diabetes control and better blood pressure control than elderly patients aged ≥ 65 years. Primary care patients aged ≥ 65 years had a significantly higher frequency of stroke than those aged < 65 years. The elderly group of secondary/tertiary care patients had a significantly higher frequency of coronary heart disease and stroke. Duration of diabetes and hypertension were the leading risk factors for complications in diabetes patients treated in both primary and secondary/tertiary care settings.

Conclusion: Diabetes control was poorer in primary care than in secondary/tertiary care patients, but control of blood pressure was better in primary care patients. The shorter duration of diabetes and better control of blood pressure in primary care patients and in patients aged < 65 years compared with their elderly counterparts might be related to a lower prevalence of complications. [*J Formos Med Assoc* 2006;105(2):105–117]

Key Words: blood pressure control, diabetes management, glycemic control, Taiwan, type 2 diabetes

Type 2 diabetes is a worldwide epidemic. According to projections by the World Health Organization (WHO), the number of individuals with diabetes will rise from 135 million in 1995 to 300 million in 2025,¹ and much of the increase is expected to be experienced in Asia.²

In Taiwan, diabetes is a major health problem with an estimated 900,000 diabetic patients among its 23 million inhabitants.³ Diabetes and its complications represent a major threat to public health resources, and the economic and societal costs of managing this disorder and its complications are

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expected to escalate along with their rising prevalence. Indeed, the annual incidence of diabetes has reached 0.5–1% of Taiwan's total population, suggesting that there are at least 100,000 new cases every year.³ Of greater concern has been the sharp rise in the prevalence of diabetes among Taiwanese citizens aged 65 years and older (from 8.7% in 1989 to 15.1% in 1999), as reported by the Taiwanese Department of Health.⁴ This will inflict an even greater burden on healthcare resources since the cost of attending a patient with diabetes is estimated to be 4.3 times greater than that for a non-diabetic patient.⁵ Treatment of diabetes and its complications takes up 11.5% of Taiwan's total medical expenses.⁵

The Diabcare-Taiwan 2001 (DCT'01) study was initiated within the larger framework of the Diabcare-Asia 2001 project – a collaborative study between Novo Nordisk Asia Pacific Pte Ltd (Singapore) and nine participating Asian countries working through their respective national diabetes associations.⁶ The study marked Taiwan's first major endeavor to comprehensively evaluate the healthcare status of patients with type 2 diabetes at primary healthcare stations. The DCT'01 study was similar to the Diabcare-Asia (Taiwan) 1998 (DCT'98) study in design,⁷ except that the DCT'01 study was carried out in the primary care setting while the DCT'98 study was conducted in secondary/tertiary care settings (medical centers and district hospitals). The primary aim of this study was to compare diabetes control, management and complications in Taiwanese type 2 diabetes patients in the DCT'98 and DCT'01 studies, followed by an examination of the differences between elderly (≥ 65 years old) and non-elderly groups.

Methods

Enrollment

Of the 312 primary healthcare stations located in 15 counties island-wide in Taiwan, 57 were randomly selected. However, the six stations in Hualien and Chiayi counties were excluded because

of a manpower shortage. Therefore, this study was conducted in 51 primary healthcare stations (i.e. medical care facilities where diabetic patients were managed by general physicians) across four regions in Taiwan from November to December in 2001. These four regions referred respectively to northern (Taipei, Taoyuan, Hsinchu and Miaoli counties), central (Taichung, Nantou, Chuanghua and Yulin counties), southern (Tainan, Kaohsiung and Pingtung counties), and eastern (Ilan and Taitung counties) Taiwan. Local working committees comprising endocrinologists and diabetes opinion leaders were responsible for patient recruitment that would result in a study sample that was representative of the diabetic population. In proportion to the size of the local population in each region, the numbers of the participating stations in northern, central, southern and eastern Taiwan were set at 19, 12, 14 and 6 respectively. Each participating station provided data for patients who had been followed-up regularly for more than 12 months at the station for diabetes management. Data were collected on a retrospective-prospective basis by reviewing patients' medical records, as well as through interviews with patients and laboratory assessments. Due to incomplete data, 163 cases out of 1502 eligible patients were excluded, resulting in an enrollment rate of 89.1%.

Data collection

The data collected on patients included demographic characteristics, type of diabetes, diabetes management, frequency and types of interventions, cardiovascular risk factors, renal function, glycemic control in the previous 3 months, as well as eye, foot, and other severe late complications experienced in the previous 6 months. All data were recorded on data collection forms provided for each patient.

Finger capillary blood samples were collected from patients during their visits for central assessment of glycosylated hemoglobin (HbA_{1c}) using the Bio-Rad HbA_{1c} kit (Bio-Rad Diagnostic Group, Hercules, CA, USA). All collected samples were stored at 2–8°C and mailed in batches to the central laboratory at the Diagnostic Department of the

Taipei Municipal Chung Hsing Hospital in Taipei City. HbA_{1c} analyses were performed by automatic high-performance liquid chromatography (HPLC) (Bio-Rad VARIANT™, Bio-Rad Laboratories, Hercules, CA, USA). The HPLC system was standardized against the Diabetes Control and Complications Trial (DCCT) method.⁷

Type 1 diabetes was defined as primary diabetes in a patient who required insulin therapy within 1 year of diagnosis and continued this treatment thereafter.⁸ All remaining patients with primary diabetes were defined as having type 2 diabetes. Secondary diabetes induced by drugs, pancreatic disorders and so on was defined as diabetes other than type 1 or type 2. Diabetic retinopathy was diagnosed by ophthalmologists or detected by non-mydratric color fundus photography during routine screening as documented in the patients' medical records. Advanced eye diseases included neovascularization, retinal detachment and retinal hemorrhage; legal blindness was defined as loss of vision. Neuropathy was diagnosed based on standard clinical examination and use of monofilaments. Foot complications included one or more of the following: impalpable foot pulse, healed ulcer, acute ulcer/gangrene, angioplasty/bypass surgery.

Statistical analysis

All data were entered into SAS version 6.12 (SAS Institute Inc, Cary, NC, USA) by electronic scanning (TELE form Elite, version 5.2, Cardiff Software, San Marcos, CA, USA). Data were validated by means of both the scanning software and SAS.

Data were presented as mean ± standard deviation (SD), range or percentage. When the data were normally distributed, two-sample *t* test was used to compare differences between two groups; the chi-square test was used otherwise.

Multiple logistic regression analysis was performed to investigate the relationship between the binary outcome (presence or absence of a complication) and risk factors. All tests were two-sided, and a *p* value of less than 0.05 was considered to be significant.

Results

Among the 1339 primary care patients in the DCT'01 study, 1302 had type 2 diabetes (97.2%), 27 had type 1 diabetes (2.0%) and 10 had other types of diabetes (0.7%). The mean age of patients with type 2 diabetes was 65.6 ± 9.7 years (Table 1), and there was a predominance of patients aged ≥ 65 years (60.3%) and females (66.2%).

Comparison between DCT'01 (primary care) and DCT'98 (secondary/tertiary care)

Diabetes control, management and complications

Compared with their secondary/tertiary care counterparts, primary care type 2 diabetes patients were older at the onset of diabetes (57.2 ± 10.3 vs. 52.1 ± 11.1 years, *p* < 0.001), had a shorter duration of diabetes (8.4 ± 5.9 vs. 10.3 ± 7.3 years, *p* < 0.001), and a much smaller percentage received insulin therapy (insulin only: 1.5% vs. 10.2%, *p* < 0.001; combination of insulin and oral hypoglycemic agent: 0.6% vs. 11.7%, *p* < 0.001). Despite having worse HbA_{1c} data (8.4 ± 1.8% vs. 8.1 ± 1.6%, *p* < 0.001), primary care patients were generally less extensively managed with fewer patients performing home glucose monitoring (6.2% vs. 27.2%, *p* < 0.001) and more patients consuming alcohol (9.6% vs. 7.0%, *p* = 0.008). Nevertheless, primary care patients still experienced lower rates of complications, including kidney, retina, leg, coronary and cerebrovascular diseases (Table 1).

Age ≥ 65 and < 65 years

As illustrated in Table 2, primary care patients aged ≥ 65 years had a longer history (9.3 ± 6.5 vs. 7.2 ± 4.6 years, *p* < 0.001) and greater age at onset of diabetes (62.7 ± 8.1 vs. 48.9 ± 7.4 years, *p* < 0.001), and tended to exercise more regularly (56.5% vs. 47.2%, *p* = 0.005) than those aged < 65 years. Exercise was defined as regular if performed ≥ 3 times weekly for at least half an hour each time. However, compared to their older (aged ≥ 65 years) counterparts, patients aged < 65 years had a significantly higher mean body mass index (BMI)

Table 1. Demographic and clinical characteristics of type 2 diabetes patients in the Diabcare-Asia (Taiwan) (DCT) 1998 and DCT 2001 studies

	DCT'98	DCT'01	<i>p</i>
Age (yr)			< 0.001
<i>n</i>	2369	1302	
Mean ± SD	62.2 ± 10.6	65.6 ± 9.7	
Duration of diabetes (yr)			< 0.001
<i>n</i>	2360	1277	
Mean ± SD	10.3 ± 7.3	8.4 ± 5.9	
Age at onset of diabetes (yr)			< 0.001
<i>n</i>	2360	1277	
Mean ± SD	52.1 ± 11.1	57.2 ± 10.3	
BMI (kg/m ²)			0.003
<i>n</i>	2349	1256	
Mean ± SD	25.2 ± 3.6	25.5 ± 3.7	
HbA _{1c} (%)			< 0.001
<i>n</i>	2024	1250	
Mean ± SD	8.1 ± 1.6	8.4 ± 1.8	
Smokers, <i>n</i> (%)	358 (15.3)	200 (15.7)	0.773
Alcohol consumption > 3 times/wk, <i>n</i> (%)	163 (7.0)	121 (9.6)	0.008
Complications, <i>n</i> (%)			
Serum creatinine ≥ 180 μmol/L	83 (4.2)	14 (1.6)	< 0.001
Proteinuria ≥ 30 mg/dL	599 (37.6)	251 (32.6)	0.020
Photocoagulation and/or advanced eye disease	248 (13.2)	64 (5.9)	< 0.001
Retinopathy	570 (30.5)	104 (9.8)	< 0.001
Foot complications*	214 (9.7)	49 (4.0)	< 0.001
MI/CABG/angioplasty	87 (3.7)	12 (1.0)	< 0.001
Stroke	134 (5.7)	51 (4.0)	0.027
ESRD	15 (0.6)	4 (0.3)	0.239
Leg amputation	23 (1.2)	5 (0.4)	< 0.001
Home blood glucose monitoring, <i>n</i> (%)	600 (27.2)	77 (6.2)	< 0.001
Type of treatment, <i>n</i> (%)			
Insulin, no OHA	240 (10.2)	20 (1.5)	< 0.001
Insulin and OHA	277 (11.7)	8 (0.6)	< 0.001
OHA, no insulin	1806 (76.5)	1238 (95.1)	< 0.001

*Included one or coexistence of the following: impalpable foot pulse, healed ulcer and acute ulcer and/or angioplasty. BMI = body mass index; CABG = coronary artery bypass graft; ESRD = end-stage renal disease; HbA_{1c} = glycosylated hemoglobin; MI = myocardial infarction; OHA = oral hypoglycemic agent; SD = standard deviation.

(25.9 ± 3.8 kg/m² vs. 25.3 ± 3.6 kg/m², *p* = 0.010) and a higher percentage regularly consumed alcohol (13.5% vs. 7.0%, *p* < 0.001). These same age-related trends were also found in patients in secondary/tertiary care (data not shown). Less than 70% of primary care patients in both age groups had fasting blood glucose and lipids checked in the previous 3 months; however, more than 90%

of secondary/tertiary care patients had these items checked during the same period of time.

Comparison of glycemic control by age groups

Compared to those aged ≥ 65 years, primary care patients aged < 65 years had significantly greater elevation in metabolic parameters including HbA_{1c} (8.6 ± 1.8% vs. 8.2 ± 1.7%, *p* < 0.001), fasting

Table 2. Demographic and clinical characteristics of type 2 diabetes patients aged < 65 years and ≥ 65 years in the Diabcare-Asia (Taiwan) (DCT) 2001 study

	< 65 yr	≥ 65 yr	<i>p</i>
Duration of diabetes (yr)			< 0.001
<i>n</i>	510	767	
Mean ± SD	7.2 ± 4.6	9.3 ± 6.5	
Age at onset of diabetes (yr)			< 0.001
<i>n</i>	510	767	
Mean ± SD	48.9 ± 7.4	62.7 ± 8.1	
BMI (kg/m ²)			0.010
<i>n</i>	495	761	
Mean ± SD	25.9 ± 3.8	25.3 ± 3.6	
HbA _{1c} (%)			< 0.001
<i>n</i>	501	749	
Mean ± SD	8.6 ± 1.8	8.2 ± 1.7	
Fasting blood glucose (mmol/L)			< 0.001
<i>n</i>	357	502	
Mean ± SD	10.1 ± 3.4	9.0 ± 3.1	
Total cholesterol (mmol/L)			0.025
<i>n</i>	370	592	
Mean ± SD	5.4 ± 1.2	5.2 ± 1.1	
Triglyceride (mmol/L)			0.022
<i>n</i>	337	559	
Mean ± SD	2.0 ± 1.2	1.8 ± 1.1	
Lifestyle modification, <i>n</i> (%)			
Smokers	83 (16.5)	117 (15.2)	0.529
Alcohol consumption > 3 times/wk	67 (13.5)	54 (7.0)	< 0.001
Regular diet adherence	288 (56.4)	466 (60.4)	0.074
Regular exercise	237 (47.2)	435 (56.5)	0.005
Complications, <i>n</i> (%)			
Serum creatinine ≥ 180 μmol/L	10 (0.8)	4 (1.4)	0.583
Proteinuria ≥ 30 mg/dL	90 (18.2)	161 (21.6)	0.873
Retinopathy*	51 (9.9)	99 (12.7)	0.106
Foot complications	15 (2.9)	37 (4.8)	0.096
MI/CABG/angioplasty	6 (1.2)	6 (0.8)	0.560
Stroke	10 (1.9)	41 (5.3)	0.003
ESRD	1 (0.2)	3 (0.4)	0.540
Neuropathy	61 (12.2)	93 (12.3)	0.957

*Including photocoagulation and/or advanced eye disease. BMI = body mass index; CABG = coronary artery bypass graft; ESRD = end-stage renal disease; HbA_{1c} = glycosylated hemoglobin; MI = myocardial infarction; SD = standard deviation.

plasma glucose (10.1 ± 3.4 mmol/L vs. 9.0 ± 3.1 mmol/L, *p* < 0.001), total cholesterol (5.4 ± 1.2 vs. 5.2 ± 1.1 mmol/L, *p* = 0.025), and triglyceride (2.0 ± 1.2 mmol/L vs. 1.8 ± 1.1 mmol/L, *p* = 0.022) (Table 2). These age-related profiles remained similar in secondary/tertiary care patients, except for

triglyceride levels which showed no age-related difference (data not shown). Consistent with the mean HbA_{1c} data, a significantly lower proportion of primary care patients (9.4% vs. 14.0%, *p* < 0.05) in the < 65 years age group had optimal glycemic control (HbA_{1c} < 6.5%) as defined by the

Table 3. Comparison of HbA_{1c} profiles of type 2 diabetes patients in the Diabcare-Asia (Taiwan) (DCT) 2001 and DCT 1998 studies by age group*

Age group	HbA _{1c} profile	DCT'01	DCT'98	p [†]
< 65 yr	Mean ± SD	8.6 ± 1.8	8.2 ± 1.7	
	< 6.5%	9.4 [‡]	11.6 [§]	
	6.5–7.5%	19.8	29.0	
	> 7.5%	70.9	59.4	< 0.001
≥ 65 yr	Mean ± SD	8.2 ± 1.7	7.9 ± 1.6	
	< 6.5%	14.0	16.5	
	6.5–7.5%	24.7	32.1	
	> 7.5%	61.3	51.4	< 0.001

*Asia-Pacific Type 2 Diabetes Policy Group⁹; [†]p value indicates comparison of HbA_{1c} profile for respective age groups of DCT'01 and DCT'98 studies; [‡]for DCT'01 study, HbA_{1c} profiles between patients < 65 yr vs. ≥ 65 yr, p = 0.004; [§]for DCT'98 study, HbA_{1c} profiles between patients < 65 yr vs. ≥ 65 yr, p < 0.001.

Asia-Pacific Type 2 Diabetes Policy Group.⁹ The HbA_{1c} profiles of patients in the DCT'98 study were better than those of patients in the DCT'01 study, for patients < 65 years (8.2 ± 1.7% vs. 8.6 ± 1.8%, p < 0.001) and for patients ≥ 65 years (7.9 ± 1.6% vs. 8.2 ± 1.7%, p < 0.001) (Table 3).

Diabetes management and treatment

A significantly greater percentage of primary care patients in the ≥ 65 years age group had received proteinuria checks (66.8% vs. 55.7%, p < 0.05), eye examinations (57.0% vs. 46.0%, p < 0.05), and foot examinations (39.3% vs. 26.9%, p < 0.05) in the previous 6 months, as compared to those in the < 65 years group. While the proportion of pa-

tients receiving the aforementioned examinations was higher in secondary/tertiary care patients, this difference was not significant (data not shown).

The most frequently prescribed oral hypoglycemic agents for patients in both age groups were sulfonylureas and biguanides. Very few patients received meglitinide, thiazolidinedione and α-glucosidase inhibitor. There was no significant difference in the proportion of patients receiving insulin therapy between the two age groups in either the primary or the secondary/tertiary care settings.

Blood pressure control

As shown in Table 4, diabetic patients treated in a primary care setting had better control of blood pressure than those treated in a secondary/tertiary setting (blood pressure ≥ 140/90 mmHg, 42.3% vs. 46.6%, p < 0.05). For the < 65 years age group, patients in the DCT'98 study had poorer control than those in the DCT'01 study (blood pressure ≥ 140/90 mmHg, 44% vs. 37.5%, p < 0.05). Three out of four patients (< 65 years and ≥ 65 years: 74.1% vs. 75.9%, not significant) did not meet the American Diabetes Association treatment target for blood pressure (< 130/80 mmHg),¹⁰ and approximately two out of five (< 65 years and ≥ 65 years: 37.5% vs. 45.4%, p < 0.05) had blood pressure that exceeded the WHO/International Society of Hypertension criteria for hypertension¹¹ (≥ 140/90 mmHg) (Table 4). Worryingly, a substantial percentage of patients (16.0% in DCT'01 and

Table 4. Blood pressure control in type 2 diabetes patients in the Diabcare-Asia (Taiwan) (DCT) 2001 and DCT 1998 studies by age group

Study	Age (yr)	N	Blood pressure, n (%)	
			≥ 130/80 mmHg	≥ 140/90 mmHg
DCT'01	< 65	517	383 (74.1)	194 (37.5)*
	≥ 65	784	595 (75.9)	356 (45.4)
	Total	1301	978 (75.2)	550 (42.3) [†]
DCT'98	< 65	1296	985 (76.0)	570 (44.0)*
	≥ 65	1038	800 (77.1)	518 (49.9)
	Total	2334	1785 (76.5)	1088 (46.6) [†]

*Blood pressure ≥ 140/90 mmHg for those aged < 65 years, DCT'01 vs. DCT'98, 37.5% vs. 44.0%, p = 0.023; [†]blood pressure ≥ 140/90 mmHg, DCT'01 vs. DCT'98, 42.3% vs. 46.6%, p = 0.012. N = number of patients available for analysis.

19.0% in DCT'98, $p < 0.05$) with high blood pressure ($\geq 140/90$ mmHg) were not taking any anti-hypertensive agent. Calcium antagonists were the most commonly used medications for hypertension, followed by angiotensin-converting enzyme inhibitors, beta-blockers and diuretics. Among those treated with antihypertensive agents whose blood pressure remained high, 57.9% took only one drug and 88.0% took two or fewer drugs.

Diabetes complications

In the primary care setting, patients in the ≥ 65 years group had a higher frequency of foot complications (4.8% vs. 2.9%, $p = 0.096$) and a greater percentage of stroke (5.3% vs. 1.9%, $p = 0.003$) than those in the < 65 years group (Table 2). In the secondary/tertiary care setting, patients ≥ 65 years showed a significantly higher prevalence of myocardial infarction/coronary artery bypass graft/angioplasty (5.5% vs. 2.3%, $p < 0.05$) and stroke (7.0% vs. 4.7%, $p < 0.05$) than the < 65 years group.

As detailed in Table 5, multiple logistic regression analysis of patients treated in primary care revealed that hypertension was the borderline risk factor for stroke (OR, 4.17; 95% CI, 0.91–19.23; $p = 0.066$). Significant risk factors for cataract were age at diabetes onset (OR, 1.11; 95% CI, 1.06–1.16; $p < 0.001$), duration of diabetes (OR, 1.15; 95% CI, 1.09–1.21; $p < 0.001$), gender (OR, 1.54; 95% CI, 1.00–2.37; $p = 0.052$) and triglyceride (OR, 1.23; 95% CI, 1.01–1.50; $p = 0.039$). Risk factors for retinopathy were duration of diabetes (OR, 1.16; 95% CI, 1.08–1.25; $p < 0.001$) and total cholesterol (OR, 0.68; 95% CI, 0.48–0.96; $p = 0.030$). Risk factors for foot complications were age at diabetes onset (OR, 1.12; 95% CI, 1.01–1.23; $p = 0.029$) and diabetes duration (OR, 1.20; 95% CI, 1.06–1.35; $p = 0.003$). The risk factor for proteinuria was diabetes duration (OR, 1.07; 95% CI, 1.02–1.13; $p = 0.012$).

Table 6 shows the risk factors for each complication in the DCT'98 study. Similar to the results of the DCT'01 study, duration of diabetes emerged as a risk factor for cataract, retinopathy, foot complications and proteinuria. The striking difference in risk factor profile might be attributable to the

fact that total cholesterol, while being a risk factor for retinopathy, foot complications and proteinuria in the DCT '98 study, showed only significant relation to retinopathy in the DCT'01 study; and hypertension as a risk factor for stroke, cataract, retinopathy and proteinuria in the DCT'98 study became barely significant for these complications in the DCT'01 study (Tables 5 and 6).

Discussion

Due to the lack of an orthodox system of family physicians in Taiwan, patients can visit a hospital directly without referral from general practitioners. However, as Table 1 indicates, compared with those treated in a secondary/tertiary care setting, patients with type 2 diabetes treated in a primary care setting had less severe diabetes as reflected by shorter duration, older age at onset, and fewer complications. Medical intervention, including both medical treatment and lifestyle modification, was less extensive in the primary care setting where the proportion of patients receiving insulin injections was much lower (Table 1). This situation might explain the slightly higher mean HbA_{1c} level of primary care patients compared to that of secondary/tertiary care patients. The shortage of well-trained staff and adequate resources for diabetes management at the primary care level may be a contributing factor to this result.¹² Reluctance of patients to receive insulin injections, and lack of familiarity of primary care physicians in prescribing insulin or managing insulin-treated patients might play a major role in the lower rate of insulin injections, although less severe disease status may also be important. More emphasis should be placed on medical education for primary care physicians and patients. Training in insulin administration and the importance of home glucose monitoring are particularly needed.

While nearly all patients treated in a secondary/tertiary care setting had HbA_{1c} data, less than one fourth of primary care patients had the same data, indicating HbA_{1c} testing that was even lower than the 32% examination rate of patients enrolled

Table 5. Individual risk factors for each complication in the Diabcare-Asia (Taiwan) (DCT) 2001 study

Variable	Stroke	Cataract	Retinopathy	Foot complications	Proteinuria
Age					
OR	1.66	1.0	0.46	0.44	0.59
95% CI	0.27, 10.27	0.49, 2.04	0.14, 1.49	0.06, 3.05	0.27, 1.32
<i>p</i>	0.587	0.992	0.195	0.403	0.202
Age at DM onset					
OR	1.00	1.11	1.06	1.12	1.01
95% CI	0.92, 1.10	1.06, 1.16	1.0, 1.13	1.01, 1.23	0.97, 1.06
<i>p</i>	0.936	< 0.001*	0.063	0.029*	0.566
Duration of DM					
OR	1.04	1.15	1.16	1.20	1.07
95% CI	0.93, 1.16	1.09, 1.21	1.08, 1.25	1.06, 1.35	1.02, 1.13
<i>p</i>	0.505	< 0.001*	< 0.001*	0.003*	0.012*
Gender					
OR	0.48	1.54	0.75	0.49	0.88
95% CI	0.17, 1.33	1.0, 2.37	0.38, 1.49	0.17, 1.40	0.53, 1.45
<i>p</i>	0.157	0.052	0.414	0.179	0.611
BMI					
OR	1.09	1.01	1.00	1.01	1.03
95% CI	0.97, 1.23	0.96, 1.07	0.92, 1.09	0.87, 1.17	0.97, 1.09
<i>p</i>	0.165	0.605	0.965	0.901	0.394
HbA_{1c}					
OR	0.80	1.03	0.99	0.93	1.14
95% CI	0.55, 1.16	0.89, 1.18	0.80, 1.22	0.65, 1.34	0.98, 1.33
<i>p</i>	0.238	0.725	0.907	0.712	0.100
Fasting blood glucose					
OR	1.07	0.95	1.10	1.06	1.02
95% CI	0.89, 1.28	0.88, 1.03	0.98, 1.24	0.89, 1.25	0.94, 1.10
<i>p</i>	0.462	0.201	0.113	0.522	0.660
Total cholesterol					
OR	1.12	1.06	0.68	1.50	1.09
95% CI	0.72, 1.75	0.88, 1.28	0.48, 0.96	0.99, 2.27	0.88, 1.35
<i>p</i>	0.622	0.540	0.030*	0.055	0.445
Triglyceride					
OR	1.01	1.23	1.03	1.13	1.12
95% CI	0.63, 1.61	1.01, 1.50	0.74, 1.43	0.71, 1.79	0.90, 1.39
<i>p</i>	0.967	0.039*	0.859	0.608	0.308
Hypertension					
OR	4.17	0.84	1.99	1.51	1.60
95% CI	0.91, 19.23	0.55, 1.31	0.93, 4.26	0.45, 5.10	0.94, 2.72
<i>p</i>	0.066	0.447	0.077	0.504	0.086

*Statistical significance at the 5% level. BMI = body mass index; CI = confidence interval; DM = diabetes mellitus; HbA_{1c} = glycosylated hemoglobin; OR = odds ratio.

For the "age" variable, odds ratio was expressed as the relative risk of complication for patients ≥ 65 years vs. those < 65 years; for the "gender" variable, females vs. males; for the "hypertension" variable, patients with hypertension vs. patients with no hypertension; for the "proteinuria" complication, patients with urinary protein excretion ≥ 30 mg/dL vs. patients with no proteinuria.

For the continuous variables (age at DM onset, duration of DM, BMI, HbA_{1c}, fasting blood glucose, total cholesterol, triglyceride), the odds ratio indicates risk for every 1 unit increase (e.g. an odds ratio for triglyceride of 1.2 implies a 20% increase in risk for every 1 mmol/L increase in triglyceride).

Table 6. Individual risk factors for each complication in the Diabcare-Asia (Taiwan) (DCT) 1998 study

Variable	Stroke	Cataract	Retinopathy	Foot complications	Proteinuria
Age					
OR	0.66	1.14	0.76	0.60	1.08
95% CI	0.33, 1.34	0.75, 1.72	0.50, 1.14	0.34, 1.05	0.71, 1.64
<i>p</i>	0.254	0.537	0.178	0.075	0.727
Age at DM onset					
OR	1.05	1.10	1.0	1.02	1.01
95% CI	1.01, 1.09	1.07, 1.13	0.98, 1.02	0.99, 1.04	0.98, 1.03
<i>p</i>	0.009*	< 0.001*	0.750	0.266	0.634
Duration of DM					
OR	1.03	1.11	1.06	1.04	1.04
95% CI	0.99, 1.08	1.09, 1.15	1.04, 1.09	1.01, 1.08	1.01, 1.07
<i>p</i>	0.147	< 0.001*	< 0.001*	0.012*	0.004*
Gender					
OR	1.11	1.09	0.89	0.86	0.66
95% CI	0.72, 1.71	0.85, 1.41	0.69, 1.15	0.60, 1.22	0.51, 0.86
<i>p</i>	0.635	0.490	0.380	0.394	0.002*
BMI					
OR	0.95	0.98	0.99	0.97	1.05
95% CI	0.90, 1.01	0.94, 1.01	0.96, 1.03	0.93, 1.02	1.01, 1.09
<i>p</i>	0.118	0.230	0.688	0.267	0.011*
HbA_{1c}					
OR	1.16	1.09	1.14	1.08	1.10
95% CI	1.003, 1.345	0.99, 1.19	1.04, 1.24	0.96, 1.21	1.00, 1.21
<i>p</i>	0.046*	0.073	0.005*	0.222	0.049*
Fasting blood glucose					
OR	0.98	0.97	1.0	1.04	1.0
95% CI	0.91, 1.06	0.93, 1.02	0.96, 1.05	0.98, 1.10	0.95, 1.05
<i>p</i>	0.648	0.265	0.851	0.249	0.947
Total cholesterol					
OR	0.85	1.0	1.24	1.18*	1.26
95% CI	0.69, 1.05	0.88, 1.13	1.10, 1.40	1.00, 1.39	1.11, 1.43
<i>p</i>	0.127	0.989	< 0.001*	0.046*	< 0.001*
Triglyceride					
OR	1.12	1.12	0.99	1.03	1.35
95% CI	0.94, 1.33	1.00, 1.26	0.89, 1.11	0.89, 1.20	1.20, 1.52
<i>p</i>	0.201	0.047*	0.900	0.660	< 0.001*
Hypertension					
OR	3.19	1.44	1.65	1.45	1.93
95% CI	1.79, 5.71	1.10, 1.89	1.24, 2.18	0.97, 2.14	1.45, 2.57
<i>p</i>	< 0.001*	0.009*	< 0.001*	0.071	< 0.001*

*Statistical significance at the 5% level. BMI = body mass index; CI = confidence interval; DM = diabetes mellitus; HbA_{1c} = glycosylated hemoglobin; OR = odds ratio.

in the Diabcare-Asia 2001 study.⁶ The lack of reimbursement for HbA_{1c} testing from the National Health Insurance System of Taiwan seems one

likely explanation. The level of glycemic control was unsatisfactory in this study, with only 9.4% of patients < 65 years and 14.0% of patients ≥ 65 years

having HbA_{1c} values within the optimal range defined by the Asia-Pacific Type 2 Diabetes Policy Group (HbA_{1c} < 6.5%).⁹ The respective figures obtained from patients in the Diabcare-Asia 1998 study were also low (11.6% and 16.0%). Mirroring worldwide trends, the overall glycemic control of our patients in both primary and secondary/tertiary care was inadequate. Several landmark studies have pointed to the importance of tight glycemic control.^{13,14} Better glycemic control may reduce the need for more intensive care of diabetic complications later, helping to facilitate a decrease in healthcare costs as a whole. There is also evidence indicating that sustained reduction in HbA_{1c} level among adult diabetic patients can lead to significant cost savings within 1–2 years of improvement.¹⁵

The rates of screening for eye and kidney complications among patients treated in a primary care setting were comparable to those for all patients in the Diabcare-Asia 2001 study, while the screening rate for foot complications was lower than in Diabcare-Asia 2001. The screening rates for the abovementioned complications were slightly better than those for female African Americans in primary care.¹⁶

Several studies have suggested that earlier onset of diabetes,¹⁷ longer duration of diabetes,^{17–19} female gender^{18,19,20–25} and hypertriglyceridemia^{26–28} are risk factors for cataract, a finding that was also reflected in our primary care patients (Table 5). Similar risk factors for cataract were found in secondary/tertiary care patients in our previous study, except an additional association with hypertension and a negative association with female gender (Table 6). No known mechanism provides an explanation for the excess risk of cataract in female diabetic subjects.²⁴ In a cross-sectional study, patients undergoing surgery for posterior capsule cataract had a significantly higher average concentration of fasting serum triglycerides.²⁶ Elevated triglycerides were associated with increased risk of posterior subcapsule cataract in men but not in women.²⁸ However, this is not a readily apparent explanation for how triglycerides might affect cataract development, despite the fact

that a close association was found in both primary and secondary/tertiary care settings. In contrast to the normal subjects, we found no significant impact of age on the prevalence of cataract. This may be related to the more important role of age at diabetes onset and duration of diabetes (Tables 5 and 6).

As Tables 5 and 6 reveal, patients with a longer duration of diabetes also had a significantly higher prevalence of cataract, retinopathy, foot complications and proteinuria. Previous studies also found that hypertension was a significant risk factor for stroke,^{29–32} retinopathy³³ and proteinuria.^{34–36}

As in much previous research, our study of diabetes patients treated in a secondary/tertiary care setting also found that male type 2 diabetics were more susceptible to renal complications (Table 6).^{37–40} However, a negative association of renal complications with gender, similar to that found in primary care patients in this study, has also been reported.⁴¹ Further studies are needed to explain the reasons for this discrepancy.

The most striking difference in the risk factors related to diabetic complications between the DCT'01 and DCT'98 (Tables 5 and 6) studies was that a close association of higher serum cholesterol levels with foot complications and proteinuria was found in patients treated in a secondary/tertiary care setting but not in patients treated in a primary care setting. High serum cholesterol or hyperlipidemia have been associated with microalbuminuria⁴² or renal disorders.^{36,38,43} However, the association of higher serum cholesterol with retinopathy in this study contradicts the findings of a previous study.⁴⁴

Hypertension is a risk factor for nephropathy in normal subjects^{34,35} and in subjects with type 2 diabetes.³⁶ The importance of maintaining an optimum blood pressure of $\leq 130/80$ mmHg and at least a normal blood pressure of $\leq 140/90$ mmHg is well-established management of diabetes. This study demonstrated poor rates of blood pressure control in type 2 diabetes patients treated in both primary and secondary/tertiary care settings (Table 4). The most commonly used antihypertensive

agent was calcium-channel blockers in primary care patients and angiotensin-converting enzyme inhibitors in secondary/tertiary care patients. More attention is needed to provide adequate antihypertensive treatment for Taiwanese patients. Moreover, as the UK Prospective Diabetes Study Group has shown, tight control of blood pressure is associated with reduced risk of stroke and microvascular diseases.³³ Further study of the importance of blood pressure control in Taiwanese diabetic patients is required.

The major limitations of our study are that some data on diabetic complications were self-reported by patients or obtained from chart review, and comprehensive, centralized laboratory examinations were not performed. While HbA_{1c} was a risk factor for stroke, retinopathy and proteinuria in the DCT'98 study (Table 6), it had no relation to any complication in the DCT'01 study (Table 5). Therefore, care must be taken in generalizing the findings. This may have been related to the use of a cross-sectioned design, retrospective recording of laboratory data except for HbA_{1c}, and incomplete collection of various data, such as for retinopathy and proteinuria.

In conclusion, diabetes control was poorer among patients treated in primary care than in secondary/tertiary care, while blood pressure control was better in primary care. Similar diabetes control and clinical features existed in patients aged < 65 years and ≥ 65 years in both care settings. The shorter duration of diabetes and better control of blood pressure in primary care patients and in patients aged < 65 years as compared with their respective counterparts might be related to the lower prevalence of complications. A high percentage of patients in both care settings had inadequate glycemic and blood pressure control.

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References

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998;21:1414–31.
2. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabet Med* 1997;14 Suppl 5:S1–85.
3. Tai T. Current status of diabetes in Taiwan. *Diabetes Res Clin Pract* 2000;50 Suppl 2:S1–2.
4. Wu L. One in Seven Senior Citizens in Taiwan Suffer from Diabetes. <http://www.taipei.org/teco/cicc/news/english/e-03-15-02/e-03-15-02-19.htm> [Date accessed: June 25, 2002]
5. Lin T, Chou P, Lai MS, et al. Direct costs-of-illness of patients with diabetes mellitus in Taiwan. *Diabetes Res Clin Pract* 2001;54 Suppl 1:S43–6.

6. Diabcare-Asia 2001. *Country Report on Outcome Data and Analyses*. Singapore: Novo Nordisk Asia Pacific Pte Ltd, 29 January 2003.
7. Chuang LM, Tsai ST, Huang BY, et al. The status of diabetes control in Asia—a cross-sectional survey of 24317 patients with diabetes mellitus in 1998. *Diabet Med* 2001;19: 978–85.
8. Morrish NJ, Stevens LK, Head J, et al. A prospective study of mortality among middle-aged diabetic patients (the London Cohort of the WHO Multinational Study of Vascular Disease in Diabetics) II: Associated risk factors. *Diabetologia* 1990;33:542–8.
9. Asia-Pacific Type 2 Diabetes Policy Group. *Type 2 Diabetes—Practical Target and Treatment*, 3rd edition. Sydney, Australia: Health Communication Australia Ltd, 2002.
10. American Diabetes Association. Treatment of hypertension in adults with diabetes. *Diabetes Care* 2002;25:199–201.
11. Kjeldsen SE, Farsang C, Sleight P, et al. World Health Organization; International Society of Hypertension. 1999 WHO/ISH hypertension guidelines—highlights and ESH update. *J Hypertens* 2001;19:2285–8.
12. Soegonds S, Soewondo P, Semiardji G, et al. The status of diabetes control in Indonesia: a national audit of patients with type 2 diabetes mellitus in the year 2001. *Maj Kedoht Indon* 2003;53:283–9.
13. Ohkubo Y, Kishikawa H, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract* 1995;28:103–17.
14. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;352:837–53.
15. Wagner EH, Sandhu N, Newton KM, et al. Effect of improved glycemic control on health care costs and utilization. *JAMA* 2001;285:182–9.
16. Melkus GD, Mailliet N, Novak J, et al. Primary care cancer and diabetes complications screening of black women with type 2 diabetes. *J Am Acad Nurse Pract* 2002;14:43–8.
17. Klein BE, Klein R, Wang Q, et al. Older-onset diabetes and lens opacities. The Beaver Dam Eye Study. *Ophthalmic Epidemiol* 1995;2:49–55.
18. McCarty CA, Mukesh BN, Fu CL, et al. The epidemiology of cataract in Australia. *Am J Ophthalmol* 1999;128:446–65.
19. Miglior S, Marighi PE, Musicco M, et al. Risk factors for cortical, nuclear, posterior subcapsular and mixed cataract: a case-control study. *Ophthalmic Epidemiol* 1994;1: 93–105.
20. Hiller R, Sperduto RD, Ederer F. Epidemiologic associations with nuclear, cortical, and posterior subcapsular cataracts. *Am J Epidemiol* 1986;124:916–25.
21. Leske MC, Chylack LT Jr, Wu SY. The Lens Opacities Case-Control Study. Risk factors for cataract. *Arch Ophthalmol* 1991;109:244–51.
22. Klein BEK, Klein R, Linton KLP. Prevalence of age-related lens opacities in a population: the Beaver Dam Eye Study. *Ophthalmology* 1992;99:546–52.
23. Harding JJ, Egerton M, van Heyningen R, et al. Diabetes, glaucoma, sex, and cataract: analysis of combined data from two case control studies. *Br J Ophthalmol* 1993;77: 2–6.
24. Giuffrè G, Giammanco R, Di Pace F, et al. Casteldaccia eye study: prevalence of cataract in the adult and elderly population of a Mediterranean town. *Int Ophthalmol* 1994–95; 18:363–71.
25. Delcourt C, Cristol JP, Tessier F, et al. Risk factors for cortical, nuclear, and posterior subcapsular cataracts: the POLA study. *Pathologies Oculaires Liées à l'Age. Am J Epidemiol* 2000;151:497–504.
26. Jahn CE, Janke M, Winowski H, et al. Identification of metabolic risk factors for posterior subcapsular cataract. *Ophthalmic Res* 1986;18:112–6.
27. Tsutsumi K, Inoue Y, Yoshida C. Acceleration of development of diabetic cataract by hyperlipidemia and low high-density lipoprotein in rats. *Biol Pharm Bull* 1999;22:37–41.
28. Hiller R, Sperduto RD, Reed GF, et al. Serum lipids and age-related lens opacities: a longitudinal investigation: the Framingham Studies. *Ophthalmology* 2003;110:578–83.
29. Brown RD, Whisnant JP, Sicks JD, et al. Stroke incidence, prevalence, and survival: secular trends in Rochester, Minnesota, through 1989. *Stroke* 1996;27:373–80.
30. Kannel WB, Wolf PA, Verter J, et al. Epidemiologic assessment of the role of blood pressure in stroke. The Framingham Study. *JAMA* 1970;214:301–10.
31. Menotti A, Jacobs DR Jr, Blackburn H, et al. Twenty-five-year prediction of stroke deaths in the Seven Countries Study: the role of blood pressure and its changes. *Stroke* 1996;27:381–7.
32. Collins R, MacMahon S. Blood pressure, antihypertensive drug treatment and the risks of stroke and of coronary heart disease. *Br Med Bull* 1994;50:272–98.
33. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* 1998; 317:703–13.
34. Jungers P, Hannedouche T, Itakura Y, et al. Progression rate to end-stage renal failure in non-diabetic kidney diseases: a multivariate analysis of determinant factors. *Nephrol Dial Transplant* 1995;10:1353–60.
35. Ishida K, Ishida H, Narita M, et al. Factors affecting renal function in 119985 adults over three years. *QJM* 2001;94: 541–50.
36. Ravid M, Brosh D, Ravid-Safran D, et al. Main risk factors for nephropathy in type 2 diabetes mellitus are plasma cholesterol levels, mean blood pressure, and hyperglycemia. *Arch Intern Med* 1998;158:998–1004.
37. Kikuchi M, Matsumoto T, Ohashi Y. Risk factors for development of proteinuria in NIDDM analyzed by Poisson

- regression. *J Diabet Complications* 1991;5:128–30.
38. Gall ML, Hougaard P, Borch-Johnsen K, et al. Significant risk factors for development of microalbuminuria and diabetic nephropathy in patients with non-insulin-dependent diabetes. *Ugeskr Laeger* 1998;160:4524–7. [In Danish]
39. Pijls LT, de Vries H, Kriegsman DM, et al. Determinants of albuminuria in people with type 2 diabetes mellitus. *Diabetes Res Clin Pract* 2001;52:133–43.
40. Basit A, Hydrie MZ, Hakeem R, et al. Frequency of chronic complications of type II diabetes. *J Coll Physicians Surg Pak* 2004;14:79–83.
41. Simon S, Stephenson S, Whyte K, et al. Prevalence of chronic renal failure in the diabetic population at the University Hospital of the West Indies. *West Indian Med J* 2004;53:85–8.
42. Barrera JA, Separza R. Renal functional reserve in patients with recently diagnosed type 2 diabetes mellitus with and without microalbuminuria. *Nephron* 2001;87:223–30.
43. Ismail N, Becker B, Strzelczyk P, et al. Renal disease and hypertension in non-insulin-dependent diabetes mellitus. *Kidney Int* 1999;55:1–28.
44. Chen MS, Kao CS, Chang CJ, et al. Prevalence and risk factors of diabetic retinopathy among non-insulin-dependent diabetes subjects. *Am J Ophthalmol* 1992;114:723–30.