行政院國家科學委員會專題研究計畫 成果報告

加入某醫學中心糖尿病論質計酬改善方案計畫之糖尿病患者其死亡與糖尿病併發症發生之研究
研究成果報告(精簡版)

計 畫 類 別 ：個別型
計 畫 編 號 ：NSC 97-2314-B-039-019-
執 行 期 間 ：97 年 08 月 01 日至 98 年 07 月 31 日
執 行 單 位 ：中國醫藥大學中國醫學研究所

計 畫 主 持 人：李采娟
共 同 主 持 人：林正介、陳清助、劉秋松
計畫參與人員：學士級-專任助理人員：楊幸玉

報 告 附 件 ：出席國際會議研究心得報告及發表論文

處 理 方 式 ：本計畫可公開查詢

中 華 民 國 98 年 10 月 20 日

Contents

Introduction

The prevalence of Diabetes mellitus (DM) is rapidly increasing in Taiwan, affecting over 900,000 people in Taiwan, and every year there would appear to be an increase of over 110,000 new cases (Chou PS, 2001). DM has become the fourth major leading cause of death for men and women in Taiwan since 2002 (Department of Health, 2002-2006). Using the world standard population reported by WHO as a standard, the standard mortality ratio of diabetes rose from $23.6/10^5$ in 1985 to $39.4/10^5$ in 2006, making diabetes the most rapid increase compared to other chronic diseases. Diabetes accounts for one in every four hospital-bed occupants and one in every sixteen office visits (one-quarter for diabetes care and three-quarters for the care of its complications), and led to 11.5% of all health care expenditure in Taiwan in 1998 (Bureau of National Health Insurance, 2002).

Diabetes is associated with substantial morbidity and mortality. In US, adults with diabetes have heart disease death rates about 2-4 times higher than those without diabetes (CDC/National Center for Chronic Disease Prevention and Health Promotion, 2000; Haffner SN, 2003). Incidence rate for stroke is also 2-4 times higher among individuals with diabetes. Diabetes is the leading cause of incidence cases of blindness among adults aged 20-74 years and the leading cause of end-stage renal disease, accounting for about 40% of new cases. And about 60%-70% of individuals with diabetes have neuropathy and diabetes accounts for more than 50% of lower limb amputations in US.

Because diabetes is a complicated disease, that medical treatments provided by different departments with multidiscipline professional medical teams (physicians, nurses, dieticians, pharmacists, social workers, laboratory technicians, etc.) is required to enhance patient's care quality. Share care is a way to achieve this goal. Hickman (Hickman M, 1994) define share care as "the joint participation of hospital consultants and general practitioners in the planned delivery of care for patients with a chronic condition, informed by an enhanced information exchange over and above routine discharge and referral notes". In Taiwan, Bureau of National Health Insurance has introduced "The Improvement Program of National Health Insurance Payment for Diabetes Medical Treatment", based on "Diabetes Share Care" since 2001. Its goal is to integrate related departments, expertise and hospitals at different levels which can provide continuous, approachable and high quality care for diabetes.

The importance of measuring variability of blood glucose level

Previous studies indicated that long-term variability of fasting plasma glucose was a predictor of all-cause and cardiovascular mortality in elderly patients with type 2 diabetes, independent of mean plasma glucose (Muggeo M, 1995; 1995; 1997). These findings have strong clinical implications because it might suggest that the stability of blood glucose level over time is one of the goals in the care management of diabetes. The possible mechanism that can make this association biological plausible is that blood glucose level could be a factor directly involved in the development of chronic diabetes complications or in precipitating one or more acute events leading to death. In such a case, glucose stability should become a major goal of diabetes treatment. Alternatively, high variability of glucose could be the result of recurrent relapses of chronic coexisting illness and thus might be responsible for death. In such a case, although the maintenance of stable glucose levels would not prevent the underlying disorder from progressing, it could be a significant predictor of mortality. This is consistent with recent studies identifying a relationship between the variability of blood glucose concentration and short-term mortality in critically ill patients (Egi M, 2006). These studies show strict glucose control in reducing the

variability of glucose significantly reduces ICU and hospitalization mortality.

Specific objectives:

The goal of this study is to establish an open diabetes cohort in order to characterize the clinical features of type 2 diabetes. A special attention will be given to describe the long-term diabetic complications and mortality and to evaluate their relationship with risk factors.

Overall mortality and morbidity from diabetes:

1. To estimate all-cause annual mortality and overall all-cause and cause-specific mortality in patients with type II diabetes enrolled in Share Care Disease Management (SCDM) program of a medical center at subsequent follow-up years. And compare these mortality estimates to those in Healthy people 2010 proposed by US Department of Health and Human Services.
2. To estimate prevalence of diabetic complications (foot ulcer, retinopathy or macular edema, hypertension, nephropathy, ischemic heart disease, myocardial infarction, and stroke) in patients with type II diabetes enrolled in SCDM program of a medical center at baseline and incidence rates for subsequent follow-up years. And compare these incidence estimates to those in Healthy people 2010 proposed by US Department of Health and Human Services.

Relationship of variability of glucose control with mortality and morbidity from diabetes:

1. To provide estimates of the annual variability for fasting plasma glucose and hemoglobin A_1C (HbA1c) in patients with type II diabetes enrolled in SCDM program of a medical center at baseline and subsequent follow-up years.
2. To assess whether the annual variability of fasting plasma glucose and HbA1c are associated with all-cause and cause-specific mortality and incidence rates of diabetic complication.

Methods

Study Subjects

The study design is a retrospective cohort study. The study cohort was the enrollee population of SCDM program in China Medical University Hospital. SCDM, a nurse case management program was set up by Bureau of National Health Insurance in 2002. Enrollees are patients with a diagnosis of DM (International Classification Disease, Ninth Revision, Clinical Modification, abbreviated as ICD-9-CM; Code of 250). SCDM program enrollees at the end of August, 2006 were identified from an automated registry. All patients enrolled in the registry during the study period between August, 2002 and August, 2006 have to be continuously enrolled in SCDM until December, 2008 for the first year study, or until their death. Thus, this is an open or dynamic cohort, each individual entering the study at different time. The rationale for this criterion was that we only will include patients who can provide at least one-year of follow-up for estimating the annual variability for fasting plasma glucose and glycemic control. Enrollees younger than 18 years on the date of diagnosis and those who died before one-year of follow-up were excluded (Wagner EH, 2001). These criteria were met by 6,613 continuously enrolled diabetic patients.

We limited the study sample to continuously enrolled diabetic patients who had at least 2 measurements of fasting plasma glucose and glycemic control in order to evaluate the annual variability during follow-up period.

Measurement

Hypertension

Blood pressure was measured by a mercury sphygmomanometer in the sitting position. Subjects were considered to have high blood pressure if the average of three readings exceeded 130 mmHg Systolically and/or 85 mmHg diastolically (Adult Treatment Panel III, 2001).

Biochemical Markers

Urine test consists of protein on urinalysis and 24-hour urinary protein excretion. Blood was drawn with minimal trauma from an antecubital vein in the morning after a 12-hour overnight fasting and was sent for analysis within four hours of blood collection. Biochemical markers such as cholesterol, triglyceride, fasting glucose, creatinine, and uric acid were analyzed by a biochemical autoanalyzer (Beckman Cou, Fullerton, CA, USA) at the Department of Clinical Laboratory of China Medical University Hospital. Urinary creatinine (Jaffe's kinetic method) and albumin (colorimetyl bromcresol purple) were measured by an auto-analyser. The interassay precision coefficient of variation was <3.0%. The clinical cutpoints for defining abnormality were given below:

Anthropometric Index & Obesity

Weight and height were measured during physical check-up. Body mass index (BMI) was derived from the formula of weight (kg) ÷ $(\text{height})^2$ (m^2). BMI≥24 was defined as overweight; BMI≥30 was defined as overweight.

Diabetic Control

Diabetic control is measured by hemoglobin A_1C (glycosylated hemoglobin, HbA1c), which is one of several forms of hemoglobin A that results from the nonenzymatic attachment of glucose to hemoglobin A.

Measures of annual variability for fasting plasma glucose and glycemic control

Three measures of variability for fasting plasma glucose (FPG) and HbA_{1c} will be used: standard deviation (SD), coefficient of variation (CV), and slope of repeated measurements (S). Thus, there are a total 6 variability measures: FPG-SD, FPG-CV, FPG-S, HbA_{1c}-SD, HbA_{1c}-CV, and HbA_{1c}-S. Annual measurements of FPG and HbA_{1c} for each patient in the electronic records will be collected and analyzed. SD is a well accepted measure of variability. CV measures the relative variability (CV=SD*100/mean). In addition to these 6 measures of variation, annual mean and maximum value in each patient will be also determined (FPG-Mean, FPG-Max, HbA_{1c}-Mean, HbA_{1c}-Max).

Sociodemographic Factors

Age, gender, employment, education, and family history for diabetes, hypercholesterolemia, and hypertension were collected in the dataset of SCDM program.

Medication History for Co-morbidity

The information for use of pharmacologic (antihypertensive agents, lipid-lowering medicines, and aspirin), etc will be derived from the dataset of SCDM program.

Diabetic Complications

Complications consist of foot ulcer, retinopathy or macular edema, hypertension, nephropathy, ischemic heart disease, myocardial infarction, and stroke. Macrovascular

complications tend to affect the heart (coronary artery disease [CAD]), the central nervous system (cerebrovascular disease), and the lower limbs (peripheral vascular disease). The definitions of diabetic complications are defined as follows:

Treatment for Diabetes

Types of treatment such as types of oral hypoglycemic agents (including doses) and insulin therapy were extracted from medical record.

Duration of Diabetes

Duration of diabetes is defined as the time interval between the time point of first diagnosis and the time point of being recruited.

Vital Status Ascertainment

The vital status of all persons who are eligible for inclusion criteria will be obtained via linkage with Death Dataset of National Health Department (2002-2007). The precise date of death was used to calculate survival time from study entry. Those whose status was not confirmed were censored. In addition all-cause death, we will group deaths into 7 major categories using ICD-9 codes. The 7 categories are cardiovascular disease (CVD) (ICD-9:53-74), cancer (ICD-9:19-43), diabetes (ICD-9:46), kidney diseases (ICD-9:97-113), chronic respiratory disease (ICD-9:82-86), acute respiratory and infectious disease(ICD-9:1-18,76-81,87-89), and all other diseases (all other numbers not in the above).

Statistical Analysis

Estimation of mortality and morbidity from diabetes:

Cumulative incidence rate (CIR) was be used to estimate the mortality and incidence of diabetic complications.

The formula for CIR is defined as follow:

$$\text{CIR} = \frac{\textit{Number of death or new cases of a disease during given time period}}{\textit{Number of total persons or persons at risk}}$$

Association of variability of glucose control with mortality and morbidity from diabetes:

Standard deviation, coefficient of variation, and slope of simple linear regression will be used to estimate the variability of glucose control. Pearson correlation coefficient will be used to examine correlations between two consecutive years' variability for glucose control. Student's t test and analysis of variance (ANOVA) will be employed to examine whether the annual variability of glucose control differ across various sociodemographic and clinical groups.

To assess the association of annual variability of glucose control with subsequent year of all-cause mortality and incidence rates of diabetic complication, measures of variability of glucose control (FPG-SD, FPG-CV, FPG-S, HbA_{1c}-SD, HbA_{1c}-CV, and HbA_{1c}-S) will be classified into 3 categories according to tertiles. Simple statistical analysis such as the Chi-square test will first be employed and Cox's proportional hazard models will be further applied to test the contribution or explanatory effects of variability of glucose control on mortality and incidence of diabetic complication by adjusting for sociodemographic and clinical factors. At last, time-dependent Cox's proportional hazard model will used to test the overall effect of annual variability of glucose control on mortality and incidence of diabetic complication. The time-dependent Cox's proportional hazard model is as follows:

$$H(\mathrm{t}, \mathrm{x}) = \mathrm{h}_0(\mathrm{t}) * \exp(\alpha + \beta_1 age + \beta_2 g\mathrm{ender} + \beta_3 \mathrm{variability\ of\ glucose\ control}$$

$$+ \beta_4 \mathrm{variability\ of\ glucose\ control} * \mathrm{t} + \sum_{j=5}^{p} \beta_j X_j$$

Results

The distributions of sociodemographic factors, life style behaviors, diabetes related variables and drug related variables in diabetic patients enrolled in SCDM program of a medical center are summarized in Table 1, and the prevalence and incidence rates of acute and chronic diabetic complications are in Table 2. The overall prevalence was highest for peripheral neuropathy (15.27%) and next was for nephropathy (9.11%) and myocardial infarction (7.84%). The incidence rates was highest for nephropathy (15.55%), and next was peripheral neuropathy (10.27%) and neuropathy (9.04%).

Table 3 shows the hazard ratios (HRs) of developing acute and chronic diabetic complications according to various indicators of fasting plasma glucose (FPG). Mean annual FPG (FPG-M), FPG-SD, FPG-CV, and FPG-S significantly predict incidence of nephropathy, after adjusting for age and gender. Adjusted HRs for the top tertile of FPG-M, FPG-SD, FPG-CV, and FPG-S were 1.37 (95% CI 1.16-1.62), 2.25 (1.89-2.67), 2.21 (1.86-2.63), and 1.20 (1.02-1.41), respectively. There were also significant linear trend for FPG-M, FPG-SD, FPG-CV, and FPG-S (p values for trend were 0.002, <0.0001, <0.0001 and 0.03, respectively). Only FPG-SD and FPG-CV can predict incidence of DKA, severe hypoglycemia, stroke, and coronary artery disease (CAD). Adjusted HRs for the top tertile of FPG-SD and FPG-CV were 3.57 (1.16-10.94), and 4.04 (1.34-12.18) for DKA; 2.91 (1.30-6.54), and 3.27 (1.48-7.25) for severe hypoglycemia; 1.99 (1.14-3.50) and 2.18 (1.22-3.89) for stroke; and 2.00 (1.21-3.30) and 2.12 (1.29-3.51) for CAD. FPG-M, FPG-SD, FPG-CV, and FPG-S significantly predict incidence of myocardial infarction, peripheral neuropathy, neuropathy, and nephropathy. There were also significant linear trend for FPG-M, FPG-SD, FPG-CV, and FPG-S except for FPG-M for myocardial infarction and FPG-S for stroke, peripheral neuropathy and neuropathy. FPG-M, FPG-SD, and FPG-CV significantly predict all-cause mortality. Adjusted HRs for the top tertile of FPG-M, FPG-SD, and FPG-CV were 1.95 (1.55-2.46), 3.41 (2.63-4.43), and 3.58 (2.73-4.69), respectively. Their linear trends were also all significant (all p<0.0001).

Table 4 shows the hazard ratios (HRs) of developing acute and chronic diabetic complications according to various indicators of HbA1c. Mean annual HbA1c (HbA1c-M), HbA1c-SD, HbA1c-CV, and HbA1c-S only significantly predict incidence of nephropathy, after adjusting for age and gender. Adjusted HRs for the top tertile of HbA1c-M, HbA1c-SD, HbA1c-CV, and HbA1c-S were 1.68 (95% CI 1.42-1.98), 1.40 (1.18-1.67), 1.30 (1.09-1.54), and 1.23 (1.04-1.45), respectively. There were also significant linear trend for HbA1c-M, HbA1c-SD, HbA1c-CV, and HbA1c-S (p values for trend were <0.001, <0.0001, <0.0001 and 0.02, respectively). Only HbA1c-M can predict incidence of HHNK (HR for top tertile: 3.25, 1.73-6.13) and myocardial infarction (HR for top tertile: 1.40, 1.02-1.93), while HbA1c-S can predict the incidence of Severe Hypoglycemia (HR for top tertile: 2.60, 1.10-6.11) and CAD (HR for top tertile: 1.78, 1.06-2.97). HbA1c-M, HbA1c-SD, and HbA1c-CV can predict incidence of peripheral neuropathy and neuropathy. Adjusted HRs for the top tertile of HbA1c-M, HbA1c-SD, and HbA1c-CV were 1.75 (1.42-2.16), 1.37 (1.11-1.68) and 1.34 (1.09-1.64) for peripheral neuropathy; 2.36

(1.89-2.94), 2.00 (1.60-2.49) and 1.67 (1.35-2.07) for neuropathy. HbA1c-M, HbA1c-SD, HbA1c-CV, and HbA1c-S can predict all-cause mortality. Adjusted HRs for the top tertile of HbA1c-M, HbA1c-SD, HbA1c-CV and HbA1c-S were 2.70 (2.01-3.62), 1.66 (1.23-2.22), 1.52 (1.12-2.05), and 0.73 (0.59-0.90), respectively. Their linear trends were also all significant (all $p<0.001$).

Table 1. Distributions of sociodemographic factors, life style behaviors, diabetes related variables s and drug related variables in diabetic patients enrolled in Share Care Disease Management program of a medical center

	Diabetic patients enrolled in Share Care Disease Management program of a medical center (N=6613)	
Variables	N	%
Sociodemographic factors		
Gender		
Male	3272	49.88
Female	3288	50.12
Age (yrs)†	57.80±13.15	
Life style behaviors		
Smoking		
No	5453	82.46
Yes	1160	17.54
Number of tobacco per day	20.27±13.33	
Alcohol drinking		
No	5962	90.16
Yes	651	9.84
Alcohol drinking per week (cc)†	687.18±1553.88	
Time of blood test per week†	1.17±3.90	
Time of urinalysis per week†	0.10±0.95	
Diabetes related variables		
Diabetes medical history(yrs)†	6.78±7.10	
Drug related variables		
Central nervous system	16	0.24
Cardiovascular drug	1071	16.20
Kidney drug	9	0.14
Hypotensive agent	2795	42.27
Vasodilating agent	10	0.15
Type of DM treatment		
Oral hypoglycemic drug	5327	80.55
Treatment period (yrs)†	6.53±7.20	
Inject insulin	216	3.27
Treatment period (yrs)†	3.99±5.93	
Both	648	9.80
Both not	422	6.38

†:mean±SD

Table 2. The prevalence and incidence rates of acute and chronic complications in diabetic patients enrolled in SCDM

Complication	N	Prevalence (%)	95% CI	Incidence (%)	95% CI
DKA	6613	1.56	1.31-1.80	0.49	0.32-0.66
HHNK	6613	1.98	1.70-2.26	1.10	0.84-1.35
Severe Hypoglycemia	6613	2.15	1.86-2.44	0.82	0.60-1.04
Stroke	6613	6.80	6.30-7.31	1.58	1.27-1.89
Coronary artery disease	6613	6.30	5.81-6.78	1.70	1.38-2.02
Myocardial infarction	6613	7.84	7.30-8.38	4.35	3.84-4.86
Peripheral neuropathy	6613	15.27	14.55-15.99	10.72	9.91-11.52
Intermittent claudication	6613	1.49	1.25-1.74	0.86	0.64-1.08
Neuropathy	6613	7.54	7.01-8.07	9.04	8.33-9.76
Nephropathy	6613	9.11	8.53-9.68	15.55	14.63-16.46

Table 3. The hazard ratios (HRs) of developing acute and chronic diabetic complications according to various indicators of fasting plasma glucose (FPG)

	FPG-M		P for trend	FPG-SD		P for trend	FPG-CV		P for trend	FPG-S		P for trend
	138.67<Q2≦166.42	Q3>166.42		21.74<Q2≦42.11	Q3>42.11		14.97<Q2≦26.16	Q3>26.16		-28.13<Q2≦15.44	Q3>15.44	
DKA												
crude	0.95 (0.38-2.39)	1.40 (0.59-3.33)	0.43	2.31 (0.82-6.56)	2.78 (0.99-7.80)	0.05	1.99 (0.68-5.81)	3.19* (1.16-8.77)	0.02	0.67 (0.28-1.61)	1.01 (0.45-2.30)	0.96
adjusted	1.09 (0.42-2.83)	1.63 (0.66-3.99)	0.28	2.98 (0.96-9.25)	3.57* (1.16-10.94)	0.03	2.56 (0.80-8.17)	4.04* (1.34-12.18)	0.01	0.60 (0.24-1.48)	1.02 (0.45-2.32)	0.93
HHNK												
crude	1.75 (0.91-3.35)	2.22* (1.18-4.18)	0.01	2.03 (0.92-4.48)	5.01*** (2.44-10.29)	<0.0001	1.55 (0.67-3.58)	5.60*** (2.74-11.43)	<0.0001	0.89 (0.50-1.59)	1.06 (0.60-1.87)	0.84
adjusted	1.95 (1.00-3.79)	2.53** (1.32-4.86)	0.005	1.93 (0.87-4.30)	5.09*** (2.48-10.45)	<0.0001	1.53 (0.66-3.53)	5.43*** (2.66-11.09)	<0.0001	0.90 (0.50-1.62)	1.10 (0.61-1.96)	0.74
Severe Hypoglycemia												
crude	1.31 (0.65-2.60)	1.41 (0.71-2.80)	0.34	2.58* (1.14-5.82)	3.08** (1.38-6.89)	0.007	2.27 (0.99-5.21)	3.49** (1.58-7.71)	0.001	0.56 (0.29-1.07)	0.68 (0.36-1.29)	0.21
adjusted	1.31 (0.66-2.61)	1.37 (0.68-2.75)	0.39	2.50* (1.11-5.65)	2.91** (1.30-6.54)	0.01	2.14 (0.93-4.93)	3.27** (1.48-7.25)	0.003	0.53 (0.28-1.03)	0.62 (0.32-1.19)	0.13
Stroke												
crude	1.15 (0.69-1.93)	1.36 (0.82-2.27)	0.24	1.78* (1.03-3.07)	1.88* (1.09-3.26)	0.03	2.07* (1.18-3.63)	2.20** (1.25-3.86)	0.008	0.60* (0.35-0.92)	0.68 (0.42-1.10)	0.10
adjusted	1.28 (0.75-2.17)	1.58 (0.94-2.66)	0.08	1.90* (1.09-3.31)	1.99* (1.14-3.50)	0.02	2.16** (1.21-3.84)	2.18** (1.22-3.89)	0.01	0.54* (0.33-0.88)	0.68 (0.42-1.11)	0.11
Coronary artery disease												
crude	1.53 (0.95-2.48)	1.28 (0.77-2.14)	0.35	1.39 (0.83-2.33)	1.84* (1.13-3.01)	0.01	1.40 (0.83-2.37)	2.05** (1.25-3.36)	0.004	1.24 (0.76-2.00)	1.14 (0.69-1.87)	0.64
adjusted	1.72* (1.05-2.80)	1.48 (0.89-2.48)	0.14	1.50 (0.89-2.51)	2.00** (1.21-3.30)	0.006	1.47 (0.86-2.50)	2.12** (1.29-3.51)	0.003	1.16 (0.71-1.88)	1.13 (0.68-1.86)	0.65
Myocardial infarction												
crude	1.44* (1.06-1.96)	1.32 (0.96-1.81)	0.09	1.28 (0.94-1.73)	1.39* (1.02-1.89)	0.04	1.09 (0.80-1.49)	1.36* (1.01-1.83)	0.04	1.33 (0.98-1.81)	1.28 (0.93-1.75)	0.15
adjusted	1.46* (1.07-1.98)	1.34 (0.98-1.85)	0.08	1.28 (0.94-1.74)	1.40* (1.03-1.91)	0.03	1.08 (0.79-1.48)	1.36* (1.01-1.84)	0.04	1.29 (0.95-1.76)	1.25 (0.91-1.71)	0.19
Peripheral neuropathy												
crude	1.10 (0.90-1.35)	1.33** (1.09-1.62)	0.005	1.80*** (1.45-2.23)	2.30*** (1.86-2.84)	<0.0001	2.06*** (1.66-2.56)	2.43*** (1.95-3.02)	<0.0001	0.84 (0.69-1.02)	0.87 (0.71-1.06)	0.16
adjusted	1.15 (0.94-1.41)	1.41** (1.15-1.72)	0.0009	1.81*** (1.46-2.25)	2.37*** (1.91-2.93)	<0.0001	2.07*** (1.66-2.58)	2.46*** (1.98-3.05)	<0.0001	0.85* (0.69-0.98)	0.85 (0.69-1.04)	0.11
Intermittent claudication												
crude	1.39 (0.70-2.75)	1.58 (0.80-3.10)	0.19	1.94 (0.97-3.89)	1.68 (0.82-3.46)	0.18	2.30* (1.09-4.83)	2.32* (1.10-4.90)	0.03	0.82 (0.44-1.55)	0.88 (0.46-1.67)	0.69
adjusted	1.47 (0.74-2.91)	1.72 (0.88-3.40)	0.12	1.95 (0.98-3.90)	1.71 (0.83-3.52)	0.17	2.24* (1.07-4.71)	2.25* (1.07-4.76)	0.04	0.78 (0.41-1.48)	0.86 (0.45-1.63)	0.64
Neuropathy												
crude	1.33* (1.06-1.66)	1.95*** (1.57-2.42)	<0.0001	1.84*** (1.44-2.34)	2.88*** (2.29-3.63)	<0.0001	1.83*** (1.43-2.33)	2.93*** (2.32-3.68)	<0.0001	0.78* (0.64-0.96)	0.91 (0.74-1.11)	0.37
adjusted	1.38** (1.10-1.74)	2.10*** (1.69-2.60)	<0.0001	1.86*** (1.46-2.37)	2.99*** (2.37-3.77)	<0.0001	1.84*** (1.44-2.35)	2.97*** (2.35-3.74)	<0.0001	0.75** (0.61-0.93)	0.89 (0.72-1.09)	0.28
Nephropathy												
crude	1.09 (0.92-1.28)	1.25** (1.06-1.48)	0.007	1.51*** (1.27-1.81)	2.12*** (1.79-2.52)	<0.0001	1.53*** (1.28-1.83)	2.16*** (1.82-2.57)	<0.0001	1.07 (0.91-1.25)	1.22* (1.03-1.43)	0.01
adjusted	1.13 (0.96-1.34)	1.37*** (1.16-1.62)	0.0002	1.56*** (1.31-1.86)	2.25*** (1.89-2.67)	<0.0001	1.57*** (1.31-1.87)	2.21*** (1.86-2.63)	<0.0001	1.01 (0.86-1.19)	1.20* (1.02-1.41)	0.03
All cause mortality												
crude	0.65** (0.49-0.86)	1.65*** (1.31-2.07)	<0.0001	1.34 (0.99-1.81)	3.27*** (2.52-4.24)	<0.0001	1.56** (1.15-2.12)	3.71*** (2.83-4.85)	<0.0001	0.59*** (0.48-0.72)	0.97 (0.81-1.16)	0.71
adjusted	0.75* (0.56-0.99)	1.95*** (1.55-2.46)	<0.0001	1.38* (1.02-1.86)	3.41*** (2.63-4.43)	<0.0001	1.59** (1.17-2.16)	3.58*** (2.73-4.69)	<0.0001	0.55*** (0.45-0.68)	0.96 (0.80-1.15)	0.63

The model adjusted for age and gender; *:p<0.05; **:p<0.01; ***:p<0.001.

Table 4. The hazard ratios (HRs) of developing acute and chronic diabetic complications according to various indicators of HbA1c.

	HbA_{1c}-M			HbA_{1c}- SD			HbA_{1c}-CV			HbA_{1c}-S		
	7.13<Q2≦8.23	Q3>8.23	P for trend	0.38<Q2≦0.79	Q3>0.79	P for trend	5.08<Q2≦9.91	Q3>9.91	P for trend	-1.07<Q2≦0.22	Q3>0.22	P for trend
DKA												
crude	1.01 (0.40-2.56)	1.30 (0.54-3.13)	0.56	0.66 (0.26-1.70)	1.07 (0.47-2.48)	0.88	0.74 (0.30-1.84)	1.98 (0.42-2.32)	0.95	1.53 (0.61-3.84)	1.57 (0.62-3.98)	0.36
adjusted	1.16 (0.45-3.01)	1.50 (0.60-3.74)	0.38	0.74 (0.28-1.94)	1.18 (0.50-2.80)	0.70	0.83 (0.33-2.09)	1.08 (0.45-2.60)	0.87	1.47 (0.58-3.75)	1.62 (0.64-4.12)	0.32
HHNK												
crude	1.43 (0.70-2.92)	3.12*** (1.66-5.86)	0.0001	1.40 (0.76-2.58)	1.67 (0.92-3.04)	0.09	1.08 (0.60-1.97)	1.40 (0.79-2.49)	0.25	1.47 (0.77-2.82)	1.78 (0.94-3.39)	0.08
adjusted	1.46 (0.72-2.99)	3.25*** (1.73-6.13)	0.0001	1.54 (0.83-2.87)	1.88* (1.02-3.46)	0.04	1.16 (0.64-2.13)	1.56 (0.87-2.79)	0.14	1.38 (0.72-2.65)	1.71 (0.90-3.25)	0.10
Severe Hypoglycemia												
crude	1.35 (0.71-2.59)	0.92 (0.45-1.88)	0.84	0.97 (0.49-1.92)	1.12 (0.58-2.18)	0.73	1.36 (0.70-2.67)	1.14 (0.56-2.31)	0.71	3.00* (1.30-6.95)	2.78* (1.18-6.55)	0.03
adjusted	1.29 (0.67-2.49)	0.96 (0.47-1.97)	0.93	1.06 (0.53-2.13)	1.31 (0.67-2.57)	0.44	1.48 (0.75-2.94)	1.36 (0.66-2.78)	0.40	2.65* (1.14-6.16)	2.60* (1.10-6.11)	0.04
Stroke												
crude	0.94 (0.56-1.59)	1.10 (0.67-1.83)	0.70	1.14 (0.68-1.91)	1.17 (0.70-1.97)	0.56	1.45 (0.85-2.47)	1.44 (0.84-2.47)	0.20	1.18 (0.70-1.99)	1.38 (0.82-2.31)	0.22
adjusted	1.01 (0.59-1.72)	1.28 (0.76-2.14)	0.36	1.36 (0.80-2.31)	1.35 (0.79-2.30)	0.28	1.70 (0.98-2.93)	1.67 (0.95-2.91)	0.08	1.03 (0.61-1.74)	1.20 (0.71-2.03)	0.47
Coronary artery disease												
crude	1.00 (0.63-1.60)	0.87 (0.53-1.41)	0.57	1.03 (0.64-1.64)	0.92 (0.57-1.50)	0.76	0.93 (0.59-1.49)	0.85 (0.53-1.38)	0.52	1.46 (0.86-2.48)	1.90* (1.14-3.17)	0.01
adjusted	1.09 (0.68-1.74)	1.00 (0.62-1.64)	0.98	1.14 (0.71-1.83)	1.05 (0.64-1.71)	0.84	1.00 (0.63-1.60)	0.95 (0.59-1.55)	0.86	1.31 (0.77-2.22)	1.78* (1.06-2.97)	0.02
Myocardial infarction												
crude	1.50* (1.10-2.04)	1.36 (0.99-1.87)	0.07	1.31 (0.98-1.76)	0.88 (0.63-1.21)	0.48	1.16 (0.87-1.54)	0.84 (0.61-1.15)	0.32	1.43* (1.04-1.96)	1.38* (1.00-1.90)	0.06
adjusted	1.52** (1.11-2.07)	1.40* (1.02-1.93)	0.04	1.33 (0.99-1.78)	0.93 (0.67-1.28)	0.73	1.17 (0.87-1.56)	0.89 (0.65-1.23)	0.54	1.36 (1.00-1.87)	1.33 (0.97-1.84)	0.10
Peripheral neuropathy												
crude	1.43*** (1.16-1.77)	1.64*** (1.34-2.02)	<0.0001	1.31** (1.07-1.60)	1.27* (1.04-1.56)	0.02	1.23* (1.01-1.51)	1.25* (1.02-1.54)	0.03	1.21 (0.99-1.49)	1.21 (0.98-1.49)	0.08
adjusted	1.50*** (1.22-1.85)	1.75*** (1.42-2.16)	<0.0001	1.39** (1.13-1.70)	1.37** (1.11-1.68)	0.003	1.29* (1.06-1.58)	1.34** (1.09-1.64)	0.005	1.15 (0.94-1.41)	1.16 (0.94-1.43)	0.20
Intermittent claudication												
crude	1.59 (0.79-3.20)	1.71 (0.85-3.41)	0.14	0.80 (0.40-1.60)	1.29 (0.69-2.40)	0.41	0.95 (0.49-1.85)	1.12 (0.59-2.13)	0.74	1.27 (0.65-2.50)	1.39 (0.71-2.73)	0.35
adjusted	1.66 (0.83-3.34)	1.92 (0.96-3.83)	0.07	0.85 (0.42-1.71)	1.42 (0.76-2.66)	0.26	0.99 (0.51-1.92)	1.22 (0.64-2.33)	0.55	1.17 (0.59-2.30)	1.29 (0.66-2.54)	0.46
Neuropathy												
crude	1.38** (1.09-1.75)	2.15*** (1.72-2.68)		1.39** (1.11-1.75)	1.84*** (1.48-2.29)		1.17 (0.93-1.46)	1.56*** (1.26-1.93)		0.91 (0.74-1.12)	1.03 (0.83-1.26)	0.78
adjusted	1.45** (1.15-1.84)	2.36*** (1.89-2.94)	<0.0001	1.48*** (1.18-1.86)	2.00*** (1.60-2.49)	<0.0001	1.22 (0.98-1.53)	1.67*** (1.35-2.07)	<0.0001	0.87 (0.70-1.07)	0.98 (0.79-1.21)	0.88
Nephropathy												
crude	1.10 (0.93-1.31)	1.48*** (1.25-1.75)		1.25** (1.06-1.48)	1.28** (1.08-1.51)		1.21* (1.03-1.43)	1.20* (1.01-1.42)		1.28** (1.09-1.51)	1.29** (1.10-1.53)	0.003
adjusted	1.16 (0.98-1.39)	1.68*** (1.42-1.98)	<0.0001	1.36*** (1.14-1.61)	1.40*** (1.18-1.67)	<0.0001	1.28** (1.08-1.52)	1.30** (1.09-1.54)	<0.0001	1.20* (1.01-1.41)	1.23* (1.04-1.45)	0.02
All cause mortality												
crude	1.16 (0.84-1.62)	2.22*** (1.66-2.98)	<0.0001	1.20 (0.88-1.63)	1.56** (1.17-2.09)	0.003	1.35 (1.00-1.82)	1.51** (1.12-2.04)	0.007	0.61*** (0.48-0.76)	0.79* (0.64-0.98)	0.03
adjusted	1.29 (0.93-1.80)	2.70*** (2.01-3.62)	<0.0001	1.30 (0.95-1.76)	1.66*** (1.23-2.22)	0.007	1.37* (1.01-1.85)	1.52** (1.12-2.05)	0.007	0.56*** (0.44-0.70)	0.73** (0.59-0.90)	0.004

The model adjusted for age and gender; *:p<0.05; **:p<0.01; ***:p<0.001.

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計畫成果自評

本研究為單一族群之回顧性追蹤研究，共收集6,613 位第二型糖尿病患者資料，描述加入中國醫藥大學附設醫院糖尿病論質計酬改善方案計畫的第二型糖尿病患者之糖尿病併發症包括足部病變、視網膜病變、高血壓、腎病變、周邊神經病變、缺血性心臟病、心肌梗塞和中風的健康狀態變化情形；估算其併發症盛行率與發生率；並完成分析糖尿病患者血糖控制情形(包括斷食飯前血糖和糖化血色素)每年之變異，並評估每年血糖控制變異情形與死亡率和併發症發生率間之相關，完全達成計畫書的目標。

行政院國家科學委員會補助國內專家學者出席國際學術會議報告

98 年 7 月 10 日

附件三

報告人姓名	李采娟	服務機構及職稱	中國醫藥大學生物統計研究所 教授
時間 會議地點	98/07/05~98/07/09 France	本會核定補助文號	NSC 97-2314-B-039-019
會議名稱	(中文)第十九屆世界老年學暨老年醫學會 (英文) 19th IAGG World Congress of Gerontology and Geriatrics		
發表論文題目	(中文) 年齡對腎絲球過濾速率的影響－以台灣都會區成年人為樣本 (英文)Effect of age on renal function estimated by glomerular filtration rate in a Taiwanese Metropolitan Adult Population		

報告內容應包括下列各項：

一、參加會議經過

七月五日到大會報到，並聆聽了「公立長期照護服務計畫的品質和照護工作者(Care workers and quality of services in public long-term care program)」及「治療老人的骨質疏鬆：醫療需求和合乎邏輯的解答(Treating osteoporosis in the elderly: a medical need, a logical answer)」。第二天(7/6)參加了由我共同指導學生之口頭報告「代謝症候群/糖尿病（Metabolic syndrome/Diabete）」場次，報告主題為「Elderly is associated with higher prevalence of microalbuminuria in a Taiwanese Metropolitan Adult Population」。七月七日我有一篇共同作者的海報展示為「Association between adiponectin gene variants in subjects of metabolic syndrome in elderly Taiwanese -A Hospital-based Study」，便參觀和瀏覽了當天展示的海報；隔天(7/8)，亦有第一作者和共同作者的兩篇海報展出，分別是「Effect of age on renal function estimated by glomerular filtration rate in a Taiwanese Metropolitan Adult Population」和「Elderly is associated with higher prevalence of metabolic syndrome in a Taiwanese Metropolitan Adult Population」，除了觀看別的作者海報外，並參加「肌肉無力：定義危險因子和治療(Sarcopenia: definitions, risk factors and treatment)」場次。

二、與會心得

在 19th IAGG 會議中，發表近年來本研究團隊在代謝性症候群研究成果，還參與大會多場熱門主題會議，吸收各類中老年醫藥衛生相關的研究經驗與研究成果，並得到當前最新健康資訊。在與各國醫學領域專家相互討論切磋時，明瞭世界各地學者最關心的健康議題，並互留聯絡方法，期望未來還有機會能互訪與交流。在此次世界會議中所獲得資訊，未來將活用於課堂教學與研究上。

三、考察參觀活動(無是項活動者省略)

四、建議

建議政府或學術單位能多舉辦大型世界健康會議，或多鼓勵及補助學術研究人員參與國際學術研討會，以期能增進國內醫藥衛生研究人員見聞，並為世界醫藥衛生盡一份心力。

五、攜回資料名稱及內容

19th IAGG 大會節目手冊與論文摘要

六、其他