

Thailand Diabetic Registry Cohort: Predicting Death in Thai Diabetic Patients and Causes of Death

Thongchai Pratipanawatr MD*, Petch Rawdaree MD**,
Thanya Chetthakul MD***, Pongamorn Bunnag MD***,
Chardpraorn Ngarmukos MD***, Yupin Benjasuratwong MD****,
Rattana Leelawatana MD*****, Natapong Kosachunhanun MD*****,
Nattachet Plengvidhya MD*****, Chaicharn Deerochanawong MD*****,
Sompongse Suwanwalaikorn MD*****, Sirinate Krittiyawong MD*****,
Sirima Mongkolsomlit BSc*****, Chulaluk Komoltri PhD*****

* Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

** Department of Medicine, Bangkok Metropolitan Medical College and Vajira Hospital, Bangkok, Thailand

*** Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

**** Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand

***** Department of Medicine, Prince of Songkla University, Songkhla, Thailand

***** Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

***** Department of Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

***** Department of Medicine, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand

***** Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

***** Theptarin General Hospital, Bangkok, Thailand

***** Faculty of Public Health, Thumasart University, Phatumthani, Thailand

***** Division of Research and Development, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Introduction: The prevalence of type 2 diabetes in Thailand is 9.8 percent which is double the number forecast by World Health Organization. There is inadequate information to statistically represent all Thai diabetic patients for their causes of death.

Objective: To determine the clinical characteristics that predicted death and causes of death in Thai diabetic patients.

Material and Method: This prospective cohort was a 3-year follow-up study of the Thai Diabetes Registry project done between April, 2003, and February, 2006, which registered 9,419 diabetic patients attending 11 diabetic clinics in tertiary medical centers in Bangkok and major provinces of Thailand. The dead or alive status (99.5%) was determined. The causes of death were defined by reviewing the medical records.

Results: Of the 9,370 diabetic patients registered, 425 patients died, 1.84 percent per year. There was an increased risk of death associated with age, type of healthcare plan, lower education, insulin use, smoking, history of coronary artery disease and cerebrovascular disease, serum creatinine and high HbA_{1c}. Lipid-lowering medication and metformin decreased the risk of death. Cardiovascular disease, infection and cancer were the prevalent causes of death.

Conclusion: The present study showed risk factors that influenced death and causes of death in Thai diabetics.

Keywords: Death rate, Diabetes mellitus, Risk factors of death, Causes of Death.

J Med Assoc Thai 2010; 93 (Suppl. 3): S12-20

Full text. e-Journal: <http://www.mat.or.th/journal>

Diabetes mellitus is epidemic worldwide owing to the growing elderly population and to lifestyle changes. The WHO has predicted a doubling of the number of diabetic patients over the next twenty years especially in developing countries in Asia⁽¹⁾. Increased caloric intake and sedentary lifestyles are precursors

Correspondence to: Pratipanawatr T, Department of Medicine, Faculty of Medicine, Khon Kaen University, Mitrapap Road, Khon Kaen 40002, Thailand. E-mail: thongcha@kku.ac.th

to abdominal obesity, which is associated with the development of diabetes mellitus⁽²⁾. As a rapidly industrializing and modernizing country, Thailand is inevitably experiencing this growing public health problem. According to the Inter-Asia Study, the prevalence of type 2 diabetes in Thailand is 9.8 percent⁽³⁾ which is double the number forecast by WHO.

Evidence from studies on Caucasians shows that cardiovascular disease (CVD) is 2- to 4-fold greater

in diabetics⁽⁴⁾ and more than half die of CVD⁽⁵⁻⁷⁾. Coronary artery disease is the most common type of CVD in diabetics, with a mortality risk equivalent to non-diabetic subjects who have a history of coronary artery disease⁽⁸⁾. Patients who have both diabetes and a history of coronary artery disease are at an even greatest risk. Differences in ethnicity, economic status and the healthcare delivery systems may affect mortality regionally and between countries.

Thailand is situated in Southeast Asia and has a rapidly developing economy strongly influenced by Asian traditions so may have some different causes and risk factors of death than those based only on the epidemiology of the West. Unfortunately, information is lacking regarding the death rate, risk factors of death and causes of death among Thai diabetic patients, which is in fact essential for decision-making and budget allocations, since resources in developing nations are even more limiting than in the West.

A small, single-center cohort-conducted in Songkla, a city in southern Thailand-showed infection, cardiovascular disease and cancer are the major causes of death; however, there is inadequate information to statistically represent all Thai diabetic patients⁽⁹⁾.

Between April and December, 2003, the Thailand Diabetic Registry Project enrolled 9,419 Thai diabetic patients to identify the characteristics of Thai diabetic patients attending tertiary care medical centers, who would then be followed-up for 2□ years in order to identify the risk factors and causes of death.

Material and Method

Setting and Subjects

This was a 3-year cohort study among the 9,419 Thai diabetes patients participating in the Diabetic Registry Project, a hospital-based study conducted between April, 2003, and February, 2006. This multi-center registry was conducted through the diabetic clinics of eleven tertiary care hospitals across Thailand. The patients were diabetics being treated in these clinics and they had given informed consent before participating in the registry. The study was approved by the ethics committees at each of the hospitals.

Baseline measurements and definitions

The registry data were recorded on a case record form while interviewing and examining the patients and reviewing their medical records. This included: demographic data; alcohol consumption, cigarette smoking, specific medications (including insulin, oral hypoglycemic agents, antihypertensive

agents, lipid-lowering agents and aspirin); pertinent parts of physical examinations; laboratory examinations performed over the 12 months prior to recruitment; and, diabetic complications verified by physicians' reports. The diagnosis of diabetes mellitus was made according to the ADA criteria⁽¹⁰⁾.

Fasting serum glucose, serum total cholesterol, HDL cholesterol (HDL-C) and triglyceride levels, glycosylated hemoglobin (HbA1c), and serum creatinine were determined by the central laboratory of each hospital using standard methods with local quality control. LDL cholesterol (LDL-C) was calculated using the Friedewald's formula.

Blood pressure was measured on the right arm after resting 5 minutes (twice, 30 seconds apart) using an automated blood pressure machine (OMRON T4). Mean values of both the systolic and diastolic blood pressure were used to define blood pressure levels. Hypertension was defined by means of blood pressure levels greater than or equal to 140/90 mmHg or the use of antihypertensive agents. Height and weight were measured in light clothing.

Smoking status was categorized as: 1) current smoker-those still smoking the day of examination or who had quit less than one year prior; 2) ex-smokers-those who had stopped smoking for at least one year; and, 3) non-smokers-those who had never smoked.

Healthcare plans were categorized as: 1) *Universal Coverage*; 2) *Social Security Welfare*; 3) *Civil Service Healthcare Plan*; and, 4) patients paying by themselves and/or through private health insurance. The *Civil Service Healthcare Plan* is for civil servants and their families and covers all healthcare costs. *Social Security Welfare* is a healthcare plan provided workers by their employer. The *Universal Coverage Health Plan* is a government plan for persons not covered by another plan and covers only essential healthcare and not expensive care such as chronic kidney replacement.

Outcome events

The vital status of the 9,370 diabetic patients (99.5%) was determined using the database of each participating hospital and the Bureau of Registration Administration, and the Ministry of Interior. The primary outcome was death from all causes. In order to avoid inaccuracies from the death certificate, the cause of death was defined by a panel of two independent physicians after reviewing the medical records. The causes of death were categorized according to the International Classification of Disease, Tenth Revision

(ICD-10).

Death from cardiovascular disease included cardiac disease, stroke and sudden death. Coronary artery disease was recognized as myocardial infarction-*viz.*, serial electrocardiographic changes leading to development of Q waves, characteristic increase in serum myocardial markers with a suggestive clinical history or evidence at autopsy of new or recent infarction-while unstable angina pectoris was defined by a clinical history of acute coronary syndrome without definite criteria of myocardial infarction. Stroke was categorized into ischemic and hemorrhagic stroke by CT or MRI scan. Malignancy and infection were subcategorized according to the primary organ of malignancy or infection.

Statistical analysis

The patients were divided into two groups; dead and alive. Descriptive statistics were used. Proportions of studied variables were compared using the Chi-squared and Fisher's exact tests. Differences in mean values of studied variables were compared using the t-test and Mann-Whitney U-tests.

The crude hazard ratio was calculated to define each factor that influenced the death rate. Confounding factors were then adjusted by applied multiple Cox regression models (backward elimination) and this was calculated to define the factors that influenced the death rate. Whenever two variables were very similar and had multi-co-linearity, only one of them was included in the model. For the final Cox proportional hazard model, assessment of model adequacy was constructed and the proportional hazard assumption and goodness-of-fit were tested. Statistical analyses were performed using STATA version 9.0 (Stata Corporation, College Station TX, USA).

Results

Of the 9,370 registered diabetic patients, 425 patients died within 2.5 years of the follow-up and the time at risk was 23,071.3 person-years. The death rate among this group of diabetic patients was 1.84 percent per year. The characteristics of the live and dead patients are presented in Table 1. Differences in the treatment history between the two groups are shown in Table 2.

Factors predicting death among Thai diabetes patients

A backward elimination multiple Cox regression (keeping sex in the model) was performed.

Starting in the multiple regression model were age, sex, history of coronary artery disease and cerebrovascular disease, history of hypertension, healthcare plan, obesity, duration of diabetes, smoking status, education level, systolic and diastolic blood pressure, use of anti-diabetic agents, anti-hypertensive agents, lipid-lowering medication, aspirin, HbA_{1c}, serum creatinine and serum lipid.

In the final model, there remained age, sex, HbA_{1c}, serum creatinine, healthcare plan, education status, smoking status, previous history of coronary artery disease and cerebrovascular disease, lipid-lowering medication, insulin, and metformin (Table 3). The proportional hazard assumption and goodness-of-fit of the final model were tested. The model did not depart from the proportional hazard assumption and fit well with the authors' patient data.

The results of the final multiple Cox regression model indicate that the risk of death increased by 55% for every 10-year increase in age. The crude HR showed that females had a lower death rate by about 26%; however, the death rates for both sexes were similar when adjusted for other parameters in the final model. The analyses showed that patients who were on the *Universal Coverage Healthcare Plan* had a higher death rate than those on the *Civil Service Healthcare Plan* by almost 2-fold (HR 1.96 95% CI 1.48-2.58) (Fig. 1A).

A previous history of coronary artery disease increased the risk of death by about two-fold (HR 1.97 95% CI 1.52-2.56) (Fig. 1B), which increased to 78% (HR 1.78 95% CI 1.24-2.54) in patients who had a previous history of cerebrovascular disease (Fig. 1C). Current smokers had an increased death rate of 74%, which dropped to the level of non-smokers if they quit smoking. Having a bachelor degree or higher education was associated with a 50% lower death rate than those with less education. Kidney function, as determined by serum creatinine, was an important predictor of death in Thai diabetics. Mild to moderate kidney impairment (serum Cr between 1.5 and 3.0) increased the rate of death by 86% and severe kidney impairment (serum Cr > 3.0) by almost seven-fold (Fig. 1D).

Half of the authors' patients (55%) were taking lipid-lowering medications. Lipid-lowering medication decreased death by 50% (HR 0.56 95% CI 0.45-0.69). Interestingly, metformin was the only anti-diabetic medication that lowered the risk of death (HR 0.59 95% CI 0.47-0.74). By contrast, patients treated with insulin had a 50% increased rate of death, which may reflect the chronicity and complexity of the disease.

Table 1. Patient characteristics at entry divided by vital status at the end of study period

	Alive (%)	Dead (%)	p-value
Number	8,945	425	
Age (years)	58.9 ± 13.5	65.9 ± 11.7	<0.05
Female (%)	5,954 (66.2)	253 (59.5)	<0.05
Duration (years)	10.4 ± 7.4	13.3 ± 8.8	<0.05
BW (kg)	63.6 ± 12.7	60.9 ± 12.5	<0.05
Height (cm)	157 ± 9	158 ± 8	NS
BMI	25.6 ± 4.4	24.5 ± 4.5	<0.05
HbA1c (%)	8.2 ± 1.9	8.5 ± 2.2	<0.05
SBP (mmHg)	142.1 ± 22.7	147.7 ± 27.3	<0.05
DBP (mmHg)	78.8 ± 11.3	77.8 ± 12.4	NS
Cholesterol (mg/dL)	197.1 ± 41.4	198.6 ± 55.2	NS
TG (mg/dL)	149.7 ± 100.5	172.9 ± 180.0	<0.05
HDL(mg/dL)	54.0 ± 15.3	50.9 ± 15.6	<0.05
LDL (mg/dL)	114.5 ± 35.3	115.0 ± 45.7	NS
Serum Cr (mg/dL)	1.1 ± 0.8	1.9 ± 1.8	<0.05
≤ 1.5	7,707 (86.2)	261 (62.7)	
1.5 - 3.0	852 (9.5)	104 (25.0)	
> 3.0	386 (4.3)	60 (14.1)	
Health care plans			<0.05
Civil Service	5,028 (56.2)	228 (53.7)	
Self pay& Insurance	2,529 (28.3)	98 (23.0)	
Social welfare	523 (5.9)	17(4.0)	
Universal coverage	861 (9.7)	82 (19.3)	
Education: BSc* or higher	1,649 (18.4)	37 (8.81)	<0.05
Previous history of coronary artery disease	679 (7.6)	79 (18.7)	<0.05
Previous history of cerebrovascular disease	373 (4.2)	37 (8.7)	<0.05
Hypertension	5,646 (63.1)	303 (72.7)	<0.05
Smoking			<0.05
Non-smoking	7,179 (80.3)	308 (72.4)	
Ex-smoking	1,234 (13.8)	81 (19.1)	
Current-smoking	532 (5.9)	36 (8.5)	
Type of diabetes			NS
Type 1	409 (4.6)	14 (3.37)	
Type 2	8,461(94.6)	406 (96.7)	

*BSc = Bachelor degree

Causes of death

The medical records of the 425 dead patients were reviewed (Table 4): 58 died at home without medical attention or autopsy and had an undefined cause of death. Of the other cases, cardiovascular disease was the most common cause of death (29.0%), followed by infection (21.9%), cancer (19.5%) and chronic kidney disease (8.6%).

Coronary artery disease (86.4%) was the major cause of death from heart disease, while about 13.6% died from other heart diseases (*i.e.*, congestive heart failure, bradycardia, rupture aortic aneurysm and valvular heart disease). All but one patient had a radio-

logically-confirmed type of stroke: hemorrhagic stroke (54.8%) slightly higher than ischemic stroke (42.0%).

Among the patients who died from cancer, hepatobiliary and other gastrointestinal tract cancers (31.7%) were the most common, followed by respiratory cancer (15.9%), hematologic cancer (15.9%), gynecological cancer (7.3%), breast cancer (3.7%), head-neck cancer (3.7%) and other cancer (9.6%). Eleven patients (12.2%) died from metastatic cancer without a clear indication of the primary site.

One-third of the patients who died from infection manifested with septicemia without a definite primary site (32.6%) while respiratory tract infection

Table 2. Characteristics of treatment at entry divided by vital status at the end of study period

Treatment	Alive (%)	Dead (%)	p-value
Lipid lowering agent(statin and/or fibrate)	4,919 (55.0)	193 (45.4)	<0.05
Statin	3,981 (44.5)	157 (36.9)	<0.05
Fibrate	1,180 (13.2)	46 (10.8)	NS
Anti-diabetic agents			
Insulin	2,519 (28.2)	194 (45.7)	<0.05
Sulfonylurea	5,926 (65.9)	225 (52.9)	<0.05
Metfomin	6,191 (69.2)	182 (42.8)	<0.05
TZD	496 (5.6)	9 (2.1)	<0.05
α -Glucosidase inhibitor	616 (6.85)	17 (4.0)	<0.05
Anti-hypertensive agents			
ACE inhibitor	3,147 (35.2)	149 (35.1)	NS
ARB	718 (8.0)	43 (10.1)	NS
Beta-blocker	1,699 (19.0)	117 (27.5)	<0.05
Alpha-blocker	284 (3.2)	23 (5.4)	<0.05
Calcium channel blocker	1,920 (21.5)	125 (29.4)	<0.05
Diuretic	2,438 (27.3)	171(40.2)	<0.05
Aspirin	3,111 (34.8)	180 (42.4)	<0.05

Table 3. Crude and adjusted hazard ratio of factors effecting mortality and 95% CI.

Variables	Crude HR	Adjusted HR	95% CI	p-value
Females	0.75	0.93	0.72-1.21	NS
Age (10years)	1.58	1.55	1.40-1.70	< 0.05
Hba _{1c} (1%)	1.07	1.06	1.01-1.12	< 0.05
Serum Creatinine				
< 1.5	1	1		
1.5-3.0	3.43	1.82	1.40-2.37	< 0.05
> 3.0	10.86	6.85	4.86-9.66	< 0.05
Health plan				
Civil Service	1	1		
Self pay & Insurance	0.86	1.07	0.83-1.39	NS
Social welfare	0.73	1.04	0.58-1.85	NS
Universal coverage	2.04	1.96	1.48-2.58	< 0.05
Education				
Below BSc	1	1		
BSc or Higher	0.43	0.65	0.45-0.94	< 0.05
Smoking				
Non-smoking	1	1		
Ex-smoking	1.52	1.10	0.81-1.50	NS
Current-smoking	1.55	1.74	1.17-2.61	< 0.05
Previous history of coronary artery disease	2.60	1.97	1.52-2.56	< 0.05
Previous history of cerebrovascular disease	2.13	1.78	1.24-2.54	< 0.05
Lipid lowering agent(statin and/or fibrate)	0.69	0.56	0.45-0.69	< 0.05
Insulin	2.10	1.49	1.18-1.87	< 0.05
Metfomin	0.34	0.59	0.47-0.74	< 0.05

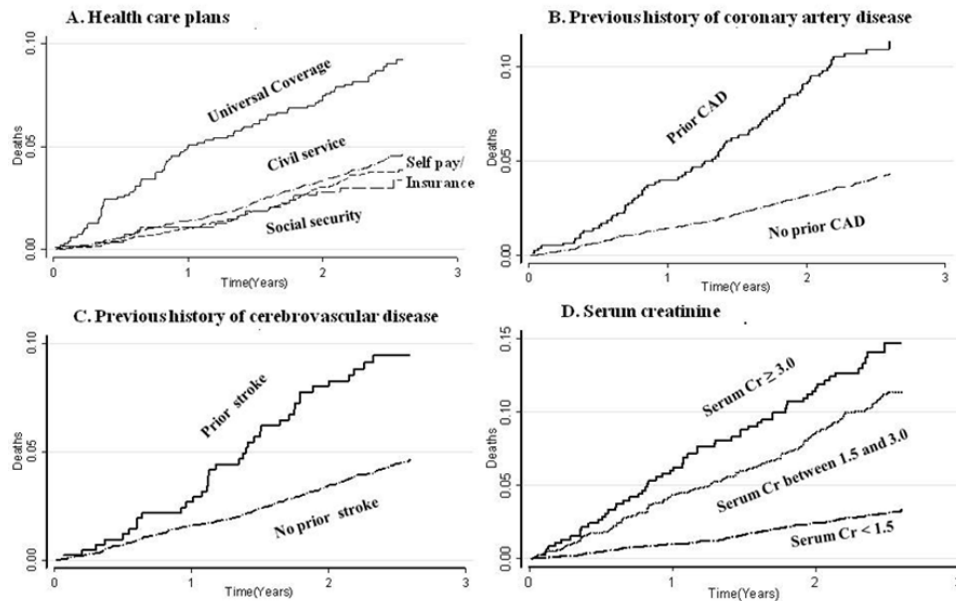


Fig. 1 Cumulative incident of death from any causes, according to, A. Health care plans, B. Previous history of coronary artery disease, C. Previous history of cerebrovascular disease, D. Serum creatinine.

Table 4. Causes of death

Disease	Dead (%)
Cardiovascular disease	122 (28.7)
- Cardiac disease	57 (13.4)
- Sudden death	31 (7.3)
- Stroke	31 (7.3)
Infection	91 (21.4)
Cancer	83 (19.5)
Chronic kidney disease	40 (9.4)
Chronic liver disease	8 (1.9)
Accident	7 (1.6)
Hyperglycemia	2 (0.5)
Hypoglycemia	2 (0.5)
Others	15 (3.5)
Undetermined	58 (13.6)
Total	425

(27.2%) was the most common defined primary site followed by urinary tract infections (14.1%), gastrointestinal tract (10.9%), skin/fascia (10.9%) and other sites infection (4.3%).

Discussion

Among the surveyed patients, 425 patients died resulting in a death rate of 1.84 patients 100⁻¹ year⁻¹.

Cardiovascular disease, infection, cancer and chronic kidney disease were the common causes of death. The major mortality risk factors were age, previous history of cardiovascular disease, being under the *Universal Healthcare Plan*, smoking, taking insulin, low education level, high HbA_{1c} and renal insufficiency. Lipid-lowering medication and metformin treatments were associated with a lower mortality.

There are at least two explanations for the authors' finding that an increased risk of mortality was associated with the *Universal Healthcare Plan*. First, patients on the *Universal Healthcare Plan* had a lower education and socioeconomic status both of which also had a higher risk of mortality. Second, these patients may have less opportunity to get beneficial treatments such as lipid-lowering agents⁽¹¹⁾ and/or kidney replacement. A further study needs to be conducted to look into the details of healthcare including admission information.

The importance of lipid-lowering medication was clear as patients who got lipid-lowering medication had about a 40% lower risk of death, consistent with previous large clinical trials^(12,13). Recent clinical trials in high-risk patients⁽¹⁴⁻¹⁶⁾ have demonstrated the benefit of aggressive lipid lowering with high doses of HMG CoA reductase inhibitors leading to more aggressive

lipid lowering strategy by American Diabetic Association. The authors' data agree with the current American Diabetic Association lipid lowering strategy: Statin therapy should be added to lifestyle therapy for diabetic patients: with overt CVD and without CVD for those who are over 40 years of age together with one or more other CVD risk factors. The primary goal is an LDL cholesterol < 100 mg/dL for diabetic individuals without overt CVD and < 70 mg/dL for individuals with overt CVD⁽¹⁷⁾.

Serum creatinine is the simplest way to evaluate kidney function. It was also an important predictor of death among Thai diabetics. Mild to moderate kidney impairment (serum Cr between 1.5 and 3.0) increased the risk of death by almost 2-fold. In the group with more severe kidney impairment (serum Cr >3.0), the risk of death increased by almost seven-fold.

Metformin was the only oral hypoglycemic agent that decreased the death rate (by about 40%) in the authors' diabetic population, in agreement with previous reports^(18,19). In obese patients with type 2 diabetes, metformin monotherapy reduced cardiovascular events as compared to those treated with sulfonylurea and insulin treatment⁽²⁰⁾. The association between insulin resistance, hyperinsulinemia, dyslipidemia and cardiovascular morbidity and mortality has been recognized for some time^(6,21). Cardiovascular-related mortality is the leading cause of death in individuals with type 2 diabetes. Metformin, which increases insulin sensitivity, should therefore have a beneficial effect on cardiovascular-related mortality outcomes in type 2 diabetes, as previously shown in the UKPDS, where metformin monotherapy reduced cardiovascular events in obese patients with type 2 diabetes compared with sulfonylurea and insulin treatment⁽²⁰⁾. The authors' findings fit well with the current guidelines of the EASD/ADA consortium that recommended metformin with lifestyle intervention as the first line of treatment⁽²³⁾.

Cardiovascular disease was the most common cause of death followed by infection and cancer; however, death from CVD seemed lower than in Caucasian populations. The authors' findings are consistent with a previous study⁽⁹⁾ that CVD death are lower than in Caucasian population. Deaths from CVD might, however, have been underestimated because the causes of death were not defined in 13.6% of the authors' patients. The variance from Caucasians may also be due to differences in genetics, socioeconomics and lifestyles of Thai diabetics. The authors' findings revealed the significant contribution of infection and

cancer in the deaths of Thai diabetic patients. Since the authors' analysis was based entirely on clinical information at the time of registry and limited by a lack of direct clinical information during the three-year follow-up period, changes in the modifiable factors (*i.e.*, level of glycemic control, blood pressure level, plasma lipid level, smoking and medication) were not taken into account.

Conclusion

The authors ascertained the risk factors of death among diabetic patients and showed the association of lipid-lowering agents and metformin in lowering the risk of death. Infection and cancer were the other important causes of death in addition to cardiovascular disease.

Acknowledgments

The present study received a grant from the National Research Council of Thailand and the Clinical Research Collaboration Network (CRCN) and was supported by the Endocrine Society of Thailand. The authors are indebted to the many staff and the nurses at each center for their contributions and Mr. Bryan Roderick Hamman and Mrs. Janice Loewen Hamman for assistance with the English-language presentation and copy editing

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. Bajaj M, Banerji MA. Type 2 diabetes in South Asians: a pathophysiologic focus on the Asian-Indian epidemic. *Curr Diab Rep* 2004; 4: 213-8.
3. Aekplakorn W, Stolk RP, Neal B, Suriyawongpaisal P, Chongsuvivatwong V, Cheepudomwit S, et al. The prevalence and management of diabetes in Thai adults: the international collaborative study of cardiovascular disease in Asia. *Diabetes Care* 2003; 26: 2758-63.
4. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *JAMA* 1979; 241: 2035-8.
5. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993; 16: 434-44.
6. DeFronzo RA, Ferrannini E. Insulin resistance. A

- multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991; 14: 173-94.
7. Geis LS, Herman WH, Smith PJ. Mortality in non-insulin dependent diabetes. In: Harris M, editor. *Diabetes in America*. 2nd ed. Bethesda, MD: National Institute of Health; 1995: 233-58.
 8. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998; 339: 229-34.
 9. Leelawattana R, Rattarasarn C, Lim A, Soonthornpun S, Setasuban W. Causes of death, incidence and risk factors of cardiovascular diseases in Thai type 2 diabetic patients: a 5 year follow-up study. *Diabetes Res Clin Pract* 2003; 60: 183-9.
 10. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care* 2003; 26: 3160-7.
 11. Pratipanawatr T, Rawdaree P, Chetthakul T, Bunnag P, Ngarmukos C, Benjasuratwong Y, et al. Thailand diabetes registry project: current status of dyslipidemia in Thai diabetic patients. *J Med Assoc Thai* 2006; 89(Suppl 1): S60-5.
 12. Collins R, Armitage J, Parish S, Sleight P, Peto R. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet* 2003; 361: 2005-16.
 13. Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, Livingstone SJ, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004; 364: 685-96.
 14. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004; 350: 1495-504.
 15. de Lemos JA, Blazing MA, Wiviott SD, Lewis EF, Fox KA, White HD, et al. Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the A to Z trial. *JAMA* 2004; 292: 1307-16.
 16. Nissen SE, Tuzcu EM, Schoenhagen P, Brown BG, Ganz P, Vogel RA, et al. Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. *JAMA* 2004; 291: 1071-80.
 17. American Diabetes Association. Standards of medical care in diabetes—2008. *Diabetes Care* 2008; 31(Suppl 1): S12-54.
 18. Johnson JA, Simpson SH, Toth EL, Majumdar SR. Reduced cardiovascular morbidity and mortality associated with metformin use in subjects with Type 2 diabetes. *Diabet Med* 2005; 22: 497-502.
 19. Johnson JA, Majumdar SR, Simpson SH, Toth EL. Decreased mortality associated with the use of metformin compared with sulfonylurea monotherapy in type 2 diabetes. *Diabetes Care* 2002; 25: 2244-8.
 20. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 1998; 352: 854-65.
 21. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* 1988; 37: 1595-607.
 23. Nathan DM, Buse JB, Davidson MB, Heine RJ, Holman RR, Sherwin R, et al. Management of hyperglycemia in type 2 diabetes: A consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* 2006; 29: 1963-72.

โครงการลงทะเบียนผู้ป่วยเบาหวานในประเทศไทย: ปัจจัยทำนายการเสียชีวิต และสาเหตุการเสียชีวิตของผู้ป่วยโรคเบาหวานในประเทศไทย

ธงชัย ประภูภานวัตร, เพชร รอดอารีย์, ธัญญา เชษฐากุล, พงศ์อมร บุญนาค, ฉัตรประอร งามอุโฆษ, ยุพิน เบ็ญจสุรัตน์วงศ์, รัตนา ลีลาวัฒนา, ณัฐพงศ์ โฆษณานันท์, ณัฐเชษฐ์ เป็ล่งวิทยา, ชัยชาญ ติโรจนวงศ์, สมพงษ์ สุวรรณวัลย์กร, สิริเนตร กฤติยาวงศ์, สิริมา มงคลสัมฤทธิ์, จุฬาลักษณ์ โกมลตรี

ภูมิหลัง: ความชุกของผู้ป่วยโรคเบาหวานชนิดที่ 2 ในประเทศไทยเท่ากับร้อยละ 9.8 ซึ่งเป็น 2 เท่าของที่ประมาณการโดยองค์การอนามัยโลก ยังไม่มีข้อมูลเพียงพอที่จะบอกสาเหตุการตายของผู้ป่วยเบาหวานที่จะใช้เป็นตัวแทนทางสถิติในระดับประเทศได้

วัตถุประสงค์: เพื่อศึกษาลักษณะทางคลินิกที่เป็นปัจจัยเสี่ยงของการเสียชีวิต และสาเหตุของการเสียชีวิตในผู้ป่วยโรคเบาหวานที่ติดตามรักษาที่คลินิกโรคเบาหวาน ในโรงพยาบาลมหาวิทยาลัย และโรงพยาบาลระดับทุติยภูมิในประเทศไทย

วัสดุและวิธีการ: การศึกษานี้เป็นการติดตามผู้ป่วยที่อยู่ในโครงการลงทะเบียนผู้ป่วยโรคเบาหวาน ในประเทศไทย ระหว่างเดือนเมษายน พ.ศ. 2546 ถึง กุมภาพันธ์ พ.ศ. 2549 จากคลินิกโรคเบาหวานในโรงพยาบาลมหาวิทยาลัย และโรงพยาบาลระดับทุติยภูมิในประเทศไทย จำนวน 10 แห่ง ในกรุงเทพฯ และเมืองใหญ่ๆ ทั้ง 4 ภาคของประเทศไทย โดยมีผู้ที่สามารถติดตามสถานภาพ ของการมีชีวิตด้วยการค้นคว้าจากฐานข้อมูลของโรงพยาบาลที่ร่วมในการศึกษาและจากฐานข้อมูลของกระทรวงมหาดไทยได้ถึงร้อยละ 99.4 และสาเหตุของการเสียชีวิตจะได้รับการสืบค้นจากเวชระเบียนโดยแพทย์จำนวนสองคนโดยความเห็นพ้องต้องกัน

ผลการศึกษา: ผู้ป่วย 9,370 ราย มีผู้เสียชีวิตทั้งหมด 425 ราย ในระยะเวลา 2.5 ปีของการติดตาม และเป็นระยะเวลาเสี่ยง 23,071.3 ราย-ปี โดยเป็นอัตราการเสียชีวิต 1.84 รายต่อปี ปัจจัยเสี่ยงในการเสียชีวิตในผู้ป่วยโรคเบาหวาน ได้แก่ อายุ ระบบประกันสุขภาพ ระดับของการศึกษา ต้องได้รับการรักษาด้วยการฉีดอินซูลิน การสูบบุหรี่ มีประวัติเคยป่วยเป็นโรคหลอดเลือดหัวใจและหลอดเลือดสมอง การทำงานของไต (ระดับ creatinine) และระดับ HbA_{1c} ขณะที่การรักษาด้วยยาลดไขมัน และ metformin สัมพันธ์ในการเสียชีวิตที่ลดลง สาเหตุของการเสียชีวิตที่สำคัญได้แก่โรคหลอดเลือด การติดเชื้อ และมะเร็ง

สรุป: การศึกษานี้แสดงปัจจัยเสี่ยงต่อการเสียชีวิตและสาเหตุของการเสียชีวิตในผู้ป่วยโรคเบาหวานในประเทศไทย
