THE RELATIONSHIP BETWEEN AMBULATORY CARE LAPSES AND MEDICAL UTILIZATION IN DIABETIC PATIENTS

by

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ABSTRACT

It remains unclear whether lapses in ambulatory care for diabetic patients influences the subsequence medical utilization. Therefore, the objective of this study was to clarify whether different duration of ambulatory care lapses were associated with the stroke utilization in diabetic patients.

We conducted a retrospective cohort study by using Taiwan National Health Insurance Research Database. Study population were diabetic patients aged 20 and over with subsequence ischemic stroke. According to lapses between the last diabetic ambulatory care and the ischemic stroke, patients were classified into five groups(from group A to group E), which were lapse A) within 90 days, B) within 91 to 180 days, C) within 181 to 270 days, D) within 271 to 365 days, and E) over 365 days. The interests outcomes were stroke hospitalization expenditure, length of stay, and severity. Groups were compared on characteristics at the ischemic stroke, the use of diabetic care and stroke utilization by using analysis of variance test for continuous variables and chi-square test for categorical variables, as appropriate. The multivariate regression models and multinomial logistic regression model was used to estimate the association between different duration of ambulatory care lapses and interested outcomes.

A total of 76,194 diabetic patients with subsequence ischemic stroke during 2002 to 2012 were included for analysis. Average hospitalization cost per day was 1.03% higher for patients in group E when compared to patients in group A. Patients in group B, group D, and group E, comparing to group A, had statistically significant longer length of stay for stroke, which were 0.79, 1.05 and 0.65 days, respectively. Stroke severity was higher associated with diabetic patients in group B, group D, and group E when compared to patients in group A.

In conclusion, this study found that diabetic patients with subsequence ischemic stroke having the last ambulatory care over 365 days tend to have higher severity, higher hospitalization cost per day, and longer length of stay for ischemic stroke. Therefore, this study suggests to enhance better monitoring and better management for all diabetic patients especially for those patients with longer lapses.

Keywords: ambulatory care, diabetes mellitus, healthcare management, lapses

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Chapter 1: Introduction

Statement of the Problem

Primary care plays an important role in the health care system all over the world. It is not only the first contact but also continuous care for patients. Patients with chronic conditions, such as diabetes mellitus, is highly recommended to manage their disease with regular appointments in ambulatory care setting for continuous care. Although studies for continuous care have been studied a lot in past decades, little is focused on discontinuous care. Therefore, this study tries to understand the pattern of ambulatory care.

Diabetes mellitus is a global health care issue and an important public health challenge because of its complexity and requiring continuous medical care with glycemic control. Patients with diabetes mellitus are recommended to have frequent diabetic visits for medications or screenings in order to prevent the complications. Diabetes mellitus has also been listed one of ambulatory care sensitive conditions which indicates appropriate ambulatory care can prevent or reduce the need for hospital admission. Therefore, it is important to understand the lapses of ambulatory care among diabetic patients.

Cardiovascular disease, including stroke, is the leading cause of illness and death in people with diabetes mellitus. It knows that people with diabetes mellitus have an increased risk of developing ischemic stroke. Stroke may cause physical disability, burdens to self, family and society, decreased national productivity and economic losses. Although mortality from stroke is dropping, the number of people having strokes is rising each year due to the aging of population and other signs that strokes have increased in younger groups. Previous studies had indicated the relationship between diabetic mellitus and risk of stroke. However, little is known the role of specific ambulatory care prior to ischemic stroke. It is also unknown how ambulatory care lapses influences stroke medical utilization for diabetic patients.

Since Taiwan conducted a National Health Insurance Program for twenty years with standard formats documented, patients' medical treatment profile on admission, ambulatory care and prescription can be easily retrieved for analysis. Therefore, this study expects to examine the relationship between the duration of ambulatory care lapses and stroke medical utilization in diabetic patients with subsequence ischemic stroke through Taiwan National Health Insurance Database. The results will provide a reference for policy maker and clinic professionals in improving diabetes care and management.

Research Objective and Study Aims

The purpose of this study is to understand whether ambulatory care lapses influence stroke medical consumption among diabetic patients. Diabetic patients with appropriate ambulatory care and regular physicians visit for diabetes management can prevent or reduce the need for hospital admission and result in reduced medical utilization. Therefore, the research objective is to test the hypothesis that diabetic patients with shorter ambulatory care lapses prior to stroke are related with reduced stroke consumptions. The specific study aims are list below.

Aim1: To understand the baseline characteristics for different pattern of ambulatory care in diabetic patients

Aim2: To understand the utilization of ambulatory care among diabetic patients prior to stroke hospitalization

Aim3: To understand whether ambulatory care lapses in diabetic patients prior to stroke hospitalization is related with stroke medical consumption

Chapter 2: Literature Review

Diabetes mellitus has become a global health care issue and an important public health challenge. Several studies have indicated that patients with diabetes mellitus have a high risk of microvascular and macrovascular which influence the whole body. The reason is that diabetes mellitus will make the renal artery and systemic arteriosclerosis, and result in peripheral vascular resistance and systolic blood pressure rise. High blood pressure will accelerate the vascular disease in diabetic patients, and cause complications in the brain, eyes, heart, kidney and other organs. Many studies had indicated that diabetic patients with more complications will incur the higher medical consumption.[1-3] Diabetes mellitus is a well-established risk factor for future ischemic stroke. Among patients with cardiovascular disease, 30% of them had type 2 diabetes mellitus.[4] It was known that diabetic patients with proper diabetes care and good glycemic control can reduce cardiovascular disease and medical consumptions.[5-9] However, study of ambulatory care lapses in diabetic patient is lacking from previous studies.

In order to improve the quality and cost-effectiveness of care, private and public policy makers and health insurance plans in many countries have executed disease management to help treat chronic illnesses, such as diabetes mellitus and stroke. The

overall perceived health status of diabetic patients is a significant predictor of complication risk and an important indicator for diabetes care management. Therefore, it is vital to have face-to-face encounters with care managers and health educators in communicating about patients' health status and self-care. Therefore, this study expects to examine the relationship between lapses in ambulatory care and medical consumptions through national insurance administrative data in order to provide a reference for policy maker and clinic professionals in patient care. To better understand the issue of diabetic care lapses prior to stroke hospitalization in diabetic population, a literature review that have been published and related on this topic was conducted below.

Diabetes mellitus

Numbers of diabetes population is growing throughout the world. The rise of diabetes mellitus is associated with economic development, ageing populations, increasing urbanization, dietary changes, reduced physical activity, and changes in other lifestyle patterns.[10] The International Diabetes Federation (IDF) indicates that 8.3% of adults, 382 million people, have diabetes in 2013,[11] and the number of adults with disease worldwide in 2015 rises to 415 million, and estimates to have 642 million people living with diabetes by 2040.[12] According to a report from the American Heart Association, an

estimated 23.4 million adults have diagnosed diabetes mellitus based on data from 2011 to 2014 in the United States. The prevalence of diabetes mellitus increased from 8.4% (between 1988 and 1994) to 12.1% (between 2005 and 2010). This increase was most pronounced among those ≥ 65 years of age, especially for the oldest age group.[13] It is estimated that one of 10 adults is affected by diabetes.[14] According to Taiwan Health Promotion Administration, the prevalence of diabetes mellitus in adults aged 18 and older is 12.4% (male 14.4%, female 10.3%), and it is about 1.5 million (6.5%) Taiwanese suffered from this disease.[15]

Diabetes may be diagnosed based on plasma glucose criteria, either the fasting plasma glucose (FPG≥126 mg/dL) or the 2-h plasma glucose (2-h PG≥200 mg/dL) value after a 75-g oral glucose tolerance test (OGTT) or hemoglobin A1c criteria (HbA1c ≥6.5%).[16] Diabetes can be classified into four general categories: (1) Type 1 diabetes, accounts for 5–10% of diabetes, which is due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency; (2) Type 2 diabetes, accounts for 90–95% of all diabetes, which is due to a progressive loss of β-cell insulin secretion, frequently on the background of insulin resistance; (3) Gestational diabetes mellitus which is diabetes diagnosed in the second or third trimester of pregnancy, but was not clearly overt diabetes

prior to gestation; (4) Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes, diseases of the exocrine pancreas, and drug- or chemical-induced diabetes.[16] Type 1 diabetes and type 2 diabetes are heterogeneous diseases in which clinical presentation and disease progression may vary considerably. Although pharmacologic therapy for type 1 diabetes and type 2 diabetes are different, there is no different for glycemic targets and diabetic ambulatory care based on the American Diabetes Association (ADA) guideline.[16]

Patients with diabetes mellitus have a high risk of microvascular, including retinopathy, nephropathy, and neuropathy, and macrovascular, including coronary heart disease, cerebrovascular disease, and peripheral arterial disease, complications. The distinct macrovascular complications of diabetes are related to the pathogenesis of stroke, a cerebrovascular disease. Therefore, diabetes is a well-established risk factor for future ischemic stroke.

The relationship between stroke and diabetes mellitus

All of the data shown that population is aging worldwide[17], and stroke has become a common health problems among older people. Stroke, also known as cerebrovascular accident, is the fifth cause of death and the leading cause of adult disability in the United

States. It is estimated that 795,000 people experience a stroke each year, and 77% of these people are the first event while remain of 23% are recurrent stroke events.[14] In 2011, one of 20 deaths in the United States is caused by stroke.[14] Over the past decades with a striving for stroke management, stroke mortality has gradually fallen due to the improvement of stroke survival, reduction of stroke incidence and lower fatality rates.[14]

Depending on the conditions of the blood vessel, strokes can be divided into two categories clinically. Ischemic strokes account for 75% of strokes while hemorrhagic strokes account for the remaining 25%. Factors for strokes can be divided into two categories: risk factors that cannot be changed, such as age and sex, and risk factors that can be modified, including hypertension, diabetes, and hyperlipidemia.[14,17] Many studies have also indicated that strokes are closely correlated to hypertension, diabetes, and heart disease.[18,19] According to research form Taiwan stroke registry, about 80% of stroke patients have medical history in hypertension and 40 to 50% of stroke patients have diabetes mellitus and hyperlipidemia.[20]

Diabetes mellitus is a major cause of stroke, and the seventh leading cause of death in adults in the United States.[21] People with diabetes mellitus have an increased risk of developing stroke by approximately 3% each year.[10,22,23] Also, self-reported history of

diabetes mellitus was associated with an increased risk of all stroke and ischemic stroke.[24] Previous diabetes was also associated with post-stroke mortality.[25] The overall relative risk of stroke is 1.5 to 6 times greater in patients with diabetes mellitus, while the relative risk for stroke is 10 times higher in diabetic patients younger than 55 years old.[26-28] Recurrent stroke is also twice more frequent in diabetic patients.[28] In addition, diabetic patients who survive a stroke are more likely to be debilitated subsequently and have poorer functional outcomes than non-diabetics. [29-32]

Inadequate glycemic control is a risk factor for poor outcome and increased mortality.[28] In Chinese adults, diabetes mellitus is associated with a substantially increased risk of death, especially from cardiovascular disease, almost half of which is due to stroke.[33] Cardiovascular diseases, including stroke, accounted for about 65% of diabetes-related mortality,[34,35] is the leading cause of illness and death in patients with type 2 diabetes.[36]

Patients with diabetes mellitus are more prone to ischemic rather than hemorrhagic stroke. Following are some reasons. First, long-term hyperglycemic can cause endothelial dysfunction and increased small-vessel resistance, which lead to atherosclerosis and ischemic stroke. Second, diabetic patients are easily to have polyuria,

which lead to water deficient and increased blood viscosity. Inadequate autoregulation of blood flow renders the brain vessels more vulnerable to damage and, eventually, occlusion. Third, cardiac autonomic neuropathy, is a complication of diabetes, may contribute to the pathogenesis of diabetic nephropathy as well as to the pathogenesis of stroke; Fourth, diabetes easily causes heart disease and leads to cardiogenic brain infarction.[28,37-40] It is known that an appropriate management for diabetes care can reduce the incidence of stroke and complications in diabetic patients.[41]

Diabetes care

A previous report pointed that 20.8% of adults with diabetes mellitus had their disease treated and controlled, 46.4% had their diabetes, 9.9% were aware they had diabetes but were not treated, and the rest were undiagnosed.[13] Poor diabetes managements could lead to serious complications, poorer clinical outcomes and early death.[33] Diabetes care got more attention from St. Vincent Declaration in 1989, which pointed out the importance of reduced complications from diabetes as well as controlling glycemic, hyperlipidemia and blood pressure. In 1999, the United States conducted Diabetes Quality Improvement Program in improving diabetes care through accountability measures, such as percentage of patients having at least once HbA1c test in a year. In 2000,

eye examinations, HbA1c testing, and lipid testing have been required to collect and report in all 50 states.[42] The ADA guidelines also suggest to measure and control glycohemoglobin, cholesterol and microalbuminuria for patients with diabetes.[32] Fallowing are main points for diabetes care.

Blood pressure control

Hypertension is a common comorbidity that affects the majority of diabetic patients, and a major risk factor for both cardiovascular disease and microvascular complications. Hypertension is often the result of underlying diabetic kidney disease in patients with type 1 diabetes, and it usually coexists with other cardiometabolic risk factors for patients with type 2 diabetes. Individuals with diabetes should be treated to a systolic blood pressure goal of <140 mmHg and a diastolic blood pressure goal of <90 mmHg. According to American Diabetes Association, diabetic patients with high risk of cardiovascular disease was suggested to control systolic blood pressure at <130mmHg and diastolic blood pressure <80mmHg. Besides, blood pressure should be measured at every routine visit.[16]

Glycemic control

To monitor and control glycemic is fundamental to diabetes management.[43] It is known that glycemic control is an important predictor for many complications of diabetes,

and its improvement has been found to lead to cost savings.[44] Therefore, HbA1C testing should be performed routinely in all patients with diabetes. Because HbA1C reflects average glycaemia over approximately three months, the ADA guideline recommends to measure HbA1c approximately every three months in order to determine whether patients' glycemic targets have been reached and maintained.[16] For those patients have stable glycemic control, it is suggested to perform the HbA1c test at least two times a year, and lower HbA1c to approximately 7%.[45] The international guidelines also suggest comprehensive management of patients with DM in order to maintain glycemic control, often measured by HbA1c, and reduce the risk of diabetes-related complications.[32,43]

Cholesterol Control

Patients with type 2 diabetes have an increased prevalence of lipid abnormalities. Dyslipidemia can lead to atherosclerotic cardiovascular disease, which including acute coronary syndromes, myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease.[16] Control of diabetes and high cholesterol appear to have contributed to the decline in stroke mortality.[14] The American Diabetes Association suggested that appropriate target goal for low-density lipoprotein cholesterol among diabetic patients is <100mg/dl.[16] In

adult patients with diabetes, it is recommended to have a screening lipid profile (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides) at the time of diabetes diagnosis, at an initial medical evaluation, and/or at age 40 and periodically (e.g., every 1 year) thereafter.[45,46]

Conduct Eye exam

Diabetic retinopathy is a highly specific vascular complication of diabetes, with prevalence strongly related to the duration of diabetes.[46] Hyperglycemic increases the risk of eye problems. The actual risk of getting microvascular complications, like microalbuminuria and retinopathy progression, starts at HbA1c level of 7%.[31] Therefore, a dilated eye exam can tell whether you have diabetes retina problems. It is known that having a dilated eye exam at least once a year can prevent most instances of severe vision loss or blindness from diabetes.

Exam Microalbuminuria

Diabetic nephropathy occurs in 20–40% of patients with diabetes and is the single leading cause of end stage renal disease.[46] Albuminuria was a significant predictor for the evaluated renal endpoints. Persistent albuminuria in the range of 30–299 mg/24h has been shown to be an early stage of diabetic nephropathy in type I diabetes and a marker for

development of nephropathy in type 2 diabetes. The first clinical manifestation of diabetic kidney disease is usually the development of microalbuminuria.[47]

Intervention Program

Among individuals at high risk for developing type 2 diabetes, structured programs that emphasize lifestyle changes with dietary strategies can reduce the risk for developing diabetes. Patients with diabetes and high-risk conditions should be educated regarding their risk factors and appropriate management.[46] Taiwan have executed the Diabetes Shared Care Program(DSCP) in 2001 in order to increase the quality of diabetes care. DSCP is a diabetes care model involving multidisciplinary approach and qualified diabetes caregivers, including physician, diabetes educator, and dietitian, in order to provide continuity of care, and to reduce the occurrence of diabetes complications for diabetes patients. By 2013, about 1.18 million of diabetic patients have ever participated in DSCP in Taiwan.[48] It is known that participants in the DSCP was associated with lower risks of cardiovascular events, stroke, and all-cause mortality.[49] In order to achieve diabetes optimal control goals, a long-term control of diabetes by comprehensive education program and regular screening of diabetes-related complications are needed.

The Role of Community Health Workers

According to American Public Health Association, community health workers (CHWs) are frontline public health workers who are trusted members of and/or have an unusually close understanding of the community served. This trusting relationship enables CHWs to serve as a liaison, link, or intermediary between health/social services and the community to facilitate access to services and improve the quality and cultural competence of service delivery.[50] Therefore, CHW typically work in their own communities, share cultural, economic, linguistic and other characteristics with the patients they work with, and are able to build close, trusting relationships with communities because of a deep knowledge of that community.[50] The five main roles of CHWs includes patient care, education, support for care delivery provided by other health professionals, care coordination, and social support.[51] CHWs, who are vital links between health services and the community, serve in a variety of capacities, typically focusing on strategies to improve self-management.[52]

Self-management for diabetic patients is an evolutionary process of development of knowledge or awareness in order to manage diabetes and prevent or delay the complications.[53] Because the majority of day-to-day care in diabetes is handled by

patients and/or families[54], it is important to have a self-management of diabetes for diabetic patients. It was known that seven essential self-care behaviors in people with diabetes can predict good outcomes namely healthy eating, being physically active, monitoring of blood sugar, compliant with medications, good problem-solving skills, healthy coping skills and risk-reduction behaviors.[55] However, numerous barriers may influence diabetes control, such as failure to adhere to treatment, lack of support for self-management, lack of access to care, and so on.[56] Therefore, CHWs, serve as a 2-way liaison between the community and health care system[57], can help overcome barriers to controlling diabetes. In the United States, CHWs have helped to meet the national health goals by conducting community-level activities and interventions that promote health and prevent diseases and disability.[56] Also, there is ample evidence of their contributions to improved health outcomes, especially among those with diabetes.[52,58]

Medical consumption of stroke

Disease manifestation has become more complicated due to changes in modern diets and lifestyles. Diabetes and its associated complications are known to have a significant relationship on the consumption of healthcare resources.[59] Compared to non-diabetics, diabetic patients hospitalized for a cardiovascular event incur higher costs

for care.[60] Following are contributing factors that related to medical consumption of stroke.

Medical expenditure

When a person suffered a stroke and undergoes emergency care at a medical institution during the acute period, to control the patient's condition, treatment resources were needed during the episode period including emergency room, neurology specialists, intensive care, rehabilitation and outpatient service. The costs of hospitalizations involving stroke are high and vary greatly by type of stroke, diagnosis status, and comorbidities.[61] The total US healthcare cost of all strokes was estimated at $53.9 billion in 2010.[62] A study indicated that ischemic, hemorrhagic, or other strokes having average costs, in turn, of $18,963±$21,454, $32,035±$32,046, and $19,248 ± $21,703, respectively.[61]

Length of stay

Dependency in daily life affects length of stay of stroke patients.[63] Costs of inpatient days were the largest contributor to hospital costs.[64] Previous study indicated that average medical expenses during the hospital stay is US$8,740 where 62% variance was explainable by length of stay.[65] In a recent Taiwan study, the average length of stay for

stroke was 13.9±14.1 days, and average cost was US$1408.7±US$2084.3. The most common length of stay was 5-10 days in 39.5% of all patients, and major cost was from US$312.50-US$781.25 resulted from 37.0% of overall and 23.2% of first-ever stroke patients.[66] In addition, complications such as atrial fibrillation, stroke treatment, and subtypes were the significant predictive factors affecting hospital costs and length of stay.[66] Four factors significantly predicted prolonged hospital stay: older age (>65), diabetes mellitus, in-hospital infection, and disability on discharge. Diabetes and in-hospital infection are possible targets for interventions to reduce the burden of illness and healthcare costs of stroke.[32]

Severity of stroke

The severity of stroke could influence the consumption of medical resources. Stroke severity is a strong and reliable predictor of length of stay.[67] Severity of illness and medical complications were the primary issues causing increased length of stay in stroke patients.[68] The severity of stroke, clinically rated by the score of National Institutes of Health Stroke Scale, is an important factor that influences length of stay after acute stroke hospitalization.[69]

Comorbidities

For patients with hypertension, heart disease, diabetes or high blood cholesterol, their disease status is more complicated. Length of stay is also commonly longer.[70] A study indicated that the significant predictive factors for length of stay were diabetes mellitus, atrial fibrillation, recurrence, and stroke subtype.[66] Besides, Charlson Comorbidity Index (CCI) at the time of hospital admission independently influences the length of stay after stroke.[70] Another study showed that 75% of patients admitted with transient ischemic attack stay in the hospital for ≥ 2 days, with the most important determinants being pre-existing medical comorbidities, and longer duration of hospital stay is associated with 2- to 5-fold greater hospitalization charges.[71]

Chapter 3: Methods

Conceptual Framework

This study created a model for conceptual framework which retrieved from Donabedian model and Andersen healthcare utilization model with little modification. (Figure 1)

The Donabedian model provides a framework for examining health services and evaluating quality of health care, which can be drawn from three categories: “structure,” “process,” and “outcomes".[72] The model assumes that structure (e.g. attributes of material) influences process (actually done in receiving care), which affects outcome (e.g. medical consumption). The Donabedian model is widely used for both researchers and policymakers to conceptualize the mechanisms that may contribute to quality of care for diabetic patients. Therefore, this study use “structure-process-outcome” framework described by Donabedian[73] in order to assess the quality of care for diabetic patients. In this study, there was no specific variable in structure part which affect process of care. The potential actions in process part was defined by different duration of lapses in diabetic ambulatory care for diabetic patients received care. The important indicator for quality outcome was defined as consumptions of subsequence ischemic stroke

hospitalization which contains expenditure, length of stay and severity.

The Andersen healthcare utilization model aimed at demonstrating the factors that lead to the use of health services. According to the initial Andersen model[74], three dynamic factors, including predisposing factors, enabling factors and need, will influence the utilization of health services by people. In this study, we used the initial Andersen model for developing an integrated model. Predisposing factor was defined as patients' characteristics, including age and sex. Enabling factor facilitates individuals to use services. It could be low-income status and shared care program for diabetic patients in the study. Need factor represents both perceived and actual need for health care services, which were patients' comorbidities in this study.

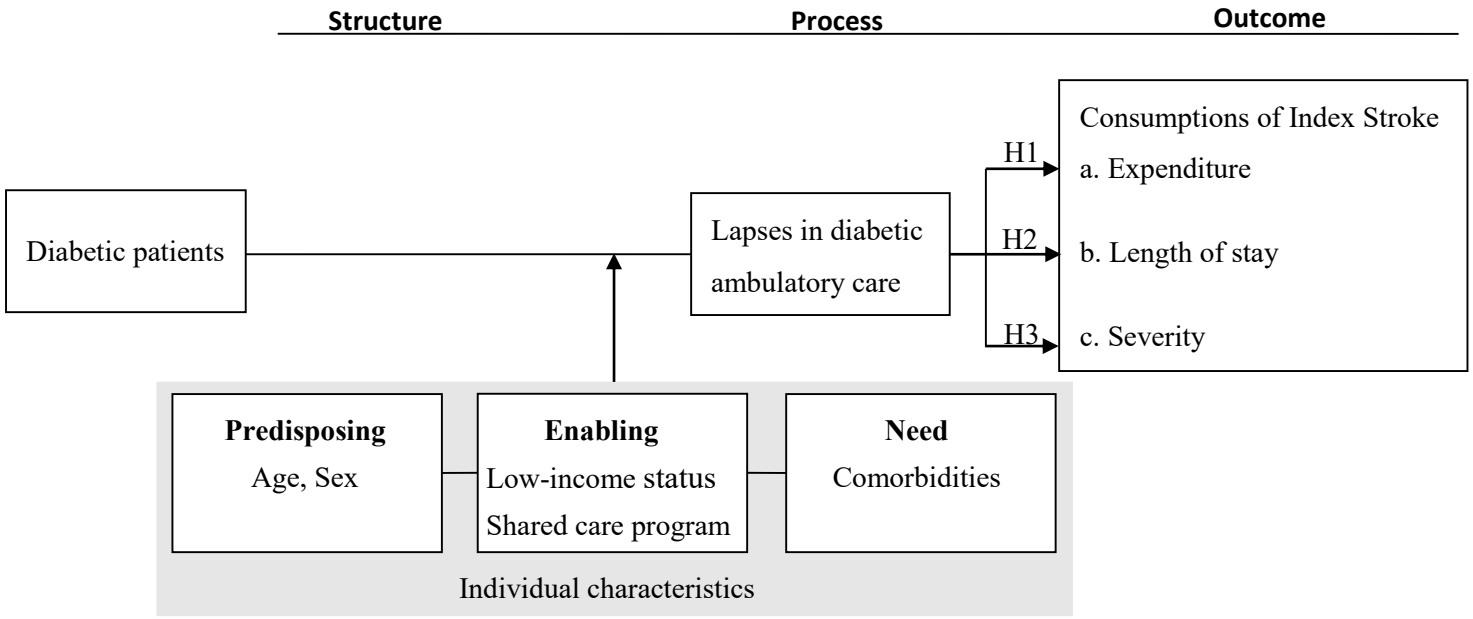

Figure 1 Conceptual framework of the study

It was known that people with diabetes mellitus were recommended to visit physician regularly for diabetes management. DSCP plays a role in structure part to influence the duration of lapses in diabetic ambulatory care. Besides, the duration of lapses in diabetic ambulatory care among diabetic patients may vary by individual characteristics, which including age, sex, low-income status and comorbidities. In other words, individual characteristics may influence people's health care behavior and result in different duration of lapses in diabetic ambulatory care. Individual characteristics were represented by predisposing factors, enabling factors, and need. Moreover, the different duration of lapses in diabetic ambulatory care may further influence the consumption of subsequence ischemic stroke, including hospitalized stroke expenditure (H1), length of stay for stroke (H2), and severity during stroke hospitalization (H3). Therefore, we assumed that diabetic patients with shorter lapses in diabetic ambulatory care before stroke hospitalization may be related with less medical consumptions of subsequence stroke.

Hypotheses/Research Questions

In order to test the assumptions that diabetic patients with shorter lapses of ambulatory care before stroke hospitalization may reduce the consumption of subsequence stroke, three hypotheses for this study were listed below.

Hypothesis 1: Diabetic patients with shorter lapses of diabetic ambulatory care will have lower hospitalized stroke expenditure.

Hypothesis 2: Diabetic patients with shorter lapses of ambulatory care will have shorter length of stay in subsequence stroke.

Hypothesis 3: Diabetic patients with shorter lapses of ambulatory care will incur less severity in stroke hospitalization.

Study Design and Methods

Data Source

To understand the relationship between lapses in diabetic ambulatory care on stroke consumption among diabetic patients, we conducted a retrospective cohort study by using a longitudinal National Health Insurance Database(NHIRD) from Taiwan.

Taiwan has launched a compulsory National Health Insurance program since 1995, which covers 99% of the population and reimburses for outpatients, inpatients services as well as prescription drugs. All contracted institutions must file claims according to standard formats which later transform into NHIRD. The data are collected from the reimbursement records of the National Health Insurance program in Taiwan, where the personal identification information is encrypted, and these data are maintained by the National Health Research Institutes for research purposes.

This study used a specific database that recruited all populations with stroke hospitalization and all their medical services. Over the past 15 year, there was little reimbursement change in diabetes and stroke care in Taiwan. The accuracy of diagnosis of major diseases in the NHIRD, such as diabetes and stroke, had been validated.[75-77] With a

large and consistency database from Taiwan, it is helpful for understanding the relationship between lapses in ambulatory care and stroke medical consumptions in diabetic patients.

Study Design and Study population

Previous Taiwanese study found that the ischemic stroke incidence in diabetes was 11.4% during 4 year follow-up.[78] It is estimated to have more resource and expense in order to prospectively follow diabetic patients for subsequence ischemic stroke in their life-time. Therefore, this study was a retrospective design in analyzing secondary administrative claims from Taiwanese National Health Insurance program for calendar year 2002 to 2012. Study population was defined as patients with diabetes mellitus and subsequence ischemic stroke hospitalization.

Patients with diabetes mellitus were identified in the 13th to 24th months prior to stroke hospitalization based on following inclusion criteria：patients had at least one hospital admission or had at least four times of outpatient visits for diabetes-related illness (The International Classification of Diseases, 9th Revision, Clinical Modification,(ICD-9-CM) code 250.xx).[79,80] (Figure 2) Those patients with fewer than four visits in the 12-month period were excluded and considered as undetermined diagnosis.[79] Besides, it is hard to distinguish type 1 diabetes and type 2

diabetes only by diagnose codes. Previous studies suggested to identify patients with type 1 DM by using catastrophic registry (ICD-9 codes 250.x1 or 250.x3) in Taiwan.[81-83] However, the previous results found that the Type 1 DM was present in less than 1% of the diabetic population in Taiwan during 2000 to 2009[81], and the incidence rate was 3.34 per 100,000 during 2009 to 2010.[82] The latest study only identified 4,007 patients with type 1 DM during 1999 to 2012.[83] Therefore, this study did not distinguish patients with type 1 diabetes and type 2 diabetes. Moreover, based on guideline, the diabetic ambulatory care between type 1 diabetes and type 2 diabetes are not different, so we consider patients with type 1 diabetes and patients with type 2 diabetes should have the same pattern of diabetic ambulatory care. We also examined all stroke hospitalized patients aged 20 and older with a primary diagnosis in ischemic stroke (ICD-9-CM codes 433.x1, 434.x1, 436) for the first time between 2002 and 2012. The first ischemic stroke during the study period is defined as the index stroke. Those patients with ischemic stroke during 1997 to 2001 were also excluded in order to create a wash-out period. Each year, it is about 24,000 new-onset stroke patients in Taiwan, and about 34% of stroke patients have diabetes mellitus.[84] The sample size was estimated to have 89,760 diabetic patients with

ischemic stroke, which power was equal to 1. This is a nationwide study that included all available and eligible patients.

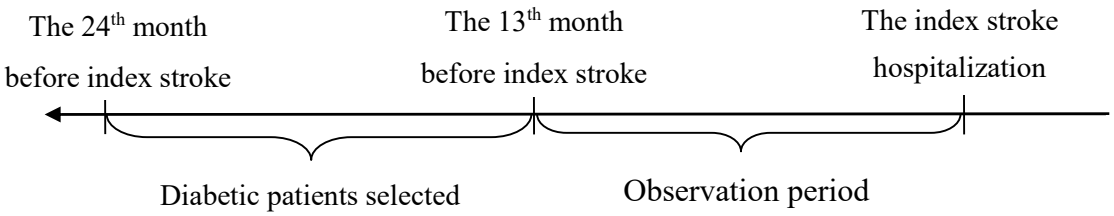

Figure 2 Define study population

Observation period was defined as 12 months prior to the index stroke hospitalization. Main exposure was defined as the last diabetic ambulatory care in observation period. According to the ADA guideline, for continuous glucose monitoring, patients with diabetes were suggested to visit a doctor at least every three months to have a HbA1C testing and to determines whether patients' glycemic targets have been reached and maintained.[16] Besides, Taiwan's National Health Insurance has encouraged physicians to use "chronic medication prescriptions" for patients with stable chronic diseases. Patients are allowed to refill such prescriptions at community pharmacies for a maximum of three months' supply of medications without revisiting the doctor.[85] Therefore, we classified the study population into four groups according to the duration between the last diabetic ambulatory care and index stroke hospitalization: A) diabetic patients had the last diabetic ambulatory care within 90 days prior to the index stroke, B) diabetic patients had the last diabetic ambulatory care within 91 to 180 days prior to the index stroke, C) diabetic patients had the last diabetic ambulatory care within 181 to 270 days prior to the index stroke, and D) diabetic patients had the last diabetic ambulatory care within 271 to 365 days prior to the index stroke. Those diabetic patient with no ambulatory care during the

observation period was defined as E) diabetic patients had diabetic ambulatory care over 365 days prior to the index stroke.

Key Measures

The study variables used in this study were summarized in Table1, including variables, description, and data type. Independent variables included duration of ambulatory care lapses, which divided into five group, and diabetic care exams. Diabetic care exams, including HbA1c test, cholesterol test, eye exam, and urine microalbumin test, are used to understand whether diabetic patients received recommend care for diabetes mellitus during the observation period. (Appendices Table 1) We also collected individual characteristic for related covariates, including predisposing factor (age, sex), enabling factors (participating in DSCP and low-income status), and need (comorbidities). Comorbidities, including hypertension, hyperlipidemia, and atrial fibrillation, ischemic heart disease, stroke history, chronic kidney disease and heart failure, were confirmed by ICD-9-CM codes based on more than 3 times of outpatient visits before the index stroke or list diagnoses of the index stroke. We also calculated number of diabetic care exams, number of emergency room

visits due to diabetes and number of hospitalization due to diabetes during observation period, and type of medical institution of the index stroke.

Table 1 Summary definition of study variables

Variables	Description	Data Type
Independent variables		
A. Duration of ambulatory care lapses	During the observation period, the duration between the last diabetic ambulatory care and the index stroke were divided into 5 groups: patients with the last ambulatory care within 90 days, patients with the last ambulatory care within 91 to 180 days, patients with the last ambulatory care within 181 to 270 days, patients with the last ambulatory care within 271 to 365 days, and patients with the last ambulatory care over 365 days.	Nominal
B. Diabetic care exams		
- HbA1c test	Whether diabetic patients received two or more HbA1c tests during observation period	Dichotomous
-Cholesterol test	Whether diabetic patients received at least one cholesterol tests during observation period	Dichotomous
-Eye exam	Whether diabetic patients received at least one dilated eye exam during observation period	Dichotomous
-Urine microalbumin test	Whether diabetic patients received at least one urine microalbumin test during observation period	Dichotomous
Dependent variables		
Medical consumption of the index stroke		
-Expenditure	Average hospital cost per day of the index stroke	Continuous
-Length of stay	Length of stay of the index stroke	Continuous

Table 1 Summary definition of study variables (continued)

Variables	Description	Data Type
-Severity	Severity of the index stroke evaluated by the Stroke Severity Index (SSI)[86], which classified into 3 categories: severity 1 (SSI≤5), severity 2 (SSI> 5 to SSI≤ 13), or severity 3(SSI>13)[87,88]	Nominal
Covariates		
Age	Patients' age of the index stroke	Continuous
Sex	Patients' sex	Dichotomous
Low-income status	Whether patients were classified low-income status in national health insurance	Dichotomous
Comorbidities		
-hypertension	Whether diabetic patients have more than 3 times of list diagnoses in outpatient visits before the index stroke or list diagnoses of index stroke	Dichotomous
-hyperlipidemia	Whether diabetic patients have more than 3 times of list diagnoses in outpatient visits before the index stroke or list diagnoses of index stroke	Dichotomous
-atrial fibrillation	Whether diabetic patients have more than 3 times of list diagnoses in outpatient visits before the index stroke or list diagnoses of index stroke	Dichotomous
-ischemic heart disease	Whether diabetic patients have more than 3 times of list diagnoses in outpatient visits before the index stroke or list diagnoses of index stroke	Dichotomous
-stroke history	Whether diabetic patients have more than 3 times of list diagnoses in outpatient visits before the index stroke or list diagnoses of index stroke	Dichotomous

Table 1 Summary definition of study variables (continued)

Variables	Description	Data Type
-chronic kidney disease	Whether diabetic patients have more than 3 times of list diagnoses in outpatient visits before the index stroke or list diagnoses of index stroke	Dichotomous
-heart failure	Whether diabetic patients have more than 3 times of list diagnoses in outpatient visits before the index stroke or list diagnoses of index stroke	Dichotomous
DSCP	Whether diabetic patients ever participated in diabetes shared care program	Dichotomous
Number of diabetic care exams	The summary of diabetic care exams, including HbA1c test, cholesterol test, eye exam, and urine microalbumin test, for each diabetic patients	Continuous
Number of emergency room visits due to diabetes	Number of emergency room visits due to diabetes-related disease listed in the primary diagnose during observation period which classified into three categories: 0, 1, and ≥2	Nominal
Number of hospitalization due to diabetes	Number of hospitalization due to diabetes-related disease listed in the primary diagnose during observation period which classified into three categories: 0, 1, and ≥2	Nominal
Type of medical institution of the index stroke	The medical institution for diabetic patient visited for the index stroke which classified into 3 categories: medical center, regional hospital, and district hospital	Nominal

Main outcome measures

The primary outcome of interests in this study is medical expenditure of the index stroke. The secondary outcomes are length of stay and severity of index stroke. Stroke severity was evaluated by the Stroke Severity Index(SSI), which comprised seven claims items including airway suctioning, bacterial sensitivity test, general ward stay, intensive care unit stay, nasogastric intubation, osmotherapy, and urinary catheterization, developed specifically to evaluate the severity of strokes for Taiwan NHIRD.(Appendices Table 2)[86] The SSI correlated with admission stroke severity, as assessed using the National Institutes of Health Stroke Scale(NIHSS), with a Pearson correlation coefficient of 0.742[86] and improved case-mix adjustment of mortality models in patients with ischemic stroke.[88,89] The SSI was categorized as severity 1 (SSI $\leq$5), severity 2(SSI$>$ 5 to $\leq$ 13), or severity 3(SSI $>$ 13) in accordance with prior studies.[87,88] The study period started from 12 month prior to the index stroke to the date of the index stroke hospitalization.

Statistical analysis

The distribution of study population within 5 categories of different diabetic ambulatory care lapses prior to stroke (patients with the last ambulatory care within 90

days prior to stroke, patients with the last ambulatory care within 91 to 180 days prior to stroke, patients with the last ambulatory care within 181 to 270 days prior to stroke, patients with the last ambulatory care within 271 to 365 days prior to stroke, and patients with the last ambulatory care over 365 days prior to stroke) were examined. Characteristics of diabetic patients were compared by analysis of variance (ANOVA) test for continuous variables and chi-square test for categorical variables, as appropriate. Diabetic care exams that patients received prior to the index stroke hospitalization were described between five categories of different diabetic ambulatory care lapses.

The multivariate regression models were used to understand the relationship between different lapses in diabetic ambulatory care prior to the index stroke and stroke medical consumptions, including medical expenditure and length of stay. The relationship between different lapses in diabetic ambulatory care prior to the index stroke and stroke severity was analyzed by using multinomial logistic regression model. Patients' age, sex, hypertension, atrial fibrillation, ischemic heart disease, chronic kidney disease, heart failure, DSCP, number of diabetic care exams, numbers of emergency room visits due to diabetes, numbers of hospitalization due to diabetes, and type of medical institution for the index stroke were included in regression models for controlling. Model diagnostics

will be used to test regression assumptions. All statistics analyses were performed with SAS statistical software, version 9.4 (SAS Institute Inc., Cary, NC). A two-sided p value < 0.05 was considered to be statistically significant.

Human Subjects

This is a retrospective study. Study population are identified from NHIRD. All personal identification data in the NHIRD are encrypted to ensure the confidentiality of individuals in order to avoid ethical concerns. The study protocol was approved by the Institutional Review Boards of Johns Hopkins University.

Chapter 4: Results

Characteristics of five study groups

Among 277,745 eligible patients aged 20 and older suffered from ischemic stroke during 2002 to 2012, there were 76,786 patients who had diagnosed diabetes mellitus one year prior to stroke. Patients who had missing data in sex or had a length of stay over 120 days were excluded. Therefore, 76,194 (27.4%) diabetic patients with subsequence stroke hospitalization were included for analysis. The selection flow of study population was showed in Figure 3. In order to understand how diabetic ambulatory care was managed for diabetic patients prior to stroke hospitalization, diabetic patients were divided into five groups based on the different duration of diabetic ambulatory care lapses prior to the index stroke. The five groups were diabetic patients with the last ambulatory care within 90 days prior to stroke, diabetic patients with the last ambulatory care within 91 to 180 days prior to stroke, diabetic patients with the last ambulatory care within 181 to 270 days prior to stroke, diabetic patients with the last ambulatory care within 270 to 365 days prior to stroke, and diabetic patients with the last ambulatory care over 365 days prior to stroke.

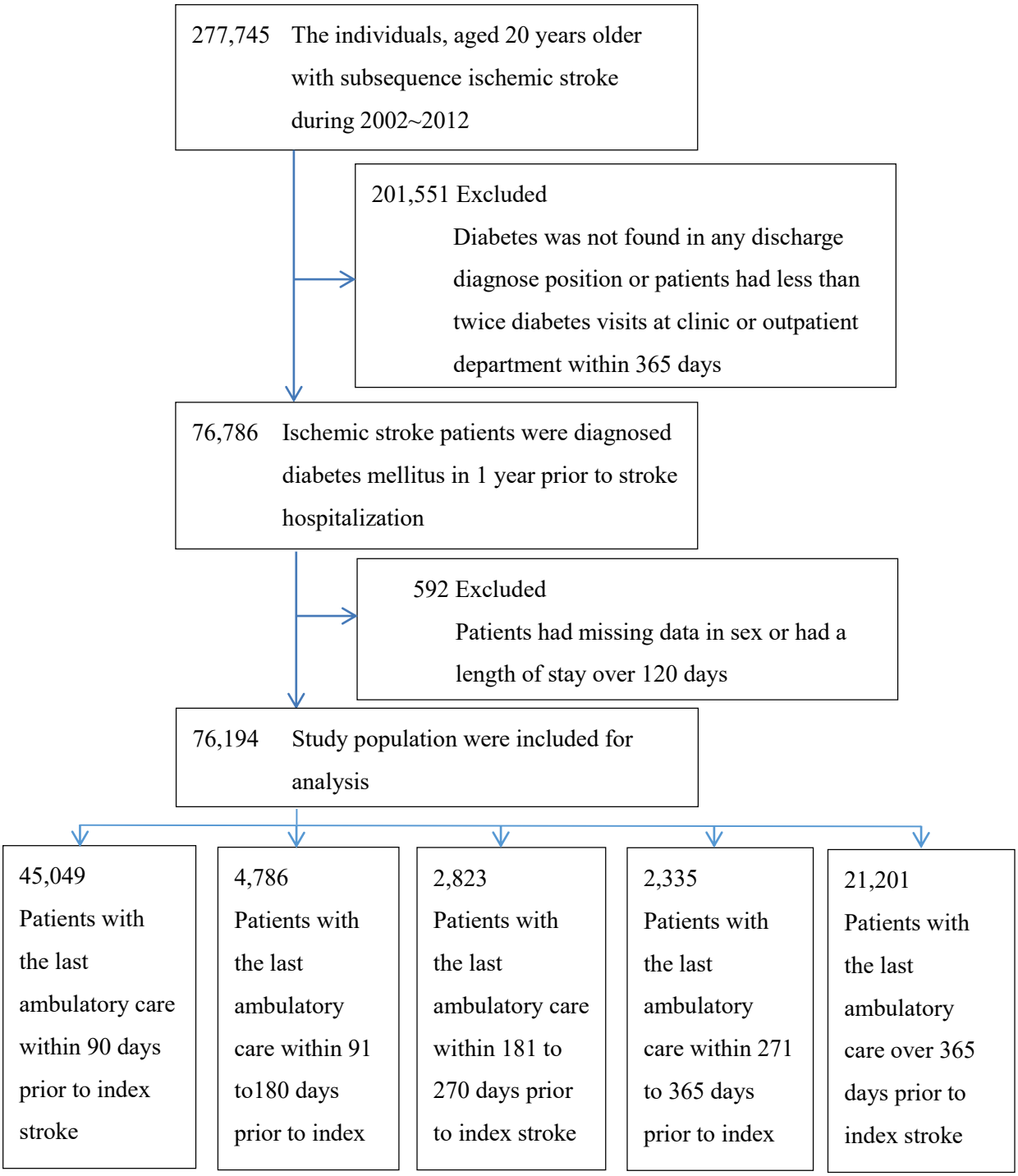

Figure 3 Flow chart of study population and data management process

More than half (59.1%) of the patients had the last ambulatory care within 90 days prior to stroke, and more than one-fourth (27.8%) of patients had the last ambulatory care over 365 days prior to stroke. Patients had the last ambulatory care within 91 to 180 days prior to stroke was 6.3%; patients had the last ambulatory care within 181 to 270 days prior to stroke was 3.7%; patients had the last ambulatory care within 271 to 365 days prior to stroke was 3.1%. The characteristics of the study population with different ambulatory care lapses were shown in Table 2.

Table 2 Study population characteristics stratified by different pattern of ambulatory care lapses prior to stroke hospitalization

	The last ambulatory care prior to stroke												
	Overall		≤ 90 days		91~180 days		181~270 days		271~365 days		> 365 days		P value
Characteristic	n=76194		n=45049 (59.1)		n=4786 (6.3)		n=2823 (3.7)		n=2335 (3.1)		n=21201 (27.8)		
Age, years, Median (IQR)	71	(62-78)	70	(62-77)	70	(61-77)	71	(62-78)	71	(62-78)	73	(63-80)	<0.0001
Age group, n (%)													<0.0001
<65	23315	(30.6)	14428	(32.0)	1569	(32.8)	869	(30.8)	725	(31.1)	5724	(27.0)	
65-74	24586	(32.3)	15613	(34.7)	1591	(33.2)	866	(30.7)	717	(30.7)	5799	(27.4)	
75-84	22535	(29.6)	12543	(27.8)	1340	(28.0)	888	(31.5)	740	(31.7)	7024	(33.1)	
≥85	5758	(7.6)	2465	(5.5)	286	(6.0)	200	(7.1)	153	(6.6)	2654	(12.5)	
Male, n (%)	39991	(52.5)	23241	(51.6)	2544	(53.2)	1482	(52.5)	1189	(50.9)	11535	(54.4)	<0.0001
Low-income status, n (%)	628	(0.8)	493	(1.1)	41	(0.9)	26	(0.9)	29	(1.2)	39	(0.2)	<0.0001
Comorbidities, n (%)													
Hypertension	50869	(66.8)	29971	(66.5)	3430	(71.7)	2108	(74.7)	1733	(74.2)	13627	(64.3)	<0.0001
Hyperlipidemia	23205	(30.5)	15976	(35.5)	1587	(33.2)	876	(31.0)	720	(30.8)	4046	(19.1)	<0.0001
Atrial fibrillation	3725	(4.9)	1611	(3.6)	250	(5.2)	155	(5.5)	180	(7.7)	1529	(7.2)	<0.0001
Ischemic heart disease	18697	(24.5)	9902	(22.0)	1361	(28.4)	858	(30.4)	720	(30.8)	5856	(27.6)	<0.0001
Stroke history	12175	(16.0)	6161	(13.7)	924	(19.3)	591	(20.9)	490	(21.0)	4009	(18.9)	<0.0001
Chronic kidney disease	6685	(8.8)	3042	(6.8)	552	(11.5)	364	(12.9)	328	(14.1)	2399	(11.3)	<0.0001
Heart failure	7685	(10.1)	3406	(7.6)	587	(12.3)	396	(14.0)	337	(14.4)	2959	(14.0)	<0.0001

Table 2 Study population characteristics stratified by different pattern of ambulatory care lapses prior to stroke hospitalization (continued)

	The last ambulatory care prior to stroke												
	Overall		≤ 90 days		91~180 days		181~270 days		271~365 days		> 365 days		P value
Characteristic	n=76194		n=45049 (59.1)		n=4786 (6.3)		n=2823 (3.7)		n=2335 (3.1)		n=21201 (27.8)		
Location of DM visit, by type of clinic, n (%)													<0.0001
Hospital-based clinic	35065	(46.0)	28844	(64.0)	2946	(61.6)	1769	(62.7)	1506	(64.5)	0	(0)	
Clinics	19928	(26.2)	16205	(36.0)	1840	(38.5)	1054	(37.3)	829	(35.5)	0	(0)	
Number of emergency room visit in the previous year due to diabetes													<0.0001
0	71263	(93.5)	40919	(90.8)	4401	(92.0)	2612	(92.5)	2192	(93.9)	21139	(99.7)	
1	4132	(5.4)	3433	(7.6)	325	(6.8)	185	(6.6)	135	(5.8)	54	(0.3)	
>=2	799	(1.1)	697	(1.6)	60	(1.3)	26	(0.9)	8	(0.3)	8	(0.04)	
Number of hospitalization in the previous year due to diabetes													<0.0001
0	71764	(94.2)	41759	(92.7)	4390	(91.7)	2612	(92.5)	2193	(93.9)	20810	(98.2)	
1	3606	(4.7)	2653	(5.9)	324	(6.8)	181	(6.4)	115	(4.9)	333	(1.6)	
>=2	824	(1.1)	637	(1.4)	72	(1.5)	30	(1.1)	27	(1.2)	58	(0.3)	

Patients with longer lapses seemed to be older, and the results showed statistically significant difference between groups. The median age of overall study population was 71 years old. The median age of the five groups ranged from 70 to 73 years old. Patients with the last ambulatory care over 365 days prior to stroke had the lowest percentage in age less than 65 and age 65 to 74 and had the highest percentage in age 75 to 84 and age over 85. Besides, more than half (52.5%) of the overall patients were male in the study. There was no trend relationship between ambulatory care lapses and sex although the results showed statistically significant difference between groups. The percentage of male patients in five groups ranged from 50.9% to 54.4%. Patients with the last ambulatory care over 365 days prior to stroke had the highest percentage of male sex. Moreover, there was no trend relationship between ambulatory care lapses and low-income status although the results showed statistically significant difference between groups. Less than 1 % of the overall patients in this study was classified a low-income status, while 0.2% to 1.2% was found in five groups. Patients with the last ambulatory care over 365 days prior to stroke had the lowest percentage of low-income status. In summary, the distribution of age, sex and low-income status varied between five groups. The results indicated that

patients who had the last ambulatory care over 365 days prior to the index stroke were older, more male and less low-income status.

The results showed that comorbidities in hypertension and hyperlipidemia were less common among diabetic patients with the longest lapses, and patients with longer lapses seemed to have lower percentage of comorbidities in hyperlipidemia. Besides, patients with longer lapses seemed to have higher percentage of comorbidities in atrial fibrillation, ischemic heart disease, stroke history, chronic kidney disease, and heart failure, except the longest lapse group. It was found that about two-thirds (66.8%) of overall study population had hypertension. Diabetic patient with the last ambulatory care within 181 to 270 day prior to stroke had the highest percentage of hypertension (74.4%), and those patients with the last ambulatory care over 365 days prior to stroke had the lowest percentage of hypertension (64.3%). For comorbidity in hyperlipidemia, less than one-third (30.5%) of overall study population had hyperlipidemia. Diabetic patients with the last ambulatory care within 90 days prior to stroke showed the highest percentage in hyperlipidemia (35.5%), and those patients with the last ambulatory care over 365 days prior to stroke were the lowest percentage (19.1%). In summary, the prevalence of comorbidities in hypertension, hyperlipidemia, atrial fibrillation, ischemic heart disease,

stroke history, chronic kidney disease, and heart failure varied between five groups. The results indicated that patients with the last ambulatory care over 365 days prior to the index stroke had less comorbidities in hypertension and hyperlipidemia, whereas patients with the last ambulatory care within 90 days prior to the index stroke had less comorbidities in atrial fibrillation, ischemic heart disease, stroke history, chronic kidney disease, and heart failure.

More than 60% of patients in each group frequently visited hospital-based clinic for diabetic ambulatory care, expect the longest lapse group. Among overall population, less than half (46.0%) of patients frequently visited hospital-based clinic for diabetic ambulatory care during observation period of 365-days, whereas over one-fourth (26.2%) of patients frequently visited clinic. Since 27.8% of diabetic patients had the last diabetic ambulatory care over 365 days, the summary percentage of frequently visit location in observation period for overall study population were not 100%. The results showed that diabetic patients with the last ambulatory care within 271 to 365 days prior to stroke had the highest percentage (64.5%) of patients went to hospital-based clinic for ambulatory care and the lowest percentage (35.5%) of patients went to clinics. On the other hand, patients with the last ambulatory care within 91 to 180 days prior to stroke had the lowest

percentage (61.6%) of patients went to hospital-based clinics for diabetic care and the highest percentage (38.5%) of patients went to clinics. The results indicated that diabetic patients with different diabetic ambulatory care lapses tended to visit hospital-based clinic for their diabetic care although the percentage of frequently visited location varied between groups.

During the observation period, diabetic patients with longer lapses seemed to have less diabetes-related emergency room visit and less diabetes-related hospitalization visits. However, there was no trend relationship between ambulatory care lapses and diabetes-related hospitalization visits. Most of study population did not have diabetes-related emergency room visit (93.5%) and diabetes-related hospitalization visit (94.2%). Diabetic patients with the last ambulatory care within 90 days prior to stroke had the highest percentage in diabetic-related emergency room visit (1 time: 7.6%; 2 or more times: 1.6%), and those with the last ambulatory care over 365 days prior to stroke had the lowest percentage in diabetic-related emergency room visit (1 time: 0.3%; 2 or more times: 0.04%). For diabetic-related hospitalization during 365 days prior to stroke, diabetic patients with the last ambulatory care within 91 to 180 days prior to stroke had the highest percentage in diabetic-related hospitalization (1 time: 6.8%; 2 or more times:

1.5%), and those with the last ambulatory care over 365 days had the lowest percentage in diabetic-related hospitalization (1 time: 1.6%; 2 or more times: 0.3%). The results showed that diabetes-related emergency room visit and hospitalization visits varied between five groups. Diabetic patients with longer lapses prior to stroke tended to have less emergency room visit and hospitalization visit due to diabetes.

In summary, the study results found that diabetic patients with the last ambulatory care over 365 days prior to stroke were older, more male, having more highly symptomatic comorbidities, such as atrial fibrillation, ischemic heart disease, stroke history, chronic kidney disease, and heart failure, and having less diabetic-related emergency visit and hospitalization when compare to those with the last ambulatory care within 90 days prior to stroke.

Utilization of diabetic care exams in five study groups

According to Table 3, patients with longer lapses seemed to have lower percentage in DSCP participation and in diabetic care exams. It was found that 13.7% of overall population had participated DSCP, and the percentage of four diabetic care exams ranged from 27.7% to 59.5%. The participating rate for DSCP and receiving diabetic care exams varied between 5 groups. Diabetic patients with the last ambulatory care within 90 days prior to stroke had the highest percentage (20.8%) in participating in DSCP, and those patients with the last ambulatory care over 365 days prior to stroke had the lowest percentage (0.6%). It was found that diabetic patients with shorter lapses before the index stroke had higher participating rate in DSCP. For four kinds of diabetic care exams in 365 days prior to the index stroke, diabetic patients with the last ambulatory care within 90 days had the highest percentage in having two or more HbA1c test (63.3%), having cholesterol test (67.0%), having dilated eye exam (35.2%), and having a urine routine test (36.2%), whereas diabetic patients with the last ambulatory care over 365 days had the lowest percentage in having two or more HbA1c test (24.5%), having cholesterol test (43.4%), having dilated eye exam (14.6%), and having a urine routine test (11.3%). It seemed that diabetic patients with longer lapses before the index stroke had lower

percentage to receive 4 kinds of diabetic care exams. In summary, the results showed that diabetic patients with the last ambulatory care over 365 days were associated with the lowest percentage in DSCP participation and the lowest percentage in receiving diabetic care exams.

Table 3 Diabetic care exams prior to stroke hospitalization stratified by different pattern of ambulatory care lapses

	The last ambulatory care prior to stroke												
	Overall		≤ 90 days		91~180 days		181~270 days		271~365 days		> 365 days		P value
Participation in DSCP	10448	(13.7)	9352	(20.8)	614	(12.8)	216	(7.7)	136	(5.8)	130	(0.6)	<0.0001
Diabetic care exams, n (%)													
Having HbA1c tests in the past year	38311	(50.3)	28526	(63.3)	2436	(50.9)	1254	(44.4)	907	(38.8)	5188	(24.5)	<0.0001
Having cholesterol test in the past year	45322	(59.5)	30182	(67.0)	2987	(62.4)	1701	(60.3)	1250	(53.5)	9202	(43.4)	<0.0001
Having dilated eye exam in the past year	21609	(28.4)	15871	(35.2)	1366	(28.5)	740	(26.2)	548	(23.5)	3084	(14.6)	<0.0001
Having urine microalbumin /urine routine test in past year	21077	(27.7)	16313	(36.2)	1320	(27.6)	626	(22.2)	422	(18.1)	2396	(11.3)	<0.0001

Medical utilization of the index stroke in five study groups

Medical utilization of the index stroke in diabetic patients between five groups were displayed in Table 4. The most frequent medical institution for index stroke visiting were regional hospital, and followed by medical center and district hospital. There was no trend relationship between ambulatory care lapses and type of medical institution for index stroke although the results showed statistically significant difference between groups. Patients with longer lapses seemed to have longer length of stay, higher average hospitalization cost per day, and severer stroke although there were no trend relationships between lapses of diabetic ambulatory care and stroke medical consumptions. Besides, patients with longer lapses seemed to have higher percentage of patients with in-hospital death and discharge under critical condition.

The results showed that less than half (47.7% to 48.9%) of patients visited regional hospital for the index stroke, 29.5% to 32.6% of patients visited medical center, and 19.7% to 22.4% of patients visited district hospital. Patients with the last ambulatory care within 90 days prior to stroke had the highest percentage to visit medical center (32.6%) and the lowest percentage to visit regional hospital (47.7%) and district hospital (19.7%) when they suffered from ischemic stroke. Besides, the median length of stay for

the index stroke were 8 days (IQR 5-16) in overall patients. Diabetic patient with the last ambulatory care within 90 days had a shorter length of stay and small IQR when compared to other groups. Moreover, the median of average hospitalization cost per day for the index stroke was 4,303 New Taiwan Dollar (NTD) (IQR 3,316- 5,834). Diabetic patients with the last ambulatory care within 90 days prior to stroke had the lowest average hospitalization cost (4,251 NTD), whereas those with the last ambulatory care over 365 days had the highest hospitalization cost (4,417 NTD). For severity of the index stroke, 64.6% of study patients were in stroke severity 1; 15.1% of study patient were in stroke severity 2; and 20.3% of study patients were in stroke severity 3. Diabetic patients with the last ambulatory care within 90 days had the highest percentage in stroke severity 1 and the lowest percentage in stroke severity 2 and stroke severity 3, whereas diabetic patients with the last ambulatory care over 365 days had the lowest percentage in stroke severity 1 and the highest percentage in stroke severity 2 and stroke severity 3.

The index stroke caused 2.7% of study patients had in-hospital death and 1.9% of study patients discharged under critical condition. Diabetic patients with the last ambulatory care within 90 days had the lowest percentage of in-hospital death (2.2%) and discharge under critical condition (1.6%), whereas those with the last ambulatory care

over 365 days had the highest percentage of in-hospital death (3.7%) and discharge under critical condition (2.3%).

In summary, the results showed that diabetic patients with the last ambulatory care over 365 seemed to have longer length of stay, higher average hospitalization cost for the index stroke, higher severity of stroke, and more critical condition when comparing to those with the last ambulatory care within 90 days.

Table 4 Medical utilization of index stroke in diabetic patients

	The last ambulatory care prior to stroke											
	Overall		≤ 90 days		91~180 days		181~270 days		271~365 days		> 365 days		P value
Medical institution type for stroke hospitalization, n (%)													<0.0001
Medical center	24056	(31.6)	14689	(32.6)	1471	(30.7)	833	(29.5)	701	(30.0)	6362	(30.0)	
Regional hospital	36580	(48.0)	21474	(47.7)	2305	(48.2)	1359	(48.1)	1141	(48.9)	10301	(48.6)	
District hospital	15558	(20.4)	8886	(19.7)	1010	(21.1)	631	(22.4)	493	(21.1)	4538	(21.4)	
Length of stay, median (IQR)	8	(5-16)	8	(5-15)	8	(5-17)	8	(5-16)	9	(5-17)	9	(5-17)	<0.0001
Average hospitalization cost per day, median (IQR)	4303	(3316-5834)	4251	(3299-5689)	4362	(3309-5962)	4304	(3276-5862)	4338	(3325-5997)	4417	(3360-6100)	<0.0001
Stroke severity													<0.0001
1 (SSI≤5)	49252	(64.6)	30736	(68.2)	3000	(62.7)	1792	(63.5)	1423	(60.9)	12301	(58.0)	
2 (5<SSI≤ 13)	11494	(15.1)	6489	(14.4)	745	(15.6)	442	(15.7)	379	(16.2)	3439	(16.2)	
3 (SSI>13)	15448	(20.3)	7824	(17.4)	1041	(21.8)	589	(20.9)	533	(22.8)	5461	(25.8)	
Outcomes of index stroke													
In-hospital death	2088	(2.7)	1010	(2.2)	147	(3.1)	75	(2.7)	79	(3.4)	777	(3.7)	<0.0001
Discharge under critical condition	1409	(1.9)	729	(1.6)	93	(1.9)	59	(2.1)	51	(2.2)	477	(2.3)	<0.0001

Factors associated with average hospitalization cost per day

The results showed that average hospitalization cost per day was 1.03% higher for diabetic patients with the last ambulatory care over 365 days ($p<0.0001$) compared to those patients with the last ambulatory care within 90 days. Table 5 also showed that factors in age, hypertension, atrial fibrillation, ischemic heart disease, stroke history, chronic kidney disease, heart failure, participating in DSCP, and medical institution for stroke were associated with average hospitalization cost per day derived from multivariate regression analysis.

By age factors, average hospitalization cost per day was 1.01% statistically significant higher among diabetic patients aged 65 to 74 years old ($p=0.0101$), 1.02% statistically significant higher among diabetic patients aged 75 to 84 years old ($p<0.0001$), and 1.06% statistically significant higher among diabetic patients aged 85 and older ($p<0.0001$) when comparing to those aged under 65 years old. No statistically significant association existed for average hospitalization cost per day by sex of the diabetic patients.

Table 5 The multivariate regression between logarithm average hospital cost per day and diabetic patients with different pattern of lapses

	Natural log average hospital cost per day			
Parameter	Estimate	Standard Error	t value	Pr > |t|
The last ambulatory care prior to stroke (compared to ≤ 90 days)				
91~180 days	0.01	0.01	1.40	0.1618
181~270 days	-0.003	0.01	-0.35	0.7245
271~365 days	0.01	0.01	0.73	0.4629
> 365 days	0.03	0.004	6.15	<0.0001
Age (compared to age<65 years old)				
65-74	0.01	0.004	2.57	0.0101
75-84	0.02	0.004	5.00	<0.0001
>=85	0.06	0.007	8.34	<0.0001
Male	-0.0009	0.003	-0.26	0.7986
Comorbidities				
Hypertension	0.01	0.004	2.46	0.0141
Atrial fibrillation	0.11	0.008	13.61	<0.0001
Ischemic heart disease	0.03	0.004	5.98	<0.0001
Stroke history	-0.02	0.005	-5.26	<0.0001
Chronic kidney disease	0.19	0.006	31.63	<0.0001
Heart failure	0.08	0.006	12.35	<0.0001
Participated in DSCP	-0.02	0.006	-4.26	<0.0001
Number of diabetic care exams	0.003	0.002	1.80	0.0726

Table 5 The multivariate regression between logarithm average hospital cost per day and diabetic patients with different pattern of lapses (continued)

	Log average hospital cost per day			
Parameter	Estimate	Standard Error	t value	Pr > |t|
Number of emerge visit due to DM				
1	-0.002	0.008	-0.26	0.7942
≥2	-0.02	0.02	-1.15	0.2502
Number of hospitalization due to DM				
1	0.007	0.008	0.92	0.3584
≥2	-0.02	0.02	-1.31	0.1918
Type of medical institution for index stroke				
Medical center	0.25	0.005	52.71	<0.0001
Regional hospital	0.18	0.004	40.17	<0.0001
Intercept	8.19	0.006	1308.59	<0.0001
	N=76194	P value <0.0001		
	R^2=0.0627	F=231.95		

By comorbidity factors, average hospitalization costs were statistically significant higher among diabetic patients with hypertension (1.01%, $p=0.0141$), atrial fibrillation (1.12%, $p<0.0001$), ischemic heart disease (1.03%, $p<0.0001$), chronic kidney disease (1.21%, $p<0.0001$), heart failure (1.08%, $p<0.0001$), and statistically significant lower among those with stroke history (0.98%, $p<0.0001$). Diabetic patients participating in DSCP were more likely to have a lower average hospitalization cost per day (0.98%, $p<0.0001$). No statistically significant association existed for average hospitalization cost by numbers of diabetic care exams, numbers of emerge visits due to diabetes, and number of hospitalization visit due to diabetes within 365 days before the index stroke.

By reported medical institution for stroke care, average hospitalization cost was statistically significant higher among diabetic patients who visited medical center (1.29%, $p<0.0001$) and regional hospital (1.20%, $p<0.0001$) when compared to district hospital.

Factors associated with length of stay

The multivariate regression results of factors associated with stroke length of stay are exhibited in Table 6. Compared to diabetic patients with the last ambulatory care within 90 days, length of stay were statistically significant 0.79 days longer in those with the last ambulatory care within 91 to 180 days, 1.05 days longer in those with the last ambulatory care within 271 to 365 days, and 0.65 days longer in those with the last ambulatory care over 365 days. Length of stay was longer for diabetic patients with longer lapses compared to those with shortest lapses although there was not statistically significant in those with the last ambulatory care within 181 to 270 day.

By age factors, length of stay was 1 days statistically significant longer among diabetic patients aged 65 to 74 years old, 2.18 days statistically significant longer among diabetic patients aged 75 to 84 years old, and 3.36 days statistically significant longer among diabetic patients aged 85 and older when comparing to those aged under 65 years old. Male sex of diabetic patients was more likely to have a shorter length of stay for the index stroke hospitalization when compared to female diabetic patients.

Table 6 The multivariate regression between length of stay and diabetic patients with different lapses

	length of stay			
Parameter	Estimate	Standard Error	t value	Pr > |t|
The last ambulatory care prior to stroke (compared to ≤ 90 days)				
91~180 days	0.79	0.22	3.68	0.0002
181~270 days	0.32	0.28	1.15	0.2510
271~365 days	1.05	0.30	3.47	0.0005
> 365 days	0.65	0.13	4.94	<0.0001
Age (compared to age<65 years old)				
65-74	1.00	0.13	7.65	<0.0001
75-84	2.18	0.14	16.11	<0.0001
>=85	3.36	0.21	15.73	<0.0001
Male	-0.30	0.10	-2.91	0.0036
Comorbidities				
Hypertension	-0.28	0.11	-2.48	0.0130
Atrial fibrillation	3.09	0.25	12.33	<0.0001
Ischemic heart disease	-0.12	0.13	-0.91	0.3618
Stroke history	0.88	0.14	6.19	<0.0001
Chronic kidney disease	0.96	0.19	5.11	<0.0001
Heart failure	1.92	0.19	10.31	<0.0001
Participated in DSCP	0.04	0.17	0.21	0.8343
Number of diabetic care exams	-0.16	0.05	-3.44	0.0006

Table 6 The multivariate regression between length of stay and diabetic patients with different lapses (continued)

	length of stay			
Parameter	Estimate	Standard Error	t value	Pr > |t|
Number of emerge visit due to DM				
1	1.11	0.23	4.78	<0.0001
≥2	1.48	0.51	2.89	0.0039
Number of hospitalization due to DM				
1	1.51	0.25	6.04	<0.0001
≥2	2.32	0.51	4.58	<0.0001
Type of medical institution for index stroke				
Medical center	5.15	0.15	34.99	<0.0001
Regional hospital	2.46	0.14	18.08	<0.0001
Intercept	9.02	0.19	47.12	<0.0001
	N=76194 P value <0.0001			
	R^2=0.0309 F=110.54			

By comorbidity factors, there were no statistically significant association between length of stay and hypertension (-0.28 day, p=0.0130) and ischemic heart disease (-0.12 day, p=0.3618). Length of stay were statistically significant longer among diabetic patients with atrial fibrillation (3.09 days, p<0.0001), stroke (0.88 day, p<0.0001), chronic kidney disease (0.96 day, p<0.0001), and heart failure (1.92 days, p<0.0001). No statistically significant association existed for length of stay by diabetic patients participating in DSCP (0.04 days, p=0.8343). Diabetic patients with receiving more diabetic care exams in 365 days before the index stroke were more likely to have a lower length of stay (-0.16 days, p=0.0006). Length of stay were statistically significant longer among diabetic patients with 1-time emergency room visit due to diabetes in 365 days before the index stroke (1.11 days, p<0.0001) and with 2 or more times emergency room visits due to diabetes in 365 days before the index stroke (1.48 days, p=0.0039) when compared to those with no emergency room visit. Length of stay were statistically significant longer among diabetic patients with 1-time hospitalization visit due to diabetes in 365 days before the index stroke (1.51 days, p<0.0001) and with 2 or more hospitalization visits due to diabetes in 365 days before the index stroke (2.32 days, p<0.0001) when compared to those with no hospitalization visit.

By reported medical institution for stroke care, length of stay was statistically significant higher among diabetic patients who visited medical center (5.15 days, $p<0.0001$) and regional hospital (2.47 days, $p<0.0001$) when compared to district hospital.

Factors associated with the index stroke severity

Table 7 showed multivariable logistic regression results of factors associated with the index stroke severity. Stroke severity was statistically significant severer associated with diabetic patients with the last ambulatory care within 91 to 180 days, diabetic patients with the last ambulatory care within 271 to 365 days, and diabetic patients with the last ambulatory care over 365 days when compared to those with the last ambulatory care within 90 days.

By age factors, stroke severity was statistically significant severer for diabetic patients who aged 65 to 74 (severity 2 vs. severity 1: OR=1.18, 95%CI:1.12-1.24; severity 3 vs. severity 1: OR=1.62, 95%CI: 1.54-1.71), aged 75 to 84 (severity 2 vs. severity 1: OR=1.52, 95%CI:1.44-1.60; severity 3 vs. severity 1: OR=2.56, 95%CI: 2.43-2.70), and aged over 85 (severity 2 vs. severity 1: OR=2.10, 95%CI:1.93-2.28; severity 3 vs. severity 1: OR=4.59, 95%CI: 4.27-4.94), when compare to patients aged less than 65. The results showed a trend relationship between stroke severity and age. Compared to female sex, male sex was statistically significant less severe for subsequence stroke(severity 2 vs. severity 1: OR=0.72, 95%CI:0.70-0.76; severity 3 vs. severity 1: OR=0.81, 95%CI: 0.78-0.84).

Table 7 Estimated odds ratios from multivariable multinomial logistic regression

	Severity 2 vs Severity 1			Severity 3 vs Severity 1		
	Odds Ratio	95% Wald Confidence Interval		Odds Ratio	95% Wald Confidence Interval	
The last ambulatory care prior to stroke						
≤ 90 days	1.00			1.00		
91~180 days	1.123	1.031	1.224	1.239	1.146	1.340
181~270 days	1.067	0.957	1.190	1.088	0.983	1.203
271~365 days	1.133	1.006	1.275	1.203	1.080	1.340
> 365 days	1.144	1.086	1.204	1.343	1.282	1.407
Age						
<65	1.00			1.00		
65-74	1.179	1.118	1.244	1.618	1.535	1.707
75-84	1.518	1.438	1.603	2.558	2.428	2.696
>=85	2.095	1.927	2.278	4.590	4.268	4.937
Sex						
Female	1.00			1.00		
Male	0.724	0.695	0.755	0.808	0.778	0.839
Comorbidities						
Hypertension	0.955	0.912	1.000	0.938	0.899	0.979
Atrial fibrillation	1.473	1.330	1.630	2.266	2.093	2.455
Ischemic heart disease	0.964	0.916	1.015	1.065	1.018	1.115
Stroke	1.317	1.246	1.391	1.345	1.280	1.414
Chronic kidney disease	1.113	1.033	1.200	1.390	1.304	1.481
Heart failure	1.256	1.166	1.353	1.789	1.684	1.901
Participated in DSCP	0.972	0.905	1.044	0.940	0.878	1.006
Number of diabetic care exams	0.917	0.900	0.935	0.896	0.880	0.912

Table 7 Estimated odds ratios from multivariable multinomial logistic regression (continued)

	Severity 2 vs Severity 1			Severity 3 vs Severity 1		
	Odds Ratio	95% Wald Confidence Interval		Odds Ratio	95% Wald Confidence Interval	
Number of emerge visit due to diabetes						
0	1.00			1.00		
1	1.200	1.095	1.313	1.305	1.202	1.417
2 or more	1.219	0.995	1.493	1.532	1.289	1.821
Numbers of hospital visit due to diabetes						
0	1.00			1.00		
1	1.213	1.099	1.339	1.546	1.419	1.683
2 or more	1.295	1.060	1.582	1.701	1.434	2.018
Medical institution for the index stroke						
District hospital	1.00			1.00		
Regional hospital	0.831	0.789	0.876	1.195	1.135	1.259
Medical center	0.992	0.937	1.050	1.481	1.401	1.564

By comorbidity factors, diabetic patients with comorbidities in hypertension had lower odds in severity 3 of stroke (OR=0.94, 95%CI: 0.90-0.98), and lower odds in severity 2 of stroke (OR=0.96, 95%CI: 0.91-1.00) when compared to severity 1 of stroke, though the letter was not statistically significant. Diabetic patients with comorbidities in atrial fibrillation (severity 2 vs. severity 1: OR=1.47, 95%CI:1.33-1.63; severity 3 vs. severity 1: OR=2.27, 95%CI: 2.09-2.46), stroke history (severity 2 vs. severity 1: OR=1.37, 95%CI:1.25-1.39; severity 3 vs. severity 1: OR=1.35, 95%CI: 1.28-1.41), chronic kidney disease (severity 2 vs. severity 1: OR=1.11, 95%CI:1.03-1.20; severity 3 vs. severity 1: OR=1.39, 95%CI: 1.30-1.48), and heart failure (severity 2 vs. severity 1: OR=1.26, 95%CI:1.17-1.35; severity 3 vs. severity 1: OR=1.79, 95%CI: 1.68-1.90) were associated with higher odds in stroke severity 2 and stroke severity 3 when compared to severity 1 of stroke. Diabetic patients with ischemic heart disease had higher odds in severity 3 (OR=1.07, 95%CI: 1.02-1.12), and lower odds in severity 2 (OR=0.96, 95%CI: 0.92-1.02) when compared to severity 1 of stroke, though the letter was not statistically significant. No statistically significant association existed for stroke severity and participating in DSCP. Stroke severity was statistically significant associated with number of diabetic care in 365 days before the index stroke. Diabetic patients with

increased diabetic care exams had statistically significant lower odds in severity 2 (OR=0.92, 95%CI: 0.90-0.94), and severity 3 (OR=0.90, 95%CI: 0.88-0.91) when compared to severity 1 of stroke.

Diabetic patients with 1-time emergency room visit due to diabetes in 365 days prior to stroke had statistically significant higher odds in stroke severity 3 (OR=1.31, 95%CI: 1.20-1.42) and stroke severity 2 (OR=1.20, 95%CI: 1.10-1.31) when compared to severity 1 of stroke. Diabetic patients with 2 or more emergency room visit due to diabetes had statistically significantly higher odds in stroke severity 3 (OR=1.53, 95%CI: 1.29-1.82) and stroke severity 2 (OR=1.22, 95%CI: 0.99-1.49) when compared to severity 1 of stroke, though the latter was not statistically significant. Stroke severity was significantly higher associated with diabetic patients who had 1-time hospitalization visit (severity 2 vs. severity 1: OR=1.21, 95%CI:1.10-1.34; severity 3 vs. severity 1: OR=1.55, 95%CI: 1.42-1.68), and two or more hospitalization visits (severity 2 vs. severity 1: OR=1.30, 95%CI:1.06-1.58; severity 3 vs. severity 1: OR=1.70, 95%CI: 1.43-2.02) due to diabetes in 365 days prior to stroke when compare to those who had no hospitalization visit due to diabetes.

By reported medical institution for stroke care, diabetic patients who visited medical center were more likely with higher odds in stroke severity 3 (OR=1.48, 95%CI: 1.40-1.56) when compared to severity 1 of stroke, though odds in stroke severity 2 (OR=0.99, 95%CI: 0.94-1.05) was not statistically significant. Diabetic patients who visited regional hospital were more likely with higher odds in severity 3 (OR=1.20, 95%CI: 1.14-1.26), and lower odds in severity 2 (OR=0.83, 95%CI: 0.79-0.88) when compared to severity 1 of stroke.

Chapter 5: Discussion of results and policy implications

This study identified consistent results with previous studies in several aspects for diabetic patients with subsequence stroke. Among ischemic stroke patients, this study identified 27.4% (n=76,194) of patients with diagnosed diabetes mellitus. The percentage is consistent with a previous hospital-based study that reported 27.3% of ischemic stroke patients with diabetes.[69] A national study examined the quality of care and outcomes in patients with diabetes hospitalized with ischemic stroke by using data from Get With the Guidelines–Stroke program, and indicated that there were 31% ischemic stroke patients with diabetes[90]. Another research form Taiwan Stroke Registry pointed out that 45.4% of stroke patients had diabetes mellitus.[20] The differences may come from a 365-day exposure period in our study, so stroke patients with first diabetes diagnosed in this period or during the stroke hospitalization were not included in this study. Also, this study did not include stroke patient with transient ischemic attack.

The percentage of diabetic patients with no ambulatory visit for 365 days is also consistent with previous study. In this study, we found that 27.8 % of diabetic patient had no diabetic ambulatory visit in 365 days prior to the index stroke. Similarly, another study in Bhutan indicated that near one-third of DM patients did not visited the clinic at least

once within a year of registration in National Diabetes Control Programme.[91] Also, a previous study tried to determine the frequency and correlates of persistent, long-term gaps in diabetes care which used “persistent gap” to define diabetic patients persistently fail to get recommended care. The result found that 30% of diabetic patients had at least 1 persistent gap for not receiving preventive services over the 3-year analytic period.[92] It was known that diabetes control may be accompanied by more frequent medical visits which linked with better control of diabetes mellitus[93-96], but we found more than one-fourth of diabetic patients in this study still had no diabetic ambulatory visit within a 365-days period.

The characteristics of different diabetic ambulatory lapses groups

The result of median age (age: 71) in this study is consisting with a previous U.S. study focused on ischemic stroke patients with diabetes (age: 69.8).[90] The results of this study showed that diabetic patients with the last ambulatory care within 90 days were younger and had a lower percentage of patients aged 75 and older, whereas diabetic patients with the last ambulatory care over 365 days had a higher percentage of patients aged 75 and older. Age is an important factor in health care utilization, especially for those who are older than 65 years. A study profiled older adults receiving assistance with physician visits and prescribed medications, and the results found that older adults receiving help with both physician visits and prescribed medications typically have high health and functioning needs.[97] Another study pointed out that nearly one-third (31.3%) of community-dwelling adults aged 65 and older were accompanied during routine physician visits, and older adults' companions were overwhelmingly family members (93.3%).[98] Besides, a recent study assessed the association between loneliness and physician visits among community-dwelling older adults in Singapore. The study indicated a significant association between loneliness and lower odds of physician visits.[99] Older population may have a higher probability to suffer a serious household medical event (e.g. heart attack),

shift in family structure (e.g. death of a partner), or desire to reduce aging associated functional decline which result in ambulatory care unaccompanied and longer ambulatory care lapses. A recent study investigated knowledge of modifiable cardiometabolic risk factors among rural men in the western United States and identify their concerns related to heart health and motivation to reduce risk. The results found that catalysts for behavior change included a serious medical event in the household and desire to reduce aging-associated functional decline.[100]

Hypertension is the most common comorbidity for diabetic patients in this study (66.8%) which is consistent with other studies. Two Canadian studies reported that hypertension was the most common comorbid disease in older adults with diabetes (79.1% and 83%)[101,102]. However, the percentage of diabetic patients with hypertension was lower in this study when compared to other studies. The reason may be that this study included patients aged 18 to 65 years which increased the population size. Besides, our study has a strict definition for comorbidities, which were defined by more than 3 times of list diagnoses in outpatient visits before the index stroke or list diagnoses of index stroke, and led to a lower percentage of hypertension. In this study, diabetic patients with the last ambulatory care within 90 days had the highest percentage in hyperlipidemia (35.5%)

when compared to the rest of groups. It seemed that there was a trend relationship between ambulatory care lapses and hyperlipidemia. However, there was no trend relationship in other comorbidities, such as atrial fibrillation, ischemic heart disease, stroke history, chronic kidney disease, and heart failure, although diabetic patients with the last ambulatory care within 90 days had the lowest percentage. Because of the characteristic of claim data, data was recorded because patients visited physicians for their needs. It is possible that patients visit physician for highly symptomatic disease, which take priority to record. This situation may result in an overestimate of other disease, which have no immediate effects. When compared to other comorbidities in this study, hyperlipidemia seemed to have no immediate effects to diabetic patients. It is known that comorbidity includes conditions that are highly symptomatic with large effects (e.g., ischemic heart disease) and those that have no immediate effects (e.g., hyperlipidemia),[103] and comorbidities with highly symptomatic are usually recorded by clinical practitioners. Comorbidities in this study were defined according to clinic visits or hospitalizations, so the results may reflect the real world situation.

Patients with poorly controlled diabetes mellitus may present repeatedly to the emergency department for management and treatment of hyperglycemic. A newly study

from Canada identified risk factors that predict unplanned recurrent emergency department visits for hyperglycemia in patients with diabetes within 30 days of initial presentation.[104] The result found that patients with a previous hyperglycemia visit in the past month were associated with an increased emergency room visit which is similar with our study showed that more emergency room visits were observed in diabetic patients with shorter ambulatory care lapses. Besides, less diabetes-related emergency room visits and hospitalizations were observed in diabetic patients with longer ambulatory care lapses in this study. Diabetic patients with shorter ambulatory care lapses did not indicate taking medication regularly and having well-controlled diabetes. A recent study identified medication adherence trajectories among patients with newly diagnosed diabetes, and found that the persistent adherence trajectory only accounted for 39.9% of the subjects.[105] For diabetic patients with poor blood sugar control, they may visit ambulatory care more often, and physicians may recommend or transfer these patients to emergency room or hospitalization for serious condition. On other hand, diabetic patients with longer lapses may not know their poor-controlled diabetes, and result in less use of emergency visit and hospitalization.

Utilization for diabetic care exams

The percentage of patients participating in DSCP, HbA1c test, and cholesterol test in this study were different with previous study, but the percentage of dilated eye test and microalbumin test in this study were consistent with previous studies. The results of this study in Table 3 showed that 13.7% of patients were participating in DSCP, 50.3% of patients were having two or more HbA1c test, 59.5% of patients were having cholesterol test, and 28.4% of patients were having dilated eye exam among overall study population. Besides, diabetic patients with shorter ambulatory care lapses had a higher percentage of patients participated in the DSCP, and received diabetic care exam in HbA1c test, cholesterol test, dilated eye test, and microalbumin/urine routine test. It is known that diabetic patients participating in DSCP are required to attend a clinic or hospital every 3 months for adjustment of drugs by a physician, and to receive diabetes education from a diabetes educator, as well as a diet consultation with a dietitian.[6] Therefore, patients with ambulatory care lapses less than 90 days is possible to be observed a higher percentage of patients who participated in the DSCP, as well as received diabetic care exams in HbA1c test, cholesterol test, dilated eye test, and microalbumin/urine routine test.

A small study examined the relationship between medication adherence and healthcare outcomes, and the DSCP enrollment rate was 6%.[106] Besides, a recently study examined the trends of healthcare use and costs for patients with type 2 diabetes mellitus in Taiwan, and indicated that about 19% of diabetic patients were enrolled in DSCP.[79] The percentage of DSCP in this study (13.7%) is higher than the small study, but lower than recent study. The reason may be that the population of the small study only focused on patients with newly diagnosed type 2 diabetes mellitus. The difference between this study and the recently study may come from different definition and calculation. However, the percentage of DSCP participation rate in diabetic patients with the last ambulatory care within 90 days prior to stroke (20.8%) is similar with the recently study.

A previous study analyzed claim data to understand accountability and utilization of health resources during 2000 to 2009 among diabetic patients in Taiwan.[107] The percentage of HbA1c test in previous study (67.6%) is higher than our study (50.3%), but it is close to patients in diabetic patients with the last ambulatory care within 90 days prior to stroke (63.3%). The reason may be come from that previous study identified diabetic patients and calculated the utilization in the same period, but diabetic patients were identified a year before calculating period. Beside, our study showed a lower percentage of

cholesterol test (59.5%) when compare to the percentage of total cholesterol test in the previous study (79.1%). The different may come from that we used strict definition in calculating cholesterol test, such as total cholesterol test, triglyceride test, and low-density lipoprotein cholesterol test should prescribe in the same order. The percentage of dilated eye test in previous study is similar with our study (28.4%), and patients with the last ambulatory care within 90 days prior to stroke had a higher percentage (35.2%) in receiving dilated eye test. The percentage of microalbumin test in our study (27.7%) was similar with previous study (25.6%), and patients with the last ambulatory care within 90 days prior to stroke had a higher percentage (36.2%).

In other hands, the results indicated that diabetic patients with the last ambulatory care over 365 days were associated with a lower participation rate in DSCP and a lower percentage to receive diabetic care exams. That is to say, this group of patients did not have diabetic ambulatory care, but they received some kinds of diabetic care exams. The reason may be that they visited other specialties due to other sever disease, and diabetic care exams were provided by other specialties. With further investigation in patent with the last ambulatory care over 365 days, we found that diabetic care exams were frequently provided through ambulatory care. The primary disease for executing diabetic care exams

included hypertensive disease, chronic kidney disease, chronic ischemic heart disease, senile cataract, diabetic retinopathy, and glaucoma. Since diabetes management is well-established, many specialties are trained to provide appropriate diabetes management for diabetic patients. With involving in more specialties in providing diabetes care, it is possible to make diabetes management more comprehensive.

Expenditure of different diabetic ambulatory lapse groups

The median of average hospitalization cost per day (4,303 NTD =143 USD) was higher than previous Taiwanese study, which found that the mean hospitalization cost is 1532.60 USD per person with mean length of stay for 15.7 days.[66] The difference may come from that the Taiwanese study was a hospital-based study and study subjects comprised patients with first-ever stroke and recurrent stroke.

Diabetic patients with the last ambulatory care over 365 day had the highest median of average hospitalization cost per day while those with the last ambulatory care within 90 days had the lowest. Although we had controlled for age, sex, comorbidities in hypertension, atrial fibrillation, ischemic heart disease, chronic kidney disease, heart failure, participated in DSCP, number of diabetic care exams, number of diabetes-related emergency room, number of diabetes-related hospitalization visit, and type of medical institution for the index stroke, our multivariate adjusted analyses detected no association with average hospitalization cost per day in patients with the last ambulatory care within 90 days, patients with the last ambulatory care within 91 to 180 days, patients with the last ambulatory care within 181 to 270 days, and patients with the last ambulatory care within 271 to 365 days. It is possible that neurologists treat their patients according to

their professional knowledge and clinical guideline, and the standard for stroke care were similar in Taiwan. Many evidence-based stroke care guidelines have been updated in accordance with these considerations to successfully guide clinical practice procedures for stroke.[108-111]

However, the result of this study showed that a statistically significant increased average hospitalization cost per day were found in diabetic patients with the last ambulatory care over 365 days while controlling all confounding factors. A previous study pointed out that lapses in Medicaid coverage can result in inadequate access to care and may be associated with overall greater expenditure in the post-lapse periods. The result also found that the longer the length of the lapse was negatively associated with the likelihood of any total expenditure within a 3-month post-lapse time period.[112] The difference between the previous study and this study may be that ambulatory care lapses in our study only indicated for diabetes-related visit, and we only consider the expenditure for the first ischemic stroke hospitalization after lapses. Beside, a recent Taiwanese study examined the trends of healthcare use and costs for patients with type 2 diabetes mellitus. The results pointed out that diabetic patients with fewer than 3 diabetes-related physician visits in a year, which considered as irregular diabetes care,

tended to consume more inpatient services.[79] The result is similar with our study showed that longer ambulatory care lapses may incurred the expenditure of hospitalization. The difference from previous study and this study is that our study only considered the expenditure of ischemic stroke hospitalization, and not included cost from other diseases. Therefore, the statistically significant increased expenditure was observed in diabetic patients with the last ambulatory care over 365 days.

The result of this study is consistent with previous studies that average hospitalization cost increased with the age increased.[66] It is also the same as previous studies that diabetic patients with comorbidities in hypertension[113,114], atrial fibrillation[56,97], ischemic heart disease[114,115], chronic kidney disease[114], and heart failure[115] were statistical significantly increase average hospitalization cost. However, diabetic patients with stroke history showed a negative effect on average hospitalization cost. The result was different with previous small study, which showed no association between stroke history and hospitalization cost.[66] Besides, this study showed that diabetic patients participated DSCP were associated with lower average hospitalization cost per day which is the same as previous study.[116]

Length of stay of different diabetic ambulatory lapse groups

The overall median length of stay for the index ischemic stroke (8 days, IQR 5-16 days) was consistent with previous studies. The result was similar with a small study with 295 subjects, which indicated acute length of stay for stroke patients was 8 days in median.[67] The result was also close to a Taiwanese hospital-based study which reported median length of stay for ischemic stroke patients was 7 days [69]. Besides, a recent Taiwanese study investigated cost and length of stay in first-ever and recurrent stroke patients. The results found that the average length of stay was 13.9 days, and the most common length of stay for ischemic stroke was 5-10 days.[66] Although the median length of stay between 5 groups did not showed big different (8 to 9 days), the longer lapses seemed to have a longer length of stay.

After controlling for age, sex, comorbidities in hypertension, atrial fibrillation, ischemic heart disease, chronic kidney disease, heart failure, participated in DSCP, number of diabetic care exams, number of diabetes-related emergency room, number of diabetes-related hospitalization visit, and type of medical institution for the index stroke, we found that diabetic patient with longer diabetic ambulatory lapses were associated with increased length of stay for subsequence ischemic stroke. The results of multivariate

regression showed that diabetic patients with the last ambulatory care within 91 to 180 days, diabetic patients with the last ambulatory care within 271 to 365 days and diabetic patients with the last ambulatory care over 365 days seemed to prolong the length of stay for the index stroke when compared to diabetic patients with the last ambulatory care within 90 days.

A previous study assessed whether a lapse in Medicaid coverage is associated with an increase in expenditures and acute care utilization among beneficiaries with diabetes. The results of the study found that individuals with diabetes having a lapse in Medicaid coverage was associated with longer inpatient stays. It also found that the length of the coverage lapse was not significant associated with the length of inpatient stay.[112] Our study showed similar results. As compared to patients with the last ambulatory care within 90 days in this study, the longer ambulatory care lapses showed statistically significant increased length of stay, especially for diabetic patients with the last ambulatory care within 91 to 180 days, diabetic patients with the last ambulatory care within 271 to 365 days and diabetic patients with the last ambulatory care over 365 days. However, the increased length of stay did not present a trend relationship with ambulatory care lapses increased.

Besides, this study is consistent with previous studies[32,66] showed that patients with older age were associated with the longer length of stay for the index stroke. This study showed the same result as a previous study[117] that male patients have shorter length of stay when compared to female patient. Comorbidity in hypertension showed a negative effect on the length of stay for the index stroke which is the consistent with a Korean study.[118] It is known that heart disease is an important factor to increase length of stay for stroke. This study is consistent with previous studies showed that atrial fibrillation[66,119] and heart failure[119] had been approved to have a positive effect on stroke length of stay. Although ischemic heart disease in this study showed a negative effect, it did not have statistically significant. The results showed that diabetic patient with more diabetic-related emergency room visit and hospitalization visit were associated with an increased length of stay. This is intuitive as one would expect patients with more emergency room visit and hospitalization prior to stroke to be more functionally impaired and hence stay longer.

Stroke severity of different diabetic ambulatory lapse groups

Although previous results showed only little difference in average hospital cost per day and length of stay among different lapses of ambulatory care groups, the odds ratio of stroke severity showed a statistically significant increase in patients with longer lapses, especially for those patients with the last ambulatory care over 365 days. The results from Table 4 showed that diabetic patients with the last ambulatory care within 90 days had the highest percentage of patients in severity 1 and the lowest percentage of patients in severity 2 and severity 3 when compared to the other groups. Besides, diabetic patients with the last ambulatory care within 90 days had a lower percentage of in-hospital death and discharge under critical condition.

With controlling for age, sex, comorbidities in hypertension, atrial fibrillation, ischemic heart disease, chronic kidney disease, heart failure, participated in DSCP, number of diabetic care exams, number of diabetes-related emergency room, number of diabetes-related hospitalization visit, and type of medical institution for the index stroke, the multinomial logistic regression model found that diabetic patients with the last ambulatory care within 91 to 180 days, diabetic patients with the last ambulatory care within 271 to 365 days and patients with the last ambulatory care over 365 days reported a

severer ischemic stroke when compared to diabetic patients with the last ambulatory care within 90 days.

It is known that frequent visits to diabetes care clinics linked with better control of diabetes mellitus. The United State studies indicated that diabetic patients who had a clinic visit of 1 to 2 weeks achieved better and faster control in HbA1C, blood pressure, and low-density lipoprotein cholesterol compared to those had a clinic visit every 3 to 6 months.[76,77] A previous study evaluated the relationship between missed appointments and glycemic control. The results found that patients who missed more than 30% of their appointments were less likely to practice daily self-monitoring of blood glucose and to have poor oral medication refill adherence.[120]

On the contrary, diabetic patients with longer ambulatory care lapses may imply that they do not have diabetes care for a longer time. A previous study identified young adults with type 1 diabetes who had been lost to follow-up during their transfer from pediatric to adult care and compared the clinic outcomes to participants receiving continuous care. The results showed that lapse care participants as compared with continuous care participants had a higher HbA1C and reported a greater proportion of severe hypoglycemia.[121] Long-term hyperglycemic can cause endothelial dysfunction,

and organs within bodies will also be damaged. When diabetic patients suffer from an ischemic stroke, the severity may increase within these groups of patients. A newly study assessed whether HbA1c-based adjusted glycemic variables were associated with unfavorable outcomes of stroke hospitalization. The result found that glycemic gap in diabetic patients were associated with acute ischemic stroke severity.[122] Besides, frequent ambulatory care visit for chronic diseases is to prevent its complications. A recent study assessed the impact on foot complications of time between the onset of symptoms of diabetes and the physician visit, and indicated that waiting for >1 month after symptoms onset dramatically increases the risk of diabetic foot complications.[123] Moreover, a previous study examined whether ambulatory visits are associated with decreased stroke and death in hypertensive patients , and found that ambulatory visits prior to event were associated with decreased death.[124]

Age is a predictors factors of index stroke severity which is consistent with intuitive as older patients to be more impaired from stroke. The result of this study is the same as a previous study that male patients seemed to have a less severe stroke than female patients.[125] The result of this study is consistent with previous studies that patients with comorbidities in atrial fibrillation[126], stroke history, chronic kidney disease[127] and heart

failure[128,129] seem to increase the severity of stroke. The results are also consistent with intuition that diabetic patients with more diabetic care was associated with less severe of stroke, and more diabetic-related emergency room visits and hospitalizations seem to associate with more severity of subsequence stroke.

Diabetic Patients with subsequence ischemic stroke having diabetic ambulatory lapse over 365 days prior to stroke

According to the above results, this group of patients were older, having higher percentages of highly symptomatic disease, less use of diabetes-related emergency visit and hospitalization. Also, they were associated with a lower participation rate in DSCP and a lower percentage to receive HbA1c test, cholesterol test, dilated eye test, and microalbumin test. Moreover, the study results found this group of patients were likely associated with higher average stroke hospital expenditure, the increase of stoke length of stay, and severer of ischemic stroke.

The significant results in diabetic patients with subsequence ischemic stroke having the last ambulatory care over 365 days prior to stroke could be due to following reasons. First, this group of diabetic patients may be lack of access to care which resulted in longer lapses. Insurance coverage, such as Medicaid in the U.S., can result in inadequate access to care.[112] However, there is little influence from insurance coverage since Taiwan conducted National Health Insurance program. Also, this group of patients may have difficulties in accessing healthcare, including problems getting appointments in primary care, costs of transportation and other expenses[56,130,131], and problems accessing medications.[130-133]

Besides, this group of diabetic patients may have limited mobility or disability[131,134]. They may need someone accompanied for healthcare, but lack of family support[135-137]. Moreover, diabetic patients with longer lapses may have other factors that preoccupied their diabetic ambulatory care. They may have a higher probability to suffer a serious household medical event (e.g. heart attack), shift in family structure (e.g. death of a partner) since this group of patients were older.[100]

Other factors that may influence this group of patients included insufficient knowledge on prevention and on support from social and health care systems[56,130,131,137], differences in perceptions of health that are culturally based, difficulty coping with comorbid conditions[131], or desire to reduce aging associated functional decline which result in longer ambulatory care lapses.[100]

Conclusions

This dissertation sought to understand the relationship between ambulatory care lapses and stroke medical utilization in diabetic patients with subsequence ischemic stroke. Although this study identified consistent results with previous studies in several aspects for diabetic patients with subsequence stroke, there was no study focused on the pattern of diabetic ambulatory care lapses. Only few studies investigated on the relationship between lapses and medical utilization. One study pointed out that lapses in Medicaid coverage were associate with increased expenditure in post-lapse periods.[112] The other Taiwanese study examined the healthcare use and cost in patients with type 2 diabetes, and found that patients with less than 3 visits per year tended to consume more inpatient services.[79]

In this analysis of a nationwide cohort study of stroke patients with diagnosed diabetes mellitus, we retrieved 76,194 (27.4%) patients aged 20 and older from 2002 to 2012 for analysis. Patients were divided into five groups based on the different duration of diabetic ambulatory care lapses prior to the index stroke. Among overall diabetic patients with subsequence ischemic stroke, we found that more than half (59%) of diabetic patients had the last diabetic ambulatory care within 90 days prior to stroke, and

more than one-fourth (27.8%) of diabetic patients had the last diabetic ambulatory care over 365 days prior to stroke. The results were summarized below to answer the study aims.

Aim1: To understand the baseline characteristics for different pattern of ambulatory care in diabetic patients

Among overall diabetic patients with subsequence ischemic stroke, diabetic patients with the last ambulatory care over 365 days prior to stroke were older, more male when compared to other groups. Diabetic patients, who had subsequence ischemic stroke, with longer diabetic ambulatory care lapses prior to stroke tended to have higher percentage in highly symptomatic comorbidities, such as atrial fibrillation, ischemic heart disease, stroke history, chronic kidney disease, and heart failure, when compared to those patients with the last ambulatory care within 90 days prior to stroke. Besides, diabetic patients, who had subsequence ischemic stroke, with the last diabetic ambulatory care over 365 days prior to stroke was found to have less diabetic-related emergency visit and hospitalization prior to stroke when compared to other groups.

Aim2: To understand the utilization of ambulatory care among diabetic patients prior to stroke hospitalization

The results showed that diabetic patients with subsequence ischemic stroke having shorter diabetic ambulatory care lapses had higher percentage of participating in diabetic shared care program and receiving diabetic care exams. The study results found that diabetic patients with subsequence ischemic stroke having the last diabetic ambulatory care over 365 days prior to stroke had the lowest percentage (0.6%) in participating diabetes shared care program, whereas diabetic patients having the last diabetic ambulatory care within 90 days prior to stroke were 20.8%. Diabetic patients with subsequence ischemic stroke having the last diabetic ambulatory care over 365 days prior to stroke had lower percentage of diabetic care exams, including HbA1c test (24.5%), cholesterol test (43.4%), eye exam (14.6%), and microalbumin/urine test (11.3%).

Aim3: To understand whether ambulatory care lapses in diabetic patients prior to stroke hospitalization is related with stroke medical consumption

Among diabetic patients with subsequence ischemic stroke, this study found following relationship between diabetic ambulatory care lapses and stroke medical consumption. The results found that diabetic patients with the last ambulatory care over 365 days prior to stroke was significantly associated with higher average stroke hospital

expenditure. Compared to diabetic patients with the last ambulatory care within 90 days prior to stroke, the average stroke hospital cost per days was 1.06 times higher in those with the last ambulatory care over 365 days prior to stroke.

Besides, the results of this study indicated that diabetic patients with the last ambulatory care over 90 days prior to stroke was likely associated with the increase of length of stay in subsequence stroke hospitalization. Compared to diabetic patients with the last ambulatory care within 90 days prior to stroke, the length of stay was 0.79, 1.04, and 0.61 days longer in those with the last ambulatory care within 91~180 days prior to stroke, the last ambulatory care within 271~365 days prior to stroke, and the last ambulatory care over 365 days prior to stroke. However, increased length of stay did not present a trend relationship with ambulatory care lapses increased.

Moreover, the results showed that diabetic patients with the last ambulatory care over 90 days was associated with increased severity of ischemic stroke. Compared to diabetic patients with the last ambulatory care within 90 days, the odds ratio of stroke severity 2 to stroke severity 1 was 1.12, 1.13, 1.14 in those with the last ambulatory care within 91~180 days, the last ambulatory care within 271~365 days, and the last ambulatory care over 365 days; the odds ratio of stroke severity 3 to stroke severity 1 was

1.24, 1.20, 1.34 in those with the last ambulatory care within 91~180 days, the last ambulatory care within 271~365 days, and the last ambulatory care over 365 days.

In summary, the results found that diabetic patients with subsequence ischemic stroke having the last diabetic ambulatory care over 365 days prior to stroke were associated with increased hospitalized expenditure, length of stay, and severity for stroke although we had controlled possible confounding factors. Although this study using Taiwanese data as an example, our findings could be consistent with other countries. Therefore, the recommendations from this study may be more closely applicable to countries with healthcare insurance system, public health systems, electronic health record systems, and cloud-based medication records systems.

Recommendations

Based on the above results, diabetic patients with the last ambulatory care over 365 days prior to stroke had higher stroke expenditures, longer length of stay and severer stroke. So, diabetic ambulatory care lapses could be an important indicator for diabetic patients care management. It is needed to be great concerned for diabetic patients with the last ambulatory care over 365 days prior to stroke. Therefore, this study provided several suggestions in management and clinical aspects.

For health care administrators, this study suggests that they should initiative to understand how frequently miss appointments occurred for diabetic patients and to follow diabetic patients with ambulatory care lapses over 365 days. We also suggest that health care facilitates establish a community health worker system in order to get close with diabetic patients. The community health worker system includes a nurse case manager and several community health workers, with providing basic diabetes information and content of diabetes-related behaviors for diabetic patients, especially for those with longer ambulatory care lapses. According a previous study[138] which adapted community health worker diabetes intervention, it significantly increased primary care physician visits, and decreased emergency department visits among those with high emergency

department utilization. The community health worker system suggests important and beneficial impacts on health system utilization from the diabetes intervention in a low resource and high-risk population. Besides, the community health worker system expects to enhance continuous of diabetes care and to reduce medical expenditure for the subsequence ischemic stroke.

For government policy, this study suggests that an indicator of ambulatory care return rate should be added in recent program, and additional reward for health care facilitates should be provided by National Health Insurance Administration if a lower percentage of miss appointment for ambulatory care within 365 days in diabetic patients. The Diabetes Shared Care Program had provided financial incentive in several ways, such as body mass index, diet and exercise, smoking, blood pressure, weight management counseling, medication reconciliation, HbA1c testing and annual lipid profile. Besides, several previous studies had indicated that pay-for-performance program for diabetes was associated with a significant increase in regular follow-up visits and evidence-based services, and significantly lower hospitalization costs.[116,139] Since ambulatory care lapses could be an important indicator in diabetes care management, the financial incentive expects to motive health care facilitates on ambulatory care monitoring for diabetic

patients, especially for those with ambulatory care lapses over 365 days. It will also offer financial relief for further diabetes complications and hospital visits in long term.

For medical professionals, this study suggests that medical professionals should make the best of a cloud-based medication system to understand diabetic care exams for diabetic patients. It is known that a cloud-based medication records system is a convenient platform for sharing data among healthcare providers in different institutions,[140] and many countries are devoted to develop, such as Austria and India. Taiwan National Health Insurance Administration launched PharmaCloud system in 2013 to integrate patients' medication lists, exams, and operations among different medical institutions. The system enables physicians at contracted medical services providers to search patients' medication records over the previous three months.[141] A previous study indicated a moderate satisfaction toward the PharmaCloud system. However, physicians and community pharmacists had a lower satisfaction rate than hospital pharmacists.[142] Therefore, it is important to encourage medical professionals to use PharmaCloud system and to provide appropriate diabetic care exams for diabetic patients, especially for those patients with longer lapses.

Finally, this study suggests that further researches can focus on diabetic patients with ambulatory care lapses over 365 days prior to stroke in order to understand the discontinuity of ambulatory care. Because of the characteristic of the database, we cannot get a deeper understanding of this group. It is suggested to use a database linking claim data with detailed community-based survey data, such as Community Health Needs Assessment in the U.S., for further researches. Based on the study results, more than one-fourth of diabetic patients with the last ambulatory care over 365 days prior to stroke. This group of patients were associated with an increased stroke medical expenditure, length of stay, and severity. Therefore, it is better to investigate the reason of longer ambulatory care lapses behind this group of patients. Besides, further researches could consider how to divide the population since there were few patients in the middle of three groups. This study used a strict three-months period for grouping, but some patients may not have a follow-up visit within three months. Moreover, it could be further investigated whether patients with type 1 diabetes or type 2 diabetes have different behavior of diabetic ambulatory care because of different clinical presentation and disease progression.

Limitations and Strengths

There are several strengths for this study. First, this is the first study to demonstrate the relationship between duration of diabetic ambulatory lapses and subsequence ischemic stroke from a nationwide database. Patients with chronic disease is highly recommended to manage their disease with regular appointments in ambulatory care setting. However, few studies focus on ambulatory lapses, especially on specific diseases. Second, Taiwanese National Health Insurance Research Database is a national database with standard formats for all reimbursement records. The longitudinal database with large sample size provided a good opportunity to study diabetic patients' behavior, especially for ambulatory care and their subsequence stroke utilization. The Taiwanese National Health Insurance Database has been used a lot in researching the relationship between diabetes and risk of stroke in the past years. However, the diabetic ambulatory care behavior is lacking. Finally, this study is a retrospective cohort study design. The design provided us to study multiple outcomes of stroke, such as expenditure, length of stay, and severity. Also, it is less time consuming and costly then prospective design. With the understanding of duration of diabetic ambulatory care lapses before stroke

hospitalization among diabetic patients with subsequence stroke, this study will increase the awareness in diabetic ambulatory care.

On the other hands, this study has some limitations. First, this is a retrospective cohort study design by using claim data, both the exposure and outcome have already occurred at the outset of the study. We must rely on others for accurate recordkeeping. Also, information on several confounding variables may be unavailable, inadequate or difficult to collect. Therefore, we cannot explain why patients miss follow-up appointments and why physicians provide some kinds of medical care. Therefore, a prospective research is recommended to conduct. Second, comorbidities that have no immediate effects, such as hyperlipidemia, may be underestimated. This is because that comorbidities are defined by numbers of physician visits, and patients may ignore comorbidities with less highly symptomatic. Therefore, the adjusted models did not include comorbidity in hyperlipidemia, but we adjust all obtainable demographic and other comorbidities. Third, the index stroke may be not the first stroke for study population. We had excluded patients with late effects of cerebrovascular disease in any place of diagnoses. Also, we excluded patients with any stroke hospitalization in calendar year 1997 to 2001. Therefore, the index stroke may be not the first stroke was more possibly in the early calendar year. Finally, the claim

database does not contain data on clinical stroke scales for severity, as well as ischemic stroke types. Therefore, this study adopted a validated proxy for stroke severity, the stroke severity index, to estimate patient stroke severity.

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Appendices

Table 1 Order code for diabetic care exams in claim data

Items	**Order codes**
HbA1c test	09006
Cholesterol test	1) 09001 and 09004 and 09043 2) 09001 and 09004 and 09044 3) 21 and IC21, 22 and IC22, 25 and IC23, 27 and IC24, 21 and L1001C and IC21, 25 and L1001C and IC23
Eye exam	23501, 23502, 23702
Urine microalbumin test	12111, 27065, 06013C

Table 2 Order code for Stroke Severity Index in claim data

Items	**Order codes**
Airway suctioning	47041C, 47042C
Bacterial sensitivity test	13009B, 13009BB, 13010B, 13010BA, 13011B, 13011BB, 13020B
General ward stay	03002A, 02006K, 02007A, 02008B, 03001K, 03003B, 03004B, 03005K, 03006A, 03007B, 03008B, 03026K, 03027A, 03028B, 03029B 03002AB
Intensive care unit stay	02012A, 02011K, 02013B, 03010E, 03010K, 03011A, 03011F, 03012B, 03012G, 03013B, 03013H, 03047E, 03048F, 03049G, 03050H
Nasogastric intubation	47017C, 47018C, 47018CA
Osmotherapy	A009633266, A009633255, A009633277, A009745277, A013354277, A015561255, A015561266, A015561277, A016476238, A016476266, A016476277, A031387238, A033425266, A042601238, B014379277, B020322265, B020322277, N012343266, A023733263, A023733265, A023733266, A023733277, A024986209, A024986265, A024986266, A024986277, A025104266, A025104277, A025355266, A025355277, A026793265, A026793266, A026793277, A028475265, A028475277, A029475265, A029475277, A034722277, AC23733263, AC23733266, AC23733277, AC24986265, AC24986266, AC24986277, AC28475277, AC29475265, B006604277, B017082263, B017082277, B017728265, B017728277
Urinary catheterization	47013C, 47014C

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Education:
DrPH in Health Policy and Management, Johns Hopkins Bloomberg School of Public Health**,** Baltimore MD, USA, July 2011- present

MS in Health Care Administration, University of New Haven**,** West Haven CT, USA, September 2010-June 2011

MS in Health Care Management, Chang Gung University, Taoyuan, Taiwan, September 2006-June 2008

BS in Health Services Administration, China Medical University, Taichung, Taiwan, September 2001-June 2005

Work experience

Chang Gung University, Taoyuan (Aug, 2016 – now)
Experienced data analyst at Research Services Center for Health Information

Chang Gung Memorial Hospital, Chiayi (June, 2012 – Jul, 2106)
Research assistant, supervised by Meng Lee MD

- Worked on project entitled – *Clinical Management, Recurrence, Readmission, Mortality and Health Care Costs after Acute Stroke in Taiwan- 5-year Follow-up based on the National Health Insurance Longitudinal Cohort Dataset* (CMRP6B0111, CMRPG6B0112) 05/2012~04/2014

- Worked on project entitled – *Does statin use prevent recurrent stroke in ischemic stroke patients with atrial fibrillation* (NSC 102-2628-B-182-012) 08/2013~07/2014

- Participated in project entitled – *Does Left atrial enlargement predict new-onset atrial fibrillation among ischemic stroke patients?* (CORPG6D0101-103) 05/2014~04/2017

- Worked on project entitled – *Impact of Discontinuation of or Switching to Low-dose Statin Therapy after Ischemic Stroke Therapy* (MOST 103-2314-B-182-056) 08/2014~07/2015

- Worked on project entitled – *Serial Electrocardiogram Versus Holter to Detect Atrial Fibrillation in Acute Ischemic Stroke: A Randomized Controlled Trial* (MOST104-2314-B-182 -019) 08/2015~07/2016

Chang Gung University, Taoyuan (Jul 2006 – Aug 2009)
Part-time research assistant, supervised by Hui-Hsuan Wang PhD

- Participated in project entitled – *Modeling Personal Health Information Management for the Next Decade: An Exemplary Demonstration for Cerebral Vascular Disease Patients, HiMD*

- Participated in project entitled – *Health Survey of Taoyuan County*, with the Department of Public Health, Taoyuan County

China Medical University, Taichung (Sep 2004 – Jun 2006)
*Research assistant, supervised by Tso-Chiang, Ma PhD (*Jul 2005 – Jul 2006*)*

- Worked on project entitled – *Medical Resource Utilization and Effectiveness for Menstrual Disorder patients in Chinese and Western Medicine*, with Taiwan Traditional Chinese Medicine Association, Taipei

- Participated in project entitled – *Abuse Prevention for Controlled Drugs*, with

the National Bureau of Controlled Drugs, Department of Health (Taiwan)

- Participated in project entitled – *Healthy City Promotion program in Miaoi County*, with the Bureau of Health Promotion, Department of Health (Taiwan)

*Part-time research assistant (*Sep. 2004 – Jun. 2005*)*

- Participated in project entitled – *Evaluating the performances of community health promotion and developing improve the strategy – from residence's perspective*, with the Bureau of Health Promotion, Department of Health (Taiwan)

Additional skills

Computers: SAS, SPSS, Stata, RevMan, Endnote, Photoshop, Microsoft Office (Word, Excel, PowerPoint)

Certificate

English Language Program, University of Washington, Seattle, USA (Sept 2009- Dec 2009)
Teachers of Chinese to Speakers for Other Languages, USA (2012)
Smoking cessation specialist training program, Chiayi County, Taiwan (2014)

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Research Papers

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Conference Abstracts

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2. Lee M, **Wu YL**, Saver JL, Lee HC, Lee JD, Chang KC, Wu CY, Lee TH, Wang HH, Rao NM, Ovbiagele B. Ischemic Strokes while on Aspirin: Initiation of Clopidogrel is better than Re-initiation of Aspirin for Prevention of Future Vascular Events. International Stroke Conference, San Diego, USA, February 2014, poster

3. Lee M, Saver JL**,** Hong KS, **Wu YL**, Liu HC, Ovbiagele B. Cognitive Impairment and Incident Stroke: A Systematic Review and Meta-analysis. International Stroke Conference, San Diego, USA, February 2014, poster
4. Hsu JY, **Wu YL**, Lee JD, Huang YC, Cheng CY, Wu CY, Hsu HL, Lin YH, Huang YC, Yang JT, Lee M, Ovbiagele B. Low Baseline Urine Creatinine Excretion Rate Independently Predicts Severe Disability or Death among Critically Ill Acute Stroke Patients. International Stroke Conference, San Diego, USA, February 2014, poster
5. Lee M, **Wu YL**, Saver JL, Lee JD, Wang HH, Ovbiagele B. Statin Use is Linked to Lower Risk of Recurrent Vascular Events among Ischemic Stroke Patients with Atrial Fibrillation. International Stroke Conference, Tennessee, USA, February 2015, poster
6. Lee M, Saver JL, Hong KS, **Wu YL**, Ovbiagele B. Impact of Warfarin Use in Patients with End Stage Renal Disease and Atrial Fibrillation. International Stroke Conference, Tennessee, USA, February 2015, oral presentation
7. Lee M, Chiu SW, Saver JL, Hong KS, **Wu YL**, Ovabiagele B. Folic Acid Therapy Prevents Stroke in Countries without Mandatory Folic Acid Food Fortification: A Meta-analysis of Randomized Controlled Trials. International Stroke Conference, Los Angeles, USA, February 2016, poster
8. Lee M, **Wu YL**, Ovbiagele B. Characteristics of Incident and Recurrent Stroke in Taiwan, 2000 to 2011. International Stroke Conference, Los Angeles, USA, February 2016, poster
9. Lee M, Huang WY, Tang SC, Sung SF, Chang KH, Lee JD, Lee TH, Huang YS, Jeng JS, Chung CM, **Wu YL**, Ovbiagele B. Atrial Fibrillation Trial to Evaluate Real-world Procedures for their Utility in helping to Lower Stroke Events (AFTER-PULSE): study protocol for a randomized controlled trial. International Stroke Conference, Los Angeles, USA, February 2016, ongoing trial poster

Unpublished works

1. Wu YL, August 2008," Relationship Between Imaging Diagnosis and Resource Utilization for Stroke Patients", Unpublished Master Dissertation, Chang Gung University, Taoyuan. (Chinese)