Development of an Ontario Diabetes Economic Model (ODEM) and Application to a Multidisciplinary Primary Care Diabetes Management Program

Report

Prepared for the Ontario Ministry of Health and Long-term Care

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Disclaimer

This Health Technology Assessment (HTA) report provides the methodology used to adapt the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model to the Ontario setting and an application of the model using primary data collected from a multidisciplinary primary care management program in Ontario. This report was prepared by the Program for Assessment of Technology in Health (PATH) at St. Joseph's Healthcare/McMaster University on behalf of the Medical Advisory Secretariat, Ontario Ministry of Health and Long-Term Care (MOHLTC) for the Ontario Health Technology Advisory Committee (OHTAC).

PATH takes sole responsibility for the final form and content of this report. The statements and conclusions in this report are those of PATH and not of the MOHLTC, OHTAC, McMaster University, St. Joseph's Healthcare Hamilton or ICES. Please contact PATH at www.path-hta.ca if you are aware of new research findings that should inform the report or would like further information.

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NOTE: *Any information pertaining to the incidence of diabetes in Ontario in this report requires further review and will be updated shortly.*

Dedication

This report is dedicated to the late Dr. Bernie O'Brien and Dr. Hui Lee whose tragic and untimely deaths occurred during the current study. Drs. O'Brien and Lee were young, enthusiastic and brilliant individuals. Their memory is an inspiration to those who knew them.

EXECUTIVE SUMMARY

Introduction

Diabetes is estimated to affect more than 734,000 Ontarians and this number is expected to increase to 1.2 million by 2010, with 90-95% having type 2 diabetes.(1) Approximately 40 percent of people with diabetes will develop diabetes-related complications at some point. This chronic disease doubles the chance of heart attack or stroke, is the leading cause of adult blindness and non-traumatic limb amputations, and increases the risk of end stage renal disease.(2) Health care costs for the treatment of persons with diabetes in Canada amount to approximately $9 billion annually.(3) These expenditures represent the costs associated with the daily treatment and control of the disease as well as the management of chronic complications that occur with increasing frequency and severity as the disease progresses.

In recognition of the burden associated with diabetes in Ontario and the potential to decrease this burden, the Ontario Ministry of Health and Long-Term Care (MOHLTC) made the treatment and management of diabetes a priority. To this end, the MOHLTC established a Diabetes Task Force in 2003 to advise the Ministry as to the best method for reducing the impact of diabetes in Ontario. The Task Force was comprised of a number of subcommittees (e.g. clinical, economic, primary prevention) who were asked to identify pressing issues and provide recommendations which would achieve maximum impact in improving outcomes for people with diabetes.(1) The economic subcommittee was given the task of proposing a method that the MOHLTC could use to prioritize investments with respect to the treatment and management of diabetes. In essence, the MOHLTC required a model that could measure the long-term cost-effectiveness of various diabetes management strategies.

Decision analytic models, that simulate the impact of alternative interventions on the probability and cost of experiencing diabetes-related complications, are increasingly being used both to model the progression of diabetes and to estimate lifetime costs and outcomes associated with different disease management strategies.(4;5) These models estimate the future occurrence of complications and quantify outcomes in terms of mean life-years gained or mean quality-adjusted life-years (QALYs) gained

from an intervention. They can also be used to estimate future healthcare costs of patients with type 2 diabetes, but their main purpose is to estimate the long-term cost-effectiveness of different interventions, especially when evidence of the impact of the interventions is on surrogate endpoints and the clinical trial evidence has to be extrapolated over patients' lifetimes.

After reviewing the economic literature, the economic subcommittee recommended to the Task Force that an economic model developed elsewhere be adapted to Ontario. Specifically, a model from the United Kingdom based on a large prospective randomized trial was selected, the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model.(6)

The objectives of this report are fourfold: (1) to identify and describe a model to evaluate the costs and consequences of various diabetes management strategies; (2) to adapt the diabetes model to the Ontario setting; (3) to review the literature surrounding the efficacy and effectiveness of multidisciplinary primary care diabetes management programs; and (4) to illustrate how the Ontario model can be used to estimate the long-term costs and consequences of a diabetes management strategy (i.e. multidisciplinary diabetes program) from the Ontario context.

UKPDS Outcomes Model

Patient data from the United Kingdom Prospective Diabetes Study (UKPDS), the largest type 2 diabetes clinical trial in the literature with more than 5,100 patients enrolled and followed for a median of 10.3 years, was used to develop a computer simulation model, the UKPDS Outcomes Model. Through a system of equations, the model predicts the lifetime occurrence and timing of seven diabetes-related complications and death, and thereby calculates life expectancy and quality-adjusted life expectancy for patients with type 2 diabetes. A key aspect of this model is that it is designed to capture the association between different types of complications at an individual patient level. Complications may be associated, not only because they share common known risk factors, but also due to the event-related dependence which arises when a complication substantially increases the likelihood of another occurring.(7) For example, the probability of a patient experiencing congestive heart failure (CHF), or a myocardial infarction (MI), is positively associated with systolic

blood pressure, but the risk of an MI is higher for patients with a history of CHF due to event-related dependence. To account for these dependencies, the model makes use of time varying risk factors (e.g. blood pressure, glycosylated haemoglobin [HbA1c]) which also facilitates its application to patient groups at different stages of the disease.

Adaptation of the UKPDS to Ontario

Background

Although the UKPDS Outcomes Model is based on data on over 5,000 patients with over 53,000 years of patient follow-up, there are five important reasons why the model needs to be adapted when considering its use in another geographic area such as Ontario. First, the incidence and prevalence of diabetes is different across countries. Second, there are differences in baseline demographic (e.g. age, gender, ethnicity) and diabetes risk factors (e.g. smoking status, body mass index, HbA1c, blood pressure, cholesterol, heart disease, stroke, and renal failure) across countries. Third, there may be differences in overall mortality, diabetes mortality or mortality from diabetes-related complications. Fourth, there are obvious differences in costs across countries, both in terms of treatment costs and in the costs of managing events and complications. And fifth, both the cost and effects of treatment programs will likely be different between countries.

Methods

Diabetes Population

In collaboration with researchers at the Institute for Clinical Evaluative Sciences (ICES), all incident and prevalent cases of diabetes in Ontario from April 1, 1992 to March 31, 2002 were identified and followed for up to 10 years, until death, or out migration. A patient was identified as having diabetes if he/she had one hospital admission with a diagnosis of diabetes or an Ontario Health Insurance Plan (OHIP) claim with a diagnosis of diabetes followed within two years by either an OHIP claim or a hospital admission with a diabetes diagnosis. This population created what is known as the Ontario Diabetes Database (ODD).

Diabetes Healthcare Resource Utilization and Costs

The ODD was subsequently linked to various administrative databases (e.g. Canadian Institute for Health Information (CIHI), Ontario Drug Benefit (ODB) plan) to create individual "patient histories" to provide an annualized profile of an individual's experience of diabetes complications and use of healthcare resources in 5 healthcare sectors (i.e. hospital, long-term care, prescription drugs, home care, and outpatient physician visits). Ontario costing sources were used to assign unit costs to all healthcare resource utilization.

Using a two-part model, the hospital and non-hospital costs for each clinical event were estimated. Complication-specific costs were divided into two time periods: 1) *immediate* costs that accrue within the year in which a complication first occurs; and 2) *long-term* costs that are intended to reflect the ongoing costs in subsequent years that are associated with ongoing management of the complication.

Results

It was estimated that there were 498,590 incident and 734,113 total patients with diabetes in Ontario in the database and over 1.39 million diabetes-related events, of which 95% were cardiovascular in nature. Of the newly diagnosed patients without complications, the mean healthcare cost was $3,115 in the year of diagnosis and approximately $2,109 in subsequent years. On average, complications resulted in an additional $2,062 per patient per year of follow-up. Generally, the total healthcare cost of a complication in the year of the event was substantially higher than in subsequent years (e.g. cost of amputation in the first year was $34,470 and $4,721 in following years). The estimated costs differ as the demographic and clinical characteristics of individual patients vary. For incident cases, the annual probability of diabetes-related events remained fairly constant over the study period and the 10-year cumulative probability of death was 47%.

Summary

The results confirm the high cost of seven diabetes-related complications (i.e. myocardial infarction, ischemic heart disease, stroke, heart failure, amputation, renal failure and blindness). Our large sample and ability to link administrative databases provide a unique opportunity to estimate the incidence of events and the cost of

diabetes over time. The relationship between healthcare costs and the seven clinical event categories estimated here were used as parameters in the ODEM.

Field Evaluation

Application of the ODEM to a Multidisciplinary Primary Care Diabetes Management Program

Background

Healthcare providers at the Group Health Centre in Sault Ste. Marie collaborated in an initiative to improve the quality of care, patient satisfaction, quality of life and clinical outcomes of persons with diabetes. This primary care program was multidisciplinary and included the employment of a Specialty Diabetes Nurse Liaison, and included components aimed at the patient, the providers, and the healthcare system. An 18-month field evaluation of this program was conducted to estimate the short-term clinical outcomes before and after the introduction of this new program and to use these short-term outcomes as inputs into the ODEM to predict long-term costs and consequences.

Methods

A retrospective chart review of all 404 patients with diabetes enrolled in the program was performed to collect individual patient-level data. Information included: demographic characteristics, diabetes medical history, history of other medical conditions, historical values of five key intermediate clinical outcomes (i.e. HbA1c, blood pressure, total cholesterol, HDL cholesterol, smoking status), as well as each patients' values for these key clinical measures before and after the 18-month study period. Healthcare resource utilization of study participants was collected and assigned unit costs. These data were used as inputs in the ODEM in order to conduct a cost-effectiveness analysis.

Results

The multidisciplinary primary care diabetes management program reduced HbA1c by approximately 1.02% (95% CI: -1.25% to -0.79%, $p<0.001$), systolic blood pressure by 1.32 mmHg (95% CI: -3.42 to 0.78, $p=0.219$), and total cholesterol by 0.47 mmol/L (95% CI -0.58 to -0.35, $p<0.001$) while HDL cholesterol increased by 0.06

mmol/L (95%CI: 0.03 to 0.09, p<0.001). The ODEM predicted that these changes in risk factors would prevent 16.2 per 1,000 deaths, 15.5 per 1,000 myocardial infarctions and a relative risk reduction of 50% in first amputations. The lifetime incremental cost per QALY gained for improved diabetes management for the program effect lasting for 1 year was $5,992. However, if the program and treatment effect continued for 10 years, the ODEM estimated the ICER to be $5,203 per QALY.

Summary

The multidisciplinary primary care diabetes management program introduced in Sault Ste. Marie improved short-term clinical outcomes for study participants. The application of the ODEM using the results from this intervention predicted that improvements in short-term clinical outcomes (e.g. HbA1c, blood pressure) impact eventual costs of care in the form of prevented complications and hospitalizations in later years. The base case analysis of $5,992 per QALY represents good value for money compared to commonly quoted thresholds.

Conclusions

The UKPDS Outcomes Model was identified as being the best diabetes economic model in existence for our purposes. Using resource utilization data for a large number of Ontarians with diabetes and assigning Canadian unit costs, this model was adapted to the Ontario setting. The resulting Ontario Diabetes Economic Model described in this report provides policymakers with a vehicle for assessing the long-term economic benefits, in terms of health outcomes (i.e. life years gained and quality-adjusted life-years gained) and healthcare costs, of any diabetes intervention. The application of the model to a primary care diabetes management program in Ontario predicted that the intervention represented good value for money. Other applications of the ODEM will enable policymakers to make similar healthcare resource allocation decisions.

In addition to the development of an Ontario-specific long-term diabetes economic model, there are a number of other important results from this report, two of which are: 1) the calculation of an estimate of the cost of treating diabetes in Canada; and 2) a variety of cost estimates that may be readily translated into patient-level cost inputs for any type of economic model.

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1. INTRODUCTION

1.1. Background

Diabetes mellitus is a chronic metabolic condition in which the body does not produce insulin or is unable to utilize the insulin it does produce. There are three types of diabetes mellitus: type 1, type 2, and gestational. Diabetes is estimated to affect more than 734,000 Ontarians and this number is expected to increase to 1.2 million by 2010, with 90-95% having type 2 diabetes.(1) Approximately 40 percent of people with diabetes will develop diabetes-related complications at some point. This chronic disease doubles the chance of heart attack or stroke, is the leading cause of adult blindness and non-traumatic limb amputations, and increases the risk of end stage renal disease.(2) Health care costs for the treatment of persons with diabetes in Canada amount to approximately $9 billion annually.(3) These expenditures represent the costs associated with the daily treatment and control of the disease as well as the management of chronic complications that occur with increasing frequency and severity as the disease progresses.

Fortunately, there is evidence that early management of the condition, including intensive control of blood glucose levels and other risk factors (e.g. cigarette smoking, dyslipidemia, and high blood pressure) can delay or even prevent these complications.(8-14) Any treatment that aims to slow disease progression, thereby delaying the onset of costly complications, is likely to be of major clinical and economic benefit. Consequently, medical resources invested in the intensive management of diabetic patients may be offset by reductions in the cost of treating future complications. In fact, economic evaluations of policies for the management of type 2 diabetes mellitus have shown that the increased costs of implementing more intensive blood glucose and blood pressure control policies are partly offset by savings associated with treating fewer diabetes-related complications.(15;16)

In recognition of the burden associated with diabetes in Ontario and the potential to decrease this burden, the Ontario Ministry of Health and Long-Term Care (MOHLTC) made the treatment and management of diabetes a priority. To this end, the MOHLTC established a Diabetes Task Force in 2003 to advise the Ministry as to the best methods for reducing the impact of diabetes in Ontario. The Task Force was comprised of a number of subcommittees (e.g. clinical subcommittee, economic

subcommittee, primary prevention subcommittee) to identify pressing issues which would achieve maximum impact in improving outcomes for people with diabetes and provide recommendations.(1) The economic subcommittee was given the task of proposing a method that the MOHLTC could use to prioritize investments with respect to the treatment and management of diabetes. In essence, the MOHLTC required a tool with which to measure the long-term cost-effectiveness of various diabetes management strategies.

In determining the long-term provision of care for patients with chronic diseases such as type 2 diabetes, healthcare policymakers must assess a range of factors. These factors include determining the future demand for services, assessing the impact of new technologies on costs and outcomes, and estimating the effects of implementing prevention and management programmes. The degree of uncertainty in all these areas makes predictions difficult, the change being compounded by the accumulation of uncertainties across several decades. Disease models, however, can help policymakers identify the likely long-term consequences of different resource allocation decisions.(17)

Decision analytic models, that simulate the impact of alternative interventions on the probability and cost of experiencing diabetes-related complications, are increasingly being used both to model the progression of diabetes and to estimate lifetime costs and outcomes associated with different disease management strategies.(4;5) These models estimate the future occurrence of complications and quantify outcomes in terms of mean life-years gained or mean quality-adjusted life-years (QALYs) gained from an intervention. They can also be used to estimate future healthcare costs of patients with type 2 diabetes, but their main purpose is to estimate the cost-effectiveness of different interventions, especially when evidence of the impact of the interventions is only on surrogate endpoints and the clinical trial evidence has to be extrapolated over patients' lifetimes. Consequently, the Diabetes Task Force's economic subcommittee reviewed the literature to identify a model that could be used in Ontario to estimate the cost-effectiveness of various types of diabetes interventions.

A review of the economic literature revealed that there are at least seven diabetes simulation models being used for the purposes of economic evaluation.(4;6;18-23) A number of the models have centered on the primary prevention of diabetes(24-27), or have focused on the secondary prevention of a specific complication (e.g. retinopathy).(28) More general models that incorporate a wider spectrum of complications have been developed for other geographic areas(4;19-22;29;30), but were not available for the Canadian or Ontario setting. It was thus recommended to the Task Force that an economic model developed elsewhere be adapted to Ontario in order to assess the long-term costs and outcomes associated with different strategies for the management of type 2 diabetes. Specifically, a model from the United Kingdom based on a large prospective randomized trial was selected.(6) The first part of this report describes the model in detail as well as how the model was parameterized to make it Ontario-specific. Following this, the report illustrates how the newly created Ontario Diabetes Economic Model (OEDM) was applied to a diabetes management strategy in Ontario.

1.2. Objectives

The objectives of this report are fourfold: (1) to identify and describe a model to evaluate the costs and consequences of various diabetes management strategies; (2) to adapt the diabetes model to the Ontario setting; (3) to review the literature surrounding the efficacy and effectiveness of multidisciplinary primary care diabetes management programs; and (4) to illustrate how the Ontario model can be used to estimate the long-term costs and consequences of a diabetes management strategy (i.e. multidisciplinary diabetes program) from the Ontario context.

2. DEVELOPMENT OF THE ONTARIO DIABETES ECONOMIC MODEL

Diabetes computer simulation models are very complex and usually require the synthesis of data from a variety of sources to create a series of modules in order to estimate the costs and consequences of strategies for managing people with type 2 diabetes.(4;18-22;24;31) For example, the first published model of the progression of type 2 diabetes had separate modules for cardiovascular disease, retinopathy, nephropathy and neuropathy,(4) and used a probabilistic Monte-Carlo analysis to simulate event histories over the remaining lifetime of newly diagnosed patients with type 2 diabetes. While that model represented a landmark in the use of computer simulation to model the progression of the disease, it had several limitations. In particular, it placed considerable reliance on data from a type 1 diabetes trial(29) and on cardiovascular risk estimates derived from the Framingham cohort study.(30) The fact that there were only 337 people with type 2 diabetes in the Framingham study, places doubt on the predictive accuracy of models that rely on the Framingham study.(30) While subsequent simulation models have been able to address some of these limitations(19), there was still a need for a comprehensive integrated system of equations from a large and well-validated diabetes-specific data source to forecast major diabetes-related complications.

Data from the United Kingdom Prospective Diabetes Study (UKPDS), the largest type 2 diabetes clinical trial in the literature with more than 5,100 patients enrolled and followed up for a median of 10.3 years, revealed that improved treatment of blood glucose(7) and blood pressure(32) lowers the risk of diabetes-related complications in individuals newly diagnosed with type 2 diabetes. A computer simulation model, the UKPDS Outcomes Model, was developed based on patient data from this trial. Through a system of equations, the model predicts the lifetime occurrence and timing of seven diabetes-related complications and death, and thereby calculates life expectancy and quality-adjusted life expectancy for patients with type 2 diabetes. A key aspect of this model is that it is designed to capture the association between different types of complications at an individual patient level. Complications may be associated, not only because they share common known risk factors, but also due to the event-related dependence which arises when a complication substantially increases the likelihood of another occurring.(7) For example, the probability of a patient experiencing congestive heart failure (CHF), or

a myocardial infarction (MI), is positively associated with systolic blood pressure, but the risk of an MI is higher for patients with a history of CHF due to event-related dependence. To account for these dependencies, the model makes use of time varying risk factors (e.g. blood pressure, glycosylated hemoglobin [HbA1c]) which also facilitates its application to patient groups at different stages of the disease.

The remaining portion of chapter 2 is made up of five separate sections. The first provides some background pertaining to the UKPDS study followed by an in-depth description of the UKPDS Outcomes Model and how the risks for each of the diabetes-related complications were calculated. The third section outlines the methodology used to adapt the UKPDS Outcomes Model to the Ontario setting. The results from the analysis of Ontario-specific diabetes data are presented in the fourth portion of the chapter. The chapter ends with a summary of the parameters obtained to create the Ontario Diabetes Economic Model.

2.1. Design of the UKPDS

The UKPDS was a large-scale randomized clinical trial evaluating policies for more intensive blood glucose and tight blood pressure control.(33) Briefly, between 1977 and 1991, 5,102 patients with newly diagnosed type 2 diabetes aged 25-65 years who were subsequently shown to have a fasting plasma glucose > 6 mmol/l on two occasions and who had no recent history of MI, ischemic heart disease (IHD), CHF, more than one major vascular event or a severe concurrent illness that would limit life expectancy, were recruited to the study. Patients had biochemical measurements including HbA1c, systolic blood pressure, lipid and lipoprotein fractions at entry to the study, at randomization after three months of dietary therapy, and in each subsequent year. Data from a sub-population (n=3,642) of patients who participated in the UKPDS were included in the creation of the UKPDS Outcomes Model.

2.2. Structure of the UKPDS Outcomes Model

The purpose of the UKPDS Outcomes Model is to estimate the first occurrence of each of seven diabetes-related complications (fatal or non-fatal myocardial infarction [MI], other ischaemic heart disease, stroke, heart failure, amputation, renal failure and eye disease measured in terms of blindness in one eye) and death in order to

estimate lifetime outcomes, life-years gained and quality-adjusted life-years gained. The model is based on an integrated system of parametric equations which predict the annual probability of complications occurring based on the patient's characteristics (e.g. age and sex), and time varying risk factors such as HbA1c and a patient's history of previous diabetes-related complications.

To improve model stability, values for time varying risk factors (HbA1c, systolic blood pressure, and total:HDL cholesterol) were calculated as the mean of the previous two years' values (e.g. the value for the variables in the fourth year was the average of these variables in second and third years), while smoking status is based on three year periods from diagnosis of diabetes. To model the long-term dependence(34) between different complications, time varying covariates indicating whether a patient had acquired a history of other complications following diagnosis of diabetes were also included in the model: these covariates were set equal to 0 until an event occurred, and then set to 1 from that point onwards.

The procedures used in fitting equations to the observed events in the UKPDS population and the estimated parameters are reported in greater detail in appendix 1.(6) In brief, each type of diabetes-related event was modeled using one or more equations that included time varying risk factors. In the case of diabetes-related complications, a Weibull proportional hazard regression was used to model the occurrence of a composite outcome covering both fatal and nonfatal events. The coefficients for risk factors were then estimated using maximum likelihood methods that account for censoring (e.g. due to factors such as loss to follow-up or death). Risk factors with a *p*-value less than 0.05 were considered statistically significant. Separate equations were used to model diabetes and non-diabetes related mortality using a combination of Gompertz and logistic regression equations. Finally, the time paths of four risk factors (i.e. HbA1c, systolic blood pressure, total:HDL cholesterol, and smoking status) were also estimated using these data.

A key aspect of the UKPDS Outcomes Model is its ability to capture the interaction of different types of complications at the individual patient-level. This may arise not only because many events share common risk factors, but also due to event-related dependence, i.e. when the occurrence of an event substantially increases the

likelihood of another event occurring. The model is a probabilistic discrete-time illness-death model(34) rather than a Markov model, which simulates a patient's life experience using annual cycles to calculate the probability of death or of experiencing any of the specified complications in the UKPDS Outcomes Model. Patients start with a given health status (e.g. no complications) and can have one or more non-fatal complications or die in any model cycle by comparing estimated probabilities with random numbers drawn from a uniform distribution ranging from zero to one to determine whether an event occurs. When a patient experiences a complication, their quality of life is permanently decremented such that they accumulate QALYs at a slower rate.

2.2.1. Modeling cardiovascular disease in the UKPDS Outcomes Model

The increased risk of cardiovascular disease among people with type 2 diabetes is well established and is increasingly recognized as one of the major hazards of type 2 diabetes. In developed countries, cardiovascular disease accounts for the majority of deaths amongst patients with type 2 diabetes (35) and is a significant contributor to diabetes-related healthcare costs.(36) Within the cardiovascular disease category there are three Weibull equations to estimate the absolute risk of: (i) myocardial infarction (MI), defined as non-fatal MI (ICD-9 code 410), or fatal vascular cardiac event (ICD-9 code ≥410 and ≤414.9, or ≥428 and ≤428.9), or sudden death (ICD-9 code ≥798 and ≤798.9); (ii) ischaemic heart disease (IHD) defined as an ICD-9 code ≥411 and ≤414.9; and (iii) congestive heart failure (CHF) defined as an ICD-9 code ≥428 and ≤428.9. IHD and CHF events were only recorded if they occurred prior to an MI event: that is, a patient who had experienced an MI was not classified subsequently as developing IHD.

2.2.2. Modeling cerebrovascular disease in the UKPDS Outcomes Model

People with type 2 diabetes are at higher risk of stroke and previous epidemiological studies have found that this risk increases with age, elevated blood pressure, smoking and lipoproprotein levels.(37) In this model, a single Weibull equation is used to estimate the absolute risk of a first non-fatal stroke (ICD-9 code ≥430 and ≤434.9, or 436) or fatal stroke (ICD-9 code ≥430 and ≤438.9) based on patient characteristics.

2.2.3. Modeling amputation in the UKPDS Outcomes Model

Patients with diabetes have an amputation rate many times higher than that of patients without diabetes, and it has been reported that the primary risk factors for amputation include age, sex (male), smoking, the presence of peripheral vascular disease and blood pressure.(38) The model contains a single Weibull equation to estimate the absolute risk of a first amputation of a digit or limb (ICD-9 code ≥5.845 and ≤5.848, or 250.6) or a fatal peripheral vascular event (ICD-9 code 997.2 or 997.6 or 250.6 or 440.2).

2.2.4. Modeling blindness in the UKPDS Outcomes Model

The model contains a Weibull equation to estimate the risk of blindness in one eye, which is defined as a visual acuity Snellen 6/60 or ETDRS logMAR 1.0 or worse for any reason, persisting for 3 months (ICD-9 codes ≥369 and ≤369.9).

2.2.5. Modeling nephropathy in the UKPDS Outcomes Model

Increasing duration of diabetes, hypertension and poor glycaemic control have been shown to elevate the risk of developing renal disease(39) and subsequent mortality.(40) The model contains a single Weibull equation to predict renal failure, defined as creatinine >250 μmol/l not ascribable to any acute inter-current illness (ICD-9 codes 250.3 and ≥ 585 and ≤ 586) and death due to renal failure (ICD-9 codes ≥ 580 and ≤ 593.9).

2.2.6. Risk-factor progression in the UKPDS Outcomes Model

Previous simulation models of the progression of diabetes have made a variety of assumptions regarding how risk factors such as HbA_{1c} and systolic blood pressure change over time.(19;20) While carrying forward current values provides a simple means of extrapolation(41;42), it does not account for the likely change in some of these risk factors over time (for example, the upward trend in the level of HbA_{1c} many patients experience). In the UKPDS Outcomes Model, the four risk factors (HbA_{1c}, systolic blood pressure, total:HDL cholesterol ratio and smoking status) are treated as panel data (longitudinal data), and a random effects model was fit to enable a time path to be estimated.(43) While the exact specification differs between risk factors, these equations generally include the value or status of the risk

factor at the time a decision was made regarding randomization in the UKPDS (which took place after a 3 month dietary run-in), years since diagnosis, and the value of the risk factor in the preceding period.(14) For HbA_{1c}, an indicator variable for the second year was also included to account for the initial decline in HbA_{1c} observed in the UKPDS. Equations for HbA_{1c}, systolic blood pressure, and total:HDL cholesterol ratio were based on annual measures of each risk factor, while smoking status (due to its less frequent ascertainment) was based on three-year periods from diagnosis of diabetes.

2.2.7. Modeling mortality in the UKPDS Outcomes Model

People diagnosed with type 2 diabetes in middle age typically have a life expectancy between 5 and 10 years shorter than people without diabetes, with heart disease being the major underlying cause of death.(44) The UKPDS Outcomes Model contains three equations for estimating absolute risk of mortality. Two of these equations estimate the likelihood of death after several diabetes-related complications that have been shown to elevate the risk of mortality. The first equation, based on logistic regression, estimates the probability of death in the first year in which either an MI, CHF, stroke, amputation or renal failure first occurs. The second equation estimates the risk of diabetes-related mortality of patients with a history of any of these events in all subsequent years. The third mortality equation estimates the risk of death from causes unrelated to diabetes (primarily due to cancers and accidents).

2.2.8. Using the UKPDS Outcomes Model to simulate outcomes

The main purpose of the model is to estimate the likely occurrence of major diabetes-related complications over a lifetime for patients with specified prognostic risk factors, in order to calculate health outcomes. While increases in mean life expectancy are widely recognized as a useful measure of benefit, (45) it is important also to encapsulate the potential impact of diabetes-related complications on quality of life. This model uses the quality-adjusted life-year (QALY) to adjust length of life for quality of life by assigning a value of health utility, on a scale on which 0 represents death and 1 represents full health, for each year of life.

The impact on quality of life of different diabetes-related complications has been reported in a number of studies, including one study in which the EQ-5D health status questionnaire(46), a standardized health-related quality of life questionnaire, was used to survey 3,192 patients still participating in the UKPDS in 1997.(47) Using these data, the mean utility for patients free of microvascular and macrovascular complications was reported to be 0.785. Patients with a history of complications were found to have lower utility and the following decrements in utility were estimated: -0.055 for a myocardial infarction; -0.090 for other ischaemic heart disease or angina; -0.164 for stroke; -0.108 for heart failure; -0.280 for amputation, and –0.074 for blindness in one eye. It was assumed that having renal failure decremented utility to 0.26 based on the results of another recent study.(48) For simplicity and in the absence of sufficient data to estimate empirically, the model assumes that the occurrence of multiple complications has an additive effect on disutility (e.g. the utility of a patient who had ischaemic heart disease and then has an MI would first be decremented by 0.090 and then by a further 0.055) and the same decrements were applied to patients with comparable health states regardless of their treatment. However, the UKPDS Outcomes Model is sufficiently flexible to allow other assumptions to be adopted regarding the impact different complications (and combinations of complications) have on quality of life.

When estimating QALYs, it is important to model the sequence of endpoints for each patient. For example, consider the simulated profiles for two patients who are free of complications. Using the model, the first patient is predicted to have an amputation in the second year post follow-up and IHD and an MI in the fourth year post follow-up, and is predicted to die in the fifth year. The second patient is predicted to have IHD in the third year post follow-up, an amputation in the fourth year, and a fatal MI in the fifth year. Using the utility weights reported above, while both patients experience the same set of diabetes-related complications over their remaining lifetimes, the QALY profile is different: the profile of the first patient is equivalent to 2.19 QALYs and the second is equivalent to 2.66 QALYS. By simulating individual patient histories, the model is able to take these differences into account.

Figure 1 provides an algorithm that illustrates the sequence of modeling events. The first cycle of the model is run, in which the probability of death or experiencing the

seven complications is calculated. Each probability is compared with a random number drawn from a uniform distribution ranging from zero to one to determine whether an event occurs.

There is a need to account for event-related dependency between some complications, as noted above. The actual event-related dependencies were estimated empirically during the equation fitting procedure, and included if they had a significance level of $p<0.05$. All significant dependencies against the known epidemiology were checked and are discussed in more detail below. In the model, if a non-fatal event is predicted to have occurred, the patient acquires a history of that event (that is, the time-varying covariate for that endpoint is updated from 0 to 1), and thereafter carries that history in their set of characteristics. In addition, the two diabetes-related mortality equations are applied to all patients who have a history of complications that were found to elevate the risk of death (MI, CHF, stroke, amputation or renal failure) from the point at which the complication is predicted to have occurred; these equations deal both with the likelihood of immediate death following the first event, and the long-term elevation of risk of death consequent on acquiring a history of these complications. Finally, a non-diabetes mortality equation is used to forecast the incidence of death from cancer, accidents, or other causes not addressed elsewhere in the model.

If the model predicts that a death has occurred, the years lived and quality-adjusted years lived (that is, life years decremented in each cycle by the reduced quality of life associated with particular complications) by that patient are calculated. If the patient is predicted to have survived that cycle, the risk factor equations are used to update their current risk factor values (e.g. systolic blood pressure) and these are carried forward to the next cycle of the model along with the updated event history.

It is important to note that the order in which the event equations listed in Figure 2 (Equations 1 to 10) is not predetermined. Further, some of these events are competing risks (e.g. within a cycle of the model if a patient dies they can have no additional events). To take this into account, the equations are run in random order in each cycle.

2.2.9. Internal validation of the UKPDS Outcomes Model

The consistency of the forecasted cumulative incidence of different complications and death to the cumulative incidence calculated using nonparametric (life-table) methods was tested by the model developers. This test of internal validity(49) was based on the forecast number of events from 2nd to the 12th year after diagnosis using the information from the first year after diagnosis on the 3,642 patients used to estimate the model.(50)

2.2.10. Handling uncertainty in the UKPDS Outcomes Model

Appropriate handling of uncertainty in complex patient simulation models such as the UKPDS Outcomes Model is not straightforward. In these applications that involve extrapolation of outcomes of patients alive at the end of the study, a combination of bootstrap methods and multiple imputation methods were used. The confidence intervals around the QALY estimates were adjusted to take into account the variance within and across imputed data sets.(51) This method removes Monte-Carlo error (first order uncertainty), so that confidence intervals from the Outcomes Model reflect parameter uncertainty in the model. Confidence intervals are based on a two-stage process of evaluation. First, the original data used to fit the risk equations were bootstrapped and the risk equations refitted and the coefficients recorded. Repeating this process twenty times generated a vector of coefficients that represents the parameter uncertainty in those coefficients, but which also accounts for the covariance between risk equations. Since the model is being applied to predict lifetime outcomes of UKPDS patients, in the second stage the predictions were treated as imputations of missing values and the twenty sets of results as multiple imputations. Standard methods for combining the results of multiple imputations were then employed.(51)

Figure 1. Overview of Diabetes Model

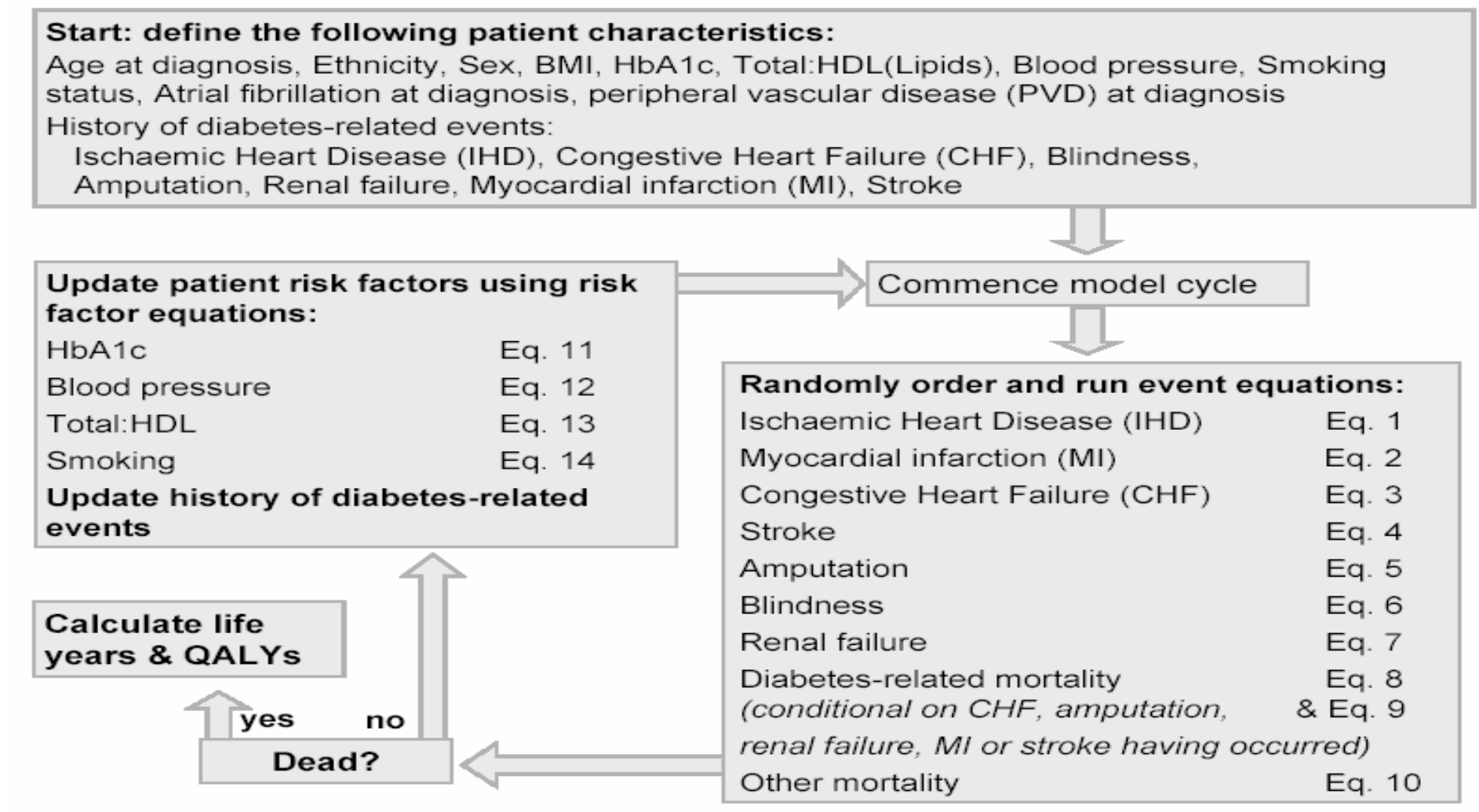
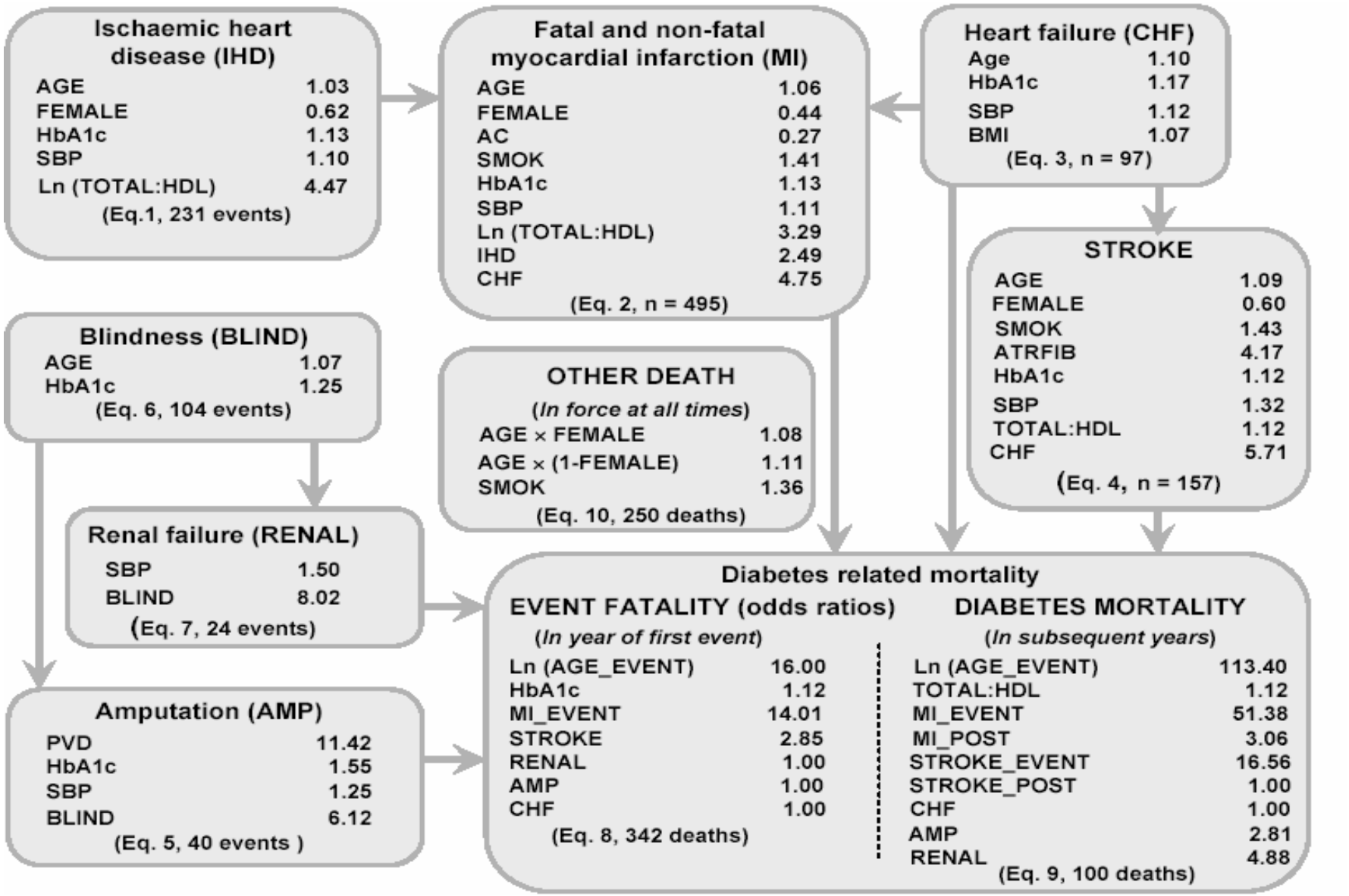


Figure 2. System of Parametric Equations (7 complications and death)



2.3. Ontario adaptation of the UKPDS Outcomes Model

Although the UKPDS Outcomes Model is based on data on over 5,000 patients with over 53,000 years of patient follow-up, there are five important reasons why the model needs to be adapted when considering its use in another geographic area such as Ontario. First, the incidence and prevalence of diabetes is different across countries. Second, there are differences in baseline demographic (e.g. age, gender, ethnicity) and diabetes risk factors (e.g. smoking status, body mass index, HbA1c, blood pressure, cholesterol, heart disease, stroke, and renal failure) across countries. Third, there may be differences in overall mortality, diabetes mortality or mortality from diabetes-related complications. Fourth, there are obvious differences in costs across countries, both in terms of treatment costs and in the costs of managing events and complications. And fifth, both the cost and effects of treatment programs will likely be different between countries.

The adaptation of the UKPDS Outcomes Model to the Ontario setting involved a collaborative effort between the Program for Assessment of Technology in Health (PATH), the Group Health Centre (GHC) in Sault Ste. Marie, and the Institute for Clinical Evaluative Sciences (ICES) in order to determine the baseline risk factors, complication rates, resource utilization, and cost of treating diabetes and each diabetes-related complication. This was a significant endeavour and involved the merging of numerous different databases in a number of steps. It is important to note that all costs collected were direct healthcare costs; it was not possible to measure productivity costs or other patient costs from the data available.

The next sections summarize how health care resource utilization for persons with diabetes in Ontario was identified followed by a description of how the costs associated with the resources were collected and applied. Finally, the methods used to analyse the cost data will be outlined.

2.3.1. Identification of the healthcare resource utilization associated with the diabetes-related complications in Ontario

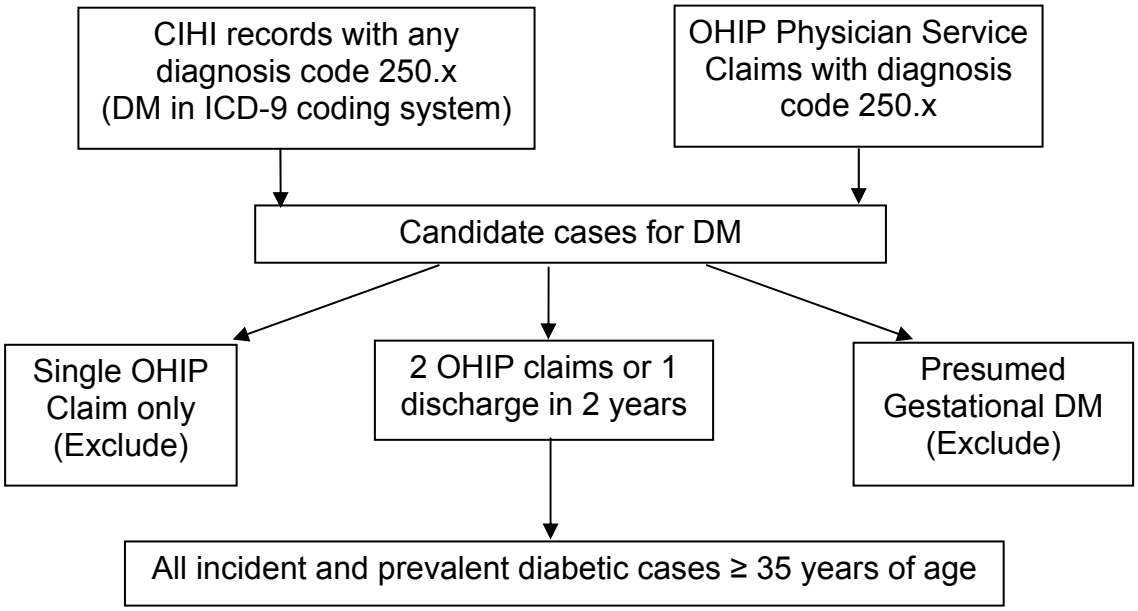
Data from the Ontario Diabetes Database (ODD), developed by ICES, was used in the current study. The ODD is a validated electronic registry created from administrative data sources to identify all adults ≥ 20 years of age with diabetes in the province of Ontario since April 1, 1992. Briefly, hospital discharge abstracts prepared by the Canadian Institute for Health Information (CIHI) were used to identify patients admitted to hospital with a new or pre-existing diagnosis of diabetes based on the presence of an International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) code of 250.X on any of 16 diagnostic fields. Physicians' service claims records were used to identify visits for diabetes (diagnostic code "250"). Any individuals having at least one hospitalization or two physicians' service claims bearing a diagnosis or diabetes with a 2-year period were included in the ODD. To exclude women from the diabetes database who have only gestational diabetes, any records bearing a diabetes diagnostic code followed by a physician service claim or hospital discharge record within 5 months, indicating an obstetrical event, were eliminated (Figure 3).

Individuals identified as having diabetes were linked by a unique identifier to the Registered Persons Database (RPDB), the annual registry of all individuals eligible for coverage under the provincial health plan. The RPDB provided each patient's sex, date of birth, date of death (where applicable), and postal code. All subjects entering the ODD remain in the database until death or migration out of province. The ODD has been well validated and shown to have a high sensitivity (86%) and specificity (97%) for identifying individuals in whom diabetes was recorded in primary care charts.(52)

For the purposes of the current study, all adults ≥ 35 years of age with diabetes in the ODD between April 1, 1992 and March 31, 2002 were included. Individual "patient histories" were developed for each patient based on his/her experience

of diabetes complications and use of healthcare services. Seven diabetes-related complications were tracked over time (i.e. myocardial infarction, stroke, angina, heart failure, blindness, amputation, and nephropathy).

Figure 3. Algorithm for the Development of ODD, 1991-2001



2.3.1.1. Inpatient and outpatient hospital utilization

Individuals identified as having diabetes were linked by a unique identifier to both the Canadian Institute for Health Information hospital discharge abstract database (CIHI DAD) and the same day surgery (SDS) database. The CIHI DAD and SDS database from April 1, 1992 to March 31, 2002 allowed for the identification of all inpatient hospitalizations and same day surgery encounters for the various complications of interest. The ICD-9-CM codes for the principal diagnosis and principle procedure used to define the complications are listed in Table 1.

Table 1. Definitions of Variables and Complications used to Identify Diabetes-Related Complications Treated in Hospital

Variable	Definition
MI	Canadian Institute for Health Information (CIHI): any non-fatal AMI (ICD-9CM 410), or fatal vascular cardiac event (ICD-9CM ≥410-≤414.9 or ≥428-≤428.9 with death) or sudden death (ICD-9CM codes ≥798-≤798.9)
Stroke	From CIHI: Hospitalization for first non-fatal stroke (ICD-9CM ≥430-≤434.9 or 436) or fatal stroke (ICD-9CM ≥430-≤438.9)
Ischaemic Heart Disease	From CIHI: any ICD-9CM code of ≥411-≤414.9 if no prior MI
Heart Failure	From CIHI: Hospitalization for or with CHF (ICD-9CM ≥428-≤428.9) if no prior MI
Blind in 1 eye	CIHI co-morbidity of blindness (ICD-9CM codes ≥369-≤369.9).
Amputation	Amputation in CIHI: codes for minor (96.11 – 96.12) and major (96.13-96.15) amputations with exclusions for malignancy and trauma as reason for procedure OR a fatal peripheral vascular event (ICD-9CM codes 997.2, 997.6, 250.6 or 440.2).
Nephropathy	CIHI records with ICD–9CM codes 250.3 and ≥585-≤586 and death due to renal failure ICD–9CM codes ≥580-≤593.9
Cataract Extraction	OHIP fee code E140

Abbreviations: ICD-9CM=International Classification of Diseases, 9th Revision; Clinical Modification; ODD=Ontario Diabetes Database; OHIP=Ontario Health Insurance Plan

2.3.1.2. Emergency room visits

The Ontario Health Insurance Plan (OHIP) billing records provided information on the place the service was provided, allowing for the identification of Emergency Room (ER) visits. An OHIP Emergency Claims Database was created in-house at ICES. This dataset has one record per ER visit and contains variables from the OHIP claims data. Again, data from April 1, 1992 to March 31, 2002 were used for calculating ER costs.

2.3.1.3. Outpatient physician utilization

OHIP fee codes provided information on out-of-hospital physician services (general practitioner and specialist visits) and laboratory tests. They also describe physician services provided in-hospital by fee-for-service physicians,

including the fees associated with the interpretation of diagnostic tests. OHIP data from April 1, 1992 to March 31, 2002 were used in order to identify billings for angina, blindness, nephropathy and cataract surgery.

2.3.1.4. Prescription drug costs and long-term care utilization

Prescription drug costs for people aged 65 and older are covered by the Ontario Drug Benefit (ODB) Program. As a result, the total drug costs represent an underestimate since the cost of drugs for people less than 65 years of age is not included. The ODB database also records whether the individual was living in a long-term care residence when the prescription was filled. The ODB, from April 1, 1992 to March 31, 2002, was linked to the ODD and was used for calculating the prescription drug costs and identifying persons residing in a long-term care facility.

2.3.1.5. Home care services utilization

Home care services are recorded in the Ontario Home Care Administration System (OHCAS) database. The database records the dates of all home care visits, and the type of visit (e.g. nursing, homemaking, physiotherapy). The data in the OHCAS database between April 1, 1992 and March 31, 2002 was used to identify all types of home care services used by persons with diabetes in Ontario so that costs could be assigned to each type of visit.

2.3.1.6. Calculation of mortality rate

Finally, individuals were linked to the Registered Persons Database (RPDB). The RPDB was used for updating the death dates (where applicable) and getting the date of last contact in order to calculate mortality rates. Individuals for whom no death record was identified remained in the diabetes database, regardless of whether they have claims with a diagnosis of diabetes in subsequent years.

The final database resulting from the merging of all of the aforementioned databases permitted the measurement of resource utilization, complication rates

and, healthcare costs for prescription medicines and professional billings that are recorded directly in administrative databases. Unit costs for other healthcare resources were estimated separately (see next section).

2.3.2. Estimating the cost of healthcare resource utilization for people with diabetes mellitus in Ontario

The following sections present the sources of costing data as well as the methods used to calculate the costs associated with the healthcare resource utilization for people with diabetes in Ontario over the 10-year observational period. All calculated costs were inflated to 2004 dollars.

2.3.2.1. Inpatient hospital costs

Acute care inpatient hospital stays were assigned cost values using the Resource Intensity Weight (RIW) recorded in the CIHI DAD. The RIW was multiplied by the average cost per RIW in each fiscal year. The cost per RIW was obtained for the years 1995-2000 from the Finance and Information Management Branch, Ministry of Health and Long-Term Care (MOHLTC). The missing years were inflated or deflated where necessary using the Health Care Component of the Consumer Price Index (HCC CPI).(53)

Included in the hospital cost is the cost of receiving rehabilitation services as an inpatient. Rehabilitation hospital stays were evaluated using the length of stay (LOS) recorded in the DAD. The LOS was multiplied by the average cost per day in each fiscal year. The average cost per rehabilitation day was obtained from the London Health Sciences Centre, an Ontario Case Costing Hospital participating in the Ontario Case Costing Project.(54)

2.3.2.2. Outpatient hospital costs

Same day surgery (SDS) hospital stay costs were evaluated by estimating the RIW on the basis of the Diagnostic Procedures Group (DPG) found in the record, and then multiplying the RIW by the average cost per RIW in each year. The

average cost per RIW for this variable was obtained from an Ontario Case Costing Project participant and multiplied by each RIW.(54)

2.3.2.3. Emergency room costs

Emergency room visits were identified from the distinct billing codes from OHIP claims that indicate ER use (algorithm created at ICES). The number of ER visits were calculated for each person in each fiscal year and then multiplied by the average cost per visit in each fiscal year. The average cost per ER visit per year was provided by CIHI.(55)

2.3.2.4. Outpatient physician costs

The OHIP database indicates the amount paid to physicians and non-hospital labs for each service provided. The costs for the services provided by physicians who are covered under Alternative Fee Programs were imputed by using the billing codes and the median payments of each billing code from those services. Again, the values were adjusted using the Health Care Component of the Consumer Price Index.(53)

2.3.2.5. Prescription drug costs

The ODB reimburses prescription drug claims for persons eligible for the program, primarily for those aged 65 and older. ODB coverage is subject to a co-payment that varies depending on a person's income level. The ODB database indicates the total cost of the prescription (plus pharmacy fee), and the amount covered by the provincial plan. Since we were interested in costs from the perspective of the provincial insurer, only the amount covered by the province was included. The cost was derived directly from ODB claims. Costs were adjusted for each year by using the Prescribed Medicines component of the CPI.(56)

2.3.2.6. Long-term care (LTC) costs

LTC residency was determined from ODB claims. Records in the ODB contain a flag indicating whether or not the individual was in an LTC facility when the

prescription was filled. If more than half of the prescriptions within a year had the LTC flag set, it was assumed those people lived in LTC facilities. If those people had been in a LTC facility one year before the study year, the start date was April 1 in the study year, if not, the start date was the first prescription date with a LTC flag in the study year. The LTC discharge date was the earliest of: death date, date of last health contact or ending date of the study fiscal year. The days spent in a LTC facility for each person in a study year was calculated by subtracting the start date from the end date and adding 1. The number of days was then multiplied by the cost per day in a LTC facility. These costs were obtained from Statistics Canada for each of the study years. The values were adjusted for inflation by multiplying by the Health Care Component of the CPI.(53)

2.3.2.7. Home care services costs

The Ontario Home Care Administrative System (OHCAS) database indicated the type of home care service (e.g. nursing, meals on wheels) that was provided at each visit. The cost of each service was estimated using information collected from various sources (e.g. Ontario Association of Community Care Access Centres across the province, Ontario Association of Medical Laboratories, Ontario Home Care Association). Again, the cost of a visit for each service was multiplied by an inflation factor from the HCC CPI.(53)

2.3.3. Analysis of cost data

To examine the relationship between healthcare costs and the seven clinical event categories considered in the UKPDS Outcomes Model, costs were separated into those associated with hospital inpatient stays and those arising from non-inpatient healthcare use. The latter included fees paid for general practitioner and specialist visits as well as diagnostic tests, long-term care, emergency room visits, home care services, and prescriptions medications. We divided complication-specific costs into two time periods: 1) *event costs* that accrue within the year in which a complication first occurs; and 2) *state costs* that are intended to reflect the ongoing costs in subsequent years that are associated with the ongoing management of the complication (including subsequent events

of the same type). Hospital inpatient and non-inpatient event and state costs were estimated for each of the seven complications.

2.3.4. Statistical methods

Health care cost data often have several characteristics that must be addressed through the careful selection of appropriate statistical analyses. Typically, within a defined period of time (e.g. one year) significant proportions of individuals have no contact with some types of healthcare providers and so incur no costs. However, amongst the individuals who do make use of health services, the distribution of costs is frequently highly skewed due to the presence of a relatively small number of individuals incurring very high healthcare costs.(57-59)

To estimate the cost of various complications a two-part model was employed in the analysis. In the first part, logistic regression was used to model the probability of incurring some healthcare costs within a single patient-year time period. The dependent variable was set equal to 1 in any patient year an individual incurs costs. To determine the impact of various clinical events on the probability of incurring some healthcare costs we included an indicator variable for each type of complication and variables to adjust for sex and age. In the second part, the total costs incurred, conditional on incurring any costs, was estimated.

When modeling the second part of the model it is important to recognize that the positive component of healthcare costs is skewed and hence some episodes with extremely high costs can overly influence the model's parameters. To model these data we employed an ordinary least squares (OLS) regression model. Estimates of the probability of incurring costs, the costs conditional on a cost being incurred and the expected cost (the product of probability and conditional cost) were calculated using this model.

The clinical events included fatal myocardial infarction (MI) and fatal stroke. A fatal MI was identified as a death occurring within 30 days after an MI. Similarly, a fatal stroke was identified as a death occurring within 30 days of a stroke.

2.4. Results

This section starts with a description of the patients included in the ODD (e.g. demographic characteristics, complications, incidence and prevalence) as well as the average annual and total costs of treating diabetes over a 10-year period. Following some results pertaining to incident cases, we report the results from the two-part logit and ordinary least squares (OLS) regression model that was used to estimate the relationship between healthcare costs and the seven clinical event categories considered in the ODEM. The results from the two-part model are presented in section 2.4.3.

2.4.1. Diabetes in Ontario, 1992-2001

Between the years 1992 and 2001, 734,113 persons with diabetes were identified in the ODD. The mean age of diagnosis was 63.4 years and just over half of the population was male (Table 2). There were 19,301 deaths due to a first myocardial infarction, more than 1.32 million non-fatal cardiovascular-related events and greater than 39,000 diabetics with a diagnosis of renal disease in the province. The average annual direct medical costs per patient was estimated to be $5,687 ($5,371 to $6,343) for an average annual total cost of $2.48 billion (Table 3).

Table 2. Demographic Characteristics and Diabetes-Related Complications from the ODD, 1992-2001 (N=734,113)

Mean age of diagnosis of DM (SD)	61.2 (13.1)
Mean age (SD)	63.4 (12.7)
% Male	52.7
Incident cases	498,590 (67.9%)
Fatal first events	**Total number of events**
Stroke	8,278
Myocardial Infarction	19,301
Non-fatal events	
Nephropathy	39,202
Amputation	15,252
Blindness	17,401
Stroke	54,367
Heart Failure	70,951
Myocardial Infarction	80,825
Angina	1,116,847

Table 3. Annual Costs of Diabetes for the ODD Cohort, 1992-2001

Year	# of patients	Total healthcare costs (billions)	Average cost per patient
1992	281,703	$1.79	$6,343
1993	320,624	$1.92	$5,998
1994	355,470	$2.08	$5,857
1995	386,640	$2.30	$5,947
1996	417,446	$2.35	$5,623
1997	451,894	$2.52	$5,579
1998	486,281	$2.61	$5,371
1999	523,744	$2.84	$5,422
2000	559,420	$3.14	$5,612
2001	586,259	$3.30	$5,626
Total	**4,369,481**	**$24.85**	**$5,687**

2.4.2. Incidence of diabetes in Ontario, 1992-2001

Of the 734,113 people with diabetes, 67.9% (N= 498,590) received a diagnosis of diabetes mellitus during the observation period (approximately 49,859 new cases per year). For this population, the average annual cost of diabetes in the

year of diagnosis was estimated to be $5,329 and roughly $4,060 in each year thereafter (Table 4). Of the newly diagnosed patients without complications (N=331,003, 66.4%), the mean healthcare cost was $3,115 in the year of diagnosis and approximately $2,109 in each subsequent year. On average, complications resulted in an additional $2,061 per patient per year. The annual probability of diabetes-related events remained fairly constant over the period for these patients and the 10-year cumulative probability of death was estimated to be 47.0% (Table 5).

Table 4. Healthcare Costs of Treating People Newly Diagnosed with Diabetes

Years since diagnosis	Average Healthcare costs (no complications) (N=331,003)	Average Healthcare costs (with and without complications) (N=498,590)
1	$3,115	$5,329
2	$2,354	$4,155
3	$2,203	$3,998
4	$2,132	$3,958
5	$2,069	$3,938
6	$2,037	$3,965
7	$2,022	$3,979
8	$2,008	$4,033
9	$2,098	$4,171
10	$2,061	$4,339
Total	**$2,210**	**$4,271**

Table 5. Annual Probability of Diabetes-Related Complications for Incident Cases of Diabetes in Ontario, 1992-2001 (N=498,590)

Years since diagnosis	N	Amputation (%)	Angina (%)	Blindness (%)	Cataract (%)	Heart failure (%)	MI (%)	Fatal MI (%)	Nephropathy (%)	Stroke (%)	Fatal stroke (%)	Deaths (%)
1	498,590	0.22	15.76	0.29	2.39	1.15	1.57	0.33	0.16	1.12	0.16	4.56
2	445,855	0.12	14.50	0.26	2.17	0.84	0.99	0.23	0.12	0.71	0.12	2.93
3	390,312	0.12	14.27	0.24	2.08	0.82	0.99	0.23	0.12	0.70	0.12	3.16
4	336,226	0.13	14.16	0.23	2.09	0.84	1.05	0.26	0.13	0.70	0.13	3.42
5	284,840	0.14	13.92	0.22	2.13	0.88	1.01	0.24	0.15	0.71	0.13	3.55
6	236,027	0.17	13.73	0.24	2.16	0.89	1.07	0.27	0.15	0.73	0.13	3.85
7	189,806	0.19	13.51	0.22	2.21	0.86	1.05	0.28	0.18	0.72	0.12	4.08
8	142,255	0.16	13.16	0.21	2.20	0.95	1.08	0.27	0.18	0.71	0.12	4.46
9	92,864	0.21	13.18	0.22	2.23	0.91	1.14	0.26	0.22	0.70	0.11	5.67
10	35,969	0.25	13.18	0.22	2.41	0.98	1.21	0.30	0.26	0.74	0.13	11.31

2.4.3. Predicted impact of diabetes-related complications on healthcare costs in Ontario based on patient-specific characteristics using a two-part model

Using the two-part model described in section 2.3.4, total annual healthcare costs were estimated for the first occurrence for each of the seven complications for a specific type of patient. All equations in the model included variables representing the patients' age and sex, and sets of indicator variables for the occurrence of diabetes-related complications in the year in question, or in any previous year. These equations were used to measure the annual hospital and non-hospital costs based on the patients' characteristics and history of complications. The hospital costs and non-hospital costs were estimated separately and then combined to provide a total annual healthcare cost for each complication for a given set of patient characteristics. The cost estimates from this two-part model were used as parameters in the ODEM.

Table 6 reports the predictions from the logistic regression equations for hospital inpatient costs for an individual with characteristics set to reflect the average values for the ODD population (i.e. a male aged 63 years) for the first complication of any type. The second column of the table shows the annual probability of this individual incurring any hospital inpatient costs. Patients who had no complications had a probability of incurring some hospital inpatient costs in any single year of 0.14; that is, approximately 14% of patients who did not have any diabetes-related complications in a given year were admitted to hospital as an inpatient and consequently incurred some hospital costs. Column 2 also reports the annual probability of incurring any hospital costs for each type of event for someone who has not previously had any of these complications. The immediate impact of complications such as a myocardial infarction (MI) is to greatly increase the probability of incurring some hospital inpatient costs (e.g. a 100% probability of incurring hospital costs for a non-fatal MI.

Table 6 Estimated Probability of Incurring Some Hospital Inpatient Costs, Estimated Annual Hospital Inpatient Costs Conditional on Costs Being Incurred, and Expected Mean Cost, for a Representative Individual* by First Diabetes-Related Complications

Complication	Mean probability of incurring some hospital inpatient costs	Estimated annual hospital inpatient costs conditional on cost being incurred	Expected mean hospital inpatient cost of complications
Column 1	Column 2	Column 3	Column 4
No complications	0.14	$5,828	$834
Estimates for the year in which the event occurred			
Fatal MI	1.00	$7,393	$7,393
Non-fatal MI	1.00	$13,528	$13,528
Fatal Stroke	1.00	$6,937	$6,937
Non-fatal stroke	1.00	$19,421	$19,421
Ischaemic heart disease	0.39	$7,970	$3,126
Heart Failure	1.00	$12,398	$12,398
Blindness in one eye	0.22	$6,223	$1,378
Amputation	1.00	$30,449	$30,449
Nephropathy	1.00	$18,235	$18,235
Cataract extraction	0.89	$1,726	$1,542
Estimates for each year subsequent to the year in which the event occurred			
Non-fatal MI	0.19	$7,138	$1,338
Non-fatal stroke	0.20	$9,068	$1,831
Ischaemic heart disease	0.24	$6,334	$1,539
Heart failure	0.28	$9,744	$2,762
Blindness in one eye	0.15	$5,940	$912
Amputation	0.28	$12,945	$3,575
Nephropathy	0.39	$14,473	$5,683
Cataract extraction	0.26	$4,603	$1,174

Abbreviations: MI=myocardial infarction

* The characteristics of the representative individual were set to the ODD mean population, i.e., a male who is 63 years of age

The bottom section of column 2 in Table 6 shows the probability of incurring hospital inpatient costs in the years following an event. This indicates that the rate of hospitalization continues to be significantly higher than the 14% rate

experienced by individuals who have not had any complications. For example, patients who have heart failure are predicted to have a 28% probability of incurring hospital inpatient cost for all subsequent years.

Column 3 provides the estimated mean hospital inpatient costs associated with each complication, conditional on some hospital inpatient costs being incurred calculated using the Ordinary Least Squares (OLS) equation from the two-part model. Thus, if a male with diabetes aged 63 years in Ontario incurred hospital inpatient costs in the year in which he had a non-fatal MI, these costs averaged $13,528, while if a patient with similar characteristics experienced an amputation, the average hospital inpatient costs of treatment would be $30,449 in that year. For all complications, except cataract extraction, these hospital costs are higher than the $5,828 incurred by the 14% of patients with no complications who were admitted to hospital.

Finally, column 4 of Table 6 represents the product of columns 2 and 3 (i.e. the expected hospital inpatient costs associated with each complication). For example, a male aged 63 years who receives a diagnosis of ischaemic heart disease has a 39% probability of incurring hospital inpatient costs in the year the diagnosis occurred. The average cost for this event for this type of patient was $7,970 and so the expected hospital inpatient costs associated with ischaemic heart disease are the product of these, or $3,126.

Similar methodologies were used for each of the other 5 healthcare sectors included in our costing analyses and the results combined in order to calculate an average annual per patient cost of treating diabetes and diabetes-related complications. Given that there are numerous combinations of patient characteristics, an example is provided in Tables 7 and 8 to illustrate how this was done. Table 7 presents the estimated average 1-year healthcare costs for a person suffering a non-fatal stroke in the year the stroke was incurred and Table 8 provides the calculations for the annual cost of treating a person in the years

subsequent to the event. The total healthcare cost in the year the non-fatal stroke occurred was estimated to be $22,221 while the average cost in each year subsequent to the non-fatal stroke was $3,083.

Table 7. Average 1-Year Cost for Person Suffering a Non-Fatal Stroke in the Year of the Event (male, aged 63 years)

Healthcare Sector	Mean probability of incurring some costs	Annual costs conditional on costs being incurred	Expected mean cost of complications
Hospital	1.00	$19,421	$19,421
Outpatient visits	1.00	$2,546	$2,546
Drugs	0.12	$838	$102
LTC	<0.01	$17,649	$0
ER	0.79	$194	$153
Home care	0.19	$0	$0
Estimated total costs in year			**$22,221**

Abbreviations: ER=emergency room; LTC=long-term care

Table 8. Average Annual Cost for Person Suffering a Non-Fatal Stroke in Subsequent Years

Healthcare Sector	Mean probability of incurring some costs	Annual costs conditional on cost being incurred	Expected mean cost of complications
Hospital	0.20	$9,068	$1,831
Outpatient visits	0.99	$1,156	$1,153
Drugs	0.05	$1,180	$54
LTC	<0.01	$29,829	$0
ER	0.24	$182	$44
Home care	0.05	$0	$0
Estimated total costs in subsequent years			**$3,083**

Abbreviations: ER=emergency room; LTC=long-term care

This methodology allowed us to calculate the immediate costs that accrue within the year an event occurs for a patient with specified characteristics, as well as the long-term costs that reflect the costs in subsequent years associated with the ongoing management of each of the seven complications. For example, for a male aged 63 years with no diabetes-related complications, the total healthcare

cost for treatment was estimated to be $1,773 per year. A person receiving a diagnosis of renal failure will incur $22,117 in the year of diagnosis and will cost approximately $10,038 in each of the following years (Table 9). Also, if the person experiences a fatal myocardial infarction, the mean total cost in the year the event occurred was estimated to be $8,556, whereas if a person had a non-fatal myocardial infarction then the cost in the first year was $16,314 with an annual cost of $2,551 in each subsequent year.

Table 9. Estimated Average Annual per Patient Cost of Diabetes and Diabetes-Related Complications in Ontario (based on male aged 63 years)

Annual cost of DM without complications: $1,773			
	At time of event		**In subsequent years**
Complication	**Fatal**	**Non-fatal**	
Ischaemic Heart Disease	---	$5,106	$2,948
Myocardial Infarction	$8,556	$16,314	$2,551
Heart Failure	---	$14,924	$4,184
Stroke	$8,051	$22,221	$3,083
Amputation	---	$34,470	$4,721
Blindness	---	$2,730	$1,945
Renal Failure	---	$22,117	$10,038
Cataract Extraction	---	$3,609	$2,272

2.5. Summary and conclusions

This section of the report provides a detailed description of how the Ontario Diabetes Economic Model (ODEM) was created. The section starts with an explanation of how the seven diabetes-related complications and mortality rates are represented in the diabetes disease model. This is followed by an account of how the healthcare resource utilization and complications were identified and measured in Ontario. The costs associated with the resource utilization for the treatment of diabetes and its complications were assigned and subsequently analysed to provide the Ontario-specific costing parameters for the ODEM. The estimated costs differ as the demographic and clinical characteristics of individual patients vary.

The results described provide Canadian data on the direct medical costs of treating diabetes using a very large number of diabetes patients followed over an extended period of time. The estimates presented here represent the care actually delivered and all unit costs, in 2004 dollars, in this analysis are from Canadian sources.

3. APPLICATION OF THE ODEM: COST-EFFECTIVENESS OF A MULTIDISCIPLINARY PRIMARY CARE DIABETES MANAGEMENT PROGRAM

The purpose of this section is to illustrate how the ODEM can be used to measure the long-term costs and consequences of a primary care, multidisciplinary diabetes management program. The chapter begins with a brief introduction to multidisciplinary diabetes programs, followed by a systematic literature review of the efficacy/effectiveness of this intervention. The remainder of the chapter pertains to the application of the ODEM to a specific intervention in Ontario.

3.1. Systematic review of the literature of the efficacy of multidisciplinary diabetes management program interventions

3.1.1. Background

Over the past decade there has been a shift in the responsibility for care of patients with diabetes away from hospital-based care to primary care. Currently, the trend is to deliver coordinated diabetes care using a team approach that includes dietitians, psychologists, and nurses as well as physicians. A multidisciplinary approach may be even more critical for achieving normoglycemia in type 2 diabetes, given the greater need for behavioral change and self-management in this disorder. Additionally, in an era of fiscal restraint, the increased role of other healthcare professionals in addition to physicians may represent a more cost-effective option for managing patients with diabetes. A wide range of interventions targeting the structure of care has been implemented to achieve better metabolic control or to improve care delivered to patients with diabetes. This review aimed to identify and describe multidisciplinary primary care interventions to improve the management of patients with type 2 diabetes mellitus in various delivery settings (e.g. primary care, outpatient and hospital). The clinical efficacy/effectiveness was also summarized where reported.

3.1.2. Search strategy for identification of studies

A preliminary literature search was undertaken to provide information on the efficacy/effectiveness of multidisciplinary primary care diabetes management interventions in the treatment of type 2 diabetes. This preliminary search allowed the determination of the potential size of the available literature and clarified the search terms to be used in the complete search.

Building on these preliminary search strategies, a complete search was undertaken by the research teams from the Evidence-based Practice Centre (EPC) and the Program for Assessment of Technology in Health (PATH) for the different databases. An initial strategy was developed for MEDLINE with advice from research librarians; this was then modified for the other databases (EMBASE, Cumulative index to nursing and allied health literature [CINAHL], Cochrane Database of Systematic Reviews [CDSR]). We employed a two-step approach. Firstly, a search strategy for type 2 diabetes was created. Secondly, we developed search terms for the multifaceted interventions as well as a composite search scheme for the primary care aspect of the search strategy. To achieve this, a combination of the use of medical subject headings (MeSH), MeSH terms, keywords and text strategy was adopted. The final strategy involved a combination of the type 2 diabetes, multidisciplinary interventions and the primary care search strategies (see Appendix 2). The goal of the review was to describe the impact of various multifaceted primary care interventions on a number of clinical parameters that could be used to compare with results from the Ontario Diabetes Outcomes Model.

English language and human studies between 1993 and 2005 inclusive were selected for review. It was felt that a search period beginning in 1993 would ensure that any references found would be in accordance with recent standardized definitions of type 2 diabetes. Reference manager, version 10 (ISI Researchsoft, Thomson Scientific, U.S.A) was used to manage the results of the searches and the obtained citations were subsequently cleansed of duplicates.

3.1.3. Methods of review

The titles and abstracts were screened by 2 reviewers to identify publications that discussed the use of a multifaceted intervention for the management of type 2 diabetes in the primary care setting. Excluded were review articles, comments, editorials, guidelines, letters, and case reports. If it was uncertain following the review of the titles and abstracts as to whether a publication provided comparative information, the full text was retrieved and a review of the paper was completed. If it was still not clear whether a study should be included or not, consensus was reached by discussion with another reviewer. No restriction based on clinical study design was used and both randomized and non-randomized trials were included.

3.1.3.1. Data analysis

Given the likely heterogeneity of interventions, settings and patient populations, we decided a priori not to use meta-analytic techniques to pool the results of the studies. Instead we present the results of studies in tabular form (Appendices 4 & 5) and make a qualitative assessment of the effect of studies, based upon the size and direction of effect observed and the statistical significance of the studies.

We present the data pertaining to changes from baseline to endpoint in glycosylated hemoglobin (HbA1c). However, where other relevant clinical parameters were reported e.g. fasting plasma glucose (FPG), body mass index (BMI), blood pressure, lipid parameters, these results were included in the description of the studies. All measures of change were continuous in nature and thus were described as means and standard deviations when reported.

The included studies were presented in two groups as we classified the studies based on design. Specifically, studies were categorized as either a randomized controlled trial or a nonrandomized controlled trial. In the appropriate section, a detailed description is given of the individual studies followed by a more general summary of the efficacy/effectiveness of that group of studies.

3.1.3.2. Description of studies

The literature search identified a total of 1,732 unique citations for screening. An initial screening of the titles and abstracts excluded 1,496 (55.2%) articles because they did not deal specifically with type 2 diabetes or they dealt with screening for diabetes. The remaining 236 articles were further reviewed using more specific criteria and 176 were thought to provide a measure of effect for the integration of a multidisciplinary primary care management program. Excluded from further evaluation was an additional 119 articles because the interventions were not multifaceted. The resulting 57 papers were obtained for full text screening and 24 of these were included in this review, 11 nonrandomized controlled trials and 13 randomized controlled trials (Appendix 3).

3.1.3.2.1. Nonrandomized controlled trial studies

Eleven nonrandomized controlled trial studies dealt with the implementation of a multidisciplinary primary care diabetes management program and provided measures of clinical effectiveness (Appendix 4). The first of these studies was conducted by Day et al(60) in 1992. The authors measured the effects of an integrated system of diabetes care with an enhanced role of a diabetes specialist nurse on diabetes control by integrating the educational with the clinical processes. Glycemic control was evaluated in : 1) a cohort of insulin-treated and non-insulin treated diabetic subjects (age < 65 years) studied prospectively before and 3 years following the introduction of the new system of care; 2) a second cohort of more elderly patients aged greater than 65 years studied for the 3 years after the change over; 3) a cross-sectional study of the clinic population the year before and 3 years after the change over; and 4) a group of patients attending standard unaltered clinics in the same district. Significant and sustained falls in HbA1c were observed in all groups of subjects attending the centre, with the means of those aged less than 65 falling from 11.9% (SD 2.3%) to 9.9% (SD 1.9%) and for those aged over 65 from a mean of 11.7% (SD 2.0%) to 10.3% (SD 2.3%) 3 years later. The cross sectional population provided similar results with a mean HbA1c of 12.2 % (SD 3.0) prior to the changeover

and 10.4% (SD 4.4%), 3 years later. Smaller but significant changes were observed in patients continuing to attend the routine clinic, from 12.2 % (SD 2.3%) to 11.3% (SD 2.6%) over a similar period. The authors concluded that the introduction of the new system of care resulted in a progressive, sustained, and highly significant improvement in glycemic control in all groups of subjects attending the centre.

An observational, retrospective chart review study conducted in Texas, US, evaluated the introduction of a diabetes resource nurse case manager in a suburban 12-physician family practice.(61) The diabetes resource nurse case manager implemented comprehensive protocols for patient assessment, chronic diabetes care, patient education, and medication management. Additional nurse visits, in the office or by phone consultation, occurred as necessary for patient care. The nurse periodically reviewed each case with the patient's primary care physician. After six months of follow-up HbA1c values significantly improved overall, from a mean of 7.9% (from 5.4% to 15.2%) to a mean of 6.7% (from 4.6% to 11.1%). Improvements in other clinical and process measures were also found. The authors concluded that the nurse intervention protocols were key components in the improvement of diabetes treatment in primary care settings and that the results suggest that the diabetes resource nurse case manager was promising.

Another study evaluated the impact of diabetes care directed by nurses. The nurses followed detailed protocols and algorithms under the supervision of a diabetologist in a Los Angeles county clinic.(62) A second county clinic, not using nurse-directed care was used as a control group. The study populations were comprised primarily of people of Hispanic decent and were followed for at least 6 months. Change from baseline results indicated that the HbA1c in the nurse-directed care population decreased by 3.5% (SD 3.8%) from 13.3 to 9.8% compared to a decrease of 1.5% (SD 2.9%) from 12.3 to 10.8% in the usual care group.

Three articles were identified that were related to a study referred to as Project Dolce (initiated in 1997): a community-based, culturally appropriate, nurse care management approach to diabetes care in San Diego County, CA.(63-65) The patient population was predominantly Latino and of low socioeconomic status. The first paper, published in 2001(63) merely presented the results of laboratory investigations before and after the delivery of 12 weeks of diabetes education classes. The authors did not report actual baseline and endpoint values but concluded that patients enrolled in educational classes had significantly improved HbA1c ($p < 0.0001$) as well as total cholesterol and triglycerides ($p<0.002$).

Another study examined the provision of case management and self-management training as part of the Project Dolce study.(64) The nurse case management component consisted of a nurse-led team with a registered nurse/certified diabetes educator (RN/CDE), bilingual/bicultural medical assistant, and bilingual/bicultural dietitian who traveled to a different clinical site each day to see patients. The RN/CDE used protocols for glucose levels, lipid levels, and hypertension management. The peer educators were individuals with diabetes completing the Project Dolce training curriculum and met established competencies. Classes were taught in patient's native language and covered diabetes and its complications, the role of diet, exercise, and medication, and the importance of self-monitoring of blood glucose. The investigators observed significant improvements in HbA1c (from 12.0% to 8.3%) and total cholesterol (from 5.79 to 4.81 mmol/L) as well as an increase in diabetes knowledge among intervention patients.

The final paper(65) from the Project Dolce Study compared the clinical outcomes and costs among participants in Project Dolce with those of a cohort of historical control patients. The authors found that 1 year of participation in the study was related to significant improvements in HbA1c, both systolic and diastolic blood pressure, total cholesterol, and LDL cholesterol. HbA1c in the intervention group decreased by 1.2% compared to 0.5% in the control group ($p<0.001$). At the

same time, systolic blood pressure decreased by 7.1 mmHg, cholesterol by 28.9 mg/dL, LDL by 18.2 mg/dL and HDL by 1.2 mg/dL. The total cost of the program was higher than control patients ($5,711 vs. $4,365) but it was the expenditures for pharmacy/supplies and disease management that increased in the program, while expenditures on hospital and emergency department care visits that declined.

Graber et al(66) reported the results of an endocrinologist-directed team of nurse and dietitian educators for a 3-month program of intensive diabetes care. Patients with unsatisfactory glycemic control, frequent hypoglycemia, or inadequate self-management were enrolled in this uncontrolled study. Seventy-one percent of the 350 patients had type 2 diabetes. The 12-week intensive outpatient program consisted of instruction and support in diabetes self-management coupled with adjustment of diabetes medications, provided by the educators and supervised by an endocrinologist. Weekly contact with the patients was made either by a clinic visit, a telephone call, or an exchange of e-mail or faxed messages regarding home blood glucose results. Overall, there was a mean decrease in HbA1c of 1.7% (95% CI: 1.4% to 1.9%) from a starting value of 9.4% (SD 1.9%) during the program. Individuals with type 2 diabetes who were taking insulin at the start of the program had a decrease of 1.4% (95% CI: 1.0% to 1.7%), while individuals with type 2 diabetes who were not taking insulin at the start had a greater decrease in HbA1c, a mean decrease of 2.3% (95% CI: 1.9% to 2.7%). The additional nurse and dietitian clinical visits cost an average of $319.70 per patient over the 3-month period.

The impact of a diabetes management program using physician-supervised diabetes nurse specialists with a computer system in an Health Management Organization (HMO) was evaluated in a study by Peters et al(67) In this system, referred to as the Comprehensive Diabetes Care Service (CDCS), the diabetes nurses followed specific protocols and used a computer system to send reminders to patients of scheduled or missed appointments as well as to order

required bimonthly laboratory tests. The CDCS utilizes diabetes nurse specialists as the primary contact with the patient. The role of the diabetologist in this program was to support and manage the clinical team as they cared for patients. The authors found that the nurses' implementation of algorithms with computerized tracking methods and follow-up among patients at high risk for diabetes complications achieved an average decrease in HbA1c values of 3.0%, from 12.5% to 9.5% ($p<0.05$), over a 1-year period.

Vrijhoef et al(68) evaluated, using a 12-month non-equivalent control group design, the impact of the substitution of a nurse specialist for an internist in stable outpatients with type 2 diabetes. The care was based on a developed protocol where the tasks of the nurse specialist were concerned with direct patient care (medial history taking, interpretation of laboratory tests, etc), organization and co-ordination of care for individual patients, consultation, and advancement of expertise (education of patients). The researchers found that the traditional care model and the nurse specialist model achieved equal patient outcomes in terms of lipid parameters, body mass index, blood pressure, quality of life, self-care behaviour, knowledge of diabetes, patient satisfaction, and overall number of consultations with care providers, while glycemic control of patients in the nurse specialist model was somewhat better than for patients receiving traditional care. The authors reported that HbA1c of patients in the nurse specialist model improved, from 8.6% (SD 1.4%) to 8.3% (SD 1.0%), after 1 year but deteriorated in the traditional model group from 8.6% (SD 1.1%) to 8.8% (SD 1.3%). This study provides some evidence that the nurse specialist model may replace the traditional outpatient model effectively in patients with stable type 2 diabetes.

Yong et al(69) conducted a prospective structured audit on the effectiveness of nurse-based treatment alterations in insulin-treated diabetic outpatients with poor metabolic control (HbA1c >7.5%) in the UK. Of the forty-three patients in the analysis, 14 (33%) had type 1 diabetes, and 29 with insulin-treated type 2 diabetes. At referral to the diabetes specialist nurse (DSN), patients had a one-

on-one meeting with the DSN that lasted approximately 20 minutes, and involved initial discussions on the patient's perception of blood glucose control and its relationship with long-term complications. Patients were provided with some educational information, asked to intensify self-monitoring records, and were referred to a dietitian if it was thought to be beneficial. A second meeting was held 2 weeks later to discuss home monitoring results, and insulin dose alterations made. Further contacts were arranged at times and places that were convenient for the patient. During this period, routine diabetic clinic appointments continued unchanged, and no increased doctor-contact occurred. After 6 months post-intervention, 27 (63%) achieved successful improvement, defined as HbA1c < 7.0, or HbA1c fall of > 1.0%. It was found that type 2 patients were more likely to show improvement than type 1 patients. Overall, this paper has reported the particular benefit of DSN care in achieving improved blood glucose control of established diabetic patients on insulin treatment.

In a 1996 study, Ziemer et al(70) evaluated the impact of a non-physician provided structured diabetes care model delivered to a primarily urban African American, low income, type 2 diabetes population. Patients enrolled in the study were assigned to follow-up with one healthcare provider, a nurse practitioner or registered nurse with special interest and training in diabetes care. All patients attended diabetes education classes at the initial visit, and were seen by an assigned dietitian in a one-on-one setting at each of their return visits. Individual treatment plans were developed by healthcare providers, guided by a uniform protocol. At each visit, patients were also seen by an endocrinologist, who reviewed the treatment plan. Primary management was provided by nurse practitioners and dietitians. Visits with the nurse were scheduled frequently (at 1, 2, and 4 weeks, and at 2, 4, and 6 months) to maximize the educational components of therapy and to avoid metabolic decline. Improvements in HbA1c were seen to decrease from 9.6% to 8.1%, a fall of 1.5% after 12 months. The authors concluded that successful management of type 2 diabetes in urban African-American patients often can be achieved with dietary therapy alone, even

among individuals presenting on pharmacologic therapy. Additionally, Ziemer et al suggested that reliance on non-pharmacologic therapy and a team approach emphasizing non-physician providers likely resulted in cost savings.

3.1.3.2.2. Summary of nonrandomized controlled trial studies

Maintaining good glycemic control in patients with diabetes is a challenging task that requires persistent follow-up and efforts to motivate patients to adhere to the necessary treatment regimen. All of the papers reviewed support the sentiment that multidisciplinary primary care interventions in the management and coordination of care for patients with type 2 diabetes has great rewards in terms of clinical outcome measures (i.e. decreases in HbA1c values ranged from 0.3% to 3.7%). However, due to their non-experimental design, it is not possible to clarify exactly which elements of the multidisciplinary intervention contribute to improved metabolic control. For example, there may be a non-specific 'support' element that favours diabetes management. Therefore, the next section reports the results of a review of randomized controlled trials for multidisciplinary primary care interventions for diabetes management.

3.1.3.2.3. Randomized controlled trial studies

Thirteen articles were identified from the literature search that used a randomized controlled trial study design to evaluate the efficacy of multidisciplinary primary care interventions (Appendix 5). One US group(71) conducted a 2-year study to determine whether multifaceted, culturally sensitive, primary care-based behavioural interventions implemented by a nurse case manager (NCM) or a community health worker (CHW) or a combination of both could improve HbA1c and other indicators of diabetic control (i.e. lipids and blood pressure) in 186 urban African Americans with type 2 diabetes. This study consisted of four arms: 1) usual medical care (control); 2) usual medical care + NCM intervention; 3) usual medical care + CHW intervention; and 4) usual medical care + NCM + CHW (combined team intervention). Interventions focused on the diet, physical activity, foot care, vision care, blood glucose self-monitoring, blood pressure

control, adherence to medication and appointments, referrals, and where appropriate, smoking cessation. Of the 84% of patients who completed the 2-year follow-up visit, HbA1c was reduced by 0.21%, 0.30% and 0.80% in the NCM, CHW, and combined group respectively. The largest effect on triglycerides was also seen in the combined group. The CHW and the combined NCM/CHW intervention had a substantial effect on diastolic blood pressure (-3.2 and -5.0 mmHg, respectively). These results suggest that combined NCM/CHW interventions in primary care may produce significant improvements in HbA1c, lipids, and blood pressure. Overall, the combined intervention produced greater effects than the NCM or the CHW interventions alone.

Weinberger et al(72) also evaluated a nurse-coordinated intervention. This intervention was delivered by telephone between visits to patients in a Veterans Affairs general medical clinic. Nurses attempted to telephone intervention patients monthly (or more often if the nurse deemed it clinically indicated), in order to: educate patients; facilitate compliance; monitor patients' health status; facilitate resolution of identified problems; and facilitate access to primary care. Patients were encouraged to call the study nurses, should questions arise. Typically the usual care patients saw their physicians every three to four months. Compared to the usual care group, the intervention patients experienced a greater reduction in fasting blood glucose of 19 mg/dL and 0.6% in HbA1c at the 1-year follow-up. Both results were statistically significant.

Likewise, Aubert et al(73) conducted a 12-month randomized controlled trial comparing a nurse case management model of diabetes care with usual diabetes management in a primary care setting. The nurse case manager was a certified diabetes educator trained in adhering to detailed management algorithms. A family physician and an endocrinologist were responsible for all diabetes management decisions for patients in the intervention group. Case management consisted of an initial assessment, a 2-week follow-up visit, follow-up telephone calls every 1 to 2 weeks, and quarterly in-person visits. The intervention reduced

HbA1c by 1.7% over 1 year compared to a decrease of only 0.6% in the usual care group. On average, patients in the intervention group had a decrease of 48.3 mg/dL in fasting blood glucose level compared with a decrease of 14.5 mg/dL in the usual care group. No statistically significant differences were seen between nurse case management and usual care with respect to changes in systolic or diastolic blood pressure, serum cholesterol and triglyceride levels, or body weight.

Despite using a similar approach to the aforementioned study by Aubert, Krein et al(74) found that the extra attention and assistance provided by case managers failed to improve glycemic, lipid, or blood pressure control in a group of Veterans Affairs ambulatory patients. At the end of the 18-month intervention period, glycemic control remained poor (HbA1c >=9%) in both case management and usual care patients.

One study evaluated the Diabetes Outpatient Intensive Treatment (DOIT) program.(75) Eligible patients with type 1 (14%) and type 2 diabetes (86%) with poor glycemic control (HbA1c > 8.5%) were randomly assigned to one of two treatment arms. The experimental arm consisted of a 3.5-day group education and skills training experience combined with daily medical management. Following the program, a nurse case manager arranged to contact each patient on at least a quarterly basis to address problems as they arose, provide support, and adjust the regimen as necessary. The other group, entitled EDUPOST, received standard diabetes care with the addition of quarterly educational mailings. Over the 6-month study period, patients randomly assigned to the intervention group had a significantly greater drop in HbA1c values than the comparison group (2.3% vs. 1.7%, $p<0.02$).

A South Korean study conducted in 2003(76) evaluated the effect of a telephone intervention by a diabetes nurse on glycosylated hemoglobin levels and adherence to treatment control recommendations in people with type 2 diabetes

mellitus. Data were collected from October 2000 to July 2002. Patients in the intervention group were provided a diabetes care booklet, and a 12-week telephone intervention. The telephone intervention consisted of continuing education and reinforcement of diet, exercise and medication adjustment recommendations, as well as frequent self-monitoring of blood glucose levels. The nurse contacted intervention group members at least twice a week for the first month and then weekly for the second and third month. Patients kept a log of their blood glucose levels as well as daily diet and exercise logs. The control group received routine care (visiting a physician every 3 months). Thirty-six of the fifty randomized patients provided data for analysis. Patients in the treatment group had a mean decrease of 1.2% in HbA1c levels and those in the control group had a mean increase of 0.6%. The authors concluded that a nurse telephone intervention can improve HbA1c.

In 2005, the same South Korean research group published a second paper using the same methodology over a 12-week period on patients from the time period March 2002 to December 2002. (77) The authors found similar results to the study published in 2003: patients in the intervention group had a mean decrease of 1.2% in HbA1c levels and those in the control group had a mean increase of 0.5%. This study also measured fasting blood glucose and lipid parameters but no significant differences for any of these outcome measures.

An evaluation of a chronic disease management program involving a nurse practitioner-physician team with those of an existing model of care was conducted by Litaker et al(78). The components of the program focused on the use of clinical practice algorithms, patient education regarding disease self-management strategies, and regular monitoring and feedback delivered primarily by the nurse practitioner. Consultation with the primary care physician was initiated when management decisions or problems not addressed in the algorithms arose. Changes from baseline to 12 months in HbA1c, high density lipoprotein cholesterol, and systolic and diastolic blood pressure control were the

clinical outcomes of interest. The researchers found that team-treated patients benefited from an increase in HDL cholesterol level and a small but significant improvement HbA1c values (-0.63% vs. -0.15%, p=0.02). Of interest, the authors observed that the effect of team management on diabetic control disappeared within 12 months after study completion. The potential value of an ongoing interaction with this team is substantiated by this rapid return of HbA1c levels to pre-study ranges once team contact was terminated. Using a cost accounting strategy, the average personnel costs per patient for 1 year's treatment were significantly higher and amounted to USD $134.68 for team-treated patients and USD $93.70 for those treated by their primary care physician alone (mean difference = USD $40.38, p<0.001). The total additional personnel costs associated with this program were nearly 50% higher than for the usual approach to providing care (USD $10,639.70 vs. USD $7,308.53).

In 2000, Piette et al(79) published a paper that reported the results of a randomized, controlled trial of automated telephone assessment and self-care education calls with nurse follow-up among diabetic patients treated in a public healthcare system. The study was conducted in general medicine clinics of a county health care system. The objective was to determine whether this intervention could improve self-care, glycemic control, and symptoms. Follow-up HbA1c levels were 0.3% lower in the intervention group than in the usual care group (p=0.1). Diabetes care supported by automated telephone assessments and patient education may be an effective means of improving patients' self-care and glycemic control.

Piette and colleagues(80) extended their work by conducting a similar 12-month study among patients treated in Department of Veterans Affairs (VA) outpatient clinics. Unlike the nurse in the prior county clinic trial, the VA nurse had the ability to schedule clinic appointments. The results of this randomized trial of automated telephone disease management-supported diabetes care were that the mean end-point HbA1c values were similar among intervention and control

patients (8.1 vs. 8.2, p=0.3). However, the intervention increased the frequency with which patients self-monitored their blood glucose and checked their feet for problems.

In the only Canadian study identified, Taylor et al(81) evaluated the effects of a nurse-physician collaborative approach to care for patients with type 2 diabetes. The nurse worked in a collaborative manner as a case manager, educator, and support person. Also included in the support team were a dietician and an exercise specialist. The usual care group received standard medical care, which included scheduled office visits at 3-month intervals. Over the 4-month study period, the control group's average fasting blood glucose increased slightly whereas the experimental group's decreased. HbA1c showed an increase in the control group (7.69% to 8.41%) and a small decrease in the experimental group (7.69% to 7.40%). Mean systolic and diastolic blood pressure, total cholesterol, and LDL cholesterol decreased in the experimental group while they increased in the control group. With the exception of diastolic blood pressure, none of these changes were statistically significant.

The effectiveness of a cluster visit model led by a diabetes nurse educator in an outpatient setting to patients with poorly controlled diabetes was evaluated by Sadur et al(82). This nurse-led multidisciplinary program, referred to as the Diabetes Cooperative Care Clinic (DCCC), includes a dietitian, a behaviourist, and a pharmacist and supported by two diabetologists. The diabetes nurse assessed patients and made referrals to various healthcare providers as necessary and continued monitoring via telephone over the 6-month intervention period. For the 85% of patients with HbA1c values available at 6 months post-randomization or beyond, levels declined by 1.3% from baseline for the intervention group but by only 0.22% for the control group ($p<0.0001$ for the difference in change between the two groups). Although the intervention group had somewhat higher ambulatory care utilization and more intensive pharmaceutical management than control subjects during the 6-month

intervention, this excess utilization was offset by fewer hospital admissions after the intervention. The researchers suggested that improved glycemic control may lead to an early reduction in health care utilization, which would offset costs of the intervention promptly and thus remove a key barrier in adopting and implementing these effective innovations in treatment.

Taylor et al(83) evaluated the efficacy of a nurse-case management system designed to improve outcomes in patients with complicated diabetes. Patients were either randomized to usual care or a special nurse case management intervention. The intervention group had an initial meeting with the nurse to develop a self-management plan, attended group session once a week for up to 4 weeks, and received telephone follow-up calls to manage medications and self-care activities. The nurse-case managers used treatment algorithms to titrate the patient's medications for diabetes, cholesterol, and hypertension. At 1 year, the mean decrease in HbA1c for the intervention group was significantly greater than the usual care group (1.14% versus 0.35%). Both groups had an average HbA1c value at baseline of 9.5%. Furthermore, 43% of intervention patients were able to achieve an HbA1c ≤ 7.5%. Decreases in total and LDL cholesterol were also significantly greater for the intervention group than for the usual care group.

3.1.3.2.4. Summary of randomized controlled trial studies

The results from the review of the literature confirm that multidisciplinary primary care approaches appear to be an effective approach toward promoting better diabetes care, contributing to a positive impact on glycaemic control (e.g. decreases ranged from 0.02% to 2.3%) (Table 10) and other important clinical markers (e.g., blood pressure and lipids). It is, however, a resource-intensive intervention that demands significant time, commitment, and careful coordination with many healthcare professionals. Providing ongoing follow-up contact with the patients by a healthcare team member appears to be important. Further research is needed to understand how glycemic improvement is achieved and to clarify the long-term influence of the initial programs from the impact of ongoing

follow-up. Whether it is behavioral change on the part of the patients or closer medical management is unclear. What is evident, however, is the mostly consistent trend toward improvements in glycemic control with a more collaborative approach.

Table 10. Changes in HBA1c from Randomized Controlled Trials

Author	Intervention(s)	Control	Mean change in HbA1c (%) (relative to control)
Gary, TL 2003(71)	- nurse case manager (NCM) - community health worker (CHW) - NCM + CHW	usual care (UC)	NCM = -0.31, CHW = -0.30, NCM + CHW = -0.80
Weinberger, M 1995(72)	Nursing telephone intervention	UC	telephone = -0.6
Aubert, RE 1998(73)	NCM	UC	NCM = -1.1
Krein, SL 2004(74)	NCM with primary care providers	UC with educational material	NCM = 0
Polonsky, WH 2003(75)	Diabetes outpatient intensive treatment (DOIT) + NCM follow-up	Diabetes education pamphlet mailings + UC	DOIT = -0.4
Kim, HS 2003(76)	Nurse coordinated intervention (NCI)	UC	NCI = -1.8
Kim, HS 2005(77)	Nurse coordinated intervention (NCI)	UC	NCI = -1.7
Litaker, D 2003(78)	Nurse practitioner + primary care physician (NP + MD)	Usual primary care physician (MD only)	NP + MD = -0.48
Piette, JD 2000(79)	Automated telephone intervention with nurse telephone follow-up	UC	Telephone = -0.3
Piette, JD 2001(80)	Automated telephone intervention with nurse telephone follow-up	UC	Telephone = -0.2
Taylor, KI 2005(81)	Clinical nurse specialist (CNS)	UC	CNS = -1.01
Sadur, CN 1999(82)	Diabetes cooperative care clinic (DCCC)	UC with primary care physician	DCCC = -1.08
Taylor, CB 2003(83)	NCM	UC with primary care physician	NCM = -0.79

3.1.3.2.5. Conclusions

In chronic conditions such as diabetes, complex relationships exist among variables related to glycemic control, and time constraints prevent the primary care physician from addressing each of these on every visit. The team approach allows the physician to address the acute issues and the nurse to address the long-term ongoing aspect of a patient's diabetes on a more individual basis. Additionally, these types of interventions could prove cost-effective in caring for the increasing number of people developing type 2 diabetes.

The following sections will describe a primary care diabetes management program coordinated by a diabetes nurse specialist implemented in Sault Ste. Marie, Ontario as well as the impact of that program on patient clinical outcome measures and cost-effectiveness.

3.2. Short- and Long-Term Costs and Effects of a Nurse-Led Multifaceted Intervention Aimed at Improving Diabetes Management in Sault Ste. Marie

3.2.1. Background

Sault Ste. Marie's population of approximately 76,000 is ageing and is comprised of a higher proportion of seniors (persons aged 65 years and over) than the provincial average. The area's population has declined between census years (1996 to 2001) and the decline has been largely in the younger working age population (persons aged 20-44 years). More than half of Sault Ste. Marie's population is enrolled or "rostered" at the Group Health Centre (GHC), (approximately 60,000 residents enrolled) and it is reported that these patients closely resemble the composition of the Ontario population in terms of age structure. The age structure of the non-rostered population is distinctly different from that of the rostered and provincial population.(84)

The GHC is a not-for-profit, multi-specialty, multi-disciplinary health service organization and is funded on a capitation basis. This means the Centre receives a sum of money every month per enrolee. This money is used to

provide primary care and helps provide all of the services at the Group Health Centre, like, Audiology, Cardiology, Communication Disorders, Counselling, Day and Evening Clinic, Diagnostic Imaging, Geriatrics Assessment Clinic, Laboratory, Nutrition Services, Phototherapy, Physical Therapy, Surgery, and Vision and Eye Care, to name a few. Enrolment entitles rostered patients access to many services not covered by the Ontario Health Insurance Plan (OHIP) either free-of-charge or at a reduced rate.

3.2.2. Diabetes quality improvement program

Thirty-three family physicians and thirty-one specialists at the GHC agreed to collaborate in an initiative to improve the quality of care, patient satisfaction, quality of life, and clinical outcomes of persons with diabetes. The multifaceted program included the introduction of a Specialty Nurse Liaison, and included components aimed at the patient, the GHC providers, and the GHC health care system.(85) The study was entitled "the Continuity of Health Care in Capitated Patients with Diabetes (CHIC)". The duration of the study period was 18 months (January 2000 to July 2001) and the components of the program are described below.

***Patient education*:** Patient education materials were developed and disseminated. One patient education newsletter with various topics related to diabetes care was placed in the local newspaper and numerous brochures and posters were placed around the GHC promoting diabetes management. The GHC organized a Diabetes Awareness Day, Patient Open House. Patients interested could call and sign up for a tour of all available services at the GHC for patients with diabetes. Volunteers guided each group through the building to each station. The areas that participated were: vision and eye care, pharmacy, dietitian, chiropody, physiotherapy, research, Health Promotions Initiative – Diabetes (HPID) program, and counselling.

***Provider education*:** The providers (physicians, nurses and other allied health care professionals) participated in a Diabetes Education Day conducted by key opinion leaders and stakeholders from across Ontario. The Diabetes Education Day was attended by 24 general practitioners and 2 internal medicine specialists, as well as 6 nurse practitioners, 13 registered nurses, 32 registered practical nurses, and 10 allied health professionals. During this day, 7 guest speakers presented diabetes-related information relevant to their respective area of expertise.

Specialty nurse liaison: A diabetes nurse liaison was formally trained for this particular endeavour and hired full-time to provide telephone and in-person follow-up visits to patients identified as having difficult-to-control diabetes (approximately 10% of the HPID patients). The diabetes nurse liaison used an electronic medical record (EMR) to communicate her findings from her initial assessments and follow-ups to other members of the healthcare team and served as a general resource to all health care providers and patients at the GHC.

Health Promotions Initiative-Diabetes (HPID) Template Updating: A special diabetes tracker computer screen, referred to as the Health Promotions Initiative-Diabetes (HPID) Template, was programmed into the EMR to be the initial screen displayed to the health care providers for a visit by a diabetes patient (Appendix 6). The diabetes tracker contained 9 elements related to acceptable optimal processes and clinical outcomes of diabetes care.(86) The items were displayed with date last done and date due for the following: weight/body mass index (BMI), blood pressure, HbA1c, eye exam, lipids, foot exam, albumin/proteinuria, smoker, and flu shot. Weight, blood pressure, HbA1c and lipids also contained the last known values. The EMR was updated twice during the life of the project to input any missing data from the paper version of the medical records. The physicians should have already seen the results in real time but this was to ensure that any data available only in paper form was

inputted into the EMR so that the EMR was fully up-to-date. This information was used as a practice audit and feedback for physicians. The Information Technology (IT) department compiled a list of all study patients in the EMR and forwarded it to the project office so that the data could be cleaned and statistics calculated for the overall population as well as for individual practices.

3.3. Methods

3.3.1. Data source and study population

All rostered GHC patients in the year 2000, over the age of 17 years were eligible to participate. Inclusion criteria consisted of a diagnosis of diabetes based on the Canadian Diabetes Association definition of diabetes mellitus and provided informed consent. Patients were excluded if they had gestational diabetes, could not communicate in English or had a life expectancy or residency in Sault Ste. Marie of less than three years. Additionally, patients who had an age of diagnosis less than 10 years were removed from all analyses as it was assumed that these patients were likely to have type 1 diabetes mellitus.

3.3.2. Data collection

3.3.2.1. Ontario-specific patient-level baseline risk factors

In order to use the Ontario Diabetes Economic Model (ODEM) to determine the long-term cost-effectiveness of this multidisciplinary primary care diabetes management program, individual patient-level data pertaining to various risk factors were required. As a result, a retrospective medical chart review was conducted to collect patient-level data necessary to populate the ODEM. A data abstraction form was created to collect demographic characteristics, diabetes medical history, and history of other medical conditions, historical values of five key intermediate outcomes (i.e. HbA1c, blood pressure, total cholesterol, HDL cholesterol, and smoking status) (Appendix 7). A second data abstraction form was used to record each patient's values for these key clinical measures before and after the 18-month study period (Appendix 8). All data collected were subsequently entered into a Microsoft© Office Excel (2002) spreadsheet.

3.3.2.2. Missing data

Where variables were missing, multivariate imputation sampling techniques were employed to impute missing data.(87) The data were transferred into STATA 8.2 Special Edition (Statacorp LP, Texas) in order to conduct the multiple imputations. This method imputes missing values by using switching regression, an iterative multivariable regression technique. The missing data were filled in 3 times to generate 3 complete datasets. The 3 datasets of imputations were generated each having 25 cycles of regression switching, updating the imputed values at the end of each cycle. The estimates for each regression were made after taking a bootstrap sample of the non-missing observations, thereby avoiding the necessary assumption that the distribution of the variables is multivariate normal. Variables, that were rare (<10) and other variables that were perfectly collinear to others, were deleted for the purposes of the imputation. The objective was to ensure valid standard errors, confidence intervals and p-values.

3.3.2.3. Healthcare resource utilization during the study period

Data were collected using the GHC EMR and the Sault Area Health (SAH) Health Records system as well as community pharmacy records to measure healthcare resource utilization throughout the 18 month study period. The resource data was divided into three 6-month phases. The first phase was considered the 'pre' phase occurring prior to and at the beginning of the quality improvement initiative. The third phase was considered the 'post' phase occurring following the program implementation.

The total number of family physician visits, specialist visits, hospitalizations, administration of injections (e.g. immunizations, chemotherapy), laboratory tests and procedures were recorded by phase of the study. As well, each healthcare resource item was given a designation as being either diabetes-related or not diabetes-related. This allowed for the analysis of any changes in the use diabetes-specific resources between the study phases.

3.3.2.4. Healthcare costs during the study period

All healthcare costs were collected in 2000/01 dollars and then inflated to 2004 dollars using the healthcare component of the Consumer Price Index (CPI).(53) Professional fees for consultations, assessments, visits, diagnostic interpretation, and surgical procedures were taken from the Ontario Health Insurance Plan (OHIP) Schedule of Benefits (SOB).(88) The cost of a family physician visit was set at $26.87 and the cost of an initial specialist consultation was set at $114.21 and a specialist follow-up visit was $58.08. The cost of an outpatient visit to the hospital (SAH) was assigned a value of $20.81 and the cost of an emergency visit to SAH was set at $54.67.

The cost of an inpatient hospital admission was calculated based on the average cost/hospital day (total expense includes direct expenses and overhead) for the hospital where the patient was admitted as reported by the Ontario Ministry of Health and Long-Term Care (MOHLTC) multiplied by the length of stay for that patient. The cost of a day surgery or emergency walk-ins was attributed as the OHIP billing costs of $55.48.

Medication utilization was based on prescription records, while over-the-counter and herbal medications were gathered from patient interview and pharmacy records. Patient costs as well as private or public drug plan costs were included. The cost of giving injections (e.g. immunization, chemotherapy) was calculated using the OHIP billing codes for the specific injection that was given. Costs varied slightly over the course of the study according to the OHIP fee adjustments.

The costs of laboratory tests and procedures were calculated based on the cost associated with the OHIP code for each test.

3.3.2.5. Upfront program implementation costs

Various sources were used to collect detailed costing data for each of the different items put into practice as part of the multidisciplinary primary care diabetes management program in Sault Ste. Marie. Direct and some indirect costs (i.e. time off work) were considered in the implementation of the program.

Patient education: The GHC was contacted in order to obtain a detailed listing of all resources and costs associated with the development of all educational material including the "Take Care" newsletter, recruitment posters for the CHIC study, information pamphlets, HPID promotion material, and patient reminder cards. The total cost of creating and disseminating the Patient Education-related material was $740.

Fifty-five people attended the Diabetes Awareness Day. The detailed costing of all items required to host the Diabetes Awareness Day including: snacks and drinks after the tour, directional and display signs, miscellaneous expenses such as door prizes, as well as the hourly wage for the professionals to staff the various stations, was conducted. The total expense for the Diabetes Awareness Day was estimated to cost $2,575.

Provider education: The hourly wages for each health care professional that attended the Group Health Centre Diabetes Education Day were identified from various sources (e.g. Ontario Medical Association, Ontario Pharmacists' Association) and multiplied by the duration of the Education Day (i.e. 5 hours) to estimate indirect costs. Miscellaneous expenses required for the Day were also tabulated (e.g. lunch for all in attendance, room and equipment rental, honorariums for guest speakers). The total cost for the GHC Diabetes Education Day was calculated to be $19,092.

Specialty nurse liaison: The total cost required to formally train a nurse to become a diabetes specialty nurse as well as the salary and benefits for the

duration of the project (i.e. 1.5 years) was calculated. The training costs include travel, examinations, conferences, educational workshops, and resource materials. The training costs were estimated to be $4,614 and the salary and benefit costs were $104,407, for a total cost of $109,021.

Health Promotions Initiative—Diabetes (HPID) Template Updating: The HPID template was updated twice (2000 and 2001) in the summer months by clinical research students. In the summer of 2000, 5 students updated 2002 patients' charts and in the summer of 2001, 8 students were hired to update 2,191 patients' charts. The total cost of the updating over the 2 time periods was $41,160.

It took the Information Technology department 16 hours, at a rate of $76/hour, to compile a list of all CHIC patients in the EMR for a total of $1,214. The data was cleaned and verified at the project office and subsequently statistics were calculated for the audit and feedback to the healthcare providers. The complete process was estimated to take 14 hours at a rate of $16.25 per hour plus 22% benefits for a total of $277.

As a result, the total cost to update the HPID template and obtain data on study patients was estimated to be $42,651.

Diabetes-related medications

The incremental costs of all diabetes-related medications used in the third phase of the study were included in the program implementation costs as it was assumed that the diabetes liaison nurse would have notified the primary care physician to any gaps in drug therapy and the nurse would have emphasized the need to adhere to prescribed medications. The result would mean an increase in drug utilization and thus improved management of diabetes. The incremental diabetes-related drug cost was an average of $228 per patient per year.

Total Program Costs: When all of the aforementioned costs were added together, the total cost of the implementation of the CHIC program was $266,236 or $659 per patient per year.

3.3.2.6. Intermediate outcome measures

The primary outcomes of interest were changes from study entry to study exit on the following clinical parameters: HbA1c, blood pressure, total cholesterol, HDL cholesterol, and smoking status.

3.3.2.7. Data analysis

This study used a before-and-after design and thus each of the intermediate outcomes of interest was measured as changes in the value at the end of the study when compared to the beginning of the study. Each person's value at the beginning of the study was subtracted from the end-of-study value and then the average change for the population was calculated with an associated measure of variance. This was done for each of the three multiply imputed datasets created to deal with missing data. This provided 3 intermediate results, which were subsequently combined into a final result. Because each multiple imputation represents a random sample of missing values, this process results in valid statistical inferences that properly reflect the uncertainty due to missing values. Statistical comparisons were made using paired t-tests and results were reported as means and standard errors due to the pooled results from the multiply imputed datasets.

3.4. Study Results

3.4.1. Study population

At the time of the study, there were 44,000 GHC patients in the EMR and 3,100 patients identified as having diabetes. Patients under the age of 18 or who had gestational diabetes (n=1,119) were excluded. Of the remaining 1,981 patients who were approached, 404 patients consented to participate and were included in the study. 3 patients were further removed from our analyses since their age

at diagnosis was less than 10 years and it was thought that these patients had type 1 diabetes mellitus.

3.4.2. Demographic characteristics

Table 11 illustrates that the study population was comprised mostly of people of Caucasian decent (92.9%), with an approximately equal number of males and females (50.6%). The mean age at diagnosis of diabetes was 52 years, and the average age upon entry into the study was 61 years.

3.4.3. Clinical characteristics

On enrolment, the average glycosylated haemoglobin level (HbA1C) was 8.14% and the average blood pressure was 139/78 (Table 11). The mean total cholesterol value was 5.43 mmol/L and the mean HDL cholesterol was 1.14 mmol/L. One hundred seventy-eight (44.4%) people had at least 1 diabetes-related complication prior to entering the study, with the majority being ischaemic heart disease (24.9%). Eleven percent (n=45) of the study participants had a history of myocardial infarction (MI) upon study entry with the mean number of years since MI being 9.6 years.

Table 11. Patient Characteristics at Time of Enrolment into CHIC Diabetes Program (n=401) Based on Pooled Estimates from the Multiply Imputed Datasets (estimated mean values and standard errors unless otherwise indicated)

Characteristic	Mean of pooled estimate
Male	203 (50.6%)
Caucasian	92.9% (1.9%)
Age at diagnosis of DM	52.3 (0.63)
Age on enrolment (mean, SD)	61.4 (10.9)
Years with diabetes	9.17 (0.43)
HbA1c	8.14% (0.1%)
Smoker	19.4% (2.6%)
Mean systolic BP mmHG	138.7 (0.98)
Mean diastolic BP mmHG	77.9 (0.52)
Mean total cholesterol mmol/L	5.43 (0.06)
HDL cholesterol mmol/L	1.14 (0.02)

History of other medical conditions	N(%)	Years with condition (SD)
Atrial Fibrillation	47 (11.7%)	3.8 (2.5)
Ischaemic heart disease	100 (24.9%)	4.5 (3.4)
Peripheral vascular disease	35 (8.7%)	3.3 (2.7)
Myocardial infarction	45 (11.2%)	9.6 (10.2)
Stroke	30 (7.5%)	4.4 (3.9)
Congestive heart disease	46 (11.5%)	3.6 (2.8)
Amputation of digit or limb	4 (1.0%)	3 (3.4)
Blindness	5 (1.3%)	5.2 (2.4)
Renal failure	57 (14.2%)	3.2 (2.1)

3.4.4. Short-term effectiveness of the multidisciplinary primary care diabetes management program

The average amount of time each person was enrolled in the program was 370 days. As a result, it was decided to assume that the patients were exposed to

the enhanced management for a period of 1 year. By the end of the study period, HbA1c values decreased by an average of 1.02% (p<0.001), systolic blood pressure decreased by 1.32 mmHg (p=0.219), total cholesterol was reduced by 0.47 mmol/L (p<0.001), while HDL cholesterol increased by 0.06 mmol/L (p<0.001). At the same time, the proportion of patients smoking dropped from 19.4% to 13.8% by the end of the study (p=0.070) (Table 12).

Table 12 Changes in Intermediate Outcome Measures from Entry to Exit of Study

Risk Factor	Before (SE)	After (SE)	Change (95% CI)	P-value
HbA1c	8.14% (0.10)	7.12% (0.07)	-1.02% (-1.25, -0.79)	<0.001
Systolic BP (mmHg)	138.68 (0.98)	137.36 (0.95)	-1.32 (-3.42, 0.78)	0.219
Total cholesterol (mmol/L)	5.43 (0.06)	4.97 (0.05)	-0.47 (-0.58, -0.35)	<0.001
HDL cholesterol (mmol/L)	1.14 (0.02)	1.20 (0.02)	0.06 (0.03, 0.09)	<0.001
Smoking status=yes	19.4% (2.6)	13.8% (1.8)	-5.6% (-11.6, 0.01)	0.070

3.4.5. Healthcare resource utilization costs during the program

Costs associated with doctor visits, laboratory tests, procedures, medications and pharmacists fees, and hospitalizations were tabulated for the first 3 months of the program (phase 1) as well as for the final 3 months of the program (phase 3). Total costs were slightly lower as a result of improved quality of care when the costs for phase 1 were compared to phase 3 ($2,497 [SD $6,618] per patient to $2,342 [SD $4,022] per patient) however this change was not statistically significant (p=0.660)(Table 13). While expenditures for medications increased by 19.8%, expenditures for hospital stays and physician visits declined by 30.4% and 18.3% respectively.

Table 13. Average per patient cost by healthcare resource type by phase of study

Healthcare resource	Phase 1	Phase 3	Mean Difference (95% CI)
Physician visits (SD)	$278 ($302)	$227 ($267)	-$51 (-$83, -$19) p=0.0018*
Hospitalizations (SD)	$1,003 ($5,953)	$698 ($2,973)	-$306 (-$932, $321) p=0.3381
Procedures (SD)	$215 ($377)	$259 ($649)	$44 (-$12, $100) p=0.1269
Medications (SD)	$817 ($971)	$979 ($1,085)	$162 ($108, $216) p<0.000*
Injections (SD)	$1 ($7)	$1 ($6)	$0 (-$0.66, $0.68) p=0.9806
Laboratory/diagnostic tests (SD)	$183 ($281)	$179 ($414)	-$4 (-$41, $33) p=0.8301
Average total costs per patient (SD)	$2,497 ($6,618)	$2,342 ($4,022)	-$155 (-$846, $537) p=0.6604

3.4.6. Summary

There is growing interest in defining the costs and potential savings involved in various delivery models of diabetes care aimed at improving health outcomes. This study demonstrated improvements in clinical risk factors and may result in costs savings (-$155 per patient, p=0.66) within the first year of implementation of a multidisciplinary primary care diabetes management program in Sault Ste. Marie, Ontario. Any long-term cost savings from improved glycemic and lipid control are only realized many years later, in patients who do not become blind, require dialysis, lose a limb to amputation or develop atherosclerotic vascular disease. However, it is difficult to quantify these benefits and prove cost-effectiveness based on future events that are prevented. Therefore, the changes in risk factors or intermediate markers due to the diabetes program were used as inputs into the Ontario Diabetes Economic Model in order to estimate the long-term costs and health outcomes over the course of the disease. The results of the economic disease model are provided in the following sections.

3.5. Economic evaluation

3.5.1. Calibration of treatment effects within the model

Demographic and clinical characteristics for each of the 401 patients in the study were entered into the Excel-based ODEM. The treatment period for this study was 1 year, and as a result this represented the base case for analysis in the model. Initially, the baseline clinical parameter values (i.e. HbA1c, blood pressure, cholesterol, and smoking status) were run through the model to provide a "control" measure of life years gained, quality-adjusted life-years (QALYs) gained, and costs. These values represented the outcomes if no diabetes management program had been implemented.

In order to calculate the incremental costs and effects of the diabetes management program, the end-of-study values were used as starting points in the model so as to represent the impact for the "intervention" group. The benefit is assumed to be instantaneous and constant over the treatment period. Also, it was assumed that after the 1-year intervention period, each patient's key clinical parameter values would return to their baseline, or pre-treatment, measurements. Based on an individual's demographic and clinical characteristics at the start of the model, the model predicted if and when a person dies or suffers a diabetes-related complication during their lifetime. If a person suffers an event, the model assigns the costs associated with treating the complication using the costing data produced from the two-part model outlined in chapter 2 of this report, as well as the number of life-years gained and quality-adjusted life-years gained. The calculated average program implementation cost of $659 per patient per year was added to the "intervention" group costs. Patients without a history of complications started with an initial utility of 0.785 and incurred a cost of $1,773 per year. The costs assigned to persons with a history of a complication would be similar to those outlined in Table 9 and the utilities are described in section 2.2.8 of this report.

To reduce Monte Carlo error, or first order uncertainty, the number of inner loops was set at 1,000. Second order, or parameter, uncertainty was handled by setting the number of bootstraps to 100. The time horizon for the model was 40 years.

3.6. Results

3.6.1. Forecasted first-time complication and mortality rates as follow-up up times are altered

The primary objective of the model is to estimate the likely occurrence of the major diabetes-related complications over a lifetime for patients with specified prognostic risk factors in order to calculate costs and health outcomes (i.e. life expectancy and quality-adjusted life expectancy). Tables 14, 15, and 16 report the forecasted cumulative first event rates from the model when the amount of follow-up time is varied by 1 year, 10 years, and 40 years respectively. The short-term benefits following one year of treatment are dramatically reduced over the long-term if the treatment is removed after one year and patient outcomes from the intervention group begin to resemble those of the control over time. For example, the intervention group experienced 15.5 fewer first myocardial infarctions than the control group after one year (Table 14). The differences in cumulative event rates however get smaller between the intervention and control groups for myocardial infarction when the patients are followed for 10 and 40 years (Tables 15 and 16 respectively). Two possible explanations for this phenomenon are: 1) the people who did not have a first event in year 1 in the intervention group are now at risk for having a first event in subsequent years since the treatment effect has been removed after year 1; and 2) there were fewer deaths in the intervention group and again, there were more people at risk for a future first event.

Table 14. Forecasted One-Year Cumulative First Event Rates as a Result of the Program and Treatment Effect Duration of One Year (base case analysis)

Complication	Control (per 1,000)	1-year program (per 1,000)	First events avoided	RRR
IHD	7.8	5.3	2.5	32%
MI	51.2	35.7	15.5	30%
Heart failure	18.0	14.5	3.5	19%
Stroke	25.1	17.9	7.2	29%
Amputation	2.2	1.1	1.1	50%
Blindness	7.8	5.9	1.9	24%
Renal failure	0.9	0.7	0.2	22%
Mortality	143.8	127.6	16.2	11%

Abbreviations: IHD=ischemic heart disease; MI=myocardial infarction; RRR=relative risk reduction

Table 15. Forecasted Ten-Year Cumulative First Event Rates as a Result of the Program and Treatment Effect Duration of One Year

Complication	Control (per 1,000)	1-year program (per 1,000)	First events avoided	RRR
IHD	48.9	47.1	1.8	4%
MI	221.2	213.1	8.1	4%
Heart failure	97.0	96.1	0.9	1%
Stroke	106.6	102.4	4.2	4%
Amputation	16.3	15.3	1.0	6%
Blindness	41.9	42.0	0.1	0
Renal failure	7.5	7.7	(0.2)	(3%)
Mortality	567.7	565.4	2.3	0

Abbreviations: IHD=ischemic heart disease; MI=myocardial infarction; RRR=relative risk reduction

Table 16. Forecasted Forty-Year Cumulative First Event Rates as a Result of the Program and Treatment Effect Duration of One Year

Complication	Control (per 1,000)	1-year program (per 1,000)	First events avoided	RRR
IHD	73.6	72.2	1.4	2%
MI	302.4	295.3	7.1	2%
Heart failure	141.1	140.6	0.5	0
Stroke	144.9	140.8	4.1	3%
Amputation	27.8	26.8	1.0	4%
Blindness	58.6	57.6	0.9	2%
Renal failure	15.4	15.6	(0.2)	(1%)

Abbreviations: IHD=ischemic heart disease; MI=myocardial infarction; RRR=relative risk reduction

3.6.2. Forecasted first-time complication and mortality rates as treatment duration is altered

Treatment duration, and thus treatment effect duration, impacts the cumulative first event rate when follow-up time is altered. We compared the forecasted cumulative first event rates for ten years and forty years when the treatment effect was assumed to last for ten years (Tables 17 and 18). In both scenarios, we assumed the treatment effect would last for ten years. When the follow-up time was set to 10 years, the absolute reduction in cumulative first myocardial infarction events was 49.4 per 1,000 population, the number of deaths avoided was 30.1 per 1,000 population, and the stroke rate was decreased by 21.8 per 1,000 population when compared to the group who did not receive the treatment (Table 17). Despite a seemingly unimpressive reduction of 7.8 first amputations per 1,000 population, the relative risk reduction as a consequence of the 10-year program was 48%.

Again, when the forecast time was increased to forty years following the ten-year treatment, it becomes evident that the effect on event rates becomes diminished when compared to the ten-year forecasted rates. However, there is still substantial benefit. For example, there is a 22% relative risk reduction in first amputation rates and a 13% and 12% relative risk reduction in ischemic heart disease and myocardial infarction respectively (Table 18).

Table 17. Forecasted Ten-Year Cumulative First Event Rates as a Result of the Program and Treatment Effect Duration of Ten Years

Complication	Control (per 1,000)	10-year program (per 1,000)	First events avoided	RRR
IHD	48.9	36.1	12.8	26%
MI	221.2	171.8	49.4	22%
Heart failure	97.0	84.4	12.6	13%
Stroke	106.6	84.8	21.8	20%
Amputation	16.3	8.5	7.8	48%
Blindness	41.9	34.8	7.1	17%
Renal failure	7.5	7.2	0.3	40%
Mortality	567.7	537.7	30.1	5%

Abbreviations: IHD=ischemic heart disease; MI=myocardial infarction; RRR=relative risk reduction

Table 18. Forecasted Forty-Year Cumulative First Event Rates as a Result of the Program and Treatment Effect Duration of Ten Years

Complication	Control (per 1,000)	10-year program (per 1,000)	First events avoided	RRR
IHD	73.6	64.0	9.6	13%
MI	302.4	264.6	37.8	12%
Heart failure	141.1	133.7	7.4	5%
Stroke	144.9	128.5	16.4	11%
Amputation	27.8	21.6	6.2	22%
Blindness	58.6	53.4	5.2	9%
Renal failure	15.4	15.4	0	0
Mortality	993.0	992.7	0.3	0

Abbreviations: IHD=ischemic heart disease; MI=myocardial infarction; RRR=relative risk reduction

3.6.3. Cost-effectiveness results

The model predicted that the improvements in glycemic control, blood pressure, lipids, and smoking status resulting from the one-year multidisciplinary primary care diabetes quality improvement program implemented in Sault Ste. Marie resulted in a reduction in the cumulative incidence of complications over the 40-year time horizon (Table 16). This reduction generated 0.1142 additional life-years and 0.1075 QALYs and an incremental cost effectiveness ratio (ICER) of $5,640 per life-year gained and a cost per QALY of $5,992 (Table 19).

Table 19. Incremental Cost-Effectiveness Analysis Results from the ODEM using the Base Case for CHIC (1-year program and treatment effect) Extrapolated over 40 Years

	Mean lifetime cost/patient	QALYs	Life Years
Control	$46,078	8.2371	10.8929
Intervention	$46,722	8.3446	11.0071
Incremental	$644	0.1075	0.1142
ICER		$5,992	$5,640

Abbreviations: ICER=incremental cost-effectiveness ratio; QALY(s)=quality-adjusted life-years(s)

3.6.4. Sensitivity analyses

One consequence of modeling the cumulative incidence of diabetes-related complications over the lifetime of a patient is that apparently small changes in input parameters can have a disproportionately large impact on the estimated outcomes. In order to test the robustness of our results to changes in key model drivers, a series of univariate sensitivity analyses were performed. Both the program and treatment effect duration were varied simultaneously in order to estimate the incremental cost-effectiveness associated with varying treatment/effect duration (Table 20). Both the costs and effects were discounted at a rate of 3% per year and the time horizon was kept constant at 40 years.

Table 20. Incremental Cost-Effectiveness Analysis Results: Sensitivity Analyses Surrounding Treatment Duration

Program & treatment effect duration	Incremental cost/effect per patient over lifetime			ICER per	
	COST	QALYs	LYs	QALY	LY
1 year	$644	0.11	0.11	$5,992	$5,640
5 years	$2,584	0.47	0.50	$5,507	$5,198
10 years	$4,124	0.79	0.84	$5,203	$4,903

Abbreviations: ICER=incremental cost-effectiveness ratio; LY(s)=life year(s); QALY(s)=quality-adjusted life-years(s)

The results from these analyses demonstrate that the longer the treatment effect was sustained, the more complications avoided resulting in an increase in life expectancy and enhancement in quality of life. The reductions in complications also led to an improved incremental cost-effectiveness ratio.

3.7. Summary

The multidisciplinary primary care diabetes management program introduced in Sault Ste. Marie improved short-term clinical outcomes for study participants. The application of the ODEM using the results from this intervention proved that improvements in clinical outcomes (e.g. glycemic control, blood pressure) impact eventual costs of care in the form of prevented complications and hospitalizations in later years. The base case analysis cost $5,992 per QALY which represents good value for money.

4. DISCUSSION

4.1. Ontario diabetes economic model (ODEM)

In long-term chronic diseases, such as type 2 diabetes, related morbidity and mortality take years to develop. Therefore, clinical trials often assess changes in surrogate risk factors such as HbA1c, lipids, and blood pressure. Modelling facilitates the linkage between intermediate biological endpoints and final health outcomes necessary for economic evaluation.

The long-term modeling of diabetes involves a number of assumptions to be made which extrapolate beyond the existing evidence base. Such assumptions affect model parameters, functional relationships between model variables, and indeed the essential structure of the model. Results from complex models are often more influenced by the assumptions about the natural history and course of the disease, reflected in the model structure, than by simple uncertainty about specific parameter values (the usual basis for sensitivity analysis). The use of epidemiological data from the largest type 2 diabetes clinical trial in the literature with more than 3,600 patients enrolled and followed up for a median of 10.3 years enhances the internal validity of our model.

It is not normally possible to verify a model against independent data which has not earlier been used to calibrate the model or define its structures. Direct comparison of models and extensive sensitivity analyses help to identify those features on which further research or methodological development is required to improve future models. In this respect there is no “gold standard” for diabetes modelling: there is only a process of iterative evolution in which the major sources of conflict between results from different models are identified, new evidence sought, and then further comparisons made.

The volume of data available from the UKPDS removed many constraints on the modelling approach adopted and allowed the construction of a model based on a set of equations estimated using a consistent methodology. In particular, the use

of time-varying covariates allowed the model to create linkages between different diabetes-related complications. These have increasingly been recognised as crucial to such simulation models. This issue was addressed by incorporating linkages where there is a high degree of statistical significance and supporting clinical and epidemiological evidence. For example, the results for stroke are consistent with those from the Framingham study showing that a history of heart failure and atrial fibrillation increase the risk of subsequent stroke.(37)

One of the limitations of the ODEM is that the model only predicts the first event in any single category of diabetes-related complications, and does not allow series of events such as sequential amputations to be modelled directly. However, this limitation should not be overstated, as: 1) such multiple events in the UKPDS data were relatively infrequent; 2) subsequent fatal events in specific categories of diabetes-related complications are included in the diabetes-related mortality equation; and 3) additional post-study monitoring data will in time allow this issue to be re-visited.

The costs included in the model reflect the actual resource utilization profiles for a large prospective cohort of individuals with diabetes over a 10-year time period representing over 4.4 million patient-years to measure the cost of treating diabetes and diabetes-related complications in Ontario. Specifically, individual "patient histories" were created to provide an annualized picture of an individual's experience of diabetes complications and healthcare resource utilization in 5 sectors (i.e. hospital, outpatient, prescription drugs, long-term care, and home care services). The costs represent the impact of seven diabetes-related complications on healthcare costs, not only in the year in which the event occurs, but in permanently raising the average level of healthcare costs in subsequent years.

The calculated average cost per patient per year for patients with and without diabetes-related complications described here is detailed enough to be

meaningful to decision makers and to those conducting economic analyses. To our knowledge, this report provides the first Canadian data on the direct medical costs of treating diabetes and related complications using a very large number of diabetes patients followed over time. The estimates provided here represent the care actually delivered and all unit costs in this analysis are from Canadian sources. Previously reported burden of illness estimates in Canada have ranged from $1.12 billion in 1993.(89) to $5.23 billion in 1998.(90) The earlier estimate represents an underestimate of the value as it does not include the costs related to the treatment of complications of diabetes.(3) The second calculation used a top-down costing methodology that allocated 1998 total medical expenditures to diabetes. The prevalence of diagnosed and undiagnosed diabetes and the relative risk of complications in people with diabetes were used to estimate the proportion of medical services that were consumed by people with diabetes.

4.2. Application of the Ontario diabetes economic model (ODEM)

The short-term results from the multidisciplinary primary care diabetes management program implemented in Sault Ste. Marie, Ontario were consistent with those found in the scientific literature. That is, coordinated care of patients with type 2 diabetes contributes to a positive impact on surrogate clinical outcomes (e.g. decreases in blood glucose levels, increases in HDL cholesterol). Using the ODEM, these beneficial changes in intermediate clinical markers translated into favourable long-term outcomes. For example, there was a 4% relative risk reduction of amputation, and a 3% risk reduction of stroke over the 40-year time horizon as a result of the one-year program. The incremental cost-effectiveness ratio associated with the reduction in these first events avoided was estimated to be $5,992 per quality-adjusted life-year. This suggests that the primary care diabetes management program represents good value for money according to commonly quoted thresholds.

5. CONCLUSIONS

The UKPDS Outcomes Model was identified as being the best diabetes economic model in existence for our purposes. Using resource utilization data for a large number of Ontarians with diabetes and assigning Canadian unit costs, this model was adapted to the Ontario setting. The resulting Ontario Diabetes Economic Model described in this report provides policymakers with a vehicle for assessing the long-term economic benefits, in terms of health outcomes (i.e. life years gained and quality-adjusted life-years gained) and healthcare costs, of any diabetes-management intervention. The application of the model to a primary care diabetes management program in Ontario predicted that the intervention represented good value for money. Other applications of the ODEM will enable policymakers to make better healthcare resource allocation decisions.

In addition to the development of an Ontario-specific long-term diabetes economic model, there are a number of other important results from this report, two of which are: 1) the calculation of an estimate of the cost of treating diabetes in Canada; and 2) a variety of cost estimates that may be readily translated into patient-level cost inputs for any type of economic model.

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APPENDICES

Appendix 1. Details of the Statistical Modeling for UKPDS Model

Parametric methods for risk estimation have been applied previously in modelling events such as MI and stroke.(51) In this analysis, a proportional hazards Weibull regression model was used to model diabetes-related complications with a baseline hazard of the form $h_0(t) = \lambda\gamma t^{\gamma-1}$, where γ is a shape parameter and the scale parameter $\lambda = \exp(\beta_0)$ or the exponentiated intercept coefficient β_0. Under the proportional hazards assumption the hazard of an event at time *t* for the *i*th individual is $h(t \mid x_{tj}) = h_0(t)\exp(x_{tj}\beta_j)$, where x_{tj} is a vector of *j* covariates and β_j their respective coefficients. Some of these covariates (such as age and sex) remain constant as time elapses; others potentially vary over time (such as HbA_{1c} and Systolic blood pressure). Thus the unknown parameters requiring estimation are λ, γ, β_0 and β_j.

Two types of risk estimation were used to model the risk of diabetes related death. First, logistic regression was used to estimate the probability that the first MI, IHD, CHF, amputation or renal failure event was fatal. Second, a Gompertz regression model – a functional form widely used to model mortality – was used to calculate the risk of diabetes-related mortality in subsequent years for patients with a history of these complications. Non diabetes-related mortality was also modelled using Gompertz regression. For these models the baseline hazard is $h_0(t) = \lambda\exp(\varphi t)$ and in the proportional hazards model $h(t \mid x_{tj}) = h_0(t)\exp(x_{tj}\beta_j)$ and the unknown parameters requiring estimation are $\lambda, \varphi, \beta_0$ and β_j.

The unconditional probability of an event occurring between *t* and *t*+1 can be calculated using the integrated hazard. For example, the integrated hazard at time *t* is $H(t \mid x_{tj}) = \exp(\beta_0 + x_{tj}\beta_j)t^{\gamma}$ and the unconditional probability of an event occurring in the interval *t* to *t*+1 is $1 - \exp(H(t \mid x_{tj}) - H(t+1 \mid x_{tj}))$.

Finally, equations representing risk factor progression were estimated using random effects panel data regression. Equations for risk factors were estimated using the form:

$$RF_{it} = \alpha + \beta_j x_{itj} + \mu_i + \nu_{it}$$

where RF_{it} is the risk factor for i th patient ($i = 1..n$) in year t of the study ($t = 1,...,T$) and x_{itj} are explanatory variables (*j*=1.. *J*). Predicted values of RF_{it} were used in conjunction with the event equations in order to complete the simulations. The smoking status equation used a logistic regression panel data model to estimate the probability of smoking in three-year periods from the diagnosis of diabetes.

Appendix 2 Search Strategy for Multifaceted Diabetes Management

Database: Ovid MEDLINE(R) <1966 to November Week 3 2004>

Search Strategy:

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1 exp diabetes mellitus/ (175728)
2 exp diabetes mellitus, type II/ (33201)
3 (("type 2 diabet:" or "type 2 DM" or diabet:) adj2 "type 2").af. (14855)
4 (("type II diabet:" or "type II DM" or diabet:) adj2 "type II").af. (34545)
5 NIDDM.af. (6419)
6 "non insulin dependent diabet:".af. (9180)
7 "adult onset diabet:".af. (342)
8 3 or 4 or 5 or 6 or 7 (40467)
9 1 and 8 (36812)
10 2 or 9 (36812)
11 multifacet$.mp. (2894)
12 intervention$.mp. (196458)
13 comprehensive$.mp. (54670)
14 ((diabet$ or manag$) adj3 program$).af. (29486)
15 ((diabet$ or program$) adj3 educat$).mp. (26817)
16 (secondary adj2 prevent$).mp. (7308)
17 (diabet$ and manag$).mp. (12120)
18 multifactor$.mp. (12338)
19 patient education.mp. (42249)
20 exp health promotion/ (23609)
21 exp health education/ (85207)
22 exp patient care management/ (282348)
23 (pc or dm).fs. (567655)
24 or/11-23 (1122527)
25 9 and 24 (7719)
26 10 and 24 (7719)
27 limit 26 to (human and english language and yr=1993 - 2005) (5435)

28 from 27 keep 1-1000 (1000)

29 from 27 keep 1001-2000 (1000)

****

Database: EMBASE <1980 to 2004 Week 52>

Search Strategy:

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1 exp diabetes mellitus/ (154809)

2 exp diabetes mellitus, type II/ (31388)

3 (("type 2 diabet:" or "type 2 DM" or diabet:) adj2 "type 2").af. (14678)

4 (("type II diabet:" or "type II DM" or diabet:) adj2 "type II").af. (4100)

5 NIDDM.af. (6007)

6 "non insulin dependent diabet:".af. (33249)

7 "adult onset diabet:".af. (232)

8 3 or 4 or 5 or 6 or 7 (36963)

9 1 and 8 (35189)

10 2 or 9 (35189)

11 multifacet$.mp. (2365)

12 intervention$.mp. (172301)

13 comprehensive$.mp. (41166)

14 ((diabet$ or manag$) adj3 program$).af. (6884)

15 ((diabet$ or program$) adj3 educat$).mp. (13801)

16 (secondary adj2 prevent$).mp. (7015)

17 (diabet$ and manag$).mp. (11183)

18 multifactor$.mp. (11205)

19 patient education.mp. (18823)

20 exp health promotion/ (15781)

21 exp health education/ (48095)

22 exp patient care management/ (139423)

23 (pc or dm).fs. (291929)

24 or/11-23 (653026)

25 9 and 24 (8329)

26 10 and 24 (8329)

27 limit 26 to (human and english language and yr=1993 - 2005) (6234)

28 from 27 keep 1-1000 (1000)

29 from 27 keep 1001-2000 (1000)

****

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature

<1982 to December Week 2 2004>

Search Strategy:

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1 exp diabetes mellitus/ (16300)

2 exp diabetes mellitus, type II/ (0)

3 (("type 2 diabet:" or "type 2 DM" or diabet:) adj2 "type 2").af. (3700)

4 (("type II diabet:" or "type II DM" or diabet:) adj2 "type II").af. (863)

5 NIDDM.af. (1234)

6 "non insulin dependent diabet:".af. (5071)

7 "adult onset diabet:".af. (80)

8 3 or 4 or 5 or 6 or 7 (7001)

9 1 and 8 (5362)

10 2 or 9 (5362)

11 multifacet$.mp. (700)

12 intervention$.mp. (42060)

13 comprehensive$.mp. (9057)

14 ((diabet$ or manag$) adj3 program$).af. (15473)

15 ((diabet$ or program$) adj3 educat$).mp. (12481)

16 (secondary adj2 prevent$).mp. (963)

17 (diabet$ and manag$).mp. (3271)

18 multifactor$.mp. (706)

19 patient education.mp. (18840)

20 exp health promotion/ (9100)

21 exp health education/ (33824)
22 exp patient care management/ (0)
23 (pc or dm).fs. (79470)
24 or/11-23 (174501)
25 9 and 24 (2779)
26 10 and 24 (2779)
27 limit 26 to (english and yr=1993 - 2005) (2648)
28 from 27 keep 1-1000 (1000)
****

Database: CDSR, ACP Journal Club, DARE, CCTR
Search Strategy:

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1 exp diabetes mellitus/ (3011)
2 exp diabetes mellitus, type II/ (0)
3 (("type 2 diabet:" or "type 2 DM" or diabet:) adj2 "type 2").af. (1897)
4 (("type II diabet:" or "type II DM" or diabet:) adj2 "type II").af. (3100)
5 NIDDM.af. (971)
6 "non insulin dependent diabet:".af. (1538)
7 "adult onset diabet:".af. (60)
8 3 or 4 or 5 or 6 or 7 (4188)
9 1 and 8 (837)
10 2 or 9 (837)
11 multifacet$.mp. (236)
12 intervention$.mp. (36536)
13 comprehensive$.mp. (3162)
14 ((diabet$ or manag$) adj3 program$).af. (1513)
15 ((diabet$ or program$) adj3 educat$).mp. (2660)
16 (secondary adj2 prevent$).mp. (1041)
17 (diabet$ and manag$).mp. (1374)
18 multifactor$.mp. (494)

19 patient education.mp. (3056)

20 exp health promotion/ (783)

21 exp health education/ (3513)

22 exp patient care management/ (3978)

23 (pc or dm).fs. (34160)

24 or/11-23 (71916)

25 9 and 24 (292)

26 10 and 24 (292)

27 8 and 24 (1181)

28 from 27 keep 1-1000 (1000)

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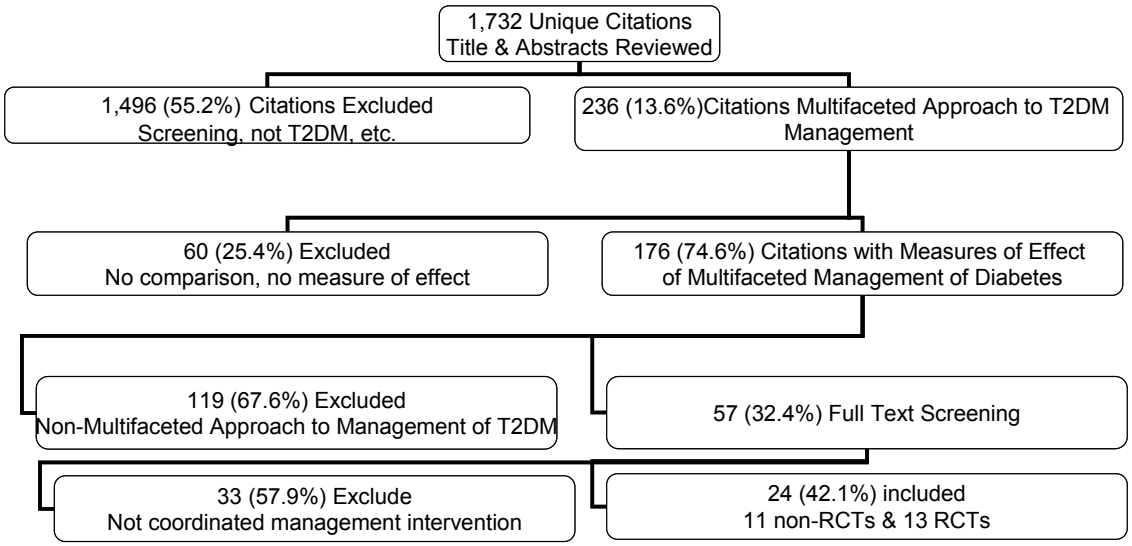
Appendix 3. Decision Tree of Systematic Literature Review for Multidisciplinary Primary Care Diabetes Management Program



Appendix 4. Characteristics of Non-Randomized Controlled Trials of Multidisciplinary Primary Care Diabetes Management

Author	Pub. Year	Country	Study design	Setting	Patient Pop.	Duration of Study	Study Description	Intervention	Outcomes	Total number of patients	Age of subjects	Clinical Results
Day JL et al(60)	1992	UK	Pre-post; non-equivalent control	Out-patient clinic	Aged < 65 after new system of care; a second cohort >65 after the system change; a third cross-sectional cohort; and a fourth routine care group	3 years	Integrating the educational with the clinical processes	Re-organization of role of the diabetes specialist nurse: to be counsellors in diabetes care, working in parallel with the physician, for patients whose needs were not predominantly medical.	Glycemic control, diabetic emergency admissions, attendance, and cancellation rates	Group 1 n=210, Group 2 n=144, Group 3 n=700, Group 4 n=157	Not reported	Group 1: 11.9% (SD 2.3) to 9.9% (SD1.9); Group 2: 11.7% (SD2.0) to 10.3% (SD 2.3); Group 3: 12.2 % (SD 3.0) to 10.4% (SD4.4); Group 4: 12.2 %(SD 2.3) to 11.3% (SD 2.6)
Couch, C et al.(61)	2003	USA	Retrospective chart review	Family practice centre (community)	Geriatric (>=65 years) and non-geriatric (<65 years)	6 months	Comprehensive protocols for patient assessment, diabetes care, education, and medication management implemented by diabetes resource nurse (DRN). Additional DRN patient visits as necessary. DRN periodically reviewed each case with the primary physician.	DRN case manager using management protocols	Clinical and process outcome measures	137 patients enrolled, 106 completed 6 months, 84 patients completed the 12-month visit.	Of the 106 patients, 58% were aged >= 65 years, and 42% were aged <65 years	HbA1c decrease from 7.9% to 6.7% (-1.2% (2.1%SD)); BMI decrease of 0.4 (SD 2.3)
Davidson, MB(62)	2003	USA	Retro-spective chart review	2 county clinics (community)	Minority population (mostly Hispanic and minority African American)	Average follow-up time was 7 months in Clinic A, 1 year in Clinic B	Nurse-directed care in Clinic A (experimental) matched to cases in Clinic B (control).	Diabetes care directed by nurses following detailed protocols and algorithms and	Clinical and process outcome measures	252 diabetic patients from clinic A were matched to 252 diabetic patients from Clinic	Mean age was 52 years	Nurse-directed care population followed for at least 6 months had HbA1c decrease by 3.5% (3.8%SD) (13.3 to 9.8)

Author	Pub. Year	Country	Study design	Setting	Patient Pop.	Duration of Study	Study Description	Intervention	Outcomes	Total number of patients	Age of subjects	Clinical Results
								supervised by a diabetologist		B		versus a decrease of 1.5% (2.9%SD) (12.3 to 10.8) in usual care group
Philis-Tsimikas, A and Walker, C(63)	2001	USA	Before-after	Comm-unity health centres	Indigent Latinos (uninsured)	12 weeks	12-week diabetes educational program to low-income diabetics.(Project Dolce)	Nurse-managed diabetes educational and treatment program	Primary outcome: HbA1c change; secondary outcomes: total cholesterol and TRGs and blood pressure	194	not reported	HbA1c (n=194): decreased at end of study (p< 0.0001), and total cholesterol and triglycerides decreased significantly (p<0.002).
Philis-Tsimikas, A et al.(64)	2004	USA	Case control	Comm-unity health centres	Indigent Latinos (uninsured)	1 year	Comprehensive program that provides outreach and education, recruitment, screening, diagnosis, clinical care, and educational services to low-income diabetics. (Project Dolce)	Nurse-managed diabetes educational and treatment program	HbA1c, lipid parameters, blood pressure	153 of 214 high-risk patients enrolled	51 (SD 12.9) years of age	HBa1c decreased 12.0% (SD 1.8) to 8.3% (SD 1.7), p< 0.0001, BMI: 35.3(17.3) to 34.7 (8.6); diastolic BP: 80 (11.8) to 76 (9.5); total cholesterol: 5.73 (1.37) to 4.81 (0.93); LDL: 3.35 (1.03) to 2.79 (0.78); triglycerides: 3.58 (5.20) to 2.04 (1.23); HDL: 1.07 (0.31) to 1.13 (0.30)
Gilmer, TP(65)	2005	USA	Pre-post clinical outcome s were compare d with a cohort of historical controls	Commun ity health centres	Indigent Latinos (uninsured)	1 year	Nurse-led diabetes case management program of low income diabetes patients compared to historical control cohort based on chart review (Project Dolce)	Stepped-care diabetes nurse case management program (protocols) and peer-led self-empowerment training program using	Primary: HbA1c; secondary: blood pressure and cholesterol parameters	188 in intervention group and 160 in control group	Intervention : 51 years of age and control: 52 years of age	HbA1c: adjusted difference between groups -0.8, SE 0.2; Systolic BP: adjusted difference between groups -5.4, SE 1.6; Diastolic BP: adjusted

Author	Pub. Year	Country	Study design	Setting	Patient Pop.	Duration of Study	Study Description	Intervention	Outcomes	Total number of patients	Age of subjects	Clinical Results
								nurse-led team with a registered nurse/certified diabetes educator, bilingual/bicultural medical assistant and bilingual/bicultural dietitian				difference between groups -8.0, SE 1.0; Total cholesterol: adjusted difference between groups -28.1, SE 4.9; HDL: adjusted difference between groups -1.6, SE 1.4; LDL: adjusted difference between groups -15.6, SE 4.1
Graber, AL(66)	2002	USA	Case series, before-after	Out-patient setting	Patients with un-satisfactory glycemic control, frequent hypo-glycemia, or inadequate self-manage-ment. 29% type 1 DM, 71% type 2 diabetes	3 months	Collaboration between primary care providers and endocrinologtst-directed team of nurse and dietitian educators	Patients had at least weekly contact with a nurse and received changes in medications, and individualized instruction for 12 weeks. Direct consultation with an endocrinologis t when necessary.	Primary outcome measure was the change in HbA1c from entry to baseline.	The first 350 patients who completed the program	51 years of age	9.4% (1.9) at start with mean decrease of 1.7% (95% CI, 1.4%-1.9%)
Peters, AL(67)	1995	USA	Obser-vational	Managed care setting (HMO)	People with diabetes from 22 HMOs	4 years	Managed care setting with a diabetes program with nurse specialists supervised by a physician using a computer system to enhance compliance	Physician-supervised diabetes nurse specialists. Diabetes nurses followed protocols and computer system sent reminders to patients of	Decrease in HbA1c from beginning to end of study; costs were also estimated	Not clear from study (244 or 750??)	Not reported	Decrease from baseline (12.5%) to endpoint (9.1%)

Author	Pub. Year	Country	Study design	Setting	Patient Pop.	Duration of Study	Study Description	Intervention	Outcomes	Total number of patients	Age of subjects	Clinical Results
								scheduled and missed appointments and to order required bimonthly laboratory tests				
Vrijhoef, HJM et al(68)	2001	The Netherlands	Non-equivalent control-group design	Out-patient	Patients with stable T2DM	1 year	Patients were referred to either the traditional model of outpatient care, or a new model in which the nurse specialist plays the central role in caring for the patients	Patients received 3 quarterly consultations from a nurse specialist based on a developed protocol.	HbA1c, lipid parameters, blood pressure, BMI	52 intervention and 47 control	68.2 (SD 9.7) years of age in intervention group and 66.4 (SD 9.3) in the control group	HbA1c decreased from 8.3% (SD 1.5) to 8.2% (SD 1.0) after 1 year compared to an increase from 8.2% (SD 1.1) to 8.5% (SD 1.4) in the control group no significant differences in other clinical parameters were found
Yong, A et al(69)	2002	UK	Pre-post	Out-patient	Diabetic outpatients poorly controlled on insulin treatment (HbA1c > 7.5%) (33% type 1 and 66% type 2)	6 months	Prospective audit of insulin-treated patients referred to diabetes nurse specialist with HbA1c >7.5%	Diabetes nurse intervention involved re-education, dietary advice and insulin dose adjustment	Improve-ment defined as a final HbA1c < 7.0% or a fall of HbA1c of >1.0% at 6 months post-intervention ; other outcomes were BMI, insulin dose and severe	43 poorly controlled insulin-treated diabetic patients	49 (SD 17) years of age	27 (63%) achieved successful improvement (HbA1c < 7.0, or HbA1c fall of > 1.0%) at 6 months

Author	Pub. Year	Country	Study design	Setting	Patient Pop.	Duration of Study	Study Description	Intervention	Outcomes	Total number of patients	Age of subjects	Clinical Results
									hypo-glycemic frequency			
Ziemer, DC et al(70)	1996	USA	Pre-post	Out-patient clinic	Low income African American T2DM urban patient population	6 months	Structured care delivered by non-physician providers. Primary management was provided by nurse practitioners and dietitians.	Management implemented by nurse practitioner and dietician that emphasizes non-pharma-cologic approaches to therapy.	HbA1c, FPG, and changes in body weight	112 of 325 with HbA1c values at all time points	57.7 years of age	HbA1c: 9.6% to 8.1%; Obese patients 9.6% to 8.2%; and nonobese subjects 8.0% to 7.9% at 12 months

Appendix 5. Characteristics of Randomized Controlled Trials of Multidisciplinary Primary Care Diabetes Management

Author	Pub. Year	Country	Setting	Patient Pop.	Duration of Study	Study Arms	Intervention	Outcomes	# of patients	Age of subjects	Clinical Results
Gary, TL et al.(71)	2003	USA	Primary care outpatient clinics at one of two centres	African Americans with Type 2 diabetes	2 years	Usual care (UC) UC + nurse case manager (NCM) UC + community health worker (CHW) UC + NCM/CHW	Patient counselling regarding self-care practices and physician reminders	Primary: HbA1c Secondary: Mean fasting blood glucose, Blood pressure, Body Mass Index, Lipid profile, Dietary risk assessment, physical activity	UC = 34 NCM = 38 CHW = 41 NCM/CHW = 36	Mean (SD) UC = 57 (8) NCM = 59 (11) CHW = 59 (9) NCM/CHW = 60 (7)	HbA1c Baseline: Mean (SD): UC = 8.5 (2.0), NCM = 8.8 (2.2), CHW = 8.4 (2.0), NCM/CHW = 8.6 (1.9) HbA1c change relative to usual care Mean (SE): UC = reference, NCM = -0.31 (0.49), CHW = -0.30 (0.48), NCM/CHW = -0.80 (0.52)
Weinberger M et al.(72)	1995	USA	Veterans Affairs general medical clinic	Veterans with type 2 diabetes receiving diabetes medication and obtaining primary care from the general medical clinic	1 year	Nursing telephone intervention vs. Usual care (UC)	Nurses telephoned patients on a monthly basis (or more frequently) to: educate, facilitate compliance, monitor health status, facilitate resolution of problems, and to facilitate access to primary care.	HbA1c, Fasting blood glucose (FBG), Quality of Life:	Nursing intervention: 204 Usual care: 71	Mean (SD) Nursing intervention: 63.2 (8.3) UC: 63.9 (8.6)	HbA1c baseline: Nursing Intervention: 10.7 (3.4), UC:10.7 (3.3) HbA1c at 1 year: Nursing Intervention: 10.5 (0.2), UC: 11.1 (0.3) (P=.046); FBG baseline: Nursing Intervention: 185.2 (67.0), UC: 183.9 (75.8) FBG at 1 year: Nursing Intervention: 174.1 (4.3), UC: 193.1 (7.3) (P=.011)
Aubert RE et al.(73)	1998	USA	Primary care clinics in a group-model HMO	17 patients with Type 1 diabetes & 121 patients with Type 2 diabetes	12 months	Nurse case management (NCM) or Usual care (UC)	NCM for blood glucose monitoring; medication adjustments; meal planning and exercise. Telephone follow-up. Management in conjunction with a family physician and an endo-crinologist.	Primary: HbA1c Secondary: Mean fasting blood glucose, Blood pressure, Weight, Lipid profile Health related quality of life	NCM: 71 UC: 67	Median: NCM arm 53 UC arm 54	Baseline Median HbA1c: NCM arm 8.8, UC arm 8.4. Mean Change HbA1c: NCM arm -1.7, UC arm -0.6 (P<.001) Mean Change FBG: NCM arm -48.3, UC arm -14.5 (P=.003) Mean Change diastolic BP: NCM arm -0.83, UC arm 1.5 (P>.2)
Krein SL(74)	2004	USA	General medicine	Subjects with	18 months	Nurse case management	NCM scheduled follow-up according	Primary: HbA1c	NCM: 123 Control	Mean: NCM: 61 (10) UC:	Mean Baseline HbA1c: NCM 9.3

Author	Pub. Year	Country	Setting	Patient Pop.	Duration of Study	Study Arms	Intervention	Outcomes	# of patients	Age of subjects	Clinical Results
			clinics from 2 Veterans Affairs Medical Centres	poorly con-trolled type 2 diabetes		(NCM) with primary care providers or educational material plus usual care (UC)	to patients' needs. Encouraged self-management, diet and exercise, reminders for screenings/ tests; appointment scheduling; medication and dose changes as needed.	Secondary: Low-density lipoprotein (LDL), blood pressure, health status and patient satisfaction questionnaires	(UC): 123	61 (11)	(1.5), UC 9.2 (1.4); Mean exit HbA1c (95% CI): NCM 9.3 (8.9-9.7), 9.2 (8.8-9.6); (P=.65) Mean Baseline LDL: NCM 123 (37), UC 123 (38); Mean exit LDL (95% CI): NCM 106 (100-112), 109 (102-116); (P=.50) Mean Baseline SBP: NCM 145 (21), UC 145 (20); Mean exit SBP (95% CI): NCM 146 (142-151), 144 (140-149); (P=.56) Mean Baseline SBP: NCM 86 (12), UC 86 (11); Mean exit SBP (95% CI): NCM 83 (81-86), 83 (81-85); (P=.70)
Polonsky WH et al.(75)	2003	USA	Tripler Army Medical Centre in Hawaii	Patients with type 1 and 2 diabetes with a HbA1c > 8.5% within previous 3 months	6 months	Diabetes Outpatient Intensive Treatment (DOIT) + nurse case manager (NCM) follow-up vs. Diabetes education pamphlet mailings (EDUPCST) + usual care	3.5 day group education and skills training with medical management and regular follow-up with a NCM. Individualized half day evaluation with physician, NCM, dietician and exercise physiologist.	Primary Outcome: HbA1c Diabetes self-care behaviour:	DOIT: 89 EDUPOST: 78	Mean (SD) DOIT: 48.8 (15.2) EDUPOST: 53.4 (15.9)	Baseline HbA1c: DOIT 10.2 (1.7), at 6 months: 7.9 Baseline EDUPOST 10.6 (1.9) , at 6 months: 8.7
Kim H-S et al.(76)	2003	South Korea	Out-patient depart-ment of a tertiary care university teaching hospital	Non-obese patients with type 2 diabetes	12 weeks	Nurse coordinated intervention (NCI) or control	Diabetes care booklet and daily log Telephone counselling re: maintaining blood glucose levels; diet exercise, medication adjustment, Recommendation by registered	Primary: HbA1c Secondary: Patient adherence.	Enrolled: NCI arm: 25 Control arm: 25 Completed: NCI arm: 20Control arm: 16	Mean (SD): NCI arm 59.7 (7.3); Control arm 60.9 (5.8)	Mean (SD) HbA1c Baseline: NCI arm 8.8 (1.2), Control arm 8.2 (0.8); Follow-up HbA1c: NCI arm 7.6 (1.0); Control arm 8.8 (0.9) (P=.252)

Author	Pub. Year	Country	Setting	Patient Pop.	Duration of Study	Study Arms	Intervention	Outcomes	# of patients	Age of subjects	Clinical Results
							dietician regarding daily caloric intake (mailed to subjects).				
Kim H-S et al.(77)	2005	South Korea	Out-patient depart-ment of a tertiary care university teaching hospital	Non-obese patients with type 2 diabetes	12 weeks	Nurse coordinated intervention (NCI) or control	Diabetes care booklet and daily log Telephone counselling re: maintaining blood glucose levels; diet exercise, medication adjustment, Recommendation by registered dietician regarding daily caloric intake (mailed to subjects).	Primary: HbA1c Secondary: Fasting plasma glucose, 2-hour postprandial glucose, triglycerides, high-density lipoprotein cholesterol, patient satisfaction with care.	NCI arm: 15 Control arm: 10	Mean (SD): NCI arm 61.0 (6.1) Control arm 60.4 (6.4)	Mean (SD) HbA1c Baseline: NCI arm 8.9 (1.3), Control arm 8.2 (0.9) Follow-up HbA1c: NCI arm 7.7 (1.1); Control arm 8.7 (0.7) (P=.004) Follow-up FBG NCI arm 145.9 (37.2); Control arm 161.0 (45.9) (P=.766) Follow-up HDL: NCI arm 48.8 (14.6); Control arm 50.9 (17.4) (P=.822)
Litaker D et al.(78)	2003	USA	General Internal medicine Depart-ment at a tertiary care teaching hospital	Patients with mild to moderate hyper-tension and non-insulin dependent diabetes mellitus	12 months	Nurse Practitioner+ Primary care physician (NP-MD) or Usual primary care physician care	Use of clinical practice algorithms, patient education and regular monitoring and feedback delivered primarily by the NP, discussion with MD when necessary.	HbA1c, HDL and systolic and diastolic BP. Health related quality of life measures: Patient education topics.	NP-MD: 79 MD only: 78	NP-MD: 60.5 (8.5) MD only: 60.6 (9.6)	Baseline HbA1c: MD-NP 8.4 (1.4), MD only 8.5 (1.6); HbA1c Change: MD-NP -0.63 (1.5), MD only -0.15 (1.0) HDL Change: MD-NP 3.0 (7.2), MD only 0.4 (6.6)
Piette JD et al(79).	2000	USA	Two general medicine clinics of a County health care system	Patients with a diagnosis of diabetes upon chart review or receiving a diabetic agent.	12 months	Automated telephone intervention with interactive response from patients with nurse telephone follow-up in response to reports generated by the automated system vs. usual care	Structured automated telephone calls to determine patients' health status. Report from telephone calls determined urgency of the problems and prioritize nurse contacts.	Self-care: glucose self monitoring, foot inspection, weight monitoring, medication adherence. Glycemic control; Hyperglycemia, hypoglycemic	Telephone intervention: 124 Usual care: 124	Mean (SD) Telephone: 56 (10) Usual Care 53 (10)	Unadjusted: Baseline HbA1c: Telephone: 8.8 (1.8), Usual care: 8.6 (1.8), 12 months Telephone: 8.2 (1.9), Usual care: 8.3 (1.9) (P=.8); Unadjusted: Serum Glucose 12 months Telephone: 181 (68), Usual care: 220 (110) (P=.009);

Author	Pub. Year	Country	Setting	Patient Pop.	Duration of Study	Study Arms	Intervention	Outcomes	# of patients	Age of subjects	Clinical Results
								a, and vascular symptoms			
Piette JD et al.(80)	2001	USA	Three general medicine clinics and one diabetes specialty clinic at a university-affiliated VA system.	Patients with a diagnosis of diabetes upon chart review or receiving a diabetic agent.	12 months	Automated telephone calls with interactive response from patients with nurse telephone follow-up in response to reports generated by the automated system vs. usual care	Structured automated telephone calls to determine patients' health status. Report from telephone calls to prioritize nurse contacts.	Glucose self monitoring, foot inspection, weight monitoring, medication adherence. Glycemic control; Hyperglycemia, hypoglycemia, and vascular symptoms	Telephone intervention: 132 Usual care: 140	Mean (SD) Telephone: 60 (10) Usual Care 61 (10)	Unadjusted: Baseline HbA1c: Telephone: 8.2 (1.7), Usual care: 8.1 (1.7), (P=.5); 12 months Telephone: 8.1 (0.1), Usual care: 8.2 (0.1) (P=.3); Adjusted Serum Glucose 12 months Telephone: 180 (9), Usual care: 172 (10) (P=0.6)
Taylor KI et al.(81)	2005	Canada	Family Practice Clinic	Patients with type 2 diabetes	4 months	Clinical nurse specialist (CNS) vs. Usual care (UC)	Visits from CNS & 1 visit from dietician and exercise specialist. CNS used Supportive Care Model to assess: knowledge & behaviour. Dietitian assessed dietary needs. All visits discussed with physician.	Fasting blood sugar; HbA1c; Blood pressure; Lipid profile; & Quality of Life	CNS: 20 UC: 19	Mean CNS: 67 UC: 58	Baseline HbA1c: CNS: 7.69, UC 7.69; 4 months follow-up HbA1c: CNS 7.40, UC: 8.41 Baseline DBP: CNS: 79, UC 70; 4 months follow-up HbA1c: CNS 74, UC: 75 (P<.05)
Sadur CN et al.(82)	1999	USA	HMO - Kaiser Permanente	Patients aged 16-75 years with HbA1c > 8.5% or no test in the past year.	6 months	Diabetes Cooperative Care Clinic (DCCC) clustered group or Usual care with the primary physician	Multidisciplinary, diabetes nurse educator (DNE) - led team. Monthly 2-hour cluster visits of 10-18 patients. DNE reviewed questionnaires and made referrals. Follow-up phone calls by DNE as needed	Outcomes: HbA1c; Diabetes self-care behaviour; inpatient and outpatient resource utilization	DCCC: 97 UC: 88 Follow-up values available: DCCC: 82 UC: 74	Mean (SD) DCCC: 55.7 (9.1) UC: 56.4 (9.1)	Baseline HbA1c: DCCC 9.7 (1.8), UC 9.6 (1.5) (P=.73) Baseline values for those with follow-up data Baseline HbA1c: DCCC 9.48, UC 9.55 HbA1c at 6 months: DCCC: 8.18, UC: 9.33 (P<.0001)
Taylor CB et al.(83)	2003	USA	HMO - Kaiser Permanente	Patients with a HbA1c > 10 % and	1 year	Nurse-care management system (NCMS) or	Initial assessment by NCM to develop a self-care plan. 4 group classes	Outcomes: HbA1c, LDL, HDL cholesterol,	NCMS: 84 PCP: 85	Mean (SD) NCMS: 54.8 (11.4) PCP: 55.5	Mean (SD) HbA1c Baseline: NCMS arm 9.5 (0.3), PCP 9.5 (0.3)

Author	Pub. Year	Country	Setting	Patient Pop.	Duration of Study	Study Arms	Intervention	Outcomes	# of patients	Age of subjects	Clinical Results
				an ICD-9 diagnosis of diabetes and one of: hyper-tension, dys-lipidemia, or cardio-vascular disease.		Usual care with primary care physician (PCP)	following a workbook created for the program. Follow-up telephone calls by NCM. Use of treatment algorithms by NCM to titrate medication.	triglycerides, glucose, urinalysis, SBP and DBP.		(8.9)	Change HbA1c: NCMS arm -1.14; PCP -0.35 (P=.01) Mean (SD) Total Cholesterol Baseline: NCMS arm 210.4 (6.0), PCP 224.1 (6.7) Change Total Cholesterol: NCMS arm -20.6; PCP -11.5 (P=.01) Mean (SD) LDL Cholesterol Baseline: NCMS arm 124.1 (5.2), PCP 123.9 (4.7) Change Total Cholesterol: NCMS arm -19.4; PCP -6.5 (P=.02)

Appendix 6. Electronic Medical Record Diabetes Tracker Display

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                                                                    Page  1
(99999998) CLINIC PATIENT            AltID-                      LV *not found*
APT 243 83 WILLOW AVE                Female (51) 25Nov49      Home:(705)759-1234
SAULT STE MARIE ON  P6B 1Y5      Ins: ON NA                   Work:(   )    -
```

```
 303 - RESEARCH STUDENTS
LAST REVISED [       ]   PROVIDER ID[998]
             DATE DONE   DATE DUE   LAST VALUE
WT/BMI    *  [       ]  [       ]  [     ]
BP        *** [       ]  [       ]  [   ]/[   ]
HbA1C     *** [       ]  [       ]  [    ]
EYE EX.   *  [       ]  [       ] :
LIPIDS    *  [       ]  [       ] TC[    ] TG[    ] HDL[    ] LDL[    ]
FEET      *** [       ]  [       ] :
ALB.URIA  *  [       ]  [       ] :
SMOKER       [       ]  [       ] Y/N[  ]:
FLU SHOT  *  [       ]  [       ]

BG MONITOR   :Y/N[ ]   [   ]0-7   [   ]8-21   [    ]>21   PER WEEK
THERAPY      :
```

Appendix 7. Abstraction form for risk factors: CHIC Diabetes Program

PATIENT DEMOGRAPHIC INFORMATION

Date of Birth: _____ / _____ / _____
dd mm yy

Gender: ☐ Female ☐ Male

Ethnic Group
☐ White / Caucasian
☐ Chinese, Japanese, Korean, Filipino
☐ Black
☐ South Asian, South East Asian
☐ Latin America
☐ Arab, West Asian
☐ Native, Aboriginal
Other, specify _____

CHIC STUDY DATA

Study ID # _____
Date enrolled in CHIC Study _____ / _____ / _____
dd mm yy

Patient deceased during the course of study	☐ ☐	Yes No

↳ If yes, date _____ / _____ / _____, and cause _____
dd mm yy

DIABETES MEDICAL HISTORY INFORMATION

Age at diabetes diagnosis: _____
↳ If not available, approximate years since diagnosis at CHIC study enrollment _____

Smoking status at diabetes diagnosis*	☐ ☐ ☐	Previous smoker Current smoker Non-smoker

Body mass index at diabetes diagnosis*

BMI =	_____	Kg/m^2	or	Height (e.g..1.8)	_____	Meters
				Weight (e.g., 90)	_____	Kg

HbA1c % at diabetes diagnosis* (e.g., 0.07 or 7%)	_____%
Blood pressure at diabetes diagnosis* (e.g., 140/80)	_____ / _____

Total cholesterol	_____ mmol/L
HDL cholesterol	_____ mmol/L

Atrial fibrillation at diabetes diagnosis*	☐ ☐	Yes No
Peripheral vascular disease at diabetes diagnosis*	☐ ☐	Yes No

* At time of diagnosis or closest time point where this information is available

HISTORY OF OTHER MEDICAL CONDITIONS

At the time of enrolment into the CHIC study (or as close as possible to that date), did the patient have a history of the following conditions:

CONDITION:			If yes, approximate number of years with condition
Atrial Fibrillation	☐	Yes	_____ years
	☐	No	
Ischemic Heart Disease	☐	Yes	_____ years
(ICD-9 >=411 & <411=414.9)	☐	No	
Peripheral Vascular Disease	☐	Yes	_____ years
(ICD-9 997.2 or 997.6 or 250.6 or 440.2	☐	No	
Myocardial Infarction	☐	Yes	_____ years
(ICD-9 >=410 & <=414.9	☐	No	
or >=428 & <=428.9			
or >=798 & <=798.9)			
Stroke	☐	Yes	_____ years
(ICD-9 >=430 & <=438.9 or 436)	☐	No	
Congestive Heart Failure	☐	Yes	_____ years
(ICD-9 >=428 & <=428.9)	☐	No	
Amputation of digit or limb	☐	Yes	_____ years
(ICD-9 >=5.8946 & <=5.848 or 250.6)	☐	No	
Blindness in one or more eyes	☐	Yes	_____ years
(ICD-9 369 – 369.9)	☐	No	
Renal Failure	☐	Yes	_____ years
(ICD-9 250.3 & 525 to 586 & 580 – 593.9)	☐	No	

Appendix 8. Effectiveness data from CHIC

STUDY ENTRY AND EXIT STATUS

At the time of enrolment into the CHIC study and exit from the study (or as close as possible to these dates), what was the patient's status for the following:

	ENTRY:	EXIT:
CHIC study entry and Exit dates:	_____ / _____ / _____ dd mm yy	_____ / _____ / _____ dd mm yy
HbA1C (e.g., 0.07 OR 7%)	_____%	_____%
Blood pressure (e.g., 140/80)	_____ / _____	_____ / _____
Total cholesterol	_____ mmol/L	_____ mmol/L
HDL cholesterol	_____ mmol/L	_____ mmol/L
Smoking status	☐ Yes ☐ No	☐ Yes ☐ No

Please provide up to six clinical values for the 2 years prior to the study enrolment:

	HbA1c (e.g., 7%)		**Blood Pressure (e.g., 140 / 80)**		**Cholesterol (mmol/L)**	
	1998 values	1999 values	1998 values	1999 values	1998 values Total : HDL	1999 values Total : HDL
1)	_____%	_____%	_____/_____	_____/_____	_____ : _____	_____ : _____
2)	_____%	_____%	_____/_____	_____/_____	_____ : _____	_____ : _____
3)	_____%	_____%	_____/_____	_____/_____	_____ : _____	_____ : _____
4)	_____%	_____%	_____/_____	_____/_____	_____ : _____	_____ : _____
5)	_____%	_____%	_____/_____	_____/_____	_____ : _____	_____ : _____
6)	_____%	_____%	_____/_____	_____/_____	_____ : _____	_____ : _____


path