DIABETES EDUCATION CENTRE ATTENDANCE AND THE EFFECT ON MEDICATION UTILIZATION IN THE ELDERLY IN ONTARIO

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ABSTRACT

Diabetes education centres (DECs) provide patients with self-management skills to control diabetes and manage complications. To evaluate the effect of DEC attendance on prescriptions for diabetes treatments, prescriptions for cardiovascular risk reduction, and visits for retinopathy screening, a population based cohort study of residents of Ontario, Canada with diagnosed diabetes aged ≥65 years was performed using administrative databases. DEC attendance was identified using a registry of visits to all DECs in the province in 2006. Demographic and clinical confounders and pre-index utilization were used to adjust the logistic regression and also to construct a propensity score matched cohort. Patients attending DECs had greater filling of prescriptions for statins than non-attendees in both analyses. DEC attendance was also associated with greater drug dispensation of glucose lowering medications, glucose monitoring strips and ACE inhibitors/ARBs, and visits to ophthalmology/optometry in both analyses. Diabetes self-management education at DECs is associated with better quality of care in the elderly in Ontario.

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List of Abbreviations

A1C	glycated hemoglobin
ABCD	Appropriate Blood Pressure Control in Diabetes
ACCORD	Action to Control Cardiovascular Risk in Diabetes Study
ACE	angiotensin converting enzyme
ADVANCE	Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation
ARB	angiotensin II receptor blocker
ASCOT-LLA	Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm
BMI	body mass index
CARDS	Collaborative Atorvastatin Diabetes Study
CI	confidence interval
CIHI	Canadian Institute for Health Information
DCCT	Diabetes Control and Complications Trial
DEC	Diabetes Education Centre
DESMOND	Diabetes Education and Self-management for Ongoing and Newly Diagnosed type 2
d.f.	degrees of freedom
DIN	Drug Identification Number
DSME	diabetes self-management education
EDIC	Epidemiology of Diabetes Interventions and Complications study

HDL	high density lipoprotein
HOT	Hypertension Optimal Treatment
HPS	Heart Protection Study
HR	hazard ratio
kg	kilogram
LDL	low density lipoprotein
LHIN	Local Health Integration Network
MI	myocardial infraction
mm Hg	millimeters of mercury
mmol/L	millimole/litre
NHANES	National Health and Nutrition Examination Survey
NPHS	National Population Health Survey
ODB	Ontario drug benefits program database
ODD	Ontario Diabetes Database
OHIP	Ontario Health Insurance Plan
OR	odds ratio
QALY	quality adjusted life year
RCT	Randomized control trial
RPDB	Registered Persons Database
SMBG	self-monitoring of blood glucose
TNT	Treating to New Targets
UKPDS	United Kingdom Prospective Diabetes Study
VADT	Veteran's Affairs Diabetes Trial

Chapter 1: Introduction

1.1 Diabetes Burden and Prevalence

Diabetes mellitus is a metabolic disease of hyperglycemia from defective insulin secretion, or action or both (Goldenberg *et al*., 2013). The long-term effects of this hyperglycemia are associated with the damage, dysfunction and failure of many organs including the kidneys, eyes, nerves, heart and blood vessels. Diabetes is classified into various types, the most common of which are type 1 and type 2. Type 1 diabetes is a result of pancreatic beta cell destruction from autoimmune or idiopathic process, leading to a lack of insulin secretion and susceptibility to ketoacidosis. Type 2 diabetes is mainly a problem of insulin resistance with relative insulin deficiency. Type 2 diabetes is more common than type 1 diabetes and comprises the majority of the diabetes population greater than 65 years of age.

The prevalence of diabetes is increasing in Ontario, with the age-adjusted and sex-adjusted diabetes prevalence increasing by 69%, from 5.2% in 1995 to 8.8% in 2005 (Lipscombe *et al*., 2007). The prevalence of diabetes in adults greater than 50 years of age increased from 10.6% in 1995 to 17.1% in 2005, a prevalence rate increase of 62.8%. The prevalence of diabetes is 20% in women and 25% in men in the over 65 population in Ontario (Creatore *et al*., 2010). The cost of diabetes in Ontario is estimated at $4.9 billion in 2010 and expected to increase to over $6.9 billion by 2020 (Canadian Diabetes Association, 2009). As the prevalence and cost of diabetes increases in Ontario, the need to provide quality care through interventions such as diabetes self-management education (DSME) also increases.

1.2 Diabetes Education

Management of diabetes, as in many chronic diseases such as asthma and rheumatoid arthritis, is dependent on the responsibility patients take in their own care (Newman *et al*., 2004). Patient involvement in the management of their care is termed self-management and includes the patients' ability to manage the symptoms, treatment, physical and psychosocial effects and lifestyle changes essential to living with a chronic condition. For self-management to be effective it must include not only the ability to monitor ones condition and follow the treatment guidelines but to institute the psychological and social changes of living with a chronic illness to manage the effect on their lives.

The chronic disease self-management program, a community based patient self-management education course involves three principal assumptions: different chronic diseases have similar self-management problems and disease-related responsibilities; patients can take responsibility for the daily management of their disease; and patients practicing self-management will have improved health status (Lorig *et al*., 1999). This model has been shown to increase healthful behaviors and maintain or improve health status and decrease rates of hospitalization in a heterogeneous group of diseases.

Diabetes education provides patients with self-management skills necessary for management of diabetes such as diet and lifestyle changes, medication compliance, and self-monitoring of blood glucose (SMBG) (Ismail *et al*., 2004). The self-care responsibilities for optimum control include modification of lifestyle with diet, exercise, and weight loss, SMBG, foot care, and the administration of oral medications and insulin injections. The objectives of DSME are to increase individual's involvement, confidence

and motivation for control of their diabetes. Diabetes education for self-management is a fundamental component of diabetes care and most beneficial when working in conjunction with the healthcare team (Jones *et al.*, 2013). It can be individualized to patient's metabolic stability, treatment recommendations, readiness for change, learning style, ability, resources and motivation. It incorporates the physical, psychological and social management of living with a chronic illness. It uses didactic and non-didactic education sessions along with social, behavioral and psychological interventions.

1.2.1 Meta-analyses of diabetes education

Several trials have been published examining the effect of DSME on clinical outcomes including glycemic control, body weight, blood pressure, lipids, and requirement for blood glucose lowering medications (Norris *et al*., 2001). As most trials use glycemic control as a primary outcome, this outcome of diabetes education has been examined in meta-analyses.

A meta-analysis of 21 randomized control trials (RCTs) published between 1990 and 2000 examined 28 diabetes educational interventions on glycemic control (Ellis *et al*., 2004). The trials included a total of 2439 participants with the trial size ranging from 23 to 320. They included a heterogeneous group of interventions including didactic teaching, dictated goal setting, goal setting negotiated teaching method, situation problem solving, cognitive reframing interventions and other techniques with some studies incorporating more than one teaching method. The content included various combinations of information on diet, exercise, SMBG, basic diabetes knowledge, medication adherence, and psychosocial topics. The duration and number of interventions ranged from 1 month

to 1 year and 1 to 36 visits. The time period to the first post intervention glycated hemoglobin (A1C) ranged from 3 to 15 months with a net decrease in A1C of -0.320% (95% confidence interval (CI) -0.571%, -0.069%) using the fixed effects meta-analysis (test for heterogeneity Q=14, degrees of freedom (d.f.)=19, p=0.78). The net A1C decrease of trials with a 3 and 12 month follow up were not significant, but those with a 6 month follow up had a significant net A1C decrease of -0.486% (95% CI -0.923%, -0.049%). There was also a significant improvement in A1C in the control group from baseline at -0.66% (95% CI -1.054, -0.265) suggesting beyond standard of care some "control groups" also received education and increased visits.

The random effects meta-analysis of glycemic change from baseline showed a drop in A1C of -1.136% (95% CI -1.481% to -0.790%) at the end of time period 1 (Q= 132, d.f. 27, p<0.001). The change was also statistically significant at the end of 3, 6 and 12 months with change in baseline A1C -1.238% (95% CI -1.665% to -0.811%), -0.892% (95% CI -1.428% to -0.356%) and -1.544% (95% CI -2.26% to -0.828%) respectively. Face to face interventions, using a cognitive reframing teaching model or that included content on exercise had a larger effect on decrease in A1C.

A meta-analysis also including earlier studies published between 1980 and 1999 involving health education in diabetes mellitus with glycemic control as a primary outcome incorporated 31 studies containing a total of 4263 patients (Norris *et al.*, 2002). At the end of the intervention the A1C was decreased by 0.76% (95% CI 0.34 – 1.18%) more in the intervention group compared to the control group. At 1-3 months of follow up the A1C was a 0.26% (95% CI 0.21-0.73%) less in the intervention group than the control group and 0.26% (95% CI 0.05-0.48%) less in the intervention group than the control

group at >4 months of follow up. The meta-regression using the change in A1C as the dependent variable showed only total contact time was significant. Each additional hour of DSME reduced A1C by 0.04% (95% CI 0.01%-0.08%).

A more recent meta-analysis of DSME by Minet *et al.,* (2010) included 47 studies published up until 2007, with its earliest included study published in 1988, involving a total of 7677 participants. Eighteen studies used behavioral psychosocial techniques which included cognitive, behavioral and motivational approaches or psychology centered counseling in the intervention and 29 studies used educational techniques which used a didactic-oriented intervention focused on knowledge acquisition. Studies included individual and group sessions. The pooled mean difference in A1C between patients assigned to self-care management intervention was 0.36% (95% CI 0.21-0.51) compared to the control group by a random-effects model. The chi-squared for heterogeneity was significant ($p<0.001$). The pooled estimate with a fixed-effects model was similar at 0.30% (95% CI 0.237-0.367). The factors which may influence the effect size of A1C change were studied by meta-regressions. The univariate meta-regression found a greater reduction in A1C in studies with a follow up period ≤ 12 months (effect size 0.49%, $p=0.017$). Those studies with a sample size ≤ 99 had a greater reduction in A1C (effect size 0.42%, $p=0.007$) compared to studies with a sample size >99. The difference in A1C reduction in studies using education techniques compared to behavioural psychosocial techniques and length of intervention were not significant.

These meta-analyses showed a decrease in A1C with diabetes education intervention. However, the degree of decrease varied between the meta-analyses and at different time points within them. Part of this difference may be due to the different time

periods over which the results were included or a difference in the regression models used. Ellis *et al*., (2004) found the effect on A1C to be related to face to face interventions, using a cognitive reframing teaching model or that included content on exercise while Norris *et al.,* (2002) found the effect on A1C to be related to only the total contact time and Minet *et al*., (2010) found the effect on A1C to be related to shorter follow up period after the intervention and small sample size.

1.2.2 Individual diabetes education

Individual diabetes education was examined in a meta-analysis by Duke *et al*., (2009) which included RCTs and controlled clinical trials that had at least a 6 month follow up period published until 2007. Individual education was compared to usual care in 7 studies. The 3 studies that assessed A1C at 6-9 months, included 295 participants, showed a trend toward decrease in A1C but this did not reach significance. The 4 studies involving 632 patients that examined A1C at 12 to 18 months found no significant change in glycemic control. There was a significant benefit to individual education on glycemic control in a sub analysis of 3 studies involving participants with a mean baseline A1C of >8% with a decrease of -0.3% (95% CI -0.5 to -0.1%, p=0.007). The 2 studies that compared individual education to group education found no significant difference in A1C at 12 to 18 months. There was no significant difference in body mass index (BMI), and blood pressure between the care types. In this meta-analysis individual care is as effective as group care and usual care for effect on A1C.

1.2.3 Group based diabetes education

The effect of group-based diabetes education on clinical and lifestyle outcomes has been assessed in a meta-analysis by Deakin *et al.* (2005). It included 11 RCTs and control clinical trials of 1532 participants of group education with groups of at least 6 participants compared to routine care, waiting list control or no intervention with follow up periods of at least 6 months. The meta-analysis of 3 studies with low heterogeneity (I^2= 36.7%) shows group based diabetes education reduced A1C at 4 to 6 months by 1.4% (95% CI 0.8-1.9%, p<0.00001) compared to the control groups. This decrease was also seen at 12 to 14 months with a reduction of 0.8% (95% CI 0.7-1.0%; p<0.00001) in the 7 studies with low heterogeneity (I^2=18%) and at 2 years with a reduction of 1.0% (95% CI 0.5 to 1.4%, p<0.0001) in the 2 studies that examined it (I^2=0%). Due to heterogeneity between studies, fasting blood glucose results could only be combined between 4 studies at 1 year with a reduction of 1.2 mmol/L (95% CI 0.7-1.6, p<0.0001) in favour of group education. Group education had a positive effect on body weight but no effect BMI at 12-14 months in 4 studies with a 1.6 kg (95% CI 0.3-3.0, p=0.02) weight loss in those who received group education. There was a reduction in systolic blood pressure at 4-6 months (5 mm Hg, 95% CI 1-10, p=0.01) but the difference was not significant at 12 months. No difference in lipid profiles was found between groups at any time point. There was a reduction in the need for diabetes medications in those receiving group education with an odds ratio (OR) of 11.8 (95% CI 5.5-26.9, p<0.00001). This meta-analysis shows positive effects of group education compared to usual care on glycemic control, body weight, blood pressure and use of diabetes medications.

A recent meta-analysis by Steinsbekk *et al*. (2012) examined group based DSME compared to routine treatment. It included 21 RCTs from 1988-2007 in 26 publications with a total of 2833 participants. A1C was reduced by – 0.44% (95% CI -0.69 to -0.19%, p= 0.0006, I^2 =56%, 13 studies) at 6 months with group based DSME. At 12 months A1C was reduced by -0.46% (95% CI -0.74 to -0.18%, p=0.001, I^2= 65%, 11 studies). However, when 2 studies were removed due to the outlying results contributing to the high heterogeneity the 9 remaining studies showed a reduction in A1C of -0.50% (95% CI -0.73 to -0. 27%, p<0.0001, I^2=33%). In the 3 studies that followed patients to 2 years there was a -0.87% (95% CI -1.25 to -0.49%, p<0.0001, I^2=0) reduction in A1C. Sub group analysis suggested that group DSME delivered by a single educator, over more than 12 hours in less than 10 months in 6 to 10 sessions gave the best improvement in glycemic control.

Group based diabetes education was found to reduce A1C in these meta-analyses with positive effects also seen on body weight, blood pressure and use of diabetes medications. Steinsbekk *et al*. (2012) found that group DSME delivered by a single educator, over more than 12 hours in less than 10 months in 6 to 10 sessions, gave the best improvement in glycemic control.

1.2.4 Effect of diabetes education on cardiovascular risk factors

The Steinbekk *et al*. (2012) meta-analysis also examined various lifestyle outcomes and cardiac risk factors. There was a significant improvement in diabetes knowledge and self-management skills with group DSME but the heterogeneity was high. Self-efficacy and empowerment was significantly increased with a standard mean

difference of 0.28 (95% CI 0.06 to 0.50, p=0.012, I^2=0). Treatment satisfaction was increased at 6 and 12 months with a standard difference in the mean of 0.65 (95% CI 0.44 to 0.85, p<0.0001, I^2=0, 2 studies) and 0.39 (95% CI 0.21 to 0.57, p<0.0001, I^2=0.0, 3 studies). However, there was no difference in quality of life. Weight was significantly improved at 12 months but not at 6 months. There was no significant difference in mortality, BMI, blood pressure and lipid profile.

A systematic review of diabetes education trials published between 1980 and 1999 found several studies that examined cardiovascular risk factors (Norris *et al.,* 2001). Thirteen studies had a positive effect on weight loss, while many did not. The studies with a positive effect generally involved regular contacts or reinforcement sessions or a short follow up period with those studies of ≥6 months follow up having no significant difference between groups. Some studies found an improvement in total cholesterol, low density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol with self-management training where others found an initial positive result but no significant difference at the final follow up. The individualized and repetitive interventions were more likely to improve lipid levels where as didactic interventions did not improve lipid profiles.

1.2.5 Recent trials of diabetes education

Some more recent studies on DSME have been published that were not included in the earlier meta-analysis and systematic reviews. They include DESMOND (Diabetes Education and Self-management for Ongoing and Newly Diagnosed type 2) from the United Kingdom (Davies *et al*., 2008) and Rethink Organization to iMprove Education

and Outcomes (ROMEO) from Italy (Trento *et al*., 2010) as well as studies from Germany, the Netherlands and Malaysia. These studies instituted a variety of DSME interventions as outlined and examined the effect on glycemic control as well as cardiovascular risk factors.

DESMOND, a multicentre cluster RCT of 824 patients at 207 general practices in 13 primary care sites in United Kingdom compared a structured education program delivered by 2 healthcare professional educators to usual care (Davies *et al*., 2008). The program consisted of 6 hours delivered in 1 day or 2 half days using a non-didactic approach to present the curriculum focused on lifestyle factors as part of self-management. DESMOND showed no difference in the primary outcome of A1C at 12 months with a non-significant decrease in both group education and usual care. Weight loss was greater in the group education setting at −2.98 kg (95% CI −3.54 to −2.41 kg) compared with −1.86 kg (95% CI −2.44 to −1.28 kg), (p=0.027) at 12 months. There was no difference in cholesterol profile, blood pressure or waist circumference between groups. The OR for using an oral hypoglycaemic agent at month 12 of the trial was 0.79 (Gillett *et al*., 2010). The OR of using a statin at month 12 of the trial was 0.99. The OR of antihypertensive use was 1.18 (95% CI 0.71 to 1.98). Smoking was higher in the control group compared to the intervention group at 12 months with an OR of 3.56 (95% CI 1.11 to 11.45, p=0.033) (Davies *et al*., 2008). The intervention group had a significantly improved understanding of diabetes with a greater improvement in the illness belief scores and lower depression score than the control group. The estimated mean incremental lifetime cost per person receiving the DESMOND intervention was £209 (95% CI −£704 to £1137) (Gillett *et al*., 2010). The incremental gain in quality

adjusted life years (QALY) per person is 0.0392 (95% CI −0.0813-0.1786) with a mean incremental cost per QALY of £5387. Using simulated long term effect there is 66% likelihood that the DESMOND intervention is cost effective.

A RCT of patients with non-insulin dependent type 2 diabetes managed by systemic group education or usual care of individual consultations and education was performed in 112 patients in Italy (Trento *et al.,* 2001) with follow up at two, four (Trento *et al.,* 2002) and five years (Trento *et al.,* 2004). At 2 years the A1C had increased in the control group from 7.4% ± 1.4% to 8.3% ± 1.8% but remained unchanged in the intervention group at 7.4% ± 1.4% to 7.5% ± 1.4% ($p<0.002$). HDL cholesterol was increased in group patients but not control patients. There was no significant difference in fasting blood glucose, total cholesterol, triglycerides, creatinine, albuminuria, body weight, BMI, foot ulcers or diabetic retinopathy between groups. Knowledge of diabetes, health behaviors and quality of life were also significantly improved with group care. At four years, A1C remained stable in the group patients from 7.4% ± 1.4% at baseline to 7.0 ± 1.1% and continued to rise in the individual care patients from 7.4% ± 1.4% at baseline to 8.6% ± 2.1% ($p<0.001$) (Trento *et al.,* 2002). Body weight and BMI decreased and HDL increased in the group patients over 4 years but there was no significant difference in the individual care patients. The knowledge of diabetes, health behaviours and quality of life improved in the group care patients and declined in the individual care group. Diabetes medication use was decreased in the group care patients compared to the individual care patients suggesting improved compliance to lifestyle modification with diabetes education leading to better control of diabetes (Trento *et al*., 2002). At five years follow up A1C in the group patients continued to remain stable at 7.3% ± 1.0% compared

to an increase in control patients to 9.0% ± 1.6% ($p<0.001$) (Trento *et al*., 2004). At five years knowledge of diabetes, problem solving ability, and quality of life continued to improve in the group patients and decrease in the control patients. Body weight but not BMI was decreased from baseline in the group patients at five years. The group patients maintained better long-term glycemic control than the individual care patients suggesting group care may be more effective.

The ROMEO trial is a multicenter trial performed to examine if the results of group care model of diabetes lifestyle intervention from a single center described by Trento *et al.* (2004) was transferable to other clinics (Trento *et al*., 2010). It was a 4 year RCT of group care vs. routine individual care of 815 patients with non-insulin dependent type 2 diabetes performed in 13 diabetes clinics in Italy. At 4 years the group patients had a lower A1C at 7.3% ± 0.9% compared to 8.8% ± 1.2% in the routine care patients ($p<0.001$) and the OR of having an A1C ≤ 7.0% was 29.4 (95% CI 14.2-60.8, $p<0.001$) in favour of group care. Group care subjects also had significantly higher HDL cholesterol, lower fasting glucose, LDL cholesterol, triglycerides, blood pressure, body weight, BMI, and creatinine compared to control subjects. At the end of the study, group care patients were more likely to have reached all treatment targets whereas fewer control patients had an A1C ≤ 7.0% at study end compared to at the initiation and there was no change in the proportion reaching the other treatment targets. Health behaviours, quality of life and diabetes knowledge were significantly improved for group care patients compared to no change in health behaviours and a worsening of quality of life and knowledge seen in control patients. Prescriptions for hypoglycemic, antihypertensive and lipid lowering medications were similar between groups suggesting healthier behaviors with group care.

ROMEO demonstrates that continuing interactive patient-centered education by group care significantly improves outcomes.

A prospective RCT of three education programs for 181 type 2 diabetes patients in Germany compared a didactic-oriented training program, a self-management-oriented program delivered in a group setting and a more individualized self-management program where half the sessions were conducted in an individual setting (Kulzer *et al*., 2007). The didactic program focused on the knowledge, skills and information about the treatment of diabetes in four 90 minute lessons in a group setting in a program which has been previously studied and used since the late 1980's. The self-management program focused on the emotional, cognitive and motivational process of behavior change and was delivered twelve 90 minute lesions in a group setting. The final program had the same content of the second program but was delivered in 6 group sessions and 6 individual sessions. The group based self-management program had a 0.7% fall in A1C that was sustained at 12 months after completion of the intervention ($p=0.013$). There was no change in A1C in the didactic program. The individualized program had a drop in A1C at 3 months but this was not maintained at 12 months. There were also benefits seen for BMI, fasting blood glucose, psychological variables and exercise in the group self-management program.

A RCT of 54 patients in the Netherlands with type 2 diabetes treated with maximum oral agents with an A1C$\geq$7.0% was performed to examine the long term outcome of DSME (Goudswaard *et al*., 2004). Patients were randomly assigned to 6 month education program by diabetes nurse or usual care by their general practitioner with a primary outcome of the proportion of patients with an A1C<7% 1 year after the

end of the intervention. An A1C < 7% was achieved by 60% of the patients in the diabetes education group and by 17% of the patients in the usual care group (OR 6.6; 95% CI 1.8-24.5, p=0.004). The mean A1C in the diabetic education group fell from 8.2% ± 1.1% to 7.2% ± 1.3% and in the usual care group from 8.8% ± 1.5% to 8.4% ± 1.7%. The difference in the mean change in A1C was not statistically significant at 0.2% (95% CI -0.7% to +0.4%) in favor of the diabetes education group when adjusted for baseline values.

A RCT of a 12 week DSME program in Malaysia consisting of two in-person individual education sessions and one telephone follow up was compared to usual care in 164 patients (Tan *et al.*, 2011). At the end of the 12 week intervention there was a significant reduction in total daily calorie intake and increase in activity in the intervention group based on self-reported food diaries and questionnaires. Based on self-reported questionnaires, 91% (95% CI 89-94%) of the intervention group were adherent to prescribed medications (defined as consuming ≥ 90% of prescribed medications in the previous week) compared to 84% (95% CI 82-87%) (p=0.008) of the usual care group at week 12. There was also more SMBG in the intervention group at the end of 12 weeks compared to no change in the control group based on the count of returned glucose test strips and self-monitoring diaries. At 12 weeks the A1C was lower in the intervention group at 8.75% ± 1.75% compared to 9.67% ± 2.01% in the control group (p<0.001). The A1C difference at 12 weeks persisted after adjusting for medication adherence, SMBG frequency and body weight.

These more recent studies of DSME had variable effects on glycemic control and other outcomes. Trento *et al*. (2001, 2002, 2004) had shown improvements in glycemic

control and other outcomes with patient centered group diabetes education that were confirmed in the ROMEO trial (Trento *et al*., 2010). DESMOND, did not find a significant difference in the decrease in A1C between groups (Davies *et al*., 2008). It did find a significant benefit with the structured diabetes education program with weight loss and smoking cessation. The smaller studies did show a significant difference in A1C however one study had only a 12 week follow up. These studies also showed benefit in other outcomes such as BMI and other self-management behaviors. These recent studies together with the meta-analysis suggest a positive effect of DSME on various outcomes.

1.2.6 Methodological issues with diabetes education trials

There are many methodological issues with these trials examining diabetes education (Norris *et al.*, 2001). Descriptive information is frequently lacking in many trials, including details of the study population such as the type of diabetes, as well as details of interventions. The usual care of the control groups in each study varies and is not always defined. The study populations may not be representative of the target population due to selection, performance, and attrition bias (Juni *et al.*, 2001). Selection bias may exist when there are systemic differences in the control and intervention groups at baseline. This possibility may only be excluded with randomization. The generalizability of the results may be limited by provider and patient selection simply due to their willingness to participate in a trial (participation bias). Differences in provider and patient behavior can also result from the Hawthorne effect, i.e. subjects that know they are part of a study behave differently due to this fact alone. These studies were often performed at tertiary care centres or university hospitals, which may differ from

community settings in the types of patients and the care they receive. Some studies limited enrollment to newly diagnosed patients with type 2 diabetes which limits the generalizability to the larger population with diabetes. Performance bias may result from differences in care provided to the control and intervention groups other than the intervention being evaluated. To prevent this there should be no evidence of contamination or co-intervention, including no additional contacts with researcher or providers for the intervention group compared with the control group or compared to routine care. Additional clinical resources, intensity of follow-up, and other factors related to a study can make all trial participants (regardless of randomization arm) different from the real world patients in clinical care. Attrition bias results from different rates of withdrawal from the study between groups. To avoid this, the attrition rates should generally be <20% of the total number and dropouts must resemble completers in baseline characteristics. These numerous factors that make the study population different from the general population of real-world clinical care can threaten the external validity of the studies of DSME.

In studies of diabetes education, the internal validity was threatened by a variety of factors. The assessors were often not blinded and it is impossible to blind the study subjects. There was a lack of information on the process of randomization and allocation concealment. There were high attrition rates in some studies and evidence of co-interventions with some control groups being more frequently than standard of care and receiving some form of education. There was a potential for response-set bias where the intervention group self-reported dietary, exercise and glucose self-monitoring habits that

match the goals of the intervention rather than actual behavior. The instruments used to measure diabetes knowledge, self-care and dietary habits, have not been validated.

The actual DSME intervention also takes many forms, including individual sessions, group sessions, didactic teaching and cognitive behaviour therapy. Many studies included fewer than 100 participants and few studies included a statistical power calculation. While these interventions may be efficacious in selected study populations under the supervision of study investigators, they may not be as effective in the general population where there is a wider variety of clinicians and patients. There is little real world evidence of the effectiveness of diabetes education.

1.3 Ontario Diabetes Education Centres

A survey with linked health care administrative data of 781 patients with diabetes greater than 2 years duration in Ontario in 2003-2004 examined predictors of Diabetes Education Centre (DEC) attendance and quality of care indicators for effectiveness of DSME (Shah *et al.*, 2009). Of the respondents, 30% had attended a DEC in 2002. Predictors of DEC attendance included recently diagnosed diabetes, receiving regular specialist care, receiving regular primary care visits and marital status. A propensity score model derived from demographics, health service utilization, diabetes clinical features, and other medical conditions was used to examine quality of care indicators such as capillary glucose testing, retinal screening examination, acute diabetes complications and continuity of primary care between the attendees and non-attendees. DEC attendees were more likely to receive retinal screening examination in the 2 years following than those who did not attend a DEC. There was no difference in the other quality of care indicators.

Attendance at DECs in Ontario has previously been shown to be associated with more glucose self-monitoring in attendees vs. non-attendees (86.2% vs. 53.5%, adjusted OR 6.45, 95% CI 5.61-7.42, $p < 0.0001$) in a cross-sectional study of a subset of the over 65 population in Ontario (Millar *et al.,* 2010). Anti-hypertensive medications (88.3% vs. 83.0%, adjusted OR 1.30, 95% CI 1.12–1.51, p=0.0006) and lipid-lowering drugs (77.2% vs. 65.6%, adjusted OR 1.68, 95% CI 1.50–1.88, $p <0.0001$) were also used more by the DEC attendees. DEC attendees were also more likely to have an eye examination (adjusted OR 1.13, 95%CI 1.02–1.26, p=0.0229). This study showed an association between DEC attendance and objective evidence of better management of diabetes.

A population based cohort study of all adults with diabetes who attended DECs in Ontario in 2006 examined DEC attendance by those with newly diagnosed diabetes (Cauch-Dudek *et al*., 2013). Only 20.6% of those with newly diagnosed diabetes attended a DEC within 6 months of diagnosis. Patients of older age, lower socioeconomic status and recent immigrants were less likely to attend. Mental health conditions and other medical comorbidities were also associated with not attending DECs suggesting those most in need of DSME are not receiving this resource.

1.4 Diabetes guidelines

Many studies have shown the benefits of glycemic control, antihypertensive medications and cholesterol lowering medications in lowering morbidity and mortality in diabetes. The targets of the Canadian Diabetes Association Guidelines are based on this evidence (Cheng *et al.*, 2013). The recommended glycemic target is an A1C of ≤7.0% to reduce microvascular complications and, in type 1 diabetes, macrovascular complications

(Imran *et al*., 2013). In Canada, males with diabetes greater than 45 years of age and females with diabetes greater than 50 years of age are considered to be at high risk for cardiovascular disease and should be considered for vascular protection (Stone *et al.*, 2013). This includes optimization of blood pressure to the target of <130/80 mmHg which often requires multiple antihypertensive agents, starting with angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) therapy, and lipid-lowering medication, primarily statins, to target an LDL cholesterol of ≤ 2.0 mmol/L. All patients with type 2 diabetes and patients with type 1 diabetes greater than 15 years of age should undergo screening for retinopathy every 1 to 2 years (Boyd *et al*., 2013). The information and recommendations in the guidelines, based on the evidence for glycemic control, lipid and blood pressure management, complication screening and management as outlined below provide a basis for the goals of DSME.

1.5 Benefits of glycemic control

1.5.1 Type 1 diabetes

The Diabetes Control and Complications Trial (DCCT) randomized 1441 patients with type 1 diabetes, to intensive (goal A1C<6.0%) or conventional therapy for a mean of 6.5 years between 1983 and 1993 (DCCT group, 1993). At the end of the study the difference in A1C was 1.7% (7.4% in the intensive-treatment group vs. 9.1% in the conventional-treatment group, p<0.01). The intensive-treatment group had a 76% risk reduction (95% CI 62 to 85%, p<0.001) for the development of retinopathy compared to conventional therapy. With intensive therapy there was also slowed progression of pre-existing retinopathy with a 54% risk reduction (95% CI 39 to 66%, p<0.001). The risk reduction in the development of proliferative or severe non-proliferative retinopathy was

47% (95% CI 14 to 67%, p=0.011). The absolute risk reduction in the development of severe nephropathy was 4.04% in the intensive group. The risk of microalbuminuria was reduced by 39% (95% CI 21 to 52%, p≤0.002) and albuminuria by 54% (95% CI 19 to 74%, p<0.04) in the intensive group. The risk of clinical neuropathy at 5 years was also reduced by 60% (95% CI 38 to 74%, p≤0.002). The absolute risk reduction in the development of clinical neuropathy in the primary prevention group was 7% (p=0.006) with intensive treatment and 9% in the secondary prevention cohort (p<0.001). During DCCT, there were fewer cardiovascular events in the intensive group but the young age of the cohort and small number events did not lead to a statistically significant difference. The DCCT showed that tight glycemic control with an A1C of 7.4% in the intensive treatment group is associated with a reduced risk of neuropathy, nephropathy and retinopathy in type 1 diabetes.

Ninety-three percent (n=1397) of participants were followed until February 1, 2005, during the observational Epidemiology of Diabetes Interventions and Complications (EDIC) study (Nathan *et al*., 2005). At the end of DCCT, the conventional group was advised to follow intensive control and the intensive group went back to regular clinical care. At the end of the EDIC study period there was no difference between groups in A1C, 7.9% in the intensive group and 7.8% in the conventional group. The time to first to cardiovascular event became statistically significant during the follow up observational period, suggesting a lasting benefit of tight control as the 2 groups had no difference in A1C during this period (Nathan *et al*., 2005). The intensive arm had a 42% risk reduction (95% CI 9-63%; p=0.02) compared to the control group at a mean 17 years of follow up, 7 years after the study intervention was completed. The event rates

for the first cardiovascular event were 0.38 and 0.80 per 100 patient-years in the intensive and control group respectively (p=0.007). The risk reduction for first occurrence of nonfatal myocardial infarction (MI), stroke, or death from cardiovascular disease was even greater at 57% (95% CI 12-79%; p=0.02). The effects on microvascular disease were also preserved in follow up (Writing team for DCCT/EDIC Research Group, 2002). EDIC demonstrated that early intensive glycemic control is associated with a reduction in both microvascular and macrovascular disease in patients with type 1 diabetes.

1.5.2 Type 2 Diabetes

The United Kingdom Prospective Diabetes Study (UKPDS) examined intensive glucose control to conventional therapy in newly diagnosed type 2 diabetes (UKPDS 33 and 34, 1998). The participants were followed for an average of 10 years from 1977-1997. The average A1C was 7.0% in the intensive group vs. 7.9% in the control group in the sulfonylurea/insulin study (UKPDS 33, 1998) and A1C 7.4% vs. 8.0% in the metformin study (UKPDS 34, 1998). The relative risk of any diabetes-related end point was 0.88 (95% CI 0.79-0.99, p=0.029) in the intensive treatment group with sulfonylurea and insulin (UKPDS 33, 1998). The relative risk of microvascular disease was 0.75 in the sulfonylurea/insulin arm (95% CI 0.60-0.93, p=0.0099). This was mainly driven by the reduction in the need for retinal photocoagulation and cataract extraction. There was no difference in diabetes related death mortality, all-cause mortality or macrovascular disease. UKPDS showed that tight glycemic control with an A1C of 7% early in diagnosis of type 2 diabetes reduces the risk of microvascular disease.

78% of the participants in UKPDS agreed to enroll in post-trial monitoring and were followed for 10 more years, the predicted 50% mortality rate point (Holman *et al*., 2008). The difference in A1C between groups was lost after the first year following the completion of the study intervention. At 10 years post study, there was a significant decrease in any diabetes related end point in the patients originally in the insulin/sulfonylurea group with a 9% relative risk reduction (p=0.04). Diabetes related death was reduced by 17% (p=0.01), death from any cause by 13% (p=0.007), MI by 15% (p=0.01), and microvascular disease by 24% (p=0.001). In the patients originally in the metformin treated group, the reduction in any diabetes related end point persisted at 10 years post study with a relative risk reduction of 21% (p=0.01). The difference in diabetes related death, MI and all-cause mortality with metformin persisted at 10 years with relative risk reductions of 30% (p=0.01), 33% (p=0.005) and 27% (p=0.002) respectively. The intensive glycemic control early in type 2 diabetes continued to provide benefit in macrovascular and microvascular disease 10 years after cessation of the trial despite a loss of difference in A1C between groups suggesting a legacy effect of tight glucose control (Chalmers *et al*., 2008).

ACCORD (Action to Control Cardiovascular Risk in Diabetes Study) randomized 10,251 patients with a median A1C 8.1% and 10 year duration of type 2 diabetes to intensive glucose control with a target A1C of <6.0% or standard therapy (Gerstein *et al.*, 2008). An A1C of 6.4% was achieved in the intensive group compared to 7.5% in the control group. The primary outcome, a composite end point of nonfatal MI, stroke, or death from cardiovascular disease, had a hazard ratio (HR) of 0.90 (95% CI 0.78-1.04; p=0.16) when the trial was stopped at 3.5 years due to an increase in death in the

intervention group. There was a 22% increase in mortality with a 35% increase in cardiovascular mortality with a HR of 1.22 for all-cause mortality (95% CI 1.01-1.46; p=0.04) and a HR of 1.35 for cardiovascular mortality (95% CI 1.04–1.76; p=0.02) with intensive treatment. Hypoglycemia was significantly higher in the intensive group. Post hoc analysis of episodes of severe hypoglycaemia and differences in the use of drugs including rosiglitazone, weight change, and other factors could not explain the increased mortality with intensive therapy. ACCORD provides evidence that older patients with long standing type 2 diabetes may not benefit from tight glycemic control with an A1C <6%.

ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) randomized 11,140 patients with an 8 year mean duration of diabetes, a mean A1C 7.5%, and 32% had a history of macrovascular disease, to standard glucose control or intensive glucose control using gliclazide MR plus other drugs as required to achieve A1C ≤ 6.5% (Patel *et al*., 2008). During the 5 year study the groups obtained an average A1C 6.5% and 7.3% respectively. The occurrence of combined major macrovascular and microvascular events was reduced by intensive control with a HR of 0.90 (95% CI 0.82 to 0.98; p=0.01). Major microvascular events were also reduced by intensive control with a HR of 0.86 (95% CI 0.77 to 0.97; p=0.01). This was driven by a reduction in the incidence of nephropathy (HR 0.79; 95% CI 0.66 to 0.93; p=0.006). ADVANCE demonstrated that an A1C of 6.5% in patients with type 2 diabetes of 8 years duration is associated with a reduction in nephropathy but did not affect macrovascular disease and other microvascular disease.

Veteran's Affairs Diabetes Trial (VADT) randomized 1791 military veterans with a 11.5 year duration of type 2 diabetes, 40% incidence of a prior cardiovascular event, and a baseline A1C 9.4% to intensive control with an A1C of <6% vs. standard control (Duckworth *et al*., 2009). They achieved an A1C of 6.9% in the intensive group vs. 8.4% in the standard group with a mean follow up of 5.6 years. There was no difference in the primary outcome of major cardiovascular events, in any component of the primary outcome, death from any cause, or microvascular complications.

An A1C of <7% has been shown to reduce microvascular complications of type 1 and type 2 diabetes in multiple trials (DCCT group, 1993; UKPDS 33, 1998; UKPDS 34, 1998; Patel *et al*., 2008). More intensive glucose control has not shown any significant reduction of cardiovascular disease compared to standard glycemic control during the randomized portion of the trials (DCCT group 1993; UKPDS 33, 1998; Gerstein *et al*., 2008; Patel *et al*., 2008; Duckworth *et al*., 2009) despite the association of high A1C with cardiovascular disease. The post-trial follow-up periods of DCCT/EDIC and UKPDS did show a reduction in cardiovascular disease suggesting a legacy effect of early glycemic control (Nathan *et al*., 2005; Holman *et al*., 2008).

1.6 Multifactorial intervention

STENO2 randomized 160 patients with type 2 diabetes and microalbuminuria to intensified, multifactorial intervention or conventional treatment in accordance with national guidelines on risk factors for cardiovascular disease in an open label parallel trial conducted in Denmark from 1993-2001 (Gaede *et al.*, 2003). The intensive treatment consisted of stepwise implementation of behaviour modification and pharmacologic

therapy to target hyperglycemia to A1C <6.5%, hypertension, dyslipidemia, microalbuminuria, smoking cessation and secondary prevention of cardiovascular disease with aspirin. The A1C at the end of the study period was 9.0% ± 1.8% in the conventional group and 7.9% ± 1.2% (p <0.001) in the intensive group with about 15% obtaining the goal A1C <6.5%. The risk of cardiovascular disease was significantly reduced with intensive therapy with a HR of 0.47 (95% CI 0.24 to 0.73, p=0.008). Nephropathy (HR 0.39; 95% CI 0.17 to 0.87), retinopathy (HR 0.42; 95% CI 0.21 to 0.86), and autonomic neuropathy (HR 0.37; 95% CI 0.18 to 0.79) were also reduced in the intensive intervention group.

STENO2 patients were then followed for 5.5 years after the end of the study to a total of 13.3 years follow up (Gaede *et al.*, 2008). By the end of the follow up period there was no difference in A1C between the groups. The risk of death from any cause was decreased with intensive therapy (HR 0.54; 95% CI 0.32 to 0.89; p=0.02). Intensive therapy also lowered the risk of death from cardiovascular causes, cardiovascular events, and end-stage renal disease, and the need for retinal photocoagulation.

STENO2, which achieved an A1C 7.9% as well as targeting multiple risk factors, significantly lowered the risk of cardiovascular disease (Gaede *et al.*, 2003) with the effect preserved in post study follow up (Gaede *et al.*, 2008). Nephropathy, retinopathy and autonomic neuropathy were also reduced in the intensive intervention group (Gaede *et al.*, 2003) with a reduction in progression to end stage renal disease and need for retinal photocoagulation seen in the post study follow-up (Gaede *et al.*, 2008). STENO2 program of behavioural modification and pharmacologic therapy to target a multiple risk factors requires a multidisciplinary approach that would include diabetes education to implement

the required teaching and behaviour modification to achieve outcomes that are not be achieved with glycemic control alone.

1.7 Lipid management in Diabetes

The Heart Protection Study (HPS) diabetes cohort of 5963 subjects showed treatment with 40 mg simvastatin daily resulted in a 27% reduction in cardiovascular events and a 25% reduction in stroke relative to placebo, which was similar to the cohort without diabetes (Collins *et al*., 2003). The Collaborative Atorvastatin Diabetes Study (CARDS) was conducted in people with type 2 diabetes with a mean baseline LDL of 3.1 mmol/L without known vascular disease and at least 1 additional risk factor for cardiovascular disease (Colhoun *et al.,* 2004). Treatment with atorvastatin 10 mg daily to a mean LDL of 2.0 mmol/L reduced the risk of first cardiovascular disease events by 37% and risk of stoke by 48%.

The Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm (ASCOT-LLA) of 10,305 hypertensive patients with no history of coronary heart disease but at least three cardiovascular risk factors were randomly assigned to receive 10 mg atorvastatin or placebo for a mean follow up of 3.3 years (Server *et al*., 2005). The subgroup analysis of 2,532 patients with type 2 diabetes at the time of randomization showed similar benefit of atorvastatin as seen in the entire cohort. The atorvastatin group had 116 (9.2%) major cardiovascular events or procedures compared to 151 (11.9%) events in the placebo group (HR 0.77, 95% CI 0.61– 0.98; p=0.036). The number of events occurring in the diabetes subgroup was small and although there were less coronary events (HR 0.84, 95% CI 0.55–1.29; p=0.14) and strokes (HR0.67, 95% CI

0.41–1.09; p=0.66) in the atorvastatin group, the reductions were not statistically significant.

The Treating to New Targets (TNT) trial included a diabetic subgroup of 1051 subjects with stable coronary artery disease treated with atorvastatin 80 mg or 10 mg daily (Shepherd *et al*., 2006). Subjects treated with atorvastatin 80 mg daily that achieved a group mean LDL of 2.0 mmol/l had 25% fewer major cardiovascular events than those treated with atorvastatin 10 mg daily who achieved a mean LDL of 2.5 mmol/L (p=0.026). Atorvastatin 80 mg also reduced the rates of all cardiovascular and cerebrovascular events compared to atorvastatin 10 mg daily. The diabetes subgroup had an increased event rate for all primary and secondary efficacy outcomes compared to the overall study population. This reinforces the evidence that people with diabetes and coronary artery disease are at high risk of subsequent cardiovascular events.

The evidence from HPS, CARDS, ASCOTT-LLA and TNT show the benefit of statin treatment for LDL cholesterol in patients with diabetes at risk for cardiovascular and cerebrovascular disease. This important risk factor for macrovascular disease is one of the topics addressed in diabetes education.

1.8 Blood Pressure management

UKPDS showed that tight blood pressure control with a mean blood pressure of 144/82 mm Hg over 8.4 years of follow up compared to 154/87 mm Hg in the conventional arm reduced the risk of microvascular disease stroke and deaths related to diabetes (Adler *et al*., 2000). For every 10 mm Hg decrease in mean systolic blood pressure there was a 12% risk reduction in any complication related to diabetes (95% CI

10-14%, p<0.0001), a 15% risk reduction in deaths related to diabetes (95% CI 12-18%, p<0.0001), a 11% risk reduction in MI (95% CI 7-14%, p<0.0001, and a 13% risk reduction in microvascular complications (95% CI 10-16%, p<0.0001).

The Hypertension Optimal Treatment (HOT) Study of 18 790 patients, aged 50-80 years with hypertension and diastolic blood pressure between 100 mm Hg and 115 mm Hg, assigned patients to 3 groups based on target diastolic blood pressure of ≤90 mm Hg, ≤85 mm Hg and ≤80 mm Hg (Hansson *et al*., 1998). In the diabetes subgroup there was a 51% reduction in major cardiovascular events in the ≤80 mm Hg group compared with the ≤90 mm Hg group (p=0.005).

The Appropriate Blood Pressure Control in Diabetes (ABCD) trial of normotensive patients with type 2 diabetes to intensive control of 10 mm Hg below the baseline diastolic blood pressure or moderate control with a diastolic blood pressure of 80-89 mm Hg (Schrier *et al*., 2002). Over a period of 5.3 years the average blood pressure in the intensive group was 128±0.8/75±0.3 mm Hg compared to 137±0.7/81±0.3 mm Hg in the moderate group (p<0.0001). There was no difference in the primary end point of change in creatinine clearance (p=0.43). Fewer patients in the intensive group reached the secondary end points of progression from normoalbuminuria to microalbuminuria (p=0.012) and microalbuminuria to overt albuminuria (p=0.028). The intensive control group also has less progression of diabetic retinopathy (p=0.019) and a lower rate of strokes (p=0.03).

The ADVANCE trial examined the effects of fixed combination of perindopril and indapamide compared to placebo on macrovascular and microvascular outcomes in 11 140 patients with type 2 diabetes mellitus and hypertension (Patel *et al*., 2007). The

primary end point was a composite of major macrovascular and microvascular events. After 4.3 years of follow up the active therapy group had a mean reduction in systolic blood pressure of 5.6 mm Hg and diastolic blood pressure of 2.2 mm Hg compared to the placebo group. The primary endpoint of major macrovascular or microvascular event had a relative risk reduction of 9% (HR 0.91, 95% CI 0.83–1.00, p=0.04). Death from cardiovascular disease was also reduced by 18% (HR 0.82, 95% CI 0.68–0.98, p=0.03) and death from any cause was reduced by 14% (HR 0.86, 95% CI 0.75–0.98, p=0.03).

The ACCORD trial randomized 4733 people with diabetes to systolic BP targets of <120 or <140 mm Hg for a mean follow up of 4.7 years (Cushman *et al*., 2010). The composite primary outcome of nonfatal MI, nonfatal stroke, or death from cardiovascular causes was not significant with an annual rate of 1.87% in the intensive therapy group and 2.09% in the standard therapy group (HR 0.88; 95% CI 0.73 to 1.06; p=0.20). The annual rate of deaths from any cause was also not significant. The annual rate of stroke was decreased with intensive therapy (HR 0.59; 95% CI 0.39 to 0.89; p=0.01).

ACE inhibitors and ARBs have been shown to reduce all-cause mortality, cardiovascular events and cardiovascular mortality in patients with diabetes (HOPE investigators 2000 and Lindholm *et al*., 2002). ACE inhibitors and ARBs have also been shown to reduce progression of kidney disease in patients with diabetic nephropathy (Lewis *et al*., 1993 and Lewis *et al*., 2001). For these reasons they are first line therapy for hypertension in patients with diabetes (Gilbert *et al*., 2013).

1.9 Achieving metabolic targets

Despite the evidence and clinical practice guidelines, many patients do not reach metabolic targets. In the United Sates, the National Health and Nutrition Examination Survey (NHANES) 2009-2010 health survey showed only 55.5% of participants with diabetes achieved the target goal of A1C <7.0% and similar rates of compliance were seen for blood pressure and lipid recommendations (Wong *et al*., 2013). The blood pressure target <130/80 mm Hg was achieved by 52.8% and LDL cholesterol of <2.6 mmol/l was achieved by 54.7% of patients with diabetes. The proportion of the NHANES 2009-2010 population with diabetes who met all three targets was 24.9%. However, there is a trend over time from 1999 to 2010 for an improvement in the proportion of the NHANES population reaching these targets.

A similar situation exists in Canada with a large proportion of the population with diabetes not meeting targets for glycemic, blood pressure and lipid control. In a chart audit of family practices in Ontario the average A1C was 7.9% with 25.7% of patients having an A1C at target of <7% and 31.5% had an A1C above 8.4% (Harris *et al.*, 2003). In a more recent cross sectional chart audit of 243 primary care physicians in Canada the average A1C was 7.3% with 51% of patients achieving a target A1C of <7% (Harris *et al.*, 2005). The proportion of patients with optimal control deteriorated over time from diagnosis from 69% with an A1C <7% in the first 2 years of diagnosis to 38% at target A1C at 15 or more years since diagnosis. In a cross sectional study of primary care physicians in 3 Canadian provinces (Nova Scotia, New Brunswick and Prince Edward Island) found 54% of patients with diabetes were at target for a blood pressure of <130/80 (Putnam *et al.*, 2011). A cross sectional study of centers in Canada and Europe found that

41.6% of patients with diabetes already on a statin were not at target for LDL (Leiter *et al*., 2011).

1.10 Medication utilization

A previous study of the clinical and demographic characteristics of patients receiving oral anti hyperglycaemic medications in Ontario residents aged 66 years and older on March 31, 2008 identified 387 778 people with diabetes out of 1 752 000 Ontarians aged 66 years and older (22.1%) (Gomes *et al*., 2009). The mean duration of diabetes was 9.3 years with a standard deviation of 5.1 years. Most individuals (60.1%) had at least one prescription for an oral hypoglycaemic agent in the previous year.

A retrospective cohort study of newly treated elderly hypertensives in Ontario was performed using health administrative databases (Friedman *et al*., 2010). The diabetes cohort of 41 236 patients aged 66 years or more in Ontario between 1997 and 2005, 76.2% were prescribed an ACE inhibitor (n=31 414), 4.9% an ARB (n=2041), 4.7% a beta blocker (n=1935), 5.7% a calcium channel blocker (n=2351), and 8.5% a diuretic (n=3495).

A population based study of 105 715 people ≥65 years with newly diagnosed diabetes in Ontario between 1994 and 2001 used administrative databases to examine the receipt of antihypertensive and lipid-lowering drugs by patients cared for by different physician specialties (Shah *et al.,* 2006). The unadjusted lipid lowering prescription rates with newly diagnosed diabetes ≥65 years was 23.9% for by those cared for family physicians, 28.6% for those cared for by internists and geriatricians and 36.1% by endocrinologists. Of the types of lipid lowering medications prescribed, statins accounted

for 86.8 to 89.9%. The unadjusted antihypertensive medication prescribing rates were 66.0% for those cared for by family physicians, 75.1% of those cared for by internists and geriatricians and 69.3% of those cared for by endocrinologists. Of these antihypertensive medications, 54.2 to 63.1% were ACE inhibitors or ARBs. This study illustrates the low rates of the use of vascular protection medications and the differences in prescribing among physician specialties.

The administrative databases of Saskatchewan were used to examine the use of anti-platelet agents, statins, and ACE inhibitors by people with type 2 diabetes with and without symptomatic atherosclerosis (Brown *et al.*, 2004). The cohort of 12 106 people with type 2 diabetes had an average age of 64 years, 55% male, with a mean duration of follow up of 5 years. Those patients with type 2 diabetes and coronary artery disease were more likely to receive antiplatelet agents at 37% compared to 15% of type 2 diabetes patients without coronary artery disease ($p < 0.001$). They were also more likely to receive a statin at 29% vs. 15% of patients with type 2 diabetes without coronary artery disease ($p<0.001$) and ACE inhibitors at 60% compared to 43% ($p<0.001$). Patients with cerebrovascular disease and type 2 diabetes were more likely to receive an antiplatelet agent at 46% compared to 20% of patients with type 2 diabetes without cerebrovascular disease ($p<0.001$) and ACE inhibitors at 58% compared to 47% ($p<0.001$) but less likely to receive a statin at 16% compared to 20% of those with type 2 diabetes without cerebrovascular disease ($p=0.001$). Patients with peripheral arterial disease and type 2 diabetes were more likely to receive antiplatelet agents (44%), ACE inhibitors (62%) than those without peripheral arterial disease (23%, $p<0.001$ and 49%, $p<0.001$ respectively)

but not statins (23% vs. 20%, p=0.12). These important cardioprotective medications are significantly underused in these populations.

1.11 Rationale

DECs are an important part of the diabetes care team (Jones *et al.,* 2013) and will continue to be as the burden of diabetes increases in Ontario (Lipscombe *et al*., 2007). DSME is designed to improve patient self-care in many areas including administration of medications to manage blood glucose, lipids and blood pressure, SMBG, and monitoring for complications (Ismail *et al*., 2004). There is evidence from RCTs that diabetes education improves glycemic control, blood glucose monitoring, blood pressure, weight and lipids (Ellis *et al*., 2004; Norris *et al.,* 2001; Norris *et al.,* 2002; Minet *et al.,* 2010). There is little evidence of the effect of diabetes education in a real world setting.

This study is designed to examine the effect of DEC attendance on prescription drug dispensation and retinopathy screening in routine clinical care in Ontario. Patients attending DECs learn about diabetes and its complications, and how best to treat it, and may become motivated to become advocates for their health. They may therefore press their primary care providers to improve quality of care.

By using drug prescription data for patients with diabetes it may be possible to draw an association between DEC attendance and quality of care. Large multi-center RCTs support the use of statins in most patients over 65 years with diabetes to decrease macrovascular risk (Collins *et al*., 2003; Colhoun *et al.,* 2004). Statins were used as the primary outcome as in the over 65 population with diabetes most people would require pharmaceutical intervention to reach the target lipid levels making it a good measure of

quality of care. People attending DECs would learn about the importance of lipid management in preventing diabetes complications and be more likely to accept or seek a prescription for a statin from their primary care provider. There is similar strong evidence to support the use of glucose lowering medications, antihypertensive medications and ACEI/ARBs in this population (UKPDS 33 and 34, Schrier *et al*., 2002; HOPE investigators 2000; Lindholm *et al*., 2002). DECs also review the importance of these interventions and they too can be used as indicators of quality of care and therefore they were included as secondary outcomes. As many patients are referred to a DEC to learn SMBG so this was also included as a secondary outcome. DEC attendance may serve as a reminder for the importance of regular retinopathy screening therefore it was also included as a secondary outcome.

1.11.1 Primary Research Question

Do diabetic patients aged ≥ 65 years have increased filling of prescriptions for statins after attending a DEC in routine clinical care in Ontario?

1.11.2 Secondary research questions

Do diabetic patients aged ≥ 65 years have increased filling of prescriptions for glucose lowering medications, blood glucose monitoring, ACE inhibitor/ARB, antihypertensive medications, and retinopathy screening after attending a DEC in routine clinical care in Ontario?

1.11.3 Hypotheses

Diabetes education center attendance will be associated with increased use of statins in the over 65 population in Ontario. DEC attendance will also be associated with

increased the use of glucose lowering medications, antihypertensive medications, ACE inhibitor/ARB, SMBG, and retinopathy screening in this population.

DEC attendance will not be associated with increased use of proton pump inhibitors, levothyroxine and otolaryngology care (to test the specificity of the response from DEC attendance).

Chapter 2: Methods

2.1 Research Design

This is a population based cohort study of residents of Ontario aged 65 years or greater diagnosed with diabetes on or before January 1, 2005. It used health care administrative databases of the Ontario Ministry of Health and Long Term Care. These databases include the Ontario drug benefits program database (ODB) which contains the prescriptions filled under the provincial formulary for all residents aged ≥65 years; the physician service claims database of Ontario Health Insurance Plan (OHIP) which includes claims for fee-for-service reimbursement for all physician and optometry services provided in Ontario; the hospital discharge abstracts prepared by the Canadian Institute for Health Information (CIHI); and a demographic database (Registered Persons Database- RPDB) which includes birth and death dates, sex and postal code of home residence. Individual patients can be linked between all of these databases and across time via their reproducibly encrypted personal health card number.

DSME in Ontario is delivered mainly through 331 DECs throughout the province at academic or community hospitals, community health centers or First Nations organizations and is funded in whole or in part by the Ministry of Health and Long Term Care. There was no previous administrative database or registry of DEC visits. Therefore, a registry of DEC attendance was created by collecting the visit dates and the health card numbers of all patients who attended any of the 331 DECs in Ontario in 2006 (Cauch-Dudek *et al*., 2013). Data were collected either manually from the DEC charts by trained

professional abstractors or directly from electronic registration information. The data were linked with the administrative data sources via the patients' health card number.

The Ontario Diabetes Database (ODD) was used to identify patients with diabetes. The ODD uses an administrative data algorithm to assemble a cohort of all individuals with diagnosed non-gestational diabetes in Ontario (Hux *et al*., 2002). Patients admitted to a hospital with a diagnosis of diabetes were identified from the discharge abstracts prepared by CIHI. Physician service claims where the diagnosis recorded was diabetes were identified from the OHIP records. Patients were identified as having diabetes if they had two physician service claims bearing a diagnosis of diabetes within a two year period, or one hospitalization with a diagnostic code for diabetes. Once a patient is diagnosed with diabetes, they remain in the ODD until death. Physician service and hospitalization claims in temporal proximity to records for an obstetrical hospitalization are excluded to avoid capturing gestational diabetes in the database. The ODD was validated against two independently derived cohorts of individuals with diabetes identified from the ODB database and the National Population Health Survey (NPHS) as well as by chart abstraction of primary care physician offices and found to have a sensitivity of 86%, specificity of 97% and a positive predictive value of 80%.

2.2 Patient Selection

The cohort included all residents of Ontario aged 65 years or greater who were diagnosed with diabetes on or before January 1, 2005 according to the ODD. The cohort was restricted to seniors to ensure that drug dispensation data was complete, as drug dispensation information is incomplete for younger patients. The cohort was restricted to

those alive until Dec 31, 2007 to insure follow up was complete. Those without a valid Ontario postal code were excluded to insure only residents of Ontario were used in the analysis.

2.3 Exposure Variable

DEC attendance in 2006 by patients in the cohort was determined by linking with the DEC database. The index date was assigned as the date of the first DEC visit. For patients who did not attend a DEC, the index date was randomly assigned following the same distribution of index dates as seen in attendees.

2.4 Covariates

Baseline characteristics were obtained and included:

1) age at index date
2) gender
3) local health integration network (LHIN) of residence at index date (LHINs are 14 geographic areas created in 2006 which plan, manage and fund health services in their region in collaboration with community members and local health care providers)
4) low income flag in ODB (based on eligibility for reduced co-payments in the drug benefits programme, requiring documented annual income less than C$16 018 for individuals or C$24 175 for couples)
5) duration of diabetes diagnosis at index date, categorized as 1 to <2 years, 2 to <5 years, and ≥ 5 years

6) comorbidity, assigned as the number of unique Drug Identification Numbers (DINs) in the 1 year prior to index date (Schneeweiss *et al*., 2001)
7) health care utilization, defined as the number of visits to a primary care physician one year prior to index date
8) diabetes specialist care at least one visit in the year prior to index date
9) cardiology care at least one visit in the year prior to index date
10) nephrology care at least one visit in the year prior to index date
11) hypoglycemia or hyperglycemia hospital admission or emergency department visit one year prior to index date
12) hospital admissions, defined as the number of days in hospital during the one year prior to index date
13) previous coronary or cerebrovascular disease in the 5 years before index date

2.5 Outcome Variables

Patients were studied in the 6 month period after their index date for prescriptions filled for medications and glucose monitoring supplies from the drug benefits database (Figure 2.1). The primary outcome was whether or not a prescription was filled for a statin in the 6 months following the index date.

The secondary outcomes were whether a prescription was filled for blood glucose lowering medications, antihypertensive medications in general, ACE inhibitors/ARBs or blood glucose monitoring strips. Visits with an optometrist or ophthalmologist for retinopathy screening in the 1 year after the index date were determined in both groups from the OHIP database.

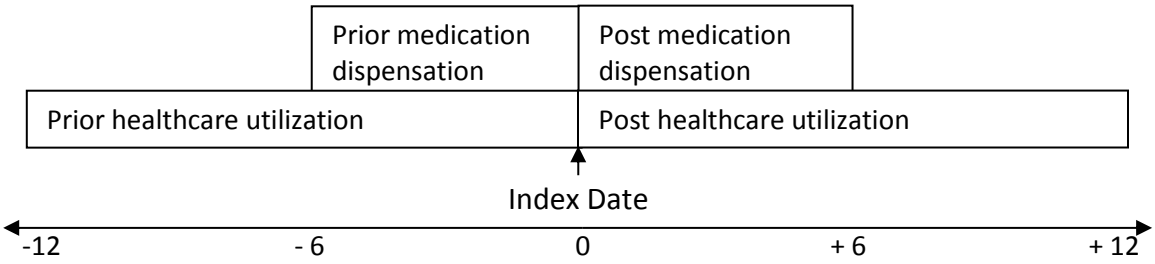

Figure 2.1: Study timeline

Index date of DEC attendance is set as time 0 with the outcome variables of prescriptions filled in the 6 months post index date and healthcare utilization in the 12 months post index date. The baseline variables of prescriptions filled in the 6 months prior to index date and healthcare utilization in the 12 months prior to index date are also included.

To test for the specificity of the response, we selected outcomes where no effect from DEC utilization was expected. Therefore, we also examined the filling of prescriptions for proton pump inhibitors and levothyroxine in the 6 months after the index date and visits with otolaryngologists in the 1 year after the index date. Each outcome variable was also examined in the 6 months or 1 year before the index date, to assess baseline drug dispensation or physician visits.

2.6 Analysis

The baseline characteristics of DEC attendees and non-attendees were compared using p-values determined by Student's *t*-test for age and Pearson's Chi Squared test for other characteristics, and using standardized difference of the means.

2.7 Logistic regression

The primary outcome of prescription filled for statins was compared between DEC attendees and non-attendees using logistic regression to adjust for pre-index dispensation of statins and all 13 baseline variables. This analysis was repeated for each secondary outcome. In each case, the model adjusted for pre-index utilization for that category only.

2.8 Matching using Propensity score

In observational studies the assignment of patients to the treatment of interest is not under the investigators control and there are differences between confounding factors between exposure groups (Shah *et al.*, 2005). Multivariate logistic regression is often used to control this bias but investigators often construct regression models with few covariates as possible to predict outcome. This makes it more understandable at the

expense of the best possible adjustment with interaction and nonlinear terms. Propensity scores were proposed by Rosenbaum and Rubin (1983a) as a method to control for confounding in observational studies. The propensity score is the conditional probability of receiving a treatment given the observed set of potentially confounding variables. It can include numerous covariates, interactions and nonlinear terms and can be estimated by logistic regression. As the predicted probability of exposure is equal with the same propensity score, differences in the exposure allocation can be deemed random. Similar to a randomized trial, there is a balance of known confounders between exposure groups after adjusting for the propensity score. Like regression modeling it cannot control for unknown confounders but the sensitivity of the model to unknown confounders can be estimated (Rosenbaum and Rubin, 1983b).

A propensity score was constructed, with DEC utilization as the dependent variable and the 13 baseline socio-demographic and clinical variables and the 9 variables for pre-index utilization as the independent variables. The balance of covariates was verified between propensity score quintiles; interaction or nonlinear terms were added as needed to achieve balance. The DEC attendees and non-attendees were greedy matched on the logit of the propensity score, using calipers with a width of 0.6 x the pooled standard deviation. This ensures that, on balance, the two groups are balanced on all of the known confounders included in the propensity score model. The baseline characteristics of the matched cohorts were compared using standardized differences of the mean. The standardized difference in the mean is the difference in the means divided by the pooled estimate of the standard deviation of the variable (Austin, 2008). Unlike significance testing, it is not affected by sample size and is therefore more useful to

compare groups when using large datasets. Values of 0.1 or greater suggest a potentially meaningful imbalance in a particular covariate between groups. The risk difference between those attending a DEC and those not attending a DEC for the frequency of filling prescriptions for statins was calculated from contingency tables. The statistical significance of this difference was ascertained using McNemar's test. The analysis was repeated for all secondary outcomes.

2.9 Ethics approval

Ethics approval was obtained from the Sunnybrook Health Sciences Centre Research Ethics Board.

Chapter 3: Results

3.1 Logistic Regression

3.1.1 Baseline characteristics

There were 350 734 people with diabetes ≥65 as of January 1, 2005. Of them, 54 575 (15.6%) were excluded because they died prior to December 31, 2007, leaving 296,159 in the cohort. Of them, 22,606 (7.6%) attended a DEC in 2006. The baseline characteristics of this population are outlined in Table 3.1. The groups differed on all variables examined. The DEC attendees were slightly younger, were more likely to be male, and were less likely to have low income. LHIN of residence was variable between non-attendees and DEC attendees. Patients who attended a DEC were more likely to have a duration of diabetes from 1-2 years or greater than 5 years. The comorbidity index expressed as the number of distinct DINs for each individual and the rate of known coronary and cerebrovascular disease was higher in DEC attendees. Patients who attended a DEC in 2006 were more likely to have a greater number of primary care visits, and received diabetes specialist care, nephrology care and cardiology care in the year prior to the index date. DEC attendees also had a higher number of hospital inpatient days and were more likely to have hospital admissions and emergency room visits for hypoglycaemia and hyperglycaemia in the year prior to the index date. The rates of prescriptions filled for medications in the 6 months prior to the index date were higher for those who attended a DEC in 2006 for statins, glucose lowering medications, antihypertensive medications in general, ACE inhibitors and ARBs and glucose monitoring strips than for those who did not attend a DEC. Proton pump inhibitor and levothyroxine prescription rates were also higher in the DEC attendee group. DEC

Table 3.1: Baseline characteristics at index date

Variable	Value	Non-attendees	DEC Attendees	P-value
	n (%)	273,553 (92.4%)	22,606 (7.6%)	
Age	Mean ± SD	75.7± 6.7	73.8 ± 5.5	<0.001
Gender	Female n (%)	140,747 (51.5%)	11,383 (50.4%)	0.002
	Male n (%)	132,806 (48.5%)	11,223 (49.6%)	
LHIN	**1. Erie St. Clair** n (%)	15,578 (5.7%)	1,481 (6.6%)	<0.001
	2. South West n (%)	19,870 (7.3%)	1,845 (8.2%)	
	3. Waterloo Wellington n (%)	11,576 (4.2%)	818 (3.6%)	
	4. Hamilton Niagara Haldimand Brant n (%)	30,297 (11.1%)	3,272 (14.5%)	
	5. Central West n (%)	14,502 (5.3%)	832 (3.7%)	
	6. Mississauga Halton n (%)	19,730 (7.2%)	1,466 (6.5%)	
	7. Toronto Central n (%)	26,427 (9.7%)	1,035 (4.6%)	
	8. Central n (%)	37,137 (13.6%)	2,115 (9.4%)	
	9. Central East n (%)	35,973 (13.2%)	2,689 (11.9%)	
	10. South East n (%)	11,567 (4.2%)	961 (4.3%)	
	11. Champlain n (%)	23,160 (8.5%)	2,246 (9.9%)	
	12. North Simcoe Muskoka n (%)	8,361 (3.1%)	1,320 (5.8%)	
	13. North East n (%)	14,006 (5.1%)	1,723 (7.6%)	
	14. North West n (%)	4,952 (1.8%)	795 (3.5%)	
	Missing LHIN n (%)	417 (0.2%)	8 (0.0%)	
Low income	n (%)	77,425 (28.3%)	5,355 (23.7%)	<0.001
Duration of diabetes	A. 1-2 y n (%)	13,620 (5.0%)	1,290 (5.7%)	<0.001
	B. 2-5 y n (%)	58,379 (21.3%)	4,055 (17.9%)	
	C. >5 y n (%)	201,554 (73.7%)	17,261 (76.4%)	
Comorbidity (#DINs)	Mean ± SD	10.8 ± 7.0	13.4 ± 6.7	<0.001
Primary Care visits	Mean ± SD	8.3 ± 8.5	8.5 ± 6.1	<0.001
Diabetes specialist	n (%)	42,302 (15.5%)	8,473 (37.5%)	<0.001
Nephrology	n (%)	11,609 (4.2%)	1,820 (8.1%)	<0.001
Cardiology	n (%)	41,276 (15.1%)	5,044 (22.3%)	<0.001
Hospital admission/ ER visit for hypo/hyperglycemia	n (%)	2,285 (0.8%)	560 (2.5%)	<0.001
Hospital Inpatient Days	Mean ± SD	1.7 ± 8.4	2.2 ± 7.6	<0.001
Coronary/ cerebrovascular disease	n (%)	27,390 (10.0%)	3,013 (13.3%)	<0.001

Variable	Value	Non-attendees	DEC Attendees	P-value
Statins	n (%)	145,875 (53.3%)	15,405 (68.1%)	<0.001
Glucose lowering medications	n (%)	158,567 (58.0%)	18,595 (82.3%)	<0.001
Antihypertensive medications	n (%)	212,112 (77.5%)	20,173 (89.2%)	<0.001
ACE inhibitors/ARBs	n (%)	174,710 (63.9%)	17,704 (78.3%)	<0.001
Glucose monitoring strips	n (%)	116,017 (42.4%)	17,115 (75.7%)	<0.001
Ophthalmology/ optometry	n (%)	164,512 (60.1%)	17,442 (77.2%)	<0.001
Proton pump inhibitors	n (%)	55,751 (20.4%)	5,790 (25.6%)	<0.001
Levothyroxine	n (%)	37,281 (13.6%)	3,655 (16.2%)	<0.001
Otolaryngology	n (%)	16,550 (6.1%)	1,849 (8.2%)	<0.001

attendees were more likely to have ophthalmology/optometry and otolaryngology visits than non-attendees in the year prior to the index date.

3.1.2 Medication and physician visits after index date by logistic regression

As all variables differed at baseline between DEC attendees and non-attendees the model was adjusted for all of these variables in the logistic regression. The results of the logistic regression are outlined in Table 3.2. The primary outcome of statin use in the 6 months following the index date was associated with DEC attendance with an OR of 1.45 (95% CI 1.37, 1.53, $p<0.001$). The secondary outcomes were also associated with DEC attendance. The use of glucose lowering medications in the 6 months following index date was associated with DEC attendance with an OR of 2.20 (95% CI 2.04, 2.37, $p<0.001$). Antihypertensive medication use is associated with DEC attendance with an OR of 1.49 (95% CI 1.38, 1.62, $p<0.001$) as were ACE inhibitors and ARBs with an OR of 1.47 (95% CI 1.38, 1.57, $p<0.001$). The use of glucose monitoring strips in the 6 months following the index date was associated with DEC attendance with an OR of 3.82 (95% CI 3.67, 3.98, $p<0.001$). Ophthalmology and optometry care in the 1 year after the index date was associated with DEC attendance with an OR of 1.56 (95% CI 1.50, 1.62, $p<0.001$). As expected, DEC attendance did not have an impact on proton pump inhibitor use in the 6 months after the index date (OR 1.01, 95% CI 0.96, 1.07, $p=0.6$) or otolaryngology visits in the 1 year after index date (OR 1.05 95% CI 0.99, 1.11, $p=0.09$) as these were used to test the specificity of the response. However, levothyroxine use was slightly associated with DEC attendance with an OR of 1.17 (95% CI 1.01, 1.36, $p=0.04$) in the 6 months after the index date.

Table 3.2: Association of medication dispensation and physician visits with DEC attendance by logistic regression

Medication	Odds Ratio	95% CI	P-value
Statins	1.45	1.37, 1.53	<0.001
Glucose lowering medications	2.20	2.04, 2.37	<0.001
Antihypertensive medications	1.49	1.38, 1.62	<0.001
ACE inhibitors/ARBs	1.47	1.38, 1.57	<0.001
Glucose monitoring strips	3.82	3.67, 3.98	<0.001
Ophthalmology/ optometry	1.56	1.50, 1.62	<0.001
Proton pump inhibitors	1.01	0.96, 1.07	0.6
Levothyroxine	1.17	1.01, 1.36	0.04
Otolaryngology	1.05	0.99, 1.11	0.09

3.2 Matching using Propensity Score

3.2.1 Baseline Characteristics

Using the propensity score to obtain a matched cohort of non-attendees to the 22 606 DEC attendees, a sample size of 45 212 was obtained with 22 606 in each group (Table 3.3). They were well matched for all baseline characteristics as demonstrated by the standardized difference of all variables being close to 0. The average age of the cohort was 73.8 years with an equal proportion of male and females. A similar proportion of DEC attendees and non-attendees were from each LHIN. 23.6% of the population had a low income tag in ODB. Both groups had a similar number of members with the same duration of diabetes and comorbidity score. Both groups had similar numbers of primary care visits and likelihood of receiving specialist care. A similar number of patients in each group filled prescriptions for statins, glucose lowering medications, antihypertensive medications, ACE inhibitors and ARBs, glucose monitoring strips, proton pump inhibitors and levothyroxine.

3.2.2 Medication dispensation and physician visits after index date in the propensity score matched cohort

The absolute rates of medication dispensation in the 6 months after index date and of physician visits in the 1 year after index date for DEC attendees and non-attendees in the cohort matched by propensity score are shown in Table 3.4. The proportion of DEC attendees who filled a prescription for a statin in the 6 months after the index date was 70.6% compared to 69.4% of non-attendees ($p=0.003$) with risk difference of 1.2%. Prescriptions for glucose lowering medications were filled by 83.7% of DEC attendees in the 6 months after index date compared to 82.0% of non-attendees ($p <0.0001$) with a risk

Table 3.3: Baseline characteristics of cohort post propensity score match

Variable	Value	Non-attendees	DEC Attendees	Standardized difference of the mean
		N=22,606	N=22,606	
Age	Mean ± SD	73.8 ± 5.6	73.8 ± 5.5	0.01
Gender	Female n (%)	11,316 (50.1%)	11,383 (50.4%)	0.01
	Male n (%)	11,290 (49.9%)	11,223 (49.6%)	
LHIN	**1. Erie St. Clair** n (%)	1,518 (6.7%)	1,481 (6.6%)	0.03
	2. South West n (%)	1,890 (8.4%)	1,845 (8.2%)	
	3. Waterloo Wellington n (%)	831 (3.7%)	818 (3.6%)	
	4. Hamilton Niagara Haldimand Brant n (%)	3,187 (14.1%)	3,272 (14.5%)	
	5. Central West n (%)	851 (3.8%)	832 (3.7%)	
	6. Mississauga Halton n (%)	1,453 (6.4%)	1,466 (6.5%)	
	7. Toronto Central n (%)	1,023 (4.5%)	1,035 (4.6%)	
	8. Central n (%)	2,148 (9.5%)	2,115 (9.4%)	
	9. Central East n (%)	2,702 (12.0%)	2,689 (11.9%)	
	10. South East n (%)	1,031 (4.6%)	961 (4.3%)	
	11. Champlain n (%)	2,162 (9.6%)	2,246 (9.9%)	
	12. North Simcoe Muskoka n (%)	1,285 (5.7%)	1,320 (5.8%)	
	13. North East n (%)	1,732 (7.7%)	1,723 (7.6%)	
	14. North West n (%)	789 (3.5%)	795 (3.5%)	
	Missing LHIN n (%)	<=5 (0.0%)	8 (0.0%)	
Low income	n (%)	5,315 (23.5%)	5,355 (23.7%)	0
Duration of diabetes	A. 1-2 y n (%)	1,286 (5.7%)	1,290 (5.7%)	0.01
	B. 2-5 y n (%)	4,131 (18.3%)	4,055 (17.9%)	
	C. >5 y n (%)	17,189 (76.0%)	17,261 (76.4%)	
Comorbidity (#DINs)	Mean ± SD	13.3 ± 6.8	13.4 ± 6.7	0.01
Primary Care visits	Mean ± SD	8.8 ± 7.0	8.5 ± 6.1	0.04
Number of primary care visits	0 visits n (%)	532 (2.4%)	685 (3.0%)	0.05
	1-2 visits n (%)	1,584 (7.0%)	1,591 (7.0%)	
	3-6 visits n (%)	7,544 (33.4%)	7,422 (32.8%)	
	7-12 visits n (%)	8,698 (38.5%)	8,477 (37.5%)	
	≥13 visits n (%)	4,248 (18.8%)	4,431 (19.6%)	
Diabetes specialist	n (%)	8,267 (36.6%)	8,473 (37.5%)	0.02
Nephrology	n (%)	1,780 (7.9%)	1,820 (8.1%)	0.01
Cardiology	n (%)	4,985 (22.1%)	5,044 (22.3%)	0.01
Hospital admission/ ER visit for hypo/ hyperglycemia	n (%)	540 (2.4%)	560 (2.5%)	0.01

Variable	Value	Non-attendees	DEC Attendees	Standardized difference of the mean
Hospital Inpatient Days	Mean ± SD	2.5 ± 9.5	2.2 ± 7.6	0.04
Coronary/ cerebrovascular disease	n (%)	2,967 (13.1%)	3,013 (13.3%)	0.01
Statins	n (%)	15,561 (68.8%)	15,405 (68.1%)	0.01
Glucose lowering medications	n (%)	18,689 (82.7%)	18,595 (82.3%)	0.01
Antihypertensive medications	n (%)	20,325 (89.9%)	20,173 (89.2%)	0.02
ACE inhibitors/ARBs	n (%)	17,838 (78.9%)	17,704 (78.3%)	0.01
Glucose monitoring strips	n (%)	17,135 (75.8%)	17,115 (75.7%)	0
Ophthalmology/ optometry	n (%)	17,527 (77.5%)	17,442 (77.2%)	0.01
Proton pump inhibitors	n (%)	5,805 (25.7%)	5,790 (25.6%)	0
Levothyroxine	n (%)	3,584 (15.9%)	3,655 (16.2%)	0.01
Otolaryngology	n (%)	1,797 (7.9%)	1,849 (8.2%)	0.01

Table 3.4: Absolute rates of medication and healthcare utilization in the propensity score matched cohort after the index date

Medication	**Non-attendees** n (%)	**DEC attendees** n (%)	**Risk Difference**	**P-value**
Statins	15687 (69.4%)	15965 (70.6%)	1.2%	0.003
Glucose lowering medications	18534 (82.0%)	18931 (83.7%)	1.8%	<0.0001
Antihypertensive medications	20286 (89.7%)	20397 (90.2%)	0.5%	0.07
ACE inhibitors/ARBs	17830 (78.9%)	18036 (79.8%)	0.9%	0.01
Glucose monitoring strips	14835 (65.6%)	18588 (82.2%)	16.6%	<0.0001
Ophthalmology/optometry	16437 (72.7%)	17797 (78.7%)	6.0%	<0.0001
Proton pump inhibitors	6055 (26.8%)	6119 (27.1%)	0.3%	0.5
Levothyroxine	3642 (16.1%)	3747 (16.6%)	0.5%	0.2
Otolaryngology	1682 (7.4%)	1763 (7.8%)	0.4%	0.2

difference of 1.8%. There was no difference in rates of antihypertensive use in the 6 months after index date between DEC attendees and non-attendees (90.2% vs. 89.7%, p=0.07). However, the rate of prescriptions filled for ACE inhibitors and ARBs was 79.8% in DEC attendees compared to 78.9% in non-attendees in the 6 months after index date (p=0.01) with a risk difference of 0.9%. Glucose monitoring strips were obtained by 82.2% of DEC attendees compared to 65.6% of non-attendees after the index date (p<0.001) with a risk difference of 16.6%. Visits to ophthalmology/optometry were higher in DEC attendees at 78.7% compared to 72.7% in non-attendees in the year following the index date (p<0.0001) with a risk difference of 6.0%. As expected, DEC attendance did not have an impact on prescriptions filled for proton pump inhibitors (27.1% vs. 26.8%, p=0.5) and levothyroxine (16.6% vs. 16.1%, p=0.2) in the 6 months following the index date or visits to otolaryngology in the 1 year following the index date (7.8% vs. 7.4%, p=0.2) as these were used to test the specificity of the response.

Chapter 4: Discussion

4.1 Characteristics of people with Diabetes over age 65 in 2006 attending DEC vs. not attending a DEC in Ontario in the cohort

This study included all of those diagnosed with Diabetes in Ontario and aged 65 years and older on January 1, 2005. Only a small portion of these people attended a DEC in 2006. This is a snapshot of a one-year time frame so it does not capture people who had attended a DEC in previous years. Inevitably, many patients who are referred to DSME ultimately do not attend. The attendance rate was lower than seen in other studies (Coonrod *et al*., 1994; Shah *et al.,* 2009; Ruppert *et al.,* 2010). This study measured DEC attendance in a 1 year period in a population based cohort. Other studies measured diabetes education since diagnosis. They are surveys with voluntary participation and diabetes education is self-reported. In a survey of people with diabetes mainly distributed through pharmacies in Ontario 30% of people reported having attended a DEC in the year prior (Shah *et al.,* 2009). A nationwide survey in the United States found that 35.1% of people with diabetes had attended diabetes education since diagnosis (Coonrod *et al*., 1994). In a study from rural Pennsylvania 65% of people with reported they had never received DSME and 76% of those had never received a referral to DSME (Ruppert *et al.,* 2010). 83% of those referred to DSME attended.

The population attending the DECs in Ontario were slightly younger, more likely to be male and less likely to be of low income status than those who did not attend a DEC in 2006. These characteristics are similar to those seen in other studies. A nationwide survey in the United States showed that diabetes education attendance was associated

with younger age, African-American ethnicity, and higher education (Coonrod *et al*., 1994). Age greater than 70 years was associated with lower participation in an American study of diabetes education in people over 60 (Glasgow *et al.,* 1991). Female sex and larger BMI predicted DEC attendance in a study in a Philadelphia academic family practice (Graziani *et al*., 1999). Those who attended a DEC in Ontario in the 6 months after diagnosis were less likely to be of low income status, less likely to be a recent immigrant, and more likely to be of rural residence than those who did not attend (Cauch-Dudek *et al.,* 2013).

DEC attendees were more likely to have a shorter duration of diabetes than non-attendees, which is not surprising as newly diagnosed are in need of DSME. Despite this, only 20.6% of all adults with newly diagnosed diabetes attended a DEC within 6 months of diagnosis in Ontario in 2006 (Cauch-Dudek *et al.,* 2013). In a survey of people with diabetes mainly distributed through pharmacies in Ontario DEC attendance was also associated with shorter duration of diabetes (Shah *et al.,* 2009). Those with a long duration of diabetes (>5 years) were also more likely to attend a DEC as these patients may need an update in their education or have comorbidities that have triggered referral. This is evident as the comorbidity score (defined as the number of distinct DINs in 1 year) was higher in those who attended the DEC in 2006 than those who did not. A nationwide survey in the United States showed that diabetes education attendance was associated with insulin use and more diabetes complications (Coonrod *et al*., 1994). In a study from rural Pennsylvania, those individuals with more risk factors and comorbidities were more likely to be referred to diabetes education (Ruppert *et al.,* 2010).

The number of primary care visits in the year prior to the index date was slightly higher in those who attended a DEC, suggesting that DECs are not replacing normal primary care but are used as an adjunct to it. The same result was seen in the cohort study of all newly diagnosed adults with diabetes in Ontario that used the same DEC registry (Cauch-Dudek *et al*., 2013). In a survey of people with diabetes mainly distributed through pharmacies in Ontario DEC attendance was associated with regular primary care visits and regular diabetes specialist care (Shah *et al.*,2009).

DEC attendees were more likely to have had a hospital admission and emergency room visits for hypoglycemia or hyperglycemia and more hospital inpatient days for all causes than non-attendees in the year prior to the index date. Overall, DEC attendees are a much sicker population than non-attendees as evidenced by their comorbidity score, rates of coronary and cerebrovascular disease, and used greater health care resources including specialist and primary care than non-attendees in the year prior to the index date. These physician and hospital visits provided more contact time with this group and provided an opportunity for referral to a DEC. The presentation with complications of diabetes demonstrated a need for diabetes education that may have prompted the visit to a DEC.

Those elderly who attended a DEC in 2006 had a higher rate of prescriptions filled in the 6 months prior to the index date than those who did not attend a DEC. This was true of all medications studied related to the management of diabetes and its complications (statins, glucose lowering medications, antihypertensive medications, ACE inhibitors and ARBs, and glucose monitoring strips) as well as proton pump inhibitors and levothyroxine which were used to test the specificity of the response. As the rates of

prescriptions filled is increased for all medications examined in the DEC attendee group, this may suggest that the DEC attendee group is a sicker group. This is also supported by their comorbidity score and rate of hospitalization. It might also suggest that this group was already more compliant with medications as prescribed and with health care follow up. Two American studies found insulin use to be associated with DEC attendance (Coonrod *et al*., 1994; Graziani *et al*., 1999).

Many studies were RCTs with groups matched for baseline characteristics in which the control group also received some form of diabetes education. Consequently it is difficult to compare those trials to this cohort population for the demographic characteristics, health care utilization, and medication dispensation at baseline. The studies using surveys of people with diabetes do not report medication use. Hence, this cohort study provides a real world picture of individuals with diabetes attending DEC compared to those who do not.

4.2 Logistic Regression results

The primary outcome of prescriptions filled for statins in the 6 months after the index date was higher in the DEC attendees, suggesting DEC attendance is associated with the increased use of statins. DECs teach about the cardiovascular complications of diabetes and self-management behaviors to reduce these risks, such as taking statins and antihypertensive medications. This knowledge may increase attendees' likelihood to fill and take the prescription for a statin and to ask their care provider about statin therapy if they have not already been prescribed a statin.

The results from routine clinical care mirror those previously reported in randomized trials of diabetes education interventions. Lipid lowering medication use in the intervention arm of DESMOND was higher than the control population but not statistically significant using NHS data (Gillett *et al.,* 2010). The lipid values were not different between the groups (Davies *et al*., 2008). A RCT of group diabetes education compared to usual care showed lipid active medication increased over the study period in both groups without significant differences in lipid profiles other than an increase in HDL in group care (Trento *et al.,* 2002).

However, the finding of increased lipid lowering medication utilization following DSME has not been universal. Many prior studies of diabetes education showed no difference in lipid lowering medication use between groups. Most were RCTs that compared a new structured diabetes education program to standard care that also included diabetes education. The primary outcome of many of these studies is reduction in A1C with statin use or lipid levels as a secondary outcome. There was no difference in statin use in patients with diabetes participating in Disease Management Programs in Germany compared to those who did not participate (Berthold *et al*., 2011). Despite this, there was an improvement in LDL cholesterol. A meta–analysis of studies of nurse led DSME showed small changes on lipid levels (Tshiananga *et al*., 2012). There was an increase in HDL of 0.009 mmol/L (p=0.018), a decrease in total cholesterol of -0.032 mmol/L (p=0.010), a decrease in LDL of -0.010 mmol/L (p=0.016), and a decrease in triglycerides of -0.237 mmol/L which was non-significant. Although the studies included in this meta-analysis did not include information on statin use, it is possible DSME had an effect given the change in lipid levels.

The secondary outcomes were also found to have an increase associated with DEC attendance. The prescriptions filled for glucose lowering medications in the 6 months after the index date was higher in the DEC attendees suggesting DEC attendance is associated with the increased use glucose lowering medications. This follows as many patients are referred to DECs for education when starting on a new diabetes therapy such as learning insulin administration and adjustment.

The use of glucose lowering medications has also found to be associated with DSME in previous studies. For example, self-reported use of glucose lowering medication was higher in the intervention group of diabetes education compared to the control group in a study of a DSME program in Malaysia (Tan *et al.*, 2011). This was correlated to the decrease in A1C in the intervention group ($r=-0.27$, $p=0.001$).

However, the effect of DSME on glucose lowering medications was variable in other studies with the increased use being attributed to greater medication compliance in some studies and the decrease use being attributed to better lifestyle choices in other studies. A RCT of group diabetes education compared to usual care showed a reduction in the doses of hypoglycemic agents over 4 years in the intervention group compared to an increase in dose in the control group (Trento *et al.,* 2002). The A1C remained constant in the intervention group but increased significantly in the control group. A similar result was seen in the Cochrane review of group DSME, where the participants required fewer diabetes medications compared to controls in the 5 included studies (OR 11.8, 95% CI 5.2-26.9; $p<0.00001$, $I^2=0$) (Deakin *et al.,* 2005). Even with fewer medications used there was a reduction in A1C which was maintained at follow up suggesting the use of fewer

diabetes medications may be related to greater diabetes knowledge and self-care behaviors that prevented further increases in medications.

In other studies there was no difference seen in the use of glucose lowering medications between groups and no statistically significant reduction in A1C seen between groups. In DESMOND, the use of glitazones and sulphonylureas were not different and there was a non-significant trend toward an increased use of metformin in the DESMOND group (Gillett *et al.*, 2010). The reduction in A1C was greater in the intervention group compared to the control group of DESMOND, −1.49% (95% CI −1.69% to −1.29%) compared with −1.21% (95% CI −1.40% to −1.02%), but after adjustment for baseline characteristics and cluster effect the difference was not statistically significant (Davies *et al*., 2008). A RCT of DSME aimed at changing the self-care behaviours of SMBG, healthy eating and smoking cessation to usual care showed that both groups changed the dose or frequency of oral agent therapy during the study with no difference between groups (Jones *et al*., 2003). Both groups also increased the frequency of insulin injection during the study. There was no reduction in A1C between groups unless the subgroup of those who reached the active or maintenance phase of the behavior change was examined.

The prescriptions filled for antihypertensive medications in the 6 months after the index date was increased in DEC attendees. Prescriptions filled for ACE inhibitors and ARBs was also increased in the 6 months after the index date in DEC attendees. DECs teach about the cardiovascular and renal complications of diabetes and self-management behaviors to reduce these risks that include blood pressure control and the use of ACE

inhibitors and ARBs. This knowledge may increase attendees' likelihood to fill and take the prescription for antihypertensive medications. A decline in persistence of antihypertensive therapy is seen after initiation in newly treated elderly hypertensive individuals in Ontario with the diabetic cohort having a therapy persistence of 74.2% over 1 year and 67.3% over 2 years (Friedman *et al*., 2010). Therefore, any intervention which improves compliance and persistence is beneficial.

Other studies have shown an increase in antihypertensive medication use in both groups. A RCT of group diabetes education compared to usual care which included individual diabetes education, showed antihypertensive medication use increased over the study period in both groups with a decrease in diastolic blood pressure in both groups (Trento *et al.*, 2002). The increase in antihypertensive use and decrease in blood pressure may be related to the effect of diabetes education in both groups.

Many of the studies of diabetes education do not measure the use of antihypertensive medications but instead look at blood pressure. DESMOND showed no difference in blood pressure between groups at the end of the study period (Davies *et al*., 2008). A meta–analysis of studies of nurse-led DSME showed the effect on blood pressure was non-significant compared to the control group with a net decrease in diastolic blood pressure of −2.291 mmHg (p=0.064) and in systolic blood pressure of −1.847 mmHg (p=0.361) (Tshiananga *et al*., 2012). These studies did not examine antihypertensive use by participants but it is possible that DSME increased their use given the trend down in blood pressure.

Prescriptions filled for glucose monitoring strips was increased in the 6 months after the index date in DEC attendees. When attending a DEC, patients are instructed to monitor their blood glucose to aid in the optimization of their treatment and often asked to bring a blood glucose log to follow up visits at the DEC or with their health care provider. Therefore it makes sense that DEC attendance would be strongly associated with the use of glucose monitoring strips in the next 6 months.

Similar increases in SMBG were seen in RCTs of diabetes education regardless of effect on A1C. SMBG increased in the intervention group at 2.88/week (95% CI 2.53-3.23) compared to the control group at 0.62/week (95% CI 0.35-0.89, $p<0.001$) during the study period of a DSME program in Malaysia (Tan *et al.*, 2011). The increase in SMBG in the intervention group was correlated with the decrease in A1C ($r = -0.28$, $p=0.001$). A RCT of DSME aimed at changing the self-care behaviours of SMBG, significantly increase testing frequency from 1.4 to 1.6 tests per day as measured by downloaded meter memory compared to a slight decrease in the control group ($p=0.002$) (Jones *et al.*, 2003). The reduction in A1C was not significant between groups in the intention treat analysis but was for the subgroup of those who reached or maintained action of self-glucose monitoring over the course of the trial with an A1C of 7.78% compared to 8.30% in those who stayed in the pre-action phase ($p< 0.003$). The reduction in A1C was seen regardless of using oral agents or insulin.

The odds of receiving care by ophthalmology or optometry in the 1 year after the index date was higher for DEC attendees. The development of diabetic retinopathy, and the importance of screening for it with appropriate eye examinations, is reviewed at DECs

so it follows that DEC attendance would be associated with an increase in care by ophthalmology or optometry as the DEC visit may serve as a reminder to the patient to see their eye doctor.

A similar association with diabetes education and eye care was seen in other studies. In a survey of people with diabetes mainly distributed through pharmacies in Ontario DEC attendance was associated with retinal screening in the following 2 years (Shah *et al.*, 2009). In a RCT of nurse case manager led DSME the rate of ophthalmological examination was 68% compared to 26% in the control group (Gabbay *et al*., 2006).

Proton pump inhibitors, levothyroxine and otolaryngology visits were used to demonstrate the specificity of the response to DEC attendance of the diabetes related outcomes. As expected, the prescriptions filled for proton pump inhibitors in the 6 months after the index date in DEC attendees and non-attendees, was not different. Receiving care by otolaryngology in the 1 year after the index date was not different between groups. Both these outcomes are not related to diabetes and its management therefore it was expected that no association would be seen with DEC attendance. However, prescriptions filled for levothyroxine in the 6 months after the index date was slightly higher in the DEC attendees than non-attendees. This was not expected to be different between groups as it is unrelated to the management of diabetes and its complications. However, as many patients with diabetes are managed by diabetes specialists who are endocrinologists or internists, they may be more likely to have been screened for hypothyroidism, and treated when diagnosed. The DEC attendees were more likely to see

these physicians than non-attendees and therefore be more likely to have their hypothyroidism diagnosed and treated. They may be a more health-aware population so more laboratory tests are performed as they see physicians more often and may be more likely to be compliant with treatments that are prescribed. Although care by a diabetes specialist and number of primary care visits in the year prior to the index date were adjusted for, they were not adjusted for in 6 months after index date which is when this difference was seen. The small increased increase in levothyroxine prescriptions also may suggest it is a sicker population overall so more attention is paid to all metabolic parameters. For these reasons levothyroxine may not have been a good choice as to test the specificity of the response to DEC attendance as it is confounded in diabetes patients.

4.3 Propensity Match results

The use of propensity scores lead to extremely well matched cohorts. For the primary outcome with propensity score matching, the rate of prescriptions filled for statins by DEC attendees was greater than in non-attendees in the 6 months after the index date. While there is a statistically significant association of statin use with DEC attendance, the effect is not large in the matched population. It is noted that in the 6 months prior to the index date 68.1% of DEC attendees and 68.8% of non-attendees filled a prescription for a statin so the dispensation of statins in this cohort was already fairly high in both groups leaving little room an effect of DEC attendance yet the small difference was statistically significant.

This study examined outcomes in patients in routine clinical care. The results are similar to what has been seen in RCTs of DSME. There was a trend toward increased use

of lipid lowering medication use in the intervention arm of DESMOND compared to the control population but this was not statistically significant (Gillett *et al.*, 2010). The lipid values were also not different between the groups (Davies *et al*., 2008). An increase in lipid-active medication was seen over the study period in both groups in a RCT of group diabetes education compared to usual care without significant differences in lipid profiles (Trento *et al.*, 2002).

Many RCTs of diabetes education showed no significant difference in lipid lowering medication use between groups with little or no effect on lipid levels. These RCTs had much smaller sample sizes than our population based cohort study so while there was often a trend toward an increase in lipid lowering medication use, it was not statistically significant. Despite an improvement in LDL cholesterol, there was no difference in statin use in patients with diabetes participating in Disease Management Programs in Germany compared to those who did not participate (Berthold *et al*., 2011).

For most of the secondary outcomes, an association with DEC attendance was seen. In most cases the effect was small using the propensity score match. The rate of prescriptions filled for glucose lowering medications in the 6 months after the index date in DEC attendees was slightly higher than in non-attendees. Many patients are referred to DECs at the time of initiation of new glucose lowering therapy so it is expected the prescriptions filled for glucose lowering medications would be higher in DEC attendees than non-attendees.

An increase in glucose lowering medications was seen in other studies of diabetes education. A study of a DSME program which showed an increase in self-reported use of

glucose lowering medication in the intervention group of diabetes education (91.42%, 95% CI 89.12–93.72) compared to the control group (84.4%, 95% CI 81.76–87.20, p=0.008) (Tan *et al.*,2011). This was correlated to the decrease in A1C in the intervention group (r= - 0.27, p=0.001). There was also an increase in oral diabetic agent and insulin prescriptions in patients with diabetes enrolled in Disease Management Programs in Germany compared to those who were not (Berthold *et al*., 2011).

Other studies showed no significant difference seen in the use of glucose lowering medications between groups and no reduction in A1C seen between groups. In DESMOND there was no difference in the use of glitazones and sulphonylureas between groups with a non-significant trend toward an increased use of metformin in the DESMOND group (Gillett *et al.*, 2010). Both groups changed the dose or frequency of oral agent therapy and increased the frequency of insulin injection during the study with no difference between groups during a RCT of DSME aimed at changing the self-care behaviours (Jones *et al*., 2003).

However, other studies showed a reduction in the dose of glucose lowering medications with diabetes education which was attributed to better adherence to improved lifestyle choices related to greater diabetes knowledge and self-care behaviors in the intervention groups as A1C improved or remained constant compared to an increase in the control group. This was seen in a RCT of group diabetes education with a reduction in the doses of hypoglycemic agents over 4 years in the intervention group compared to an increase in the control group while the A1C remained constant in the intervention group but increased in the control group (Trento *et al.*, 2002). A similar result was seen

in the Cochrane review of group DSME where participants required fewer diabetes medications compared to controls in the 5 included studies (OR 11.8, 95% CI 5.2-26.9; $p<0.00001$, $I^2=0$) (Deakin *et al.,* 2005). There was a reduction in A1C that was maintained at follow up.

The rate of prescriptions filled for antihypertensive medications was not different between DEC attendees and non-attendees. The use of hypertensive medications in this cohort was already high at baseline in both groups. However, the rate of prescriptions filled for ACE inhibitors and ARBs was slightly higher in DEC attendees compared to non-attendees. This effect though small may be due to the knowledge gained at DECs by patients of the importance of ACE inhibitors and ARBs in preventing proteinuria in diabetes.

Other studies of diabetes education which examined antihypertensive medication use also did not show a difference between groups. A RCT of group diabetes education compared to usual care, showed antihypertensive medication use increased over the study period in both groups (Trento *et al.,* 2002). Other studies of diabetes education did not measure the use of antihypertensive medications but instead examined at blood pressure with no difference in blood pressure between groups at the end of the study period in DESMOND (Davies *et al*., 2008) and in a meta–analysis of studies of nurse led DSME (Tshiananga *et al*., 2012). There was also an increase in ACE inhibitor prescriptions in those patients enrolled in a Disease Management Program for diabetes in Germany compared to those who were not (Berthold *et al*., 2011). There was an improvement in

meeting the diastolic blood pressure target but not systolic blood pressure. The use of other antihypertensive medications was not examined in this study.

The rate of prescriptions filled for glucose monitoring strips in the 6 months after the index date was higher in DEC attendees than in non-attendees. The greater association seen with glucose monitoring strips and DEC attendance than with other outcomes is possibly a result of people attending a DEC being asked to monitor their blood glucose more often to help in the adjustment of glucose lowering therapy on future visits.

Increases in SMBG were seen in other studies of diabetes education with variable of effect on A1C. A study of a DSME program showed increased SMBG in the intervention group at 2.88/week (95% CI 2.53-3.23) compared to the control group at 0.62/week (95% CI 0.35-0.89, $p<0.001$) which was correlated with a decrease in A1C (Tan *et al.*, 2011). There was an increase in testing frequency from 1.4 to 1.6 tests per day compared to a slight decrease in the control group in a RCT of DSME aimed at changing the self-care behaviours including SMBG ($p=0.002$) (Jones *et al*., 2003). In the intention treat analysis the reduction in A1C was not significant but was statistically significant for the subgroup that reached or maintained action of SMBG ($p<0.003$).

The rate of receiving ophthalmology or optometry care was increased in the DEC attendee group compared to the non-attendee group. Diabetes education reviews the importance of diabetic retinopathy screening and DEC attendance may serve as a reminder for patients to be seen for eye care.

An association with diabetes education and eye care was seen in other studies. DEC attendance was associated with retinal screening in the following 2 years in a survey of people with diabetes mainly distributed through pharmacies in Ontario (Shah *et al.*, 2009). The rate of ophthalmological examination was 68% in the intervention group compared to 26% in the control group in a RCT of nurse case manager led DSME (Gabbay *et al*., 2006).

The risk differences for the filling of prescriptions for medications between groups are not large, raising the question of whether the results are clinically significant. There was a very small difference in medication use and optometry/ophthalmology visits between groups at baseline with slightly higher use in the non-attendee group in the propensity score matched cohort. Therefore, the population is slightly biased against the DEC attendees at baseline which further strengthens the results of increased medication dispensation in DEC attendees.

Prescriptions filled for proton pump inhibitors, prescriptions filled for levothyroxine, and receiving otolaryngology care were not different between DEC attendees and non-attendees after the index date in the propensity score matched cohort. These outcomes were used to demonstrate the specificity of the response to DEC attendance of the diabetes related outcomes. Therefore, it was expected that no association with DEC attendance would be seen as these medications and type of medical care is not related to diabetes management or its complications.

4.4 Difference in results of the two methods

As expected, the different methods of analysis gave broadly similar results. The propensity score analysis attenuated the results seen in the logistic regression analysis. Both methods gave a statistically significant association of statin dispensation in the 6 months after DEC attendance but the degree of association was stronger by the logistic regression that may not be as well controlled for cofounders as the propensity matched score.

The secondary outcomes were also similar in the two methods of analysis. The association was greater with logistic regression than with propensity score matching for all secondary outcomes. The association was positive and statistically significant with both methods for all secondary outcomes except for antihypertensive medications for which no difference was seen between groups in the propensity score matched cohort but was seen in the logistic regression analysis.

There was no statistically significant difference in prescriptions filled for proton pump inhibitors or otolaryngology visits in both analyses as expected as these outcomes are not related to diabetes management. These were used to demonstrate the specificity of the response to DEC attendance of the diabetes related outcomes. Prescriptions filled for levothyroxine in the 6 months after DEC attendance was different between groups in the logistic regression analysis compared to no statistically significant difference seen in the propensity score matched cohort. It is possible that the confounders were better controlled in the propensity score matched cohort than in logistic regression or it may be that the difference seen with logistic regression is real but the more conservative measure of

association of the propensity score matching attenuated the results. The large number of unmatched non-attendees in the logistic regression analysis may have contributed to the affect seen in that analysis. The propensity-matched cohort may be a better analysis of the effect of DEC attendance on medication dispensation.

The two methods of analysis use different samples from the overall population. Logistic regression is performed on the whole cohort and is unmatched while the propensity matched is a sample of the population that is matched for 13 baseline variables and the 9 other variables for pre-index utilization. Logistic regression finds the OR by adjusting for the baseline and other variables of pre-index utilization while propensity matched adjusts the OR for propensity score.

The two methods are also not estimating the same thing, as logistic regression estimates the association for the individual but propensity score matching estimates the association for the population. The logistic regression model estimates the conditional or adjusted average with the OR estimating the average change for an individual e.g. changing a person from not being on a statin to being on a statin. The propensity score matched method estimates the marginal or population average with the risk difference estimating the average risk of change for the population e.g. changing the whole population from not being on a statin to being on a statin. If the outcome studied was continuous, the two analyses would give the same result. However, the outcome is a dichotomous outcome, so the two estimations are not the same, and the population average usually is slightly reduced in magnitude compared to the individual average. The two estimates will approach each other for dichotomous outcomes that are very rare. But

this study uses very common outcomes as about 70% of the population were on a statin so the results of the two methods will be more divergent from each other as is seen.

4.5 Strengths and Limitations

There are many strengths associated with this study over previous studies. This study shows the effectiveness DSME provided through DECs in real world conditions in a population by using the databases of the Ministry of Health and Long Term Care. RCTs show the efficacy of diabetes education only in selected individuals with a specific curriculum in an experimental setting. Because the study used population-based data, the sample size is much larger than experimental studies, and there is no selection bias, loss to follow up or missing data. The use of population databases insures inclusion of all areas of the population including rural and ethnic minorities that may be missed in smaller studies of selected populations. As it was performed in Canada with universal health coverage including drug benefits covered by the ODB to those 65 years and older, there are no financial barriers to care as would be seen in other jurisdictions. Also it is unlikely people would have access to these services that are not captured in the databases.

There are limitations associated with this study. As with all observational cohort studies, unmeasured and unknown confounders may be present. Although statistical techniques were used to adjust for these confounders, they cannot adjust for all possible confounders and unobserved variables and this problem cannot be eliminated in an observational study no matter which analysis method is used. It is non-experimental. Sampling and measurement errors can affect the results. As it only uses administrative data there are issues with data validity. Potentially useful data is also missing as it is not

captured by these databases. The generalizability is limited to the over 65 population as prescription data is not available for younger patients.

As this is an observational study the general limitations of all observational studies apply. Since it is non-experimental, sampling and measurement errors can affect the results. This study examines DEC attendance and quality of care outcomes but confounding by other explanations can limit inferences on causality. Although statistical techniques were used to adjust for these confounders, they cannot adjust for all possible confounders or unobserved variables and this problem cannot be eliminated in an observational study no matter which analysis method is used.

The cohort of patients was linked through large health care databases of the Ontario Ministry of Health and Long Term Care permitting measurement of many demographic and clinical predictor variables. However, other potentially important demographic factors that might be associated medication and health care utilization after DEC attendance could not be measured from population-level data, such as health literacy, education level, and language proficiency. Other immeasurable or unknown confounders may exist in the relationship between DEC attendance and medication use, such as patients who are more health conscious or more motivated may be more likely to attend diabetes education and to perform self-care activities, including using the recommended medication, glucose monitoring and attending eye care. These are limitations of an observational cohort study and would not be present in an interventional trail such as a RCT.

The database could only be used to tell whether prescriptions were filled, not if they were used appropriately or used at all. It also cannot measure patients who were appropriately offered a prescription and refused it or took the prescription and did not fill it. The outcome of prescriptions filled for a medication does not equate as medication compliance as many filled prescriptions may go unused from non-compliance. It also does not capture those who could not tolerate the medication and discontinued it. Unfortunately only information for medications in the elderly is available through ODP, as only medication costs for those 65 years of age and older or of low income status is covered by the program. Therefore the ability to apply these results to the general adult population is uncertain.

The appropriateness of medication use also cannot be assessed with administrative data. It is assumed that most seniors with diabetes would require statins, glucose lowering medications, and antihypertensive medications based on risk factor prevalence in this population. However, since no data is present on lipid levels, glycemic control, or blood pressure, the difference might also reflect different needs and appropriateness rather than quality of care improvements related to DEC attendance. The indications for treatment are also not available. Patients who filled a prescription for a beta-blocker for angina or an ACE inhibitor for proteinuria would both be classified as receiving antihypertensive treatment.

The influence of the variability between the curricula of diabetes education programs could not be evaluated as this data were not available. The variability may not be significant as there is a Standards Recognition Program for diabetes education that has

been developed by the Canadian Diabetes Association and each program must adhere to government-mandated standards on curriculum, staffing and access of the Ontario Ministry of Health and Long Term Care. This study looked at the effect of attendance at formal DSME programs but other sources of education such as delivered by an individual nurse working with a primary care physician, or by a pharmacist are not captured by this study. DEC attendance is known for only one year, with no data in the preceding years from which the effect may still be present. DEC attendance was defined as at least one visit to the DEC. If patients attended the DEC multiple times this information was not captured in this study and therefore the effect multiple visits may have had on the outcomes is unknown. Despite this limitation the results were still significant.

This study relied on administrative data that was collected for reasons other than research, which may lead to misclassification and compromise validity. The ODD has a sensitivity of 86% and a specificity of 97% with a positive predictive value of 80% (Hux *et al*., 2002) so only a small proportion may be misclassified. DINs have been shown to have good prediction comorbidity in terms of health care costs and visits over the next year but are not the best comorbidity score to predict mortality (Perkins *et al.,* 2004). Reasons for hospital and emergency room visits may be misclassified or entered as another presenting complaint when hypoglycaemia, hyperglycemia, coronary or cerebrovascular disease may also be present. Visits to specialists and primary care physicians are based on fee for service billing and will miss physician visits to physicians paid by alternative funding plans. Diabetes specialist care is extracted from the OHIP database as visits to an endocrinologist or internist but visits to these specialists may be

for other health issues unrelated to diabetes. Also, other physicians such as primary care physicians who focus on diabetes and provide specialized diabetes care would be missed.

As this study uses administrative data only, much clinical information is missing. As the ODD does not distinguish between types of diabetes we could not compare medication dispensation and healthcare utilization between type 1 and type 2 diabetes, but in this age group assume it is a majority of type 2 diabetes. Unfortunately, as laboratory data is not linked electronically in Ontario, we have no data on if the metabolic targets are reached in this study population or if an effect is seen with DEC attendance. Although we were able to capture health care utilization and coronary and cerebrovascular disease we were not able to capture whether blood pressure targets were met. We could measure receiving eye care but not incidence of retinopathy.

As prescription data is only available for the population aged 65 and older, the generalizability of this study is unknown in the younger population. This study was conducted in Ontario. However, the practice of diabetes educators across Canada is similar due to the guidelines set out by the Canadian Diabetes Association and likely similar to other countries. Therefore, these results are likely generalizable to areas outside Ontario. The short follow up period of this study also limits generalizability as it shows association in short term only. The change seen in the 6 months and 1 year after DEC attendance does not mean the effect will still be present in 5 years.

4.6 Conclusions

Patients in routine clinical care who attended DECs had a statistically significant greater filling of prescriptions for cardiovascular risk reduction, prescriptions for diabetes treatments, and visits for retinopathy screening than those who did not attend. DECs educate attendees on the self-management of diabetes and its complications which includes the importance of lipid management, glycemic and blood pressure control, and retinopathy screening. Those patients aware of the necessity of medications and retinopathy screening for the management of diabetes and its complications are more likely to accept or seek a prescription or appointment for eye care which could lead to an increase in drug dispensation and ophthalmology/optometry visits in DEC attendees.

This study supports that DECs improve medication dispensation and retinopathy screening in the elderly which lends support to the importance of DECs as a part of complete diabetes care and the funding of DECs as an important part of Ontario Diabetes Strategy. More research is required to assess if the improvements in medication dispensation and retinopathy screening seen leads to improvements in glycemic and metabolic control, quality of life, and reduction in diabetes related complications and mortality.

The study examined the real world effect of DSME on improving the quality of care through prescription drug dispensation and retinopathy screening in the elderly in Ontario at a population level in a longitudinal cohort. By logistic regression, DEC attendance was associated with filling prescriptions for statins in the 6 months following attendance. DEC attendance was also associated with the dispensation of glucose lowering medications, antihypertensive medications, ACE inhibitors/ARBs, and glucose

monitoring strips in the six months following attendance and utilization of ophthalmology/optometry in the one year following attendance. The propensity score matched analysis also showed an association of DEC attendance with dispensation of these medications except antihypertensive medications in the 6 months following attendance and utilization of ophthalmology/ optometry in the year following attendance. Although the propensity matched cohort attenuated the results seen with logistic regression, it may provide a better controlled analysis as all of the outcomes used to demonstrate the specificity of the response to DEC attendance of the diabetes related outcomes were not statistically significant. These findings corroborate that the benefits of DSME found in randomized trials, in carefully selected patients under experimental conditions, can be generalized to routine clinical care at a population level.

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Appendix

Cohort Dataset Creation Plan

Name and Number of Study:	Diabetes Education Center Attendance and effect on medication utilization in the elderly in Ontario # 251.261
Contacts	Baiju Shah (supervisor), Cathy Murray (student)
PIA Approved?	Yes
DCP update history	V1
Short Description of Research Question	1. To determine if diabetes education centre attendance is associated with changes in the rates of statin utilization in the over 65 population in routine clinical care in Ontario. 2. To determine if diabetes education centre attendance is associated with blood glucose monitoring, hypoglycemic and antihypertensive medication utilization and retinopathy screening in the over 65 population in routine clinical care in Ontario.
List of Datasets Used	DEC database, ODB, RPDB, OHIP, ODD

Defining the Cohort

Index Event	In ODD with diagdate on or before Jan 1, 2005 Alive until Dec 31, 2007 Age 65 or greater on or before Jan 1, 2005
Exclusions (In order)	No valid Ontario postal code

Variable Definitions

Main Exposure or Risk Factor	Diabetes education center attendance in 2006
Index date	For subjects who attended a DEC, index date = earliest date of attendance For subjects who did not attend a DEC, index date = randomly assigned following the same distribution of index dates as seen in attendees.
Baseline Characteristics	1) Age at index date 2) Gender 3) LHIN of residence at index date 4) Low income flag in ODB – based on all prescriptions from Jan2005 to index date 5) Duration of diabetes at index date: (identified via ODD) -Diagnosis→ 1 to <2 years → 2 to <5 years → ≥ 5 years

	6) Comorbidity –number of unique DINs in the 1 year prior to index date
	7) Healthcare utilization =number of visits to a primary care physician one year prior to index date: from OHIP, where the physician's main specialty in IPDB = "GP/FP" or "F.P/EMERGENCY MEDICINE" or "COMMUNITY MEDICINE"; location = office, LTC or home with %ohip_location. Only one claim per physician per day.
	0 visits
	1-2 visits
	3-6 visits
	7-12 visits
	≥13 visits
	8) Diabetes specialist care- at least one visit in the year prior to index date where the physician's mainspecialty in IPDB = "internal medicine" or "endocrinology" and location="office" "LTC" or "home" with %ohiplocation
	9) Cardiology- at least one visit in the year prior to index date where the physician's mainspecialty in IPDB = "cardiology" and location="office" "LTC" or "home" with %ohiplocation
	10)Nephrology- at least one visit in the year prior to index date where the physician's mainspecialty in IPDB = "nephrology" and location="office" "LTC" or "home" with %ohiplocation
	11)hypoglycemia or hyperglycemia = hospital admission/ER visit for hypoglycemia or hyperglycemia on year prior to index date (see below)
	12) hospital admission = number of days in hospital during the one year prior to index date. (Do not double-count overlapping hospital admissions in the DAD.) Log transform days+1.
	13) History of previous coronary and cerebrovascular disease in the 5 years before index date (see below)
Other variables	1) prescriptions filled for statins in the 6 months before index date
	2) prescriptions filled for blood glucose monitoring strips in the 6 months before index date
	3) prescriptions filled for antihypertensive medications in the 6 months before index date
	4) prescriptions filled for ACEIs/ARBs in the 6 months before index date
	5) prescriptions filled for glucose lowering medications in the 6 months before index date
	6) Prescriptions filled for proton pump inhibitors in the 6 months before index date
	7) prescriptions filled for levothyroxine in the 6 months before index date
	8) visits to ophthalmology or optometry in the 1 year before index date
	9) visits to ENT in the 1 year before index date
Outcome Definitions	Primary outcome prescriptions filled for statins in the 6 months after index date Secondary outcomes 1) prescriptions filled for blood glucose monitoring strips in the 6 months after index date

	2) prescriptions filled for antihypertensive medications in the 6 months after index date 3) prescriptions filled for ACEIs/ARBs in the 6 months after index date 4) prescriptions filled for glucose lowering medications in the 6 months after index date 5) Prescriptions filled for PPIs in the 6 months after index date 6) prescriptions filled for levothyroxine in the 6 months after index date 7) visits to ophthalmology or optometry in the 1 year after index date 8) visits to ENT in the 1 year after index date

Codes

Hypo/hyperglycemia	ICD-10 codes of interest are: E100, E101, E1063, E110, E111, E1163, E130, E131, E1363, E140, E141, E1463, E15, E160, E161, E162 CIHI record with these ICD-10 codes for dx10codes with accompanying dxtype = admitdx NACRS record in FY 2005: these ICD-10 codes for dx10code with accompanying dxprex = R *and* triage ≤ 4 *and* visittype ≠ 3 NACRS record in FY 2006 or 2007: these ICD-10 codes for visitreason *and* triage ≤ 4 *and* visittype ≠ 3
Previous coronary/ cerebrovascular disease	-Acute myocardial infarction: dxcode 410 or dx10code I21 (dxtype=all) -Stroke: dxcodes 431, 433, 434, 436 or dx10codes I61, I63, I64, G450 to G453 (dxtype=all) -History of coronary revascularization: CCP codes 48.02, 48.03, 48.09 or incodes 1IJ50, 1IJ57, 1IJ76, 1IJ80
Statins	subclnam="ANTILIPEMIC: STATINS" or "CALCIUM BLOCKERS ANTILIPEMIC COMBINATIONS"
Blood glucose monitoring strips	drugname = 'DIAGNOSTIC AGENT – DIABETES' and routeadm =: 'STRIP'
Antihypertensive medications	drugname in: acebutolol, aliskiren, amiloride, amlodipine, atenolol, benazepril, bendroflumethiazide, bisoprolol, candesartan, captopril, carvedilol, chlorothiazide, chlorthalidone, cilazapril, clonidine, debrisoquine, diltiazem, doxazosin, enalapril, eprosartan, felodipine, fosinopril, guanethidine, hydralazine, hydrochlorothiazide, indapamide, irbesartan, isradipine, labetalol, lisinopril, losartan, methyclothiazide, methyldopa, metoprolol, minoxidil, nadolol, nicardipine, nifedipine, oxprenolol, perindopril, phenoxybenzamine, pindolol, prazosin, propranolol, quinapril, ramipril, reserpine, spironolactone, telmisartan, terazosin, timolol, trandolapril, triamterene, valsartan, verapamil Include only tablet, capsule or kit forms of these drugs, not IV, ophthalmic,

	topical, etc.
ACEIs/ARBs	subclnam = “ACE INHIBITORS” or “ACE INHIBITORS COMBINATION” or “ANGIOTENSIN II ANTAGONIST” or “ANGIOTENSIN II COMBINATION”
Glucose lowering medications	drugname in: (‘INSULIN’ ‘ACARBOSE’ ‘ACETOHEXAMIDE’ ‘CHLORPROPAMIDE’ ‘GLICLAZIDE’ ‘GLIMEPIRIDE’ ‘GLIPIZIDE’ ‘GLYBURIDE’ ‘METFORMIN’ ‘NATEGLINIDE’ ‘PIOGLITAZONE’ ‘REPAGLINIDE’ ‘ROSIGLITAZONE’ ‘SITAGLIPTIN’ ‘TOLBUTAMIDE’)
Proton pump inhibitors	subclnam="PROTON PUMP INHIBITORS"
Levothyroxine	drugname =: “LEVOTHYROXINE”
Ophthalmology or optometry	OHIP feecodes = A233 to A240, C233 to C236, V401, V402, V404 to V409, V450, V451 OHIP feecodes = K065, K066 where spec=23 NOTE need to include spec=all in %getohip to include optometrists
ENT	At least one visit where the physician’s mainspecialty in IPDB = “OTOLARYNGOLOGY” and location=”office” “LTC” or “phone” with %ohiplocation

Outline of Analysis Plan

Compare baseline characteristics of DEC attendees and non attendees (with p-values and standard differences). Please run %dinexplore on all DIN lists.

Logistic regression

Compare the number of prescription filled for statins in the 6 months after index date using logistic regression adjusting for pre-index utilization of statins and all 13 baseline variables.

Repeat the above analysis for antihypertensive medications, ACIs/ARBs, glucose-lowering medications, blood glucose monitoring supplies, proton pump inhibitors and levothyroxine at 6 months, and ophthalmology/optometry and ENT at 1 year post index date. In each case, adjust for pre-index utilization for that category only.

Matching using Propensity score

Construct a propensity score for DEC utilization, using the following predictor variables: the 13 baseline variables, and the 9 “other variables” (pre-index utilization). Verify balance of covariates between PS quintiles; add interaction or nonlinear terms as needed to achieve balance. Greedy match DEC attendees and non-attendees on the logit of the PS, using calipers with a width of 0.6 x the pooled standard deviation. Compare the proportion of people with prescriptions filled for statins in the 6 months after index date using McNemar’s test.

Repeat the above analysis for all secondary outcomes.