University of Alberta

Telemedicine in Chronic Disease Management

by

Arash Ehteshami Afshar

A thesis submitted to the Faculty of Graduate Studies and Research
In partial fulfillment of the requirements for the degree of

Master of Science
in
Clinical Epidemiology

Department of Public Health Sciences

Fall 2013
Edmonton, Alberta

I would like to dedicate this thesis to Neda, my lovely wife and best friend for her endless love. With her my life is a beautiful journey; always by my side every step of the way.

I also dedicate this thesis to my loving parents, Amin and Hoda, for their infinite support through my life. I learned from them the true meaning of unconditional love

Abstract

Telemedicine is a promising but unproven tool for improving the quality of chronic disease care. The aim of this research is to investigate the potential of telemedicine for the care of patients with chronic diseases in Canada.

We did a systematic review and meta-analysis of telemedicine for management of diabetes. In pooled analysis, mean A1C level in the telemedicine group was significantly lower than those of patients in the usual care group (weighted mean difference (WMD) -0.49, 95% CI -0.64, -0.35, $p<0.00001$) with evidence of statistical heterogeneity between studies ($I^2 = 65\%$).

We also described the results of a survey that was used to demonstrate the willingness of 1849 patients to use telemedicine. The result showed that 65.1% (CI 61.4, 68.6) of Western Canadians with self-reported chronic disease are willing to use telehealth.

Finally, a clinical trial proposal was presented for a study using telemedicine for management of diabetic nephropathy.

Acknowledgements

First of all, I would like to express my sincere gratitude to my supervisor Dr. Marcello Tonelli for his continuous support throughout my graduate study and completing my thesis. Working with him enhanced my understanding of medical research in so many aspects. I could not have imagined having a better supervisor and mentor.

Also, I would like to thank the rest of my thesis committee: Dr. Scott Klarenbach, Dr. Neesh Pannu and Dr. Dean Eurich for their encouragement, insightful comments and valuable feedbacks.

I would like to thank The Kidney Health Research Group people who create such a good atmosphere for me to complete my studies and research. Especially I would like to thank Natasha Wiebe for her contribution in analysis of the data.

I would like to thank Alberta Kidney Disease Network (AKDN) and Interdisciplinary Chronic Disease Collaboration (ICDC) for the opportunity of studying clinical epidemiology in the School of Public Health in the University of Alberta.

Table of Contents

List of Tables

Page

List of Figures

Page

List of Abbreviation

A1C	Glycated hemoglobin
ADA	American Diabetes Association
AGE	Advanced Glycation End product
BCPCHC	Barriers to Care for People with Chronic Health Conditions
BMI	Body Mass Index
BP	Blood Pressure
CATI	Computer Assisted Telephone Interviews
CCHS	Canadian Community Health Survey
CDA	Canadian Diabetes Association
CHF	Congestive Heart Failure
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CRF	Chronic Kidney failure
CVD	Cerebrovascular Disease
DCCT	The Diabetes Control and Complications Trial
DM	Diabetes Mellitus
ESRD	End-Stage Renal Disease
HbA1C	A1C
ICDC	The Interdisciplinary Chronic Disease Collaboration
IT	Information Technologies
NASA	National Aeronautics and Space Administration
REENAL	Reduction of Endpoints in Non-insulin dependent diabetes mellitus with the Angiotensin II Antagonist Losartan
RCTs	randomized controlled trials
SES	Socioeconomic Status
SMS	Short Message service
UKPDS	United Kingdom Prospective Diabetes Study

CHAPTER 1.INTRODUCTION

1.1 Chapter introduction

The purpose of this chapter is to provide some general information and relevant background about diabetes and its management, as well as barriers to optimal diabetes care. This is followed by a brief history and description of telemedicine and its possibilities for chronic disease management. Next, I provide an overview of the other topics that are discussed in this research paper and the structure of the thesis as a whole.

1.2 Diabetes mellitus

1.2.1 Epidemiological and economic burden of diabetes mellitus

Diabetes mellitus is one of the most common chronic diseases and a major public health issue in Canada and elsewhere in the world. Over the past three decades, the prevalence of diabetes has more than doubled worldwide[1] and is projected to rise further from 171 million in 2000 to 366 million in 2030[2]. Currently, about two million Canadians suffer from diabetes. The number of people with diabetes is expected to nearly double by 2020, when about 10% (or 3.7 million) of Canadians are expected to have the condition. The epidemics of obesity, the low level of physical activity among young people and greater consumption of simple sugars and calorie-dense foods may be major contributors to this increase[3].

Diabetes patients' medical costs are up to three times higher than those without diabetes. A person with diabetes can face direct costs for medication and diabetes supplies ranging from $1,000 to $15,000 per year[4]. The economic burden of diabetes had an annual cost of $12.2 billion and accounts for 3.5% of Canadian public healthcare spending in 2009, and will continue to grow with the increasing incidence of the disease[5]. The American Diabetic Association cost analysis in 2009 showed that much of the direct medical cost of diabetes was attributable to long-term complications and comorbidities requiring hospital or nursing home

care[6]. Also, massive amounts of money are spent on research and marketing for new products, making diabetes an even more expensive disease for health systems in the future.

1.2.2 Types and definitions

Diabetes mellitus, or simply diabetes, is a chronic disease that occurs when the body is either unable to sufficiently produce or properly use insulin. The greatest discovery concerning the pathophysiology and management of diabetes occurred in July of 1921, when Frederick Banting, a young surgeon, and Charles Best, a medical student, from the University of Toronto, were able to extract insulin from the pancreas of a dog. One year later, the first insulin extract was administered successfully to L. Thomson, a young diabetic patient[7]. Insulin is a hormone that is produced by the pancreas gland, and is essential for maintaining blood glucose level and regulating carbohydrate and fat metabolism.

Although both type 1 and type 2 diabetes are characterized by the body's inability to maintain appropriate glycemic levels, they may differ in their risk factors and pathophysiology.

Type 1 diabetes typically arises in people under the age of 40 and once was known as "juvenile diabetes" or also referred to as "insulin-dependent diabetes mellitus". Type 1 diabetes is an autoimmune disease in which the immune system destroys the insulin-producing cells of the pancreas, thereby leaving the individual dependent on an external source of insulin for life.

Type 2 diabetes was previously referred to as adult-onset or non-insulin-dependent diabetes. Its risk is higher among people who are overweight, physically inactive and of certain ethnic populations or having positive family history of type 2 diabetes. It progresses from an early asymptomatic stage with insulin resistance and/or insufficient insulin production to frank diabetes requiring pharmacological intervention[8].

1.2.3 Prevention of diabetes

Primary prevention measures including lifestyle intervention has been shown to prevent or postpone the development of type 2 diabetes. Several trials confirmed this fact, with relative risk reduction ranging from 30% to 60% and absolute risk reduction of approximately 15–20% during active intervention[9, 10]. These interventions are likely to be cost effective if implemented on a population scale. Some experts also recommend screening for Type 2 diabetes in high risk individuals for early diagnosis and treatment[11], although this recommendation is not universal. At present, in the absence of evidence for interventions to prevent or delay type 1 diabetes, no recommendations for prevention or screening for type 1 diabetes has been made.

1.2.4 Complications of diabetes

People with diabetes have twice the risk of death as someone of the same age without diabetes. The primary cause of death in individuals with diabetes is not from diabetes itself but from the complications of the disease. Diabetes is the leading cause of new blindness in people 20 to 74 years of age and the leading cause of end-stage renal disease (ESRD). The risk of cardiovascular complications is increased by two to six fold in subjects with diabetes. Approximately, 60% of diabetic patients are affected by neuropathy. Because of accelerated lower-extremity arterial disease and neuropathy, diabetes mellitus accounts for 50% of all non-traumatic related amputations in the United States. Overall life expectancy is about 7 to 10 years shorter than for people without diabetes mellitus because of increased mortality from diabetic complications[12].

After developing diabetes, chronic elevation of blood glucose (hyperglycemia) leads to development of long-term complications including kidney disease, cardiovascular disease, limb amputation, stroke, blindness and premature death in individuals with diabetes.

Although hyperglycemia has been considered the most important factor in development of diabetic complications, the mechanisms involved remain uncertain. There are several theories as to how chronic hyperglycemia leads to micro or macro-vascular disease in diabetes, including the advanced glycation end product (AGE) theory. AGEs form on proteins, lipids, nucleic acids and interfere with their structures, functions and are accompanied by increased free radical activity that contributes towards the molecular damage in diabetes[13]. Some recent research suggested that genetic factors[14] or continuing effects of the autoimmune disease in type 1 diabetics, which initially destroyed the insulin producing cells of the pancreas [15] might also play a role in pathogenesis of diabetic complications as well. However the magnitude of this putative effect and its clinical implications remain to be discovered in future.

1.2.5 Management of diabetes

Large prospective clinical studies have shown a strong relationship between hyperglycemia and diabetic microvascular complications in both type 1 diabetes and type 2 diabetes[16-18]. Hyperglycemia also plays a role in the pathogenesis of macrovascular complications[19]. Hyperglycemia is a primary factor in the development of diabetes complications and restoring blood glucose level to as close to a normal state as possible is essential in management of diabetes. Decreases in average blood glucose have a profound effect on preventing complications of diabetes in both type 1[20] and type 2 diabetes[18]. A1C (see section 2.1.1) serves as an index of long-term glucose control.

To achieve good glucose control,, individuals with type 1 diabetes require lifelong insulin replacement therapy. In patients with type 2 diabetes, dietary modifications and exercise and oral hypoglycemic agents can also be used. Dramatic advances in the pharmacologic agents and monitoring technology available for the treatment of diabetes have made it possible to lower glucose levels safely to the near-normal range in patients. A 10-year follow-up of the UKPDS cohort demonstrated that the relative benefit of intensive management of

glucose demonstrated statistically significant benefits on cardiovascular end points and total mortality [21]. Meta-analysis of cardiovascular outcomes in randomized trials suggested that an average A1C reduction of 0.9% correlates with a 17% reduction in nonfatal MI and a 15% reduction in coronary heart disease[22].

Beside regular monitoring and controlling of blood glucose; controlling of blood pressure and cholesterol levels and early detection and management of diabetes complication are effective measures of diabetes care are essential in management of diabetes and are all supported by evidence-based clinical practice guidelines. The RENAAL study (Reduction of Endpoints in Non-insulin dependent diabetes mellitus with the Angiotensin II Antagonist Losartan) demonstrated that independent risk factors for the development of ESRD were albuminuria, increased serum creatinine, hypoalbuminemia. Systolic BP is also an important factor in determining ESRD risk particularly in patients with type 2 diabetes. In RENAAL, the presence/absence of diabetes explained 12 to 18% of the change in risk score from baseline[23].

A comprehensive review of all aspects of diabetes management and care is beyond the scope of this thesis. In the next section, we describe some key population-level barriers to receiving appropriate diabetes care that can be addressed by use of novel methods like use of telemedicine.

1.2.6 Barriers to standard diabetes care

Optimal metabolic control is essential to prevent and reduce diabetic complications. However, despite significant advances in treatment of diabetes, inadequate metabolic control continues to be very common[24, 25] , especially for those in underserved areas[26] and among all racial/ethnic groups[27]. During 2007–2010, an estimated 12.9% of U.S. adults with self-reported diagnosed diabetes exhibited poor glycemic control[28] and, approximately 1 in 3 Canadians

with diabetes reports not having undergone recommended tests for effective diabetes care[29].

Results from a national sample of 733 adults with type 2 diabetes in the United States showed high rates of health care access, utilization, screening for diabetes complications and treatment of hyperglycemia, hypertension, and dyslipidemia in type 2 diabetes. However, only 58% of these patients had A1C < 7%. Thus, barriers to diabetes care may not be entirely about access to any care (regardless of quality), but rather about access to high quality care[30].

Diabetes is a complex disease and the barriers to its management are multifactorial. The barriers to optimal diabetic care can be related to either personal characteristics, provider factors or health care system-based issues.

Several personal factors may contribute to optimal diabetes management including adherence to self-management. Self-management is defined as the personal actions to manage diabetes, its treatment, and prevent disease progression. Diabetes is a chronic disease requiring long-term treatment and a high quality care in the ambulatory setting, so efficient patient self-management is crucial[31]. Self-management in diabetes began in the 1970s with introduction of personal glucose monitors, which allowed patients to test their own blood glucose at home without supervision [32]. Better adherence to a self-care regimen can reduce mortality and disability, improve quality of life, and reduce health care costs [33-35]. It has been widely assumed that the benefits of self-management stem from the effect of putting patients in a situation in which they are in control of their own therapy.

Another personal factor is socioeconomic status (SES) of the patient. Several studies have reported that diabetic patients of lower socioeconomic status are less likely to receive specialist care [36] or to use preventive health care services [36, 37]. These patients have worse complication risk factor profiles, [38] and

glycemic control[39]. Other personal factors include ethnicity[27], attitudes and beliefs[40], knowledge[41], and presence of comorbidities[42] – which have all have been shown to be potential barriers to optimal diabetic care.

Optimal glycemic control is challenging and involves ongoing monitoring, often by a team of health care providers [47]. The gap between ideal evidence-based care and the actual care which is provided by health care professionals is not surprising in view of the complex nature of diabetes management, often needing coordinated services of primary-care physicians, allied health practitioners, and subspecialists. However, a report from the United Sates demonstrates that access to specialist care may be essential for preventive service utilization and improved glycemic control [36] . Good communication between patient and provider predicts better diabetes self-care and even better diabetes outcomes [43]. In a study involving 367 patients with types 1 and 2 diabetes in a primary care setting, poor communication was associated with poor treatment adherence [44].

In United States over two thirds of patients diagnosed with type 2 diabetes receive diabetes care exclusively from primary care providers [45]. A study in Québec reported that specialist consultation rates were statistically lower in rural areas compared to urban areas. In addition, morbidity rates were significantly higher for atherosclerosis and diabetes in small towns and rural areas[46].

A number of studies investigated barriers to diabetes care, and focused on health care system factors including the cost of and access to health care. Due to the nature of universal health care system in Canada, cost is a less important barrier than in the United States. In contrast, low population density in Canada makes travel time and distance important barriers of receiving optimal care for chronic conditions of patients living in rural and remote areas.[47, 48] In Canada approximately 1 in every 5 person lives in a rural area -- and health care providers are not equally distributed in urban and rural/remote communities across the provinces. Residents of remote areas face issues of distance and adequate

transportation when seeking health care, and therefore may have fewer treatment choices [49]. Rural residents also experience increased rates of chronic disease including diabetes[50]. After adjusting for social, demographic and clinical factors, a study in the United States showed lower insulin usage among diabetic adults with higher driving distance to primary care facilities[51].

With the high prevalence of diabetes and effectiveness of its management on decreasing related mortality and morbidity, it is reasonable for healthcare systems to improve diabetes management and decrease barriers to optimal care by novel methods of care accessible to all patients, especially those in underserved areas. Researchers suggest that new methods like reminder systems and tools such as checklists can improve diabetes care [52, 53]. For example, Ziemer and colleagues conducted a 3 year trial to determine whether sending patient-specific recommendations to providers at each visit (along with performance improvement feedback every two weeks) will lead to better process-based and clinical diabetes outcomes in a primary care setting as compared to a control group. This trial showed that giving feedback on performance to providers contributed independently to fall in A1C ($P<0.001$) and intensification of care ($P<0.001$) [54].

1.3 Telemedicine

Telemedicine is one of the most potentially revolutionary technologies to be integrated into the healthcare system. In the literature there are several definitions of telemedicine that have largely been modified according to advancements in technologies. Telemedicine (literally, meaning “healing at a distance” from Latin “medicus” and Greek “tele”) was first defined as the practice of medicine without the usual physician-patient confrontation, but instead via an interactive audio-video communication system in 1975, by the American Thomas Bird [55] . Scannell provided a more comprehensive definition in 1995:

“Telemedicine is the use of telecommunications for medical diagnosis and patient care. It involves the use of telecommunications technology as a medium for the

provision of medical services to sites that are at a distance from the provider. The concept encompasses everything from the use of standard telephone services through high speed, wide bandwidth transmission of digitized signals in conjunction with computers, fibre-optic communications and satellites and other sophisticated peripheral equipment and software[56].”

The World Health Organization has adopted the following definition:

“The delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities” [57].

Currently there is no one definitive definition of telemedicine. One 2007 study found 104 peer-reviewed definitions of the term[58]. The many definitions highlight that telemedicine is constantly evolving to incorporate new advancements in technology -- and adapts to changing health care needs over time.

Some scholars differentiate telemedicine from telehealth with the former restricted to service delivery by physicians only, and the latter signifying services provided by all the health professionals in general. However, for the purpose of this thesis, the terms telemedicine and telehealth are used interchangeably.

The first telemedicine experiments date back to the early 1960 when NASA incorporated this technology into their space program to monitor the astronauts[59]. After that, NASA began trial runs of its Space Technology Applied to Rural Papago Advanced Health Care (STARPAHC) program to help people living in remote locations with little or no medical services[60]. Later in

1977, Canada's Memorial University of Newfoundland participated in a Canadian Space Program for distance education and medical care, using the joint Canadian/United States Hermes satellite.

In early years, the equipment was expensive and rather burdensome; as the cost and size of the equipment has decreased, and the technical quality has improved, telemedicine has become much more feasible to use in health care systems [61]. Today, telemedicine is no longer limited to Indian remote villages or orbiting space shuttles. Health workers have now grasped the impact and possibilities information and communication technologies could have on health systems and potentially health outcomes – serving as a tool to improve access, reduce costs and minimize inequalities by residence location. The literature suggests that there has been a rapid expansion of telemedicine in North America[56], and in Europe[62].

Several systematic reviews found different types of telemedicine interventions to be therapeutically effective. These include remote monitoring for chronic heart failure [63] ; home telemonitoring of respiratory conditions[64];web and computer based smoking cessation programs[65]; telehealth approaches for secondary prevention of coronary heart disease[66]; telepsychiatry [67]; virtual reality exposure therapy for anxiety disorders [68]; home telehealth for diabetes, heart disease and chronic obstructive pulmonary disease [69].

Some studies have suggested that telemedicine is cost-effective, but few draw firm conclusions. One review found that 91% of the studies showed telemedicine to be cost-effective, in that it reduced hospitalization, improved patient compliance, satisfaction and quality of life [70]. Telemedicine was also found to be cost-effective for chronic disease management, but the authors cautioned that studies were few and heterogeneous[71]. Telemedicine could reduce travel time and hospital admissions compared to usual care [72].

There are several countries that are currently initiating plans for the development of telehealth at a large scale or already have a sustainable telemedicine program implemented. For instance, Scotland, Denmark, Spain and the United States have large scale telemedicine programs.

Compared with many countries the implementation of telemedicine is relatively far advanced in Scotland. Around 19% of those aged 65 and over have community alarm systems, 3.5% use more sophisticated telemedicine packages. Currently the Scottish Centre for Telehealth (SCT) is focused on four clinical areas – Stroke, Pediatrics, COPD and Mental Health[73].

Denmark has a long history in promoting and adopting telemedicine solutions. In cooperation with Odense University Hospital in Denmark a company has developed a "Patient Briefcase", as part of the discharge process from hospital, to assist those suffering from chronic obstructive pulmonary disease (COPD). Additional applications are now being looked into, including expanding to physical rehabilitation, the treatment of heart failure, and other chronic conditions[73].

In Spain, telephone and online consultations are available and are more focused on providing information and medical appointments than on achieving a diagnosis. Catalonia has a hospital-in-the home services educational support to heart failure patients via their television [74]. In Andaluciá an independent living supporting system is one of the largest telemedicine services in Europe. Patients can push an alarm button in their home, and when necessary be provided with emergencies services or health-related information and advice[73].

Kaiser Permanente in the United States, with nearly 9 million health plan members, has adopted telemedicine to improve healthcare across their members. Their system allows healthcare providers to send patient reminders about other aspects of their care. Patients can also access this secure system to email their

doctors, view lab results and order prescriptions. Their programs have focused on simple but effective approaches, for example management of high blood pressure. United States Department of Veteran Affairs has been using this technology broadly for a number of years. Home telehealth is used for long-term health conditions such as diabetes, chronic heart failure, chronic obstructive pulmonary disease (COPD), depression or post-traumatic stress disorder [75].

In 2009, the former President of France, Mr. Sarkozy, declared telemedicine a national priority and in some European countries such as Italy, some insurers give discounts on premiums to members if they agree to be monitored through telemedicine [73].

1.3.1 Telemedicine in Canada

In Canada, approximately 6.7 million people are considered to live in rural areas. For many patients living in rural and isolated regions, getting access to appropriate health care is delayed by long travel, which is exacerbated by difficult weather; high travel costs, accommodations; and by the stress of leaving home and going to an unfamiliar, larger city. These trips for ongoing care such as consultations and follow-ups can be very disruptive to a patient's personal and professional life.

Its vast geography, low population density and high portion of people living in rural areas means that Canada is an excellent place to deploy telemedicine. In fact, Canada is a pioneer in the use of some telemedicine technologies. For example, Canada was a leader in the use of video technology for telehealth[76]. There is presently a remarkably diverse set of clinicians using telemedicine in different Canadian jurisdictions[77]. Some provinces like Ontario and Manitoba have consolidated telemedicine into a centralized provincial program. Others leave telemedicine to regional discretion, with little centralized coordination.

Several examples of how telehealth is used in Canada are listed below:

1) Telehomecare: These telemonitoring solutions provide remote monitoring and transmission of clinical data to a centralized facility for review and action by a care team for the management of chronic diseases.

2) Telepsychiatry: Allows a single psychiatrist to remotely provide patient assessments and a care plan that can be administered by a family physician.

3) Telecrisis: Connects mental health crisis specialists to emergency physicians who are treating patients experiencing a mental health crisis such as a schizophrenic episode or anxiety attack.

4) Telestroke: An emergency service that immediately connects an on-call neurologist to an emergency physician who is treating a stroke patient (in a small community or a rural area). There are fewer Telestroke networks in Canada than the US.

4) Teleophthalmology: Retinal images are captured by primary care providers and forwarded to a retinal specialist or ophthalmologist for review and assessment.

In Canada, About two third of telemedicine clinical activity was generated by a few clinical service areas: Mental Health (which includes addictions, forensic mental health, general mental health services, psychiatry and psychology) (54%), Internal Medicine (15%) and Oncology (13%)[76].

In 2010, Canada had in place more than 5,710 Telehealth systems in at least 1,175 communities. Many of these systems served the 21% of the Canadian population who live in rural or remote areas or being the member of Aboriginal heritage.

Based on Ontario data, the capacity of telehealth programs could increase from the current 187,385/year consults to 1.2 million telehealth consults/year if activity of all telehealth sites below the median were brought up to the current median level. About one-half of these events are projected to be rural consults. This increase in consults would represent a true increase in access to health care for rural Canadians.

1.3.2 Telemedicine in chronic diseases

Besides diabetes, other chronic illnesses, such as COPD, heart failure and hypertension represent a significant burden of disease. Non-communicable diseases accounted for nearly 60% of deaths globally in 2001and almost half of the disease burden in low-and-middle-income countries is now from non-communicable diseases, a rise of 10% in its relative share since 1990[78].

A systematic review of 141 randomized controlled trials (RCTs) on telemedicine in chronic disease management showed that most studies have reported a beneficial effect (n=108); almost none have reported a deleterious effect (n=2); and that there were no apparent differences in the effect of telehealth between the various chronic diseases. However, most studies have been relatively short-term (median duration 6 months)[79].

Five recent systematic reviews on the use of telemedicine in heart failure [63, 80-83] ,one on COPD[84] and one on hypertension[85] showed significant positive pooled estimate of effect in favor of telemedicine. A wide range of outcomes and different approaches have been employed in these studies. However, the majority of the studies reviewed in these systematic reviews have reported beneficial effects as defined by the individual authors.

In summary, telemedicine is still very new and it is not yet being implemented on a large scale. While there is a lot of interest in the implementation of telemedicine, there is little information on exactly what role these type of systems realistically could play, or precisely which services could/should be delivered by a telehealth program. In addition, the clinical benefits that would accrue from wider uptake of telehealth programs remain to be definitively shown.

1.4 Thesis structure

Recently there has been a lot of interest in telemedicine as a method to combat several problems in the healthcare sector, including chronic diseases. The overarching aim of this thesis is to explore the potential benefits of telehealth for management of diabetes, an important chronic disease.

The first chapter has provided baseline information on diabetes and telemedicine. Chapter 2 is a systematic review of literature on the effects of telemedicine for metabolic control of diabetes. Because there is some skepticism that patients will find telehealth acceptable or desirable, chapter 3 describes a survey that was used to explore the willingness of Canadian patients to use telemedicine for management of their diabetes and three other chronic diseases. Chapter 4 describes the protocol for a hypothetical clinical trial that would study the clinical benefits of a specific form of telemedicine for the management of diabetes in patients with chronic kidney disease. Finally, chapter 5 summarizes the results of this thesis.

1. References:

1. Chen, L., D.J. Magliano, and P.Z. Zimmet, *The worldwide epidemiology of type 2 diabetes mellitus - Present and future perspectives.* Nature Reviews Endocrinology, 2012. **8 (4)**: p. 228-236.
2. Wild, S., et al., *Global Prevalence of Diabetes: Estimates for the year 2000 and projections for 2030.* Diabetes care, 2004. **27 (5)**: p. 1047-1053.
3. Canada, P.H.A.o., *Diabetes in Canada: report from the National Diabetes Surveillance System.* 2009: Ottawa, ON;.
4. *Economic costs of diabetes in the U.S. In 2007.* Diabetes care, 2008. **31**(3): p. 596-615.
5. Association, C.D., *An economic tsunami: the cost of diabetes in Canada*. 2009: Toronto, ON.
6. Herman, W.H., *The economics of diabetes prevention.* Med Clin North Am, 2011. **95**(2): p. 373-84, viii.
7. Karamitsos, D.T., *The story of insulin discovery.* Diabetes Res Clin Pract, 2011. **93 Suppl 1**: p. S2-8.
8. Bhattacharyya, O.K., E.A. Estey, and A.Y. Cheng, *Update on the Canadian Diabetes Association 2008 clinical practice guidelines.* Can Fam Physician, 2009. **55**(1): p. 39-43.
9. Lindstrom, J., et al., *Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS).* Diabetologia, 2012.
10. Gillies, C.L., et al., *Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis.* BMJ, 2007. **334**(7588): p. 299.
11. Forouhi, N.G., et al., *The threshold for diagnosing impaired fasting glucose: a position statement by the European Diabetes Epidemiology Group.* Diabetologia, 2006. **49**(5): p. 822-7.
12. Skyler, J.S., *Diabetic complications. The importance of glucose control.* Endocrinol Metab Clin North Am, 1996. **25**(2): p. 243-54.
13. Ahmed, N., *Advanced glycation endproducts--role in pathology of diabetic complications.* Diabetes Res Clin Pract, 2005. **67**(1): p. 3-21.
14. Tarnow, L., et al., *European rational approach for the genetics of diabetic complications--EURAGEDIC: patient populations and strategy.* Nephrol Dial Transplant, 2008. **23**(1): p. 161-8.
15. Adams, D.D., *Autoimmune destruction of pericytes as the cause of diabetic retinopathy.* Clin Ophthalmol, 2008. **2**(2): p. 295-8.
16. *The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group.* N Engl J Med, 1993. **329**(14): p. 977-86.
17. Genuth, S., *Insights from the diabetes control and complications trial/epidemiology of diabetes interventions and complications study on the use of intensive glycemic treatment to reduce the risk of complications of type 1 diabetes.* Endocr Pract, 2006. **12 Suppl 1**: p. 34-41.
18. *Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group.* Lancet, 1998. **352**(9131): p. 837-53.
19. Krolewski, A.S., et al., *Glycosylated hemoglobin and the risk of microalbuminuria in patients with insulin-dependent diabetes mellitus.* N Engl J Med, 1995. **332**(19): p. 1251-5.
20. *Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group.* J Pediatr, 1994. **125**(2): p. 177-88.

21. Holman, R.R., et al., *10-year follow-up of intensive glucose control in type 2 diabetes.* N Engl J Med, 2008. **359**(15): p. 1577-89.
22. Ray, K.K., et al., *Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials.* Lancet, 2009. **373**(9677): p. 1765-72.
23. Keane, W.F., et al., *Risk scores for predicting outcomes in patients with type 2 diabetes and nephropathy: the RENAAL study.* Clin J Am Soc Nephrol, 2006. **1**(4): p. 761-7.
24. Gomes, M.B., et al., *Prevalence of adults with type 1 diabetes who meet the goals of care in daily clinical practice: a nationwide multicenter study in Brazil.* Diabetes Res Clin Pract, 2012. **97**(1): p. 63-70.
25. Bo, S., P. Cavallo-Perin, and L. Gentile, *Prevalence of patients reaching the targets of good control in normal clinical practice. A cohort-based study in type 2 diabetes.* Diabetes care, 1999. **22**(12): p. 2092.
26. Ziemer, D.C., et al., *Clinical inertia contributes to poor diabetes control in a primary care setting.* Diabetes Educ, 2005. **31**(4): p. 564-71.
27. Saydah, S., et al., *Race and ethnic differences in glycemic control among adults with diagnosed diabetes in the United States.* Ethn Dis, 2007. **17**(3): p. 529-35.
28. Ali, M.K., et al., *Characteristics associated with poor glycemic control among adults with self-reported diagnosed diabetes--National Health and Nutrition Examination Survey, United States, 2007-2010.* MMWR Morb Mortal Wkly Rep, 2012. **61 Suppl**: p. 32-7.
29. Webster, G., P. Sullivan-Taylor, and M. Terner, *Opportunities to improve diabetes prevention and care in Canada.* Healthc Q, 2011. **14**(1): p. 18-21.
30. Harris, M.I., *Health care and health status and outcomes for patients with type 2 diabetes.* Diabetes care, 2000. **23**(6): p. 754-8.
31. King, D.K., et al., *Self-efficacy, problem solving, and social-environmental support are associated with diabetes self-management behaviors.* Diabetes care, 2010. **33**(4): p. 751-3.
32. Aljasem, L.I., et al., *The impact of barriers and self-efficacy on self-care behaviors in type 2 diabetes.* Diabetes Educ, 2001. **27**(3): p. 393-404.
33. Gallagher, E.J., C.M. Viscoli, and R.I. Horwitz, *The relationship of treatment adherence to the risk of death after myocardial infarction in women.* JAMA, 1993. **270**(6): p. 742-4.
34. Horwitz, R.I. and S.M. Horwitz, *Adherence to treatment and health outcomes.* Arch Intern Med, 1993. **153**(16): p. 1863-8.
35. Horwitz, R.I., et al., *Treatment adherence and risk of death after a myocardial infarction.* Lancet, 1990. **336**(8714): p. 542-5.
36. Zgibor, J.C., et al., *The association of diabetes specialist care with health care practices and glycemic control in patients with type 1 diabetes: a cross-sectional analysis from the Pittsburgh epidemiology of diabetes complications study.* Diabetes care, 2000. **23**(4): p. 472-6.
37. Freeborn, D.K., et al., *Health status, socioeconomic status and utilization of outpatient services for members of a prepaid group practice.* Med Care, 1977. **15**(2): p. 115-28.
38. Connolly, V.M. and C.M. Kesson, *Socioeconomic status and clustering of cardiovascular disease risk factors in diabetic patients.* Diabetes care, 1996. **19**(5): p. 419-22.
39. Klein, R., et al., *The relation of socioeconomic factors to the incidence of proliferative diabetic retinopathy and loss of vision.* Ophthalmology, 1994. **101**(1): p. 68-76.
40. Anderson, R.M., M.B. Donnelly, and R.F. Dedrick, *Measuring the attitudes of patients towards diabetes and its treatment.* Patient Educ Couns, 1990. **16**(3): p. 231-45.
41. Persell, S.D., et al., *Relationship of diabetes-specific knowledge to self-management activities, ambulatory preventive care, and metabolic outcomes.* Prev Med, 2004. **39**(4): p. 746-52.
42. Jerant, A.F., M.M. von Friederichs-Fitzwater, and M. Moore, *Patients' perceived barriers to active self-management of chronic conditions.* Patient Educ Couns, 2005. **57**(3): p. 300-7.
43. Schillinger, D., et al., *Closing the loop: physician communication with diabetic patients who have low health literacy.* Arch Intern Med, 2003. **163**(1): p. 83-90.

44. Ciechanowski, P.S., et al., *The patient-provider relationship: attachment theory and adherence to treatment in diabetes.* Am J Psychiatry, 2001. **158**(1): p. 29-35.
45. Shumaker S, S.E., Ockene J, McBee W, *The handbook of health behavior change*. 2004, New York: Springer.
46. Vanasse, A., et al., *Rural-urban disparities in the management and health issues of chronic diseases in Quebec (Canada) in the early 2000s.* Rural Remote Health, 2010. **10**(4): p. 1548.
47. Thompson, S., et al., *Higher mortality among remote compared to rural or urban dwelling hemodialysis patients in the United States.* Kidney Int, 2012. **82**(3): p. 352-9.
48. Rucker, D., et al., *Quality of care and mortality are worse in chronic kidney disease patients living in remote areas.* Kidney Int, 2011. **79**(2): p. 210-7.
49. Mainous, A.G., 3rd, et al., *Race, rural residence, and control of diabetes and hypertension.* Ann Fam Med, 2004. **2**(6): p. 563-8.
50. Assessment), U.S.C.O.o.T., *Health Care in Rural America.*: Washington, D.C.
51. Strauss, K., et al., *Driving distance as a barrier to glycemic control in diabetes.* J Gen Intern Med, 2006. **21**(4): p. 378-80.
52. Eytan, T.A. and H.I. Goldberg, *How effective is the computer-based clinical practice guideline?* Eff Clin Pract, 2001. **4**(1): p. 24-33.
53. Larme, A.C. and J.A. Pugh, *Attitudes of primary care providers toward diabetes: barriers to guideline implementation.* Diabetes care, 1998. **21**(9): p. 1391-6.
54. Ziemer, D.C., et al., *An intervention to overcome clinical inertia and improve diabetes mellitus control in a primary care setting: Improving Primary Care of African Americans with Diabetes (IPCAAD) 8.* Arch Intern Med, 2006. **166**(5): p. 507-13.
55. Strehle, E.M. and N. Shabde, *One hundred years of telemedicine: does this new technology have a place in paediatrics?* Arch Dis Child, 2006. **91**(12): p. 956-9.
56. Scannell K, P.D., Kissman H, *Telemedicine: past, present, future. Current bibliographies in medicine*. 1995, Maryland: National Library of Medicine.
57. WHO, *A health telematics policy in support of WHO's Health-For-All strategy for global health development: report of the WHO group consultation on health telematics*. 1998, World Health Organization
Geneva.
58. Sood, S.P., et al., *Differences in public and private sector adoption of telemedicine: Indian case study for sectoral adoption.* Stud Health Technol Inform, 2007. **130**: p. 257-68.
59. Dardelet, B. *Breaking the wall: The rise of telemedicine as the new collaborative interface* in *Hawaii International Conference on System Sciences*. 1999.
60. Kuszler, P.C., *Telemedicine and integrated health care delivery: compounding malpractice liability.* Am J Law Med, 1999. **25**(2-3): p. 297-326.
61. Doolittle, G.C., A.O. Spaulding, and A.R. Williams, *The decreasing cost of telemedicine and telehealth.* Telemed J E Health, 2011. **17**(9): p. 671-5.
62. R, W., *TeleMed 95: medicine on the superhighway*. 1995, London: Royal Society of Medicine Press.
63. Clark, R.A., et al., *Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis.* BMJ, 2007. **334**(7600): p. 942.
64. Jaana, M., G. Pare, and C. Sicotte, *Home telemonitoring for respiratory conditions: a systematic review.* Am J Manag Care, 2009. **15**(5): p. 313-20.
65. Myung, S.K., et al., *Effects of Web- and computer-based smoking cessation programs: meta-analysis of randomized controlled trials.* Arch Intern Med, 2009. **169**(10): p. 929-37.
66. Neubeck, L., et al., *Telehealth interventions for the secondary prevention of coronary heart disease: a systematic review.* Eur J Cardiovasc Prev Rehabil, 2009. **16**(3): p. 281-9.
67. Loane, M. and R. Wootton, *A review of guidelines and standards for telemedicine.* J Telemed Telecare, 2002. **8**(2): p. 63-71.
68. Opris, D., et al., *Virtual reality exposure therapy in anxiety disorders: a quantitative meta-analysis.* Depress Anxiety, 2012. **29**(2): p. 85-93.

69. Polisena, J., et al., *Home telehealth for chronic obstructive pulmonary disease: a systematic review and meta-analysis.* J Telemed Telecare, 2010. **16**(3): p. 120-7.
70. Rojas, S.V. and M.P. Gagnon, *A systematic review of the key indicators for assessing telehomecare cost-effectiveness.* Telemed J E Health, 2008. **14**(9): p. 896-904.
71. Gaikwad, R. and J. Warren, *The role of home-based information and communications technology interventions in chronic disease management: a systematic literature review.* Health Informatics J, 2009. **15**(2): p. 122-46.
72. Seto, E., *Cost comparison between telemonitoring and usual care of heart failure: a systematic review.* Telemed J E Health, 2008. **14**(7): p. 679-86.
73. Cruickshank, J., *Healthcare without walls: A framework for delivering telehealth at scale*, J. Manning, Editor. 2010. p. 110.
74. Domingo, M., et al., *[Noninvasive remote telemonitoring for ambulatory patients with heart failure: effect on number of hospitalizations, days in hospital, and quality of life. CARME (CAtalan Remote Management Evaluation) study].* Rev Esp Cardiol, 2011. **64**(4): p. 277-85.
75. Darkins, A., et al., *Care Coordination/Home Telehealth: the systematic implementation of health informatics, home telehealth, and disease management to support the care of veteran patients with chronic conditions.* Telemed J E Health, 2008. **14**(10): p. 1118-26.
76. Gartner, I., *Telehealth Benefits and Adoption, Connecting People and Providers Across Canada*. 2011.
77. Forum, C.T., *Canadian Telehealth Report,Based on the 2010-2011 Telehealth Survey* 2011.
78. Lopez, A.D., et al., *Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data.* Lancet, 2006. **367**(9524): p. 1747-57.
79. Wootton, R., *Twenty years of telemedicine in chronic disease management--an evidence synthesis.* J Telemed Telecare, 2012. **18**(4): p. 211-20.
80. Clarke, M., A. Shah, and U. Sharma, *Systematic review of studies on telemonitoring of patients with congestive heart failure: a meta-analysis.* J Telemed Telecare, 2011. **17**(1): p. 7-14.
81. Dang, S., S. Dimmick, and G. Kelkar, *Evaluating the evidence base for the use of home telehealth remote monitoring in elderly with heart failure.* Telemed J E Health, 2009. **15**(8): p. 783-96.
82. Inglis, S.C., et al., *Structured telephone support or telemonitoring programmes for patients with chronic heart failure.* Cochrane Database Syst Rev, 2010(8): p. CD007228.
83. Polisena, J., et al., *Home telemonitoring for congestive heart failure: a systematic review and meta-analysis.* J Telemed Telecare, 2010. **16**(2): p. 68-76.
84. McLean, S., et al., *Telehealthcare for chronic obstructive pulmonary disease.* Cochrane Database Syst Rev, 2011(7): p. CD007718.
85. AbuDagga, A., H.E. Resnick, and M. Alwan, *Impact of blood pressure telemonitoring on hypertension outcomes: a literature review.* Telemed J E Health, 2010. **16**(7): p. 830-8.

CAHPTER 2.EFFECT OF TELEMEDICINE IN MANAGEMENT OF DIABETES

2.1 Chapter introduction

Telemedicine offers potential novel ways to help provide care to people with diabetes -- even for those unable to travel to health care facilities due to large distances or disabilities. Previous reviews describing the benefits of telemedicine for management of diabetes have been published [1-7]. However, this is a rapidly developing field; several potentially important new studies have recently been published, suggesting the value of an updated review. [8-10] We did a systematic review and quantitative synthesis of available randomized controlled trials, comparing the impact of different methods of telemedicine with usual care on A1C and health-related quality of life in people with diabetes (Type 1 and Type 2).

2.1.1 A1C in diabetes

The periodic measurement of glycated hemoglobin for monitoring the degree of control of glucose metabolism in diabetic patients was proposed in 1976 by Anthony Cerami and colleagues[11]. Because plasma glucose concentrations range as a continuum, A1c is better measure of glucose level in time compared to fasting plasma glucose (FPG) or 2-hour plasma glucose (2-hour PG) and is more reproducible . Intra-individual coefficient of variation in one study was 6.4% for the FPG and 16.7% for the 2-hour PG value, compared with less than 2% for A1C[12]. Currently, A1C is the preferred standard for assessing glycated hemoglobin, and laboratories are encouraged to use assay methods for this test that are standardized. It has been suggested that A1C may be thought of as “average blood glucose” in order to assist people to better understand the meaning of the results of this test[13] .

We chose A1C as our primary outcome, because A1C is an accepted measure of long-term serum glucose regulation, and is proportional to average blood glucose concentration over the previous four weeks to three months.

In the normal 120 day lifespan of the red blood cell, glucose molecules react with hemoglobin, forming A1C. Once a hemoglobin molecule is glycated, it remains that way. Therefore, A1C level reflects the average level of glucose to which the cell has been exposed during its lifespan in a predictable way. In the blood of individuals with poorly controlled high concentrations of glucose, the quantities of this glycated hemoglobin are higher than in healthy people.

In diabetes, higher amounts of A1C have been associated with cardiovascular disease[14], nephropathy, and retinopathy. The Diabetes Control and Complications Trial (DCCT) [14] and the United Kingdom Prospective Diabetes Study (UKPDS) [15] demonstrated that A1C and the development of long-term complications are correlated in both type 1and type 2 diabetes. Monitoring A1C in type 1 and type 2 diabetic patients may improve outcomes[16]. In certain circumstances where the rate of red blood cell turnover is significantly shortened or extended, or the structure of hemoglobin is altered, A1C may not accurately reflect glycemic status[17].

Meta-analysis of cardiovascular outcomes in randomized trials suggest that an average A1C reduction of 0.9% correlates with a 17% reduction in nonfatal MI and a 15% reduction in coronary heart disease without significant effects on stroke or all-cause mortality [18].

In epidemiologic analyses A1C levels >7.0% are associated with a significantly increased risk of both microvascular and macrovascular complications, regardless of underlying treatment. The usual target value for A1C is < 7%, to reduce the risk of chronic complications. Furthermore, the ADA suggests that lower targets may be pursued in selected patients, such as those with recent-onset disease, long

life expectancy, and no significant cardiovascular disease, if they can be achieved without significant hypoglycemia or other adverse effects of treatment [19].

2.2 Methods

We followed an *a priori* protocol, and reported this review according to guidelines [20].

2.2.1 Data sources

The search strategy was designed by an expert librarian. We searched the following electronic databases through the Ovid interface: Medline (1950 – March 2011), Embase (1988 –March 2011), and the Cochrane library (March 2011). Similar searches were run in CINAHL, BIOSIS Previews® (1926 – March 2011), and Web of Science (1900 – March 2011); we also searched the clinicaltrials.gov registry and citations of existing systematic reviews. Since telemedicine is a broad term and can cover different interventions, we decided to include all electronic forms of communication in our search (strategy available on request). Results of the search were transferred to RefWorks online software and were checked for duplicates.

2.2.2 Study selection

Two reviewers (N.D. and A.E.) independently reviewed all citations. Studies with "diabetes", "type 1" or "type 2" in the title or abstract that studied any kind of telemedicine intervention were flagged for full text review. Search strategy for Medline is shown in appendix 1. Other search strategies are available on request. We retrieved the full-text articles of these studies and assessed them using the *a priori* selection criteria for eligibility. Eligible studies were randomized controlled trials (RCTs) or randomized crossover trials published in English; enrolled patients with type 1 or 2 diabetes with no age restriction; compared telemedicine with usual care and reported the level of metabolic control measured by A1C. We

excluded studies on gestational diabetes because of the different nature of this disease. Disagreements between two reviewers were resolved by consensus.

2.2.3 Data extraction

We used a standardized method to extract and record relevant properties of each trial into a database. Data from eligible trials was independently extracted by two reviewers using a standardized extraction sheet. We resolved disagreements by discussion. The following information was extracted from selected studies:

(1) General information: title, year of publication, sponsor;

(2) Trial characteristics: trial design, duration, randomization method, intention-to-treat design; allocation concealment and method of allocation concealment.

(3) Interventions: Telemedicine interventions for diabetes can range from receiving simple reminders systems via short message service (SMS) to complex web interfaces where patients can upload home meter data of blood glucose levels and other pertinent data such as medications, dietary habits, activity level, and medical history. In some cases, providers (physicians, nurses or software) review this data and provide feedback regarding medication adjustments and lifestyle modification guidelines. The telemedicine interventions were categorized in terms of frequency of communications and strength of intervention. The strength of intervention was assessed against the following criteria, (a) interactive follow-up with the possibility of medication adjustments, (b) non-interactive follow-up. The frequency of contact with the diabetes care provider was also graded: (a) high if ≥ once weekly; (b) weak if < once weekly. We also classified studies regarding the duration of intervention (<6 months or ≥6 months);

(4) Patients: total number in intervention groups, sex, age, socioeconomic status, ethnicity, educational status, type of diabetes, duration of diabetes, similarity of groups at baseline, withdrawals/losses to follow-up (reasons/description);

(5) Outcomes and results: A1C level (primary outcome), hypoglycemia, quality of life and satisfaction from intervention, mortality and cost of care;

2.2.4 Quality assessment

We assessed the quality of included studies using the Cochrane Collaboration's tool for assessing risk of bias[21].

2.2.5 Data analysis

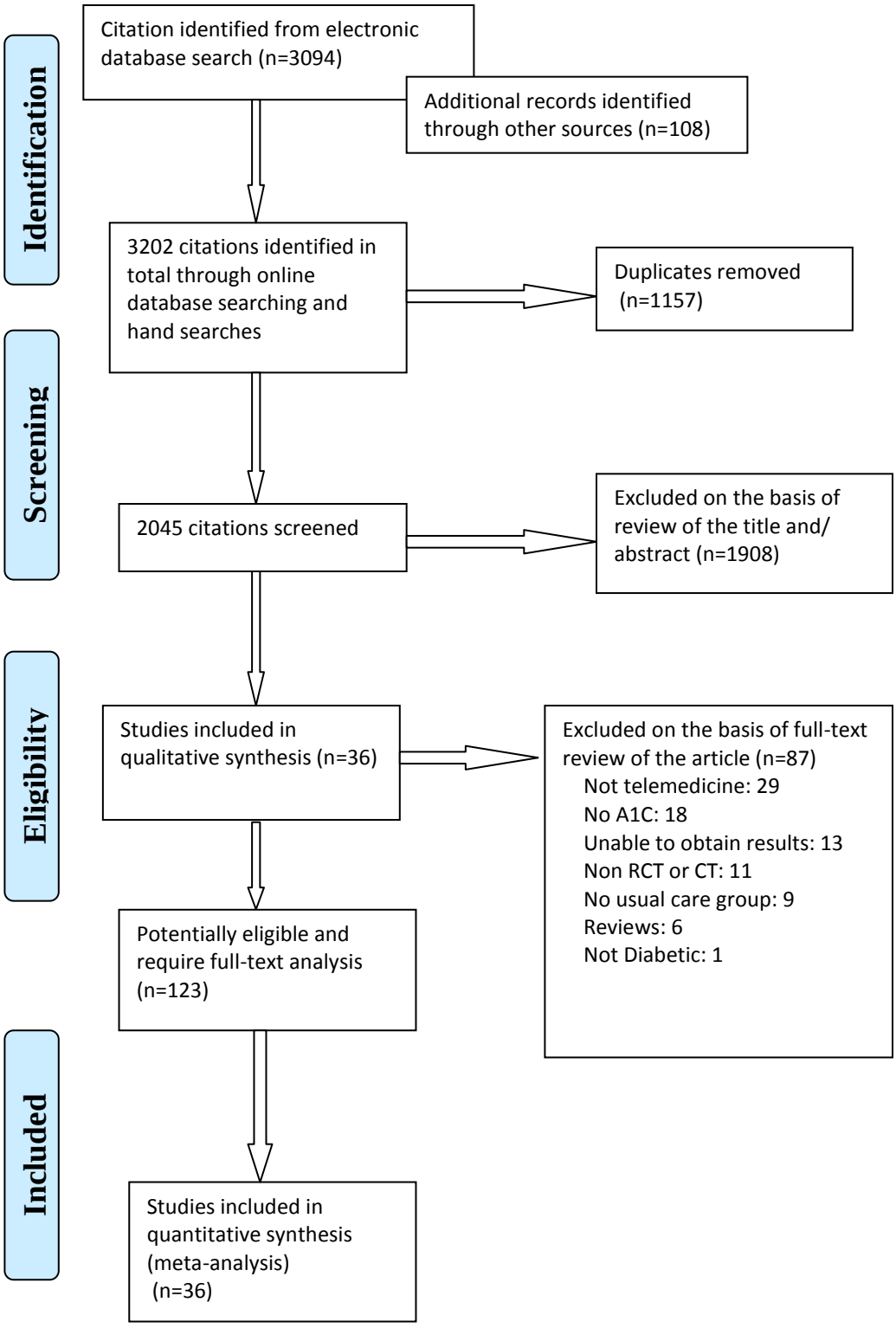
We used STATA 10.1 (www.stata.com) and Review Manager for all statistical analyses in this systematic review. Due to the differences expected between studies, we combined results using a random effects model; missing standard deviations (SD) were imputed directly from baseline SD [22]. Heterogeneity was identified by visual inspection of the forest plots and other statistical methods including χ^2-test and quantifying I^2.[23] *A priori* subgroup analyses were planned and performed for different types of DM. We categorized studies into three groups based on the type of diabetes that was studied (as defined by the primary authors): type 1; type 2; or mixed/unspecified type of diabetes.

Regression analysis of funnel plot asymmetry of A1C level allowed us to assess any evidence of publication bias and small study effects (Egger's test)[24] we used fixed effects rather than random effects to eliminate the contribution of between-study variance to the calculation of precision. To assess the impact associated with patient characteristics or specific elements of telemedicine, we used weighted linear meta-regression[25] to evaluate for effect modification on end-of-study A1C by these characteristics.

2.3 Results

The literature search of online databases and references of relevant studies identified 3202 citations. After screening abstracts, 123 potentially eligible studies were identified, and 36 studies [1, 4, 8-10, 26-57] met our inclusion criteria (Figure 2.1).

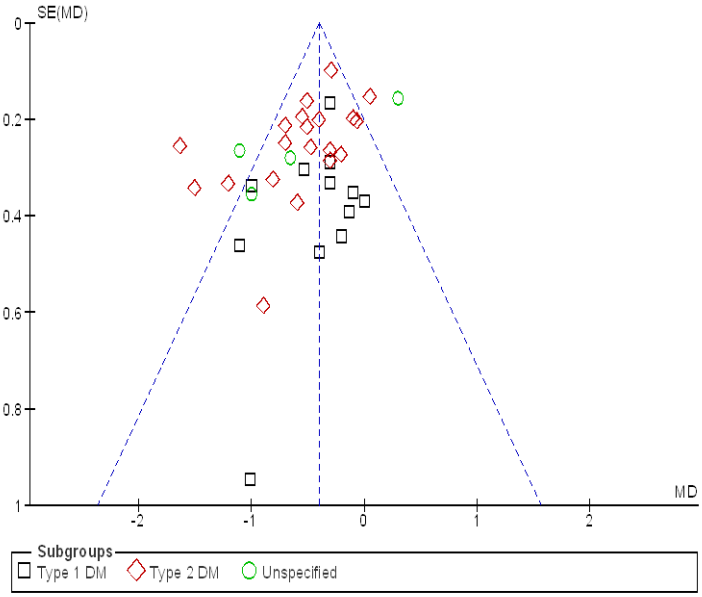
Figure 2.1: Flow diagram of study selection



About 39% (14/36) of included studies were performed in the United States and 25% in South Korea (9/36). Of the 36 included studies, three [32, 54, 57] were published before 2000 and two were randomized crossover trials [34, 35]. The median number of study participants was 75.5, ranging from 18 to 727. Sample size tended to be larger in the 20 studies of patients with Type 2 diabetes [8, 10, 36-53] than in the 12 studies of patients with type 1 diabetes [1, 9, 26-35] and the four studies of mixed or unspecified diabetes [19, 54-57].

Study characteristics are summarized in Table 2.1. Study quality is shown in Table 2.2; The funnel plot of A1C did not suggest a large degree of publication bias (Figure 2.2). However, regression analysis showed evidence of small study effects (Egger's test, P<0.006 for all studies).

Figure 2.2: Publication bias (Fixed effect model)



The range of baseline metabolic control varied substantially between trials (mean A1C ranged from 7.05% to 10.9%). However, 23(63.8%) of studies had mean A1C of > 8% at baseline.

The telemedicine interventions for diabetes management that were studied in the included trials ranged from simple methods where patients received simple reminders by phone or text message to very complex multidisciplinary interventions (Appendix 2). The comparison groups received usual care for their diabetes as defined in each study.

Table 2.1: Study characteristics

Type of DM	Study	Year	Country	Number of participants	Study Duration (days)	Age	Baseline A1C	Mean interval since diagnosis (years)	Medication adjustment	Frequency of feedback from care giver through telemedicine
1	Marrero	1999	USA	106	270	13.3	9.65	< 10	Yes	< 1/week
	Tsang	2001	China	20	365	32.5	8.68	< 10	No	> = 1/week
	Biermann	2002	Germany	48	180	30.3	8.15	>= 10	Yes	< 1/week
	Chase	2003	USA	70	180	17.3	8.95	>= 10	Yes	< 1/week
	Montori	2004	Canada	31	180	42.9	8.95	>= 10	Yes	< 1/week
	Farmer	2005	UK	93	900	23.8	9.25	< 10	Yes	< 1/week
	Jansa`	2006	Spain	40	365	25	8.65	NR	Yes	< 1/week
	Rami	2006	Austria	36	180	15.3	9.2	< 10	Yes	> = 1/week
	Franklin	2006	UK	61	90	13.4	9.93	>= 10	No	> = 1/week
	Izquierdo	2009	USA	77	180	NR	8.59	>= 10	No	< 1/week
	McCarrier	2009	USA	41	84	37.2	8.01	< 10	Yes	> = 1/week
	Rossi	2010	Italy, Spain, UK	130	365	35.7	8.29	< 10	Yes	NR
2	Piette	2001	USA	292	180	60.5	8.15	< 10	No	< 1/week
	Oh	2003	Korea	50	365	60.6	8.55	NR	Yes	> = 1/week
	Kim	2003	Korea	50	365	60.3	8.5	< 10	Yes	> = 1/week
	Kwon	2004	Korea	110	90	54.1	7.39	< 10	Yes	> = 1/week
	McMahon	2005	USA	104	84	63.5	9.95	< 10	Yes	NR
	Harno	2006	Finland	175	270	NR	7.98	>= 10	No	NR
	Cho	2006	Korea	80	90	52.9	7.60	< 10	Yes	< 1/week
	Kim	2007	Korea	80	365	48.1	NR	< 10	No	NR
	Kim	2008	Korea	40	84	47	7.85	< 10	Yes	> = 1/week
	Quinn	2008	USA	30	84	NR	9.28	< 10	Yes	> = 1/week
	Yoon	2008	Korea	100	365	47.1	7.84	>= 10	Yes	> = 1/week
	Rodriguez	2009	Spain	137	365	63.9	7.51	>= 10	Yes	NR
	Schillinger	2009	USA	1665	273	55.8	9.54	< 10	No	> = 1/week
	Istepanian	2009	UK	119	84	58.5	8	>= 10	No	NR
	Yoo	2009	Korea	225	90	58.1	7.84	< 10	No	> = 1/week
	Ralston	2009	USA	83	365	57.2	8.05	NR	Yes	> = 1/week
	Graziano	2009	USA	123	365	NR	8.64	NR	No	< 1/week
	Shea	2009	USA	328	1825	70.8	7.37	>= 10	Yes	NR
	Stone	2010	USA	150	180	NR	9.50	NR	Yes	NR
	Lim	2011	Korea	103	180	67.6	7.85	>= 10	Yes	> = 1/week
3***	Ahring	1997	Canada	42	120	41.4	10.90	< 10	Yes	> = 1/week
	Thampson	1999	Canada	46	180	48.7	9.50	< 10	Yes	> = 1/week
	Maljanian	2005	USA	274	84	57.9	7.90	NR	No	> = 1/week
	Bond	2006	USA	62	84	67.2	7.05	>= 10	No	> = 1/week

(NR = Not Reported); *Randomized crossover trials; **USA=United States of America, UK=United Kingdom; ***3=Unspecified or mixed population

Table 2.2: Risk of bias assessment

Author, Year	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias) , Percentage of dropouts	Selective reporting (reporting bias)
Ahring,1992	Unclear	Unclear	Unclear	Unclear, NR	Unclear
Marrero ,1995	Unclear	Unclear	Unclear	Unclear, NR	Unclear
Thompson,1999	Unclear	Unclear	Unclear	Unclear, 0	Unclear
Piette, 2001	Low risk	Low risk	Unclear	Low risk, 9	Low risk
Tsang,2001	Unclear	Unclear	Unclear	Low risk, 10	Unclear
Bierman,2002	Low risk	Unclear	Unclear	Low risk, 10	Unclear
Chase,2003	Unclear	Unclear	Low risk	High risk, 10	Unclear
Kim,2003	High risk	Unclear	Unclear	Unclear, 28	Unclear
Oh,2003	Unclear	Unclear	Unclear	Unclear, 24	Unclear
Kwon,2004	Low risk	Unclear	Unclear	Low risk, 8	Unclear
Montori, 2004	Low risk	Low risk	Unclear	Unclear, 35	Unclear
Farmer,2005	Low risk	Unclear	Unclear	Low risk, 13	Unclear
Maljanian,2005	Unclear	Unclear	Unclear	Low risk, NR	Unclear
McMahon,2005	Unclear	Unclear	Unclear	High risk, 19	Unclear
Bond,2006	Unclear	Unclear	Unclear	Unclear, NR	Unclear
Cho, 2006	Unclear	Unclear	Unclear	Unclear, 11	Low risk
Franklin,2006	Low risk	Low risk	Unclear	Low risk, 15	Low risk
Harno,2006	Unclear	Unclear	Unclear	Unclear, NR	Unclear
Jansa`,2006	Low risk	Unclear	Unclear	Low risk, 12	Unclear
Rami, 2006	Unclear	Unclear	Unclear	Low risk, 0	Unclear
Kim,2007	Unclear	Unclear	Unclear	Low risk, 11	Low risk
Kim,2008	Low risk	Unclear	Unclear	Low risk, 15	Low risk
Yoon,2008	Unclear	Unclear	Unclear	High risk, 49	Unclear
Quinn,2008	Unclear	Unclear	High risk	Low risk, 13	Low risk
Graziano,2009	Low risk	Low risk	Low risk	Low risk, 5	Unclear
Istepanian,2009	Low risk	Unclear	Unclear	Low risk, NR	Unclear
Izquierdo,2009	Unclear	Unclear	Unclear	Unclear, NR	High risk
McCarrier,2009	Low risk	Low risk	Unclear	Unclear, 17	Low risk
Ralston,2009	Low risk	Low risk	Unclear	Low risk, 11	Unclear
Rodriguez,2009	Unclear	Unclear	Unclear	Low risk, 12	Low risk
Shea,2009	Low risk	Unclear	Unclear	Unclear, 56	Unclear
Schillinger,2009	Low risk	Unclear	Unclear	High risk, 9	Low risk
Yoo,2009	Unclear	Unclear	Unclear	Unclear, 49	Unclear
Rossi, 2010	Low risk	Low risk	High risk	Low risk, 8	Unclear
Stone,2010	Unclear	Unclear	Unclear	Unclear, NR	Unclear
Lim,2011	Low risk	Unclear	Unclear	Unclear, 6	Unclear

NR= Not reported

2.3.1 Effect of telemedicine on A1C

The pooled result from all 36 studies revealed that the mean A1C level in the telemedicine group was significantly lower than those of patients in the usual care group (weighted mean difference (WMD) -0.49 %, 95% CI -0.62%, -0.35%, P<0.001). There was evidence of high statistical heterogeneity between studies (I^2 = 77.2%).

In subgroup analyses stratified by type of diabetes, pooled results remained significant for both type 1 diabetes (WMD -0.37%, 95% CI -0.56%, -0.19%, P<0.001) and type 2 diabetes (WMD -0.52%, 95% CI -0.70%, -0.34%, P<0.001). Heterogeneity was absent for trials with type 1 diabetes (I^2=0%) but high for trials with type 2 diabetes (I^2=82.2%). (Figure 2.3)

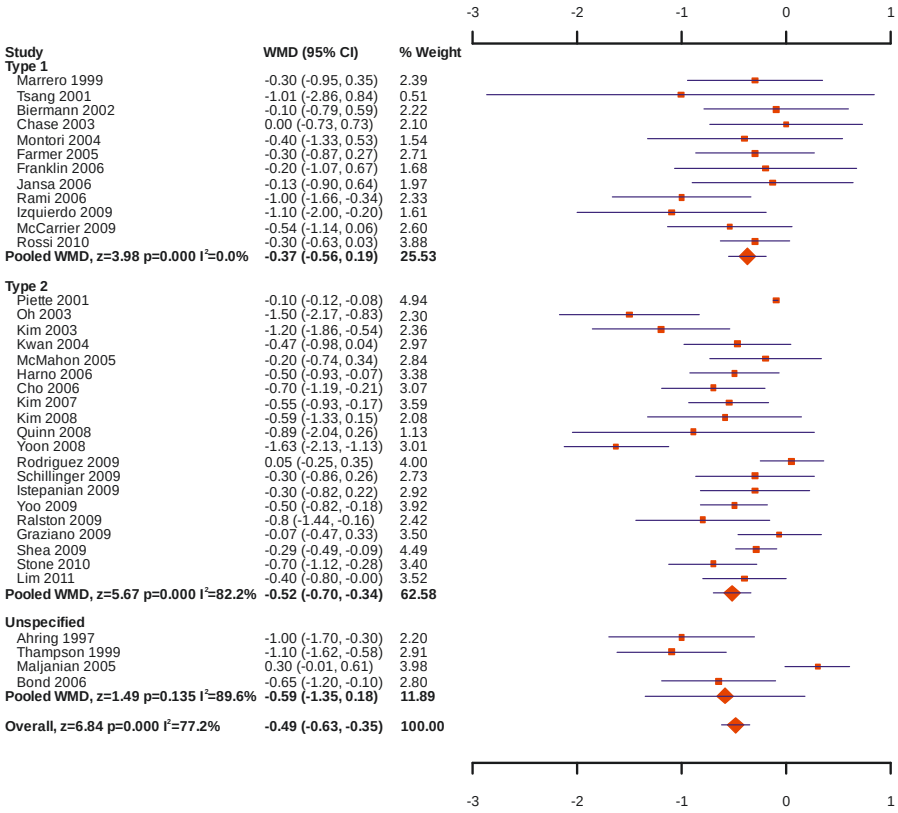
For the four studies [48-51] with unspecified or mixed populations, the pooled result did not show a statistically significant difference between the two groups (WMD -0.58 %, 95% CI -1.35%, 0.18%, P=0.13). However, after exclusion of one study [50] in which the baseline A1C was significantly higher in the intervention group as compared to controls (P=0.015), the pooled result for the remaining three studies was significant and favored the telemedicine group (WMD -0.91%, 95% CI -1.24%, -0.58%, P<0.001) and I^2 decreased from 89.6% to 0%.

Results of metaregression: factors associated with greater reduction in A1C
Using univariable metaregression, we tested four variables as possible modifiers of the effect of telemedicine on A1C: type of diabetes, mean age of participants, and frequency of intervention and possibility of medication changes or dose adjustment. Interventions that facilitated medication changes or dose adjustment were associated (at the p<0.10 level) with lower A1C at the end of the study compared to interventions without this characteristic conferring an additional

reduction of 0.26% (95% CI, -0.03% to 0.56%, P= 0.080) beyond that associated with interventions without this characteristic.

Among 28 studies reporting the frequency of contact, high frequency of contact (>1/week) was a significant modifier with an additional reduction of 0.41% (95% CI, 0.02% to 0.81%, P= 0.040). In the model that included these characteristics of the telemedicine intervention (the possibility of medication adjustments and greater frequency of contact), both variables remained significantly associated with greater reductions in A1C. Metaregression did not suggest an association between the type of diabetes or the mean age of study participants with the magnitude of the change in A1C.

Figure 2.3: Forest plot of the effect of telemedicine interventions on A1C



2.3.2 Effect of telemedicine on quality of life

Among nine [9, 27, 30-32, 34, 46, 50, 56] studies that compared health-related quality of life or patient satisfaction between arms, four [9, 30, 32, 46] found statistically significant differences in at least one category of quality of life or treatment satisfaction – all favoring the intervention group. None of the reported comparisons favored usual care. For instance, in one study [30], significant improvements in several subscales of the Pediatric Diabetes Quality of Life questionnaire were observed. Telemedicine was also associated with a significant improvement in several mental and physical components of the SF-36 Health Survey, compared with usual care. The SF-36 is a multi-purpose, short-form health well known survey with only 36 questions used for quality-of-life measurement. Due to heterogeneous methods for assessing health-related quality of life or patient satisfaction, statistical pooling of results was not possible.

2.3.3 Effect of telemedicine on risk of hypoglycemia

Importantly, most studies did not describe how hypoglycemia was defined – for instance distinguishing symptomatic or asymptomatic hypoglycemia. Acknowledging this limitation, among studies that compared the risk of hypoglycemia, there was no statistically significant difference in the incidence hypoglycemia between intervention and control groups in ten studies[1, 8, 9, 26, 27, 29, 34, 44, 52, 54]. Only one study[28] found a significant difference in the percentage of transmitted blood glucose tests that demonstrated hypoglycemia between the two groups (intervention 1,650/29,765 [5.3%] compared with 739/21,400 [3.5%], $P<0.001$). Another study[31] reported a significant decrease between the percentages of patients experiencing <3 episodes of mild hypoglycemia after 12 months of study in both groups. Overall, there was no conclusive evidence that telemedicine affected the risk of hypoglycemia.

2.3.4 Effect of telemedicine on mortality and costs

Six studies [10, 37, 49-51, 54] compared the risk of mortality between groups. However, even the largest study [51] (N=1831) did not have adequate statistical power to detect differences in mortality between groups and pooled results were similarly inconclusive. Four studies that focused on the financial aspects of telemedicine documented that the cost of telemedicine was less expensive than routine clinic care.[26, 27, 31, 46] Pooled analyses of differences in cost were not feasible because of heterogeneous reporting across studies.

2.4 Discussion

This systematic review updates prior reviews [1-7] of the potential benefits of telemedicine in people with diabetes, which found that electronic transfer of self-monitored results is feasible in diabetes, but document only weak evidence for improvements in A1C or other aspects of diabetes management[7]. We identified 11 new studies including a total of 1297 participants, allowing additional statistical power. Our study suggests that telemedicine significantly improves A1C in people with either type 1 or 2 diabetes, as compared to usual care. The 0.49% pooled estimate of the incremental decrease in A1C associated with telemedicine appears clinically relevant [58], and is comparable to improvements associated with some oral anti-diabetic agents [59], psychosocial interventions [60] or quality improvement strategies [61] for patients with diabetes. However, based on the Endocrinologist and Metabolic Drugs Advisory of the US Food and Drug Administration a 0.7% reduction in A1C is considered to be a minimal clinically important difference. Of note, we did not find any evidence that telemedicine reduced the risk of clinical events such as all-cause mortality. Although it is possible that telemedicine may also reduce health care costs and improve satisfaction and health-related quality of life, pooled analyses were not feasible given heterogeneous reporting of the individual studies and thus this suggestion remains speculative.

Options for telemedicine range from simple weekly automated reminders, and a daily message providing tips[29] to more comprehensive interventions as in the IDEATel study[51]. In IDEATel, patients randomized to the intervention group received a home telemedicine unit permitting videoconferencing with a nurse case manager, remote monitoring of glucose and blood pressure with electronic upload and integration into the electronic medical record, access to their own clinical data and educational material, and secure communication with the nurse case manager.

The results of meta-regression suggested that telemedicine improved A1C to an importantly clinically greater extent (not statistically) in people with type 2 as opposed to type 1 diabetes. Since people with Type 2 diabetes are older, this argues against the suggestion that seniors will not be attracted to new technologies to help manage their health – consistent with previous work [55]. Meta-regression in the 24 studies of non-type 1 (type 2 or mixed/unspecified populations) suggested that telemedicine interventions that facilitated medication changes or dose adjustment were more effective for improving glycemic control than those which did not – consistent with previous work studying other types of intervention [61].

We used Weaknesses of our systematic review include the uncertain quality of the constituent studies, many of which were limited by small sample size, limited duration. There are differing opinions about how best to assess risk of bias. Though the Cochrane risk of bias tool incorporates objective judgments and the extent of agreement between assessors may not be as high as for some other tools, it is one of the most comprehensive available tools and focuses on the perceived risk of bias rather than reported characteristics of the trial. In addition, many of the studies were of relatively short duration, and so it is unclear whether the improvements in A1C that we noted would persist over time. Second, there was considerable variation in the types of telemedicine technology employed, as well as the type of care the control groups received – which may explain why some studies found positive effects of telemedicine, while other studies found no

benefit. Although we attempted to elucidate using metaregression which types of telemedicine intervention were particularly efficacious, we were hampered by the relatively small number of studies, which likely reduced the statistical power of meta-regression analyses. Identifying which characteristics of telemedicine interventions are likely to improve outcomes should be a high priority for future research.

Third, we observed evidence of high statistical heterogeneity between studies (I^2 = 77%). This could be the consequence of both clinical and methodological heterogeneity. Studies included in this review are diverse in numerous aspects. This variability among studies is the source of heterogeneity. Variability in the populations and interventions can be sources of clinical heterogeneity, and variability in study design and risk of bias can be sources of methodological heterogeneity. There was considerable clinical heterogeneity in the included studies in terms of demographic of populations studied, type of DM and baseline A1C level. As seen in subgroup analyses stratified by type of diabetes, heterogeneity was absent for trials with type 1 diabetes (I^2=0%) but high for trials with type 2 diabetes (I^2=82.2%). Methodological factors (such as use of blinding and allocation concealment) of between-study differences in the way the outcomes were measured, may also have led to statistical heterogeneity.

Fourth, we found some evidence of publication bias, suggesting that some small negative studies may exist but were not identified by our search of the published literature. If this supposition is correct, it may have led to a slight overestimate of the efficacy of telemedicine interventions. Finally, although our unpooled results might be interpreted as suggesting that telemedicine improves quality of life, not all studies reported all subscales of the instruments used, raising the possibility of bias due to selective reporting.

Our results suggest that telemedicine may be a useful supplement to usual clinical practice for helping to control A1C – at least in the short term. Additional trials

are required to accurately measure the clinical impact of home telemedicine and assess which elements of telemedicine programs are particularly effective for improving diabetes management and might be justifies as means to increase equity in access to high quality healthcare in remote communities.

2. References:

1. Montori, V.M., et al., *Telecare for patients with type 1 diabetes and inadequate glycemic control: a randomized controlled trial and meta-analysis.* Diabetes care, 2004. **27**(5): p. 1088-1094.
2. Dellifraine, J.L. and K.H. Dansky, *Home-based telehealth: a review and meta-analysis.* Journal of telemedicine and telecare, 2008. **14 (2)**: p. 62-66.
3. Polisena, J., et al., *Home telehealth for diabetes management: A systematic review and meta-analysis.* Diabetes, Obesity and Metabolism, 2009. **11 (10)**: p. 913-930.
4. Azar, M. and R. Gabbay, *Web-based management of diabetes through glucose uploads: Has the time come for telemedicine?* Diabetes Research and Clinical Practice, 2009. **83 (1)**: p. 9-17.
5. Wu, L., et al., *Telephone follow-up to improve glycaemic control in patients with Type 2 diabetes: Systematic review and meta-analysis of controlled trials.* Diabetic Medicine, 2010. **27 (11)**: p. 1217-1225.
6. Liang, X., et al., *Effect of mobile phone intervention for diabetes on glycaemic control: A meta-analysis.* Diabetic Medicine, 2011. **28 (4)**: p. 455-463.
7. Farmer, A., et al., *A systematic review of telemedicine interventions to support blood glucose self-monitoring in diabetes.* Diabet Med, 2005. **22**(10): p. 1372-8.
8. Lim, S., et al., *Improved glycemic control without hypoglycemia in elderly diabetic patients using the ubiquitous healthcare service, a new medical information system.* Diabetes care, 2011. **34**(2): p. 308-313.
9. Rossi, M.C., et al., *Diabetes Interactive Diary: a new telemedicine system enabling flexible diet and insulin therapy while improving quality of life: an open-label, international, multicenter, randomized study.* Diabetes care, 2010. **33**(1): p. 109-115.
10. Stone, R.A., et al., *Active care management supported by home telemonitoring in veterans with type 2 diabetes: the DiaTel randomized controlled trial.* Diabetes care, 2010. **33**(3): p. 478-484.
11. Koenig, R.J., et al., *Correlation of glucose regulation and hemoglobin AIc in diabetes mellitus.* N Engl J Med, 1976. **295**(8): p. 417-20.
12. Sobrin, L., *Longitudinal validation of hemoglobin a1c criteria for diabetes diagnosis: risk of retinopathy.* Diabetes, 2012. **61**(12): p. 3074-5.
13. *Consensus statement on the worldwide standardisation of the HbA1c measurement.* Diabetologia, 2007. **50**(10): p. 2042-3.
14. Gillett, M.J., *International Expert Committee report on the role of the A1c assay in the diagnosis of diabetes: Diabetes Care 2009; 32(7): 1327-1334.* Clin Biochem Rev, 2009. **30**(4): p. 197-200.
15. *Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group.* Lancet, 1998. **352**(9131): p. 837-53.
16. Larsen, M.L., M. Horder, and E.F. Mogensen, *Effect of long-term monitoring of glycosylated hemoglobin levels in insulin-dependent diabetes mellitus.* N Engl J Med, 1990. **323**(15): p. 1021-5.
17. Jandric Balen, M., et al., *HbA1C - overall glycemia marker and hemolytic anemia indicator.* Med Glas Ljek komore Zenicko-doboj kantona, 2012. **9**(2): p. 406-8.
18. Ray, K.K., et al., *Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials.* Lancet, 2009. **373**(9677): p. 1765-72.
19. *Executive summary: Standards of medical care in diabetes--2010.* Diabetes care, 2010. **33 Suppl 1**: p. S4-10.

20. Liberati, A., et al., *The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration.* BMJ (Clinical research ed.), 2009. **339**: p. b2700.
21. Higgins, J.P., et al., *The Cochrane Collaboration's tool for assessing risk of bias in randomised trials.* BMJ, 2011. **343**: p. d5928.
22. Wiebe, N., et al., *A systematic review identifies a lack of standardization in methods for handling missing variance data.* Journal of Clinical Epidemiology, 2006. **59 (4)**: p. 342-353.
23. Higgins, J.P., et al., *Measuring inconsistency in meta-analyses.* BMJ (Clinical research ed.), 2003. **327 (7414)**: p. 557-560.
24. Egger, M., et al., *Bias in meta-analysis detected by a simple, graphical test.* British Medical Journal, 1997. **315 (7109)**: p. 629-634.
25. Thompson, S.G. and J.P. Higgins, *How should meta-regression analyses be undertaken and interpreted?* Stat Med, 2002. **21**(11): p. 1559-73.
26. Biermann, E., et al., *Are there time and cost savings by using telemanagement for patients on intensified insulin therapy? A randomised, controlled trial.* Computer Methods & Programs in Biomedicine, 2002. **69**(2): p. 137-146.
27. Chase, H.P., et al., *Modem transmission of glucose values reduces the costs and need for clinic visits.* Diabetes care, 2003. **26**(5): p. 1475-1479.
28. Farmer, A.J., et al., *A randomized controlled trial of the effect of real-time telemedicine support on glycemic control in young adults with type 1 diabetes (ISRCTN 46889446).* Diabetes care, 2005. **28**(11): p. 2697-2702.
29. Franklin, V.L., et al., *A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes.* Diabetic Medicine, 2006. **23**(12): p. 1332-1338.
30. Izquierdo, R., et al., *School-centered telemedicine for children with type 1 diabetes mellitus.* Journal of Pediatrics, 2009. **155**(3): p. 374-379.
31. Jansa, M., et al., *Telecare in a structured therapeutic education programme addressed to patients with type 1 diabetes and poor metabolic control.* Diabetes Research & Clinical Practice, 2006. **74**(1): p. 26-32.
32. Marrero, D.G., et al., *Using telecommunication technology to manage children with diabetes: the Computer-Linked Outpatient Clinic (CLOC) Study.* Diabetes Educator, 1995. **21**(4): p. 313-319.
33. McCarrier, K.P., et al., *Web-based collaborative care for type 1 diabetes: a pilot randomized trial.* Diabetes Technology & Therapeutics, 2009. **11**(4): p. 211-217.
34. Rami, B., et al., *Telemedical support to improve glycemic control in adolescents with type 1 diabetes mellitus.* European journal of pediatrics, 2006. **165**(10): p. 701-705.
35. Tsang, M.W., et al., *Improvement in diabetes control with a monitoring system based on a hand-held, touch-screen electronic diary.* Journal of Telemedicine & Telecare, 2001. **7**(1): p. 47-50.
36. Cho, J.H., et al., *Long-term effect of the Internet-based glucose monitoring system on HbA1c reduction and glucose stability: a 30-month follow-up study for diabetes management with a ubiquitous medical care system.* Diabetes care, 2006. **29**(12): p. 2625-2631.
37. Graziano, J.A. and C.R. Gross, *A randomized controlled trial of an automated telephone intervention to improve glycemic control in type 2 diabetes.* Advances in Nursing Science, 2009. **32**(3): p. E42-57.
38. Harno, K., R. Kauppinen-Makelin, and J. Syrjalainen, *Managing diabetes care using an integrated regional e-health approach.* Journal of Telemedicine & Telecare, 2006. **12**(Suppl 1): p. 13-15.
39. Kim, H.S. and M.S. Song, *Technological intervention for obese patients with type 2 diabetes.* Applied Nursing Research, 2008. **21**(2): p. 84-89.
40. Istepanian, R.S., et al., *Evaluation of a mobile phone telemonitoring system for glycaemic control in patients with diabetes.* Journal of Telemedicine & Telecare, 2009. **15**(3): p. 125-128.

41. Kim, C., et al., *Internet diabetic patient management using a short messaging service automatically produced by a knowledge matrix system.* Diabetes care, 2007. **30**(11): p. 2857-2858.
42. Kim, H.S. and J.A. Oh, *Adherence to diabetes control recommendations: impact of nurse telephone calls.* Journal of advanced nursing, 2003. **44**(3): p. 256-261.
43. Kwon, H.S., et al., *Establishment of blood glucose monitoring system using the internet.* Diabetes care, 2004. **27**(2): p. 478-483.
44. McMahon, G.T., et al., *Web-based care management in patients with poorly controlled diabetes.* Diabetes care, 2005. **28**(7): p. 1624-1629.
45. Oh, J.A., et al., *A telephone-delivered intervention to improve glycemic control in type 2 diabetic patients.* Yonsei medical journal, 2003. **44**(1): p. 1-8.
46. Piette, J.D., et al., *Impact of automated calls with nurse follow-up on diabetes treatment outcomes in a Department of Veterans Affairs Health Care System: a randomized controlled trial.* Diabetes care, 2001. **24**(2): p. 202-208.
47. Quinn, C.C., et al., *WellDoc mobile diabetes management randomized controlled trial: change in clinical and behavioral outcomes and patient and physician satisfaction.* Diabetes Technology & Therapeutics, 2008. **10**(3): p. 160-168.
48. Ralston, J.D., et al., *Web-based collaborative care for type 2 diabetes: a pilot randomized trial.* Diabetes care, 2009. **32**(2): p. 234-239.
49. Rodriguez-Idigoras, M.I., et al., *Telemedicine influence on the follow-up of type 2 diabetes patients.* Diabetes Technology & Therapeutics, 2009. **11**(7): p. 431-437.
50. Schillinger, D., et al., *Effects of self-management support on structure, process, and outcomes among vulnerable patients with diabetes: a three-arm practical clinical trial.* Diabetes care, 2009. **32**(4): p. 559-566.
51. Shea, S., et al., *A randomized trial comparing telemedicine case management with usual care in older, ethnically diverse, medically underserved patients with diabetes mellitus: 5 year results of the IDEATel study.* Journal of the American Medical Informatics Association, 2009. **16**(4): p. 446-456.
52. Yoo, H.J., et al., *A Ubiquitous Chronic Disease Care system using cellular phones and the internet.* Diabetic Medicine, 2009. **26**(6): p. 628-635.
53. Yoon, K.H. and H.S. Kim, *A short message service by cellular phone in type 2 diabetic patients for 12 months.* Diabetes Research & Clinical Practice, 2008. **79**(2): p. 256-261.
54. Ahring, K.K., et al., *Telephone modem access improves diabetes control in those with insulin- requiring diabetes.* Diabetes care, 1992. **15 (8)**: p. 971-975.
55. Bond, G.E., et al., *Preliminary findings of the effects of comorbidities on a web-based intervention on self-reported blood sugar readings among adults age 60 and older with diabetes.* Telemedicine Journal & E-Health, 2006. **12**(6): p. 707-710.
56. Maljanian, R., et al., *Intensive telephone follow-up to a hospital-based disease management model for patients with diabetes mellitus.* Disease Management, 2005. **8**(1): p. 15-25.
57. Thompson, D.M., S.E. Kozak, and S. Sheps, *Insulin adjustment by a diabetes nurse educator improves glucose control in insulin-requiring diabetic patients: a randomized trial.* CMAJ Canadian Medical Association Journal, 1999. **161**(8): p. 959-962.
58. Clar, C., et al., *Self-monitoring of blood glucose in type 2 diabetes: Systematic review.* Health Technology Assessment, 2010. **14 (12)**: p. 1-140.
59. Sherifali, D., et al., *The effect of oral antidiabetic agents on A1C levels: A systematic review and meta-analysis.* Diabetes care, 2010. **33 (8)**: p. 1859-1864.
60. Armour, T.A., et al., *The effectiveness of family interventions in people with diabetes mellitus: A systematic review.* Diabetic Medicine, 2005. **22 (10)**: p. 1295-1305.
61. Shojania, K.G., et al., *Effects of quality improvement strategies for type 2 diabetes on glycemic control: A meta-regression analysis.* Journal of the American Medical Association, 2006. **296 (4)**: p. 427-440.

CHAPTER 3.WILLINGNESS TO USE TELEMEDICINE

3.1 Chapter introduction

Our systematic review and meta-analysis in the previous chapter of this thesis tackled the clinical effectiveness of the telemedicine in management of diabetes, which is an important factor to consider whether assessing whether to implement a telemedicine intervention. However, without willingness to use a new technology, voluntary users will seek alternatives and forced users may not fully benefit from their treatment[1]. Behavioral willingness reflects individuals' openness to an opportunity to perform a certain behavior in situations that are favorable to that behavior[2].

Before considering telemedicine for widespread implementation, it would be potentially useful to measure whether such a strategy is likely to be accepted and utilized by the target population.

Therefore, we first summarized theoretical frameworks and conceptual models of health behavior to assess the potential importance of willingness to implement a new intervention like telemedicine. Subsequently, we used this summary to contextualize the findings of a survey that examines willingness to use telemedicine in a large national sample of patients with chronic disease in Canada.

3.2 Motivational models of health behavior

A number of models of health behavior have been suggested in an attempt to map out the variables and to identify proximal determinants of health behavior.

Among these models motivational models have been developed to predict behaviors at single points in time regarding a health-related decisions [1].

According to these models, motivational factors, such as the intention to perform a behavior, are the main determinants of health behavior and one of the proximal determinant of behavior[3].

Intention is defined as the motivation required performing a particular behavior. Therefore, the more one intends to perform a behavior, the more likely is its performance. Intentions are assumed to reflect the motivational factors that underlie actions; in other words, how much effort an individual is planning to exert to perform a specific behavior[4]. In fact, much of the research associated with motivational models uses measures of intention as the dependent variable of interest[5]. Furthermore, meta-analyses have consistently found high correlations between intentions and behavior (e.g., r+ = .47)[6].

However, some recent evidence suggests that intentions may not predict behavior as previously thought [7]. It has been suggested that for improving the predictive strength of intention, researcher should use measures of behavioral expectation and willingness in addition to (or as a substitute for) intention[2].

Behavioral expectation is defined as an individual's estimation of the likelihood that he or she will perform some specified future behavior; behavioral willingness reflects an individual's openness to opportunity, that is, his or her willingness to perform a certain behavior in situations that are favorable to that behavior[2].

It is assumed that usually people have an idea of how they might react in a situations, even though they have no intention or even expectation of being in those situations[8].

Patients who have had little or no experience with telemedicine are not likely to plan (intend), or even expect to engage in that behavior. However, they may have an idea about how they might respond if the opportunity presented itself.

Therefore, their willingness to perform the behavior (willing to interact with their health provider using telemedicine), should be a better predictor of future behavior than either their intention or expectation.

In summary, on the basis of these assumptions -- the more a person is willing to perform a specific behavior, the more likely it is that the behavior will be performed. So, by studying the willingness to use telemedicine, we gain some insight into the potential uptake of telemedicine. It is also possible (although speculative) that variables which correlate with this willingness could be manipulated to influence the uptake of telehealth.

3.3 Willingness and interest to use telemedicine in literature

Few studies have addressed the problem of patients' willingness to use telemedicine. Existing studies have had various limitations including the use of small, homogeneous and non-representative samples -- and only one study was done on patients with chronic disease.

In a statewide telephone survey of 461 non-institutionalized rural adults of the United States in 1997 only one third of the respondents had heard of telemedicine and nearly two thirds thought patients would find it less satisfactory than seeing a physician in person. For chronic conditions, 47% of the respondents would use telemedicine if no physician was available locally, whereas 27% would go out of town to see another physician in person, and 25% would wait for their own physician[9].

In another study done in the United State in 2000, 67 residents of a rural Midwestern state were surveyed by telephone to determine which factors were associated with their willingness to receive mental health services through live, two-way audio and video transmission. Forty-five of the survey respondents, or two-thirds of the sample, expressed a willingness to use telemedicine for mental health services, and 49 of 67 (nearly three-quarters) said that they would

recommend the service to a friend. The mean age of those interested in telepsychiatry was significantly lower than those who were not. Of those who said their health was good, very good, or excellent, 79 percent were willing to participate in telepsychiatry, compared with 21 percent of those who said their health was fair or poor. One-third of the respondents were not willing to participate in telepsychiatry; the most frequently cited reason was concern about confidentiality (55%)[10].

In a study, based on a sample of the non-institutionalized adults in 2003 in Israel, participants consistently expressed greater willingness to use telemedicine was significantly higher for routine than for specialized care. Also, willingness was higher to use the telephone compared to two-way video or the computer for the purposes of telemedicine. Being younger, secular, having fewer children, more years of education, working outside the home, and having a computer at home were significantly associated with higher levels of willingness to use telemedicine for routine care. Being female, having fewer children, being secular, and living at distant location were significantly associated with higher levels of willingness to use telemedicine for specialized care[1].

A total of 116 patients in four audiology centers were surveyed from December 2004 to May 2005 in Australia. Of these, 75% had not previously heard about telemedicine. The most common reasons for willingness to use telemedicine were to reduce the time waiting for an appointment and cost. The most common barrier to using telemedicine was a preference for face-to-face visits. Of those surveyed, 32% were willing to use telemedicine, 10% would sometimes be willing, 28% were unsure, and 30% were not willing. There was no relationship between willingness and age or gender, except that women over the age of 55 years were less willing. Patients who had previously heard of telemedicine and used the internet for health-related matters, especially men, were more inclined to have a telemedicine appointment[11].

In another U.S study (2006), 346 patients of a family doctor were surveyed. Of all patients with internet access, 74.6% (n = 185) were willing to pay a small annual fee for one or more of the following online services: viewing parts of their medical record, messaging with their physician, medication refills, appointment requests, and billing inquiries. Although this willingness to pay ranged from 60% for those in their 50s to 90% for those in their 30s, these differences were not statistically significant (p 0.06). This study suggests that many patients (regardless of age) may be willing to pay a small annual fee in exchange for online services with their primary care physician's office[12].

In a survey of patients of a U.S sleep clinic done between 2009 and 201, 55% of respondents indicated that they used email to communicate with providers, with the most common frequency being 1-2 times per six months. However, none reported experience with video telemedicine. Despite this lack of experience, over 60% reported feeling comfortable or willing to try it and more than half of respondents reported willingness to pay for a video visit with who. Of those who were uncomfortable about video telemedicine, the two main reasons were that in-person visits feel more natural (48%) and that the doctor might need to perform an examination (24%)[13].

3.4 Survey regarding willingness to participate in telehealth

We explore data obtained from a large survey of Western Canadians with one or more chronic diseases. Respondents were asked about their thoughts and willingness of using new technologies (including telemedicine) to deliver care. We also explored how the capacity and understanding of respondents to currently use such new technologies was associated with their willingness to use these technologies.

3.4.1 Study purpose

Survey research methodology grew from social science. Because public health largely depends on behavior, the social science principles of survey research are

directly applicable to much of public health. Survey research is also important because it not only tries to measure past and present behavior but also future behavior.

The purpose of examining the results of the present survey is to examine willingness to use telemedicine in a large sample of Western Canadians. We describe the socioeconomic and demographic factors that are associated with access or willingness to use certain new information technologies (telehealth, email, and text messages [SMS]) among patients with chronic disease.

3.4.2 Objectives

1. To describe the characteristics of survey respondents.

2. To describe sociodemographic and other characteristics of survey respondents associated with their interest and willingness to use telemedicine or other Information technologies (IT) for management of their current or future chronic disease.

3. To determine how much time would need to be saved through the use of telehealth before respondents would prefer to use telehealth rather than an in-person physician visit.

3.4.3 Characteristics of survey

3.4.3.1 Study population and target population

The study population consisted of adult respondents with at least one of the chronic medical conditions of interest (hypertension, diabetes, coronary heart disease and stroke).

The target population was residents of Alberta, British Columbia, Manitoba or Saskatchewan who are 40 years old or older and have self-identified as having been diagnosed with hypertension, diabetes, heart disease or stroke.

3.4.3.2 Sampling

We used the Barriers to Care for People with Chronic Health Conditions (BCPCHC) survey data linked to the Canadian Community Health Survey (CCHS) 2011 cycle. 4331 respondents of CCHS were considered to be in BCPCHC survey if they were not already selected for the 2011 Survey of Living with a Neurological Condition in Canada, or if they not refused to allow Statistics Canada to link their CCHS responses to other surveys, or if their household was not already selected for the 2011 Household and Environment Survey.

Of 2582 in-scope respondents, 2400 were selected. Of the 1931 unselected persons, 1749 were unavailable due to selection for another Statistics Canada survey (n=1273) or they refused permission for data linkage (n=476). The remaining 182 persons were in-scope for the BCPCHC and not selected by other surveys, but were not selected because recruitment targets were met.

3.4.3.3 Study sample

The BCPCHC survey is a voluntary, non-proxy, sample survey with a cross-sectional design. This was conducted by Statistics Canada from February 1st to March 31st, 2012. This telephone survey was administered in four western provinces of Canada (Manitoba, Saskatchewan, Alberta, and British Columbia) who were at least 40 years of age and who were self-identified as having one of the four medical conditions by answering 'yes' to one of the following questions on the CCHS:

1. Hypertension: "Do you have high blood pressure?
2. Diabetes: "Do you have diabetes?
3. Heart Disease: "Do you have heart disease?

4. Stroke: "Do you suffer from the effects of a stroke?

3.4.3.4 Survey questions designing

Statistics Canada Health Analysis Division and The Interdisciplinary Chronic Disease Collaboration (ICDC) researchers to produce a draft questionnaire intended to elicit barriers to optimal care from the target population. A qualitative testing was performed in Calgary by the Questionnaire Design Resource Centre (QDRC) of Statistics Canada in the form of focus group testing in July, 2011. The methodology profile included five cognitive one-on-one interviews, two focus groups (n=10 each) with participants having a mix of chronic conditions, including six participants from a rural area, and seven participants with more than one condition. A summary report was prepared and most recommended changes were implemented. For those that were not, written justification was provided to the QRDC and the survey was finalized. Final revisions were completed in August 2011.

3.4.3.5 Data Collection, Processing

Data collection for the BCPCHC occurred from February 1, 2012 to March 31, 2012. One week prior to data collection an introductory letter was mailed to potential respondents approximately. Data were collected by telephone interviewers using Computer Assisted Telephone Interviews (CATI) conducted by the Edmonton Regional Office of Statistics Canada. The selected respondent was required to answer the survey directly and proxy interview was not permitted therefore if the selected respondent was not available or refused to participate, they were considered a non-response. The statistical data reference period was the last 12 months prior to the interview date.

Validation, consistency and distribution edits were conducted on the data set and errors in questionnaire flow, lack of information, and identification of incoherent

entries were corrected. Only, few data items were recorded in an open-ended format which required additional coding and a small number of data items on the microdata file were derived by combining items on the questionnaire to facilitate data analysis. No imputation was necessary in processing the data from the BCPCHC survey.

Statistics Canada's requirements for consent, privacy, confidentiality, survey collection, data quality, storage access and handling of information were strictly adhered to throughout this project[11].

3.4.3.6 Data quality

Survey errors virtually happen in all survey activities and can be classified into two non-sampling and sampling errors.

Non-sampling errors arise mainly due to: non-response, coverage, measurement and processing. Non-response can cause bias because of non-respondents might have characteristics that are different from respondents. Lack of coverage specifically was present for residents of Indian Reserves and Crown land, full-time members of the Canadian Armed Forces, inmates of institutions and residents of isolated areas[14].

Measurement errors (response errors) occur when the response provided differs from the real value and processing errors includes all data handling activities after collection and prior to estimation[14].

Sampling errors is only present in sample surveys. It is defined as errors that results from estimating a population characteristic by measuring a portion of the population rather than the entire population and is quantify by sampling variance[14].

3.4.3.6 Weighting

Survey weight is a value assigned to each case in the data. For example if we had half the size of our sample from minority populations, then each case in that category would have got a weight of 1 and each person in this category represent another person beside itself. Five variables used to create the weighting classes for the BCPCHC were disease: Disease (chronic conditions and multimorbidity), age group (40 to 59 or <60 years old) and province (used for the first step only).

Five steps were done to synthesize the final weights for the BCPCHC survey which included (1) calculation of the design-based sampling weight, (2) adjustment for unresolved cases, (3) retention of persons in-scope, (3) adjustment for non-response and inflation to the calendar year 2011[14].

3.4.4 Methods and data analysis

The baseline characteristics of the survey respondents were tabulated. Variables of interest for analysis were identified from both the BCPCHC and CCHS surveys. Descriptive variables were categorized based on number of responses and respondents. Based on Statistic Canada recommendations we regroup questions with five or more answers into two or three answer categories in order to make the weighted estimates more robust.

Statistics Canada's calibrated design weights and bootstrap weights were used to obtain population-level point estimates for proportions, prevalence risk ratios (PRRs) or odds ratios (ORs) and bootstrapping was used to determine 95% confidence intervals (CI) for the estimates.

According to Statistics Canada guidelines, if the coefficient of variation (CV) was 16% to 33.3%, the results were interpreted with caution as they may be unreliable. If the CV was >33.3%, the results were considered unreliable and were not presented.

The reasons that respondents provided regarding why they were/were not interested in using the different technologies were explored and illustrated.

To examine associations between exposures and outcomes of interest, log binomial and logistic regression modeling were used. Regression models were adjusted for characteristics usually used in the behavioral models of health service utilizations[15] and motivational models[1]. These models provide frameworks for analyzing factors that may be associated with patient utilization of telemedicine. These variables are categorized into baseline characteristics, current quality of health related care and attitude toward using new technologies.

The baseline characteristics of survey respondents including age, gender, location, income, smoking status, province and type and number of chronic conditions were identified.

Current quality of health related care was determined by types of barriers reported by respondents, hospitalizations, adverse health outcomes, perceived reasonable access and by location of closest specialist relative to that of the survey respondent (i.e., categorized by location of the specialist in the same or a different city than the survey respondent).

Attitude toward using new technologies was assessed by perception and past behaviors.

Logistic regression analyses and point estimates of ORs and 95% CIs using multivariate adjusted models were used to examine the associations between above mentioned variables and respondents' interest and attitude toward using information technologies for their care.

In addition, we also investigated respondents' attitudes towards how much time would have to be saved in order to adopt telehealth (i.e., < 30 minutes, 31-60

minutes, > 60 minutes or don't know) compared to an in-person visit with a specialist.

3.4.5 Results

3.4.5.1 Response Rates

4331 respondents to the 2011 CCHS were in-scope of the 2012 BCPCHC. This number represents all persons who were contacted and verified as in-scope (alive and at least 40 years old, not living in an institution, residing in one of the four provinces) as well as a portion of persons who were unable to be contacted during the collection period and who may have been in-scope. Of 2582 in-scope and available CCHS respondents, 2400 were selected for the 2012 BCPCHC.

Specifically excluded from the survey's coverage were residents of Indian Reserves and Crown land, full-time members of the Canadian Armed Forces, inmates of institutions and residents of isolated areas. The CCHS represented approximately 98% of the Canadian population > aged 12 years.

The response rate across the four provinces of interest to the 2011 CCHS survey was 68.7%, while the response rate to the BCPCHC survey was 80.0 %. (Table 3.1)

Table 3.1: Response rates to the 2011 CCHS and to the 2012 BCPCHC [14]

Province	**CHSS Response Rate**	**BCPCHC Estimated In-scope Persons**	**BCPCHC Responding Persons**	**BCPCHC Response Rate (%)**	**Overall Response Rate (%)**
Manitoba	71.1	415.6	334	80.4	57.2
Saskatchewan	72.5	457.1	370	81.0	58.7
Alberta	66.5	563.8	454	80.5	53.5
British Columbia	67.7	874.4	691	79.0	53.5
Total	68.7	2310.8	1849	80.0	55.0

3.4.5.2 Baseline Characteristics

The majority of survey respondents were white (87%), urban dwellers (83%), married or in common-law relationships (67%). Males and females were equally represented as were income levels. The greatest number of respondents were from British Columbia (45%), followed by Alberta (32%), Manitoba (13%) and Saskatchewan (11%). Most of the respondents were post-secondary and/or university graduates (50%) and were between the ages of 40-64 years (49%). Sociodemographic characteristics of respondents are shown in Table 3.2.

Among 2400 patients selected for BCPCHC, 1244 had hypertension, 209 had Diabetes, 207 had heart diseases and 111 had stroke. 629 patients had more than one chronic disease. BMI was corrected for self-report bias [16] and most respondents were overweight or obese (77%) and approximately 70% were current or former smokers. Health related baseline characteristics are shown in Table 3.3.

Table 3.2: Socio-demographic characteristics of survey respondents

	(n=1849) % (95% CI) †
Sex	
Male	49.9 (46.0 - 53.8)
Female	50.1 (46.2 - 54.0)
Age Category (y/o)	
40-64	48.8 (45.7 - 52.1)
65-74	26.9 (23.9 - 29.8)
75+	24.3 (21.5 - 27.0)
Region	
Urban	82.5 (79.5 – 85.4)
Rural	17.5 (14.6 – 20.5)
Household Income	
<$30,000	21.8 (18.9 - 24.7)
$30-54,999	27.4 (24.3 - 30.4)
$55-94,999	24.9 (21.5 - 28.4)
$95,000+	26.0 (22.3 - 29.6)
Marital Status	
Married / Common-law	66.9 (63.2 – 70.6)
Widowed/Sep/Div/Single	33.1 (29.4 – 36.8)
Level of Education	
< HS grad	21.3 (18.6 - 24.1)
HS grad/some post-secondary	22.0 (18.9 - 25.1)
Post-secondary grad (<	37.7 (33.9 - 41.5)
Bachelors)	19.0 (15.6 - 22.4)
Bachelor's degree or higher	
Province	
British Columbia	44.5 (41.3 – 47.7)
Alberta	31.7 (28.8 – 34.6)
Saskatchewan	10.8 (9.4 – 12.1)
Manitoba	13.0 (11.1 – 15.0)
Race/Ethnicity	
White	86.7 (83.5 - 89.9)
Aboriginal	4.2 (2.9 - 5.5)
Other	9.1 (6.0 - 12.2)

BMI=Body Mass Index; CI=confidence interval; Div=divorced; Grad=Graduate; HS=High School; Post-sec=Post-Secondary; Sep=separated

†All proportions (%) and 95% CI weighted and bootstrapped as per Statistics Canada guidelines

Table 3.3: Health related baseline characteristics

	(n=1849) % (95% CI) †
Smoking Status	
Current	17.6 (14.3 – 20.8)
Former	51.6 (47.4 – 55.7)
Never	30.8 (26.9 – 34.8)
BMI Category (kg/m^2)	
Normal / Underweight	23.3 (19.8 - 26.7)
Overweight	36.7 (32.5 - 40.8)
Obese	40.1 (36.2 - 44.0)
Type of Chronic Condition	
Hypertension	81.9 (78.9, 84.5)
Diabetes	26.2 (23.7, 28.9)
Heart disease	21.4 (18.7, 24.3)
Stroke	7.9 (6.4, 9.6)
Additional chronic disease	
Yes	63.0 (59.3, 66.6)
Drinking Status	
No	26.0 (22.6, 29.6)
Occasional	19.8 (16.8, 23.2)
Regular	54.2 (50.2, 58.2)

†All proportions (%) and 95% CI weighted and bootstrapped as per Statistics Canada guidelines

3.4.5.2 Current quality of health related care

Interestingly, despite having at least one chronic condition, 77% of respondents reported their health as 'Good' or better.

Table 3.4: Current health related care variables

	(n=1849) % (95% CI) †
Self-perceived Health	
Excellent/ Very Good	36.8 (33.0 - 40.6)
Good	40.2 (36.1 - 44.2)
Fair / Poor	23.0 (20.1 - 25.9)
Having a regular medical doctor	
Yes	95.1 (93.2 to 97.1)
No	4.9 (2.9 to 6.8)
Care by the same family doctor/nurse?	
Always	78.0 (74.5 to 81.5)
Often, Sometimes, Rarely, or Never	22.0 (18.5 to 25.5)
After-hours to regular doctor access	
Yes	31.9 (27.9 to 36.0)
No	68.1 (64.0 to 72.1)
Hospital emergency department use in the past 12 months	
0	91.9 (89.9 to 93.9)
1 or more	8.1 (6.1 to 10.1)
Overnight for your chronic condition	
No	95.2 (93.7 to 96.7)
Yes	4.8 (3.3 to 6.3)
received advice from a physician regarding lifestyle modifications	
Reducing sodium intake	61.0 (57.2-64.7)
Eating a balanced diet	63.5 (59.7-67.3)
Becoming physically active	74.8 (71.3-78.3)
Weight loss or weight control (for obese)	67.7 (61.3-74.1)
Tobacco cessation (for smokers)	88.4 (84.5-92.2)
No insurance for prescription medication	14.1 (11.2-17.0)

†All proportions (%) and 95% CI weighted and bootstrapped as per Statistics Canada guidelines

Table 3.5: Barriers to care

	(n=1849) % (95% CI) †
Difficulties getting health care services from your family doctor or general practitioner in the past 12 months	9.5 (6.7-12.3)
Barriers to specialist care	20.3 (17.7, 23.2)
Unreasonably poor access to specialists	11.5 (9.0, 14.6)
Difficulty paying for services in the past 12 months	12.0 (9.3-14.7)
Specific care needed for your chronic condition(s) but did NOT get it in the past 12 months	4.6 (2.6-6.6)

†All proportions (%) and 95% CI weighted and bootstrapped as per Statistics Canada guidelines

3.4.5.2 Attitude toward using new technologies

Less than 1% of respondents had experience with telemedicine in the last 12 months. A high proportion respondent owned a computer with internet access or a cell phone. 66.3% were interested in using email to interact with a specialist. However, respondents were less enthusiastic about text messaging than about email.

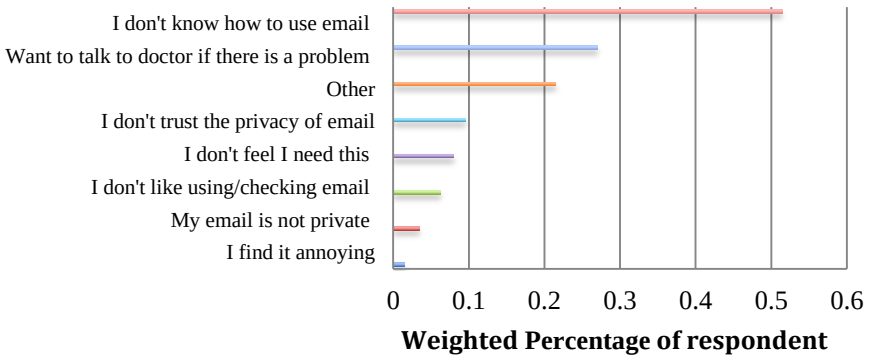
Table 3.6: Use of electronic technologies to interact with a specialist

	(n=1849) % (95% CI) †
Own computer with internet	76.4 (73.3, 79.3)
Own a cell phone	73.9 (70.7, 76.8)
Using email	66.3 (63.0, 69.5)
Using SMS	44.9 (41.2, 48.7)
Using telemedicine	65.1 (61.4, 68.6)

3.4.5.3 Willingness to use telemedicine, email and SMS

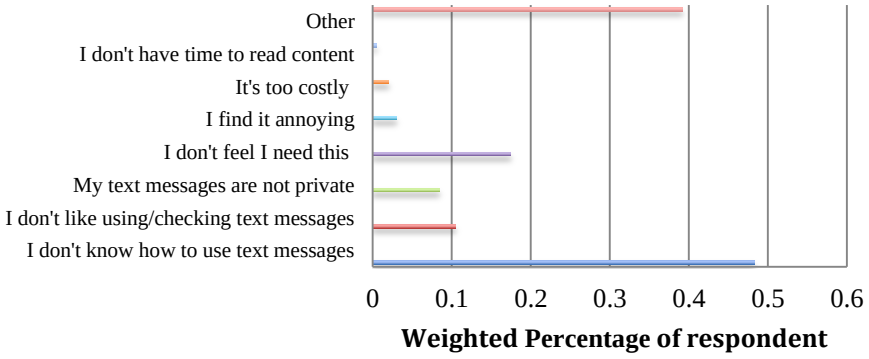
We found that respondents' willingness to use telemedicine was lower for primary care (49.9% CI 45.9, 53.9) than for specialized care (64.4% CI 60.9, 68), which is different from what was found in a previous study that was done in XXX country[9]. This might suggest that access to specialized care is more difficult (or considered more important) in Canada than in other countries. Respondents selected following reasons for unwillingness to receive the results of most recent medical test via email. (Figure 3. 1)

Figure 3.1 Reasons for unwillingness to receive test results via email



Respondents selected following reasons for unwillingness to receive advice and reminders about how to manage chronic diseases by text messaging to their via cell phone. (Figure 3. 2)

Figure 3.1 Reasons for unwillingness to receive text messages



3.4.5.4 Adjusted model of willingness to use telemedicine

Logistic regression analyses of multivariate adjusted models were used to examine the associations between respondents' characteristics and their willingness to use information technologies for their care.

Factors associated with willingness to use telemedicine for primary and specialized care were lack of a specialist in the same city as the respondent's home (a proxy for remote residence location), owning an internet connection, annual household income of more than $40,000, multimorbidity and self-perceived health status.

Table 3.7: Characteristics associated with willingness to use telemedicine for chronic care

	Interest in telehealth % (95% CI)
Specialist	
Same city	60.1 (53.7, 66.2)
Different city	70.2 (66.4, 73.7)
Barrier to specialist	
No	63.7 (59.4, 67.7)
Yes	71.4 (64.1, 77.7)
Own internet	
No	52.0 (44.8, 59.1)
Yes	69.2 (64.9, 73.3)
Own cell phone	
No	57.5 (50.6, 64.2)
Yes	68.4 (64.1, 72.4)
Sex	
Male	66.1 (60.7, 71.2)
Female	64.0 (58.8, 68.9)
Age	
40-64	70.3 (64.6, 75.4)
65-74	64.5 (57.7, 70.8)
75+	55.3 (48.5, 61.9)
Education	
< High School	49.8 (43.3, 56.3)
High School	61.8 (52.3, 70.4)
Post-secondary	68.2 (62.1, 73.8)
University degree	79.0 (71.5, 84,9)
Household income	
<$25,000	55.3 (45.9, 64.4)
$25-39,999	60.6 (52.3, 68.4)
$40-70,000	70.2 (64.1, 75.6)
>$70,000	67.2 (59.8, 73.9)
Insurance status	
No	67.1 (58.0, 75.1)
Yes	64.8 (60.7, 68.6)
Place of birth	
Born in Canada	66.5 (62.6, 70.2)
Born outside Canada	60.4 (50.4, 69.7)
Province	
Alberta	69.1 (62.0, 75.4)
Manitoba	57.0 (45.6, 67.7)
Saskatchewan	59.4 (50.9, 67.4)

British Columbia	66.0 (60.1, 71.4)
Ethnicity	
White	65.3 (61.5, 68.9)
Aboriginal/Other	63.7 (50.6, 75.0)
Type of Chronic Condition	
Hypertension	
No	63.8 (54.6, 72.1)
Yes	65.4 (61.5, 69.1)
Diabetes	
No	66.2 (61.8, 70.4)
Yes	61.9 (55.3, 68.0)
Heart disease	
No	66.9 (62.8, 70.7)
Yes	58.3 (49.9, 66.2)
Stroke	
No	66.7 (62.9, 70.3)
Yes	46.0 (33.2, 59.3)
More than one chronic disease	
No	75.4 (70.7, 79.6)
Yes	59.0 (54.0, 63.8)
Self-perceived health	
Excellent/ Very Good / Good	68.1 (64.0, 72.0)
Fair/Poor	54.8 (47.4, 61.9)

3.4.6 Discussion

The BCPCHC survey is the first large survey of western Canadians with chronic diseases that explores respondents' willingness to use new technologies for healthcare delivery (e.g. telemedicine).

Respondents expressed greater interest to use email or telemedicine than SMS (table 3.6). Because cellular phones are so widely available, SMS might be more available to the average person than the other two technologies. However, the relative lack of interest in SMS might be related to the interactive aspect of the other two technologies, and/or to a desire to have a more direct relationship with the physician.

This survey has been qualitatively tested to ensure validity. Results of validity testing suggest that the BCPCHC weighted totals represent the correct magnitude of the population of interest, and that for most domains the totals are reasonably accurate. However, there are some limitations to be considered when interpreting these results. First, the data used were cross-sectional. Consequently, conclusions regarding causality must be treated with caution. Although our response rates were relatively high, the sample was drawn from people who had already agreed to take the CCHS survey. (Table 3.1) Plus, respondents who were in both surveys may differ from general population as with any other survey. In addition, relationships with actual behavior were not examined.

Future studies should examine relationships between intentions and actual behaviors and should distinguish between different telemedicine interventions.

Despite these limitations, these findings will inform and facilitate the development and implementation of new interventions for management of chronic diseases to deliver care remotely.

3. References:

1. Werner, P. and E. Karnieli, *A model of the willingness to use telemedicine for routine and specialized care.* J Telemed Telecare, 2003. **9**(5): p. 264-72.
2. Pomery, E.A., et al., *From willingness to intention: experience moderates the shift from reactive to reasoned behavior.* Pers Soc Psychol Bull, 2009. **35**(7): p. 894-908.
3. Fishbein, M.a.A., I, *Beliej attitude, intention and behavior: An introduction to theory and research.* 1975, Reading, MA.: Addison-Wesley.
4. Ajzen, I., *The theory of planned behaviour: reactions and reflections.* Psychol Health, 2011. **26**(9): p. 1113-27.
5. Godin, G. and G. Kok, *The theory of planned behavior: a review of its applications to health-related behaviors.* Am J Health Promot, 1996. **11**(2): p. 87-98.
6. Armitage, C.J. and M. Conner, *Efficacy of the Theory of Planned Behaviour: a meta-analytic review.* Br J Soc Psychol, 2001. **40**(Pt 4): p. 471-99.
7. Webb, T.L. and P. Sheeran, *Does changing behavioral intentions engender behavior change? A meta-analysis of the experimental evidence.* Psychol Bull, 2006. **132**(2): p. 249-68.
8. Gerrard, M., et al., *A theory-based dual-focus alcohol intervention for preadolescents: the Strong African American Families Program.* Psychol Addict Behav, 2006. **20**(2): p. 185-95.
9. Brick, J.E., et al., *Public knowledge, perception, and expressed choice of telemedicine in rural West Virginia.* Telemed J, 1997. **3**(2): p. 159-71.
10. Rohland, B.M., et al., *Acceptability of telepsychiatry to a rural population.* Psychiatr Serv, 2000. **51**(5): p. 672-4.
11. Eikelboom, R.H. and M.D. Atlas, *Attitude to telemedicine, and willingness to use it, in audiology patients.* J Telemed Telecare, 2005. **11 Suppl 2**: p. S22-5.
12. Adler, K.G., *Web portals in primary care: an evaluation of patient readiness and willingness to pay for online services.* J Med Internet Res, 2006. **8**(4): p. e26.
13. Kelly, J.M., L.H. Schwamm, and M.T. Bianchi, *Sleep telemedicine: a survey study of patient preferences.* ISRN Neurol, 2012. **2012**: p. 135329.
14. StatisticsCanada, *Microdata User Guide, BARRIERS TO CARE FOR PEOPLE WITH CHRONIC HEALTH CONDITIONS*. 2012.
15. Aday L, A.R., *A Framework for the Study of Access to Medical Care.* Health Services Research, 1974. **9**(3): p. 208-220.
16. Shields, M., et al., *Bias in self-reported estimates of obesity in Canadian health surveys: an update on correction equations for adults.* Health Rep, 2011. **22**(3): p. 35-45.

CHAPTER 4. PROTOCOL FOR AN RCT EVALUATING THE BENEFITS OF TELEMEDICINE FOR MANAGEMENT OF DIABETIC NEPHROPATHY

4.1 Chapter introduction and background

The benefits of using information technologies for remote exchange of data between a patient and health care professionals, to assist in the management of an existing long-term condition like diabetes have been largely treated as self-evident. Accordingly, such technologies are widely available for use in Canada[1] and other countries.

Evidence for testing a new intervention often derives from cross-sectional studies and quasi-experimental studies. However, randomized controlled trials (RCT) are the "gold standard" study design to answer intervention questions.

Plus, because of complexity, context and environment dependent nature of telemedicine the effectiveness must be sufficiently tested in the context in which it would be implemented. No matter how many times telemedicine has been shown to be effective in different settings it should be properly tested in the setting it is planned to be implemented.

After systematically reviewing effect of telemedicine in diabetes management of -- and understanding the willingness and attitude of patients with chronic conditions in four province of Canadian we decided to design a study that would test the potential benefits of a specific telemedicine intervention among high risk patients with diabetic nephropathy.

We are planning to assess effectiveness of an intervention in the context of routine practice. Therefore, in contrast with explanatory trials, in which efficacy of interventions is tested in tightly controlled conditions this is a pragmatic RCT.

This will result in better external validity and more likely to indicate the likely intervention effects when applied in real life.

Due to lack of time and resources, only the trial design is presented in this thesis (i.e I did not execute the trial as part of my thesis).

4.1.1 Diabetic nephropathy

Diabetic nephropathy is a clinical syndrome characterized by albuminuria, hypertension, and progressive loss of kidney function. Approximately 20-30% of patients with diabetes (type 1 and type 2) develop nephropathy. The earliest clinical manifestation is the presence of low but abnormal levels of albumin in the urine. Microalbuminuria generally proceeds to overt proteinuria by 5-10 years. Once proteinuria is started, renal function gradually deteriorates over 10-15 years. This chronic complication of diabetes remains a major cause of morbidity and mortality for persons with either type 1 or type 2 DM. In Western countries, diabetes is the leading cause of ESRD. ESRD risk in men with diabetes is more than 12 times greater than in men without diabetes [2]. More than half of patients in renal replacement therapy programs have diabetes as the major cause of their kidney failure [3]. In the baseline cohort analysis of a large U.S Medicare study (n=1,091,201 aged >65 years) the presence of diabetes was found to more than double the risk of developing CRF compared with those without diabetes[4].

The progression of kidney failure is more frequent in patients with diabetes with 3.4 per 100 patient years requiring dialysis -- as compared with patients without diabetes who reached this endpoint at less than half the rate (1.6 per 100 patient years; $p<0.0001$)[4].

Intensified glycemic control has benefit in both type 1[5] and type 2 diabetes. The risk of development and progression of nephropathy increases gradually as the A1C levels rises. Better glycemic control (as reflected by lower A1C) level slow progression of nephropathy in people with diabetes. A1C level higher than 9% in

non-hemodialysis dependent patients with chronic kidney disease is common and associated with markedly worse clinical outcomes; lower levels of A1C (<6.5%) also seem to be associated with excess mortality[6].

Systemic hypertension can accelerate diabetic nephropathy. In two Scandinavian prospective study showed that aggressive Blood pressure (BP) reduction reduces the rate of progression of diabetic nephropathy [7, 8]. BP control is also known to improve the vascular status of patients with DM by varying degrees and reduce the rate of decline in glomerular filtration rate [9] .Beside the tight control of blood pressure, certain antihypertensive (e.g. angiotensin-converting enzyme inhibitors [ACEI] or angiotensin receptor blockers [ARB]) can slow the progression of nephropathy and reduce proteinuria independently of their antihypertensive effect and can impede the progression of renal disease.

In summary, better blood pressure and glycemic control in patients with diabetic nephropathy can improve clinical outcomes. Optimization of BP, use of ACEI and ARB, and control of plasma glucose levels should be the mainstay of therapy for diabetic nephropathy.

4.2 Rationale

Studies have clearly shown that increased frequency of blood glucose and blood pressure testing; dramatically improve glycemic and blood pressure control and outcomes in patients. Previous reviews have concluded that telemedicine may favorably affect A1C in unselected populations of people with diabetes. However, the benefits of telemedicine in a high risk population of patients with diabetic nephropathy have not been shown – nor has the feasibility of such an intervention been demonstrated in the community health care setting.

Telemedicine offers the potential to address several of the barriers to effective care for patients with diabetic nephropathy by providing:

1. Reinforcement and positive feedback to patients to increase adherence
2. Real-time access to blood glucose and blood pressure data optimization of treatment plans
3. Alerts to patients and providers if blood glucose and/or pressure levels are above a pre-established threshold

The proposed study will use technology-assisted case management to target patients with diabetic nephropathy residing in remote areas. Due to distance to specialized care this population is at the highest risk for complications arising from uncontrolled hypertension and diabetes.

4.2 Objectives

The purpose of this study is to determine if a chronic care model using telemedicine can improve quality of care in patients with CKD and DM and hypertension compared to usual care.

The primary objective of this study is to test the effectiveness of telemedicine for control and monitoring of of blood glucose level and blood pressure of patients with stage 3-4 of CKD with diabetes and hypertension.

4.3 Trial design

The study uses a two parallel group randomized clinical trial design

4.3.1 Subject population

120 Participants of this study will be selected from patients with stage 3 or 4 CKD with type 2 diabetes and hypertension. We will approach patents in the waiting room of the nephrology clinic of University of Alberta hospital to identify eligible study subjects. The nephrologist of eligible patients will be asked permission to enroll their patients in this 6 month study. The procedures and risks will be explained to the patient. If the patient signs the consent form, then patient will be

randomized (1:1) to one of the groups and additional information will be revealed to the patient according to the allocated group. The specific interventions that will be studied will not be disclosed to the participants, and both groups will be told that they are in the more intensive intervention group in order to control for Hawthorne effect. The Hawthorne effect is a tendency of some people to improve or modify some aspects of their behavior when they are participants in an experiment.

Inclusion criteria

- Age>18 y/o
- Diagnosed with CKD stage 3 or 4*
- Diagnosed with type 2 diabetes *
- Diagnosed with hypertension*
- Able to read, write and understand English
- Have access to internet connection at home and be able to work with a computer

* Confirmed by nephrologist

Exclusion criteria

- Unable to give consent
- Living in a nursing home or other health care facilities
- Severe mental illness
- Life expectancy less than 6 months
- Primary renal diagnosis requiring specific management (non-diabetic glomerulonephritis, vasculitis, etc.)

4.3.2 Randomization and blinding

The randomization sequence is generated by the online web application provided by the EPICORE website -- using a block randomization scheme stratified by

CKD stage. The randomized assignment for eligible participants is accessible to the study coordinator but the outcome assessors and analyzer will be blinded. Justified concept deception will be used to minimize the observer effect in which subjects improve or modify aspects of their behavior due to the fact that they know they are being studied. The details of the intervention that will be provided to other group will not be disclosed to participants in consent form so each group thinks they are receiving the intervention. This concealment bears no potential harm to the participants. A debriefing session will be held in which we will disclose to the participants the use of deception in the research and provide them with the option of withdrawing from the study.

4.3.3 Intervention and usual care group

There is an intervention group (using web-based telemedicine case management) and a usual care group. Participants in the telemedicine intervention group will use FORA D20 Blood Glucose plus pressure monitoring system to check their blood glucose and blood pressure at least once a day. Participants in the intervention group will receive half a day of training on the FORA system (http://www.foracare.com/flash/d20/start.html) and will be taught how to use the secure website.

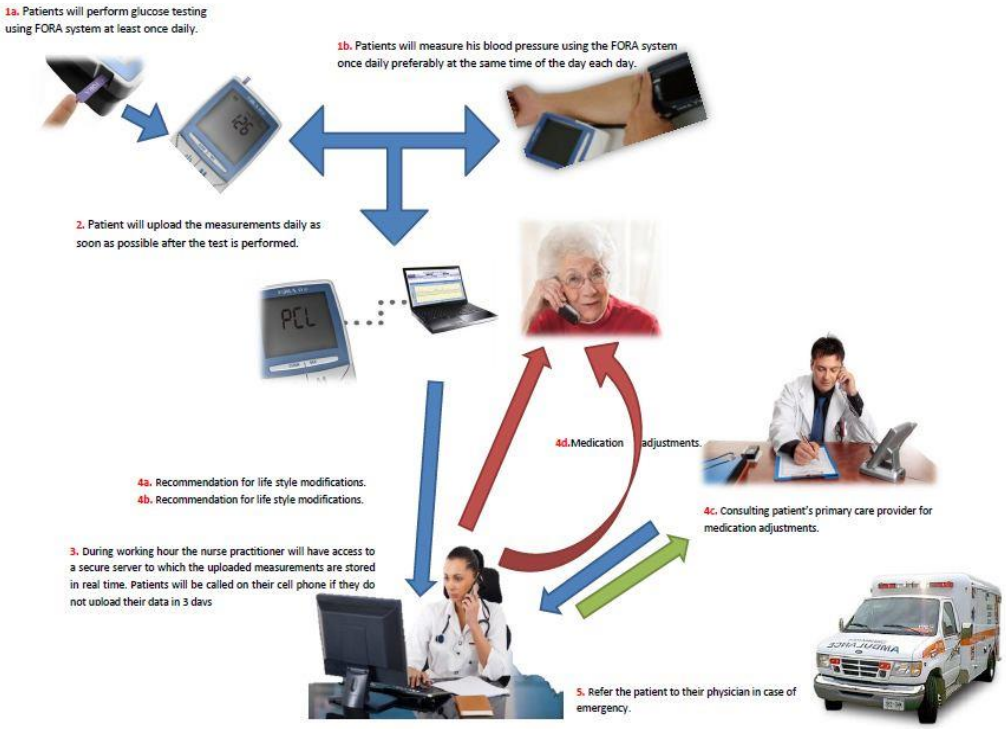
Participants and controls will receive enough glucose test strips (free of charge) to allow testing at least once a day. They will be asked to upload their daily measurements to their computer and send their data through a secure website to our study center. The nurse practitioner at study center serves as an adjunct to usual care by providing more frequent contact between the patient and health care system. The nurse practitioner will check the uploaded measurements during the office hours. The nurse practitioner will respond using the participants health records together with study algorithms based on current guidelines. The response will be prepared in one these four formats:

1) Motivation message

2) Recommendation for life style modifications (e.g. exercise and low salt intake)
3) Medication adjustments under the supervision of the patient's nephrologist
4) Referring the participant to their physician or to an emergency department

Participants will receive their response through their preferred method; text message or phone call or the study website. If any change is made to the participant's medications as part of the study, the patient's family physician will be notified by email and fax. We also will ask participants to notify the nurse practitioner if their medications have been changed by their physician outside of the study. A schematic graph of the intervention is available in below.
To simulate participation in the intervention group, participants in the usual care group will receive a series of information pamphlets each week in the by email.

Figure 4.1: Intervention chart



4.3.4 Primary study endpoints/secondary endpoints

The primary outcome will be A1C at 6 months post-randomization. Considering all of the mentioned studies including the UKPDS, A1C is a good surrogate for important endpoints. The secondary outcomes will be systolic and diastolic blood pressure at 6 months post-randomization.

Patients' and care providers' experience in this trial will be used to evaluate the technical feasibility of conducting a larger RCT or implementing a similar telemedicine intervention in the future.

At the end of the study, the participants will receive a questionnaire to assess their experience with the telemedicine intervention. The questionnaire will test four areas of overall satisfaction from using telemedicine, use of technologies, effect of feedback and change in behavior and self management. The development of this questionnaire will be based on a similar questionnaire from previous studies [10, 11]. As the experience of care providers is also important for future implementation, the providers will be invited to participate in two interviews. In these interviews, the health providers will tell about their experience with the intervention and will provide suggestions for improvement. Patients and providers will both answer questions related to their willingness to participate in/recruit to a future trial of telemedicine and factors that would make them less or more willing to participate.

4.3.5 Duration of Study

The A1C level (primary outcome) is proportional to average blood glucose concentration over the previous four weeks to six months. So we decided to follow each patient for 6 months. We estimated that we could recruit the target sample size in 1 year.

4.4 Statistical Plan

4.4.1 Statistical Methods

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline demographic variables as appropriate. Continuous variables will be summarized with descriptive statistics (mean, standard deviation). Ninety-five percent confidence intervals may also be presented. Frequency counts and percentage of subjects within each category will be provided for categorical data. Intention to treat analysis using ANCOVA statistics will be used in this study to test the statistical significance of difference between A1C level between intervention and usual care group. An advantage of the use of ANCOVA is that it adjusts for baseline differences between the two groups. ANCOVA also has more statistical power than the t-test, so sample size requirements will be lower.

4.4.2 Sample size

With 60 participant randomized to each group, considering 25% dropout, we will have 80% power to detect a difference of 0.5 in A1C between the intervention and usual care groups.

We assumed not greater than 0.5 correlation between baseline and follow-up A1C values based on previous studies. Below the output of STATA software has been provided using ANCOVA method to calculate the sample size for this study. The calculated sample size (N=48) was inflated by 25% to account for dropouts.

Sample size calculation STATA

```
Estimated sample size for two samples with repeated measures
Assumptions:
alpha =   0.0500  (two-sided)
power =   0.8000
m1 =         8
m2 =       8.5
sd1 =          1
sd2 =          1
n2/n1 =     1.00
number of follow-up measurements =         1
number of baseline measurements =         1
```

```
correlation between baseline & follow-up =    0.500
Method: ANCOVA
 relative efficiency =    1.333
    adjustment to sd =    0.866
        adjusted sd1 =    0.866
        adjusted sd2 =    0.866

 Estimated required sample sizes:
                  n1 =       48
                  n2 =       48
```

4.5 Knowledge translation plan

Once complete, we will publish the results of this study in a peer reviewed journal. If the results suggest that telemedicine is beneficial in this population, this would justify conducting a longer study with larger sample size to test the effect of telemedicine on clinically relevant outcomes including mortality, hospitalization and progression to kidney failure..

4.6 Ethical considerations

This study will be conducted according to Canadian and international standards of Good Clinical Practice for all studies. Applicable government regulations and University of Alberta research policies and procedures will also be followed. Actively participating in the telemedicine intervention can be burdensome for this group of patients. Therefore, the researchers always take into account the condition of the patient when a research activity will be undertaken.
This protocol and any amendments will be submitted to the University of Alberta ethics board for formal approval to conduct the study. All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form will be submitted with the protocol for review and approval by the ethics board. The formal consent of a subject, using the approved consent form, will be obtained before that subject is submitted to any study procedure. This consent form must be signed by the subject, and the investigator-designated research coordinator obtaining the consent.

4.7 Limitations

Barriers such as lack of funding, skilled personnel, incentives, and time exist for conducting any clinical trial. However, some limitations are predictable for this study.

Generalizability of our result to all of the CKD patients will be limited because we will be including only patients with stage 3 or 4 CKD. However, these groups

of patients are most likely to benefit from more frequent follow-ups. Plus, these groups of patients are more homogenous in terms of treatment management protocols and less likely to receive more complicated medications for their kidney disease. Therefore, they are easier for the nurse practitioner to manage.
The choice of primary outcome and short duration of study is another limitation of our study. Finally, other feasibility challenges for implementing telemedicine, including policy-related, organizational and economical cannot be evaluated in this trial.

However, telemedicine in CKD patients has not been studied extensively and it is reasonable to conduct a small and short-term trial that assesses process-based outcomes before conducting a definitive trial of the effect of telemedicine on clinically relevant outcomes.

4. References:

1. Hendy, J., et al., *An organisational analysis of the implementation of telecare and telehealth: the whole systems demonstrator.* BMC Health Serv Res, 2012. **12**: p. 403.
2. Gilbertson, D.T., et al., *Projecting the number of patients with end-stage renal disease in the United States to the year 2015.* J Am Soc Nephrol, 2005. **16**(12): p. 3736-41.
3. Collins, A.J., et al., *Excerpts from the United States Renal Data System 2004 annual data report: atlas of end-stage renal disease in the United States.* Am J Kidney Dis, 2005. **45**(1 Suppl 1): p. A5-7, S1-280.
4. Foley, R.N., et al., *Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare population, 1998 to 1999.* J Am Soc Nephrol, 2005. **16**(2): p. 489-95.
5. Barr, C.C., *Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive insulin therapy, by The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. N. Engl. J. Med 342:381-9, 2000.* Surv Ophthalmol, 2001. **45**(5): p. 459-60.
6. Shurraw, S., et al., *Association between glycemic control and adverse outcomes in people with diabetes mellitus and chronic kidney disease: a population-based cohort study.* Arch Intern Med, 2011. **171**(21): p. 1920-7.
7. Mogensen, C.E., *Long-term antihypertensive treatment inhibiting progression of diabetic nephropathy.* Br Med J (Clin Res Ed), 1982. **285**(6343): p. 685-8.
8. Parving, H.H., et al., *Effects of long-term antihypertensive treatment on kidney function in diabetic nephropathy.* Hypertension, 1985. **7**(6 Pt 2): p. II114-7.
9. Vinik, A.I. and E. Vinik, *Prevention of the complications of diabetes.* Am J Manag Care, 2003. **9**(3 Suppl): p. S63-80; quiz S81-4.
10. Nes, A.A., et al., *The development and feasibility of a web-based intervention with diaries and situational feedback via smartphone to support self-management in patients with diabetes type 2.* Diabetes Res Clin Pract, 2012. **97**(3): p. 385-93.
11. Kristjansdottir, O.B., et al., *Written online situational feedback via mobile phone to support self-management of chronic widespread pain: a usability study of a Web-based intervention.* BMC Musculoskelet Disord, 2011. **12**: p. 51.

CHAPTER 5. SUMMARY AND CONCLUSIION

Recently there has been a lot of interest in telemedicine as a method to combat several problems in the healthcare system, including management of chronic diseases like diabetes -- a leading cause premature death and disability worldwide. Despite its theoretical benefits, telemedicine is an unproven tool for improving the quality of chronic disease care, especially for remote-dwelling patients. The aim of the research was to investigate the potential of this type of system for diabetes care and other chronic conditions.

We did a systematic review and quantitative summary of the effects of different methods of telemedicine for management of diabetes, as compared with usual care. In pooled analysis of 36 randomized trials, mean of A1C levels in the telemedicine group was significantly lower than those of patients in the usual care group (weighted mean difference (WMD) -0.49, 95% CI -0.64, -0.35, $p<0.00001$) with evidence of statistical heterogeneity between studies ($I^2 = 65\%$). Plus, other systematic reviews have shown that telemedicine interventions can be effective in improving the quality of life and health outcomes and also result in cost savings in chronic conditions [1, 2].

We also described the results of a survey that was used to demonstrate the willingness of patient to use telemedicine. The result showed that 65.1% (CI 61.4, 68.6) of patients with self-reported chronic disease are willing to use telehealth for their primary and specialized care. 41.7% (CI 36.9, 46.7) of respondents would prefer telemedicine to an in-person visit with a specialist if it saves them more than 60 minutes.

Our systematic review suggests that telemedicine could be effective in diabetes management and the survey result suggest that the people with chronic disease are willing to use telemedicine for their care. However, there is a consensus amongst

reviews that further evaluations are needed to address the limitations of the current evidence for the effectiveness of telemedicine interventions. Hence, we have presented a protocol for a randomized trial to demonstrate the feasibility and effectiveness of telemedicine for improving process-based outcomes among high risk Alberta patients with diabetic nephropathy

We suggest a number of ways to improve the evidence regarding the use of telemedicine in chronic disease care before its universal implementation in Canada.

First, better quality of evidence is needed. There are limited studies that have used an appropriately large sample size and are of sufficient duration to test the effectiveness of telemedicine. In our review most evaluations have not considered the effectiveness of the intervention for a period longer than 12 months. For example, most studies of telemedicine use in patients with heart failure evaluated outcomes at either 6 or 12 months after implementation of the intervention[3]. It is unclear whether users will be willing to continue using telemedicine for longer periods of time -- and therefore patterns of use (and the effectiveness of telehealth) may change over time, both of which may affect outcomes. Therefore it is essential to develop a better understanding of whether the effectiveness and cost-effectiveness of telehealth are durable over time.

Given the potentially context-dependent nature of health systems interactions, it is important that more RCTs of the benefits of telehealth are carried out in Canada. Extrapolation of results from other settings to the Canadian health care system may not be reasonable, given differences in participant characteristics and in how the health systems are structured, funded and managed differently in each country.

Cost-effectiveness should also be evaluated in Canada before universal implementation. A review of 23 studies found that 91% showed home telecare to be cost-effective, in that it reduced use of hospitals, improved patient compliance,

satisfaction and quality of life. However, the heterogeneity among cost-effectiveness indicators limits the generalizability of these findings. [4]. A review of telemedicine use in COPD found that only 2 out of 23 identified studies examined the costs associated with the intervention [5]. Another review identified 130 evaluations of telehealth for heart failure, but only 22 provided data to allow an evaluation of economic outcomes[6].

Given the fact that telemedicine is mostly used as an add-on to usual care (resulting in additional costs), more evaluations are needed to identify which groups of patients are most willing to use and benefit from it. This might make people with specific health conditions, or health status, or with certain socio-demographic characteristics better candidates for using telemedicine. For instance, there is some evidence to suggest that telemedicine monitoring for heart failure or psychiatric conditions is more effective than for diabetes[7, 8].

It is also essential to evaluate which component of telemedicine is effective. Our systematic review found that interventions with an interactive component were significantly more effective for reducing A1C level compare to non-interactive interventions. Since telehealth interventions often comprise a number of components, making generalizations across different interventions makes it difficult to identify which interventions are the most effective or cost-effective.

In conclusion, telemedicine appears to improve A1C level among unselected patients with diabetes – and there also appears to be considerable interest in using telehealth as a supplement to usual care, at least among Western Canadians with chronic conditions. However, much research is required before universal implementation of telemedicine can be justified for management of chronic conditions like diabetes.

5. References:

1. Polisena, J., et al., *Home telehealth for diabetes management: A systematic review and meta-analysis.* Diabetes, Obesity and Metabolism, 2009. **11 (10)**: p. 913-930.
2. Barlow, J., et al., *A systematic review of the benefits of home telecare for frail elderly people and those with long-term conditions.* J Telemed Telecare, 2007. **13**(4): p. 172-9.
3. Klersy, C., et al., *Economic impact of remote patient monitoring: an integrated economic model derived from a meta-analysis of randomized controlled trials in heart failure.* Eur J Heart Fail, 2011. **13**(4): p. 450-9.
4. Rojas, S.V. and M.P. Gagnon, *A systematic review of the key indicators for assessing telehomecare cost-effectiveness.* Telemed J E Health, 2008. **14**(9): p. 896-904.
5. Jaana, M., G. Pare, and C. Sicotte, *Home telemonitoring for respiratory conditions: a systematic review.* Am J Manag Care, 2009. **15**(5): p. 313-20.
6. Bensink M, H.D., Wootton R, *A systematic review of successes and failures in home telehealth: preliminary results.* Journal of Telemedicine and Telecare, 2006. **12**(sup(3)): p. 8-16.
7. Dellifraine, J.L. and K.H. Dansky, *Home-based telehealth: a review and meta-analysis.* J Telemed Telecare, 2008. **14**(2): p. 62-6.
8. Pare, G., M. Jaana, and C. Sicotte, *Systematic review of home telemonitoring for chronic diseases: the evidence base.* J Am Med Inform Assoc, 2007. **14**(3): p. 269-77.

APPENDIX 1: Search strategy for MEDLINE

Diabetes and Telehealth

MEDLINE - FINAL Feb 16

1. diabetes mellitus/ or exp diabetes mellitus, type 1/ or exp diabetes mellitus, type 2/
2. (diabet* or IDDM or NIDDM or MODY).ti,ab.
3. Diabetes, Gestational/ or exp Diabetes Insipidus/ or gestational diabetes.ti.
4. 2 not 3
5. 1 or 4
6. Computers, Handheld/
7. telecommunications/ or electronic mail/ or telemedicine/ or remote consultation/ or telephone/ or cellular phone/ or exp videoconferencing/
8. exp Computer Communication Networks/
9. (telemedic* or tele medic* or tele health or telehealth).ti,ab.
10. (cell* phone* or telephon* or mobile or smartphone* or smart phone* or land line* or landline* or iphone* or blackberr* or palmpilot* or palm pilot* or android or pocket pc or personal digital assistant* or pda*).ti,ab.
11. Radio/
12. (2 way radio* or two way radio* or walkee talkee).ti,ab.
13. 6 or 7 or 8 or 9 or 10 or 11 or 12
14. 5 and 13
15. exp clinical trial/
16. randomi?ed.ti,ab.
17. placebo.ti,ab.
18. dt.fs.
19. randomly.ti,ab.
20. trial.ti,ab.
21. groups.ti,ab.
22. or/15-21
23. animal/
24. human/
25. 23 not (23 and 24)
26. 22 not 25
27. 14 and 26

APPENDIX 2: Details of telemedicine interventions

Study	Telemedicine intervention group	Control group
Ahring, 1992	Counseled every week over the telephone after transferring their last week's glucose measurements (five per day) through modem to adjust insulin and food intake if necessary.	No scheduled contacts or data transmission. Their blood glucose data was evaluated on their regular visits every 6 weeks
Bierman, 2002	Modem transmission of memory blood glucose-meters data at least every 2 weeks, with clinician feedback on proper dose adjustment was given by telephone every 2 to 4 weeks. A 24-h voice recorder system was available for patients.	Face-to-face visits at least every 2 months.
Bond, 2006	Accessed a study website that provided them access to an on-line library, advice and counseling from a nurse via e-mail, a personal electronic log of self-management activities, and weekly on-line problem-solving group discussions.	Received their standard diabetes. No educational or training materials associated with the intervention were provided to the control group. Had access to educational materials/classes provided by their health provider through traditional face-to-face classroom methods and/or via the Internet.
Chase, 2003	Transmitted their blood glucose information every 2 weeks, with clinician feedback to discuss and make treatment changes as needed plus 2 clinical visits at 0 and 6 months.	No scheduled contacts or data transmission. three clinic visits (at 0, 3 and 6 months), with the option to telephone or fax blood glucose results to the clinic
Cho, 2006	Logged onto the website at their convenience and uploaded their glucose levels, current medication, blood pressure, changes in their lifestyle, weight and other factors that might influence the blood glucose level. Three endocrinologists, a nurse, and a dietitian logged onto the system daily and sent appropriate recommendations based on the patients' uploaded blood glucose data) to each patient in the intervention group every 2 weeks plus clinic every 3 months.	Used a conventional note-keeping record system. Control patients were given our clinic's usual recommendations about medications, dosage, and lifestyle modification from the same endocrinologists who met with the intervention group and outpatient clinic every 3 months
Farmer, 2005	Nurse-initiated phone calls, giving advice on drugs, food intake and activity level in response to real-time blood glucose test results automatically transmitted by the phone to a remote server every 2.5 weeks on average.	The results were transmitted to the server for data storage but were not available to the nurse for feedback. . Minimal feedback presented on the phone screen consisted of a graphical time series of blood glucose readings for the previous 24 h only.
Franklin, 2006	The automated delivery of a series of appropriately tailored messages (Sweet Talk program), including a weekly reminder of the goal set in clinic, and a daily message providing tips, information or reminders to reinforce this goal.	Conventional therapy without Sweet Talk program.
Graziano, 2009	Received a daily, automated telephone message regarding diabetes	Received usual care.
Harno, 2006	An e-health application with diabetes management system and a home care link. Patients downloaded their measurements directly from the blood glucose meter into regional database using a modem. The self-management system allowed the diabetes team to transmit text messages to patients with mobile phones and Internet access.	Regular general practitioner visits about every 3 months

Istepanian, 2009	Measure their blood glucose with a sensor which transmitted the readings to a mobile phone via a Bluetooth wireless link. Clinicians were then examined and respond to the readings which were viewed with a web-based application.	Received care with their usual doctor in the outpatient and/or primary care setting.
Izquierdo, 2009	Usual care plus a telemedicine unit in the school nurse office to videoconference between the school nurse, child, and diabetes team every month.	Medical visits every 3 months and communication between school nurse and diabetes team as needed by phone.
Jansa`, 2006	Recorded and sent their blood glucose data using GlucoBeep device through Internet 9 times in 6 months of study. Patient could leave a voice message about insulin doses and events. Appropriate counseling to the patient based on stored data on the server provided by a nurse.	12 outpatient appointments.
Kim, 2007	Downloaded their daily blood glucose levels, exercise and medications. Received weekly optimal recommendations were sent via cellular phone (SMS) and the Internet.	Were provided with glucose-meters and received their usual outpatient management from their physicians.
Kim, 2003	Wrote self-management logs on blood glucose levels, diet and exercise. A dietician analyzed the diet diaries, and medication adjustments were made by the researcher. Telephone intervention was given twice a week for the first month and then weekly for the second and third months	Visited their physician every 3 months
Kim, 2008	Accessed web using personal cellular phones or internet services to input daily blood glucose levels. Weekly optimal recommendations were sent via cellular phone and the Internet.	Met the endocrinologist specialist two or four times during the 6-month period. An endocrinologist provided the participants with recommendations about their medications, medication dosages, lifestyle modifications, and other treatment modalities. Whether the doctor chose that the patient consult for special education or the patient himself or herself wished for it, the nurse or the dietitian assists the patient with more individualized and detailed information for lifestyle modification.
Kwon, 2004	Patients sent data on their blood glucose levels and drug information, and patients also could record changes in blood pressure or weight and any questions or detailed information through the internet. After reviewing all information. Appropriate recommendations by physician were sent every two weeks.	Visited the diabetes centre monthly and received their usual outpatient treatment from their physicians.
Lim, 2011	Automatically transferred blood glucose levels at least 8 times a week to a hospital-based server. Once the data are transferred to the server, an automated system, the clinical decision support system, generates and sends patient-specific messages by mobile phone.	Did not receive an intervention and were advised to follow-up according to their current medical care.
Maljanian, 2005	Received a series of 12 weekly phone calls reinforcing base education and self-management skills.	Received usual care.
Marrero ,1995	Transmitted self-monitoring blood glucose data by modem to the hospital every 2 weeks. Transmitted data were reviewed by nurse practitioners who telephoned subjects to discuss regimen adjustments based on an algorithm.	Received standard care with regimen adjustments made by physicians. No scheduled contacts or data transmission.
McCarrier, 2009	The case manager (nurse) reviewed patient-uploaded data weekly and initiated weekly e-mail contact with patients during the first month, after which she initiated contact based on individual patient goals (with a minimum of once per month) but continued to review records weekly and provide feedback to patients uploading information or initiating e-mail contact, plus usual care.	Usual clinic care alone.

McMahon, 2005	Uploaded blood pressure and blood glucose levels. The care manager responded to queries within one working day during office hours. The care manager and primary care providers communicated mainly by email. Physicians made changes in medication directly into the pharmacy's electronic ordering system.	Received usual care by their physicians
Montori, 2004	Modem transmission of blood glucose 4 times/day at least every 2 weeks, with clinician feedback within 24 h, plus every 3 months clinic visit.	Modem transmission at least every 2 weeks, without clinician feedback but free to contact the nurse on demand plus every 3 months clinic visit.
Oh, 2003	Continuous education and reinforcement of diet, exercise and medication adjustment, as well as frequent self-monitoring of blood glucose levels. Telephone intervention was performed twice per week for the first month, and then weekly for the second and third months. Subjects were requested to write self-management logs, including blood glucose, diet and an exercise diary. The diet diaries were analyzed by a dietitian, and subjects instructed about the results by telephone counseling or mail. All medication adjustments were communicated to the subjects' diabetes specialist.	Received usual care.
Piette, 2001	Automated statements and queries recorded in human voice transmitted to patients biweekly placed at a convenient time for participants and required entering of participation number. Questions about blood glucose monitoring, symptoms, problems related to diabetes as well as diabetic management were asked. Biweekly automated assessment and self-care education calls, with nurse telephone follow-up based on the assessment results. Patients also have the option to participate in a 3- to 5-min interactive self-care education module on the telephone	Received usual care and had no contact with the automated telephone disease management system for clinical assessments, patient education, appointment reminders or follow-up data collection.
Quinn, 2008	Received cell phone-based software. The software provided real-time feedback on patients' blood glucose levels, displayed patients' medication regimens, incorporated hypo- and hyperglycemia treatment algorithms, and requested additional data needed to evaluate diabetes management. Patient data captured and transferred to secure servers were analyzed by proprietary statistical algorithms. The system sent computer-generated logbooks (with suggested treatment plans) to intervention patients' health care provider.	Also received one blood glucose meters and adequate testing strips and lancets for the duration of the trial. They were asked to fax or call in their logbooks every 2 weeks to their health care provider until their BG levels were stabilized in the target ranges or until their health care provider changed testing frequency. Investigators asked treating health care provider to follow their usual standards of care for the patients' diabetes management.
Ralston, 2009	Sent blood glucose readings weekly, and send secure e-mail as needed. The care manager reviewed blood glucose levels at least once per week, adjusted hypoglycemic medications, and conferred with the primary care provider as needed.	Received usual care.
Rami, 2006	Transmission of data (date, time, blood glucose, carbohydrate intake, insulin dosage) via mobile phone, at least daily by patient6s, to a server and diabetologists sent back their advice via short message service (SMS) or a personalized message with more specific advice once a week.	Routine scheme with a daily written protocol (paper diary) and a clinical visit after 3 months.
Rodriguez-Idigoras, 2009	Sent, in real-time and via their mobile phone, their blood glucose measurements to the call center. When blood glucose levels were not within normal range, the system sent an alarm to the call center, and previously established protocol interventions were implemented. Physicians could contact their patients via mobile phone.	Received usual care.
Rossi, 2010	Diabetes (Interactive Diary automatic carbohydrate/insulin bolus calculator) on the mobile phone of the patient to Reinforcement of diet, insulin adjustment, physical activity using patient-physician communication via short text messages.	Received the standard educational approach

Schillinger, 2009	Received weekly automated telephone calls regarding disease management. Patient responses triggered either immediate, automated health education messages and/or subsequent nurse phone follow-up,	Received usual care.
Shea, 2009	Received a home telemedicine unit consisting of, videoconferencing with nurse case managers, remote monitoring of glucose and blood pressure, access to patients' own clinical data and access to a special educational web page	Patients in the usual care group received clinical care from their primary care providers, without other guidance or direction from study personnel.
Stone, 2010	Ongoing monitoring of blood glucose level, blood pressure, and weight; and daily transmission of these data to study providers via a secure network. The nurse practitioner reviewed these information and contacted participants for adjustment of glycemic, blood pressure, and lipid control medications, education and self-management counseling. Participants also could initiate contact with the study diabetes nurse educator to discuss concerns related to diabetes management.	Received usual care.
Tsang, 2001	Recorded information about their meal portions and blood glucose reading in a hand-held electronic diary and transmitted the data to the diabetes monitoring system through a telephone modem. Patients then received instant feedback about the carbohydrate, protein and fat content of the meal as well as the calorie content on daily bases.	Had conventional follow-up consultations with a diabetes team
Thompson, 1999	Regular telephone contact with the nurse as needed. Most calls involved insulin adjustment. The nurse reviewed patients' records with their physicians as needed.	Patients continued their usual contact with the endocrinologist at the clinic for insulin adjustment.
Yoo, 2009	Automatically sent their blood glucose, blood pressure twice a day and body weight once a day via their cellular phone to a central study database. As soon as participants transmitted their glucose measurement through their cellular phones, they immediately received messages of encouragement, reminders, and recommendations according to a pre-defined algorithm. Participant's also sent their exercise time using the short message service (SMS). Participants received information via SMS three times a day regarding healthy diet and exercise methods, along with general information about diabetes, hypertension and obesity. Physicians could follow participant's trends in blood glucose levels, blood pressure and body weight changes, allowing them to send individualized recommendations to patients when needed.	Patients in the control group visited their clinic according tom their routine schedule and received the usual out-patient treatment from their physicians during the study period.
Yoon, 2008	Asked to access a website by using a cellular phone or to wiring the Internet and input their blood glucose levels weekly. Participants were sent the optimal recommendations by both cellular phone and the Internet weekly.	Met the endocrinologist specialist several times during the 12 months.