UNIVERSITY OF CALGARY

Quality of care and outcomes for First Nations People and non-First Nations People with diabetes mellitus

by

Vinay Deved

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE

DEGREEE OF MASTER OF SCIENCE

DEPARTMENT OF COMMUNITY HEALTH SCIENCES

CALGARY, ALBERTA

FEBRUARY, 2012

UNIVERSITY OF
CALGARY

ABSTRACT

Background: First Nations People experience higher rates of chronic kidney disease (CKD) and mortality compared to non-First Nations People. We examined the two groups for differences in quality of care and associations with renal failure and death.

Methods: Adults with diabetes were identified through administrative data from 2005 to 2008. Differences in four diabetic quality indicators [proteinuria, LDL, hemoglobin A1C (HbA1C), creatinine] were assessed during a one year period. Differences in renal failure and death were also assessed.

Results: For those without CKD, First Nations People were less likely to receive all four quality indicators and to achieve the HbA1C target. Rates of renal failure and death were higher for First Nations People, and were associated with lack of measurement (LDL) and levels above target (HbA1C).

Conclusion: Differences in quality of care between First Nations and non-First Nations People with diabetes exist, and may contribute to worse clinical outcomes.

ACKNOWLEDGEMENTS

I would like to thank my supervisor Dr. Brenda Hemmelgarn. She is a wealth of knowledge, a pillar of support, and stadium of encouragement; without her, I would not have completed this.

I would like to thank Andrea Soo for her help with data collection and analysis.

I would also like to express my appreciation to my committee, Dr. Nathalie Jette and Dr. Hude Quan, who provided valuable commentary, advice and insight.

DEDICATION

To my mom, dad, and sister, for their love and support my entire life.

To my wife, for her love and patience while completing my thesis.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1: BACKGROUND AND LITERATURE REVIEW

1.1. Diabetes mellitus (diabetes)

Diabetes is diagnosed when an individual consistently has blood glucose levels which are higher than the normal range. Insulin is required to maintain normal blood glucose levels, as it helps shuttle glucose from blood into cells of the body for metabolism. Type 1 diabetes typically occurs in children and adolescents, accounts for less than 10% of the diabetes population, and is characterized by lack of insulin production by the pancreas. Type 2 diabetes usually occurs in middle aged adults, accounts for more than 90% of the diabetes population, and is characterized by lack of insulin production by the pancreas or failure of the body to utilize insulin appropriately. Diabetes is associated with significant morbidity and mortality because chronic exposure of the body to high blood glucose levels leads to end-organ damage primarily in the kidneys, eyes, nerves, and vascular system.

1.2. Chronic kidney disease (CKD)

When a patient is diagnosed with kidney disease the illness can be separated into acute and chronic forms, depending on its time of onset as well as its persistence. Acute kidney disease has a rapid onset (days to weeks) and has the possibility for recovery, while chronic kidney disease develops over time (months to years) and does not recover. Chronic kidney disease (CKD) is defined primarily based on an estimated or measured glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for a period of greater than 3 months (1). An estimated GFR (eGFR) of greater than 60 mL/min/1.73 m^2 is

considered abnormal if it is accompanied by abnormalities of urine sediment or abnormal results of imaging tests, or if the patients has had a kidney biopsy with documented abnormalities. The stages of CKD, which are used to guide clinical care and management, are outlined in Table 1.

Based on extrapolation from United States Renal Database System (USRDS) data, it is estimated that over 600,000 Canadians have Stage 3 or higher CKD (2). The prevalence of Stage 3 CKD in the adult population is about 8%, a rate that increases to almost 40% among individuals 70 years of age and older (3). This is concerning because there is an increased risk of mortality, cardiovascular events, and hospitalizations for patients with Stages 3 or higher CKD (4). In addition to these poor clinical outcomes, all patients with CKD are at risk of progressing to End-Stage Renal Disease (ESRD), a health state in which a patient's level of kidney function is no longer compatible with life. Therefore, patients with ESRD require treatment to replace their absent or near absent native kidney function, and this can be achieved by medical or surgical treatments such as hemodialysis, peritoneal dialysis, or kidney transplantation. In Canada, the primary causes of CKD are diabetes (26%), glomerulonephritis (21%), renal vascular disease (13%), and unknown (14%) (5).

1.3. Management of patients with CKD can be complex

CKD is a complex disease associated with multiple co-morbidities. Each of these co-morbid conditions needs to be individually optimized to prevent further clinical sequelae.

Co-morbidities associated with CKD include hypertension, anemia, bone disease, electrolyte abnormalities, and vascular disease (6 – 8).

Hypertension develops in patients because of CKD, and is a risk factor for worsening kidney function as well as disease in other vascular beds. Anemia occurs in patients with CKD because of erythropoietin deficiency, and hemoglobin levels need to be maintained within a narrow range to prevent symptoms and events caused by both hemoglobin levels which are too high or too low. Bone disease occurs because of abnormal calcium and phosphate metabolism. Electrolyte abnormalities occur because of the inability to remove enough potassium and acid from the body in CKD. Finally, CKD causes disease in all vascular beds, leading to cerebrovascular disease, coronary artery disease, and peripheral vascular disease. Given the number of co-morbidities associated with CKD, the care of the CKD patient is very comprehensive; studies have shown that adequate care of co-morbidities helps slow the progression of CKD (9 - 13).

1.4. Chronic kidney disease and diabetes mellitus among First Nations People

Assessment of kidney function as determined by a serum creatinine measurement are completed as frequently in First Nations People as they are in non-First Nations People across all age groups (14). Although the prevalence of Stage 3 CKD is similar among First Nations and non-First Nations individuals, Stage 4 and 5 CKD (reflecting more severe disease) is more prevalent in First Nations individuals. Further, incidence rates of ESRD are two-to-three times as high in First Nations People, and First Nations People starting

dialysis tend to be younger, compared to non-First Nations People (15). A further distressing fact is that adjusted mortality rates are higher in First Nations compared to non-First Nations People across all Stages of CKD (14).

The reason for the higher prevalence of CKD, ESRD and mortality in First Nations People may be in part related to the higher prevalence of diabetes in this population. In Alberta in 2009, age and sex adjusted prevalence of diabetes in the Aboriginal population was 11.9% compared to 5.7% for the general population (16). Accordingly, diabetes is the etiology of ESRD in over 60% of First Nations compared to approximately 25% of the overall ESRD population (17). Despite this strong association of diabetes in the First Nations population and adverse outcomes, it is unknown if there are other factors which contribute to the higher prevalence of CKD, ESRD and mortality. Given the high prevalence of diabetes among the First Nations population, combined with their higher rates of developing ESRD, the focus of this work is on the population with diabetes.

1.5. Quality of care

Quality of care has emerged as an important goal in health care. In the modern era of medicine, poor patient outcomes have become less acceptable. A poor clinical outcome can be related not only to the disease itself, but to the type and delivery of treatment for the particular disease. Inadequate treatment can compromise patient safety, and this is naturally becoming a larger concern. Patient safety is an individual concept and can be looked at on an individual level. Quality of care is a broad concept and speaks more to the

delivery of high quality health care to a particular group of patients. In this study, I have looked at the quality of care delivered to diabetic patients and how this delivery affected outcomes.

1.5.1. Definition and importance of quality of care

One of the most commonly cited definitions of quality of care is that provided in a quality assurance report for the Medicare program in the United States in 1990. In this report, quality of care was defined as "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge" (18). There is evidence that there is variability in the quality of care delivered to patients in the modern health care system. A study of 4185 hospitals in the United States from 2002 to 2004 showed that markers of quality of care were implemented anywhere from 28% to 99% of the time in the common conditions of acute myocardial infarction, heart failure, and pneumonia (19).

There is also a growing body of literature suggesting adherence to quality of care standards improves outcomes in many patient populations. In a retrospective cohort of 372 patients over the age of 65, improved quality of care (based on 160 quality indicators which were abstracted from medical records), was associated with lower mortality after 500 days (20). In a prospective cohort of 64,775 patients presenting with non-ST elevation myocardial infarction, quality of care was defined by 4 acute process-of-care indicators and 5 discharge process-of-care indicators recommended by the American College of

Cardiology and American Heart Association. An example of an acute process-of-care indicator was the use of aspirin on admission, and an example of the discharge process-of-care indicators was the use of lipid lowering therapy upon discharge. This study demonstrated a 10% decrease in in-hospital mortality with a 10% increase in adherence to the 9 quality of care measures (21). It is clear that quality of care is variable, and has the potential to impact patient outcomes.

1.5.2. Quality of care indicators

Quality of care indicators or "performance measures" are required to evaluate the extent to which high quality care is provided. Quality of care indicators reflect the presence or absence of various aspects of healthcare delivery, and are often divided into three categories: structural, process-of-care, and outcome (22).

Structural indicators evaluate healthcare at a system level. They evaluate interventions that can be achieved on a large scale such as providing adequate staffing to a dialysis unit and providing the dialysis unit with adequate dialysis equipment. ***Process-of-care*** indicators evaluate healthcare at a provider level. They reflect the direct care a patient receives. An example of a process-of-care indicator would be the prescription of erythropoietin for a patient with anemia caused by CKD. ***Outcome indicators*** evaluate healthcare at a patient level. They evaluate the result of healthcare interventions such as the number of hospitalizations per year for a given population with CKD.

An indicator is chosen based on the feasibility of data collection, its reliability, its validity, and its usefulness in improving patient outcomes. In general, indicators may be obtained from administrative data or abstracted from chart review (22).

1.5.3. Quality of care indicators for patients with diabetes

Clinical practice guidelines have been developed for management of patients with diabetes (23,24), and clinical practice guidelines are often used as indicators of quality of care (25 – 27). These guidelines include (but are not limited to) the following indicators (see also Table 2):

1.5.3.1. urine albumin-creatinine ratio (ACR)

Patients with diabetes can develop abnormally high amounts of protein in the urine (proteinuria); the major protein in the urine is albumin**.** The presence of proteinuria (ACR > 2 mg/mmol) is also associated with increased cardiovascular events, hospitalizations, and mortality (28). There is a strong association between treatment to reduce proteinuria and prevention of progression of diabetic kidney disease (29 – 31). The optimal frequency of measuring proteinuria is unknown, but it is clear that proteinuria quantification should be performed on a regular basis. In 2003 (during cohort period), the Canadian Diabetes Association (CDA) recommended screening diabetic patients for proteinuria with a urine albumin-creatinine ratio (23).

1.5.3.2. fasting cholesterol profile

Diabetic patients are at high risk for cardiovascular events and cardiovascular mortality (32). Hypercholesterolemia is a strong risk factor for cardiovascular disease, and abnormal cholesterol profiles are present in up to 66% of patients with diabetes (33). There is strong evidence that improving cholesterol levels in diabetic patients with normal kidney function reduces cardiovascular events (34 - 36). There is also recent evidence of the potential benefit in patients with CKD (37). For the first time in the CKD population, Baigent et al. were able to show a 17% reduction in atherosclerotic events with LDL reduction. The optimal frequency of measuring fasting cholesterol profiles is unknown, although the importance of monitoring is evident. In 2003, the CDA recommended measuring fasting cholesterol profiles at the time of diagnosis, one to three years thereafter, and more frequently for patients on therapy (23). They also indicated target levels, with the target LDL (low density lipoprotein) cholesterol less than 2.5 mmol/L and the target total cholesterol to HDL (high density lipoprotein) ratio less than 4.0 (38). These target levels and frequency of monitoring will be used for the purposes of our study.

1.5.3.3. HbA1C

Intensive blood sugar control has been shown to prevent the development of proteinuria and CKD in insulin dependent diabetic patients, and there is a trend toward decreased development of proteinuria and CKD with intensive blood sugar control in non-insulin dependent adult onset diabetics (39 – 43). In adult onset diabetics with established

proteinuria, intensive blood sugar control has been shown to decrease the progression of proteinuria (44). In patients with established CKD, poor glycemic control is associated with a higher risk of ESRD (45). Improved glycemic control is associated with decreased long-term mortality in both type 1 and 2 diabetics (46,47).

Glycated hemoglobin or HbA1C is a blood test that measures the percentage of hemoglobin that is glycated, and it reflects blood sugar control during the three months prior to the test. The normal range for HbA1C in the general population is 4.3 – 6.1%. As per CDA guidelines in 2003, the evidence based target for HbA1C in the general diabetic population was less than or equal to 7%. Although the optimal frequency of measurement is uncertain, the CDA guidelines recommend measuring the HbA1C every 3 months (23).

1.5.3.4. serum creatinine measurement

Patients with diabetes are at risk of end organ damage including diabetic nephropathy. As stated above, diabetic nephropathy accounts for 26% of CKD in Canada (5). Patients with diabetic nephropathy are at increased risk for progression to ESRD requiring dialysis. They are also at increased risk for cardiovascular disease (4). By measuring a serum creatinine, an estimation of kidney function can be made, and at risk patients can thus be identified. The optimal frequency of serum creatinine measurements for patients with diabetes is unknown, but in 2003, the CDA recommended screening all diabetic patients with a serum creatinine (23).

The above indicators are all process-of-care indicators, and were chosen for the purposes of this study as they are obtainable through available laboratory data holdings.

1.5.4. Quality of care in First Nations with diabetes and CKD

First Nations People in Canada bear a higher burden of disease with higher rates of chronic disease and all-cause mortality compared to the general Canadian population (48). Inequitable healthcare may contribute to the increased burden of chronic disease experienced by First Nations People. In the general First Nations population, decreased access to both primary ambulatory care and specialist care has been shown compared to geographically and socio-economically similar cohorts (49). In a cohort of patients with epilepsy, Aboriginal patients were more likely to visit the emergency department or become hospitalized, and they were less likely to see a neurologist (50). This has also been described in a First Nations CKD population in which access to ambulatory care and nephrology specialist care was lower compared to a non-First Nations CKD population (51).

With the higher rates of significant CKD, ESRD, and mortality in the First Nations population, and the evidence of disparity of care, it is possible that the poorer quality of care in First Nations may contribute to the higher burden of CKD and mortality in this population. Furthermore, it is also possible that improving quality of care in the First Nations population may lead to a lower burden of CKD and mortality.

1.6. Summary

Diabetes and CKD are complex, common diseases in Canada. Management of these chronic conditions requires special care not only to prevent progression of the disease itself, but also to treat renal related co-morbidities. Quality of care has emerged as important concept in the modern era of healthcare delivery, and although it can be variable, there is growing evidence that optimizing quality of care can improve patient outcomes. Quality of care indicators have been developed as yardsticks for measuring adequate care. For diabetes specifically, there are several quality of care indicators as defined by clinical practice guidelines, and these indicators can be used to measure quality of care delivered to a particular population with diabetes. Clinical Practice guidelines for management of CKD specifically have also been developed and provide indicators for quality of care, although the evidence on which they are based is more limited.

The First Nations population is a unique population known to have a higher burden of diabetes, more severe CKD and increased mortality compared to the non-First Nations population. First Nations People are also known to have poorer access to care. Using the diabetes quality of care indicators introduced here, the quality of care delivered to both First Nations and non-First Nations populations will be assessed. Furthermore, the association between quality of care indicators and clinical outcomes including progression to kidney failure (doubling of serum creatinine or ESRD) and mortality will also be assessed in these two populations.

CHAPTER 2: STUDY OBJECTIVES AND METHODS

2.1. Study objectives

2.1.1. Objective 1

To determine if quality of care indicators differ between adult First Nations and non-First Nations People with diabetes in Alberta, as assessed by the likelihood of having an ACR, HbA1C, LDL or serum creatinine measurement in a one-year period, and among the subgroup with diabetes and CKD specifically.

2.1.2. Objective 2

To determine if likelihood of achieving LDL and HbA1C measurements within target ranges differ between First Nations and non-First Nations People with diabetes in Alberta, and among the subgroup with diabetes and CKD specifically.

2.1.3. Objective 3

To determine if there is an association between inability to achieve diabetes quality of care indicator target levels (A1C > 7%, LDL > 2.5) and progression to a composite renal outcome (doubling serum creatinine or ESRD) or death, among First Nations and non-First Nations People with diabetes in Alberta.

2.2. Study design

The study design was a retrospective cohort of prevalent adult Alberta residents with diabetes mellitus during a defined cohort period. All data from this cohort was derived from laboratory and administrative data sources (defined below). Although not prospective, this study design was longitudinal, and allowed for robust associations to be made. Furthermore, given that I was interested in the likelihood of measurements and proportions of measurements within target, a long cohort period permitted more measurements for analysis. The data collection was objective since all laboratory and administrative data were collected electronically and systematically, and results should be generalizable to the Alberta population.

2.3. Sources of data

2.3.1. Alberta Kidney Disease Network (AKDN) repository of laboratory data

AKDN is a research group that brings together laboratory and administrative data from the province of Alberta (52). The AKDN database contains select laboratory data from all adult residents of Albertans including serum creatinine measurements, urine albumin-creatinine ratios (ACR), fasting cholesterol profiles, and HbA1C. Using unique identifiers (the Provincial Health Number), the AKDN database was linked to the other administrative data listed below. An overview of the AKDN repository is provided in Appendix 1.

2.3.2. Alberta Health and Wellness (AHW).

All permanent Alberta residents are eligible for insurance by AHW, and >99.9% participate in this coverage. Alberta Health and Wellness contains numerous data sources, the details of which are outlined in Appendix 2. This database contains a Registration File, and this contains Provincial Health Numbers (PHNs), which are unique identifiers for every Alberta resident registered with Alberta Health Care insurance program. The Registration File contains information on residents including date of birth, gender, postal code, and socio-economic status.

The Registration File also captures the First Nations Status of Albertans. First Nations health care is under federal jurisdiction, and all persons registered with the Department of Indian and Northern Affairs under the federal Indian Act are provided First Nations Status. The registry file was searched from April 1, 1994 to the study end-date and any individual with a First Nations status indicator at any time was classified as “First Nations”. All other people were classified as non-First Nations. First Nations People who were not registered under the federal Indian Act were included in the non-First Nations group. According to the 2001 census, about 70% of the Aboriginal population in Alberta is First Nations (53).

AHW data also included a Physicians Claims File and a Hospital Morbidity File. The diagnostic codes contained in these Files were used to identify patient characteristics including diabetes, hypertension and the Charlson co-morbidities. The AHW Vital

Statistics Death Registration File, and was used to identify patients who died, and their date of death.

2.3.3. Northern and Southern Alberta Renal Program databases

The Northern and Southern Alberta Renal Programs databases contain information about all prevalent and incident dialysis patients in Alberta, and were used to exclude prevalent dialysis and transplant patients at cohort entry as well as to identify incident dialysis and transplant patients during the follow-up period (outcome for Objective 3) (54).

2.4. Study population

The study population consisted of all Albertans 18 years and older who had at least one out-patient serum creatinine measurement from January 1 2005 to December 31 2008 and were diagnosed with diabetes mellitus. This was a cohort design, with cohort entry between January 1 2005 and December 31 2008, and study follow-up to December 31 2009 (the last date at which administrative data was available to determine outcomes, to ensure a one-year follow-up period for all subjects). The cohort was limited to those with diabetes (as defined below) and at least one out-patient serum creatinine measurement, with a sub-cohort defined by those with both diabetes and CKD (the group of patients at highest risk of death, ESRD and other adverse outcomes). The index date was defined as the date of the first out-patient serum creatinine measurement from January 1 2005 to December 31 2008. The primary exposure of interest was First Nations and non-First Nations status, as defined below. Patients were excluded if they were: age < 18; had an

implausible creatinine result (< 25 umol/L); did not link to the AHW files; migrated out of the province within one year of the index date (follow-up duration required at least one year); were treated with dialysis or a kidney transplant prior to the index date.

2.5. Variable definitions:

2.5.1. First Nations: individuals with First Nations Status as defined by AHW (see Section 2.3.2. above); First Nations status, the primary exposure of interest, was categorized as present or absent.

2.5.2. Measurement of kidney function: The eGFR for each patient was estimated using the 4-variable Modification of Diet in Renal Disease (MDRD) Study Equation (55); the equation is, eGFR = 186 x [creatinine] exp (-1.154) x [age] exp (-0.203) x 0.742 (if female), where creatinine is in mg/dL and age is in years. Although data on black race was not available, misclassification of eGFR was minimal because less than 1% of the Alberta population is black. Baseline kidney function (index eGFR) was estimated using the first outpatient serum creatinine measurement from January 1 2005 to December 31 2008. eGFR was categorized as ≥60 mL/min/1.73m^2, 45 to 59.5 mL/min/1.73m^2, 30 to 44.9 mL/min/1.73m^2, 15 to 29.9 mL/min/1.73m^2, and < 15 mL/min/1.73m^2. CKD was defined by an eGFR < 60 mL/min/1.73m^2.

2.5.3. Diabetes mellitus: individuals with at least one hospital admission with a diabetes related code or at least two physician service claims for diabetes within a two year period (56); diabetes was categorized as present or absent.

2.5.4. Hypertension: individuals with at least one hospital admission with hypertension or at least two physician service claims for hypertension within a two year period (57); hypertension was categorized as present or absent.

2.5.5. Age: determined from difference between the index date and date of birth.

2.5.6. Gender: determined from the sex of the patient as listed by AHW; gender was categorized as male or female.

2.5.7. Socioeconomic status: the 6-digit postal code for each study participant was linked to the 2006 Canadian Census using the Postal Code Conversion file to determine median neighborhood household income quintiles (levels 1 [lowest income quintile] to 5 [highest income quintile]) with a category for unknown.

2.5.8. Location of residence: the 6-digit postal code and linkage to the 2006 Canadian Census was also undertaken to define location of residence as urban or rural.

2.5.9. Charlson co-morbidity index (58): there are a number of standard co-morbidities, each with its own weight (Table 3); the co-morbidities for each patient were derived from physician service claims and hospital morbidity data prior to the index date over a three year period prior; the score for each patient was calculated as the sum of the weighted co-morbidities (Table 3) (59).

2.6. Definitions for Quality of care Indicators:

2.6.1. ACR measurement: at least one outpatient urine albumin-creatinine ratio (ACR) measurement during one year period following the index date (yes/no)

2.6.2. Urine dipstick : at least one outpatient urine dipstick measurement during one year period following the index date (yes/no)

2.6.3. LDL measurement: at least one out-patient LDL measurement during one year period following the index date (yes/no); among patients with LDL measurements, mean LDL measurement during one year period following the index date within target of ≤2.5 mmol/L (yes/no)

2.6.4. HbA1C measurements: at least one outpatient HbA1C measurement during one year period following the index date (yes/no); among patients with HbA1C measurements, mean HbA1C measurement during one year period following the index date within target of ≤ 7.0% (yes/no)

2.6.5. Serum creatinine measurement: at least one outpatient serum creatinine measurement during one year period following the index date (yes/no)

2.7. Clinical outcomes

2.7.1. Composite renal outcome (doubling of serum creatinine or progression to ESRD): doubling of serum creatinine was defined as the occurrence of an outpatient serum creatinine measurement that was twice as high as the index creatinine measurement during the study period (corresponding to a 50% decline in kidney function), as assessed at the end of follow-up (December 31 2009). ESRD was defined as the date of registration for chronic dialysis or renal transplantation (54).

2.7.2. All-cause mortality: determined from Alberta Vital Statistics maintained within the Alberta Health and Wellness Registry file, with follow-up to December 31 2009.

2.8. Data analysis

Continuous data was reported as means with standard deviations for normally distributed data and medians with interquartile ranges for non-normally distributed data, with categorical data described using proportions. All comparisons were made between First Nations and non-First Nations. All patients were followed up from the index date until study end, December 31 2009, with censoring at the primary outcome event or out-migration from the province.

Objective 1 was to determine if quality of care indicators differ between adult First Nations and non-First Nations patients with diabetes in Alberta, as assessed by the likelihood of having an ACR, HbA1C, LDL or serum creatinine measurement in a one-year period. For this analysis, separate models were developed for each of the indicators (outcomes). The primary exposure variable of interest was First Nations status (yes/no), with the outcomes a dichotomy of each of the indicators, as defined above. Logistic regression models were developed to assess the association between First Nations status and each indicator, adjusting for age, gender, SES, location of residence, hypertension, and Charlson co-morbidity score. Interaction was assessed between First Nations status and CKD status, and if present, results were stratified by CKD status.

For ***objective 2***, to determine if achievement of LDL and HbA1C measurements within target ranges differ between First Nations and non-First Nations people, a separate model was developed for each of the outcomes of LDL and HbA1C. The primary exposure of interest was First Nations status (yes/no), with the outcomes a dichotomy of the achieved targets (yes/no), as defined above. This analysis was limited to patients with LDL and HbA1C measurements, respectively. Logistic regression models with adjustment and assessment for interaction as in objective 1 were undertaken.

Objective 3 was to determine the association between the ability to achieve quality of care indicator targets and progression to the composite renal outcome (doubling of serum creatinine or ESRD), and death. We first used Poisson regression to calculate crude rates

of ESRD, the composite renal outcome (doubling of serum creatinine or ESRD), and all-cause mortality for First Nations and non-First Nations people. Rates were then adjusted for age and gender and further stratified by CKD status. We then used Cox proportional hazards models to determine the association between achievement of target levels for the indicators and risk of the outcomes, with separate models for each of the outcomes (composite renal outcome [doubling of serum creatinine or ESRD] and death). The primary exposure variables of interest were the three level variables of HbA1C (target, not target, not measured) and LDL (target, not target, not measured), with follow-up from the index date to the first of the occurrence of doubling of serum creatinine, ESRD or death. In these analyses First Nations was included as an independent variable in the models. Two-way interaction terms between First Nations and HbA1C, First Nations and LDL, CKD and HbA1C, and CKD and LDL were assessed. If the interaction was significant, results were stratified by the variable. Adjustment for variables as in objectives 1 and 2 were undertaken. Assumptions for Poisson regression (that the variance equals the mean) and for Cox regression (proportionality of hazards) were tested and met.

CHAPTER 3: RESULTS

3.1. Defining cohort

The flow-diagram for cohort inclusion is shown in Figure 1. Between January 1, 2005 and December 31, 2008, there were 1,832,495 individuals with at least one out-patient serum creatinine measurement. Of those, 2,668 participants (0.1%) were excluded because they did not have at least one serum creatinine greater than 25 µmol/L (creatinine less than 25 µmol/L considered to be clinically implausible). A further 13,916 individuals (0.8%) were excluded because they did not link to the Alberta Health and Wellness registry file. There were 44,019 participants (2.4%) excluded for being younger than 18. We also excluded 19,437 participants (1.1%) with out-migration date on or within 1 year of index date (to ensure all subjects had at least 1 year of follow-up for study outcomes in the logistic regression analysis). We excluded 3,123 individuals (0.2%) who were either on dialysis or had a renal transplant prior to the index date. Finally, 1,602,049 participants (87.4%) did not have a diagnosis of diabetes prior to the index date, and were excluded, for a final cohort of 147,283 patients (8.0%).

3.2. Baseline characteristics of cohort

The cohort consisted of 6,574 (4.5%) First Nations and 140,709 non-First Nations People (Table 4). Compared with non-First Nations, First Nations were significantly younger (mean age 53.18 vs 61.66 years, $p < 0.001$), with a greater proportion of female gender (57.5% vs 47.1%, $p < 0.001$).

The mean index eGFR was significantly higher in First Nations People compared to non-First Nations (87.91 ml/min/1.73 m^2 vs 74.75 ml/min/1.73 m^2, $p < 0.001$). When compared to non-First Nations, a greater proportion of First Nations People had an eGFR greater than or equal to 60 ml/min/1.73 m^2 (86.9% vs 76.0%) and an eGFR less than 15 ml/min/1.73 m^2 (0.6% vs 0.3%). First Nations were less likely to have an eGFR between 45 and 59.9 ml/min/1.73 m^2 (7.7% vs 15.2%), 30 and 44.9 ml/min/1.73 m^2 (3.3% vs 6.4%), and between 15 and 29.9 ml/min/1.73 m^2 (1.5% vs 2.1%).

With respect to co-morbidities, First Nations People were less likely to have a diagnosis of hypertension than non-First Nations (51.7% vs 63.2%, $p < 0.001$). Although the median Charlson co-morbidity index was the same for both First Nations and non-First Nations, there was a statistical difference according to the Kruskal-Wallis rank test ($p = 0.0001$). First Nations People were more likely to have chronic pulmonary disease, rheumatic disease, peptic ulcer disease, any degree of liver disease, and diabetes with end organ damage, and less likely to have a history of myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, diabetes without chronic complication, renal disease, and cancer.

First Nations People were much more likely than non-First Nations to be living in a rural area (56.2% vs 16.7%, $p < 0.001$). Compared to non-First Nations, a greater proportion of First Nations People were in the lowest income quintile and a smaller proportion in the highest income quintile ($p < 0.001$).

3.3. Quality of care indicators

3.3.1. Assessment of proteinuria

There were 3,049 (46.4%) First Nations People with an assessment of proteinuria, either urine dipstick or urine ACR, during the one year period following the index eGFR compared to 78,558 (55.8%) non-First Nations People (Table 5). In a crude analysis, First Nations People were 32% less likely to have an assessment of proteinuria compared with non-First Nations People (OR 0.68; 95% CI (0.65 – 0.72)].

There was a significant interaction between First Nations status and CKD ($p < 0.001$); therefore all further results are presented stratified by CKD (eGFR > 60 mL/min/1.73 m^2). Among participants with eGFR greater than or equal to 60 ml/min/1.73 m^2, after adjustment for age, gender, hypertension, Charlson score, location of residence and income, First Nations People were significantly less likely than non-First Nations People to have an assessment of proteinuria during the one year period following the index eGFR [Adjusted OR 0.78; 95% CI (0.73 – 0.83)]. Among participants with eGFR less than 60 ml/min/1.73 m^2, after adjustment there was no difference between First Nations and non-First Nations People with respect to likelihood of having an assessment of proteinuria [Adjusted OR 1.05; 95% CI (0.91 – 1.21)].

We also assessed the likelihood of having an assessment of urine ACR specifically within a one year period. Urine ACR is the recommended method for assessing presence of proteinuria among individuals with diabetes, thus is a more specific quality of care

indicator. Overall only 1,738 (26.4%) First Nations participants had a urine ACR during the one year period following the index eGFR compared to 49,384 (35.1%) non-First Nations participants (Table 5). First Nations People were 33% less likely to have this assessment completed compared with non-First Nations People [OR 0.66; 95% CI (0.62 – 0.71)]. Among participants with eGFR great than 60 ml/min/1.73 m^2, after adjustment First Nations People were significantly less likely than non-First Nations People to have a urine ACR [OR 0.77; 95% CI (0.72 – 0.83)]. For patients with eGFR less than 60 ml/min/1.73 m^2, there was no difference between First Nations and non-First Nations People with respect to likelihood of having a urine ACR completed [Adjusted OR 1.09; 95% CI (0.93 – 1.27)].

3.3.2. Assessment of cholesterol

After excluding five First Nations and 110 non-First Nations People with LDL values less than 0.5 mmol/L (considered to be clinically implausible), 2,491 (37.9%) First Nations People had an LDL cholesterol during the one year period following the index eGFR compared to 73,274 (52.1%) non-First Nations (Table 6). First Nations were almost 50% less likely than non-First Nations patients to have an LDL cholesterol [OR 0.56; 95% CI (0.53 – 0.60)]. Among participants with eGFR greater than 60 ml/min/1.73 m^2, after adjustment for age, gender, hypertension, Charlson score, location of residence and income, First Nations patients were significantly less likely than non-First Nations patients to have an LDL cholesterol [OR 0.60; 95% CI (0.56 – 0.64)]. Similar results were present for those with eGFR less than 60 ml/min/1.73 m^2, [Adjusted OR 0.82 95% CI (0.71 – 0.95)].

3.3.3. Assessment of glycemic control

There were 3,473 (52.8%) First Nations people with at least one HbA1C during the one year period following the index eGFR compared to 89,935 (63.9%) non-First Nations (Table 7). First Nations People were almost 40% less likely than non-First Nations to have a HbA1C during the one year period following the index eGFR [Crude OR 0.63; 95% CI (0.60 – 0.67)]. Among participants with eGFR greater than 60 ml/min/1.73 m^2, after adjustment for age, gender, hypertension, Charlson score, location of residence and income, First Nations People were significantly less likely than non-First Nations to have a HbA1C [Adjusted OR 0.68; 95% CI (0.64 – 0.73)]. However among the subgroup with an eGFR less than 60 ml/min/1.73 m^2, there was no difference in the likelihood of HbA1c assessment between First Nations and non-First Nations People with respect to HbA1C during the year following the index eGFR [Adjusted OR 1.10; 95% CI (0.94 – 1.27)].

3.3.4. Assessment of serum creatinine

There were 4,141 (63.0%) First Nations People with at least one out-patient serum creatinine measurement during the one year period following the index eGFR compared to 94,369 (67.1%) non-First Nations (Table 8). First Nations People were less likely than non-First Nations People to have a serum creatinine measurement obtained during a one year period [Crude OR 0.84; 95% CI (0.79 – 0.89)]. Among participants with eGFR greater than 60 ml/min/1.73 m^2, after adjustment for age, gender, hypertension, Charlson score, location of residence and income, First Nations People were significantly less likely than non-First Nations People to have a serum creatinine measurement [Adjusted OR 0.89;

95% CI (0.84 – 0.95)]. However among the subgroup with eGFR less than 60 ml/min/1.73 m^2, there was no difference between First Nations and non-First Nations with respect to likelihood of having a serum creatinine measurement [Adjusted OR 1.02; 95% CI (0.86 – 1.21)].

3.4. Quality of care indicator targets

3.4.1. Achieving LDL cholesterol target

Among subjects with at least one LDL measurement in the year following the index eGFR, the mean (SD) LDL was similar for First Nations and non First-Nations people at 2.54 (0.85) mmol/L and 2.50 (0.83) mmol/L, respectively (Table 9).

Overall, 1,279 (51.3%) of First Nations People and 39,807 (54.3%) of non-First Nations People were able to achieve a mean LDL target of less than or equal to 2.5 mmol/L. First Nations People were less likely than non-First Nations People to achieve an LDL target [Crude OR 0.89; 95% CI (0.81 – 0.97)]. However, when stratified by baseline eGFR and after adjustment there was no difference in the likelihood of achieving a mean LDL target of less than or equal to 2.5 mmol/L for First Nations and non-First Nations People.

3.4.2. Achieving HbA1C target

Among the participants who had at least one HbA1C measurement during a one year period, the mean HbA1C was higher among First Nations compared with non-First Nations People at 7.90% and 7.33% mmol/L, respectively (Table 10).

There were 1,504 (43.3%) of First Nations People and 45,725 (50.8%) of non-First Nations People who were able to achieve the HbA1C target of less than or equal to 7%. First Nations People were almost 30% less likely to achieve a target HgA1c compared with non-First Nations People [Crude OR 0.74; 95% CI (0.68 – 0.80)]. After stratifying by eGFR and adjusting for potential confounders, First Nations with eGFR greater than 60 ml/min/1.73 m^2, were significantly less likely than non-First Nations to achieve the HbA1C target [Adjusted OR 0.84; 95% CI (0.77 – 0.92)]. However among the group with eGFR < 60 there was no difference between the groups [Adjusted OR 0.93; 95% CI (0.78 – 1.12)].

In summary, for participants with eGFR greater than 60 ml/min/1.73 m^2, First Nations People were less likely than non-First Nations People to receive all four quality of care indicators, namely assessment of proteinuria, cholesterol, glycemic control, and renal function. Furthermore, in this group of individuals, First Nations People were less likely to achieve the HbA1C target than non-First Nations People.

For participants with eGFR less than 60 ml/min/1.73 m^2, First Nations People were less likely than non-First Nations People to receive an assessment of cholesterol.

3.5. Clinical outcomes

3.5.1. Rates of the composite renal outcome and mortality

Rates of ESRD, the composite renal outcome and death, by First Nations and CKD status, are presented in Tables 11 to 13.

For those with eGFR greater than 60 ml/min/1.73 m^2, First Nations People had a higher rate of ESRD than non-First Nations People (Crude 0.94 vs 0.41 per 1000 person-years, respectively) (Table 11). After adjustment for age and gender, First Nations individuals with higher eGFR were still more likely to develop ESRD than non-First Nations (Adjusted 0.55 vs 0.29 per 1000 person-years, respectively). For those with eGFR less than 60 ml/min/1.73 m^2, First Nations People had an almost four-fold higher rate of ESRD than non-First Nations People (Crude 35.93 vs 8.04 per 1000 person-years, respectively). After adjustment for age and gender, First Nations individuals were still much more likely to develop ESRD than non-First Nations (Adjusted 39.65 vs 10.91 per 1000 person-years, respectively).

For those with eGFR greater than 60 ml/min/1.73 m^2, First Nations People had a higher rate of the composite renal outcome than non-First Nations People (Crude 4.77 vs 2.71 per 1000 person-years, respectively), and this was maintained after adjustment for age and gender (Adjusted 4.80 vs 2.64 per 1000 person-years, respectively) (Table 12). For those with eGFR less than 60 ml/min/1.73 m^2, First Nations People were much more likely to reach the composite renal outcome than non-First Nations People (Crude 50.50 vs

14.88 per 1000 person-years, respectively), including after adjustment for age and gender (Adjusted 53.57 vs 15.36 per 1000 person-years, respectively).

In the crude analysis for those with eGFR greater than 60 ml/min/1.73 m^2, First Nations People had a lower mortality rate than non-First Nations People (Crude 18.11 vs 21.54 per 1000 person-years, respectively); however, when adjusted for age and gender, the mortality rate was higher in the First Nations group (Adjusted 23.83 vs 15.37 per 1000 person-years, respectively) (Table 13). For those with eGFR less than 60 ml/min/1.73 m^2, unadjusted mortality rates were much higher for both First Nations and non-First Nations (Crude 78.62 vs 74.74 per 1000 person-years, respectively). When adjusted for age and gender, mortality was lower, but the mortality rate of the First Nations group was almost twice that of the non-First Nations group (Adjusted 47.44 vs 24.55 per 1000 person-years, respectively).

3.5.2. Association between quality of care indicator targets, composite renal outcome and mortality

Cox proportional hazards models were used to determine the association between quality of care indicators (achieving target LDL and HbA1c) and the outcomes of interest, death and the composite renal outcome. In this analysis the target LDL and HbA1c were categorized as “target” (reference), “not at target”, and “not measured”. We initially assessed for potential effect modification for each of the exposure variables of interest (LDL and HbA1c) with First Nations Status and CKD.

For the composite renal outcome there was a significant interaction between CKD status and target LDL ($p<0.0001$), thus we present these results stratified by CKD status. There was no significant interaction between First Nations and target HbA1c, First Nations and LDL, or CKD and target HbA1C.

The association between quality of care markers and the composite renal outcome are presented in Table 14. For participants with eGFR < 60 ml/min/1.73 m^2, those without a LDL assessment had the greatest risk of the composite renal outcome compared to those with LDL at target [Adjusted HR 1.16; 95% CI (1.04 – 1.30)]. There was a higher risk of the composite renal outcome if the HbA1C was not at target when compared to HbA1C at target [Adjusted HR 1.27; 95% CI (1.15 – 1.41)], but a lower risk if the HbA1C was not measured at all compared to HbA1c at target [Adjusted HR 0.71; 95% CI (0.63 – 0.81)].

For individuals with eGFR > 60 ml/min/1.73 m^2, those without an LDL assessment were more likely to reach the composite renal outcome than those who met the cholesterol target [Adjusted HR 1.74; 95% CI (1.50 – 2.02)]; those with HbA1C not at target were more likely to reach the composite renal outcome than those who met the HbA1C target [Adjusted HR 1.63; 95% CI (1.41 – 1.87)].

For the death outcomes there was a significant interaction between First Nations and target LDL ($p < 0.0001$), thus we present these results stratified by First Nations status.

There was no significant interaction between First Nations and target HbA1C, CKD and target HbA1C or between CKD and target LDL. The association between quality of care indicators achieving target levels and mortality are presented in Table 15.

When compared to non-First Nations People who met the LDL target, non-First Nations People who did not meet the target had lower mortality [Adjusted HR 0.91; 95% CI (0.86 – 0.96)], and non-First Nations People who did not have a cholesterol assessment had higher mortality [Adjusted HR 2.11; 95% CI (2.03 – 2.20)]. Non-First Nations People who did not meet the HbA1C target or who did not have a HbA1C measurement were both more likely to die than non-First Nations People who met the HbA1C target {[Adjusted HR 1.05; 95% CI (1.01 – 1.09)] and [Adjusted HR 1.27; 95% CI (1.22 – 1.32)], respectively}.

When compared to First Nations People who met the LDL target, First Nations People who did not meet the target had lower mortality [Adjusted HR 0.60; 95% CI (0.44 – 0.83)], and First Nations People who did not have a LDL assessment had higher mortality [Adjusted HR 1.38; 95% CI (1.10 – 1.71)]. First Nations People who did not have a HbA1C measurement were more likely to die than First Nations People who met the HbA1C target [Adjusted HR 1.46; 95% CI (1.17 – 1.82)].

In summary, First Nations People had higher rates of ESRD, composite renal outcome, and mortality than non-First Nations People especially for individuals with eGFR less than 60 ml/min/1.73 m^2.

There was a higher risk of the composite renal outcome if LDL assessment was not done or if the HbA1C was done and not at target. For those with eGFR less than 60 ml/min/1.73 m^2, there was a lower risk of composite renal outcome if the HbA1C was not done.

There was a higher risk of mortality if there was no assessment of glycemic control or if it was done and not at target. There was also a higher risk of mortality if the LDL was not measured, but a lower risk of mortality if the cholesterol measured and not at target.

CHAPTER 4: DISCUSSION

4.1. Conclusions

In this cohort of patients with diabetes we were able to identify important differences in care and outcomes for First Nations compared with non-First Nations people, including:

A) Assessment of quality indicators and achievement of targets:

1) First Nations without CKD were less likely to have all four quality of care indicators (LDL, proteinuria, HbA1c and kidney function) measured, and were less likely to achieve HbA1c targets
2) First Nations with CKD were less likely to have LDL measured, but were equally as likely to achieve HbA1C and LDL targets

B) Association between quality indicators and renal failure and death:

3) First Nations with and without CKD had increased rates of renal failure (ESRD or doubling of serum creatinine) and death
4) The risk of renal failure (ESRD or doubling of serum creatinine) was increased if an LDL was not measured or if the HbA1C was not at target, for both First Nations and non-First Nations, similarly for those with and without CKD
5) The risk of death was increased if an LDL was not measured, and was decreased if an LDL was not at target, for both First Nations and non-First Nations, similarly for those with and without CKD
6) The risk of death was increased for First Nations and non-First Nations if an HbA1c was not at target or not measured

In summary we found that compared with non-First Nations, First Nations People with diabetes were less likely to receive assessment of indicators commonly used to monitor diabetes. These indicators in general had a variable impact on outcomes, and lack of measurement (LDL) or levels above target (HbA1C) were associated with an increased risk of renal failure or death.

4.1.1. Baseline characteristics

The population of this cohort included a large number of individuals accrued over a 3 year period of time (n=147,283); however, the number of First Nations individuals was only 6,574 or 4.5% of the total population. This is similar to the general population of Alberta which is 3.0% First Nations according to 2006 Canadian Census data (60). There were important differences between the First Nations and non-First Nations populations in age, gender, index eGFR, presence of hypertension, income and location of residence, and this made adjustment for these differences in baseline characteristics necessary. These differences, with the First Nations population being younger, primarily rural, lower income, and having a higher proportion of females and individuals with eGFR > 60 ml/min/1.73 m^2, were similar to that seen in other studies involving First Nation adults (14,61).

4.1.2. Quality of care indicators for participants with diabetes and no CKD

Likelihood of quality of care markers being measured:

For participants without CKD (eGFR greater than 60 ml/min/1.73 m^2), First Nations People were less likely than non-First Nations People to receive all four quality of care indicators, namely assessment of proteinuria, LDL, glycemic control, and kidney function. These results are similar to findings from Dyck et al. (61). In this study, the authors examined quality of care provided to a cohort of diabetic individuals from Saskatchewan's two largest health regions from 2005 to 2006. Individuals were identified as being First Nations or non-First Nations, and were stratified on the basis of stages of CKD. The authors found First Nations People without CKD were less likely than non-First Nations People without CKD to receive the same four quality indicators.

The difference in quality of care indicators between First Nations and non-First Nations People suggests a discrepancy in the care these two groups are receiving. These quality of care indicators are disease markers recommended for monitoring people with diabetes. If First Nations People are less likely to have these assessments completed, then the severity of their disease may go undiagnosed. Without timely diagnosis of disease severity, changes to therapy designed to treat severe disease cannot be made, and this may contribute to the increased risk of complications from diabetes for First Nations People.

It is well established that aggressive interventions and close monitoring can reduce morbidity and mortality in patients with type 2 diabetes. In the STENO-2 study, Gaede et al. randomly assigned 160 Danish patients with type 2 diabetes and persistent microalbuminuria to intensive or conventional therapy (62). The intensive therapy consisted of a HbA1C goal less than 6.5%, a total cholesterol goal less than 4.5 mmol/L, a triglyceride goal less than 1.7 mmol/L, a blood pressure goal less than 130/80 mm Hg, renin angiotensin system blockade for proteinuria reduction, and aspirin for primary prevention of cardiovascular events. With intensive therapy for a mean treatment period of 7.8 years and a mean follow up period of 5.5 years, there was a 46% reduction in mortality and 59% reduction in cardiovascular events. Furthermore, fewer patients in the intensive therapy group reached end-stage renal disease. Achievement of these treatment benefits however requires close monitoring – monitoring which was less likely to be obtained by First Nations People in our study, suggesting that they may be less likely to experience the potential benefits of these interventions.

First Nations People have been shown to receive insufficient quality of care compared to non-First Nations People. Shah et al. showed that Aboriginal People living in rural Ontario were more likely to be hospitalized for conditions which could have been treated in the ambulatory care setting (ex. asthma) when compared to geographical and social economical control populations (49). They were also less likely to receive procedures which depend on referral from primary care (ex. cardiac catheterization). Both the higher rate of hospitalizations for ambulatory care conditions and the lower rate of referral

based procedures are further examples of the disparity in primary care for Aboriginal People living in rural areas.

Disparity differences between First Nations People and non-First Nations People are not limited to the diabetic population. Jette et al. examined a cohort of patients with epilepsy over a one year period of time and found that Aboriginal epileptic patients were more likely to visit the emergency department or become hospitalized and less likely to be seen by a neurologist when compared to non-Aboriginal epileptic patients (50). The higher rates of hospital visits and lower rates of specialist care further highlight the discrepancy in care between the two populations for a variety of medical conditions.

Achievement of treatment targets:

Among patients without CKD, we found that First Nations participants were less likely to achieve the HbA1C target than non-First Nations People. These results are also similar to findings from Dyck et al. who found that First Nations People were less likely than non-First Nations People to achieve the diabetes target in a diabetic Saskatchewan population without CKD (61).

The difference in the ability to achieve the HbA1C target between First Nations and non-First Nations People is very important. Tight glycemic control has clearly been shown to prevent proteinuria and the development of renal disease in the diabetic population.

In the DCCT study (40), intensive glycemic control with a HbA1C goal less than 6% resulted in a 54% reduction in macroalbuminuria (≥ 300 mg albuminuria/24 hr) in an insulin dependent diabetic cohort after a mean follow period of 6.5 years. In the UKPDS study (41), there was a trend toward decreased proteinuria in a non-insulin dependent type 2 diabetic cohort. Intensive glycemic control has also been shown to improve cardiovascular disease and mortality in the diabetic population.

In the long term follow up of the DCCT study (46), ninety-tree percent of the original cohort were followed for a mean of 17 years. During this time, despite not maintaining improved glycemic control, the group who received intensive insulin treatment during the trial had a reduction in non-fatal myocardial infarction, stroke or death by 57% compared to the conventional treatment. In the long term follow up of the UKPDS study (47), seventy-eight percent of the original cohort were followed for a median of approximately 17 years. Again, despite not maintaining improved glycemic control, the intensive treatment group still had a 13 to 27% reduction in mortality compared to the conventional group. The inability to achieve glycemic control evident in our study results may contribute to the larger burden of renal disease, cardiovascular disease and mortality in the First Nations population.

4.1.3. Quality of care indicators for participants with diabetes and CKD

Likelihood of quality of care markers being measured:

For participants with CKD (eGFR less than 60 ml/min/1.73 m^2), First Nations People were less likely than non-First Nations People to receive an assessment of LDL, but were just as

likely to receive an assessment of proteinuria, kidney function and HbA1C. There were, however, only 864 First Nations People with CKD, which may result in limited power to detect statistically significant differences in quality of care indicators between groups. The lower likelihood of obtaining an LDL assessment shows a discrepancy in quality of care between First Nation and non-First Nations People, and may place them at a higher risk of complications from elevated LDL levels such as myocardial infarction, stroke or death.

The reason that First Nations People with CKD were less likely to receive an LDL assessment compared to non-First Nations People may be related to access to care. Gao et al. examined an Alberta population with CKD and found that the hospitalization rate for ambulatory care sensitive conditions were higher for Aboriginal People compared to non-Aboriginal People (51). Furthermore, for those with severe CKD, Aboriginal People were less likely to be referred to a nephrologist. These findings suggest that First Nations People do not access the health care system in the intended fashion. A fasting lipid profile requires an ordering provider, a laboratory visit, and a fasting period; given there is evidence Aboriginal People access the health care system in an urgent but not planned manner, it may be more difficult for them to obtain a fasting lipid profile.

Achievement of treatment targets:

First Nations with CKD were just as likely to achieve HbA1C and LDL treatment targets as non-First Nations with CKD. The reason for the similar ability to achieve HbA1C targets for

First Nations and non-First Nations with CKD may be related to insulin metabolism in CKD. As renal function worsens insulin clearance is prolonged, and insulin requirements become lower. Biesenbach et al. showed that in both type 1 and type 2 diabetics, insulin requirements decrease as creatinine clearance decreases (63). Therefore, for both First Nations and non-First Nations People with CKD insulin requirements decrease, and glycemic control would be easier to achieve. This is supported by the fact that the mean HbA1C in First Nations with CKD was closer to that of the non-First Nations People with CKD (7.55% and 7.20%, respectively) when compared to the mean HbA1C in First Nations and non-First Nations without CKD (7.97% and 7.38%, respectively).

4.1.4. Clinical outcomes for participants with diabetes and no CKD

We found that compared to non-First Nations, First Nations participants with diabetes but without CKD had higher age and gender adjusted rates of ESRD, composite renal outcome, and mortality. The rates of ESRD for the non-First Nations population reported in our study were similar to those of other diabetic populations at 1.6 per 1000 person years (64) and 1.8 per 1000 person years (65). The increased rates of diabetic ESRD for First Nations, compared with non-First Nations people, have also been reported in a Saskatchewan population (66)**,** and in the United States (17).

The increased mortality rates for First Nations compared with non-First Nations People have been reported in other diabetic populations (67) as well as a general population without CKD (14).

These differences in clinical outcomes may be related to the differences in quality of care that First Nations received compared to non-First Nations People. By not receiving recommended monitoring, First Nations People are at risk for progressive renal disease and mortality. In addition, given the inferior glycemic control found in the First Nations population, this would directly lead to worse renal outcomes and mortality.

4.1.5. Clinical outcomes for participants with diabetes and CKD

Similar to our results for First Nations People without CKD, we found that First Nations People with both diabetes and CKD experienced substantially higher age and gender adjusted rates of ESRD, composite renal outcome, and mortality, compared to the non-First Nations population.

As expected, diabetic individuals with CKD were more likely to experience ESRD than diabetic individuals without CKD (3.1% vs 0.2%, respectively). Further, diabetic individuals with CKD were more likely to die compared with diabetic individuals without CKD (27.1% vs 8.0%, respectively). As individuals with CKD are closer to ESRD than those without CKD, it is not surprising that the ESRD and composite renal outcome rates are higher for those with CKD.

Our results of an increased risk of death associated with CKD are consistent with other large population based studies (4). The increased rates of death for First Nations compared with non-First Nations with diabetes and CKD is similar to that reported for the

non-diabetic CKD population (14). The difference in clinical outcomes between First Nations and non-First Nations with diabetes and CKD may be related to the difference in quality of care. Although the only difference in quality of care was lower probability of LDL assessment, this may be a marker of poorer access to health care as described above. By not accessing the health care system in the intended fashion, First Nations individuals with CKD are at risk of not receiving appropriate treatments for CKD and related co-morbidities, and this could therefore increase their risk of mortality.

4.1.6. Association between quality indicators and risk of renal failure (First Nations and non-First Nations combined)

We found that the risk of renal failure (ESRD or doubling of serum creatinine) was higher if an LDL was not measured compared to the LDL being at target. This was evident in individuals with and without CKD, similarly for First Nations and non-First Nations People. Again, this may be related to a difference in quality of care. Lack of LDL assessment may be a marker of poorer use of the heath care system. If not using the health care system in the appropriate fashion, diabetic individuals without an LDL assessment may not be receiving appropriate treatments designed to slow the progression of renal disease (blood pressure control, use of particular antihypertensive medication). This could therefore increase their risk of the composite renal outcome.

The risk of renal failure was higher if the HbA1C was not at target compared to HbA1C being at target, similarly for patients with and without CKD and for First Nations and non-

First Nations People. Given that all patients in this cohort were diabetic, and that diabetes is the leading cause of kidney disease in Canada (5), a large proportion of patients with CKD in this cohort likely had diabetic nephropathy. Poor glycemic control has been shown to be associated with increased risk of ESRD in diabetic patients with CKD (45), and therefore individuals with diabetic nephropathy in this cohort with poor glycemic control would be at higher risk of the composite renal outcome. Even for those who did not have diabetic nephropathy, poor glycemic control could lead to the development of diabetic nephropathy (40,41), and thus the composite renal outcome.

Interestingly, for participants with CKD, the risk of renal failure was lower if the HbA1C was not measured compared to a HbA1C at target. It is possible that some participants were not getting regular HbA1C measurements because their diabetes was well controlled, and their health care practitioners did not find it necessary to check the HbA1C frequently. Both the Canadian Diabetes Association and the American Diabetes Association recommend that the HbA1C can be checked every six months instead of every three months for diabetics consistently meeting glycemic targets (24,68). Therefore, for participants with CKD who did not have a HbA1C measurement, it is possible that they were consistently meeting glycemic targets, and good glycemic control is associated with a lower risk of adverse renal outcomes (45).

4.1.7. Association between quality indicators and risk of mortality (CKD and no CKD combined)

We found that the risk of mortality was higher if LDL was not measured compared to an LDL measured and at target, similarly for First Nations and non-First Nations groups and those with and without CKD. Lack of an LDL assessment may be a marker of poor access to the heath care system. Without appropriate use of the health care system, diabetic individuals without an LDL assessment may not be receiving adequate treatments for diabetes and related co-morbidities designed to reduce mortality (lipid lowering therapy, blood pressure control, antihypertensive therapy). This could therefore increase their risk of mortality.

The risk of mortality was lower if LDL was not at target compared to LDL at target in both First Nations and non-First Nations People. There are likely two reasons for this. Firstly, it has been shown that patients close to death may be malnourished and have lower LDL profiles (69). In contrast higher LDL levels may reflect a healthier population, thus LDL levels may be a surrogate marker of underlying severity of disease. Age-standardized mean total cholesterol values in healthy populations worldwide for men and women were recently estimated to be 4.64 mmol/L and 4.76 mmol/L, respectively (70). Secondly, health care practitioners are guided to be more aggressive with LDL targets if an individual is deemed higher cardiovascular risk (38,71). It is plausible that those patients with higher LDL profiles were not being treated as aggressively because they were felt to be healthier. If these individuals were truly healthier, their risk of mortality would be lower.

We also found that the risk of mortality was higher if the HbA1C was not at target compared to HbA1C at target in non-First Nations People, and there was a trend toward higher mortality in First Nations People. If an individual has poor glycemic control, this can eventually lead to higher mortality (46,47).

The risk of mortality was even higher if the HbA1C was not measured compared to HbA1C at target in both First Nations and non-First Nations People. The reason for this is not clear. Less frequent HbA1C measurements are recommended for diabetics who are consistently meeting glycemic targets (24,68), and these individuals would be at lower risk of mortality (UKPDS and DCCT long terms studies). However, it is plausible that less frequent HbA1C measurements are being done for individuals who are very ill and close to death. In these individuals, glycemic control may not be at the forefront of goals of care.

4.2. Understanding the gap

To try and understand the gap in care provided to First Nations and non-First Nations People, we can use the Anderson and Aday model which looks at factors at the patient level, the health care system level, and the provider level (72).

From the patient level, First Nations People with diabetes may not be receiving the same quality of care as non-First Nations People because of cultural differences. Traditionally, First Nations People have relied on spirituality and “indigenous knowledge” for their illnesses as opposed to western medicine (73). Because of this, there are likely many

members of the First Nations community who still do not trust western medicine practices. This would a larger barrier to receiving the quality of care examined in this study, as this quality of care would be considered part of western medicine.

From a health care system level, a major factor to be examined is that of location of residence. The health care system in Alberta is much different in urban versus rural settings. In an urban center, all health care services are available, and all are accessible with respect to distance. However, in rural Alberta, health care services are limited, and services become even more limited as an area becomes more remote. Many First Nations communities are located in these remote areas. Despite adjusting for local of residence in this study, the allocation of an area as "urban" or "rural" is a crude division based only on population and not proximity. A small community living in a very remote area would be considered "rural", but a small community living close to a large urban center would also be considered "rural"; however, their access to health care would be considered much different. Therefore, for First Nations communities living in remote areas far from urban centers, the distance would be considered a barrier to receiving the quality of care examined in this study. Rucker et al. have shown that patients with chronic kidney disease were less likely to receive quality of care markers, and more likely to be hospitalized or die if they lived further from a nephrologist (74).

From a provider level, a major factor to consider is duration of practice in rural areas. Many providers working in rural areas do not stay for a long duration of time. In Alberta,

there is a very active Rural Locum Program through the Alberta Medical Association, and this is designed to provide coverage for gaps in provider care in rural Alberta via rotation of physicians. Because these physicians are providing short coverage, their duration of stay in a given rural area is often short. Many of the quality indicators described in this study require continuity of care to be effective. If a provider is not in an area for a long time, he or she may not pursue these quality indicators, knowing that they will not be present to interpret the results of the tests. Again, as many First Nations communities are in remote rural areas, they may receive lower quality of care than non-First Nations communities because of the short duration of care by providers.

4.3. Study strengths

Our study has a number of strengths. The AHW data sources used include all Alberta residents, and the AKDN database contains laboratory results from all regions in Alberta. Therefore, this study was able to capture the adult population with diagnosed diabetes in Alberta from 2005 to 2008, and all corresponding lab values for these individuals were available from 2005 to 2009. This provided a large population with adequate data to assess quality indicators and clinical outcomes.

The AHW database also contains a large amount of information including age, sex, gender, and co-morbidities, and after linking with Canadian census data we were able to obtain additional information regarding location of residence and median household income, important potential covariates. This wealth of information allowed for a more complete

assessment of baseline characteristics and allowed for more robust adjustment for logistic regression and Cox proportional hazard models.

The four chosen quality indicators (serum creatinine, proteinuria, LDL cholesterol, HbA1C) were available within the AKDN laboratory database. They are well established and valid measures of kidney function, proteinuria, cholesterol, and glycemic control, respectively. Therefore, they are ideal markers of quality of care in a diabetic population, and differences in these indicators between the First Nations and non-First Nations populations reflect differences in quality of care between the two groups.

4.4. Study limitations

The results of our study should be interpreted in context of the study limitations. Firstly, the study design was a prospective cohort with retrospective data collection, with the resultant limitations inherent in observational studies, and inability to determine a causal relationship. Secondly we used administrative data to identify the cohort participants and their co-morbidities. The study was therefore prone to inherent errors with this type of data which lacks detailed clinical information. For example, only diabetic individuals captured by the Physicians Claims and Hospital Morbidity Files from Alberta Health and Wellness were included in the cohort. Known diabetics without physician or hospital visits as well as undiagnosed diabetics would not have been included. However the algorithm used to define diabetes based on administrative data has a sensitivity of 86% and specificity of 87% (56), therefore misclassification of diabetes status is likely to be

minimal. Thirdly, we were only able to include First Nations individuals with treaty status as identified from the AHW registry file. Metis, Inuit, and First Nations people who did not have treaty status were misclassified as non-First Nations. However, given that the majority of the First Nations population in Alberta is registered under the federal Indian Act and given the size of the non-First Nations population, this potential misclassification likely had minimal impact on our results.

Fourth, although the eGFR based on the MDRD study equation is a well accepted and validated method to estimate kidney function in the general population, it has not been validated in the First Nations population. Fifth, the study follow up was of short duration, with the maximum length of follow up being 4 years. This short duration of follow up would not have affected the objectives related to likelihood of assessment of quality indicators and indicator targets during the first year of follow up. However, mortality and composite renal outcomes may have been limited by duration of follow up, and additional follow-up would have resulted in a larger number of events and more stable and robust measures of association. Sixth, the number of First Nations People was relatively small in comparison to the non-First Nations group (6,574 or 4.5% of the total population), and the number of First Nations People with CKD in particular was limited in size (864 or 0.6% of the total population). Given this small sample size of First Nations individuals relative to non-First Nations, and in particular those with CKD, the power to detect differences between First Nations and non-First Nations populations was limited.

Finally, the quality indicators included in our study were chosen because of our ability to extract them from laboratory data. Although these quality indicators are good markers of clinical care for individuals with diabetes, there are other important quality indicators such as blood pressure control and use of particular blood pressure medications. Unfortunately, these quality indicators were not available in the data sources utilized. Their inclusion would have permitted use to draw further conclusions about differences in clinical quality of care between First Nations and non-First Nations People.

4.5. Study significance and future directions

This study has provided important insight into the quality of care delivered to First Nations and non-First Nations People with diabetes. Given the identified differences between markers of quality of care between the two groups, the health care community and decision makers need to be informed of these differences so steps can be taken to improve the quality of care in First Nations People. An example of this would be to set up a mobile diabetes clinic which would bring heath care practitioners and resources directly to First Nations communities. This would be especially beneficial for those communities living in rural areas. Another example would be to set up a regular mobile laboratory unit going to First Nations communities. This would allow for the collection of valuable laboratory data necessary to provide good quality of care to First Nations People.

This study clearly showed higher rates of composite renal outcome and mortality in the First Nations population. Because of associations shown between poor clinical outcomes

and failure to either assess quality indicators or achieve indicator targets, it is reasonable to assume that improving quality of care in the First Nations population would also improve clinical outcomes.

Future studies are required to further examine quality of care and its impact on clinical outcomes in the First Nations and non-First Nations diabetic population. A prospective study would enable detailed clinical data to be obtained to identify potential barriers to care and reasons for the deficiencies in quality of care for the First Nations people. By following both First Nations and non-First Nations prospectively with regular assessments of quality indicators at pre-defined intervals additional detailed information could be obtained. In addition to the quality indicators included in this study, important quality indicators such as blood pressure and use of particular blood pressure medication could also be included. In order to accommodate various First Nations communities, a study like this could include a mobile clinic and laboratory to allow for clinical assessment and data collection of study participants in their First Nations communities as opposed to an urban center which would be difficult to travel to.

Table 1. Stages of chronic kidney disease as defined by the National Kidney Foundation

Stage	Description	GFR^ (ml/min/1.73 m^2)
1	**Kidney damage* with normal or ↑GFR**	**≥ 90**
2	**Kidney damage* with mild ↓ GFR**	**60 – 89**
3	**Moderate ↓ GFR**	**30 – 59**
4	**Severe ↓ GFR**	**15 – 29**
5	**Kidney failure**	**< 15 (or dialysis)**

^GFR = glomerular filtration rate
*kidney damage defined by urine/blood/imaging abnormalities

Table 2. Quality of care indicators for diabetes

Urine albumin-creatinine ratio
Fasting cholesterol profile
HbA1C
Serum creatinine

Table 3. Co-morbidities and associated weighting in the Charlson Co-morbidity Index

Co-morbidity	Assigned Weight
Myocardial infarction	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Rheumatic disease	1
Peptic ulcer disease	1
Mild liver disease	1
Diabetes without chronic complication	1
Hemiplegia/paraplegia	2
Diabetes with end organ damage	2
Renal disease	2
Cancer	2
Moderate or severe liver disease	3
Metastatic solid tumor	6
AIDS/HIV	6

Table 4. Baseline characteristics of population, by First Nations status

	Non-First Nations (N = 140,709)	**First Nations (N = 6,574)**	**P value**
Age in yrs, mean (SD)	**61.66 (15.02)**	**53.18 (13.85)**	**< 0.0001†**
Female, number (%)	**66,270 (47.1%)**	**3,782 (57.5%)**	**< 0.001 ^**
Index eGFR in ml/min/1.73 m^2, mean (SD) *	**74.75 (22.57)**	**87.91 (27.57)**	**< 0.0001†**
Index eGFR stage in ml/min/1.73 m^2, number (%)			
> 60	**106,946 (76.0%)**	**5,710 (86.9%)**	**< 0.001 ^**
45 – 59.9	**21,331 (15.2%)**	**507 (7.7%)**	
30 – 44.9	**9,046 (6.4%)**	**219 (3.3%)**	
15 – 29.9	**2,944 (2.1%)**	**96 (1.5%)**	
< 15	**442 (0.3%)**	**42 (0.6%)**	
HTN, number (%)	**88,987 (63.2%)**	**3,399 (51.7%)**	**< 0.001 ^**
Charlson co-morbidity index, median (IQR)	**1 (1 - 2)**	**1 (1 - 2)**	**0.0001 ϕ**
Charlson co-morbidities (N, [%]):			
Myocardial infarction	10,153 (7.2%)	383 (5.8%)	
Congestive heart failure	12,725 (9.0%)	493 (7.5%)	
Peripheral vascular disease	6,563 (4.7%)	189 (2.9%)	
Cerebrovascular disease	9,074 (6.4%)	370 (5.6%)	
Dementia	5,137 (3.7%)	115 (1.7%)	
Hemiplegia/paraplegia	1,547 (1.1%)	100 (1.5%)	
Chronic pulmonary disease	27,064 (19.2%)	2,183 (33.2%)	
Rheumatic disease	2,580 (1.8%)	202 (3.1%)	
Peptic ulcer disease	4,064 (2.9%)	407 (6.2%)	
Mild liver disease	2,152 (1.5%)	168 (2.6%)	
Moderate/severe liver disease	451 (0.3%)	53 (0.8%)	
DM w/o chronic complication	116,170 (82.6%)	5,283 (80.4%)	
DM w/ end organ damage	10,088 (7.2%)	634 (9.6%)	
Renal disease	7,043 (5.0%)	265 (4.0%)	
Cancer	10,820 (7.7%)	321 (4.9%)	
Metastatic solid tumor	1,523 (1.1%)	49 (0.7%)	
AIDS/HIV	86 (0.1%)	19 (0.3%)	

Location of residence, number (%)			
Urban	**116,484 (82.8%)**	**2,869 (43.6%)**	**< 0.001 ^**
Rural	**23,459 (16.7%)**	**3,692 (56.2%)**	
Unknown	**766 (0.5%)**	**13 (0.2%)**	
Income quintiles, number (%)			
1 (lowest)	**29,908 (21.3%)**	**3,415 (52.0%)**	**< 0.001 ^**
2	**30,519 (21.7%)**	**928 (14.1%)**	
3	**27,510 (19.6%)**	**754 (11.5%)**	
4	**26,097 (18.6%)**	**521 (7.9%)**	
5 (highest)	**23,017 (16.4%)**	**539 (8.2%)**	
Unknown	**3,658 (2.6%)**	**417 (6.3%)**	

*eGFR values ≥ 200 ml/min/1.73 m^2 set at 200 ml/min/1.73m^2

† t-test

^ chi-square test

ϕ Kruskal-Wallis rank test

Table 5. Likelihood of having an assessment of proteinuria (urine dipstick or ACR) during a 1 year period after index eGFR, by First Nations status

	Non-First Nations (N = 140,709)	First Nations (N = 6,574)	Crude OR, FN vs non-FN (95% CI)	Adjusted OR * (95% CI) eGFR > 60 ml/min/1.73 m^2	Adjusted OR * (95% CI) eGFR < 60 ml/min/1.73 m^2
Urine dipstick or ACR, number (%)	78,558 (55.8%)	3,049 (46.4%)	0.68 (0.65 – 0.72)	0.78 (0.73 – 0.83) p < 0.001	1.05 (0.91 – 1.21) p = 0.510
ACR, number (%)	49,384 (35.1%)	1,738 (26.4%)	0.66 (0.62 – 0.71)	0.77 (0.72 – 0.83) p < 0.001	1.09 (0.93 – 1.27) p = 0.273

* adjusted for age, gender, hypertension, Charlson score, location of residence, income

Table 6. Likelihood of having an assessment of cholesterol during 1 year period after index eGFR, by First Nations status ^

	Non-First Nations (N = 140,599)	First Nations (N = 6,569)	Crude OR, FN vs non-FN (95% CI)	Adjusted OR * (95% CI) eGFR > 60 ml/min/1.73 m^2	Adjusted OR * (95% CI) eGFR < 60 ml/min/1.73 m^2
LDL, number (%)	**73,274 (52.1%)**	**2,491 (37.9%)**	**0.56 (0.53 – 0.60)**	**0.60 (0.56 – 0.64) p < 0.001**	**0.82 (0.71 – 0.95) p = 0.007**

^ after exclusion of 110 non-First Nations and 5 First Nations patients with LDL values < 0.5 mmol/L

* adjusted for age, gender, hypertension, Charlson score, location of residence, income

Table 7. Likelihood of having an assessment of HbA1C during 1 year period after index eGFR, by First Nations status

	Non-First Nations (N = 140,709)	First Nations (N = 6,574)	Crude OR, FN vs non-FN (95% CI)	Adjusted OR * (95% CI) eGFR > 60 ml/min/1.73 m^2	Adjusted OR * (95% CI) eGFR < 60 ml/min/1.73 m^2
HbA1C, number (%)	89,935 (63.9%)	3,473 (52.8%)	0.63 (0.60 – 0.67)	0.68 (0.64 - 0.73) p < 0.001	1.10 (0.94 – 1.27) p = 0.207

* adjusted for age, gender, hypertension, Charlson score, location of residence, income

Table 8. Likelihood of having a serum creatinine measurement during a 1 year period after index eGFR, by First Nations status

	Non-First Nations (N = 140,709)	First Nations (N = 6,574)	Crude OR, FN vs non-FN (95% CI)	Adjusted OR * (95% CI) eGFR > 60 ml/min/1.73 m^2	Adjusted OR * (95% CI) eGFR < 60 ml/min/1.73 m^2
creatinine measurement, number (%)	94,369 (67.1%)	4,141 (63.0%)	0.84 (0.79 – 0.89)	0.89 (0.84 - 0.95) p < 0.001	1.02 (0.86 – 1.21) p = 0.822

* adjusted for age, gender, hypertension, Charlson score, location of residence, income

Table 9. Mean LDL cholesterol and likelihood of achieving an LDL target during the 1 year period after index eGFR, by First Nations status ^

	Non-First Nations (N = 73,274)	First Nations (N = 2,491)	OR, FN vs non-FN (95% CI)	Adjusted OR * (95% CI) eGFR > 60 ml/min/1.73 m^2	Adjusted OR * (95% CI) eGFR < 60 ml/min/1.73 m^2
Mean LDL, mmol/L (SD)	**2.50 (0.83)**	**2.54 (0.85)†**			
LDL ≤ 2.5mmol/L, number (%)	**39,807 (54.3%)**	**1,279 (51.3%)**	**0.89 (0.81 – 0.97)**	**1.05 (0.95 - 1.15) p = 0.307**	**1.12 (0.90 – 1.39) p = 0.318**

^ after exclusion of 110 non-First Nations and 5 First Nations patients with LDL values < 0.5 mmol/L

* adjusted for age, gender, hypertension, Charlson score, location of residence, income

† p = 0.023 based on t-test

Table 10. Mean HbA1C and likelihood of achieving HbA1C target during the 1 year period after index eGFR, by First Nations status

	Non-First Nations (N = 89,935)	First Nations (n = 3,473)	OR, FN vs non-FN (95% CI)	Adjusted OR * (95% CI) eGFR > 60 ml/min/1.73 m^2	Adjusted OR * (95% CI) eGFR < 60 ml/min/1.73 m^2
Mean HbA1C, % (SD)	7.33 (1.42)	7.90 (2.02)†			
HbA1C ≤ 7%, number (%)	45,725 (50.8%)	1,504 (43.3%)	0.74 (0.68 – 0.80)	0.84 (0.77 - 0.92) p < 0.001	0.93 (0.78 – 1.12) p = 0.438

* adjusted for age, gender, hypertension, Charlson score, location of residence, income

†p < 0.0001 based on t – test

Table 11. Rates of ESRD, per 1000 person-years, by First Nations and CKD status

	Non-First Nations		First Nations	
	Crude Rate (95% CI)	Age- and gender-adjusted Rate (95% CI)	Crude Rate (95% CI)	Age- and gender-adjusted Rate (95% CI)
eGFR > 60 ml/min/1.73 m^2	0.41 (0.35 - 0.48)	0.29 (0.24 - 0.34)	0.94 (0.53 - 1.36)	0.55 (0.31 - 0.80)
eGFR < 60 ml/min/1.73 m^2	8.04 (7.54 - 8.55)	10.91 (10.20 - 11.63)	35.93 (29.02 - 42.83)	39.65 (32.01 - 47.28)

Table 12. Rate of composite renal outcome (ESRD/doubling creatinine), per 1000 person-years, by First Nations and CKD status

	Non-First Nations		First Nations	
	Crude Rate (95% CI)	Age- and gender-adjusted Rate (95% CI)	Crude Rate (95% CI)	Age- and gender-adjusted Rate (95% CI)
eGFR > 60 ml/min/1.73 m^2	2.71 (2.55 - 2.87)	2.64 (2.48 – 2.80)	4.77 (3.84 – 5.70)	4.80 (3.85 – 5.74)
eGFR < 60 ml/min/1.73 m^2	14.88 (14.19 – 15.57)	15.36 (14.52 – 16.19)	50.50 (42.25 – 58.75)	53.57 (44.80 – 62.35)

Table 13. Mortality rate, per 1000 person-years, by First Nations and CKD status

	Non-First Nations		First Nations	
	Crude Rate (95% CI)	Age- and gender-adjusted Rate (95% CI)	Crude Rate (95% CI)	Age- and gender-adjusted Rate (95% CI)
eGFR > 60 ml/min/1.73 m^2	21.54 (21.09 – 21.99)	15.37 (14.97 – 15.76)	18.11 (16.30 – 19.92)	23.83 (21.45 – 26.21)
eGFR < 60 ml/min/1.73 m^2	74.74 (73.21 – 76.27)	24.55 (23.75 – 25.34)	78.62 (68.78 – 88.47)	47.44 (41.45 – 53.43)

Table 14. Association between quality of care indicators and composite renal outcome, by CKD status*

	HR (95% CI) eGFR > 60 ml/min/1.73 m^2	HR (95% CI) eGFR < 60 ml/min/1.73 m^2
LDL target **LDL not target** **LDL not measured**	**Reference** **0.95 (0.80 – 1.12)** **1.74 (1.50 – 2.02)**	**Reference** **0.92 (0.81 – 1.04)** **1.16 (1.04 – 1.30)**
HbA1C target **HbA1C not target** **HbA1C not measured**	**Reference** **1.63 (1.41 – 1.87)** **0.91 (0.78 – 1.08)**	**Reference** **1.27 (1.15 – 1.41)** **0.71 (0.63 – 0.81)**

* adjusted for age, gender, hypertension, Charlson score, location of residence, income, First Nations status, and other variables in table

Table 15. Association between quality of care indicators and mortality, by First Nations status*

	HR (95% CI) Non-First Nations	HR (95% CI) First Nations
LDL target **LDL not target** **LDL not measured**	**Reference** **0.91 (0.86 – 0.96)** **2.11 (2.03 – 2.20)**	**Reference** **0.60 (0.44 – 0.83)** **1.38 (1.10 – 1.71)**
HbA1C target **HbA1C not target** **HbA1C not measured**	**Reference** **1.05 (1.01 – 1.09)** **1.27 (1.22 – 1.32)**	**Reference** **1.17 (0.94 – 1.48)** **1.46 (1.17 – 1.82)**

* adjusted for age, gender, hypertension, Charlson score, location of residence, income, CKD status and other variables in the table

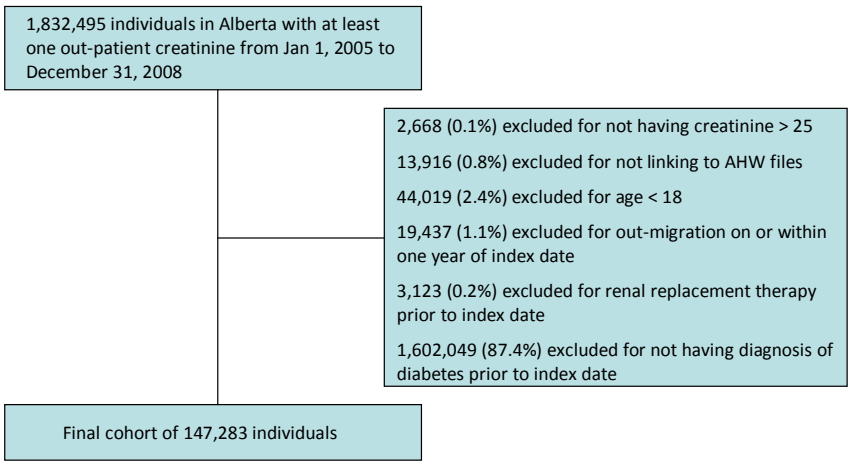
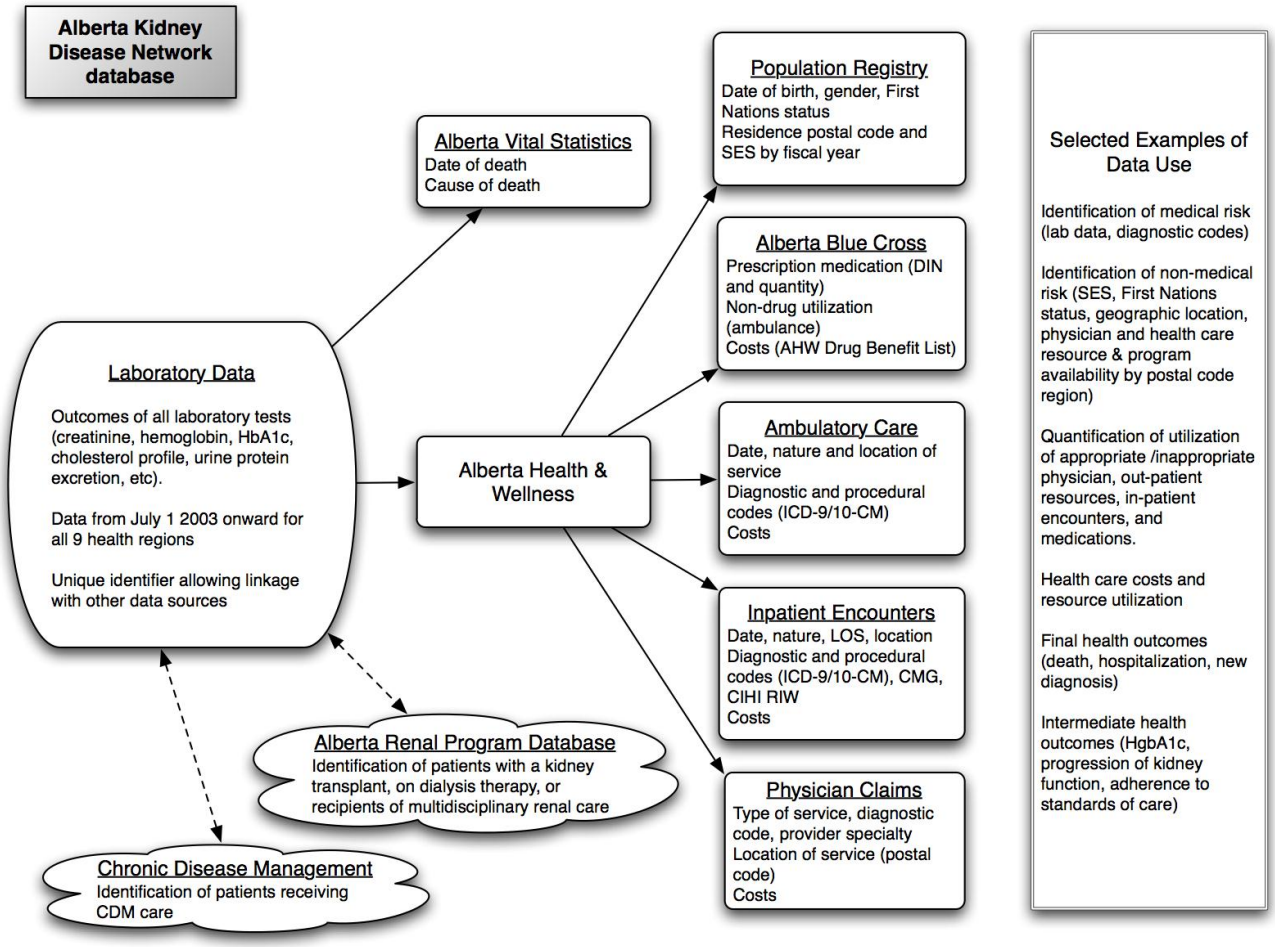


Figure 1. Flow diagram defining final cohort

APPENDICES

Appendix 1. Overview of the Alberta Kidney Disease Network (AKDN) database

The AKDN has developed a process for retrieval, storage and maintenance of laboratory data and relevant laboratory tests (serum creatinine, hemoglobin, potassium, lipid profile, hemoglobin A1C, and urine protein) for all patients who have these measurements across the province of Alberta. Linkage to administrative data permits an assessment of outcomes, including health services utilization and mortality, for patients with laboratory tests measured and those without.



CDM = Chronic Disease Management; SES = socioeconomic status defined by health insurance premium subsidy; DIN = drug information number; AHW = Alberta Health & Wellness; ICD = International Classification of Disease; CM = Clinical Modification; LOS = Length of stay; CMG = Case Mix Group; CIHI RIW = Canadian Institute for Health Research Resource Intensity Weights.

Appendix 2. Alberta Health and Wellness Data Sources

1) Alberta Health and Wellness Registration File - contains a unique recipient identifier (PHN), age, date of birth, postal code, ***identifier for First Nations Treaty Status***, and date of death (for those who have died).

2) Alberta Blue Cross - Alberta Blue Cross administers extended health benefits paid by Alberta Health and Wellness on behalf of eligible individuals, including residents aged 65 and older, for services which include formulary drugs. Information contained in this data source include a recipient identifier, as well as details regarding drugs dispensed including date, drug quantity and drug identifier. Data is available from April 1994 onward.

3) CIHI hospital inpatient - contains details regarding inpatient hospitalizations including recipient identifier, admission date, discharge date, length of stay, facility, 16 diagnostic codes and 10 procedure codes. Diagnosis and procedures are coded using ICD-9-CM until 2001/2002, following which ICD-10 was implemented. Data is available from 1988/89 onward.

4) CIHI day procedures - contains details of procedures performed in operating rooms on a registered outpatient including a recipient identifier, discharge date, 16 diagnostic codes and 10 procedure codes. All diagnoses and procedures are coded using ICD-9-CM. Data is available from 1994/95 onward.

5) Ambulatory Care Classification System - contains details of same day surgery and emergency room visits including recipient identified, intervention date, 5 diagnostic codes (ICD-9-CM) and 10 intervention codes (as defined by the Ambulatory Care Classification System). Data is available from 1997/98 onward.

6) Physician claims file – contains details of physician service claims including recipient identifier, physician identifier, service codes, diagnostic codes, date and location of service.

REFERENCES

1. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39(Suppl 1): S1-266.

2. Stigant C, Stevens L, Levin A. Nephrology: 4. Strategies for the care of adults with chronic kidney disease. *CMAJ* 2003; 168: 1553-60.

3. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA* 2007; 298: 2038-47.

4. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; 351: 1296-1305.

5. Canadian Organ Replacement Register. Annual report 2011. Ottawa: Canadian Institute for Health Information; 2011.

6. Levin A, Hemmelgarn BR, Culleton BF, et al. Guidelines for the management of chronic kidney disease. *CMAJ* 2008; 179: 1154-62.

7. James MJ, Hemmelgarn BR, Wiebe N, et al. Glomerular filtration rate, proteinuria, and the incidence and consequences of acute kidney injury: a cohort study. *Lancet* 2010; 376: 2096-2103.

8. Levey AS, Coresh J. Chronic kidney disease. *Lancet* 2011; Aug 12 (Epub).

9. Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. *N Engl J Med* 1994; 330: 877-84.

10. Maschio G, Alberti D, Janin G, et al. Effect of the angiotensin-converting-enzyme inhibitor benazepril on the progression of chronic renal insufficiency. *N Engl J Med* 1996; 334: 939-45.

11. Gruppo Italiano di Studi Epidemiologici in Neforologia (GISEN). Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. *Lancet* 1997; 349: 1857-63.

12. Gouva C, Nikolopoulos P, Ioannidis JP, et al. Treating anemia early in renal failure patients slows the decline of renal function: a randomized controlled trial. *Kidney Int* 2004; 66: 753-60.

13. de Brito-Ashurst I, Varagunam M, Raftery MJ, et al. Bicarbonate supplementation slows progression of CKD and improves nutritional status. *J Am Soc Nephrol* 2009; 20: 2075-84.

14. Gao S, Manns BJ, Culleton BF, et al. Prevalence of chronic kidney disease and survival among aboriginal people. *J Am Soc Nephrol* 2007; 18: 2953-9.

15. Tonelli M, Hemmelgarn BR, Manns BJ, et al. Death and renal transplantation among Aboriginal people undergoing dialysis. *CMAJ* 2004; 171: 577-82.

16. Alberta Diabetes Surveillance System. Alberta Diabetes Atlas 2011. Canadian Institute of Health Economics; 2011.

17. Narva AS. The spectrum of kidney disease in American Indians. *Kidney Int* 2003; 63(Suppl 83): S3-7.

18. Lohr KN, Schroeder SA. Special report: a strategy for quality assurance in Medicare. *N Engl J Med* 1990; 322: 707-12.

19. Williams SC, Schmaltz SP, Morton DJ, et al. Quality of care in US hospitals as reflected by standardized measures, 2002-2004. *N Engl J Med* 2005; 353: 255-64.

20. Higashi T, Shekelle PG, Adams JL, et al. Quality of care is associated with survival in vulnerable older patients. *Ann Intern Med* 2005; 143: 274-81.

21. Peterson ED, Roe MT, Mulgund J, et al. Association between hospital process performance and outcomes among patients with acute coronary syndromes. *JAMA* 2006; 295: 1912-20.

22. McGlynn EA. Six challenges in measuring the quality of health care. *Health Aff* 2007; 16: 7-21.

23. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2003 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2003; 27(Suppl 2): S1-152.

24. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008; 32(Suppl 1): S1-201.

25. Holloway RG, Vickrey BG, Benesch C, et al. Development of performance measures for acute ischemic stroke. *Stroke* 2001; 32: 2058-74.

26. Spertus JA, Eagle KA, Krumholz HM, et al. American College of Cardiology and American Heart Association methodology for the selection and creation of performance measures for quantifying the quality of cardiovascular care. *Circulation* 2005; 111: 1703-12.

27. Tu JV, Khalid L, Donovan LR, et al. Indicators of quality of care for patients with acute myocardial infarction. *CMAJ 2008*; 179: 909-15.

28. Gerstein HC, Mann JF, Yi Q, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. *JAMA* 2001; 286: 421-6.

29. Lewis EJ, Hunsicker LG, Bain RP, et al. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993; 329: 1456-62.

30. Atkins RC, Briganti EM, Lewis JB, et al. Proteinuria reduction and progression to renal failure in patients with type 2 diabetes mellitus and overt nephropathy. *Am J Kidney Dis* 2004; 45: 281-7.

31. de Zeeuw D, Remuzzi G, Parving HH, et al. Proteinuria, a target for renoprotection in patients with type 2 diabetic nephropathy: lessons from RENAAL. *Kidney Int* 2004; 65: 2309-20.

32. Roglic G, Unwin N, Bennett PH, et al. The burden of mortality attributable to diabetes: realistic estimates for the year 2000. *Diabetes care* 2005; 28; 2130-5.

33. Harris SB, Ekoe JM, Zdanowicz Y, et al. Glycemic control and morbidity in the Canadian primary care setting (results of the diabetes in Canada evaluation study). *Diabetes Res Clin Pract* 2005; 70: 90-7.

34. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002; 360: 7-22.

35. Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004; 364: 685-96.

36. Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005; 366: 1267-78.

37. Baigent C, Landray MJ, Reith C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomized placebo-controlled trial. *Lancet* 2011; 377: 2181-92.

38. Genest J, Frohlich J, Fodor G, et al. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: summary of the 2003 update. *CMAJ* 2003; 169: 921-4.

39. Reichard P, Nilsson BY, Rosenqvist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. *N Engl J Med* 1993; 329: 304-9.

40. Diabetes Control and Complications Trial (DCCT) Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993; 329: 977-86.

41. United Kingdom Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *Lancet* 1998; 352: 837-53.

42. Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) Research Group. Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive therapy. *N Engl J Med* 2000; 342: 381-9.

43. Epidemiology of Diabetes Interventions and Complications (EDIC) Study. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy. *JAMA* 2003; 290: 2159-67.

44. Levin SR, Coburn JW, Abraira C, et al. Effect of intensive glycemic control on microalbuminuria in type 2 diabetes. *Diabetes Care* 2000; 23: 1478-85.

45. Shurraw S, Hemmelgarn BR, Lin M, 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: 1920-7.
46. Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 2005; 353: 2643-53.

47. Holman RR, Paul SK, Bethel MA, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 2008; 359: 1577-89.

48. MacMillan HL, MacMillan AB, Offord DR, et al. Aboriginal health. *CMAJ* 1996; 155: 1569-78.

49. Shah BR, Gunraj N, Hux JE. Markers of access to and quality of primary care for aboriginal people in Ontario, Canada. *Am J Pub Health* 2003; 93: 798-802.

50. Jette N, Quan H, Faris P, et al. Health resource use in epilepsy: significant disparities by age, gender, and aboriginal status. *Epilepsia* 2008; 49: 586-93.

51. Gao S, Manns BJ, Culleton BF, et al. Access to health care among status Aboriginal people with chronic kidney disease. *CMAJ* 2008; 179: 1007-12.

52. Hemmelgarn BR, Clement F, Manns BJ, et al. Overview of the Alberta Kidney Disease Network. *BMC Nephrol* 2009; 10: 30.

53. Statistics Canada. 2001 Census. Ottawa: Canadian Institute for Health Information; 2001.

54. Manns BJ, Mortis GP, Taub KJ, et al. The Southern Alberta Renal Program database: a prototype for patient management and research initiatives. *Clin Invest Med* 2001; 24: 164-70.

55. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med* 1999; 130: 461-70.

56. Hux JE, Ivis F, Flintoft V, et al. Diabetes in Ontario: Determination of prevalence and incidence using a validated administrative data algorithm. *Diabetes Care* 2002; 25: 512-6.

57. Quan H, Khan N, Hemmelgarn BR, et al. Validation of a case definition to define hypertension using administrative data. *Hypertension* 2009; 54: 1423-8.

58. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic co-morbidity in longitudinal studies: development and validation. *J Chron Dis* 1987; 40: 373-83.

59. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Medical Care* 2005; 43: 1130-9.

60. Statistics Canada. 2006 Census. Ottawa: Canadian Institute for Health Information; 2006.

61. Dyck RF, Sidhu N, Klomp H, et al. Differences in glycemic control and survival predict higher ESRD rates in diabetic first nations adults. *Clin Invest Med* 2010; 33: E390-7.

62. Gaede P, Lund-Andersen H, Parving HH, et al. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008; 358: 580-91.

63. Biesenbach G, Raml A, Schmekal B, et al. Decreased insulin requirement in relation to GFR in nephropathic type 1 and insulin-treated type 2 diabetic patients. *Diabet Med* 2003; 20: 642-5.

64. Hoffmann F, Haastert B, Koch M, et al. The effect of diabetes on incidence and mortality in end-stage renal disease in Germany. *Nephrol Dial Transplant* 2011; 26: 1634-40.

65. Finne P, Reunanen A, Stenman S, et al. Incidence of end-stage renal disease in patients with type 1 diabetes. *JAMA* 2005; 294: 1782-7.

66. Dyck RF, Tan L. Rates and outcomes of diabetic end-stage renal disease among registered native people in Saskatchewan. *CMAJ* 1994; 150: 203-8.

67. Oster RT, Johnson JA, Hemmelgarn BR, et al. Recent epidemiologic trends of diabetes mellitus among status Aboriginal adults. *CMAJ* 2011; 183: E803-8.

68. American Diabetes Association. Standards of medical care in diabetes – 2007. *Diabetes Care* 2007; 30: S4-41.

69. Roongpisuthipong C, Sobhonslidsuk A, Nantiruj K, et al. Nutritional assessment in various stages of liver cirrhosis. *Nutrition* 2001; 17: 761-5.

70. Farzadfar F, Finucane MM, Danaei G, et al. National, regional, and global trends in serum total cholesterol since 1980: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3.0 million participants. *Lancet* 2011; 377: 578-86.

71. Fodor JG, Frohlich JJ, Genest JJ, et al. Recommendations for the management and treatment of dyslipidemia: a report of the working group on hypercholesterolemia and other dyslipidemia. *CMAJ* 2000; 162: 1441-7.

72. Aday LA, Andersen R. A framework for the study of access to medical care. *Health Serv Res* 1974; 9: 208-20.

73. CIHR guidelines for health research involving Aboriginal People. Ottawa: Canadian Institutes of Health Research; 2007.

74. Rucker D, Hemmelgarn BR, Lin M, et al. Quality of care and mortality are worse in chronic kidney disease patients living in remote areas. *Kidney Int* 2011; 79: 210-7.