CARE OF MANITOBANS LIVING WITH CHRONIC KIDNEY DISEASE

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The Manitoba Centre for Health Policy (MCHP) is located within the Department of Community Health Sciences, College of Medicine, Faculty of Health Sciences, University of Manitoba. The mission of MCHP is to provide accurate and timely information to healthcare decision–makers, analysts and providers, so they can offer services which are effective and efficient in maintaining and improving the health of Manitobans. Our researchers rely upon the unique Population Health Research Data Repository (Repository) to describe and explain patterns of care and profiles of illness and to explore other factors that influence health, including income, education, employment, and social status. This Repository is unique in terms of its comprehensiveness, degree of integration, and orientation around an anonymized population registry.

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We thank the University of Manitoba, Faculty of Health Sciences, College of Medicine, Health Research Ethics Board for their review of this project. MCHP complies with all legislative acts and regulations governing the protection and use of sensitive information. We implement strict policies and procedures to protect the privacy and security of anonymized data used to produce this report and we keep the provincial Health Information Privacy Committee informed of all work undertaken for Manitoba Health, Healthy Living & Seniors.

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ACRONYMS

ACE	angiotensin-converting-enzyme inhibitors
ACR	albumin-creatinine ratio
AHRQ	Agency for Healthcare Research and Quality
ARB	angiotensin receptor blockers
CI	confidence interval
CORR	Canadian Organ Replacement Registry
CKD	chronic kidney disease
DPIN	Drug Program Information Network
DSM	Diagnostic Services Manitoba
eGFR	estimated glomerular filtration rate
ESKD	end stage kidney disease
GLM	generalized linear model
HD	centre-based hemodialysis
HHD	home hemodialysis
KDIGO	Kidney Disease Improving Global Outcomes
MCHP	Manitoba Centre for Health Policy
MDRD	Modification of Diet in Renal Disease
MHHLS	Manitoba Health, Healthy Living and Seniors
MRP	Manitoba Renal Program
NPV	negative predictive value
OR	odds ratio
PCR	protein-creatinine ratio
PD	peritoneal dialysis
PHIN	personal health identification number
PPV	positive predictive value
ROC	receiver operating characteristic
RR	relative risk
RRT	renal replacement therapy
SCr	serum creatinine
SES	socioeconomic status
Tx	kidney transplant

EXECUTIVE SUMMARY

Introduction

Chronic kidney disease (CKD) was previously perceived as a life-threatening condition affecting a small number of people, but it is now thought of as a common disorder requiring a public health strategy (Levey & Coresh, 2012). CKD encompasses disorders that damage the glomeruli (kidney filters) and lead to gradual long-term loss of kidney function. End stage kidney disease (ESKD) or kidney failure is the last and most debilitating stage of CKD. An estimated 10% to 15% of Canadian adults (about 3 million people) have CKD, and the Canadian prevalence of ESKD is 1,182 cases per 1,000,000 people, as reported in the Canadian Organ Replacement Report (Canadian Institute for Health Infrmation (CIHI), 2015). Rates in Manitoba, already the highest in Canada, are expected to grow if current trends continue.

Renal replacement therapy (RRT) is required to treat kidney failure, and includes centre-based hemodialysis, peritoneal dialysis, home hemodialysis, and kidney transplant. The type of RRT that patients use has important health and cost implications, and centre-based hemodialysis is associated with lower quality of life and higher costs. Disorders that most commonly cause CKD include diabetes and high blood pressure, and the risk increases with advancing age.

Purpose of This Report

The purpose of this report is to gain a greater understanding of CKD and ESKD in adults and children in Manitoba. The findings will provide background knowledge to prevent new cases of CKD, to intervene early to slow the progression to ESKD, and to plan resources for renal health services in the future. We sought to address four research questions as requested by Manitoba Health, Healthy Living and Seniors (MHHLS):

- What are the future needs for renal health services (peritoneal dialysis, home hemodialysis and centre-based dialysis) in Manitoba?
- What is the geographic distribution of this population?
- What are the characteristics of the future population of Manitoba residents who will require renal replacement treatment by dialysis (peritoneal dialysis, home hemodialysis and centre-based dialysis)?
- What preventive, screening, and education measures and affiliations with existing programs might reduce the number of Manitobans who will require dialysis?

Methods

The results presented in this report were obtained using administrative data housed in the Population Health Research Data Repository (the Repository) at the Manitoba Centre for Health Policy. All records in the Repository are de-identified by removing names and addresses, as well as scrambling all Personal Health Identification Numbers (PHINs) and other personal identifiers.

The cohorts of people with ESKD and CKD defined in this report were mutually exclusive. The ESKD cohort included only people receiving renal replacement therapy, and excluded people who had ESKD but were being managed conservatively. We used administrative data and laboratory data to define the CKD cohorts of children and adults. Using the administrative data, we defined a Manitoba resident as having CKD if he or she had, within a three-year period, at least two CKD-related medical claims by a physician visit or one CKD-related hospitalization or one filled prescription of a medication specifically used in the treatment or management of CKD. Using the laboratory data, we defined CKD as having at least two estimated glomerular filtration rates (eGFR) test results indicating kidney dysfunction or two abnormal albumin or protein-creatinine ratios, at least 90 days apart.

We calculated prevalence rates of CKD for children and adults using three different methods to determine reliable minimum and maximum rates for the population. This approach was important because previous studies had cautioned that administrative data tend to underestimate the number of people diagnosed for CKD (Ronksley et al., 2012). We calculated rates of medical conditions, mental disorders, drug prescriptions, and healthcare use. Rates in the CKD or ESKD cohorts were compared to rates of people without CKD.

We used a combination of Poisson regression and Markov simulation modelling to create projections of the number of patients with ESKD from 2012 to 2024. These projections accounted for the aging population, increases in diabetes prevalence, and regional differences. Because population conditions or clinical practice approaches may change, we also tested "what if" scenarios by altering parameters of the projection models and by examining what effects these changes may have on the projections. "What if" scenarios were created based on factors that could potentially influence the prevalence of ESKD or the distribution of centre-based versus home-based treatments.

We also conducted validation tests on the definition of CKD in children and on the Kidney Failure Risk Equation (KFRE), a risk stratification tool. Sensitivity, specificity, positive predictive value and negative predictive value were calculated. Finally, factors associated with starting renal replacement therapy with centre-based hemodialysis were examined. We used logistic regression to determine the unique contribution of age, sex, socioeconomic status, health region, diagnosis of diabetes, use of angiotensin-converting enzyme (ACE) inhibitors, and length of time between the first nephrologist visit and the dialysis start.

Results

Disease Prevalence in 2012

Using three methods, we found that CKD prevalence among adults ranged between 7.4% and 13.8% in Manitoba. The CKD prevalence in the Northern Health Region and particularly remote communities, where most of the population are First Nations people, was significantly higher than the Manitoba average. The ESKD prevalence was 1.45 per 1,000 residents overall in Manitoba, 2.43 in the Northern Health Region, and 3.86 in remote communities.

Using both the administrative and laboratory data, we estimated CKD prevalence for children in Manitoba to be 1.49%. There were an additional 17 children with ESKD (prevalence: 5.8 per 100,000). All algorithms that we tested, using administrative data to define CKD in children, had low sensitivity and very high specificity. The definition used in this report successfully identified 37.6% of children who had CKD, and 99% of those who did not have CKD, as confirmed by laboratory testing.

There were 1,833 Manitoba residents (adults and children) receiving renal replacement therapy in 2012; of these, 597 (32.6%) had a functioning kidney transplant and 1,236 (67.4%) were on dialysis. Of those on dialysis, we found that 79% used centre-based hemodialysis, 19% used peritoneal dialysis, and a very small proportion (3%) used home-based hemodialysis.

Characteristics of People with Chronic Kidney Disease and End Stage Kidney Disease

People aged 65 years and older, those with diabetes, and those living in lower-income areas had higher rates of CKD and ESKD. Women had slightly but statistically significantly higher rates of CKD; however, men had significantly higher rates of ESKD. High rates of medical conditions (particularly cardiovascular diseases), mental disorders, prescription drugs and healthcare use were found among those with CKD and ESKD. People with ESKD had the highest comorbidity rates, but rates among those with CKD at high risk of requiring renal replacement therapy were also remarkably high. The results in Table E.1 suggest that rates of comorbid disorders increased as kidney function worsened.

Table E.1: Physical Health of Adults in Chronic Kidney Disease Patient Cohorts

Age- and sex adjusted prevalence, 95% confidence intervals

Indicators		No CKD	CKD by Risk of Progression to ESKD		
			Unknown	Low	High
Diabetes (%) (2009/10-2011/12)	**Prevalence**	7.02 (6.96-7.07)	12.44 (8.64-17.92)	28.59 (19.80-41.30)	37.10 (25.62-53.73)
	Relative Risk	reference	**1.77 (1.23-2.55)**	**4.08 (2.82-5.89)**	**5.29 (3.65-7.66)**
Hypertension (%) (2011/12)	**Prevalence**	21.45 (21.36-21.55)	31.06 (19.91-48.45)	43.84 (28.01-68.61)	61.46 (39.06-96.72)
	Relative Risk	reference	1.45 (0.93-2.26)	**2.04 (1.31-3.20)**	**2.87 (1.82-4.51)**
Congestive Heart Failure (%) (2009/10-2011/12)	**Prevalence**	1.38 (1.35-1.41)	4.51 (2.47-8.26)	5.19 (2.88-9.35)	25.09 (13.64-46.17)
	Relative Risk	reference	**3.27 (1.79-5.98)**	**3.76 (2.09-6.77)**	**18.17 (9.88-33.43)**
Stroke (%) (2007/08-2011/12)	**Prevalence**	0.41 (0.39-0.43)	0.92 (0.51-1.67)	2.01 (1.17-3.45)	5.59 (3.13-9.98)
	Relative Risk	reference	**2.26 (1.25-4.10)**	**4.94 (2.88-8.47)**	**13.72 (7.68-24.50)**

bolded values indicate statistically significant difference from the No CKD group

Higher rates of CKD and ESKD were found among adolescents than children under 12 years old. Compared to children without CKD, those with CKD had higher rates of diabetes, hypertension, ischemic heart disease, mood and anxiety disorders, developmental disabilities, substance abuse, at least one mental disorder, and suicide attempts. Relative risks ranged from 2.76 for having at least one mental disorder to 77.70 for hypertension. Compared to children without CKD, those with CKD had higher hospitalization rates and more physician visits, were dispensed more medications and were more likely to be taking anti-hypertensive medications. As with adults, children with ESKD had the highest rates of comorbid disorders and healthcare use compared to children with earlier stages of CKD.

Projections of the Number of Manitobans Requiring Treatment for Kidney Failure (2012 – 2024)

The number of Manitobans with ESKD who will require renal replacement therapy will continue to increase over the next decade. We estimate that 3,077 people will be receiving renal replacement therapy by 2024, a 68% increase between 2012 and 2024. This risk is more pronounced among people with diabetes and people aged 65 and older. Our 2024 projections show that increases in ESKD are most pronounced among residents of the Southern Health/ Santé Sud and Northern Health Regions (Table E.2). The Northern Health Region will continue to have the highest number of people with ESKD per capita in Manitoba.

We examined the potential benefits of implementing strategies to reduce the number of Manitobans with ESKD. These "what if" scenarios included maintaining diabetes prevalence at 2012 levels, increasing kidney transplants by 25%, increasing peritoneal dialysis starts to 30% of all dialysis starts, increasing home hemodialysis starts to 8% of all dialysis starts, and decreasing mortality rates by 20% among people with ESKD. Maintaining diabetes prevalence at 2012 levels showed the most significant decrease in the total ESKD population and in the proportion of Manitobans treated with centre-based hemodialysis. The number of people on centre-based hemodialysis also decreased when 30% of all new dialysis starts were peritoneal dialysis and when 8% started on home hemodialysis. For example, if measures were taken to ensure that 30% of all new starts are peritoneal dialysis by 2024, we would expect 95 more people on peritoneal dialysis, and 98 fewer people who would require centre-based hemodialysis during that year. Increasing kidney transplants by 25% would result in fewer people on centre-based hemodialysis. Not surprisingly, a decrease in mortality rates would increase the number of Manitobans requiring treatment.

Table E.2: Observed and Predicted Number of End Stage Kidney Disease Patients by Region and Treatment Type, 2012 and 2024

Health Region	Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	Total
Observed Number (2012)				
Southern Health/Santé Sud	68	35	77	180
Winnipeg	558	141	367	1,066
Prairie Mountain Health	112	14	74	200
Interlake-Eastern	120	35	51	206
Northern	118	35	28	181
Manitoba	976	260	597	1,833
Predicted Number in 2024 (% Annual Increase From 2012 to 2024)				
Southern Health/Santé Sud	124 (4.92)	61 (4.54)	139 (4.84)	324 (4.81)
Winnipeg	944 (4.30)	198 (2.75)	626 (4.36)	1,768 (4.13)
Prairie Mountain Health	181 (3.91)	24 (4.41)	123 (4.15)	328 (4.04)
Interlake-Eastern	198 (4.09)	49 (2.73)	86 (4.27)	333 (3.92)
Northern	207 (4.60)	54 (3.53)	64 (6.84)	324 (4.77)
Manitoba	1,653 (4.31)	386 (3.21)	1,038 (4.52)	3,077 (4.23)

Risk Factors, Screening, Prevention and Treatment Strategies

We reviewed the scientific literature and used Repository data to examine ways of reducing the prevalence of ESKD in Manitoba. Several risk factors (age, health status, comorbid medical conditions, socioeconomic status and region of residence) are associated with CKD and progression to kidney failure. Indigenous peoples are three times more likely to be new patients receiving renal replacement therapy than non-indigenous people. We found no consistent evidence of the health and cost benefits of systematic screening in the general population. However, potential benefits may exist in screening populations with earlier stages of CKD and those with risk factors such as diabetes, hypertension, cardiovascular disease and older age. In the clinical setting, diagnosis of early stage CKD is often missed because patients are asymptomatic. Early identification of CKD permits lifestyle counselling to address risk factors and the start of treatments to slow progression of the disease. Clear guidelines for primary care physicians are required to implement care for CKD patients in the early stages of the disease.

Using the Repository, we examined the relationship between demographic, social and healthcare factors and the type of renal replacement therapy that patients used when they began treatment (centre-based hemodialysis versus home-based renal replacement therapy or kidney transplant). Residents living in areas of lower socioeconomic status (Odds Ratio [OR]: 1.85) and those who had not seen a nephrologist before renal replacement therapy began (OR: 1.39) were significantly more likely to use centre-based hemodialysis than other types of renal replacement therapy. People with CKD who were younger than 65 years (OR for people aged 0 to 44: 0.42; OR for people aged 45 to 64: 0.47), lived in a region with healthy populations (Interlake-Eastern OR: 0.86), or received medications that delay CKD progression (OR: 0.62), were less likely to start on centre-based hemodialysis. Gender and diabetes status were not significant predictors of the type of renal replacement therapy received.

We also examined the Kidney Failure Risk Equation (KFRE), a risk stratification tool, to determine its usefulness in Manitoba in identifying people with CKD at greatest risk for developing ESKD. We found that the KFRE successfully identified 97% of people who required renal replacement therapy and correctly identified 62% of those who did not receive renal replacement therapy within five years.

Conclusions and Recommendations

This report confirms that the number of Manitobans with ESKD requiring renal replacement therapy will rise considerably in the next decade. Residents of the Northern Health Region and, in particular, people living in remote communities are at highest risk for developing CKD and progressing to kidney failure.

The findings of this report and previous research indicate that ESKD in Manitoba should be addressed within a comprehensive public health strategy that encompasses a range of interrelated chronic diseases. This strategy would target earlier stages of CKD, as well as underlying causes, risk factors, and comorbid conditions. Strategies would include a focus on the primary and secondary prevention of the most common underlying causes for CKD, including diabetes and hypertension in adults and children. Screening with a focus on high-risk populations (those with diabetes, hypertension, or cardiovascular disease and those from First Nations or older age groups) would include direct referral to appropriate healthcare providers according to their risk of progression to kidney failure. An active laboratory-based surveillance system would ensure that at-risk individuals are not lost to clinical follow-up and care. Timely referrals for high-risk individuals would increase time to plan for renal replacement therapy and may increase the use of home-based therapies. Finally, screening and intervention strategies would be evaluated continually.

Through this report, we have learned a great deal about how to capture cases of CKD and ESKD for research purposes. More comprehensive laboratory data, which will soon be available through the Repository, will enhance our ability to study CKD in the future. The research team hopes that this report will contribute to the prevention of CKD and improve the quality of life of Manitobans living with this disease.

CHAPTER 1: INTRODUCTION AND BACKGROUND

Chronic kidney disease (CKD) and kidney failure, the final stage of this progressive disease, are health issues of increasing importance locally and worldwide (Kidney Disease Improving Global Outcomes (KDIGO), 2013; United States Renal Data System (USRDS), 2013). Perception of CKD has shifted over time from a life-threatening condition affecting a small number of people to a fairly common disorder requiring a public health strategy (Levey & Coresh, 2012). Most epidemiological studies report that CKD is prevalent in the general population, and has increased steadily in prevalence since the 1980s (Canadian Institute for Health Information (CIHI), 2014; Rodina-Theocharaki, Bliznakova, & Pallikarakis, 2012; Schaubel, Morrison, Desmeules, Parsons, & Fenton, 1999; Schaubel, Morrison, & Fenton, 2000; United States Renal Data System (USRDS), 2013; United States Renal Data System (USRDS), 2014; White & Chadban, 2014).

In Manitoba, the prevalence of kidney failure, also called end stage kidney disease (ESKD), has been the highest or second-highest in Canada since 2003 (Canadian Institute for Health Information (CIHI), 2014; Canadian Institute for Health Information (CIHI), 2015). The Manitoba Renal Program (MRP) has projected further increases in the number of people living with kidney failure and therefore, a growing need for resources to support their treatment, including dialysis stations, trained healthcare professionals, and resources for home-based dialysis. In order to meet these future needs for renal health services in Manitoba, a better understanding of CKD trends and resource use is necessary for appropriate policy development and resource planning.

Purpose of This Report

The purpose of this report is to determine the number of Manitobans expected to require **renal replacement therapy**[1] (RRT) and to help plan the resources necessary to meet their future needs. To address this objective, this report seeks to answer the following research questions:

- What are the future needs for renal health services (dialysis and transplants) in Manitoba?
- What is the geographic distribution of people requiring renal health services?
- What are the characteristics of the future population of Manitoba residents who will require dialysis?
- What preventive, screening, and education measures and affiliations with existing programs might reduce the number of Manitobans who will require dialysis? (i.e., what are the modifiable risk factors for ESKD?)

In this report, we use the terms kidney failure, ESKD, requiring treatment for ESKD and requiring RRT interchangeably. We recognize that some people with ESKD receive conservative management rather than RRT, usually because of other medical complications or advanced age. These people are not included in the data used for this report, because our focus is on understanding the future need for RRT services in Manitoba.

What You Will Find in This Report

This report is presented in nine chapters. Chapter 1 provides background information about CKD and ESKD. Chapter 2 describes the data sources and methods used to approach the topic. Chapter 3 presents the current prevalence of CKD and ESKD in adults and children in Manitoba. Chapters 4 and 5 examine sociodemographic factors, health status and healthcare use of adults and children with CKD and ESKD. Chapter 6 presents projections of the number of Manitobans with ESKD by the year 2024. Chapter 7 provides background information about prevention, screening, and treatment strategies that have been implemented in Manitoba. Chapter 8 presents the potential benefit of a risk stratification tool for CKD and ESKD. A summary of the findings and our recommendations based on Chapters 3 to 8 are presented in Chapter 9.

1 Terms in bold typeface are defined in the Glossary at the end of this report

Disease Background

Causes

CKD encompasses disorders that damage the glomeruli (kidney filters) and lead to gradual, long-term loss of kidney function (Kidney Disease Improving Global Outcomes (KDIGO), 2013; Levey et al., 2005; Levey & Coresh, 2012; Levey, Stevens, & Coresh, 2009; Levin et al., 2008). The most common causes of kidney failure in adults in the US are diabetes and hypertension, accounting for 43% of cases (United States Renal Data System (USRDS), 2014). Other disorders that might develop into CKD include autoimmune diseases, hereditary kidney disease, recurrent kidney infections, and acute kidney damage due to toxic drugs or other acute illness (Kidney Disease Improving Global Outcomes (KDIGO), 2013). Risk factors include advanced age, obesity, material deprivation (e.g., low income), and social deprivation (Arora et al., 2013; Canadian Institute for Health Information (CIHI), 2014; Hossain, Palmer, Goyder, & El Nahas, 2011; Hossain, Palmer, Goyder, & El Nahas, 2012; Kidney Disease Improving Global Outcomes (KDIGO), 2013; Steenkamp, Castledine, & Feest, 2012; Stevens, Viswanathan, & Weiner, 2010).

Diagnosis

The current clinical definition for CKD is "abnormalities of kidney structure or function, present for > 3 months, with implications for health", and classification is based on cause, **estimated glomerular filtration rate** (**eGFR**) and **albuminuria** categories (Kidney Disease Improving Global Outcomes (KDIGO), 2013). Early stages of CKD can only be diagnosed with laboratory tests as this disease is generally without symptoms. Individuals with more advanced CKD are more likely to have symptoms of kidney damage or failure; however, the diagnosis must still be confirmed with laboratory testing. Clinical tests used to diagnose CKD include abnormalities in eGFR based on serum creatinine, urine sediments including excess protein in the urine (e.g., **proteinuria** and albuminuria) or hematuria, and imaging results (Astor et al., 2011; De Jong & Curhan, 2006; Gansevoort et al., 2011; Hemmelgarn et al., 2010; Remuzzi, Benigni, & Remuzzi, 2006; Van Der Velde et al., 2011). The estimation of GFR values based on patient factors is considered critical to the clinical diagnosis of CKD and is widely used in population-based studies, as it accounts for influences on serum creatinine such as muscle mass, body size, sex, and age (Coresh et al., 2007; Coresh, Astor, Greene, Eknoyan, & Levey, 2003; Kidney Disease Improving Global Outcomes (KDIGO), 2013; Levey et al., 2006). These laboratory values are also used in epidemiological studies to supplement administrative records of ICD (International Classification of Diseases) physician coding for CKD and kidney failure. CKD definitions based entirely on administrative data have poor sensitivity and require validation with population-based laboratory data or large-scale screening initiatives (Ronksley et al., 2012). These concepts will be discussed further in Chapter 2.

Progression, Comorbidities and Complications

Proteinuria, albuminuria and eGFR are also used to assess risk for progression of the disease. These clinical tests help to identify individuals with low risk, moderately increased risk, high risk, and very high risk for progression to ESKD, and for development of related, or comorbid, health conditions (Astor et al., 2011; De Jong & Curhan, 2006; Gansevoort et al., 2011; Hemmelgarn et al., 2010; Kidney Disease Improving Global Outcomes (KDIGO), 2013; Remuzzi et al., 2006; Van Der Velde et al., 2011). Kidneys provide important regulatory functions in the body, and people with kidney damage due to CKD often have high rates of diabetes, hypertension, and hypertriglyceridemia (high levels of fatty molecules in the blood) (Arora et al., 2013). Conversely, these comorbid diseases are risk factors for developing CKD. CKD also increases the risk of infections, cardiovascular diseases, bone loss and fractures, and cognitive impairment (Fink et al., 2012; Levin et al., 2008). The most severe consequence of CKD is death due to kidney failure.

Disease Management and Treatment

Early stages of CKD require disease management. This approach targets complications of the disease (e.g., anemia, mineral imbalance) as well as comorbid conditions that may increase the risk of developing kidney failure (e.g., high blood pressure, diabetes, cardiovascular diseases) (Fink et al., 2012; Levin et al., 2008). Several randomized controlled trials reported that a number of treatments are effective at reducing the risks of poor clinical outcomes. These treatments include angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) (Fink et al., 2012).

If the disease does progress to kidney failure, treatment to sustain life focuses mainly on renal replacement therapy (RRT), which replaces the functions that the kidneys previously performed. Several types of RRT are available:

- **hemodialysis**: This procedure uses a machine to filter bodily fluids in place of the kidneys performing this task. It requires a strict treatment schedule (it must be done every few days and takes four to six hours each time), strict diet, and the use of medications. **Hemodialysis** can be performed in a medical centre or at home with support from trained healthcare professionals (Mayo Clinic). Centre-based hemodialysis has been the most common type of RRT both in Manitoba and Canada generally in the last decade. It has the highest costs and greatest burden on patients' quality of life.
- **peritoneal dialysis:** This procedure uses blood vessels in the lining of the patient's abdomen to filter the fluids, bypassing the kidneys. Because it can be delivered at home and is less restrictive than hemodialysis in terms of diet and medication, **peritoneal dialysis** has less impact on patients' quality of life (Mayo Clinic). It also has much lower healthcare costs than hemodialysis. Peritoneal dialysis is the second-most common form of dialysis used in Manitoba.
- **home-based hemodialysis:** Home-based hemodialysis is less restrictive for patients and costs the health system less. Historically, home hemodialysis has been used rarely because of the size of the machine and the skill required for patients to self-administer the treatment. However, the use of this dialysis method has increased considerably in the last decade due to improved technology and capacity building for training; in 2012-2013 alone, use of home hemodialysis increased by 25% in Manitoba (Canadian Institute for Health Information (CIHI), 2014; Manitoba Renal Program (MRP), 2013).
- **kidney transplant:** This is major surgery and is recommended only for ESKD patients who are otherwise healthy enough for this type of procedure. Transplant as a treatment option is also restricted by the number of kidneys available from donors.

Healthcare Use and Costs

The progressive loss of kidney function, associated medical conditions and predisposition to complications translate into frequent use of healthcare services by patients with CKD. CKD disease and especially ESKD often lead to significantly higher healthcare costs compared to other chronic diseases (Fink et al., 2012; Kidney Disease Improving Global Outcomes (KDIGO), 2013; White & Chadban, 2014). These costs can be attributed to the higher rates of hospitalization, specialist services use, and medication use by CKD patients. The cost of healthcare service use increases with the progression of CKD. In Canada, costs for in-hospital hemodialysis, the most common type of RRT, reach about $95,000 to $107,000 per patient per year (Klarenbach, Tonelli, Chui, & Manns, 2014; Levin et al., 2008; Manns et al., 2010). These cost estimates vary by geographic region. We discuss the costs of the various types of RRT in Manitoba in Chapter 3.

Epidemiology

Historical Trends

Most of the epidemiological data available on patients with CKD originates from treatment records (dialysis or transplant) of ESKD populations. Information about the incidence (new cases) and prevalence (existing cases) of earlier stages of CKD in the general population is limited. Estimates of the prevalence of CKD in Canada range from 10% to 15%, representing approximately 3 million affected adults (Arora et al., 2013). National screening initiatives in the US have shown that ESKD represents a small fraction of the total CKD population, with early CKD affecting 50 times more individuals than ESKD (Castro & Coresh, 2009; United States Renal Data System (USRDS), 2013). Prevalence rates of CKD across Europe, Asia, North America and Australia range between 2.5% and 11.2% (James, Hemmelgarn, & Tonelli, 2010).

According to an international comparison of data among 43 countries, Canada ranked 21st for incidence and 11th for prevalence of ESKD in 2011 (United States Renal Data System (USRDS), 2013), and rising rates appear to be due to aging populations and increases in diabetes and hypertension (Coresh et al., 2007). The prevalence of ESKD in Canada and Manitoba continues to increase (Schaubel et al., 1999; Schaubel et al., 2000; United States Renal Data System (USRDS), 2013). While the number of new cases of ESKD has stabilized in Canada overall (United States Renal Data System (USRDS), 2014), the Manitoba incidence continues to rise. As a result, kidney failure now affects more Manitobans per capita than any other province in Canada, with a prevalence rate of 1,163 to 1,560 per 1,000,000 population (Canadian Institute for Health Information (CIHI), 2014). ESKD prevalence and the need for dialysis in Manitoba and Canada are two to three times higher among Indigenous populations compared to other groups (Canadian Institute for Health Information (CIHI), 2013).

Projections

The historical trends of increasing CKD prevalence, as well as ESKD incidence and prevalence, have raised concerns about how best to provide renal health services in the future. Due to the limited availability of CKD data and the complexity of the disease, only ESKD incidence and prevalence have been projected in a small number of modelling studies. Canadian projections of increases in ESKD prevalence for 2005 provided by Schaubel et al. (2000) were more conservative than values reported by (Canadian Institute for Health Information (CIHI), 2014). Schaubel et al. (1999) estimated average annual increases in ESKD of about 6% to 7%. The greatest increases in prevalence were predicted for peritoneal dialysis (6.0% annually), followed by hemodialysis (5.9%) and functioning kidney transplant (5.7%) (Schaubel et al., 1999).

Treatment, Screening and Prevention Strategies

The increasing prevalence of ESKD is partially related to the under-recognition of CKD in its earlier stages and to the increasing prevalence of risk factors associated with CKD (Obrador, Pereira, & Kausz, 2002). Appropriate monitoring and treatment can prevent or delay progression to ESKD in many cases. Recommendations to address the increasing prevalence of ESKD include screening individuals at increased risk for CKD, targeting upstream prevention strategies (education and lifestyle changes) to address risk factors for CKD, and slowing the progression of the disease after onset. Strategies to achieve these goals are the focus of Chapter 7.

CHAPTER 2: METHODS

This chapter describes how we prepared the report. We will explain the geographical boundaries and data sources we used, how we created our cohorts of people with chronic kidney disease (CKD) and end stage kidney disease (ESKD), and the statistical methods we used to analyze trends and project disease and treatment numbers.

Geographical Boundaries

The geographical boundaries in this report are based on the five health regions in Manitoba: Winnipeg Health Region, Prairie Mountain Health Region, Northern Health Region, Southern Health/Santé Sud Region, and Interlake-Eastern Health Region (Figure 2.1). This report also includes a geographical region called "**Remote Communities**" (indicated in grey in Figure 2.1). These are communities in northern areas of Manitoba with limited access to a major health facility (only by plane, train or winter roads) and communities that have all-season roads but are at least four hours away from a major health facility due to distance or road conditions. These communities are sparsely populated and include First Nations populations. Living conditions in some of these areas can be challenging due to unfavourable economic conditions, poor water supply, and limited access to affordable food and to health, social and recreational services.

Data Sources

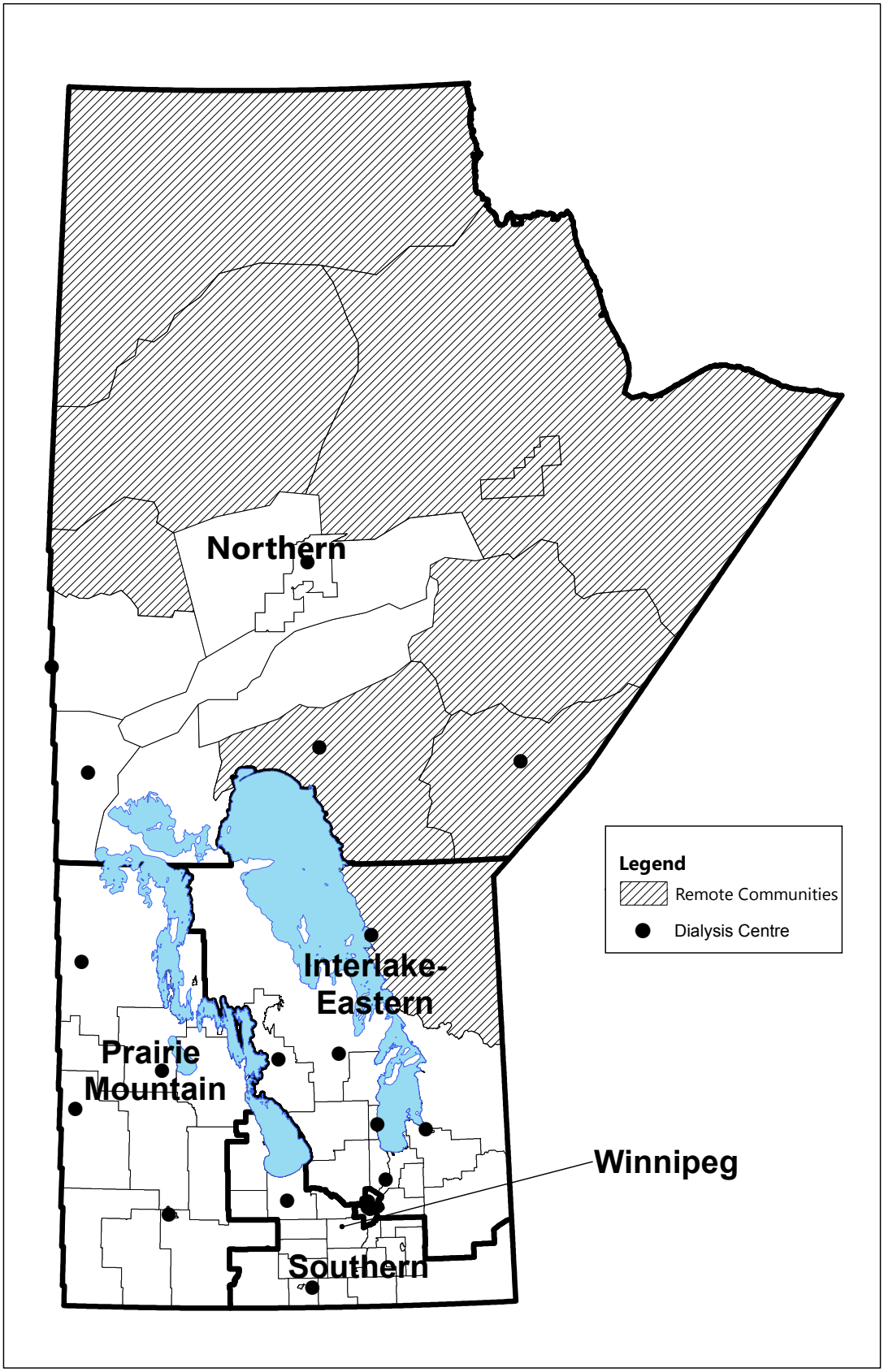
The results presented in this report were obtained using administrative data housed in the Population Health Research Data Repository (the Repository) at the Manitoba Centre for Health Policy (MCHP). These data include individual-level records of the population and their use of the healthcare, education, and social services systems in Manitoba. All records in the Repository are de-identified by removing names and addresses, as well as scrambling all Personal Health Identification Numbers (PHINs) and other personal identifiers. This ensures the privacy and confidentiality of all data. Only aggregate-level values are shown and results involving fewer than five individuals or events are suppressed (shown as "s").

The following data in the Repository were used for the analyses in this report:

- Public Canadian Census Files
- **Diagnostic Services Manitoba (DSM) Laboratory Data**
- Drug Program Information Network (DPIN) Data
- Hospital Abstracts
- Manitoba Health Insurance Registry
- **Manitoba Pediatric Chronic Kidney Disease Registry**
- **Manitoba Renal Program (MRP) Data**
- Medical Claims
- Physician Resource File
- Vital Statistics Mortality

Detailed information about these data are available on the MCHP website: http://umanitoba.ca/faculties/medicine/units/community_health_sciences/departmental_units/mchp/resources/repository/datalist.html.

Figure 2.1: Manitoba Health Regions, Remote Communities and Location of Dialysis Centres



Diagnostic Services Manitoba Data

We used the Diagnostic Services Manitoba (DSM) Delphic Chemistry data to add to our cohort of people with CKD and to determine the severity of the disease (see section about the CKD cohort, below). We were able to link 678, 821 individuals to the Repository. While most data were available for April, 2006, to December, 2011, the date range was shorter for some facilities:

- April, 2006–December, 2011 for Health Sciences Centre, St-Boniface Hospital, Seven Oaks General Hospital, Grace General Hospital, Victoria General Hospital, and Deer Lodge
- November, 2009–December, 2011 for Riverview and Beausejour Health Centres.

Blood and urine tests (biochemical) were used in this report to determine a CKD diagnosis. In using these data, we experienced some challenges related to data coverage. Since DSM data are collected in facilities that provide public laboratory services and diagnostic imaging (Diagnostic Services Manitoba (DSM), 2014), data from some hospitals, private laboratories and Westman laboratories[2] were not captured. Additionally, the geographical distribution of available DSM data was skewed towards Winnipeg residents (78% of laboratory data) when compared with the other health regions. Table 2.1 shows the availability by health region of creatinine tests, a laboratory test critical to determining if CKD is present or not. Given that these tests are not available in the same proportion as the general population, we acknowledge that estimates of CKD in Manitoba based only on DSM data would underestimate the disease burden outside of Winnipeg. It was not possible to provide a meaningful estimate of the missing laboratory data because we had no mechanism to capture all individuals who had CKD-related laboratory tests ordered and compare them to those who did not.

Table 2.1: Comparison Between the Distribution of Regional Populations and Creatinine Tests, 2006/07-2011/12

Region	Percent of Manitoba Population	Percent of Manitoba Population with Creatinine Tests
Southern Health/Santé Sud	13.4%	6.2%
Winnipeg	58.5%	78.5%
Prairie Mountain Health	13.3%	6.3%
Interlake-Eastman	9.8%	7.2%
Northern	5.0%	1.7%

Manitoba Renal Program Data

We used Manitoba Renal Program (MRP) data to create a cohort of patients with ESKD and to identify the type of renal replacement therapy (RRT) each patient received. The MRP data provide information from 20 dialysis centres across Manitoba (Figure 2.1) starting in 2004. The data include date of entry into the MRP and the type of treatment. The main challenge that we encountered with the MRP data was the lack of information about kidney transplants and dates of transition between treatment modalities. We obtained this information through linkage of MRP data to administrative data (medical claims and hospital abstracts).

2 Despite our best efforts, the data sharing agreements for the Westman Laboratory Data were not in place at the time of analysis for this report. This will be a valuable resource for future studies.

Chronic Kidney Disease and End Stage Kidney Disease Cohorts

To estimate the potential number of people in Manitoba who might develop kidney failure and require RRT over the next decade, we created two cohorts (CKD and ESKD) and sub-divided them in the following way:

- People with CKD and at low risk of progression to ESKD
- People with CKD and at high risk of progression to ESKD
- People with CKD and at unknown risk of progression to ESKD
- People with ESKD who are on dialysis
- People with ESKD who have received a kidney transplant
- People without either CKD or ESKD

Following is a description of how these groups were created.

People with Chronic Kidney Disease

Chronic kidney disease definition

We defined the CKD cohort in two ways, using administrative data (medical claims and hospital abstracts) and laboratory data.

Definition using administrative data

Using administrative data, we defined Manitoba residents (children and adults) as having CKD if, within a three-year period, the resident had at least two CKD-related medical claims by physician visit or one CKD-related hospitalization or one filled prescription of a medication specifically used in the treatment or management of CKD. These medications include erythropoietin-like drugs, potassium binders, certain vitamins including replavite and vitamin D analogues, and non-calcium-based phosphate binders. People who required RRT were excluded from this group. A list of specific diagnosis and drug codes used in this definition is provided in Appendix 1.

This definition is based on one validated by Ronksley et al. (2012). These authors compared a series of definitions for CKD using medical claims and hospitalizations from Alberta Health. The best definition included two medical claims or one hospitalization for CKD within a time frame of three years. Despite using a three year time frame, the study found that the definition had 23% sensitivity (out of all true cases, only 23% were identified) and 96% specificity (i.e., 96% of cases that did not have CKD were identified correctly). The authors noted that using administrative data to estimate prevalence of CKD tends to underreport the true rates.

Definition using laboratory data

We identified additional cases of CKD using the DSM Laboratory data (see Appendix 1 for description of tests used). For people with laboratory results, CKD was defined by calculating the estimated glomerular filtration rate (eGFR) and the level of proteinuria or albuminuria. As mentioned earlier, we expected to capture proportionally fewer residents with CKD outside of Winnipeg because fewer laboratory results are available for rural Manitoba.

We defined an individual as having CKD if he or she had at least two eGFR tests indicating poor kidney function (less than 60 ml/min/1.73m) at least 90 days apart. The three month time frame was included to ensure we were capturing people with chronic and not acute kidney dysfunction (Ronksley et al., 2012). eGFR is the flow rate of filtered fluid through the kidneys; low rates indicate poor function. It was measured with existing creatinine levels in the blood (serum creatinine, SCr).

We used the Modification of Diet in Renal Disease (MDRD) equation to estimate the eGFR:

$$\text{Men: } \left[175 \times \left(\frac{S_{cr}}{88.4}\right)^{-1.154}\right] \times (age)^{-0.203} \qquad \text{Women: multiply results by 0.74.}$$

The MDRD was chosen because it was being used by Manitoba laboratories. This equation may underestimate kidney function in the general population (Matchushita et al., 2012).

For children, our CKD definition based on laboratory data was similar — at least two eGFR tests indicating poor kidney function (less than 60 ml/min/1.73m) at least 90 days apart — but we used the Pediatric Schwartz formula instead of the MDRD:

$$36.51 \times \left(\frac{height\ (cm)}{S_{cr}(\frac{\mu mol}{L})} \right)$$ (Schwartz et al., 2009).

To calculate eGFR, we used an estimated height for children when measured heights were not available in the data. For children whose age was in months, we estimated GFR using a 3rd percentile height. The 3rd percentile was used to maximize the sensitivity of the test. A subset of children had heights recorded in the DSM data (n=98). 70% of our results were within 10% of the measured result and all of our results were within 30% of the measured result.

Other equally important laboratory tests used for assessing kidney damage are proteinuria or albuminuria. They indicate the amount of protein leakage in the urine. This can be measured by a urine dipstick, as a ratio between urine albumin and urine creatinine (albumin-creatinine ratio, ACR) or a ratio of urine protein and urine creatinine (protein-creatinine ratio, PCR). As with the eGFR, we defined an individual as having CKD if they had at least two abnormal ACR or PCR results at least 90 days apart (see Appendix 1 for details about these tests).

As a validation, we also ran our definitions using the eGFR, proteinuria and albuminuria tests and categorized the results by levels of severity. The number of people with eGFR less than 45 ml/min/1.73m, less than 30 ml/min/1.73m and less than 15 ml/min/1.73m was reasonable based on clinical experience and previous research. We proceeded in a similar manner with the tests for proteinuria and albuminuria. These validation tests are not shown in this report.

Validation of the CKD definition using administrative data for children

Previous validation studies have found that capturing CKD cases using administrative data in the adult population is challenging, and we suspect that this is the case for CKD in children as well. We conducted the following analyses to determine the validity of administrative data definitions to identify children less than 18 years of age with CKD. To our knowledge, no studies have examined the validity of using administrative data in defining cases of CKD in children.

The laboratory data were used to construct our gold standard of CKD cases in children. We included all Manitoba residents who were children less than 18 years old as of April 1, 2012, with a valid PHIN and with the necessary laboratory data. These laboratory data included at least two tests of serum creatinine or proteinuria assessment prior to April 1, 2012, at least 90 days apart during the three-year period of study (starting March 31, 2009) as per our CKD definition using laboratory data. We excluded from the analyses patients on dialysis or with kidney transplant. As shown in Table 2.2, our validation study included 918 children.

Table 2.2: Inclusion and Exclusion Criteria for Children in the Chronic Kidney Disease Validation Cohort
April 1, 2009-March 31, 2012

Inclusion and Exclusion Criteria	Number of Children
Children in Manitoba (aged 0-17)	291,781
Exclusions*:	
No laboratory data	273,682
No abnormal laboratory tests	12,957
Only 1 abnormal laboratory test	3,928
Abnormal tests occurred within 90 days	279
Children receiving dialysis or kidney transplant	17
Final Cohort**	918

* exclusion criteria are based on available laboratory data

** children meeting the Chronic Kidney Disease case definition based on laboratory data

Following the example of (Ronksley et al., 2012), we established 18 different algorithms to define our CKD group. We then determined sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the area under the receiver operating curve for the 18 definitions by comparing them to the cases found through the laboratory data. The calculations for testing the validity of the algorithms are described in Chapter 3, and ICD codes are found in Appendix 1 of this report.

$$Sensitivity = \frac{N_{true\ positives}}{N_{patients\ with\ ESKD}}$$

$$Specificity = \frac{N_{true\ negatives}}{N_{people\ without\ ESKD}}$$

$$Positive\ predictive\ value = \frac{N_{true\ positives}}{N_{true\ positives} + N_{false\ positives}}$$

$$Negative\ predictive\ value = \frac{N_{true\ negatives}}{N_{true\ negatives} + N_{false\ negatives}}$$

Risk of progression to ESKD

Using the laboratory data, we were able to categorize the CKD cases into risk categories by severity of eGFR and proteinuria. The National Kidney Foundation Kidney Disease Outcomes Quality Initiative defines CKD as the presence of an eGFR less than 60 ml/min/1.73 m2 and ESKD as the presence of an eGFR less than 15 ml/min/1.73 m2, for at least three months (Levey et al., 2005).

To determine the likelihood of progression to ESKD, it is crucial to stratify individuals by risk based on the laboratory results. We adapted a "heat map" (a colour-coded classification table) developed in January 2013 by the Kidney Disease Improving Global Outcomes (KDIGO) Work Group (Kidney Disease Improving Global Outcomes (KDIGO), 2013). This new approach for prognosis of CKD was built on the recognition that albuminuria is an important marker of kidney function and risk of progression to ESKD, and it uses both albuminuria categories and eGFR to identify four levels of risk (see Table 2.3):

- green: lowest risk (eGFR and albuminuria are normal or mildly abnormal)
- yellow: moderately increased risk
- orange: high risk
- red: the highest risk of all.

We modified this table by adding three additional categories to represent people with CKD who have an incomplete set of laboratory tests (one of the two laboratory tests, providing some indications of risk level) or who do not have any laboratory tests (unknown risk level):

- light purple: likely at lower risk
- dark purple: likely at higher risk
- white: unknown risk.

We combined these classifications into a low risk (green, yellow, and light purple) and high risk (orange, red, and dark purple). The low-risk group includes people who might be in earlier stages of CKD, and the high-risk group includes people who might be in later stages of CKD. We were not able to determine how advanced the disease is in people in the unknown-risk group (white) because of lack of laboratory data and thus no information about the impairment of kidney function.

Sociodemographic and treatment characteristics of these groups are found in Chapter 4.

Table 2.3: Heat Map (Risk of Progression to ESKD) of Chronic Kidney Disease

eGFR categories (ml/min/1.73m^2) Description and range				Persistent albuminuria categories Description and range			
				A1	A2	A3	
				Normal to mildly increased	Moderately increased	Severely increased	Albuminuria unknown
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol	
	G1/G2*	Normal or high	≥60	Low Risk	Low Risk	Low Risk	Low Risk
	G3a	Mildly to moderately decreased	45-59	Low Risk	High Risk	High Risk	Low Risk
	G3b	Moderately to severely decreased	30-44	High Risk	High Risk	High Risk	High Risk
	G4	Severely decreased	15-29	High Risk	High Risk	High Risk	High Risk
	G5	Kidney failure	<15	High Risk	High Risk	High Risk	High Risk
	eGFR unknown			Low Risk	Low Risk	High Risk	Unknown Risk**

* G1 and G2 categories are measured separately for children with CKD

** Identified using only administrative data

People with End Stage Kidney Disease

Using the Manitoba Renal Program (MRP) data and administrative data, we created a cohort of patients with ESKD based on their use of RRT (dialysis and kidney transplant) from 2004 to 2012. The MRP data hold information on all patients on dialysis in Manitoba, but not kidney transplants. When the data were collected in 2004, only new cases of ESKD on dialysis were entered. To calculate ESKD prevalence for those early years, we used administrative data to add existing cases to the MRP data. Patients who had two tariff codes for dialysis at least three months apart or a code for kidney transplant were defined as having ESKD. All patients in the MRP data were identified through the administrative data in the Repository using these tariff codes for dialysis. All children in the Pediatric CKD Registry with linkable data were found in the Repository as well. It is important to note that because our ESKD cohort includes everyone who is receiving treatment for ESKD in the province, we have the official count and do not need to estimate the rates of people with ESKD receiving RRT.

Analyses

This section describes the analyses we conducted for this report. It includes our method for calculating the current and future burden of CKD and ESKD in Manitoba (prevalence, incidence, projections, progression/risk of complications) and how we described the demographics, health status and healthcare use of people with CKD and ESKD. We also describe the modelling used to analyse ESKD treatment type.

All data management, programming and analyses were performed on MCHP's secure server using SAS® version 9.3 software.

Cohort Characteristics

We examined the sociodemographic, physical and mental health, and health service use for children and adults in each of our five groups (defined above, see "CKD and ESKD Cohorts"): people with CKD at low, high or unknown risk of progression to ESKD; people with ESKD who have had a kidney transplant or are on dialysis; and people without CKD or ESKD. When looking at the characteristics of children with ESKD, we combined the dialysis and transplant groups due to small counts. The time frames varied across indicators and are specified in Appendix 1.

Adjusted rates and statistical analyses

Event counts for each indicator were modelled using a generalized linear model (GLM), as it is suitable for non–normally distributed data such as counts. Various distributions were used for different indicators depending on which fit the data best, including Poisson distribution (very rare events), negative binomial distribution (relatively rare but highly variable), or binomial distribution (two outcomes—yes/no). We adjusted the rates of indicators for age and sex to enable valid comparisons among groups in the cohorts, because people with CKD tend to be older than the general population and consequently more health problems would be expected. Statistical differences between groups were measured using relative risk, which compared the characteristics of people without CKD to all other groups.

Chronic Kidney Disease Prevalence

We used three methods to calculate the child and adult prevalence of CKD: (a) administrative and laboratory data, (b) laboratory data only, and (c) a **capture-recapture** method. Recall that measuring CKD is challenging because no symptoms are apparent in the early stages. In addition, a CKD diagnosis may not be recorded when a patient has diagnoses for several other conditions. This may be particularly important for outpatients because outpatient claims are limited to a single diagnosis code.

a. We counted all CKD cases captured by the administrative data and by the laboratory data, added them together, and then divided by the total Manitoba population. This estimate will likely underestimate the true prevalence, because it will not include people in the early stages of CKD who have not been diagnosed by a physician.
b. We counted all CKD cases captured through the laboratory data and divided by all residents with laboratory data required to make a CKD diagnosis.
c. We used both the administrative and laboratory data to estimate CKD prevalence through a capture-recapture method. This approach is often used in estimating the size of animal populations in the wilderness (Brittain & Böhning, 2009). An example is estimating the number of turtles in a lake. We catch a sample of turtles, count them, mark them and release them back in the lake. We then catch another sample of turtles, count them and, among those caught, count how many are marked. The estimated number of turtles is calculated using the Chapman formula (eq. 5) (Chapman, 1951). We applied this capture-recapture method to our CKD data using the Chapman formula:

$$CKD\ prevalence = \left[\frac{(N_{CKD\ cases\ in\ administrative\ data} + 1) \times (N_{CKD\ cases\ in\ laboratory\ data} + 1)}{(N_{CKD\ cases\ in\ both\ data} + 1)}\right] - 1$$

End Stage Kidney Disease Incidence and Prevalence

To calculate the incidence of ESKD, we counted the number of new cases of ESKD in a given time period and divided it by the number of people living in Manitoba in the same period. The prevalence was calculated in a similar way: the number of existing cases of ESKD in a given time period divided by the number of people living in Manitoba at that time. This was calculated for the child and adult populations. For regional rates, incidence and prevalence were adjusted by age and sex to account for differences in age and sex distribution in the regions.

End Stage Kidney Disease Projections

Preparing projections by treatment type is important for health services planning because the various types of renal replacement therapy (RRT) have different implications for health, quality of life, and cost. We used a combination of observed trends in population size and ESKD burden in Manitoba for 2004 to 2012, population projections for 2012 to 2024, and statistical models to predict the number of patients who will have ESKD requiring RRT from 2012 to 2024.

We present two types of projections: basic and "what if" scenarios. Basic projections assumed no change in the health status of the Manitoba population or treatment strategies for ESKD. "What if" scenarios investigated the effect of changes in diabetes prevalence, mortality rates, and the type of RRT patients had started. All projection analyses used a SAS® algorithm developed by Mannan, Knuiman, & Hobbs (2010).

Markov model

We used a combination of Poisson regression and Markov simulation modelling to create projections of the number of patients with ESKD using each type of RRT from 2012 to 2024. Markov modelling is a commonly used method for predictions of ESKD (Gilbertson et al., 2005; Schaubel et al., 1999). It permits group-specific projections and accommodates patients switching between types of treatment, which is important because the current type of treatment is related to future treatment decisions. Accounting for transitions from one state to another adds another layer of information to create more precise predictions. Covariates incorporated in the **Markov model** were age, region and diagnosis of diabetes. See Appendix 2 for more details.

Basic projections and "what if" scenarios

We realize that changes in other conditions during the years 2012 to 2024 may influence the numbers of people who will develop ESKD and their choice of treatment. For example, new initiatives and changes in policies might help to improve the health of the population (e.g., by preventing new cases of diabetes and reducing mortality). Changes in policies and the provision of additional supports might promote the use of treatments that offer more health benefits and are less costly than centre-based hemodialysis (e.g., increasing the number of kidney transplants or making home-based dialysis more accessible). We modelled ESKD projections for five "what if" scenarios: a stable diabetes prevalence, decreased mortality rates, and increased rates of kidney transplant, peritoneal dialysis or home-based hemodialysis. The choice of each of these modifying factors is based either on recent trends in the health and healthcare use of Manitobans or viable options for future changes in policy and the provision of healthcare.

Factors Associated with Centre-Based Hemodialysis

We used logistic regression to examine factors that might be associated with the use of centre-based hemodialysis relative to other types of RRT (peritoneal dialysis, home-based hemodialysis and kidney transplant). These factors included age group, sex, diabetes status, income quintile, region of residence, use of hypertensive medication (ACE inhibitors and ARBs), and length of time between the first nephrologist visit and the start of RRT. According to Kelsey (1996), regression is the method of choice for analyzing multiple variables. This regression technique is used when the outcome is a binary or dichotomous variable, in this case, hemodialysis or other type of RRT. A strength of logistic regression is its ability to explore the association of a number of factors on treatment modalities, while controlling the effects of other confounding variables. Statistically significant variables (p-value<0.05) with an odds ratio greater than 1 are associated with hemodialysis. An odds ratio below 1 can be interpreted as an association with other types of RRT.

Kidney Failure Risk Equation

We tested the performance of a risk stratification tool, the **Kidney Failure Risk Equation** developed by Tangri et al. (2011) to validate it for use in Manitoba. The tool, methods and results of this validation study are described in Chapter 8.

CHAPTER 3: COHORT DESCRIPTION: CHRONIC KIDNEY DISEASE AND END STAGE KIDNEY DISEASE

In this chapter, we describe the cohorts of adults and children with chronic kidney disease (CKD) and end stage kidney disease (ESKD). As outlined in Chapter 2, it is straightforward to capture those being treated for ESKD as they are found in the Manitoba Renal Program (MRP) and administrative data. Capturing people in earlier stages of CKD based on the administrative and laboratory data is more challenging; however, these data are valuable from a policy and planning perspective. In this chapter, we estimate the current prevalence of CKD and ESKD (2012 data). Given the important implications for quality of life and system costs for the various types of treatment for ESKD, we show the number the people per treatment type over time and by health region. This chapter also presents our validation of the definition we used for CKD in children, as we are not aware of any other validated definition of CKD for this age group. The adult CKD definition used in this report has been validated by Ronksley et al. (2012).

Key Findings

Adult Cohort

- CKD prevalence among all adults identified in both administrative and laboratory data was 7.4% (n=71,758); two other methods were used to estimate CKD prevalence, with different results: 10% (n=37,534) using only people with laboratory data, and 13.8% (n=133,767) using the capture-recapture method.
- Of the adult CKD cases, 34% were at high risk of progression to ESKD and 47% were at low risk. The remaining 19% did not have any laboratory data and were therefore not categorized by risk.
- CKD prevalence in the Northern Health Region and remote communities was significantly higher than the Manitoba average.
- ESKD prevalence in Manitoba was 1.45 per 1,000 residents.
- Northern Health Region and remote communities, which have a high percentage of First Nations people, had the highest ESKD rates (2.43 and 3.86 per 1,000 residents, respectively).
- 1,833 Manitoba residents were receiving treatment for ESKD in 2012; of these, 597 (32.6%) had a functioning kidney transplant and 1,236 (67.4%) were on dialysis.
- Of those on dialysis in 2012, 79% used centre-based hemodialysis, 19% used peritoneal dialysis, and a very small proportion (3%) used home-based hemodialysis.

Child Cohort

- CKD prevalence among all children identified in both administrative and laboratory data was 1.49% (95% CI: 1.47 -1.53); two other methods were used to estimate CKD prevalence, with different results: 3.41% using only people with laboratory data, and 2.9% using the capture-recapture method.
- Half of the child CKD cases captured did not have laboratory data and were not categorized by risk. Of those with laboratory data, three-quarters were at low risk of progressing to ESKD.
- An additional 17 children with ESKD were identified, resulting in a ESKD prevalence of 5.8 per 100,000.
- The Northern Health Region had higher rates of CKD among children than all of Manitoba. The relative risk of CKD was 1.6 in the Northern Health Region and 2.4 in remote communities relative to the Manitoba average.
- All algorithms using administrative data to define CKD in children had low sensitivity and very high specificity. The definition used in this report has a sensitivity of 0.376 and a specificity of 0.996.

Adults with Chronic Kidney Disease and End Stage Kidney Disease

Figure 3.1 shows that the total number of adult Manitoba residents (18 years and older) with CKD found in all data was 69,905. Of these, 32,371 were identified using administrative data, 24,909 were found in the Diagnostic Services Manitoba (DSM) laboratory data, and 12,625 people were found in both data. The MRP and administrative data captured an additional 1,853 people with ESKD[3] (see Figure 3.1).

The CKD cohort included residents of Manitoba as of April 1, 2012, who met the definition for CKD (as described in Chapter 2 and Appendix 1) at any point from April 1, 2004, to March 31, 2012. Recall that the administrative data covers virtually all Manitoba residents in the province and that the DSM laboratory data covers Winnipeg residents reasonably well, the south-eastern and northern parts of the province to some extent, and the western region of the province poorly. If the DSM data covered all laboratory tests in the province, it would have been possible to capture more people meeting our definition of CKD. A more accurate picture of CKD in Manitoba will emerge once DSM's Westman Laboratory data, which covers the western region of the province, is added to the Repository.

We examined patients' contact with a nephrologist to understand the differences in the CKD populations that we identified through different data sources and definitions. The group that met the definition in both the administrative data and the DSM laboratory data had the highest percentage that had seen a nephrologist (46.6%), followed by the group identified in either the administrative data (21.2%) or the laboratory data (10.7%). All residents found in the MRP data had seen a nephrologist (Figure 3.1). Given that the percentage of CKD patients seeing a nephrologist varies across the groups, we suspect that patients may be at different stages of CKD. It is important to keep in mind that a proportion of CKD patients have earlier stages of the disease and could be managed adequately by a primary care physician. This group would not necessarily require a consult with a nephrologist. It is reasonable to assume that people with CKD found with both the administrative data and the laboratory data may have more advanced stages of CKD and should be seen by a nephrologist. Those identified only through the laboratory data have the highest likelihood of having CKD without the kidney dysfunction having been previously detected by the patient or primary care provider[4].

Prevalence of Chronic Kidney Disease in Adults

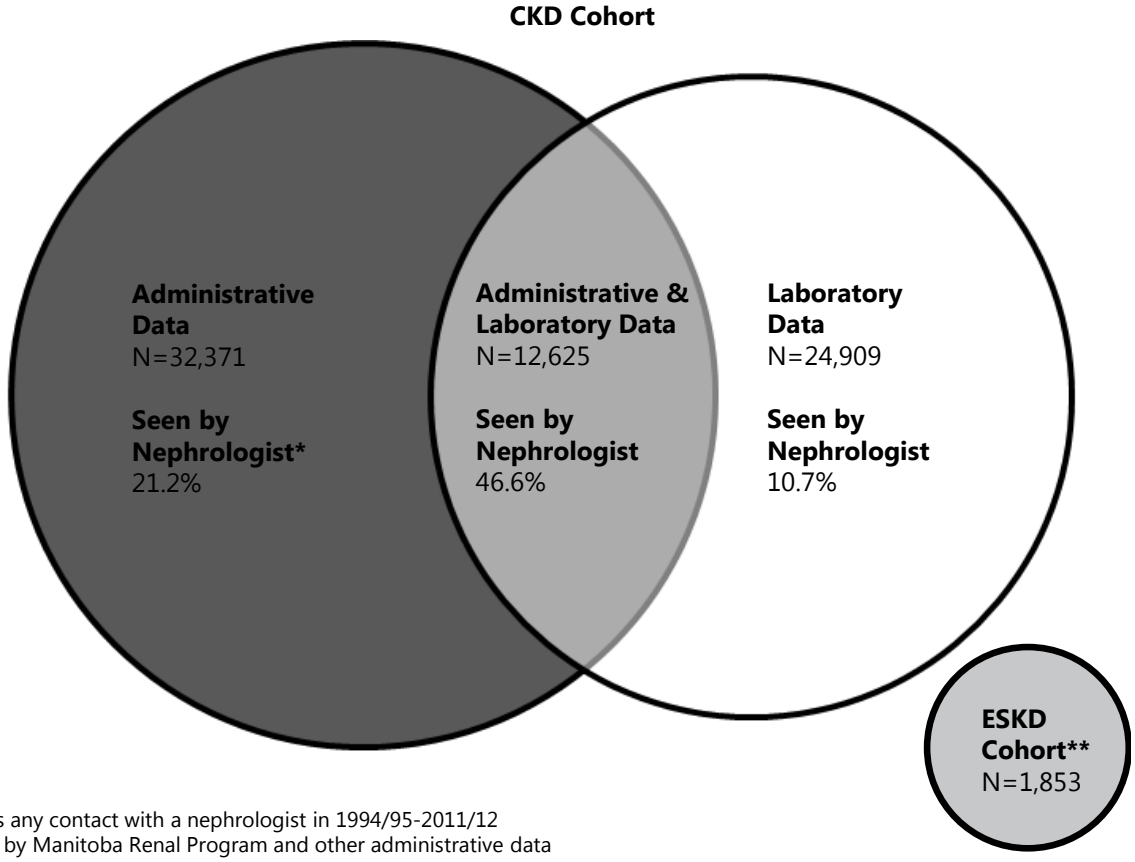
To provide the most accurate estimate of the true burden of CKD in the province, we used three different methods, described in Chapter 2, to measure the prevalence of CKD in adults 18 years and older. As also noted in Chapter 2, both of our definitions of CKD — based either on administrative data or on DSM laboratory data — may underestimate the true prevalence of CKD because of underreporting of CKD diagnoses in administrative data and limited coverage of DSM data.

Figure 3.2 shows CKD prevalence for adults by region in 2012 based on administrative and laboratory data, and on laboratory data only, as well as prevalence for Manitoba overall based on each of the three methods. The prevalence of CKD among adults in Manitoba with laboratory data was 10% (n=37,534). The prevalence among all adults with CKD who were identified in administrative and laboratory data was 7.4% (n=71,758). (This includes all CKD cases including those on dialysis in the Manitoba Renal Program (MRP) and with kidney transplants.) Prevalence based on the capture-recapture method, which uses cases defined both by administrative and laboratory data, reached 13.8% (n=133,767).

3 This count of 1,853 people with ESKD differs from the number of cases we later used in calculating projections. The 1,833 cases had the registry information that was necessary to model the projections.

4 We were puzzled that 10.8% of people captured through the laboratory data were seen by a nephrologist without a medical, hospital or prescription claim. We speculate that this group of people may have a number of health problems of which CKD is not the primary problem, and therefore the diagnosis of CKD was not coded. As we will see later in this report, people with CKD are more likely than the general population to have many other health problems.

Figure 3.1: Number of Adults with Chronic Kidney Disease (CKD) or End Stage Kidney Disease (ESKD), and Percentage Seen by Nephrologist by Data Source
Manitoba residents aged 18+ on March 31, 2012



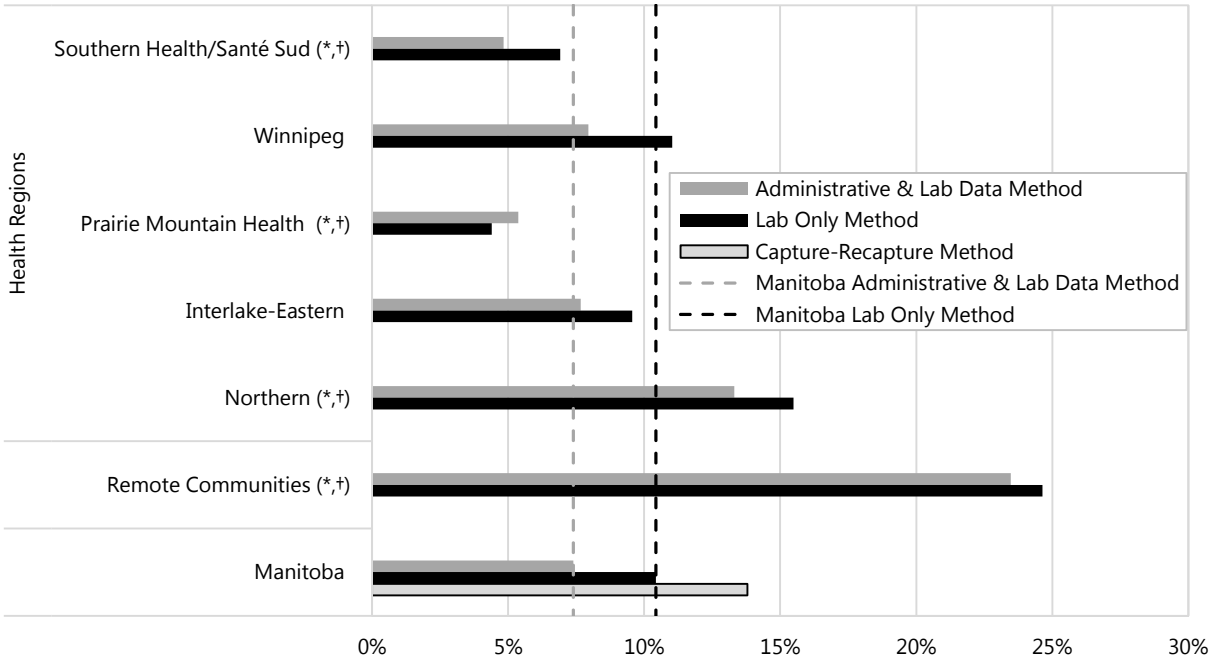
* Includes any contact with a nephrologist in 1994/95-2011/12
** Defined by Manitoba Renal Program and other administrative data

The graph in Figure 3.2 illustrates the regional differences in the prevalence of CKD, which follow the general pattern of health status by region in Manitoba: from healthier populations in southern areas of the province to more prevalent health problems in northern areas (Fransoo et al., 2013). The prevalence of CKD in the Northern Health Region and remote communities was significantly higher than the Manitoba average. This could be attributed both to the lower health status of these populations and to the smaller number of people living in these areas.

These results are consistent with other epidemiology studies, summarized in Chapter 1.

Figure 3.2: Prevalence of Adults with Chronic Kidney Disease by Region and Estimation Method

Age- and sex-adjusted, March 31, 2012



* indicates health region's rate is statistically different from Manitoba rate for Administrative & Lab Data Method
† indicates health region's rate is statistically different from Manitoba rate for Lab Only Method

Classification of Adults with Chronic Kidney Disease by Disease Severity

We classified people with CKD who have laboratory data into three groups (low, high, and unknown risk), according to their risk of progressing to kidney failure and requiring renal replacement therapy (Table 3.1). As described in Chapter 2, this classification is based on an adaptation of the "heat map" (a colour-coded classification table) developed by the Kidney Disease Improving Global Outcomes Work Group (Kidney Disease Improving Global Outcomes (KDIGO), 2013). The heat map incorporated estimated glomerular filtration rate (eGFR) and albuminuria (protein level in the urine) because these laboratory results help to evaluate kidney function and the risk of progression to kidney failure.

Of the 69,905 people with CKD, approximately 47% (n=33,097) were at low risk (green, yellow, and light purple) of progression to kidney failure and therefore more likely to be in the early stages of CKD. About 34% (n=23,551) were at high risk and potentially had more advanced CKD. The CKD stage and risk level were unknown for 19% (n=13,257) due to missing laboratory data (Table 3.1). In Appendix Table 3.1, we show sociodemographic characteristics of people at very high risk (A3/G5 category) compared to those of lower risk.

Table 3.1: Heat Map (Risk of Progression to ESKD) of Adults with Chronic Kidney Disease

				Persistent albuminuria categories Description and range			
				A1	A2	A3	
				Normal to mildly increased	Moderately increased	Severely increased	Albuminuria unknown
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol	
eGFR categories (ml/min/1.73m^2) Description and range	G1/G2	Normal or high	≥60	4,109	5,331	6,492	5,999
	G3a	Mildly to moderately decreased	45-59	4,384	3,059	4,435	3,498
	G3b	Moderately to severely decreased	30-44	2,292	2,156	3,563	1,701
	G4	Severely decreased	15-29	616	929	2,291	413
	G5	Kidney failure	<15	86	191	838	89
	eGFR unknown			1,082	2,202	892	13,257*

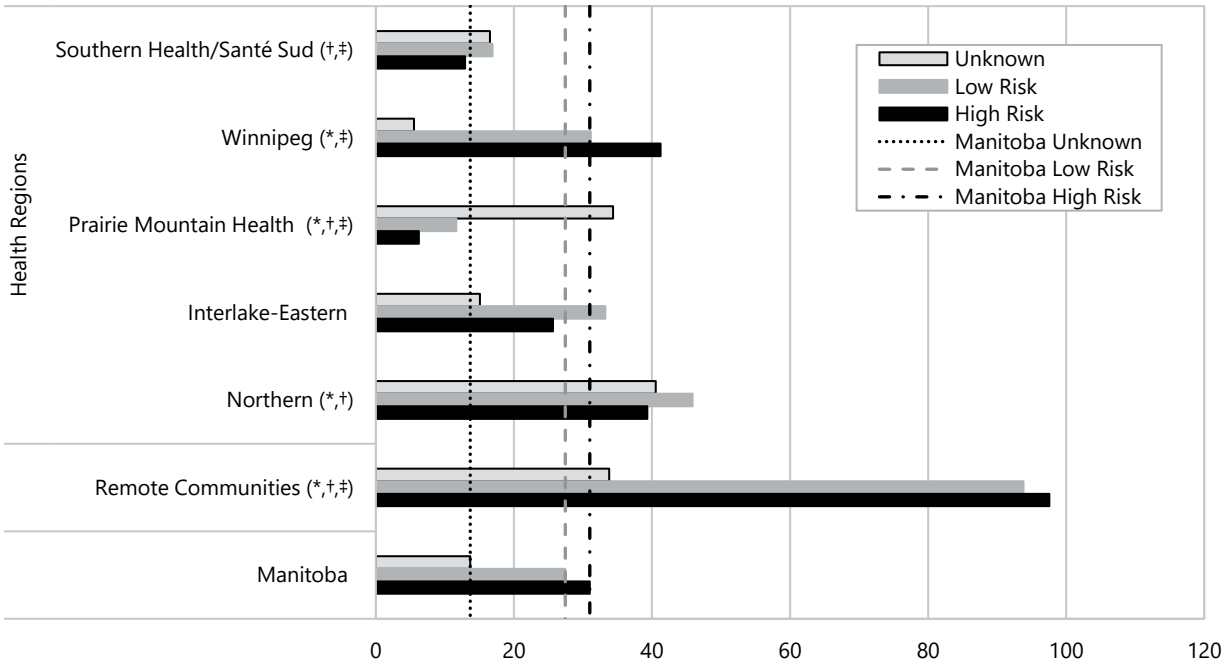
* Identified using only administrative data

Low Risk
High Risk

Figure 3.3 shows rates of CKD among Manitoba residents by region and risk of progression to ESKD. Similar to the graph of prevalence by region (Figure 3.2), the high rates of CKD in the remote communities and in the Northern Health Region are striking for all risk categories. The lower rate of the unknown-risk group in Winnipeg is due to the better coverage of laboratory data in that region, so that most Winnipeg patients could be categorized as either low or high risk. For the Prairie Mountain Health Region, the low- and high-risk groups will be underestimated because of the poor laboratory data coverage in that area; these rates should be interpreted with caution (see Chapter 2).

Figure 3.3: Adults in Risk Groups of Chronic Kidney Disease by Region

Age- and sex-adjusted rates per 1,000 residents aged 18+ on April 1, 2012

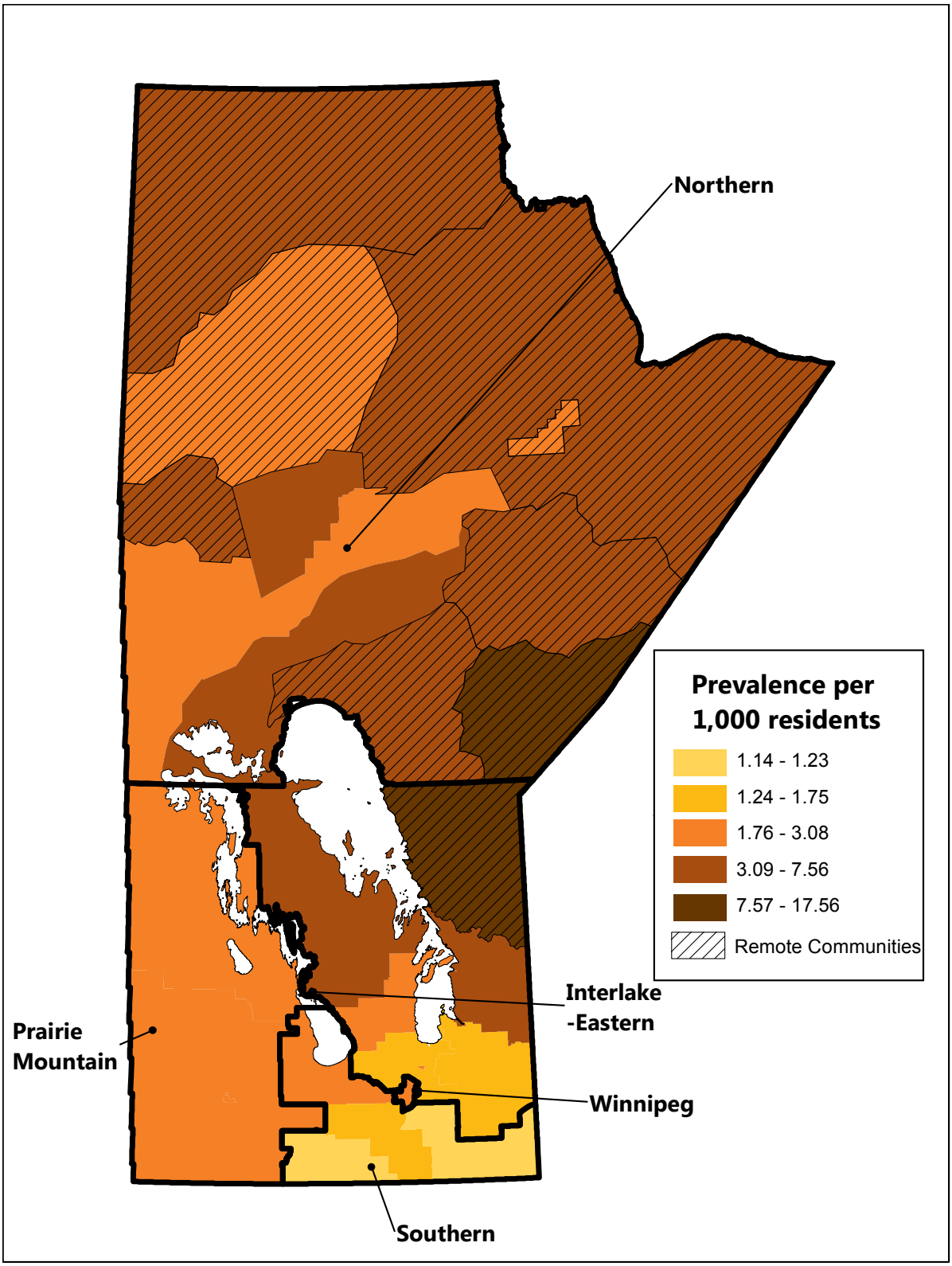


* indicates area's Unknown Risk rate was statistically different from Manitoba
† indicates area's Low Risk CKD rate was statistically different from Manitoba
‡ indicates area's High Risk CKD rate was statistically different from Manitoba

Prevalence and Incidence of End Stage Kidney Disease in Adults

The map in Figure 3.4 shows the prevalence of ESKD in Manitoba in 2012, by health region zones (sub-areas within the five health regions) and for remote communities. These zones provide more detail about the geographic distribution of ESKD. The darker areas indicate the highest rates of ESKD. The rates in northern zones and remote communities are generally higher than rates in the rest of the province, and the lowest rates (lighter shades) are in zones within the Southern Health/Santé Sud Region.

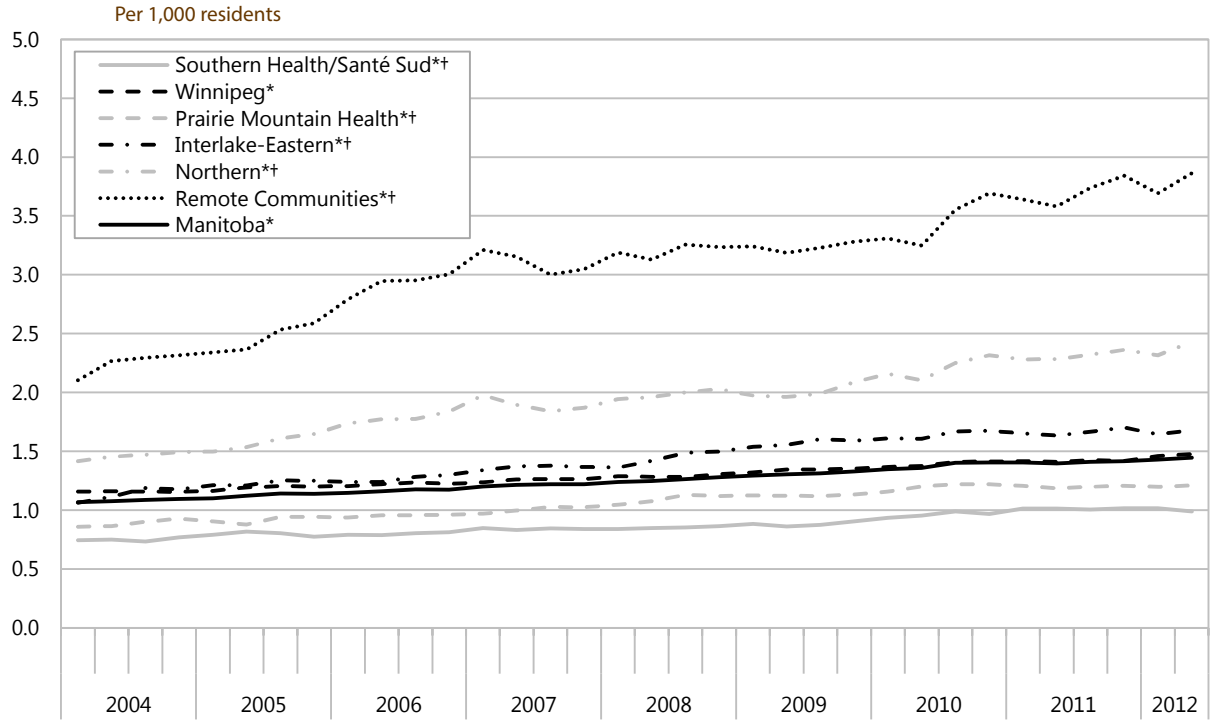
Figure 3.4: Prevalence of End Stage Kidney Disease by Health Region Zones in Manitoba, March 2012



Note: The RHA Zone is based on where people were living two years before dialysis started, so it more accurately reflects region of origin of the kidney disease population

Figure 3.5 represents the geographic distribution of ESKD over time. The prevalence of ESKD in Manitoba in 2012 was 1.45 per 1,000 residents. The Northern Health Region and remote communities, which both have a high percentage of First Nations people, have the highest ESKD rates (2.43 and 3.86 per 1,000 residents, respectively). All rates are increasing over time: the linear trend is statistically significant.

Figure 3.5: End Stage Kidney Disease Prevalence by Region, 2004-2012

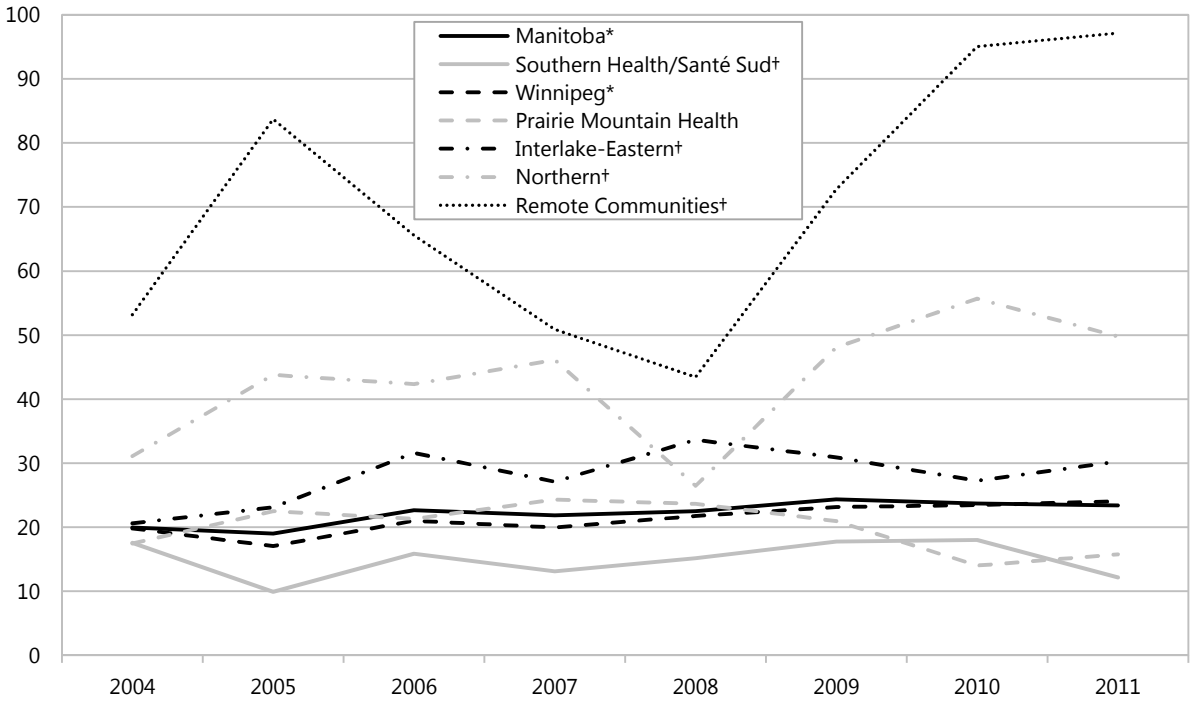


* indicates statistically significant linear trend over time
† indicates health region's rate is statistically significantly different from the Manitoba rate on March 31, 2012

Figure 3.6 shows the incidence rates, or new cases, of ESKD by region over time. The total number of new cases of ESKD in Manitoba in 2011 was 295. From 2004 to 2011, the rates were higher in remote communities, the Northern Health Region and the Interlake-Eastern Health Region, and lower in the Southern Health/Santé Sud Region. For example, in 2005 there were 43.8 per 100,000 residents with ESKD in the Northern Health Region compared to 19 per 100,000 residents in all of Manitoba. The fluctuations in the rates in the Northern Health Region and remote communities are due to the small size of populations in those areas. For example, in Northern Health Region the difference between the incidence of ESKD in 2010 (41 new cases) and 2011 (37 new cases) is only four people, but for this sparsely populated area, it looks like there are big fluctuations. A statistically significant time trend was observed for Manitoba and for Winnipeg, indicating that these rates are increasing over time.

Figure 3.6: End Stage Kidney Disease Incidence by Region, 2004-2011

Crude rate per 100,000 residents



* indicates statistically significant linear trend over time

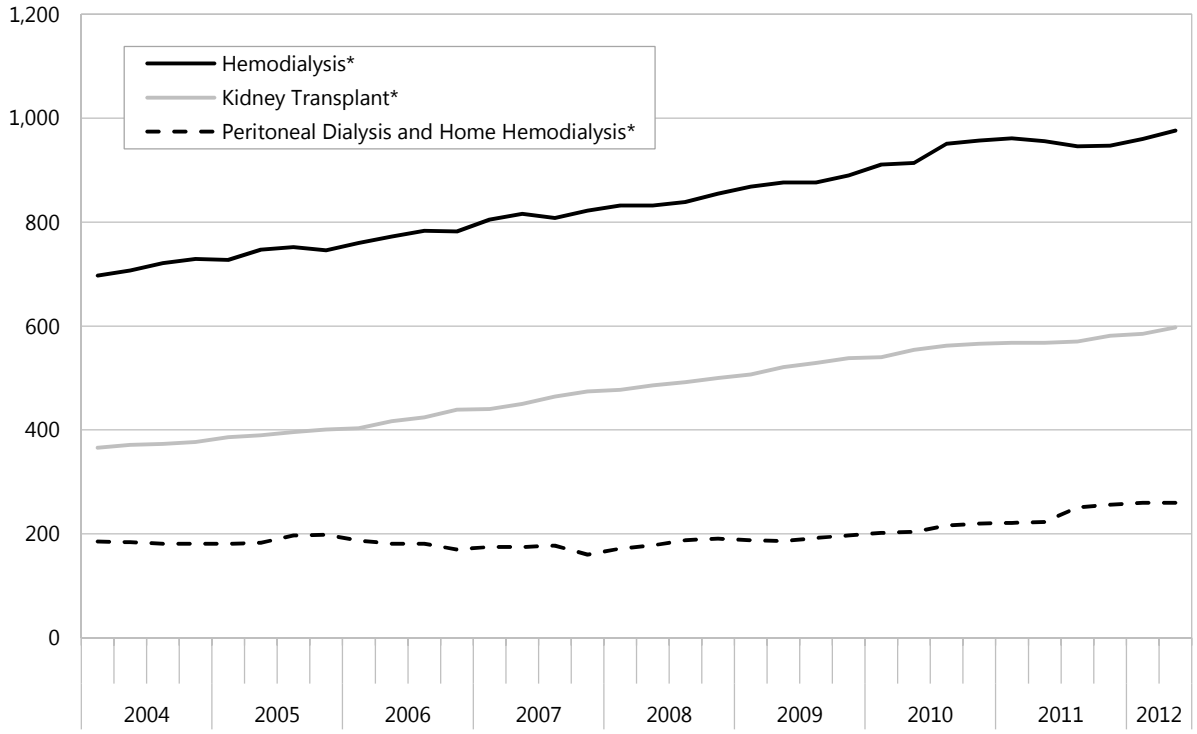
† indicates health region's rate is statistically significantly different from the Manitoba rate on March 31, 2012

Type of Renal Replacement Therapy

The type of RRT used by ESKD patients has significant implications for quality of life and cost, with centre-based hemodialysis being the most restrictive type of dialysis with respect to patients' diet and lifestyle and the most expensive for the health system (see cost details later in this chapter). When dialysis is required, beginning with peritoneal dialysis offers the best quality of life and has been shown to improve mortality over the first two years on treatment (Yeates et al., 2012).

Figure 3.7 shows the observed patterns of types of renal replacement therapy for Manitoba residents with ESKD, based on data from the Manitoba Renal Program and medical claims data. The number of residents with ESKD receiving dialysis or a kidney transplant grew by 47% between 2004 and 2012 (Figure 3.7). We note that the increase is mostly due to the increases in centre-based hemodialysis and kidney transplants. The number of people on peritoneal dialysis has increased only slightly. The home-based types of dialysis — peritoneal dialysis and home hemodialysis — are grouped together on the graph because of the small number of people using this type of therapy. In 2012, there were 1,833 Manitoba residents receiving treatment for ESKD; of these, 597 (32.6%) had a functioning kidney transplant and 1,236 (67.4%) were on dialysis.

Figure 3.7: Observed Number of Patients with End Stage Kidney Disease by Treatment Type, 2004-2012



* indicates statistically significant linear trend over time ($p<0.05$)

Figure 3.8 shows the number of people who started dialysis (and continued for at least three months) and those who stopped dialysis (for reasons of transplant, palliative care or death). Since the number of people who start is higher than those who stop, we observe an overall increase in people receiving RRT from 2004 to 2012. The fluctuation in starts and exits illustrates the degree of activity in the Manitoba Renal Program (MRP). From a resource perspective, it is important to keep in mind that the MRP also provides short-term care for patients in acute kidney failure. These patients are not included in this report.

Figure 3.9 shows ESKD rates for adults by treatment type for each region. Again, we note that remote communities, followed by the Northern Health Region, have the highest rates of ESKD, after adjusting for age and sex (Figure 3.9). We see that these areas also have the lowest proportion of kidney transplants relative to other treatment types. We calculated the relative risk to quantify how ESKD rates in each health region compare to Manitoba's overall ESKD rate (see Appendix Table 4.2). The rate ratio was 2.05 (95% CI: 1.73 to 2.43) for the Northern Health Region and 3.42 (95% CI: 2.77 to 4.23) for remote communities, meaning that the Northern Health Region's rate was 2.05 times higher and the remote communities' rate was 3.40 times higher than Manitoba's rate.

Figure 3.8: Number of Patients with End Stage Kidney Disease who Start and Stop Dialysis, 2004-2012

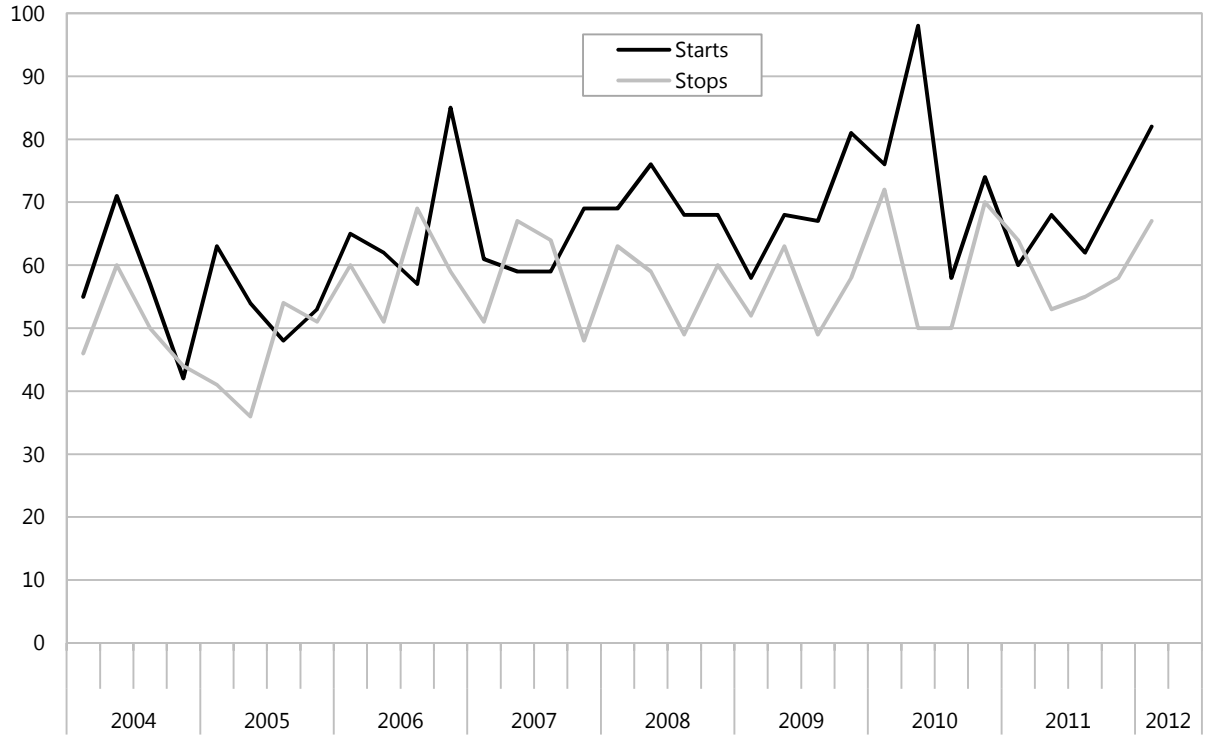
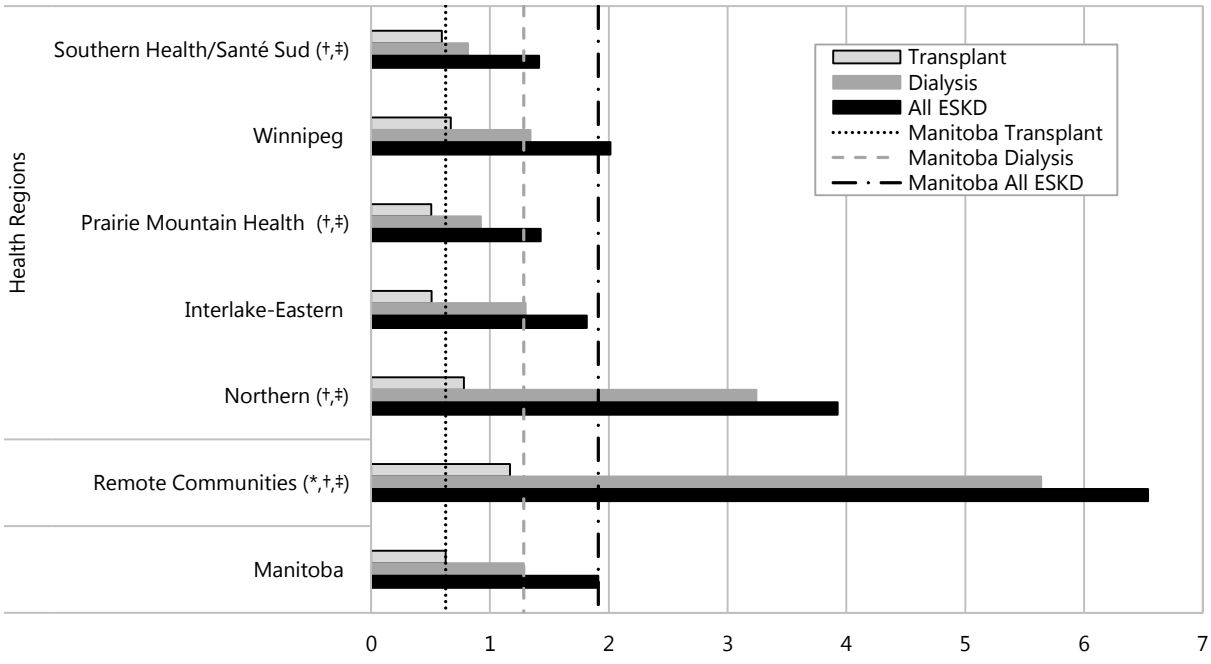


Figure 3.9: Treatment Type of Adults with End Stage Kidney Disease by Region

Age- and sex-adjusted rates per 1,000 residents aged 18+ on March 31, 2012



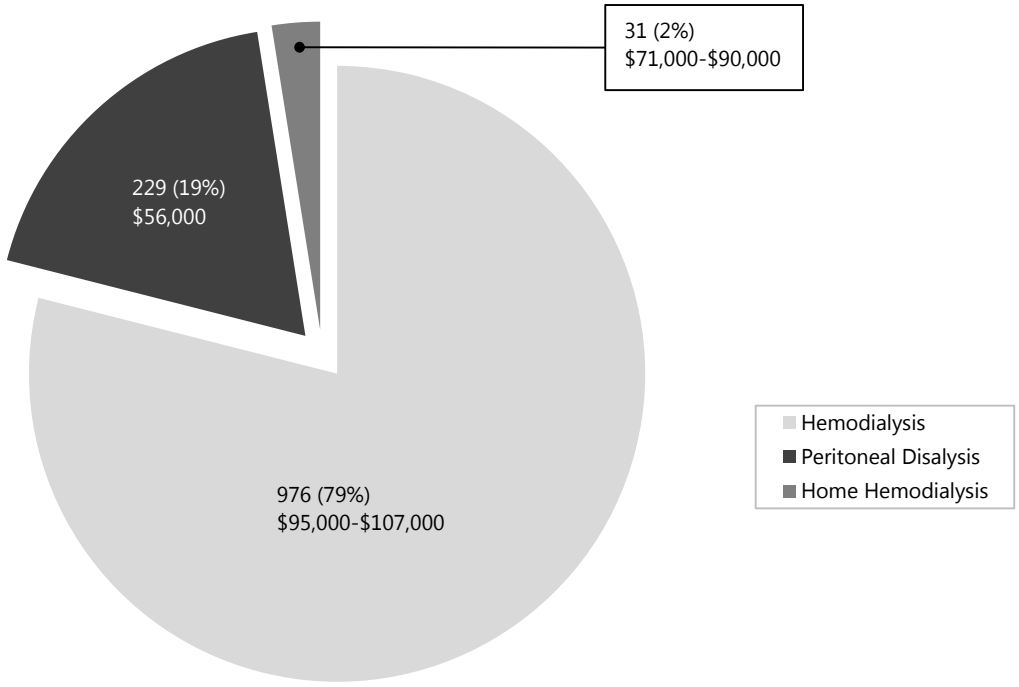
* indicates area's Transplant rate was statistically different from Manitoba
† indicates area's Dialysis rate was statistically different from Manitoba
‡ indicates area's All ESKD rate was statistically different from Manitoba

Dialysis Distribution and Costs

This pie chart (Figure 3.10) displays the distribution of Manitoba residents in the Manitoba Renal Program by dialysis type in 2012 and the estimated annual cost per patient, based on a study by (Klarenbach et al., 2014). While the costs of centre-based hemodialysis in Manitoba are generally in line with these estimates, they are higher in Manitoba because of the costs of providing treatment in remote areas. About 19% of Manitobans receive their dialysis at satellite facilities, smaller sites away from major centres. A recent review of the Manitoba Local Centres satellite dialysis program revealed that the cost of providing hemodialysis in the satellite units ranged from $80,545 to $216,885 per patient, per year. The median per-patient, per-year cost was $101,947 (inter-quartile range: $87,519 - $121,383) (Ferguson et al., 2015). These costs are not reflected in the pie chart.

We found that 79% of residents with ESKD requiring dialysis used centre-based hemodialysis, 19% used peritoneal dialysis, and a very small proportion (2%) used home hemodialysis. The proportions and costs of each type of dialysis point to the potential cost-savings associated with increasing the use of home-based treatment (peritoneal dialysis and home hemodialysis). The surgical costs of kidney transplant are lower than for dialysis and are not shown here.

Figure 3.10: Number and Percent of Adults on Dialysis (2012) and Annual Cost per Person*



* Includes all relevant healthcare costs in addition to procedure costs
Annual cost per person is based on 2013 data for Canada (Klarenback et al. 2014)

Children with Chronic Kidney Disease and End Stage Kidney Disease

Prevalence of Chronic Kidney Disease in Children in Manitoba

We identified a total of 4,330 children under 18 years of age in Manitoba living with CKD as of April 1, 2012 (see definition in Chapter 2). This translates to an overall age- and sex-adjusted prevalence of 1.49% (95% CI: 1.45 to 1.53) (Table 3.2).

The largest proportion (71.8%) of children with CKD were identified by administrative data (n=3,111), and an additional 16.4% (n=711) were identified by available laboratory data alone. The remaining 11.7% (n=508) were identified with both administrative and laboratory data (Figure 3.11).

Due to the lack of complete provincial laboratory data, there is a risk that we would underestimate the true prevalence of CKD in the province. Therefore, we performed two sensitivity analyses to estimate true prevalence of CKD (Table 3.2). The first method used only the children with laboratory tests relevant to CKD as the denominator. The second used the capture-recapture method (described in Chapter 2) to more accurately determine the true pediatric CKD population. We estimate that the actual CKD rate in children is between 1.49% and 3.41%.

Table 3.2: Prevalence of Chronic Kidney Disease in Children by Estimation Method
Rates per 100 residents aged 0-17 on March 31, 2012

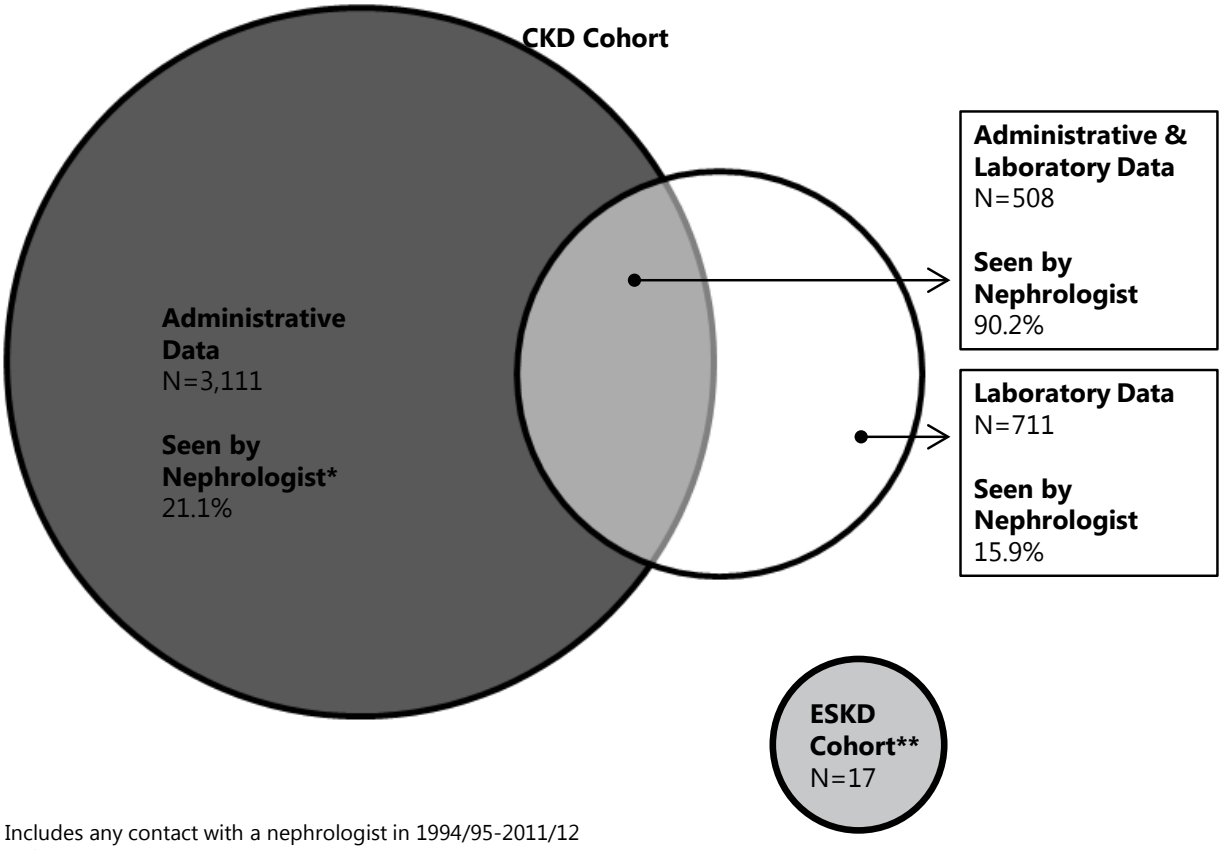
CKD Prevalence by Data Source		
Administrative and Laboratory Data	**Laboratory Data Only**	**Capture-Recapture Method**
1.49%	3.41%	2.97%

Slightly more than one-quarter of children with CKD (28.3%, n=1,225) had been seen by a nephrologist. As shown in Figure 3.11, the group identified through both administrative and laboratory data was the most likely to have been seen by a nephrologist (90.2%). In the other two groups, a much smaller proportion was seen by a nephrologist (administrative data group = 21.1% and laboratory data group = 15.9%). This is not surprising as the children seen by pediatric nephrologists in Winnipeg are the most likely to have been captured by both administrative data and laboratory data. (Specialists are the most likely to bill an ICD code for CKD or a related diagnosis and to order kidney-related laboratory tests).

End Stage Kidney Disease in Children in Manitoba

We identified an additional 17 children on dialysis or with a functioning kidney transplant in 2012, for an overall prevalence of ESKD of 58 per 1,000,000 children (95% CI: 30.6 to 85.7 per 1,000,000). The mean age of children with ESKD was 12.9 years, 53% were male, and 47% were from Winnipeg (data not shown). Kidney transplant is the gold-standard treatment for ESKD in children; most children either receive a transplant without ever starting dialysis or they do not remain on dialysis for very long.

Figure 3.11: Number of Children with Chronic Kidney Disease (CKD) or End Stage Kidney Disease (ESKD), and Percentage Seen by Nephrologist by Data Source
Manitoba residents aged 0-17 on March 31, 2012



* Includes any contact with a nephrologist in 1994/95-2011/12
** Defined by Manitoba Renal Program and other administrative data

Our results provide valuable new knowledge of the population-based prevalence of CKD in our province, with innovative methodology that can now be applied to other populations. Until now, CKD rates in children had never been evaluated using administrative data or laboratory data, and population-based North American data had not been reported previously. Active screening for CKD has been done in Canada with the Canadian Health Measures Survey but to date, results on CKD have been published for adults only (Arora et al., 2013).

The ability to compare the prevalence of CKD in Manitoba in children with other provinces or with national and international rates is challenged by limited available data on pre-dialysis populations (Harambat, van Stralen, Kim, & Tizard, 2012; Warady & Chadha, 2007), and the methodological differences in definitions and screening techniques across studies. Data on CKD in children is available from other countries around the world. Manitoba's prevalence as defined in this report of 1.49% or 14,900 per 1,000,000 age-related population (pmarp) is considerably higher than the previously reported prevalence in children of 56 to 74.7 per 1,000,000 age-related population (pmarp) for early CKD (GFR <75 ml/min/1.73m2) in Europe, 42.5 pmarp in Latin America and the highest previously reported prevalence of 188 to 329 pmarp in Middle and South East Asia in children (Harambat et al., 2012).

More reliable data are available for ESKD populations, as national registries have been developed. The Canadian Organ Replacement Registry (CORR), a validated national registry, reported a national prevalence of ESKD in 0 to 19 year olds of 63.1 per 1,000,000 population in 2012 (Canadian Institute for Health Information (CIHI), 2015). The ESKD prevalence in this report for Manitoba children aged 0 – 17 years is comparable to the Canadian prevalence (58 per 1,000,000 children). The Canadian prevalence is quite comparable to reported rates in Australia, Malaysia, and Western Europe (except Finland, with approximately 65 pmarp). The US has a prevalence of 85 pmarp and Japan has amongst the lowest at 23 pmarp (Harambat et al., 2012).

Validation of Administrative Data Definition for Chronic Kidney Disease in Children

As described in Chapter 2, we evaluated the validity of a number of administrative data algorithms to define CKD in children, using a combination of hospital records, physician claims and Drug Program Information Network (DPIN) data. A description of our valdiation population of children is found in Appendix 5. Table 3.3 shows the numbers captured through the different algorithms of administrative data and the 918 children with laboratory data. We note that Algorithm #15 captures the most cases of CKD in children with the administrative data. Numbers of children in the columns for laboratory only and both administrative and laboratory data fluctuate depending on the agreement between administrative and laboratory data.

In Table 3.4, all algorithms had very low sensitivity (0.221–0.416) but very good specificity (0.994–0.999). The positive predictive value was similarly low (0.180–0.342), whereas the negative predictive value was high (0.998). The receiver operating characteristic (ROC) curves indicate poor to fair accuracy (0.610 – 0.705). Generally speaking, the sensitivity improved slightly with increasing years of data (three years vs. one or two years). Algorithm #15 had the highest sensitivity (0.416), and included one or more hospital records, one or more physician claims and one or more DPIN fills over three years. The algorithm used in this report (#16: one or more hospital records, two or more physician claims and one or more DPIN fills over three years), had lower sensitivity (0.376) but higher specificity (0.996). Overall, these findings are in keeping with adult studies that have evaluated CKD algorithms (Ronksley et al., 2012; Vlasschaert et al., 2011). The low sensitivity is generally unacceptable for population-based surveillance for CKD and reinforces the importance of laboratory data surveillance or active screening for CKD in high-risk populations.

Table 3.3: Number of Children with Chronic Kidney Disease Identified with Administrative Data Case Definitions and Laboratory Data

Years of Adminsitrative Data	Administrative Data Case Definitions of CKD				Number of Children with CKD by Case Definition		
	Algorithm	Hospital Abstracts	Physician Claims	Medication Records	Administrative Data Only	Both Adminsitrative and Laboratory Data	Laboratory Data Only*
1 year (2011/12)	1	1 or more	1 or more	n/a	806	307	611
	2	1 or more	2 or more	n/a	390	203	715
	3	1 or more	1 or more	1 or more	913	312	606
	4	1 or more	2 or more	1 or more	498	212	706
	5	1 or more	1 or more	2 or more	836	310	608
	6	1 or more	2 or more	2 or more	421	209	709
2 years (2010/11-2011/12)	7	1 or more	1 or more	n/a	1,229	353	565
	8	1 or more	2 or more	n/a	729	302	616
	9	1 or more	1 or more	1 or more	1,378	361	557
	10	1 or more	2 or more	1 or more	880	311	607
	11	1 or more	1 or more	2 or more	1,268	356	562
	12	1 or more	2 or more	2 or more	770	305	613
3 years (2009/10-2011/12)	13	1 or more	1 or more	n/a	1,573	375	543
	14	1 or more	2 or more	n/a	991	338	580
	15	1 or more	1 or more	1 or more	1,739	382	536
	16	1 or more	2 or more	1 or more	1,160	345	573
	17	1 or more	1 or more	2 or more	1,619	378	540
	18	1 or more	2 or more	2 or more	1,039	341	577

* children not captured by administrative data case definition

n/a indicates not applicable

Table 3.4: Validity of Administrative Data Case Definitions of Chronic Kidney Disease Compared to Laboratory Data

2009/10–2011/12

Years of Adminsitrative Data	Administrative Data Algorithm	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Kappa Statistic	ROC
1 year (2011/12)	1	0.334	0.997	0.276	0.998	0.300	0.666
	2	0.221	0.999	0.342	0.998	0.267	0.610
	3	0.340	0.997	0.255	0.998	0.289	0.668
	4	0.231	0.998	0.299	0.998	0.258	0.615
	5	0.338	0.997	0.271	0.998	0.298	0.667
	6	0.228	0.999	0.332	0.998	0.268	0.613
2 years (2010/11-2011/12)	7	0.385	0.996	0.223	0.998	0.280	0.690
	8	0.329	0.997	0.293	0.998	0.308	0.663
	9	0.393	0.995	0.208	0.998	0.269	0.694
	10	0.339	0.997	0.261	0.998	0.292	0.668
	11	0.388	0.996	0.219	0.998	0.277	0.692
	12	0.332	0.997	0.284	0.998	0.304	0.665
3 years (2009/10-2011/12)	13	0.408	0.995	0.193	0.998	0.259	0.702
	14	0.368	0.997	0.254	0.998	0.298	0.682
	15	0.416	0.994	0.180	0.998	0.248	0.705
	16	0.376	0.996	0.229	0.998	0.282	0.686
	17	0.412	0.994	0.189	0.998	0.256	0.703
	18	0.371	0.996	0.247	0.998	0.294	0.684

Classification of Children with Chronic Kidney Disease by Disease Severity

Proteinuria is an indication of glomerular inflammation or scarring, and is associated with higher rates of progression of CKD over time. Even mild protein loss in a child can be associated with a significant life-long risk of progression of CKD (Wong, Moxey-Mims, Jerry-Fluker, Warady, & Furth, 2012), unless the mechanisms driving protein loss (such as obesity, diabetes and hypertension, or autoimmune processes) can be modified.

Adequate laboratory data to meet our criteria for CKD (at least two eGFR results available to calculate eGFR or urine protein tests at least 90 days apart) were available for about 28% of the pediatric cohort (Table 3.5). At least one relevant laboratory test (either eGFR or proteinuria test) was available for an additional 25%, leaving 2,057 children without any available laboratory data to classify risk severity of CKD (47.5%). The available laboratory data were used to further classify the CKD cohort into a low-risk group (green, yellow and light purple on the heat map) and a high-risk group (orange, red and dark purple) for progression to ESKD based on eGFR category (G) and albuminuria category (A).

Three-quarters of the cohort with laboratory data was in the low-risk category (n=1,755) including 142 children with normal eGFRs and normal to mildly increased protein excretion (G1/A1). The remaining one-quarter was high-risk (n=507) (Table 3.5). A small proportion of the cohort had documented eGFRs less than 45 ml/min/1.73m2 (G3b or worse; n=79) and fewer than 20 children had eGFRs less than 30 ml/min/1.73m2, consistent with advanced CKD (G4 or worse). A large proportion of the children had significant proteinuria: nearly 500 children had moderately increased protein excretion (A2) and an additional 457 children had severely increased protein excretion (A3).

We use these risk groupings in Chapter 5 to describe the characteristics of children with CKD (low-risk CKD, high-risk CKD, unknown risk due to lack of laboratory data, ESKD) compared with all children in the province without known CKD (no-CKD group).

Table 3.5: Heat Map (Risk of Progression to ESKD) of Children with Chronic Kidney Disease on March 31, 2012

eGFR categories (ml/min/1.73m²) Description and range				Persistent albuminuria categories Description and range			
				A1	A2	A3	
				Normal to mildly increased	Moderately increased	Severely increased	Albuminuria unknown
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol	
	G1	Normal or high	≥90	142	214	160	373
	G2	Mildly decreased	60-89	189	179	168	487
	G3a	Mildly to moderately decreased	45-59	15	24	30	24
	G3b	Moderately to severely decreased	30-44	s	13	19	7
	G4	Severely decreased	15-29	6	s	14	s
	G5	Kidney failure	<15	0	s	9	0
	eGFR unknown			78	54	57	2,057*

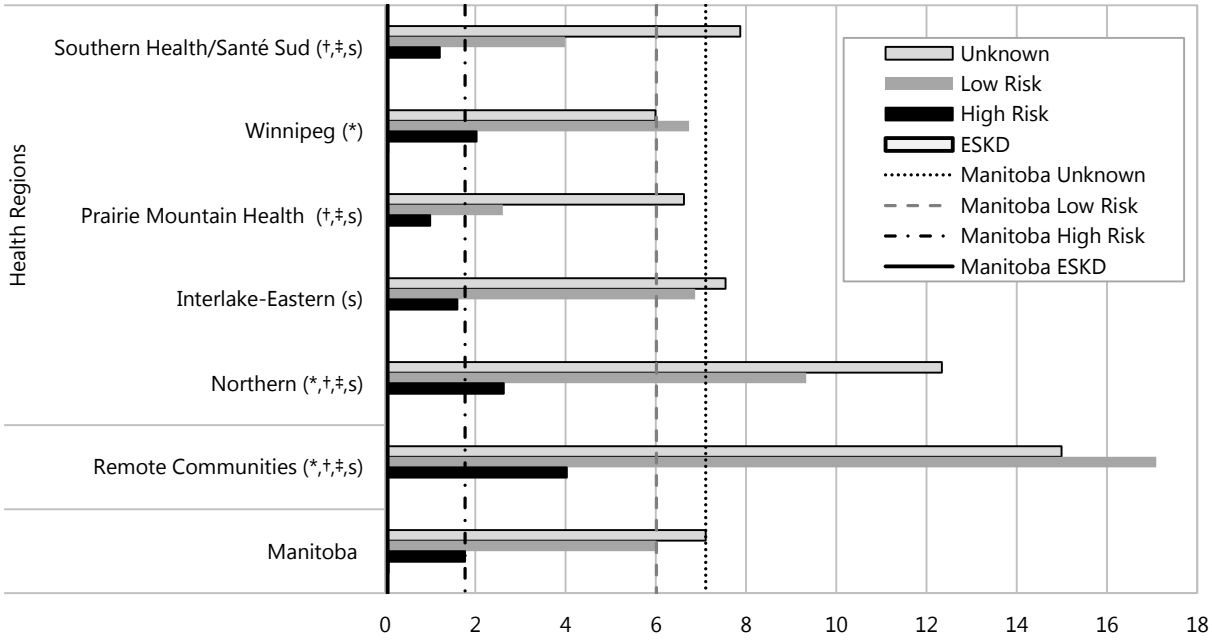
* Identified using only administrative data

Low Risk
High Risk

Figure 3.12 shows rates of CKD and ESKD for children in each region by disease severity. The distribution of high- and low-risk CKD groups (which rely on laboratory data for identification) should be interpreted with caution because of the known paucity of laboratory data in Southern Health/Santé Sud and Prairie Mountain health regions and some areas of the Northern Health Region. However, children with low-risk or high-risk CKD were identified in all health regions in the province, with the majority residing in Winnipeg. Data for the group of children with unknown risk for progression to ESKD likely reflect a lower-risk population that was not referred to a tertiary care center for laboratory testing for CKD. Despite the lack of complete laboratory data in the North, there was a significant over-representation of children with any CKD in the Northern Health Region and in the remote communities. Relative risks for each region are available in Appendix 6.

Figure 3.12: Children in Risk Groups of Chronic Kidney Disease and End Stage Kidney Disease by Region

Age- and sex-adjusted rates per 1,000 residents aged 0-17 on March 31, 2012



* indicates area's Unknown rate was statistically different from Manitoba
† indicates area's Low Risk CKD rate was statistically different from Manitoba
‡ indicates area's High Risk CKD rate was statistically different from Manitoba
s indicates ESKD rates are suppressed due to small numbers
Note: rates of ESKD are crude and below 0.1 per 1,000 children

CHAPTER 4: CHARACTERISTICS OF ADULTS WITH END STAGE KIDNEY DISEASE AND CHRONIC KIDNEY DISEASE

This chapter is dedicated to answering the question: What are the characteristics of the future population of Manitoba residents who will require renal replacement treatment (RRT) by dialysis or transplant? One way to answer this question is to describe the people who are currently receiving RRT. However, given that chronic kidney disease (CKD) is a progressive illness, it is important to also describe the population with CKD at greatest risk of progressing to end stage kidney disease (ESKD) in the future. This will provide a clearer picture of the full spectrum of CKD, and is crucial in planning prevention and early intervention strategies and treatment services for this population.

In this chapter, we describe the sociodemographic characteristics of adults with ESKD and CKD, as well as co-existing medical conditions, diagnosed mental disorders, healthcare use and medication use associated with the disease. As outlined in Chapters 2 and 3, these characteristics are described in four distinct groups: CKD with low risk of progressing to ESKD, CKD with high risk of progressing, CKD with unknown risk (no laboratory data), and ESKD. In examining comorbid disorders and healthcare services use, we compare the CKD and ESKD cohorts to all adults without known CKD (no-CKD group).

Key Findings

Adults with End Stage Kidney Disease

- Higher rates of ESKD are found among among adults aged 65 years and older (3.53 per 1,000) and middle-aged residents aged 45 to 64 years (2.48 per 1,000) than among those aged 18 to 44 years (0.87 per 1,000).
- Men have higher rates of ESKD than women (2.20 per 1,000 versus 1.63 per 1,000).
- In both rural and urban areas, higher rates of ESKD were found among adults living in the lowest income area compared to the highest income area (rural lowest: 3.51 per 1,000, rural highest: 1.24 per 1,000, urban lowest: 3.42 per 1,000, urban highest: 1.30 per 1,000). Also, rates of kidney transplants are lower relative to dialysis in the lowest income quintiles than in higher income quintiles.
- Compared to adults without CKD, those with ESKD have higher rates of diabetes, hypertension, ischemic heart disease, acute myocardial infarction, congestive heart failure, stroke, atrial fibrillation, lower limb amputation, dementia, mood and anxiety disorders, and at least one mental disorder. Relative risks range from 1.20 for having at least one mental disorder to 39.08 for lower limb amputation.
- Compared to adults without CKD, those with ESKD have higher hospitalization rates and more physician visits, are dispensed more medications, and are more likely to be taking anti-hypertensive medications. Relative risks range from 2.35 for physician visits to 15.13 for days spent in hospital.

Adults with Chronic Kidney Disease

- People in earlier stages of CKD have similar characteristics to those in ESKD. The main difference is that adults with ESKD have more comorbid conditions and use more healthcare services than those in the earlier stages of CKD. Women have higher rates of CKD than men (34.77 per 1,000 versus 27.03 per 1,000), whereas the converse was found for ESKD.
- Higher rates of CKD are found among among adults aged 65 years and older (106.86 per 1,000) and middle-aged residents aged 45 to 64 years (21.48 per 1,000) than among those aged 18 to 44 years (8.66 per 1,000).
- In both rural and urban areas, higher rates of CKD are found among adults living in the lowest income compared to the highest income area (rural lowest: 28.50 per 1,000, rural highest: 17.73 per 1,000, urban lowest: 56.67 per 1,000, urban highest: 25.54 per 1,000). Also, rates of kidney transplants are lower relative to dialysis in the lowest income quintiles than in higher income quintiles.
- Compared to adults without CKD, those with CKD have higher rates of diabetes, hypertension, ischemic heart disease, acute myocardial infarction, congestive heart failure, stroke, atrial fibrillation, lower limb amputation, suicide attempts, substance abuse, dementia, mood and anxiety disorders and at least one mental disorder. Relative risks range from 1.33 for mood and anxiety disorders to 18.17 for congestive heart failure.
- Compared to adults without CKD, those with CKD have higher hospitalization rates and more physician visits, are dispensed more medications, and are more likely to be taking anti-hypertensive medications. Relative risks range from 2.17 for number of medications dispensed to 10.82 for days spent in hospital.

Characteristics of Adults with End Stage Kidney Disease

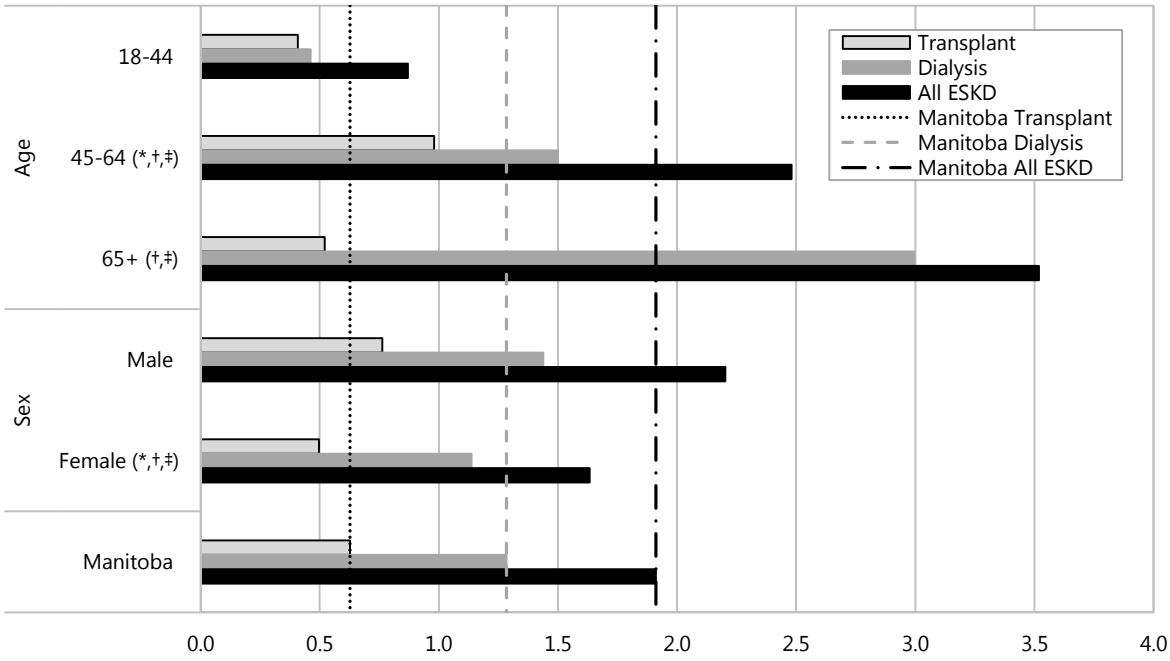
As described earlier, the ESKD cohort consists of people receiving renal replacement therapy (RRT) by dialysis or kidney transplant. The incidence and prevalence of ESKD were described in Chapter 3. In this section, we examine the sociodemographic characteristics, physical and mental health, use of prescription drugs, and use healthcare services by Manitoba adults with ESKD.

Sociodemographic Characteristics

Figure 4.1 shows rates of ESKD in Manitoba by age and sex and by type of RRT in 2012. We observe higher rates of ESKD among older residents (aged 65 years and older) and middle-aged residents (aged 45 to 64) than among younger adults (aged 18 to 44). The middle-aged group has the highest rate of kidney transplants, and proportionately fewer people in the older age group receive transplants relative to dialysis than in the younger age group. Men have higher rates of ESKD than women.

Figure 4.1: Treatment Type of Adults with End Stage Kidney Disease by Age and Sex

Rates per 1,000 residents aged 18+ on March 31, 2012

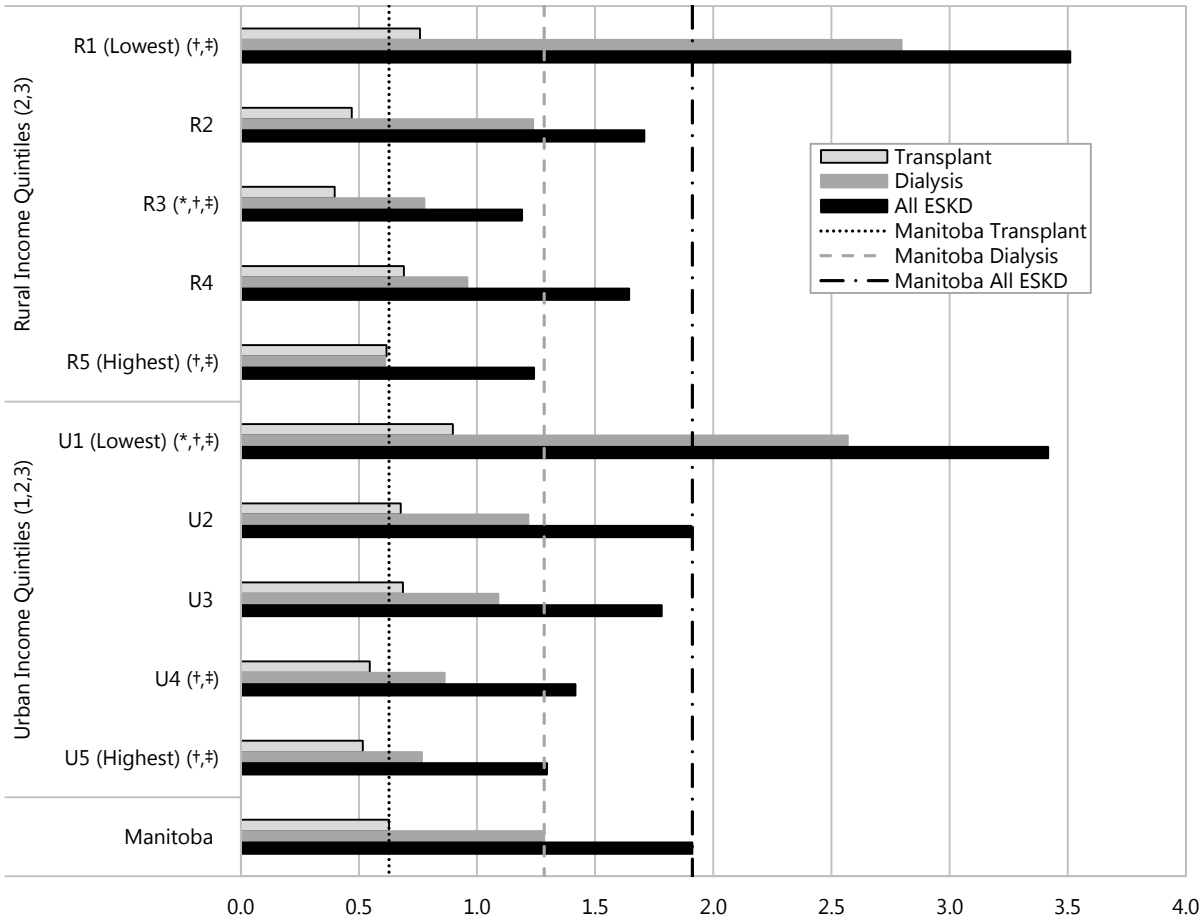


* indicates area's Transplant rate was statistically different from reference group (Age: 18-44 or Sex: Male)
† indicates area's Dialysis rate was statistically different from reference group (Age: 18-44 or Sex: Male)
‡ indicates area's All ESKD rate was statistically different from reference group (Age: 18-44 or Sex: Male)

Figure 4.2 shows the rates of ESKD and treatment type by income quintiles. These income quintiles were developed separately for urban (Winnipeg and Brandon) and rural areas (all other health regions) by assigning average household income from the 2001 and 2006 Census to dissemination areas, and ranking these from highest to lowest. In both rural and urban areas, we observe a similar pattern: the lowest income areas have higher rates of ESKD. This gradient appears to be more pronounced in the urban areas, likely because income quintiles are measured more accurately in urban than rural areas. Of note, rates of kidney transplants are disproportionately lower relative to dialysis, in the lowest income quintiles compared to higher quintiles. This is particularly true in rural areas; half of all RRT among the higher income quintiles is dialysis, whereas in the lower income quintiles, most of the treatment for ESKD is dialysis.

Figure 4.2: Treatment Type of Adults with End Stage Kidney Disease by Rural and Urban Income Quintile

Age- and sex-adjusted rates per 1,000 residents aged 18+ on March 31, 2012



* indicates area's Transplant rate was statistically different from Manitoba
† indicates area's Dialysis rate was statistically different from Manitoba
‡ indicates area's All ESKDrate was statistically different from Manitoba
1,2,3 indicates linear trend of Urban or Rural Income Quintiles: 1 - Transplant 2 - Dialysis 3 - All ESKD

Physical Health

Table 4.1 shows rates and relative risks of comorbid medical conditions among people with ESKD, by treatment type and compared to people without any known CKD. Rates of medical conditions among people with ESKD are considerably higher than among people without CKD, and the relative risk ranges from 3.98 for hypertension to 39.1 for lower-limb amputation among people with diabetes. Cardiovascular conditions are also significantly more prevalent among people with ESKD. The high rates of hypertension and diabetes are not surprising given that these are important risk factors for developing CKD. We also observe differences in the rates of comorbid medical conditions among people who are being treated with dialysis and those who have received transplants. For example, dialysis patients have considerably higher rates of diabetes (52.58%) and congestive heart failure (36.58%) compared to transplant recipients (29.90% and 10.22% for diabetes and congestive heart failure, respectively).

Table 4.1: Physical Health of Adults in End Stage Kidney Disease Patient Cohorts

Age- and sex-adjusted prevalence, 95% confidence intervals

Indicators		No CKD	ESKD by Treatment Type		
			Dialysis	Kidney Transplant	All ESKD
Diabetes (%) (2009/10-2011/12)	**Prevalence**	7.02 (6.96-7.07)	52.58 (37.22-74.28)	29.90 (20.74-43.10)	41.72 (30.06-57.91)
	Relative Risk	reference	**7.50 (5.31-10.59)**	**4.26 (2.96-6.14)**	**5.95 (4.29-8.25)**
Hypertension (%) (2011/12)	**Prevalence**	21.45 (21.36-21.55)	86.76 (54.32-100.00)	84.00 (52.53-100.00)	85.39 (56.79-100.00)
	Relative Risk	reference	**4.04 (2.53-6.46)**	**3.92 (2.45-6.26)**	**3.98 (2.65-5.98)**
Ischemic Heart Disease (%) (2007/08-2011/12)	**Prevalence**	4.72 (4.68-4.77)	49.91 (28.63-86.99)	29.77 (16.79-52.78)	40.10 (24.35-66.05)
	Relative Risk	reference	**10.57 (6.06-18.42)**	**6.30 (3.56-11.17)**	**8.49 (5.16-13.98)**
Acute Myocardial Infarction (%) (2007/08-2011/12)	**Prevalence**	0.99 (0.96-1.01)	10.75 (6.41-18.01)	3.53 (1.76-7.08)	7.71 (4.69-12.70)
	Relative Risk	reference	**10.91 (6.51-18.29)**	**3.59 (1.79-7.19)**	**7.83 (4.76-12.90)**
Congestive Heart Failure (%) (2009/10-2011/12)	**Prevalence**	1.38 (1.35-1.41)	36.58 (21.41-62.48)	10.22 (5.41-19.30)	24.70 (14.18-43.05)
	Relative Risk	reference	**26.48 (15.50-45.24)**	**7.40 (3.92-13.97)**	**17.89 (10.26-31.17)**
Stroke (%) (2007/08-2011/12)	**Prevalence**	0.41 (0.39-0.43)	3.11 (1.61-6.00)	s	2.25 (1.24-4.09)
	Relative Risk	reference	**7.62 (3.95-14.72)**	s	**5.53 (3.05-10.04)**
Atrial Fibrillation (%) (2009/10-2011/12)	**Prevalence**	1.92 (1.89-1.94)	12.98 (9.00-18.71)	5.34 (3.34-8.54)	9.74 (7.01-13.54)
	Relative Risk	reference	**6.78 (4.70-9.77)**	**2.79 (1.75-4.46)**	**5.09 (3.66-7.07)**
Lower-Limb Amputation Among Diabetics (%) (2007/08-2011/12)	**Prevalence**	0.33 (0.29-0.38)	15.18 (10.33-22.30)	8.28 (4.69-14.61)	12.97 (9.11-18.44)
	Relative Risk	reference	**45.76 (31.15-67.21)**	**24.95 (14.13-44.05)**	**39.08 (27.47-55.60)**

bolded values indicate statistically significant difference from the No CKD group

s indicates suppressed values due to small numbers

The rates of these medical conditions are much higher than the Manitoba averages reported for 2011/12 (Fransoo et al., 2013). While the rates of medical conditions are alarmingly high among people with ESKD, this is consistent with previous research showing that prolonged dialysis treatment is associated with higher levels of hypertension in patients with ESKD (Issa et al., 2008), and that chronic and acute cardiovascular diseases are more common in people with ESKD (Cheung et al., 2004; Cooper, Monge, & Panza, 2008; Seliger, Gillen, Longstreth, Kestenbaum, & Stehman-Breen, 2003; Trespalacios, Taylor, Agodoa, Bakris, & Abbott, 2003). Previous research also shows that people with both ESKD and diabetes (especially type 2 diabetes) have high rates of lower-limb amputation (Girman et al., 2012; Kaminski, Frescos, & Tucker, 2012; Speckman et al., 2004). However, there is no consistent evidence that amputations rates are higher solely due to the presence of ESKD.

Our findings show that ESKD patients with a kidney transplant have lower rates of physical health problems than those on dialysis, after adjustments for age and sex. Similarly, Rosenberger et al. (2010) found that transplant patients had less comorbidity and better perceived health than those on dialysis. These authors note that patients selected for kidney transplants are assessed as being healthy enough to undergo major surgery.

Mental Health

Table 4.2 shows rates and relative risks of mental disorders among people with ESKD, by treatment type and compared to people without any known CKD. As previously reported by Fransoo et al. (2013), the diagnostic prevalence of mood and anxiety disorders is high in the general Manitoba population. We found significantly higher rates of dementia, mood and anxiety disorders, and having at least one mental disorder among people with ESKD compared to those without CKD. There was no difference in rates of substance abuse between the no-CKD and ESKD groups. The relative risks for mental disorders are not as dramatic as for medical conditions. However, the 20% to 70% higher rates of mental disorders in people with ESKD highlights the importance of addressing of mental health concerns in this population.

Previous studies have shown an association between ESKD and mental disorders such as anxiety, depression, mood disorders, dementia, suicide and substance abuse (Butt, Evans, Skanderson, & Shakil, 2006; Chou et al., 2015; Farrokhi, Abedi, Beyene, Kurdyak, & Jassal, 2014; Palmer et al., 2013; Reckert, Hinrichs, Pavenstadt, Frye, & Heuft, 2013; Taskapan et al., 2005). The reported prevalence of depression (20%–39%) and anxiety (12%–52%) in people diagnosed with ESKD varies across studies (Fabrazzo & De Santo, 2006; Hedayati, Yalamanchili, & Finkelstein, 2012; Lee, Kim, Cho, & Kim, 2013; Stasiak, Bazan, Kuss, Schuinski, & Baroni, 2014). Chou et al. (2015) also showed that prolonged treatment with dialysis is associated with higher severity of dementia. Kurella, Kimmel, Young, & Chertow (2005) found that suicide rates among people with ESKD are higher than the general population.

It is noteworthy that we found no significant differences in mental health indicators among adults with a kidney transplant compared to those without CKD, with the exception of substance abuse rates being lower in the transplant group. These results differ from previous studies that found kidney transplant recipients and dialysis patients have similar rates of mental disorders. Depression in transplant recipients has also been associated with non-adherence to post-transplant medication, graft failure and mortality (Chilcot, Spencer, Maple, & Mamode, 2014). It has been suggested that the high rates of mental health problems in this group could potentially be associated with the stress of waiting for a transplant (Silva et al., 2014).

Table 4.2: Mental Disorders in Adults in End Stage Kidney Disease Patient Cohorts

Age- and sex-adjusted rates and prevalence, 95% confidence intervals

Indicators		No CKD	ESKD by Treatment Type		
			Dialysis	Kidney Transplant	All ESKD
Mood and Anxiety Disorders (%) (2007/08-2011/12)	**Prevalence**	22.38 (22.28-22.47)	28.29 (24.99-32.02)	24.54 (20.59-29.24)	26.99 (24.29-30.00)
	Relative Risk	reference	**1.26 (1.12-1.43)**	1.10 (0.92-1.31)	**1.21 (1.09-1.34)**
Dementia (%) (2007/08-2011/12)	**Prevalence**	3.91 (3.84-3.99)	7.23 (5.29-9.88)	4.38 (2.14-8.98)	6.64 (4.97-8.88)
	Relative Risk	reference	**1.85 (1.35-2.53)**	1.12 (0.55-2.29)	**1.70 (1.27-2.27)**
Any Disorder* (%) (2007/08-2011/12)	**Prevalence**	25.31 (25.20-25.41)	32.75 (29.14-36.81)	26.15 (22.08-30.97)	30.45 (27.53-33.67)
	Relative Risk	reference	**1.29 (1.15-1.45)**	1.03 (0.87-1.22)	**1.20 (1.09-1.33)**
Suicide and Suicide Attempts (per 10,000 person-years) (2009-2012)	**Rate**	5.24 (4.98-5.50)	s	s	s
	Relative Risk	reference	s	s	s
Substance Abuse (%) (2007/08-2011/12)	**Prevalence**	5.12 (5.08-5.17)	8.68 (6.55-11.51)	2.58 (1.53-4.34)	6.28 (4.78-8.25)
	Relative Risk	reference	**1.70 (1.28-2.25)**	**0.50 (0.30-0.85)**	1.23 (0.93-1.61)

bolded values indicate statistically significant difference from the No CKD group

* includes mood and anxiety disorders, personality disorder, schizophrenia, and substance abuse

s indicates suppressed values due to small numbers

Use of Prescription Drugs

Table 4.3 shows rates and relative risks of prescription drugs dispensed for adults with ESKD over a one-year period.[5] Looking at medication use provides insight into the general health of this population and the degree to which they are receiving drug therapies recommended for treating ESKD. As expected, people with ESKD have higher rates of prescription drug use than people without CKD. The relative risk ranges from 1.31 for angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) to 4.50 for anti-hypertensive drugs among people with diabetes. Note that prescription rates for ACE inhibitors and ARBs are generally high among people with diabetes, regardless of their CKD status. The relative risks for all prescription indicators are similar for the dialysis and transplant groups.

Given the high rates of hypertension among people with ESKD, we would expect them to take anti-hypertensive medications. ACE inhibitors and ARBs are among the most widely prescribed medications and are often considered the most protective drugs for these patients (Cravedi, Remuzzi, & Ruggenenti, 2011; Lopes et al., 2009). Overall, our findings on ACE inhibitor and ARB use follow a similar pattern to reports from the literature (Tomaszuk-Kazberuk et al., 2013; Wetmore et al., 2011): prescription rates are higher in the ESKD cohort compared with people without CKD. However, Wetmore et al. (2011) found that the rate of prescription of ACE inhibitors, ARBs and beta-blockers in their sample of people with ESKD was lower than expected based on clinical guidelines. Our findings suggest that the overall rate of ACE inhibitor prescribing to Manitobans with ESKD (61%) is higher than rates reported in the literature (14%–32%) (Foley, Herzog, & Collins, 2002; Griffith et al., 2003). Whether this is an indication of better prescribing practices in Manitoba or an overestimation is unclear (see footnote 4 in this section).

5 Some people included in these results may not have been in kidney failure for the full year; they may have progressed from earlier stages of CKD to ESKD during the one–year period. Therefore, the percentages of people on ACE inhibitors and ARBs may be overestimated. ACE inhibitors and ARBs are not as commonly used in ESKD patients as in earlier stages of CKD.

Table 4.3: Use of Prescription Drugs by Adults in End Stage Kidney Disease Patient Cohorts

Age- and sex-adjusted rates, 95% confidence intervals, 2011/12

Indicators		No CKD	ESKD by Treatment Type		
			Dialysis	Kidney Transplant	All ESKD
Anti-Hypertensive Drug Prescriptions (%)	**Rate**	18.78 (18.69-18.87)	84.92 (50.79-100.00)	83.99 (50.28-100.00)	84.45 (53.96-100.00)
	Relative Risk	reference	**4.52 (2.71-7.56)**	**4.47 (2.68-7.47)**	**4.50 (2.87-7.04)**
ACE & ARB Prescriptions (%)	**Rate**	14.01 (13.93-14.09)	61.07 (35.25-100.00)	60.41 (34.96-100.00)	60.74 (37.65-97.98)
	Relative Risk	reference	**4.36 (2.52-7.55)**	**4.31 (2.50-7.45)**	**4.34 (2.69-6.99)**
ACE & ARB Prescriptions Among Diabetics (%)	**Rate**	56.18 (55.60-56.77)	73.19 (59.31-90.32)	74.52 (57.54-96.51)	73.66 (61.13-88.75)
	Relative Risk	reference	**1.30 (1.06-1.61)**	**1.33 (1.02-1.72)**	**1.31 (1.09-1.58)**
Different Prescribed Drugs (per person)	**Rate**	3.99 (3.98-1.00)	12.10 (10.75-1.00)	10.85 (9.62-1.00)	11.49 (10.33-1.00)
	Relative Risk	reference	**3.04 (2.69-3.42)**	**2.72 (2.41-3.07)**	**2.88 (2.59-3.21)**

bolded values indicate statistically significant difference from the No CKD group

Healthcare Services Use

Table 4.4 shows rates and relative risks of healthcare services use by people with ESKD by treatment type and compared to people without any CKD. As expected given their higher rates of other health conditions, people with ESKD are hospitalized and see physicians more often than people without CKD. For example, the number of days spent in hospital by people on dialysis is 21 times higher than by people without CKD. We also note that within the ESKD cohort, people on dialysis use more healthcare services than those with transplants. Dialysis patients appear to see nephrologists less frequently than transplant recipients, but we speculate that this may be because the nephrology visits that occur during dialysis sessions are not always captured in the medical claims. Relative risks for nephrologist visits were not calculated because they are rare among people without CKD, our reference group.

The hospitalization rate for Manitobans with ESKD (867 hospitalizations per 1,000) and the average number of days spent in hospital (8.32 days per person) are dramatically higher than the Manitoba average (86 hospitalizations per 1,000; 0.567 days per person) (Fransoo et al., 2013). Our rates are comparable to values reported in the literature for ESKD cohorts (1.8 hospitalizations per person; 13 days per person) (Brophy, Daniel, Gitlin, & Mayne, 2010). Hospitalization rates often increase within the first year of ESKD diagnosis (Metcalfe, Khan, Prescott, Simpson, & Macleod, 2003; Teo, Ma, Xu, Li, & Lee, 2010) and may remain high due to complications related to dialysis or kidney transplant such as infections, catheter insertion, anemia, cardiovascular symptoms and other kidney-related comorbidities (Brophy et al., 2010; Metcalfe et al., 2003; Teo et al., 2010).

Table 4.4: Healthcare Use by Adults in End Stage Kidney Disease Patient Cohorts

Age- and sex-adjusted rates, 95% confidence intervals, 2011/12

Indicators		No CKD	ESKD by Treatment Type		
			Dialysis	Kidney Transplant	All ESKD
Inpatient Hospitalizations (per 1,000)	**Rate**	78.88 (78.30-79.46)	1,066.63 (734.53-1,548.86)	539.97 (367.99-792.32)	806.01 (556.51-1,167.35)
	Relative Risk	reference	**13.52 (9.31-19.64)**	**6.85 (4.67-10.04)**	**10.22 (7.06-14.80)**
Days in Hospital (per person)	**Rate**	0.54 (0.54-0.54)	11.59 (7.20-18.65)	4.90 (3.03-7.91)	8.28 (5.13-13.36)
	Relative Risk	reference	**21.55 (13.39-34.67)**	**9.10 (5.64-14.70)**	**15.39 (9.54-24.83)**
Ambulatory Physician Visits (per person)	**Rate**	4.55 (4.55-4.56)	8.99 (7.74-10.45)	12.40 (10.67-14.41)	10.68 (9.13-12.50)
	Relative Risk	reference	**1.98 (1.70-2.29)**	**2.72 (2.34-3.17)**	**2.35 (2.01-2.75)**
Nephrologist Visits (per person)	**Rate**	0.00 (0.00-0.00)	1.08 (0.69-1.70)	5.63 (3.61-8.80)	3.38 (1.88-6.08)
Specialist Visits (per person)	**Rate**	1.04 (1.04-1.04)	3.70 (2.95-4.65)	3.28 (2.61-4.13)	3.49 (2.86-4.27)
	Relative Risk	reference	**3.55 (2.83-4.46)**	**3.15 (2.50-3.96)**	**3.35 (2.74-4.09)**

bolded values indicate statistically significant difference from the No CKD group

Note: relative risk for nephrologist visits not calculated due to low rate for reference group

Characteristics of Adults with Chronic Kidney Disease

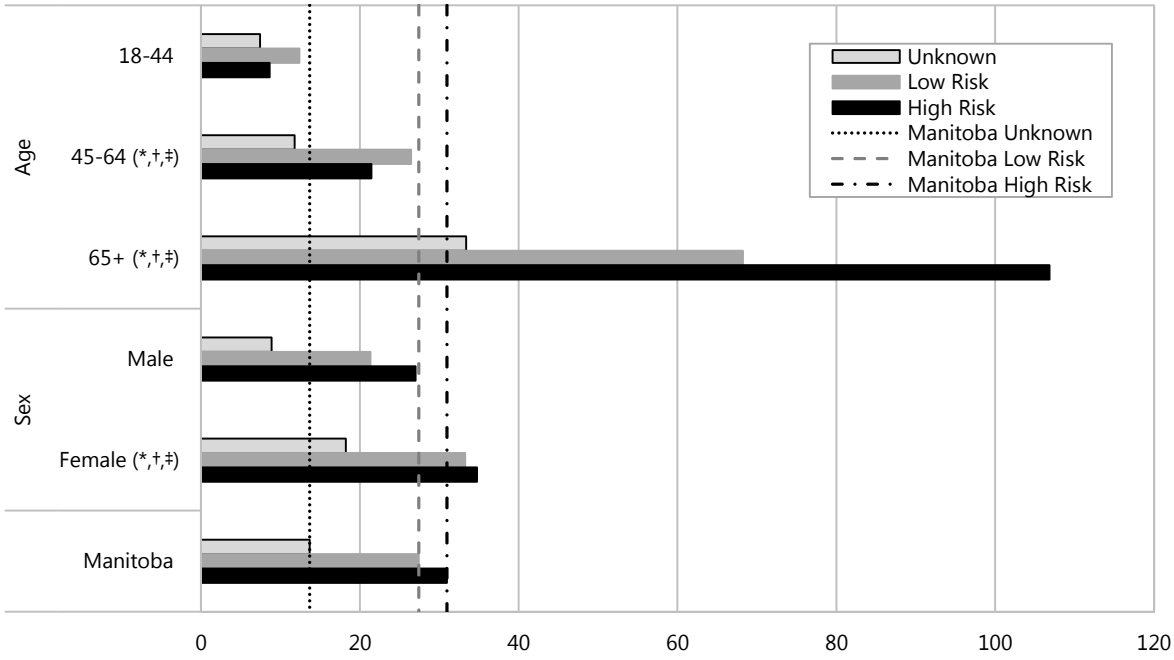
In this section, we describe the characteristics of Manitoba adults with CKD according to their risk of progression to kidney failure. As detailed in Chapter 3, we categorized people by severity of disease based on two laboratory tests (estimated glomerular filtration rate (eGFR) and proteinuria). Recall that this method did not categorize all individuals with CKD because laboratory data are not available in all areas of the province and because some at-risk people are not screened; people defined as having CKD through administrative data but lacking laboratory data comprise the unknown-risk group. We describe the age, sex, economic and regional distribution of the CKD cohort captured with administrative and/or laboratory data, as well as rates of health indicators and healthcare use associated with the cohort.

Sociodemographic Characteristics

Figure 4.3 shows rates of CKD in adults by age, sex and risk for progressing to ESKD. The rates of CKD are highest among the older population (65 years and older) for all risk groups, and particularly for those at high risk, compared to the middle-aged and young adult populations. Women have higher rates of CKD than men across all risk groups.

Figure 4.3: Adults in Risk Groups of Chronic Kidney Disease by Age and Sex

Rates per 1,000 residents aged 18+ on March 31, 2012

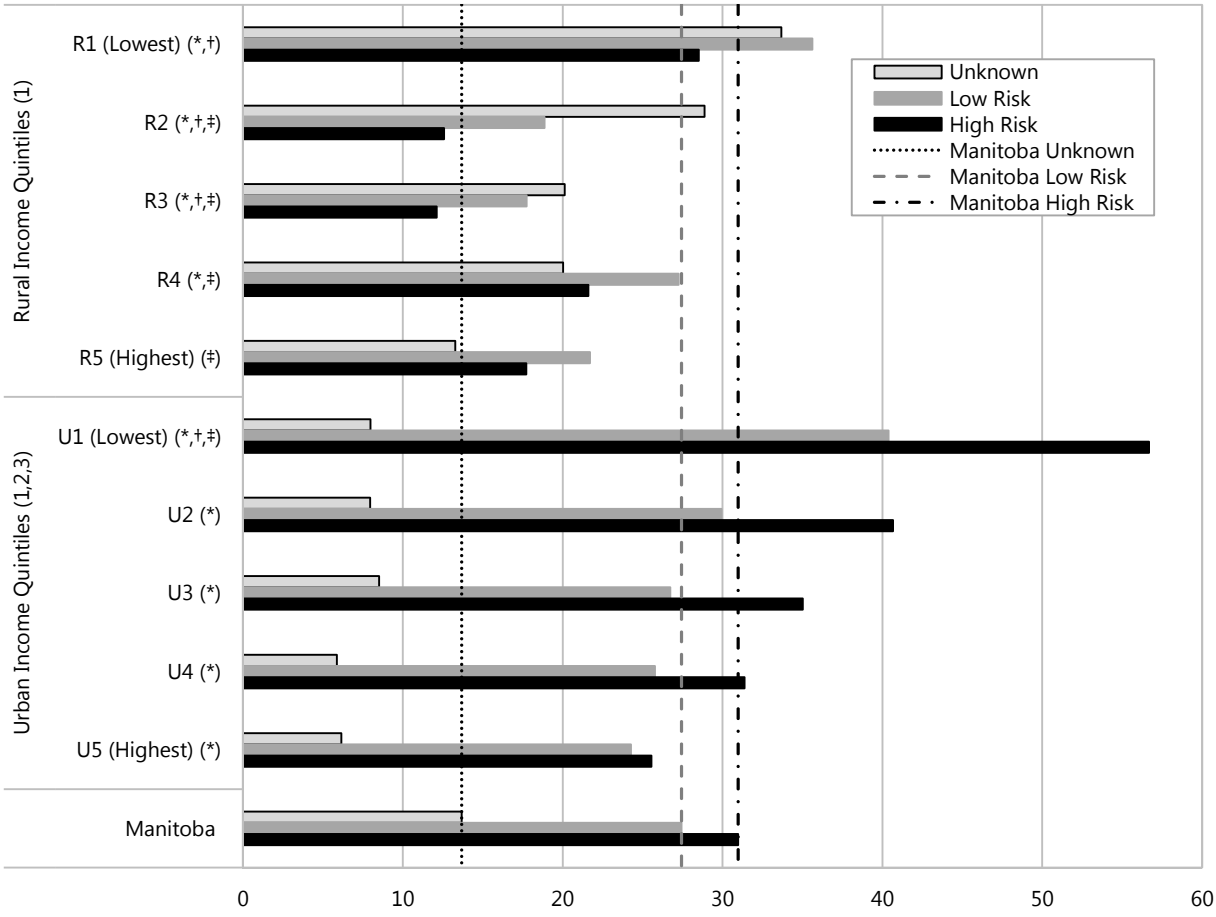


* indicates area's Unknown Risk rate was statistically different from reference group (Age: 18-44 or Sex: Male)
† indicates area's Low Risk CKD rate was statistically different from reference group (Age: 18-44 or Sex: Male)
‡ indicates area's High Risk CKD rate was statistically different from reference group (Age: 18-44 or Sex: Male)

Figure 4.4 shows risk of progression to ESKD by income quintile. The lowest income quintiles, areas where people have the lowest income, have higher rates of CKD, but we note differences between urban and rural areas. In rural areas, rates of all three risk groups are higher in the lowest income quintile compared to higher income quintiles. The unknown-risk group has a clear income gradient; however, the gradient is less pronounced in the low- and high-risk groups. The reverse is true in the urban areas, where an income gradient is clear for the low- and high-risk groups but less pronounced in the group of unknown risk. These differences may reflect the availability of data, since we know there is better coverage of laboratory data in urban than in rural areas of the province (see Chapter 2).

Figure 4.4: Adults in Risk Groups of Chronic Kidney Disease by Income Quintile

Age- and sex-adjusted rates per 1,000 residents aged 18+ on March 31, 2012



* indicates area's Unknown Risk rate was statistically different from Manitoba
† indicates area's Low Risk CKD rate was statistically different from Manitoba
‡ indicates area's High Risk CKD rate was statistically different from Manitoba
1,2,3 indicates linear trend of Urban or Rural Income Quintiles: 1 - Unknown Risk, 2 - Low Risk CKD, 3 - High Risk CKD

Physical Health

Table 4.5 shows the prevalence of co-existing medical conditions among people with CKD, by their risk of progression to ESKD. Across the risk groups, rates of medical conditions are considerably higher among people with CKD than among those without CKD. The pattern that emerges is that rates of comorbid medical conditions increase with severity of CKD. For example, relative to those without CKD, rates of hypertension are higher among people classified with CKD at lower risk of progressing to ESKD (relative risk (RR): 2.04) and higher still among people with CKD at higher risk (RR: 2.87). Similarly, rates of diabetes and lower-limb amputation are higher among all groups of CKD compared to those without CKD, but highest among people with high risk of progressing to ESKD.

People in the unknown-risk group are likely at an earlier stage of CKD and being followed in the community by primary care providers. This group has lower rates of diabetes compared with the low-risk and high-risk groups, suggesting that the unknown-risk group is comprised of people without diabetes-related kidney disease. This group also appears to have a higher rate of hypertension compared to those without CKD, but this difference is not statistically significant.

Comorbidity among adults with CKD is generally lower than among those with ESKD, as shown earlier (Table 4.1). Nonetheless, the disease burden in the CKD cohort is much higher than the average for Manitoba for all the indicators we examined (Fransoo et al., 2013). In the high-risk CKD group alone, the rate of stroke is 13 times higher than the Manitoba average in 2011/12, and rate of diabetes is five times higher than the Manitoba average. These rates and the pattern of increasing comorbidity with increasing risk of progression are consistent with findings in other studies on CKD (Arora et al., 2013; Foster et al., 2013).

Table 4.5: Physical Health of Adults in Chronic Kidney Disease Patient Cohorts

Age- and sex-adjusted prevalence, 95% confidence intervals

Indicators		No CKD	CKD by Risk of Progression to ESKD		
			Unknown	Low	High
Diabetes (%) (2009/10-2011/12)	**Prevalence**	7.02 (6.96-7.07)	12.44 (8.64-17.92)	28.59 (19.80-41.30)	37.10 (25.62-53.73)
	Relative Risk	reference	**1.77 (1.23-2.55)**	**4.08 (2.82-5.89)**	**5.29 (3.65-7.66)**
Hypertension (%) (2011/12)	**Prevalence**	21.45 (21.36-21.55)	31.06 (19.91-48.45)	43.84 (28.01-68.61)	61.46 (39.06-96.72)
	Relative Risk	reference	1.45 (0.93-2.26)	**2.04 (1.31-3.20)**	**2.87 (1.82-4.51)**
Ischemic Heart Disease (%) (2007/08-2011/12)	**Prevalence**	4.72 (4.68-4.77)	7.30 (4.29-12.43)	12.22 (7.20-20.74)	24.55 (14.25-42.27)
	Relative Risk	reference	1.55 (0.91-2.63)	**2.59 (1.52-4.39)**	**5.20 (3.02-8.95)**
Acute Myocardial Infarction (%) (2007/08-2011/12)	**Prevalence**	0.99 (0.96-1.01)	1.10 (0.63-1.93)	2.29 (1.37-3.81)	5.29 (3.12-8.97)
	Relative Risk	reference	1.12 (0.64-1.96)	**2.32 (1.40-3.87)**	**5.37 (3.16-9.11)**
Congestive Heart Failure (%) (2009/10-2011/12)	**Prevalence**	1.38 (1.35-1.41)	4.51 (2.47-8.26)	5.19 (2.88-9.35)	25.09 (13.64-46.17)
	Relative Risk	reference	**3.27 (1.79-5.98)**	**3.76 (2.09-6.77)**	**18.17 (9.88-33.43)**
Stroke (%) (2007/08-2011/12)	**Prevalence**	0.41 (0.39-0.43)	0.92 (0.51-1.67)	2.01 (1.17-3.45)	5.59 (3.13-9.98)
	Relative Risk	reference	**2.26 (1.25-4.10)**	**4.94 (2.88-8.47)**	**13.72 (7.68-24.50)**
Atrial Fibrillation (%) (2009/10-2011/12)	**Prevalence**	1.92 (1.89-1.94)	3.09 (2.20-4.33)	5.03 (3.64-6.94)	9.72 (6.97-13.57)
	Relative Risk	reference	**1.61 (1.15-2.26)**	**2.63 (1.90-3.63)**	**5.08 (3.64-7.09)**
Lower-Limb Amputation Among Diabetics (%) (2007/08-2011/12)	**Prevalence**	0.33 (0.29-0.38)	0.79 (0.44-1.42)	0.77 (0.52-1.13)	2.65 (1.83-3.84)
	Relative Risk	reference	**2.37 (1.32-4.27)**	**2.30 (1.55-3.42)**	**8.00 (5.53-11.57)**

bolded values indicate statistically significant difference from the No CKD group

Mental Health

Table 4.6 shows rates and relative risks of mental disorders by CKD risk group. Higher rates of mental disorders are found among people with CKD than those without CKD. Rates of dementia and suicide or suicide attempts are particularly high among people with high-risk CKD (3.76 and 4.96 times higher, respectively, than in people without CKD). As with physical comorbidities, we found a similar pattern of increasing rates of mental disorders with increasing risk of CKD progression. For example, 5.12% of people without CKD have been diagnosed with substance abuse, compared to 8.16% of people with CKD of unknown risk, 9.92% of those at lower risk of progressing to ESKD and 11.94% of those at high risk.

Previous research has also found a high prevalence of mental disorders in CKD cohorts (Lee et al., 2013; Peng et al., 2013; Stasiak et al., 2014). Notably, the rates of mood and anxiety disorders and substance abuse are higher among people with CKD than the general Manitoba population (Fransoo et al., 2013). The relationship between substance abuse and CKD that we observed is not found across other studies (Akkina et al., 2012; Taal & Brenner, 2006). Systematic reviews of the literature suggest that CKD might be a risk factor for developing dementia and other cognitive issues (Elias, Dore, & Davey, 2013; Etgen, Chonchol, Förstl, & Sander, 2012).

It is not surprising to find an association between CKD and mental disorders given the challenging physical health problems faced by those with CKD. We speculate that the same underlying socioeconomic conditions that predispose people to CKD, including the stresses of poverty, unemployment or poor housing, also contribute to mental health problems. We note that the relative risks for mental health problems are higher for those with CKD than for those with ESKD (Table 4.2). This is different than the pattern we found for comorbid medical conditions and difficult to explain given that ESKD is a more severe form of the disease.

Table 4.6: Mental Disorders in Adults in Chronic Kidney Disease Patient Cohorts

Age- and sex-adjusted rates and prevalence, 95% confidence intervals

Indicators		No CKD	CKD by Risk of Progression to ESKD		
			Unknown	Low	High
Mood and Anxiety Disorders (%) (2007/08-2011/12)	**Prevalence**	22.38 (22.28-22.47)	29.85 (27.77-32.08)	35.89 (33.58-38.36)	37.02 (34.49-39.74)
	Relative Risk	reference	**1.33 (1.24-1.43)**	**1.60 (1.50-1.71)**	**1.65 (1.54-1.78)**
Dementia (%) (2007/08-2011/12)	**Prevalence**	3.91 (3.84-3.99)	11.82 (9.70-14.39)	10.11 (8.41-12.16)	14.70 (12.16-17.77)
	Relative Risk	reference	**3.02 (2.48-3.68)**	**2.58 (2.15-3.11)**	**3.76 (3.11-4.54)**
Any Disorder* (%) (2007/08-2011/12)	**Prevalence**	25.31 (25.20-25.41)	33.95 (31.64-36.43)	39.73 (37.21-42.42)	41.90 (39.08-44.93)
	Relative Risk	reference	**1.34 (1.25-1.44)**	**1.57 (1.47-1.68)**	**1.66 (1.54-1.78)**
Suicide and Suicide Attempts (per 10,000 people-years) (2009-2012)	**Rate**	5.24 (4.98-5.50)	14.13 (9.23-21.62)	14.29 (9.16-22.28)	25.96 (16.87-39.95)
	Relative Risk	reference	**2.70 (1.76-4.13)**	**2.73 (1.75-4.25)**	**4.96 (3.22-7.63)**
Substance Abuse (%) (2007/08-2011/12)	**Prevalence**	5.12 (5.08-5.17)	8.16 (6.50-10.25)	9.92 (7.96-12.37)	11.94 (9.54-14.95)
	Relative Risk	reference	**1.59 (1.27-2.00)**	**1.94 (1.55-2.41)**	**2.33 (1.86-2.92)**

bolded values indicate statistically significant difference from the No CKD group

* includes mood and anxiety disorders, personality disorder, schizophrenia, and substance abuse

Use of Prescription Drugs

Table 4.7 shows rates and relative risks of prescription drug use by CKD risk group. The rates of prescriptions dispensed increase with the risk of CKD progression. For example, among people with an anti-hypertensive drug prescription, only 18.8% had no CKD, compared to 28.6% of people with CKD of unknown risk, 41.3% in the early stages of CKD (low risk of progression), 59.4% at the later stages of CKD (high-risk group) and 84.5% of people in ESKD (Table 4.3). Those with high-risk CKD have more than twice the number of drugs prescribed than those without CKD. The higher number of prescription medications indicates poor health status and multiple comorbidities in people with CKD.

The use of ACE inhibitors and ARBs is also important to examine, as these medications have been shown to decrease the risk of progressing to kidney failure among people who have CKD and proteinuria but no diabetes (James et al., 2010). The high rates of ACE inhibitors and ARB prescriptions in the CKD cohort indicate good prescribing practices in Manitoba. Among people with diabetes, taking anti-hypertensives is common, and the differences in ACE inhibitor and ARB prescribing between the CKD and no-CKD groups are less pronounced. This could be attributed to the widespread good prescribing practices for diabetes management, including ACE inhibitors for high blood pressure, among people without CKD (James et al., 2010). ACE inhibitor and ARB prescribing is often higher in patients with CKD who have visited a nephrologist or have other medical conditions that are managed with these drugs (Philipneri et al., 2008).

Table 4.7: Use of Prescription Drugs by Adults in Chronic Kidney Disease Patient Cohorts

Age- and sex-adjusted rates, 95% confidence intervals, 2011/12

Indicators		No CKD	CKD by Risk of Progression to ESKD		
			Unknown	Low	High
Anti-Hypertensive Drug Prescriptions (%)	**Rate**	18.78 (18.69-18.87)	28.56 (17.59-46.37)	41.29 (25.31-67.35)	59.39 (36.16-97.53)
	Relative Risk	reference	1.52 (0.94-2.47)	**2.20 (1.35-3.59)**	**3.16 (1.93-5.19)**
ACE & ARB Prescriptions (%)	**Rate**	14.01 (13.93-14.09)	21.26 (12.71-35.55)	32.51 (19.34-54.65)	44.79 (26.45-75.86)
	Relative Risk	reference	1.52 (0.91-2.54)	**2.32 (1.38-3.90)**	**3.20 (1.89-5.42)**
ACE & ARB Prescriptions Among Diabetics (%)	**Rate**	56.18 (55.60-56.77)	69.90 (57.47-85.02)	74.91 (62.38-89.95)	79.47 (65.95-95.77)
	Relative Risk	reference	**1.24 (1.02-1.51)**	**1.33 (1.11-1.60)**	**1.41 (1.17-1.70)**
Different Prescribed Drugs (per person)	**Rate**	3.99 (3.98-1.00)	5.84 (5.17-1.00)	6.76 (5.99-1.00)	8.66 (7.66-1.00)
	Relative Risk	reference	**1.47 (1.30-1.66)**	**1.70 (1.50-1.92)**	**2.17 (1.92-2.45)**

bolded values indicate statistically significant difference from the No CKD group

Healthcare Services Use

Health services use is considerably higher among people with CKD than among those without CKD (Table 4.8). Although the rates are lower than for people with ESKD (Table 4.4), a similar pattern is evident for the CKD cohort, with rates of healthcare service use increasing with increasing risk of disease progression. For example, relative to those without CKD, rates of inpatient hospitalization are higher among people with CKD at lower risk of progression (RR: 2.97) and highest among people with more advanced CKD (RR: 6.12). While we observe that people with high risk of progressing to ESKD have more visits per person to a nephrologist than any other CKD group, we felt that this high risk group had lower rates than expected. This rate only included ambulatory (out-patient) nephrology visits and these high risk patients may be seen by a nephrologist while in hospital.

The rate of inpatient hospitalizations of Manitobans with CKD is more than double the average reported for Manitoba in 2011/12 (Fransoo et al., 2013). The number of days spent in hospital by people in the CKD cohort is also longer than the average length of hospital stay in Manitoba for both short and long stays. These trends are consistent with other studies showing increased risk of hospitalization among CKD patients for complications such as anemia and acute cardiovascular conditions, compared with patients without CKD (Daratha et al., 2012). Mix et al. (2003) also found evidence of increasing hospitalization rates as the disease advanced, with a peak after ESKD treatment began.

The rates of physician visits for Manitobans with CKD are comparable to those reported by Zhao et al. (2008), who showed that 50% of people with CKD visited non-nephrologist physicians up to four times within one to two years before they needed to start dialysis. Navaneethan, Aloudat, & Singh (2008) found evidence that some of the factors associated with late referral of patients with CKD to nephrologists include low income, low education level, multiple comorbidities, and old age. Additionally, studies of the CKD management and primary care models demonstrate that because of the increased number of people diagnosed with CKD, there might be a shortage of consulting nephrologists (Mandell, 2014; Poulos & Antonsen, 2005); however, diagnosis of the disease in its early stages does not always require a specialist consultation (Mandell, 2014).

Table 4.8: Healthcare Use by Adults in Chronic Kidney Disease Patient Cohorts

Age- and sex-adjusted rates, 95% confidence intervals, 2011/12

Indicators		No CKD	CKD by Risk of Progression to ESKD		
			Unknown	Low	High
Inpatient Hospitalizations (per 1,000)	**Rate**	78.88 (78.30-79.46)	172.60 (113.49-262.48)	234.50 (154.12-356.79)	482.94 (316.50-736.93)
	Relative Risk	reference	**2.19 (1.44-3.33)**	**2.97 (1.95-4.52)**	**6.12 (4.01-9.34)**
Days in Hospital (per person)	**Rate**	0.54 (0.54-0.54)	1.55 (0.91-2.66)	1.97 (1.14-3.39)	5.82 (3.36-10.09)
	Relative Risk	reference	**2.89 (1.68-4.95)**	**3.66 (2.13-6.30)**	**10.82 (6.24-18.75)**
Ambulatory Physician Visits (per person)	**Rate**	4.55 (4.55-4.56)	6.14 (5.13-7.35)	8.44 (7.05-10.11)	10.31 (8.61-12.35)
	Relative Risk	reference	**1.35 (1.13-1.62)**	**1.85 (1.55-2.22)**	**2.27 (1.89-2.71)**
Nephrologist Visits (per person)	**Rate**	0.00 (0.00-0.00)	0.02 (0.01-0.05)	0.03 (0.02-0.07)	0.25 (0.13-0.50)
Specialist Visits (per person)	**Rate**	1.04 (1.04-1.04)	0.88 (0.70-1.11)	2.47 (1.97-3.11)	3.40 (2.71-4.28)
	Relative Risk	reference	0.85 (0.67-1.07)	**2.37 (1.89-2.98)**	**3.27 (2.60-4.10)**

bolded values indicate statistically significant difference from the No CKD group

Note: Relative risk for nephrologist visits not shown due to rate of zero for reference group

CHAPTER 5: CHARACTERISTICS OF CHILDREN WITH END STAGE KIDNEY DISEASE AND CHRONIC KIDNEY DISEASE

As with adults, understanding the characteristics of children with end stage kidney disease (ESKD) and chronic kidney disease (CKD) at earlier stages of the disease provides a clearer picture of the overall CKD spectrum, and is crucial in planning prevention and early intervention strategies and treatment services for this population. In this chapter, we will describe the sociodemographic characteristics of children aged 0 to 17 years with ESKD and CKD, comorbid medical conditions, diagnosed mental disorders, healthcare use and medication use. As outlined in Chapters 2 and 3, these characteristics are described in four distinct groups: CKD with low risk of progressing to ESKD, CKD with high risk of progressing, CKD with unknown risk (no laboratory data) and ESKD. When examining comorbidity and healthcare use, we compare the CKD and ESKD cohorts to children without known CKD (no-CKD group). As there are only 17 children in the ESKD cohort, relative risks for this group must be interpreted with caution.

Key Findings

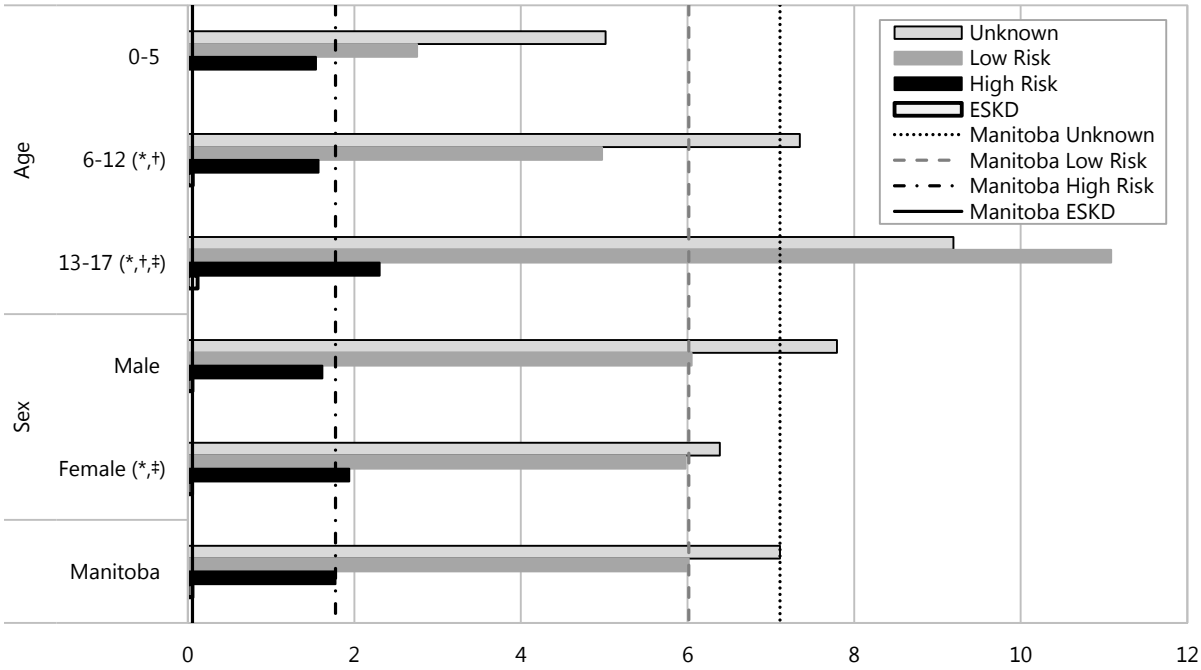
- Higher rates of CKD and ESKD are found among adolescents than among children under 12 years old.
- No income gradient was evident across both rural and urban areas.
- Compared to children without CKD, those with CKD have higher rates of diabetes, hypertension, ischemic heart disease, mood and anxiety disorders, developmental disabilities, substance abuse, attempted suicide, and at least one mental disorder. Relative risks range from 2.32 for having at least one mental disorder to 77.70 for hypertension.
- Compared to children without CKD, those with CKD have higher rates of hospitalization and more physician visits, are dispensed more medications and are more likely to be taking anti-hypertensive medications. Relative risks range from 1.70 for number of prescription medications to 79.29 for anti-hypertensive mediations.
- Children with ESKD have the highest rates of comorbid disorders and healthcare services use compared to the CKD groups. Half of the children with ESKD have hypertension and 54% have at least one mental disorder. The inpatient hospitalization rate for children with ESKD is 1,630 hospitalizations per 1,000 children.

Sociodemographic Characteristics

Rates of CKD and ESKD among children in Manitoba, by age, sex and severity of disease, are presented in Figure 5.1. We sub-divided children into three age groups: under five years (infant/preschool), six to 12 years (young school-age) and 13 to 17 years (adolescent). The youngest age group accounts for the smallest proportion of each CKD group (15.3%–29.0%), and the rate of CKD increases with increasing age (Figure 5.1). This difference is most marked in the low-risk CKD group where adolescents account for 53.7% of the cohort. The children with ESKD (and on renal replacement therapy (RRT)) are in the young school-age (41.2%) and adolescent age groups (58.8%). There were no children less than six years old with ESKD in Manitoba during the study period.

Figure 5.1: Children in Risk Groups of Chronic Kidney Disease and End Stage Kidney Disease by Age and Sex

Rate per 1,000 residents aged 0-17 on March 31, 2012

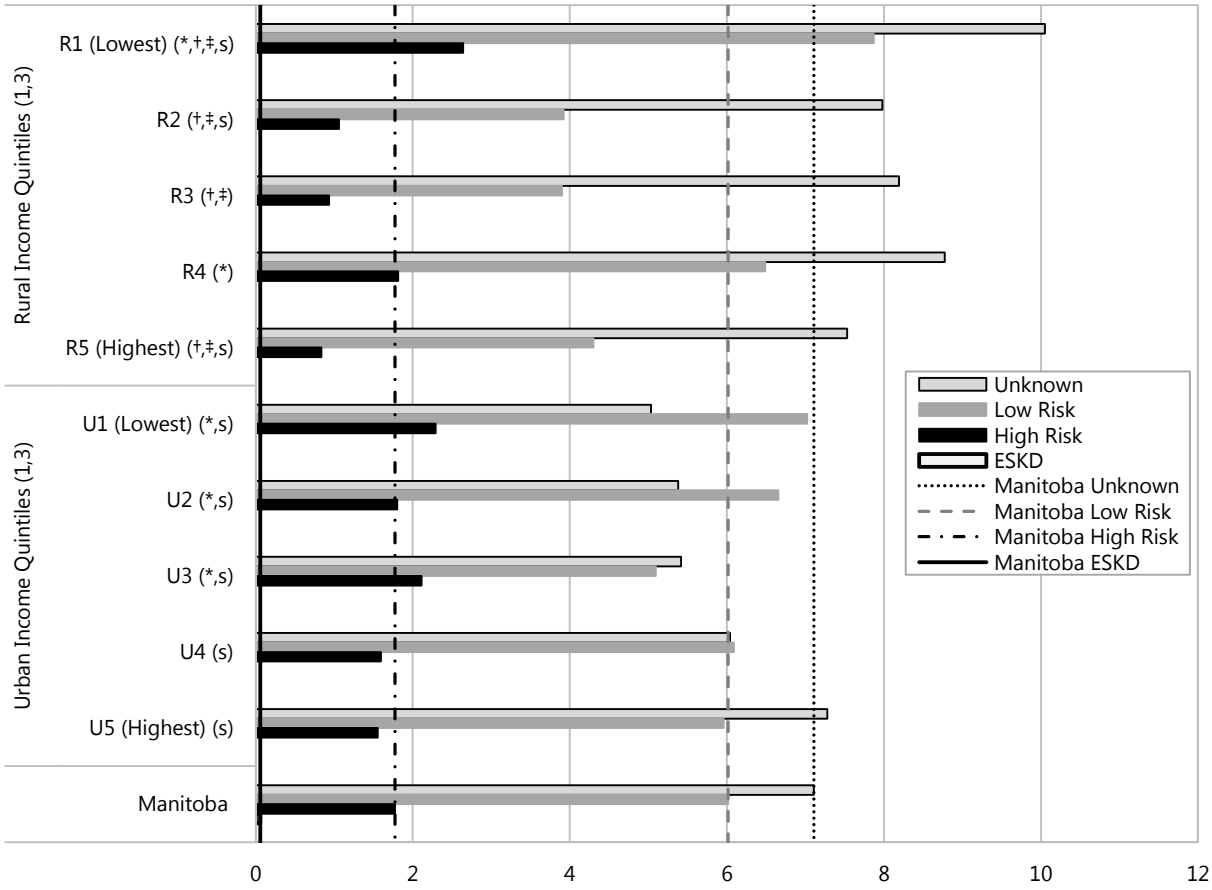


* indicates area's Unknown Risk rate was statistically different from reference group (Age: 0-5 or Sex: Male)
† indicates area's Low Risk CKD rate was statistically different from reference group (Age: 0-5 or Sex: Male)
‡ indicates area's High Risk CKD rate was statistically different from reference group (Age: 0-5 or Sex: Male)
Note: rates of ESKD are below 0.2 per 1,000 children

Across urban income quintiles, the gradient we observed for adults is not evident for children (Figure 5.2). We note a higher percentage of children across the spectrum of CKD in the lowest rural income quintile (28.7%–42.2%) relative to other rural income quintiles. The higher rates in low-income rural areas may reflect the higher rates of CKD among children in Indigenous populations (Manitoba Renal Program (MRP), 2013), which are over-represented in low-income rural areas in Manitoba (Martens et al., 2002).

Figure 5.2: Children in Risk Groups of Chronic Kidney Disease and End Stage Kidney Disease by Income Quintile

Age- and sex-adjusted rates per 1,000 residents aged 0-17 on March 31, 2012



* indicates area's Unknown Riskrate was statistically different from Manitoba
† indicates area's Low Risk CKD rate was statistically different from Manitoba
‡ indicates area's High Risk CKD rate was statistically different from Manitoba
s indicates ESKD rates are suppressed due to small numbers
1,2,3 indicates linear trend of Urban or Rural Income Quintiles: 1 - Unknown Risk 2 - Low Risk CKD 3 - High Risk CKD
Note: rates of ESKD are crude and below 0.1 per 1,000 children

Physical Health

Table 5.1 shows rates and relative risk of diabetes and hypertension in children with CKD and ESKD, compared to those without CKD. Sample sizes for cardiovascular comorbidities in Manitoba children were too small to allow them to be included in this report. Although children have risk factors for significant cardiovascular outcomes that manifest in early adulthood (Oh et al., 2002), actual numbers of these outcomes remain low during childhood (Mitsnefes, Laskin, Dahhou, Zhang, & Foster, 2013).

The diabetes prevalence is significantly higher in children with low-risk CKD (RR: 21.09) and high-risk CKD (RR: 29.18) compared to children without CKD. In contrast, the diabetes rate in the group with unknown risk of progression to ESKD is not significantly different from the group of children without CKD.

Rates of hypertension are high among all CKD groups. The relative risks of hypertension, compared with the no-CKD population, are 2.75 in the unknown-risk group, 34.49 in the low-risk and 77.70 in the high-risk CKD group. The relative risks are even higher in young children from birth to five years old (low-risk CKD, RR: 81.57; high-risk CKD, RR: 146.4), since rates in children in that age group without CKD, our reference group, are extremely low.

Population-based screening for hypertension in children has shown elevated blood pressure in 2.6% of boys and 3.4% of girls aged 8 to 17 (Ostchega et al., 2009). The rates we identified with administrative data are significantly lower (4.73 per 1,000 population for 6- to 17-year-olds without CKD). This suggests that hypertension may be inadequately diagnosed in Manitoba children. The thresholds for diagnosis of hypertension in children are complex, based on age and height percentile (National High Blood Pressure Education Program, 2004). It is possible that primary care providers are not aware of the diagnostic criteria, and this may be an important priority for knowledge translation.

If risk factors for CKD (such as diabetes) begin in early childhood, it is reasonable to suppose that the lifelong risk for CKD and progression to ESKD is increased. This is supported by a recent study in adults with diabetes, which revealed a higher lifelong risk of ESKD in young adults with diabetes, compared with later onset of diabetes (Jiang, Osgood, Lim, Stang, & Dyck, 2014). The increased risk of ESKD is due to a decreased competing risk with mortality in younger populations. A strategy to monitor early risk factors for CKD and early onset CKD in childhood is particularly relevant in Manitoba, which has the highest rates of incident youth onset type 2 diabetes in Canada (Amed et al., 2010), as well as the highest proportion of Indigenous people outside of the North West Territories, Nunavut and the Yukon (Statistics Canada, 2011). This population has a significantly increased risk for both congenital and acquired kidney disease in childhood (Bulloch, Postl, & Ogborn, 1996; Samuel et al., 2012).

Table 5.1: Physical Health of Children in Patient Cohorts

Age- and sex-adjusted prevalence, 95% confidence intervals

Indicators		No CKD	CKD by Risk of Progression to ESKD			All ESKD
			Unknown	Low	High	
Diabetes (%) (2009/10-2011/12)	**Prevalence**	0.25 (0.23-0.26)	0.26 (0.11-0.57)	5.19 (4.26-6.32)	7.18 (5.22-9.87)	s
	Relative Risk	reference	1.04 (0.47-2.33)	**21.09 (17.32-25.68)**	**29.18 (21.21-40.14)**	s
Hypertension 0-17 yrs (%) (2011/12)	**Prevalence**	0.36 (0.34-0.38)	0.99 (0.64-1.52)	12.42 (10.33-14.92)	27.98 (23.30-33.60)	55.46 (31.16-98.73)
	Relative Risk	reference	**2.75 (1.79-4.21)**	**34.49 (28.70-41.44)**	**77.70 (64.69-93.32)**	**154.03 (86.53-274.18)**
Hypertension 0-5 yrs (%) (2011/12)	**Prevalence**	0.14 (0.11-0.16)	s	11.09 (7.45-16.52)	19.90 (13.38-29.60)	0.00 (0.00-0.00)
	Relative Risk	reference	s	**81.57 (54.79-121.46)**	**146.35 (98.38-217.70)**	0.00 (0.00-0.00)
Hypertension 6-17 yrs (%) (2011/12)	**Prevalence**	0.47 (0.44-0.50)	1.14 (0.71-1.81)	14.70 (12.68-17.05)	32.71 (26.95-39.69)	70.16 (39.69-124.00)
	Relative Risk	reference	**2.40 (1.50-3.83)**	**31.08 (26.80-36.04)**	**69.14 (56.97-83.90)**	**148.30 (83.91-262.12)**

bolded values indicate statistically significant difference from the No CKD group

s indicates supressed values due to small numbers

Mental Health

We examined mental health comorbidities for children with CKD and ESKD, as we did for adults, because of the growing body of literature linking physical and mental health (Hedayati, Minhajuddin, Toto, Morris, & Rush, 2009; Katon & Ciechanowski, 2002; Patten et al., 2005), and the recognized burden of chronic illness care on patients and families (Sav et al., 2013). We found significant increases in all mental health indicators for all CKD groups, compared with children without CKD (Table 5.2). The prevalence of mood and anxiety disorders are four times higher in the low- and high-risk CKD groups and 15 times higher in children requiring renal replacement therapy (RRT), affecting 70% of children with ESKD; the prevalence in children with unknown risk of CKD progression is similar to children without CKD. The prevalence of developmental disabilities and substance abuse are also higher in children with low-risk and high-risk CKD when compared with children without CKD. The rates of suicide and suicide attempts are significantly higher in children with CKD or ESKD, but rare in children with unknown risk of progression.

The link between physical and mental health in children with CKD has not previously been examined in detail. Adult studies have shown increased rates of depression and anxiety (Knowles, Swan, Salzberg, Castle, & Langham, 2014; Stasiak et al., 2014) in individuals with CKD, and the association is hypothesized to be secondary to the impact of CKD treatments on quality of life, such as significant dietary restrictions. However, small cross-sectional studies have identified higher rates of depression and anxiety in some pediatric CKD populations (Kilis-Pstrusinska et al., 2013; Kogon et al., 2013). It is clear from our results and from previous studies that psychological factors should be evaluated and treated in adults and children with CKD. What remains to be determined is the impact of these negative psychological factors on risk for progression or cardiovascular outcomes.

Table 5.2: Mental Disorders in Children in Patient Cohorts

Age- and sex-adjusted rates and prevalence, 95% confidence intervals

Indicators		No CKD	CKD by Risk of Progression to ESKD			All ESKD
			Unknown	Low	High	
Mood and Anxiety Disorders (%) (2007/08-2011/12)	**Prevalence**	3.35 (3.27-3.44)	3.73 (2.67-5.22)	14.57 (11.26-18.86)	12.12 (8.39-17.51)	50.84 (26.78-96.48)
	Relative Risk	reference	1.11 (0.80-1.56)	**4.34 (3.36-5.62)**	**3.61 (2.50-5.22)**	**15.15 (7.98-28.76)**
Developmental Disability (%) (2007/08-2011/12)	**Prevalence**	0.86 (0.83-0.90)	0.93 (0.60-1.45)	4.43 (3.53-5.57)	4.24 (2.76-6.51)	s
	Relative Risk	reference	1.08 (0.70-1.68)	**5.14 (4.09-6.45)**	**4.91 (3.19-7.54)**	s
Attention–Deficit Hyperactivity Disorder (%) (2007/08-2011/12)	**Prevalence**	6.33 (6.22-6.44)	7.51 (6.28-8.97)	12.42 (10.73-14.37)	10.77 (7.76-14.93)	0.00 (0.00-0.00)
	Relative Risk	reference	1.19 (0.99-1.42)	**1.96 (1.70-2.27)**	**1.70 (1.23-2.36)**	0.00 (0.00-0.00)
Any Disorder* (%) (2007/08-2011/12)	**Prevalence**	9.07 (8.93-9.20)	10.17 (7.09-14.58)	22.02 (15.61-31.06)	21.03 (14.04-31.50)	53.88 (26.75-100.00)
	Relative Risk	reference	1.12 (0.78-1.61)	**2.43 (1.72-3.42)**	**2.32 (1.55-3.47)**	**5.94 (2.95-11.97)**
Suicide and Suicide Attempts (per 10,000 person-years) (2009-2012	**Rate**	10.21 (9.08-11.34)	s	62.97 (41.14-96.38)		
	Relative Risk	reference	s	**6.17 (4.03-9.44)**		
Substance Abuse (%) (2007/08-2011/12)	**Prevalence**	0.98 (0.91-1.04)	1.56 (0.88-2.75)	5.41 (4.14-7.07)	3.97 (2.06-7.66)	0.00 (0.00-0.00)
	Relative Risk	reference	1.59 (0.90-2.82)	**5.54 (4.24-7.24)**	**4.06 (2.11-7.84)**	0.00 (0.00-0.00)

bolded values indicate statistically significant difference from the No CKD group

* includes attention-deficit hyperactivity disorder, developmental disability, mood and anxiety disorders, schizophrenia, and substance abuse

s indicates suppressed values due to small numbers

Note: rates of suicide and suicide attempts are shown for low risk, high risk, and ESKD groups combined due to small numbers

Use of Prescription Medication

Children in the low-risk and high-risk CKD groups have rates of use of anti-hypertensive drugs 28 and 79 times higher, respectively, than children without CKD (Table 5.3). This is not surprising, given the high rates of high blood pressure among children with CKD, as seen earlier in this chapter and elsewhere (Mitsnefes et al., 2010). ACE inhibitors and ARBs, often the drugs of choice for treatment of hypertension in children with CKD, are used in 6% of the low-risk CKD group and 16% of the high-risk CKD group. However, as the respective rates of hypertension in these groups are 12% and 28%, the prescription numbers suggest that knowledge translation strategies may be important to ensure that children with CKD receive the standard of care. Somewhat more reassuring is the higher rate of ACE inhibitor and ARB prescribing for youth with diabetes and CKD (16%–25%). Overall, children with low-risk and high-risk CKD are managed with an average of three to four medications each in a given year (1.60–1.70 times higher rates than children without CKD).

Table 5.3: Use of Prescription Drugs by Children in Patient Cohorts

Age- and sex-adjusted rates, 95% confidence intervals, 2011/12

Indicators		No CKD	CKD by Risk of Progression to ESKD			All ESKD
			Unknown	Low	High	
Anti-Hypertensive Drug Prescriptions (%)	**Rate**	0.26 (0.24-0.27)	0.53 (0.30-0.93)	7.06 (5.90-8.45)	20.25 (16.49-24.86)	48.38 (26.63-87.91)
	Relative Risk	reference	**2.07 (1.17-3.66)**	**27.65 (23.11-33.07)**	**79.29 (64.58-97.35)**	**189.47 (104.28-344.24)**
ACE & ARB Prescriptions (%)	**Rate**	0.03 (0.03-0.04)	s	5.95 (3.80-9.33)	16.12 (10.38-25.03)	49.37 (23.72-102.76)
	Relative Risk	reference	s	**187.94 (119.87-294.67)**	**509.08 (327.75-790.72)**	**1,559.41 (749.24-3,245.63)**
ACE & ARB Prescriptions Among Diabetics (%)	**Rate**	1.84 (0.84-2.84)	0.00 (0.00-0.00)	16.41 (8.14-33.08)	24.97 (11.09-56.21)	s
	Relative Risk	reference	0.00 (0.00-0.00)	**8.92 (4.43-17.99)**	**13.58 (6.03-30.57)**	**s**
Different Prescribed Drugs (per person)	**Rate**	2.10 (2.09-2.10)	2.24 (2.00-2.50)	3.36 (3.01-3.75)	3.57 (3.18-4.02)	9.37 (7.71-11.39)
	Relative Risk	reference	1.07 (0.96-1.19)	**1.60 (1.44-1.79)**	**1.70 (1.52-1.91)**	**4.47 (3.68-5.43)**

bolded values indicate statistically significant difference from the No CKD group

s indicates suppressed values due to small numbers

Healthcare Services Use

The use of nephrologist services is low in children with CKD at unknown risk of progression (no laboratory data) and children with low-risk CKD (Table 5.4). As noted in Chapter 3 (Figure 3.11), the majority of children with CKD who were identified only through laboratory or administrative data had no contact with a nephrologist (84% and 79%, respectively). However, children with low-risk CKD have significantly higher rates of ambulatory physician visits than children without CKD, and the rate of visits to other specialists and hospitalizations at any stage of CKD progression is significantly higher (1.9- to 16-fold higher risk). The most common reasons for inpatient hospitalizations and physician visits of children with CKD include chemotherapy (and related side-effects), mental disorders, chronic renal failure, and diabetes (data not shown). These results highlight the increased morbidity associated with low-risk CKD, even in childhood, and the need for early disease management, such as referral to nephrologists, to delay CKD progression.

Previous research also highlights the significant health impacts of ESKD in children. ESKD is relatively rare in children and adolescents younger than 18 years, with a prevalence of only 58 per 1,000,000 population in Manitoba (see Chapter 3) and 18 to 100 per 1,000,000 worldwide (Harambat et al., 2012). Children and youth make up only 1% of all patients requiring dialysis or kidney transplant in Canada (Canadian Institute for Health Information (CIHI), 2015). Yet, mortality rates for children receiving dialysis are 30- to 150-fold higher than age-matched populations (McDonald & Craig, 2004). North American survival rates are 95%, 90.1% and 85.7% at one, two and three years, respectively (North American Pediatric Renal Trails and Collaborative Studies (NAPRTCS), 2006). Cardiopulmonary abnormalities and infections account for the majority of deaths in pediatric dialysis populations, with malignancy also being important in transplant populations (McDonald & Craig, 2004). The complications of ESKD also impact all aspects of life, including growth and development (Warady & Chadha, 2007). Impacts on the family including financial, psychological and emotional stress are significant (Medway et al., 2015).

Table 5.4: Healthcare Use by Children in Patient Cohorts

Age- and sex-adjusted rates, 95% confidence intervals, 2011/12

Indicators		No CKD	CKD by Risk of Progression to ESKD			All ESKD
			Unknown	Low	High	
Inpatient Hospitalizations (per 1,000)	**Rate**	22.38 (21.83-22.92)	42.48 (23.76-75.98)	344.58 (200.97-590.82)	357.27 (205.66-620.64)	1,630.36 (800.69-3,319.72)
	Relative Risk	reference	**1.90 (1.06-3.40)**	**15.40 (8.98-26.40)**	**15.97 (9.19-27.74)**	**72.86 (35.78-148.35)**
Days in Hospital (per person)	**Rate**	0.10 (0.10-0.10)	0.20 (0.07-0.62)	2.36 (0.83-6.72)	4.14 (1.45-11.84)	6.57 (2.00-21.60)
	Relative Risk	reference	2.11 (0.70-6.40)	**24.44 (8.57-69.65)**	**42.95 (15.03-122.78)**	**68.11 (20.71-224.01)**
Ambulatory Physician Visits (per person)	**Rate**	2.54 (2.54-2.55)	2.94 (2.40-3.61)	6.50 (5.30-7.97)	6.61 (5.38-8.12)	23.26 (18.10-29.89)
	Relative Risk	reference	1.16 (0.94-1.42)	**2.56 (2.09-3.13)**	**2.60 (2.12-3.19)**	**9.15 (7.12-11.76)**
Nephrologist Visits (per person)	**Rate**	0.01 (0.00-0.01)	0.03 (0.02-0.04)	0.38 (0.27-0.53)	1.27 (0.90-1.79)	12.50 (8.38-18.64)
Specialist Visits (per person)	**Rate**	0.24 (0.23-0.24)	0.44 (0.31-0.63)	2.01 (1.43-2.81)	1.54 (1.09-2.17)	8.01 (5.31-12.07)
	Relative Risk	reference	**1.89 (1.34-2.67)**	**8.55 (6.10-11.97)**	**6.56 (4.66-9.24)**	**34.13 (22.65-51.43)**

bolded values indicate statistically significant difference from the No CKD group

Note: relative risk for nephrologist visits not calculated due to low rate for reference group

CHAPTER 6: OBSERVED PATTERNS AND PROJECTIONS OF THE NUMBER OF MANITOBANS REQUIRING TREATMENT FOR END STAGE KIDNEY DISEASE

This chapter will focus on the following question: What are the future needs for renal replacement therapy (RRT) in Manitoba? We present our projections for the number of people, (adults and children combined) who will require dialysis or transplant to treat end stage kidney disease (ESKD) by 2024. We also present a series of "what if" scenarios where the future need for ESKD treatment is predicted based on changes in current treatments and population health trends.

Key Findings

- The number of Manitobans with ESKD will increase by 68% between 2012 and 2024. Our projections estimate that 3,077 people will require RRT in 2024.
- Increases will occur in all health regions. The highest increases are projected in the Southern Health/Santé Sud and Northern Health Regions. The Northern Health Region will continue to have the highest number of people needing RRT per capita in Manitoba.
- Half of ESKD patients in Manitoba also have diabetes, and by 2024 the number people who are on hemodialysis and have diabetes will increase by 89%. The need for hemodialysis among people without diabetes will see a more modest increase of 35%.
- The number of ESKD patients aged 65 and older on hemodialysis will increase by 89% by 2024. In the younger age groups, the need for hemodialysis will see increases of 50% (0 to 44 years) and 65% (45 to 64).
- We examined the potential benefits of implementing strategies that improve the health of Manitobans and the treatment of ESKD. These "what if" scenarios included maintaining diabetes prevalence at 2012 levels, increasing kidney transplants by 25%, increasing peritoneal dialysis starts to 30% of all dialysis starts, and increasing home hemodialysis starts to 8% of all starts.

Projections of the Number of Manitobans Requiring Treatment for End Stage Kidney Disease, 2012-2024

As described in Chapter 2, we calculated ESKD projections for the years 2012 to 2024 based on recent trends (2004–2012), health regions, projections of population growth (2012–2024), and projections of diabetes prevalence (2012-2024). We present projections for the number of people who will need each type of RRT, for the province as a whole, and by health region, age group and diabetes status. Projections for the two types of home-based dialysis (peritoneal and home hemodialysis) were combined because of small numbers.

We present the results in summary tables and figures. In the figures, quarterly averages for 2004 to 2012 are shown in solid lines and quarterly averages for projected values and their 95% confidence intervals are shown in dotted lines.

Projections for Manitoba and for Each Health Region

Based on observed trends and assuming no changes to current population projections, diabetes prevalence or clinical approaches to RRT, the projections indicate that by 2024, there will be 3,077 Manitoba residents receiving treatment for ESKD (Figure 6.1). This represents a 68% increase from 2012 to 2024. Of these, 1,653 (54%) will require centre-based hemodialysis in 2024. The confidence intervals show that this projection could be as low as 1,576 or as high as 1,735 residents. A further 386 residents (13%) are projected to be using peritoneal dialysis and home-based hemodialysis, with confidence intervals between 229 and 426. The projections indicate that there will be 1,038 (34%) kidney transplant (Tx) recipients by 2024 (95% CI: 988 to 1,093).

Table 6.1 shows the actual and projected numbers and projected annual increases for each health region. For the province overall, we predict a 4.3% annual increase in the number of people receiving centre-based hemodialysis, a 3.2% annual increase for home-based dialysis (peritoneal and home hemodialysis), and 4.5% for kidney transplants.

Though substantial, these projected increases are not surprising, given the growth in diabetes prevalence and the aging population in Manitoba (Fransoo et al., 2013; Manitoba Renal Program (MRP), 2013). Our predicted annual increases are lower than previous estimates by Schaubel et al. (1999) . In 1999, these authors reported an annual increase of 8.9% in the overall need for RRT in Manitoba.

Figures 6.1 to 6.6 show differences among the health regions in the need for RRT (actual and projected) over time. These graphs and Table 6.1 above provide a substantial amount of information. It is important to keep in mind the distinction between the magnitude of the increases, the actual number per treatment type per region, and the number per capita. For example, the projected number of people requiring RRT is the same in the Northern Health and Southern Health/Santé Sud Regions in 2024; however, the Northern Health Region has a considerably higher rate of ESKD because of its smaller population.

All regions have projected increases but they vary in magnitude and by type of RRT. The increases in Winnipeg are similar to those in Manitoba overall. Winnipeg will continue to have the highest number of people with ESKD because of the region's larger population and capacity for providing treatment. Although dialysis units are located throughout the province, some units are not able to meet the needs of the region, and some patients relocate to Winnipeg for treatment.[6] Of note, Southern Health/Santé Sud will experience the greatest increases in people on each type of dialysis, possibly because of its aging population. At the same time, Southern Health/Santé Sud will continue to have low rates of ESKD because the small numbers of people with ESKD relative to its population count. Kidney transplants are projected to see the largest increases in the Northern Health Region. This is likely due to the growing number of young First Nations people living in this region, as First Nations communities have high rates of ESKD and young people are more likely to be candidates for transplant surgery.

6 There are multiple reasons for not being able to meet all the needs of patients in rural and remote regions. The Local Centre Dialysis Units (LCDU) can only accommodate patients who are medically stable; therefore, those with complex medical needs are treated in Winnipeg. It is challenging to staff the units in rural and remote areas. The centres are not always located close to the patient's primary residence (Ferguson et al., 2015; Tangri N, personal communication, July, 2015).

Figure 6.1: Observed and Projected Number of Patients with End Stage Kidney Disease by Treatment Type in Manitoba, 2004-2024

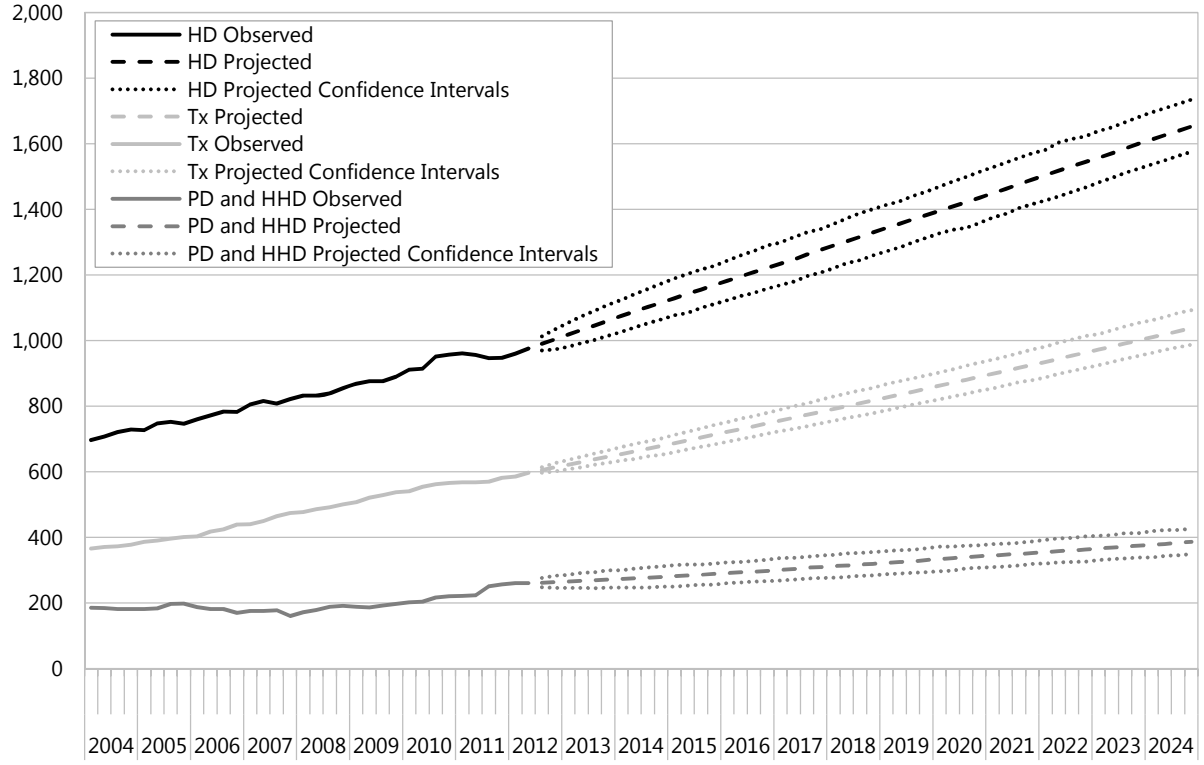


Table 6.1: Observed and Predicted Number of End Stage Kidney Disease Patients by Region and Treatment Type, 2012 and 2024

Health Region	Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	Total
Observed Number (2012)				
Southern Health/Santé Sud	68	35	77	180
Winnipeg	558	141	367	1,066
Prairie Mountain Health	112	14	74	200
Interlake-Eastern	120	35	51	206
Northern	118	35	28	181
Manitoba	976	260	597	1,833
Predicted Number in 2024 (% Annual Increase From 2012 to 2024)				
Southern Health/Santé Sud	124 (4.92)	61 (4.54)	139 (4.84)	324 (4.81)
Winnipeg	944 (4.30)	198 (2.75)	626 (4.36)	1,768 (4.13)
Prairie Mountain Health	181 (3.91)	24 (4.41)	123 (4.15)	328 (4.04)
Interlake-Eastern	198 (4.09)	49 (2.73)	86 (4.27)	333 (3.92)
Northern	207 (4.60)	54 (3.53)	64 (6.84)	324 (4.77)
Manitoba	1,653 (4.31)	386 (3.21)	1,038 (4.52)	3,077 (4.23)

Figure 6.2 shows the projected number of people with ESKD in the Winnipeg Health Region from 2012 to 2024 for each type of treatment. The number of people on centre-based hemodialysis is predicted to increase from 558 in 2012 to 944 by 2024, an increase of 69%. Kidney transplants are expected to increase by 71%, from 367 in 2012 to 626 by 2024. The 40% increase for home-based dialysis (peritoneal and home hemodialysis) is less dramatic; it will rise from 141 people in 2012 to 198 by 2024.

Figure 6.3 shows the projected number of people with ESKD in the Southern Health/Santé Sud Region from 2012 to 2024 for each type of treatment. The number of people on centre-based hemodialysis is projected to grow from 68 in 2012 to 124 by 2024, an increase of 82%. Kidney transplants are expected to increase by 80%, from 77 in 2012 to 139 by 2024. A 74% increase is projected for home-based dialysis (peritoneal and home hemodialysis) which will go from 35 people in 2012 to 61 by 2024. As noted above, these increases are considerably higher than for the Manitoba population overall. This is the only region where the projected number of people with kidney transplants in 2024 is higher than the projected number on centre-based hemodialysis. The overlap in the dotted lines for transplants and hemodialysis means that the number of people receiving these treatments could be similar.

Figure 6.4 shows projections for the Prairie Mountain Health Region. The projected number of people on centre-based hemodialysis will increase from 112 in 2012 to 181 by 2024, an increase of 62%. The confidence intervals are quite wide, indicating that the projected numbers could be much higher or lower. Kidney transplants are expected to increase by 66%, from 74 in 2012 to 123 by 2024. A 71% increase is projected for home-based dialysis (peritoneal and home hemodialysis) which will go from 14 people in 2012 to 24 by 2024. These increases are the second highest in Manitoba, after the Southern Health/Santé Sud Region. It is noteworthy that Prairie Mountain Health has proportionally lower use of home-based dialysis compared to other regions (7% of all RRT patients in 2012 versus 14% in Manitoba), likely because of the lack of home dialysis programs in this region. However, we do project a considerable increase in this type of RRT in Prairie Mountain health. One explanation might be that the projections are more heavily based on the most recent data and the use of home-based dialysis has been increasing.

Figure 6.2: Observed and Projected Number of Patients with End Stage Kidney Disease by Treatment Type in Winnipeg Health Region, 2004-2024

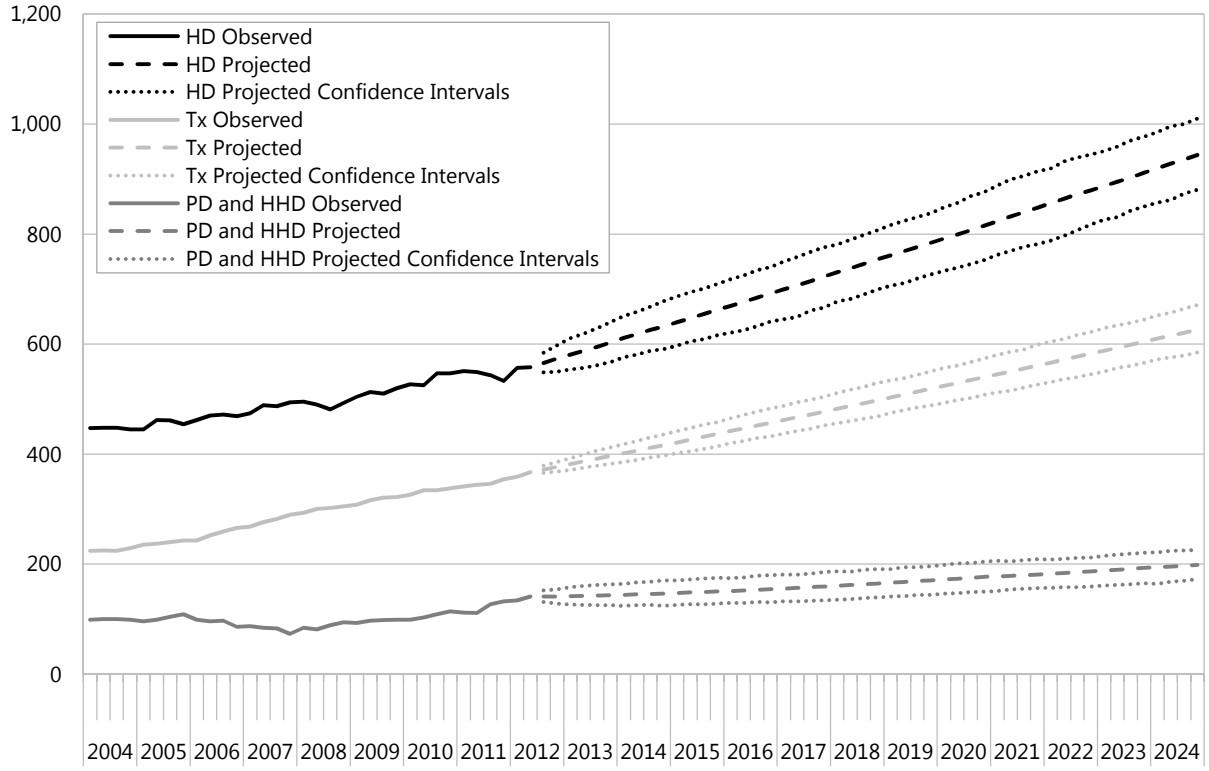


Figure 6.3: Observed and Projected Number of Patients with End Stage Kidney Disease by Treatment Type in Southern Health/Santé Sud Region, 2004-2024

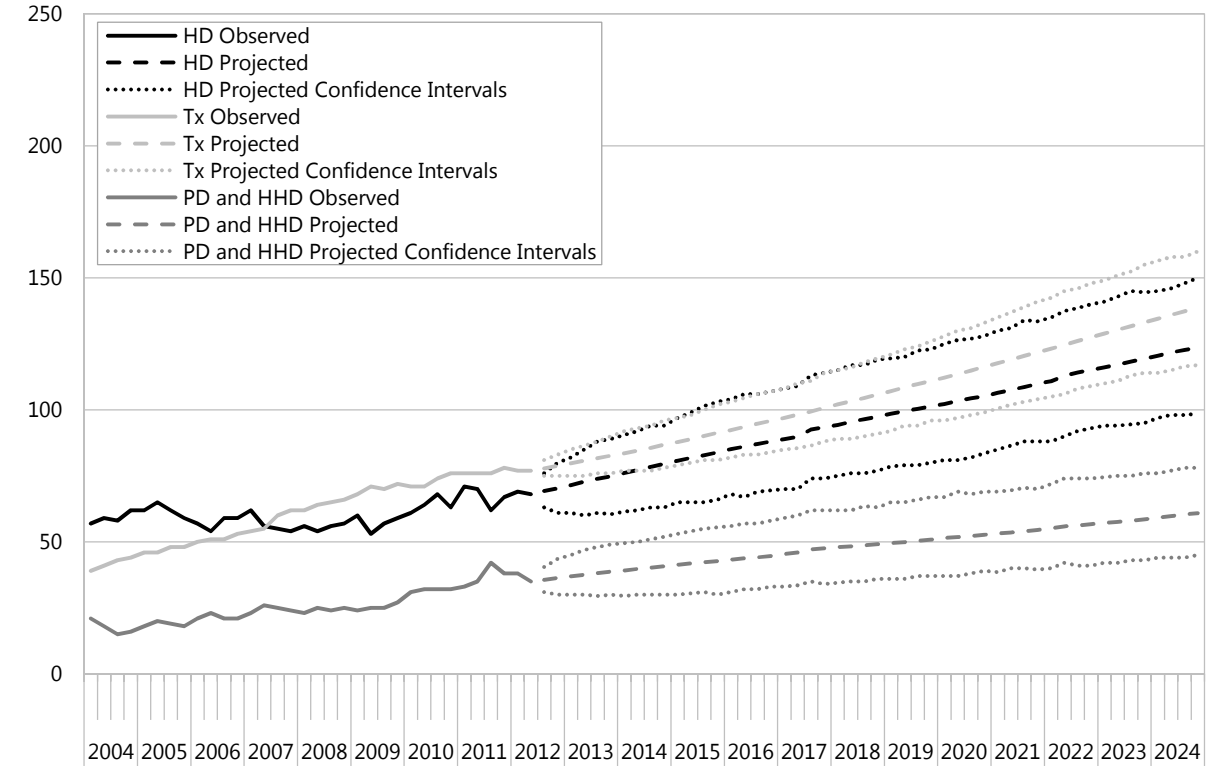


Figure 6.4: Observed and Projected Number of Patients with End Stage Kidney Disease by Treatment Type in Prairie Mountain Health Region, 2004-2024

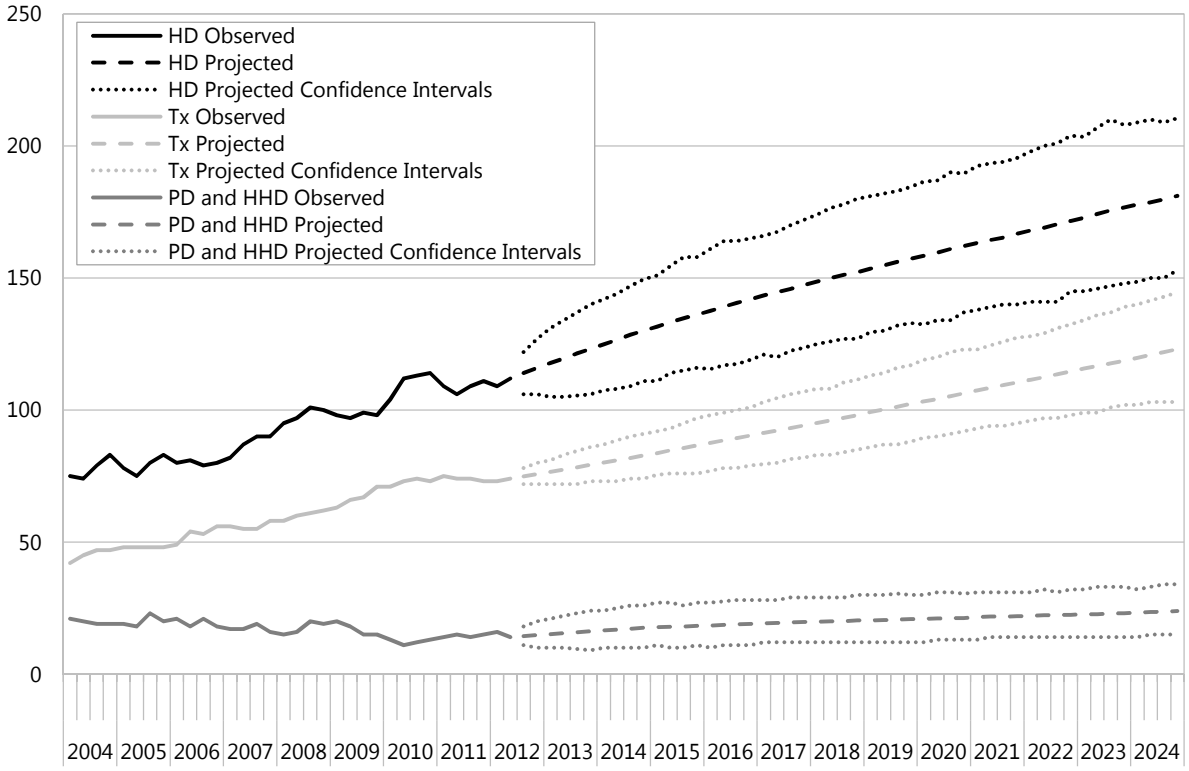


Figure 6.5 shows projections for the Northern Health Region. The models predict that the number of people on centre-based hemodialysis will increase from 118 in 2012 to 207 by 2024, an increase of 75%. Kidney transplants are expected to increase by 130%, from 28 in 2012 to 64 by 2024. As noted, this dramatic increase may be due to the region's younger population, who are better candidates for kidney transplants. A 54% increase is projected for home-based dialysis (peritoneal and home hemodialysis), from 35 people in 2012 to 54 by 2024.

Figure 6.6 shows the projected number of people with ESKD in the Interlake-Eastern Health Region from 2012 to 2024 for each type of treatment. The number of people on centre-based hemodialysis is projected to grow by 65%, from 120 in 2012 to 198 by 2024. Kidney transplants are expected to increase by 68%, from 51 in 2012 to 86 by 2024. Finally, a 40% increase is projected for home-based dialysis (peritoneal and home hemodialysis), from 35 people in 2012 to 49 by 2024. These increases are similar to the projections for Manitoba overall.

Figure 6.5: Observed and Projected Number of Patients with End Stage Kidney Disease by Treatment Type in Northern Health Region, 2004-2024

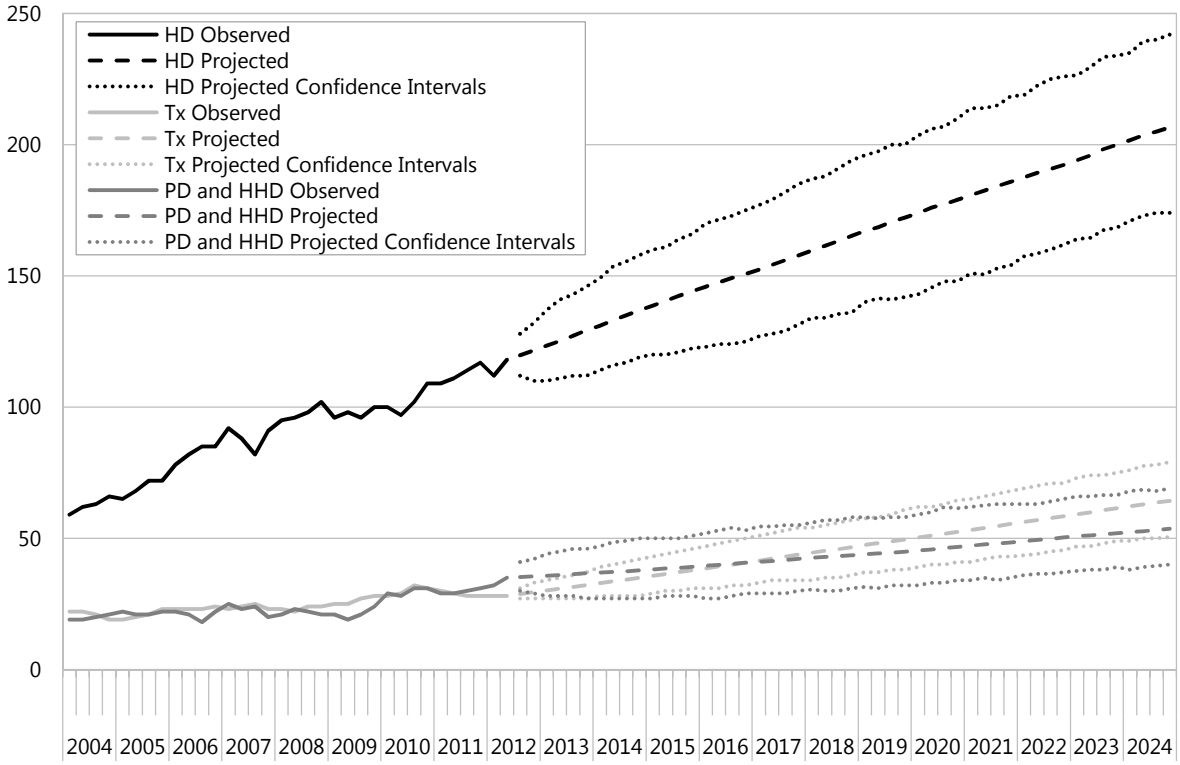
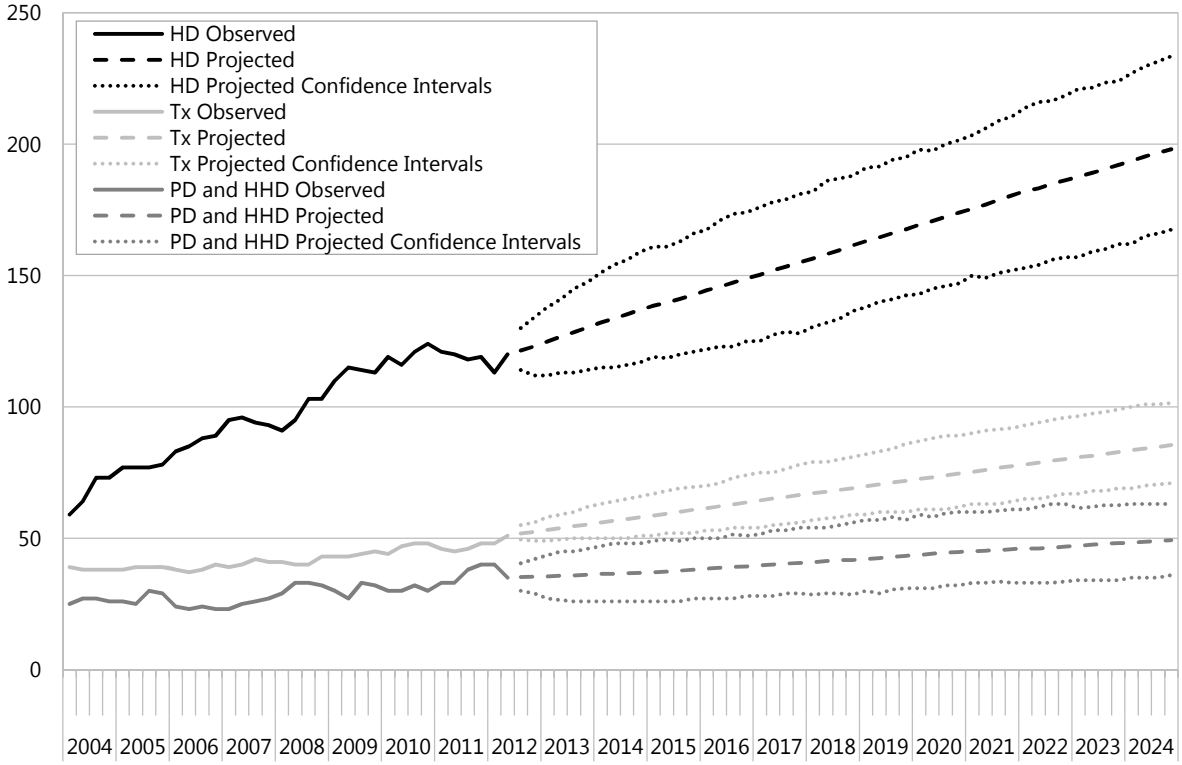


Figure 6.6: Observed and Projected Number of Patients with End Stage Kidney Disease by Treatment Type in Interlake-Eastern Health Region, 2004-2024



Projections by Diabetes Status

People with diabetes represent about 10% of Manitoba's total population (Fransoo et al., 2013), but in 2012, they comprised almost half (892) of all Manitobans requiring RRT. Of these, 752 were on dialysis and 140 received kidney transplants (Figure 6.7).

By 2024, the total number of Manitoba residents with diabetes requiring RRT is projected to increase by 95%. The number on centre-based hemodialysis is predicted to increase from 622 in 2012 to 1,176 by 2024, an increase of 89%. Kidney transplants are expected to increase by 143%, from 140 in 2012 to 340 by 2024. A 75% increase is projected for the use of home-based dialysis (peritoneal and home hemodialysis) by people with diabetes, an increase from 130 people in 2012 to 228 by 2024. The projected increases in rates of all types of RRT are greater for people with diabetes than for Manitoba overall.

Figure 6.8 shows the much smaller increases projected for the number of ESKD patients without diabetes between 2012 and 2024. The models predict that the number of people without diabetes on centre-based hemodialysis will increase from 354 in 2012 to 478 by 2024, an increase of 35%. Kidney transplants are expected to increase by 53%, from 457 in 2012 to 698 by 2024. Finally, a 22% increase is projected for home-based dialysis (peritoneal and home hemodialysis) which will go from 130 people in 2012 to 158 by 2024.

When we compare projections for Manitoba by RRT type in 2024 among people with and without diabetes, we note that a higher percentage of people with diabetes are on centre-based hemodialysis (67%) and a lower percentage have a functioning kidney transplant (20%) compared to people without diabetes. The high number of people on hemodialysis are likely due to the higher number of comorbid health problems among people with diabetes, making them ineligible for other types of treatments. These results shed some light on the importance of preventing and managing diabetes to attenuate the soaring rates of ESKD.

Figure 6.7: Observed and Projected Number of End Stage Kidney Disease Patients with Diabetes by Treatment Type in Manitoba, 2004-2024

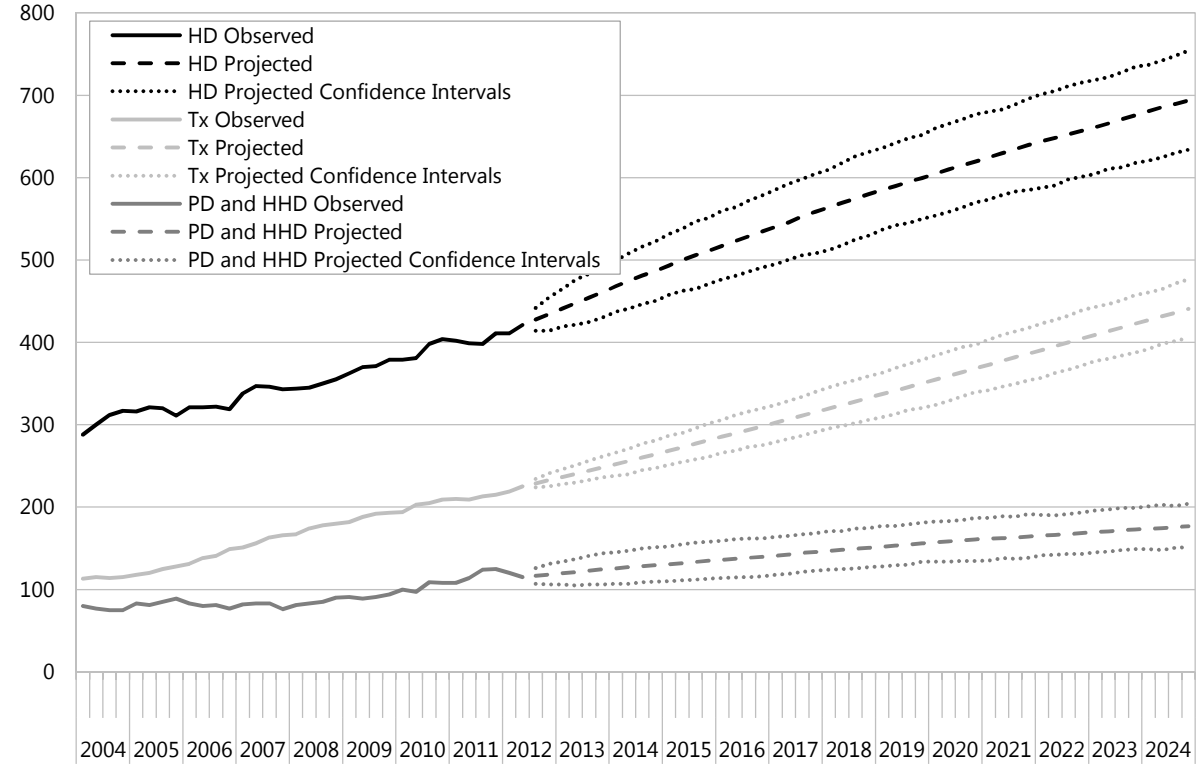
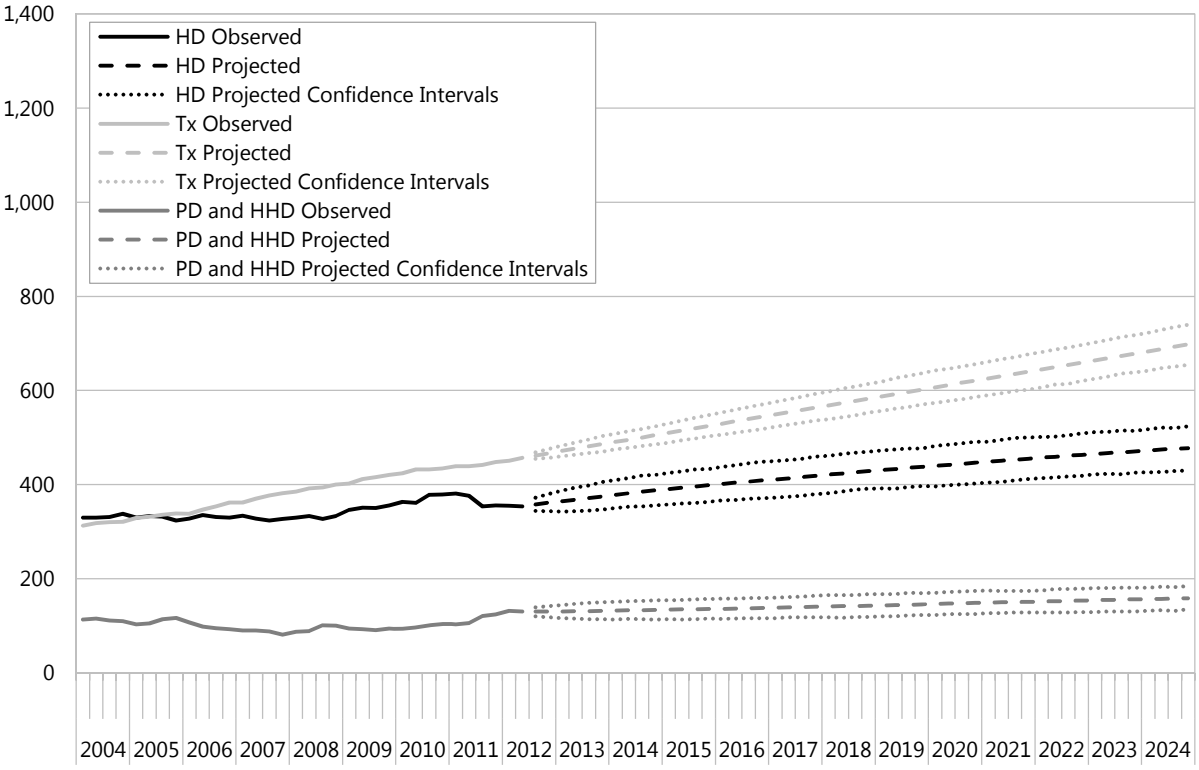


Figure 6.8: Observed and Projected Number of End Stage Kidney Disease Patients Without Diabetes by Treatment Type in Manitoba, 2004-2024



Projections by Age Group

Figures 6.9 to 6.11 show differences in the projected number of ESKD patients by age. All types of RRT are expected to increase in all three age groups (0 to 44, 45 to 64, and 65 years and older), although peritoneal dialysis shows the smallest projected increases. The largest group receiving RRT are aged 45 to 64 (n=1,311 in 2024), and RRT use in this age group will increase by 72% between 2012 and 2024. However, the age group 65 years and older will see the greatest increase in the number of people receiving RRT (87%).

Figure 6.9 shows the projected number of younger people (aged 0 to 44 years) with ESKD by treatment type between 2012 and 2024. Among younger people, kidney transplants are the most common type of RRT, and these are expected to increase by 59%, from 352 in 2012 to 559 by 2024. The number of people on centre-based hemodialysis is projected to increase from 234 in 2012 to 352 by 2024, an increase of 50%. The 22% increase for home-based dialysis (peritoneal and home hemodialysis) is less dramatic, rising from 81 younger people in 2012 to 98 by 2024.

Figure 6.10 shows projections of the number of middle-aged people (45 to 64 years) with ESKD, by treatment type, between 2012 and 2024. Centre-based hemodialysis is the most common type of RRT in this age group and its use is expected to increase by 65%, from 421 in 2012 to 694 by 2024. Kidney transplants are projected to increase by 96%, from 225 in 2012 to 441 in 2024; people in this age group are typically good candidates for kidney transplants. Finally, a 54% increase is predicted for home-based dialysis (peritoneal and home hemodialysis), from 115 in 2012 to 177 by 2024.

Figure 6.11 shows the projected number of older people (aged 65 and older) with ESKD to 2024, by treatment type. It is in this age group that we observe the largest increases for all types of dialysis. Centre-based hemodialysis, by far the most common type of treatment in this older population, is expected to increase by 89%, from 321 in 2012 to 608 in 2024. A slightly lower increase of 73% is predicted for home-based dialysis (peritoneal and home hemodialysis). Although kidney transplants are projected to increase by 89%, this translates into a net increase of 18 more people (from 20 in 2012 to 38 by 2024).

Figure 6.9: Observed and Projected Number of End Stage Kidney Disease Patients Aged 0-44 by Treatment Type in Manitoba, 2004-2024

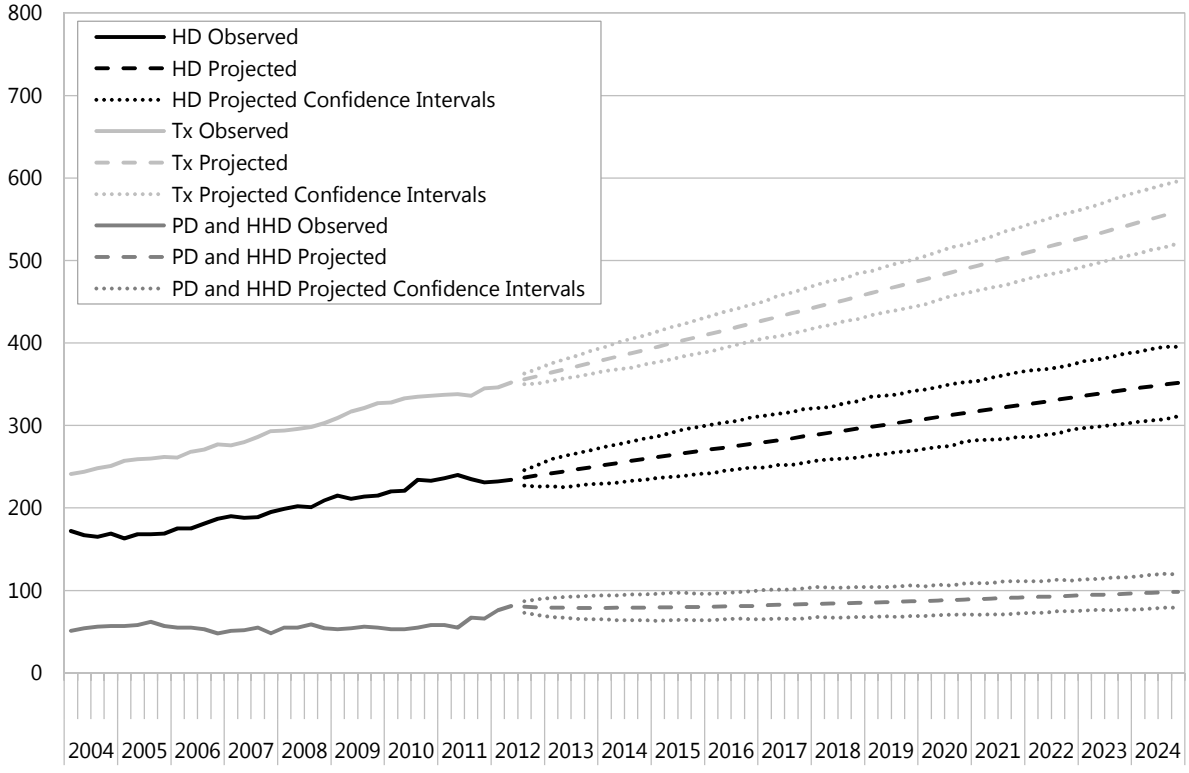


Figure 6.10: Observed and Projected Number of End Stage Kidney Disease Patients Aged 45-64 by Treatment Type in Manitoba, 2004-2024

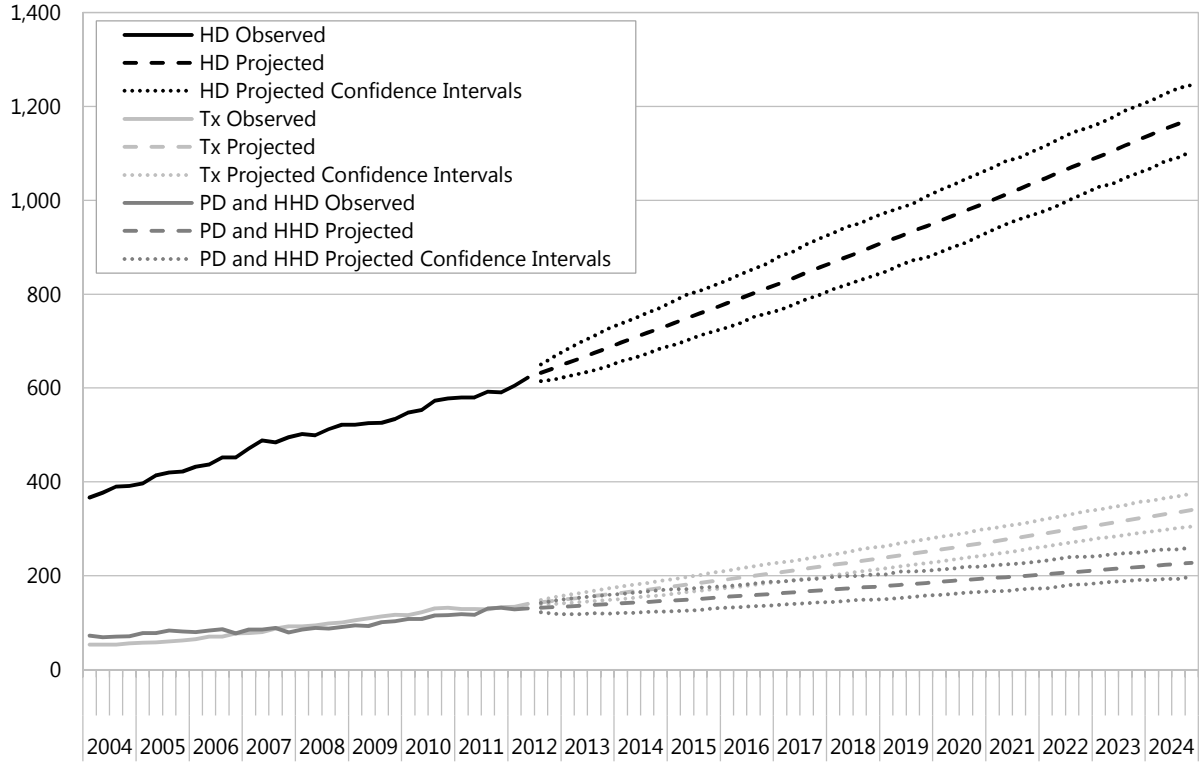
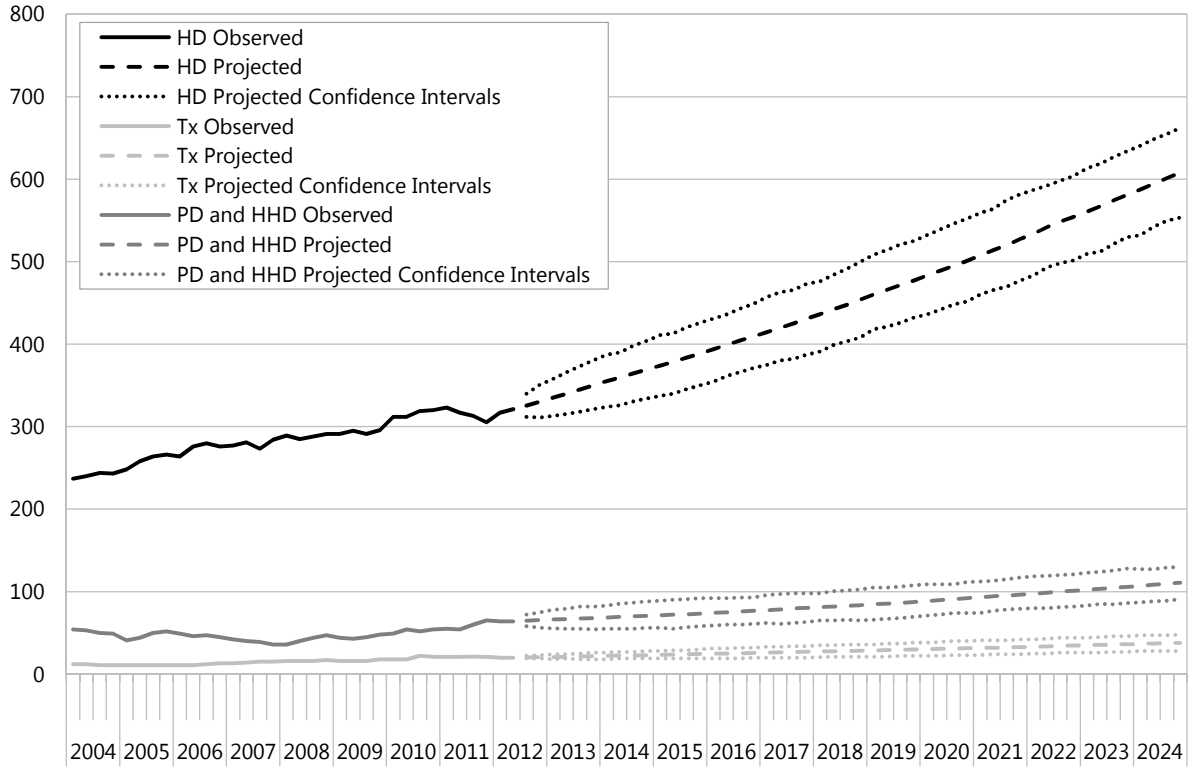


Figure 6.11: Observed and Projected Number of End Stage Kidney Disease Patients Aged 65+ by Treatment Type in Manitoba, 2004-2024



"What If" Projection Scenarios

The projections reported in the previous section are based on past trends in age, diabetes status and treatment types among Manitobans with ESKD, assuming no changes to these trends. It is entirely possible that a number of factors will change. In this section, we examine five scenarios to demonstrate how certain factors influence the ESKD projections. We calculated the projections based on the following scenarios:

- Diabetes prevalence remains at 2012 levels
- Peritoneal dialysis (PD) starts increase to 30% of all dialysis starts
- Home hemodialysis (HHD) starts increase to 8% of all dialysis starts
- Kidney transplants (Tx) rates increase by 25%
- Mortality rates for people with ESKD decrease by 20%.

Table 6.2 summarizes the impact of these "what if" scenarios on the projected number of Manitobans using each type of RRT by 2024. The first line shows the actual number of ESKD patients by treatment type in 2012. The next line shows the baseline projections: the number of ESKD patients by 2024 if treatment practices and health trends do not change. The remaining lines show the projections based on each scenario.

The scenario of constant diabetes prevalence (i.e., a change to the current trend of rising rates of diabetes) provides the most dramatic decrease in the number of people requiring any type of RRT, compared with the baseline projections. Not surprisingly, the scenario of a decrease in mortality rates among people with ESKD provides a significant increase in the number of people using RRT. All other scenarios show a decreased use centre-based hemodialysis. These results point to some promising strategies that may improve quality of life and reduce financial costs associated with ESKD, especially with centre-based hemodialysis. We discuss these strategies in Chapter 7 and in the recommendations in Chapter 9.

Projected numbers by region for each scenario are available in Appendix 7.

Table 6.2: Observed and Projected Number of Patients with End Stage Kidney Disease in Manitoba, by "What If" Projection Scenario and Treatment Type, 2012 and 2024

	Average Number of Patients (95% Confidence Interval)			Total Number of ESKD Patients
	Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	
Observed (2012)	976	260*	597	1,833
Projected (2024)	1,653 (1,576–1,735)	386 (349–426)	1,038 (988–1,093)	3,077
"What If Scenarios" (2024)				
Constant diabetes prevalence	1,445 (1,373–1,516)	346 (311–383)	1,014 (959–1,066)	2,804
30% of starts are peritoneal dialysis	1,555 (1,479–1,629)	481 (440–523)	1,053 (999–1,105)	3,089
8% of starts are home hemodialysis	1,587 (1,504–1,666)	448 (406–492)**	1,045 (993–1,098)	3,081
25% increase in kidney transplant rate	1,608 (1,526–1,684)	368 (329–407)	1,142 (1,085–1,200)	3,118
20% decrease in mortality rate	1,903 (1,820–1,990)	435 (392–479)	1,107 (1,053–1,164)	3,445

* Peritoneal dialysis: 229; home hemodialysis: 31

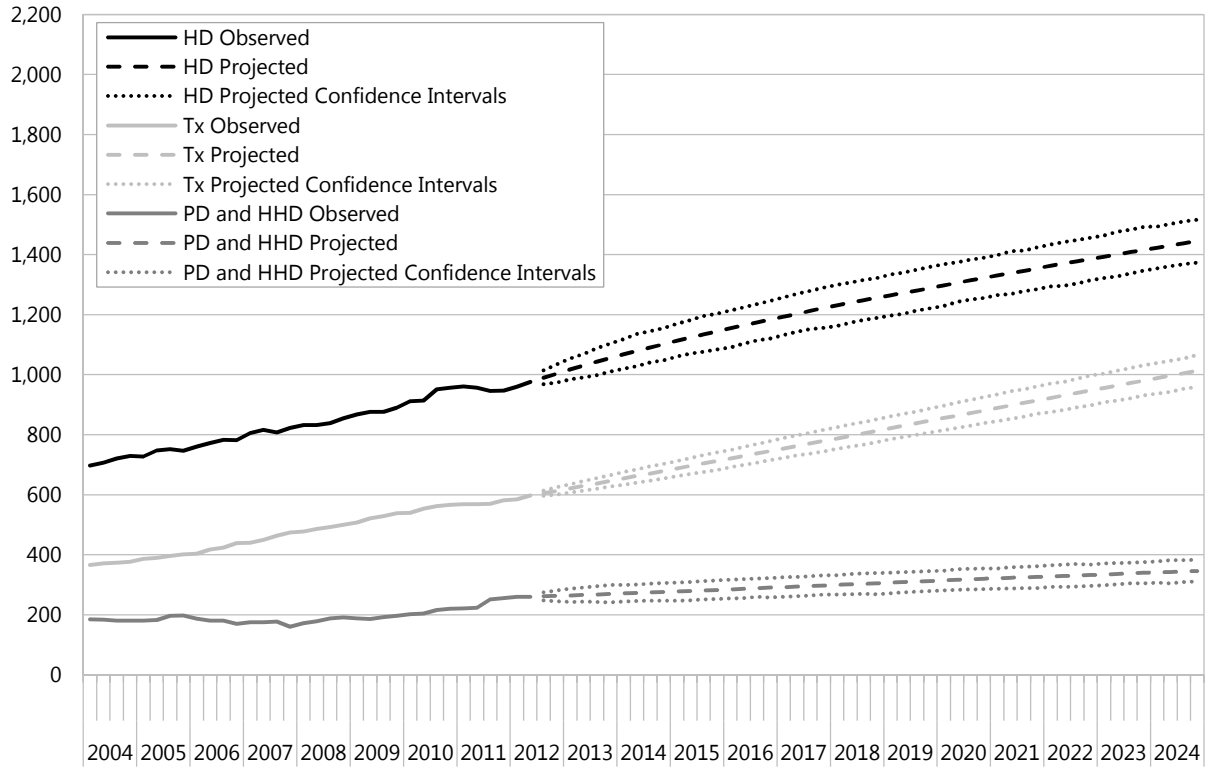
** Peritoneal dialysis: 340; home hemodialysis: 108

Diabetes Prevalence Remains at 2012 Levels

If measures can be taken to maintain diabetes prevalence at 2012 levels, there will be 272 fewer people with ESKD by 2024. Of these, 208 fewer will require centre-based hemodialysis in 2024, compared to baseline projections, 40 fewer will require peritoneal dialysis or home hemodialysis, and 24 fewer requiring kidney transplants. Figure 6.12 shows projections by treatment type for this scenario. We found that decreases at the regional level were similar to those for the province overall (see Appendix 6).

Improvements in preventing diabetes will decrease the number of people with ESKD in the future. This scenario may be attainable: Fransoo et al. (2013) has reported a decrease in the incidence of diabetes in Manitoba.

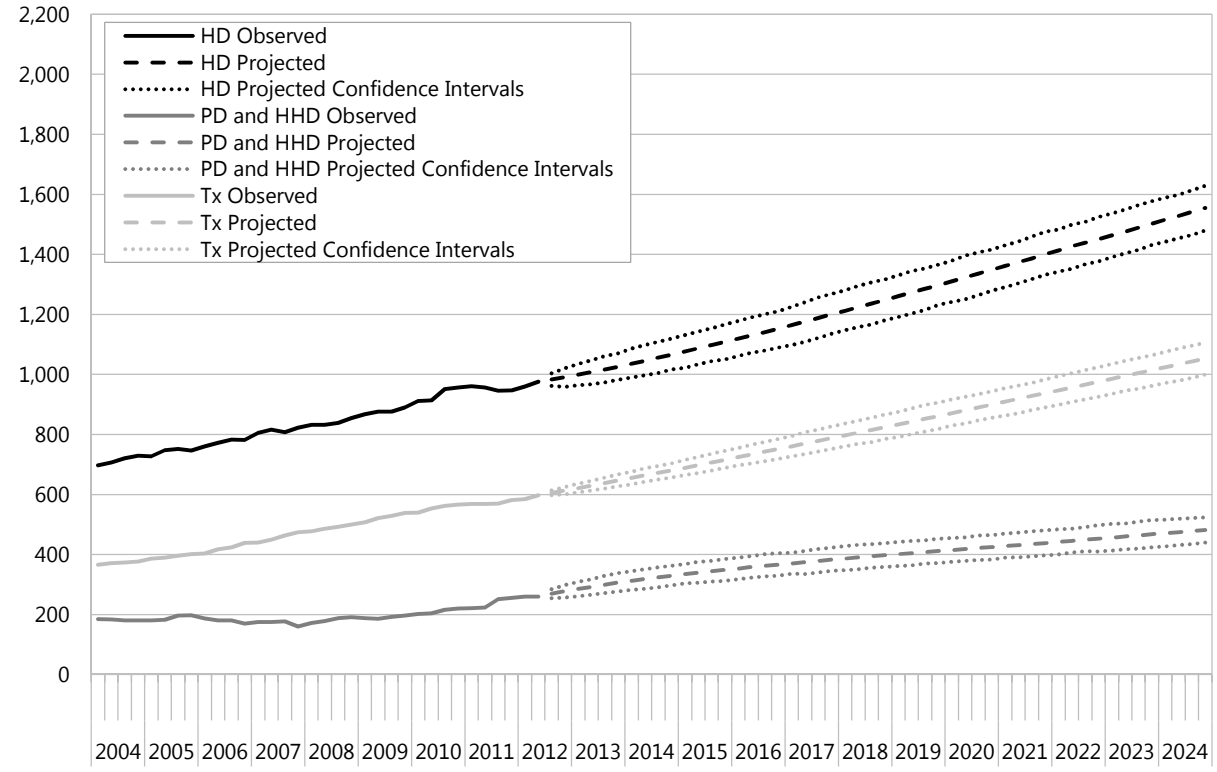
Figure 6.12: Observed and Projected Number of End Stage Kidney Disease Patients by Treatment Type in Manitoba if Diabetes Prevalence is Constant, 2004-2024



Peritoneal Dialysis Starts Increase to 30% of all Dialysis Starts

Starting peritoneal dialysis requires considerable effort and planning, but it has several important advantages. Because it is administered at home, patients can remain in their communities. It is also more economical at about half the cost of centre-based hemodialysis. If measures are taken to ensure that 30% of all new dialysis patients start on peritoneal dialysis, we project that 95 more people would use peritoneal or home-hemodialysis in 2024, compared to baseline projections, and 98 fewer people would require centre-based hemodialysis. Figure 6.13 shows projections to 2024 for each type of treatment under this scenario. We note a slight increase in kidney transplants, because, in our statistical models, being on peritoneal dialysis increases the chance of receiving a transplant.

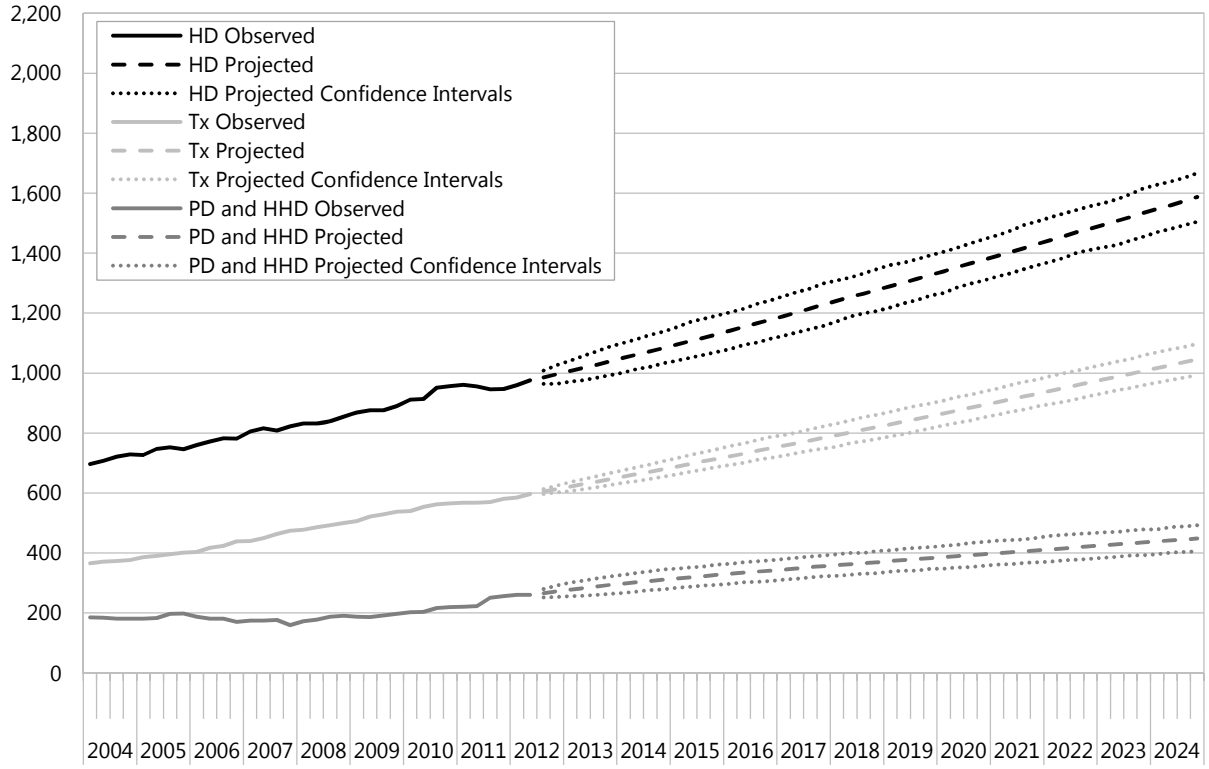
Figure 6.13: Observed and Projected Number of End Stage Kidney Disease Patients by Treatment Type in Manitoba if 30% of Dialysis Starts are Peritoneal Dialysis, 2004-2024



Home Hemodialysis Starts Increase to 8% of all Dialysis Starts

Home hemodialysis also permits patients to receive treatment at home, affords a better quality of life and is considerably less costly than centre-based hemodialysis. If measures are taken to ensure that 8% of all dialysis starts are home hemodialysis, 62 more patients would require home hemodialysis or peritoneal dialysis in 2024, compared to baseline projections, 66 fewer patients would require centre-based hemodialysis and seven more would receive kidney transplants. Figure 6.14 shows projections of the number of people using each type of RRT from 2012 to 2024.

Figure 6.14: Observed and Projected Number of End Stage Renal Disease Patients by Treatment Type in Manitoba if 8% of Dialysis Starts are Home Hemodialysis, 2004-2024

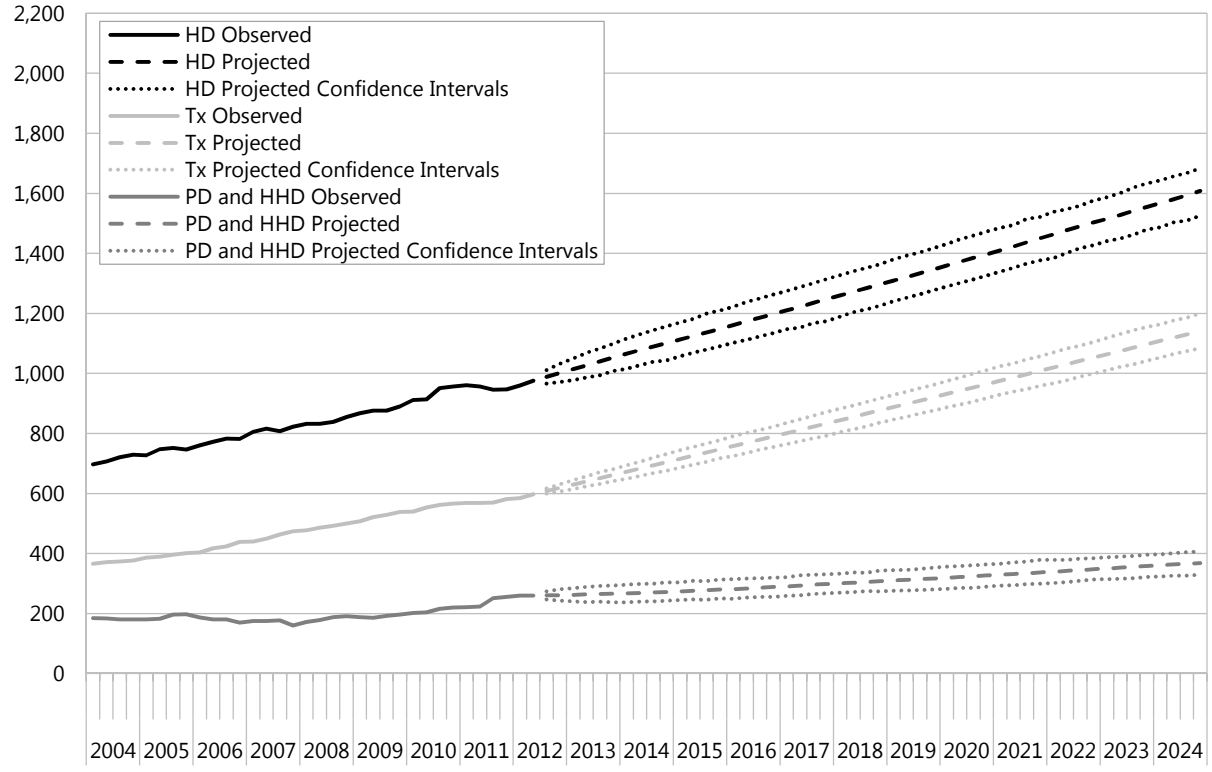


Kidney Transplants Increase by 25%

Although not all patients with ESKD are eligible for a kidney transplant, the rate of kidney transplants in Manitoba could be increased. Strategies in other jurisdictions have included less restrictive criteria for matching donors and recipients, expanded criteria for organ acceptance, donor-pair exchange programs, and education campaigns on kidney donation (Canadian Blood Services).

If measures are taken to increase the number of kidney transplants in Manitoba by 25%, there would be 45 fewer patients requiring centre-based hemodialysis in 2024 compared to the baseline projections, a 3% decrease on average across the province (see Appendix 7 for regional rates). In addition, 18 fewer people would require peritoneal and home hemodialysis, and 104 more would receive kidney transplants. Figure 6.15 shows projections to 2024 for each type of treatment under this scenario. We note that the total number of people living with ESKD would be slightly higher since the survival rate associated with kidney transplants is better than with dialysis.

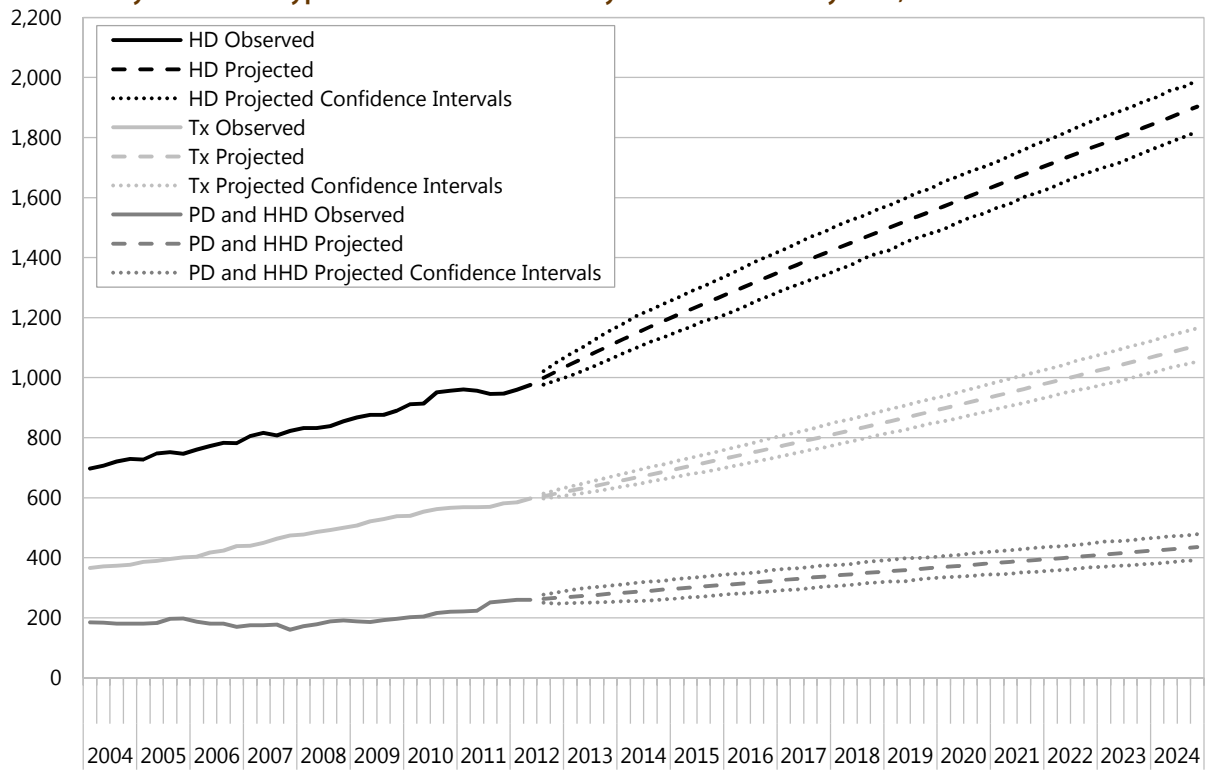
Figure 6.15: Observed and Projected Number of End Stage Kidney Disease Patients by Treatment Type in Manitoba if Kidney Transplant Rate Increased by 25%, 2004-2024



Mortality Rates for People with End Stage Kidney Disease Decrease by 20%

We calculated the baseline projections by taking into account the probability of death among people with ESKD, based on historical patterns. These mortality rates may change; for example, they may decrease if there is an improvement in healthcare for ESKD and related conditions. In the past, survival rates for people on RRT have improved by 15% over a five-year period (Sorensen, Mathiesen, Heaf, & Feldt-Rasmussen, 2007). If a 20% decrease in mortality rates for ESKD patients was realized in Manitoba, the total number of people requiring RRT in 2024 would increase by 368 people. There would be 250 more patients who would require hemodialysis, an increase of 15% on average across the health regions (see Appendix 7 for regional rates). In addition, 49 more people would require home-hemodialysis and peritoneal dialysis, and 69 more would receive kidney transplants relative to baseline projections. Figure 6.16 shows projections to 2024 for each type of treatment under this scenario.

Figure 6.16: Observed and Projected Number of End Stage Kidney Disease Patients by Treatment Type in Manitoba if Mortality Rate Decreased by 20%, 2004-2024



CHAPTER 7: RISK FACTORS AND SCREENING, PREVENTION AND TREATMENT STRATEGIES FOR CHRONIC KIDNEY DISEASE AND END STAGE KIDNEY DISEASE

This chapter is devoted to answering the question: What preventive, screening, and education measures, and affiliations with existing programs might reduce the number of Manitobans who will require dialysis or transplant for end stage kidney disease (ESKD)?

First, we summarize the literature in the inter-related areas of risk factors, screening, prevention and early intervention, to provide background for developing a strategy to reduce chronic kidney disease (CKD) and ESKD. Where possible, we compare the findings from this report to previous research, and we provide a section on children due to the severity of the illness and the potential to prevent a lifetime of comorbid health conditions. Next, using data in the MCHP Repository, which links health and socioeconomic data on Manitobans, we explore factors associated with the use of centre-based hemodialysis versus other types of renal replacement therapy (RRT). This analysis is intended to provide some insight into how to target prevention and treatment strategies to improve outcomes for people living with CKD in Manitoba. Finally, we present an overview of current screening, prevention and treatment initiatives in Manitoba.

Key Findings

- Age, health status, comorbid medical conditions, socioeconomic status and regional factors are associated with CKD and progression to ESKD.
- Indigenous people are three times more likely to be new patients receiving RRT than non-indigenous people.
- Early identification of CKD allows healthcare providers to initiate lifestyle counselling, address risk factors, and start treatment to slow the progression of the disease.
- Clear guidelines for primary care physicians on the care of CKD patients in the early stages of the disease are needed.
- No consistent evidence exists on the health and cost benefits of systematic screening for CKD in the general population. However, targeted screening may benefit people with risk factors such as diabetes, hypertension, cardiovascular disease and older age.
- Nephrologist care in advanced stages of CKD is associated with starting home-based dialysis rather than centre-based dialysis as the initial type of RRT.
- The high comorbidity of cardiovascular diseases, hypertension and diabetes among people with CKD points to the value of a coordinated public health strategy aimed at prevention and management of CKD and other chronic diseases.

Findings from Previous Studies and the Present Report

Risk Factors Associated with Chronic Kidney Disease and End Stage Kidney Disease

CKD and the progression to ESKD depend on factors such as age, socioeconomic status (SES), health status and existing medical conditions. As described in Chapter 1, medical conditions that increase the risk of CKD include diabetes, high blood pressure and cardiovascular disease. In Chapters 4 and 5, we found that CKD and ESKD were associated with a number of sociodemographic factors and physical and mental health conditions. These are important considerations when developing screening, prevention and early intervention strategies.

Age

The age and sex distribution that we found in Manitoba is similar to other studies (Hornberger, Garber, & Jeffery, 1997; Nickolas, Frisch, Opotowsky, Arons, & Radhakrishnan, 2004; Yeates et al., 2012; Zhao et al., 2008). As noted in Chapter 4, older age groups in Manitoba have higher rates of CKD and ESKD. It is well known that decreased kidney functioning is common in older people and that it is important to tailor prevention and treatment strategies to each person's age rather than modifying the diagnostic criteria for CKD in the elderly (Levey, Inker LA, & Coresh J, 2015). In some cases, older people can live for many years with decreased but stable kidney function (Tonelli & Riella, 2014). In contrast, people who develop CKD at an earlier age are at a higher lifelong risk of ESKD, because younger people are less likely than older people to die of other causes before reaching kidney failure (Hallan et al., 2012).

Decisions about CKD and ESKD management in the elderly are more complex than for younger patients (Nitta, Okada, Yanai, & Takahashi, 2013). Management strategies for older adults often depend on comorbid disorders and functional status. For example, Tonelli & Riella (2014) note that a large proportion of 80-year-olds who initiate dialysis will die within six months. Careful evaluation will determine whether conservative management, kidney transplant or dialysis improves outcomes for older adults. We found that age was a significant predictor of the type of treatment chosen in Manitoba (see "Factors Associated with ESKD Treatment Type in Manitoba," later in this chapter).

Socioeconomic Status

In Chapters 4 and 5, we report an association between area-level SES and the prevalence of CKD and ESKD. Hossain, Goyder, Rigby, & El (2009) found numerous studies consistent with our findings in their review of CKD and poverty. In fact, they also noted an association between SES and other risk factors of CKD, namely diabetes and hypertension. More recently, So, Methven, Hair, Jardine, & MacGregor (2015) reported that a large part of the differences in CKD prevalence across populations could be explained by SES, rurality, and the ratio of patients to primary care providers. Using US data, Vart, Gansevoort, Coresh, Reijneveld, & Bultmann (2013) found that income was strongly associated with CKD but education was not. Interestingly, when using data from the Netherlands, a country with universal healthcare, the authors observed that low income was weakly associated with CKD whereas low education was strongly associated (Vart et al., 2013).

These findings point to the importance of considering the social determinants of health in preparing a strategy to reduce the burden of CKD and ESKD in Manitoba. The disparity among health outcomes across income groups has been well-documented (Martens et al., 2010) and it appears that ESKD is no exception. Poor housing, stressful living conditions, lack of recreational facilities and affordable nutritious food, and stresses related to unemployment are examples of how low SES can influence health and health-related behaviours (Marmot, 2005; Raphael, 2004).

While there are no simple solutions to poverty, some approaches show promising outcomes in improving the health of low-income populations. A guaranteed annual income program was associated with declines in hospitalization, particularly for accidents, injury and mental illness (Forget, 2013). The Poverty Tool, developed in Ontario and endorsed by the Manitoba College of Family Physicians and by Manitoba Health, Healthy Living and Seniors, provides practical solutions family physicians can recommend to their patients for alleviating the harmful impacts of poverty (The Manitoba College of Family Physicians (MCFP)).

First Nations Populations

The large health disparity across regions in Manitoba points to the need for targeted prevention and early intervention efforts, particularly among First Nations communities. We found that CKD and ESKD prevalence in Manitoba are highest in the Northern Health Region, where many of the province's remote First Nations communities are found (Chapters 3, 4 and 5).

Our findings correspond with previous research showing that ESKD rates for Aboriginal people in Canada (First Nations, Métis and Inuit) are two to four times higher than for non-Aboriginal people (Gao et al., 2007; Samuel et al., 2012). Using data from the Canadian Organ Replacement Register (CORR), the Canadian Institute of Health Information (CIHI) found that Aboriginal people were three times more likely to be new patients receiving RRT than non-Aboriginal people (Canadian Institute for Health Information (CIHI), 2013). The CORR report also notes that ESKD incidence among Aboriginal people in Canada continues to rise, while it appears to have stabilized for the non-Aboriginal population (Canadian Institute for Health Information (CIHI), 2013). At all levels of proteinuria and estimated glomerular filtration rate (eGFR), Aboriginal people are at higher risk of progression to ESKD (Samuel et al., 2014), and Aboriginal children have increased odds (1.8- to 3.2-fold greater) of developing ESKD compared with Caucasian children (Samuel et al., 2012).

To determine better ways of addressing these high rates, CIHI examined the mechanisms linking CKD to First Nations people (Canadian Institute for Health Information (CIHI), 2013). The authors found that First Nations people tend to have more risk factors for CKD, such as diabetes and obesity, than non-First Nations people. First Nations youth are living longer with diabetes and are at greater risk of developing complications of this disease, including kidney damage. Access to specialized medical care is more limited given that First Nations people are also more likely to live in remote communities, and survival rates following dialysis are lower than for non-First Nations people. Living conditions in remote First Nations communities are sometimes challenging due to economic conditions, poor water supply, and limited access to affordable food and to social and recreational services. Similarly, Jiang et al. (2014) noted that the mean age of onset of diabetes for First Nations people in Saskatchewan was 47.2 years compared to 61.6 years for non-First Nations people. In addition, they reported that the risk of ESKD among First Nations people with diabetes was 2.7 times higher than non-First Nations counterparts (Jiang et al., 2014).

These findings also point to the need for measures to delay the onset of diabetes and slow the progression of CKD, particularly among First Nations people (Jiang et al., 2014). Action is required on multiple levels to address the social determinants of health and ensure the delivery of high-quality healthcare services. CIHI describes a scan of interventions aimed at improving the experiences of indigenous people with CKD (see appendices of their report) (Canadian Institute for Health Information (CIHI), 2013). Some approaches include reorienting health services to account for social and economic circumstances of communities, providing culturally appropriate practices, and collaborating with communities with high rates of CKD and other chronic diseases. Strategies to increase income in First Nations communities will likely have a beneficial effect on the prevalence of CKD and ESKD. For example, Jones-Smith, Dow, & Chichlowska (2014) found that increasing economic resources in an indigenous community by opening a casino was associated with decreased risk of childhood obesity.

Prevention of Chronic Kidney Disease

Worldwide and in Canada, the majority of initiatives for CKD prevention use mid-stream and downstream approaches that target different stages of CKD progression (Levin et al., 2008; Manitoba Renal Program (MRP), 2013; Smith et al., 2008). Mid-stream strategies include voluntary screening (i.e., local and organization-based) and legislated screening for CKD, although research is still required to study their cost-effectiveness (Fink et al., 2012). Downstream strategies include monitoring patients' risk of progression to kidney failure and preventing complications of RRT, such as infection due to dialysis. Screening and monitoring strategies are discussed further in the following section.

Several authors have recommended upstream strategies that involve education about and implementation of lifestyle management to reduce exposure to factors that increase the risk of CKD (Levin et al., 2008; Stengel, Tarver-Carr, Powe, Eberhardt, & Brancati, 2003). These lifestyle changes, which are recommended for the prevention of diabetes, high blood pressure and cardiovascular disease, as well as CKD, may include increased physical activity, weight control, control of salt intake, and decreased use of cigarettes and alcohol. As described above, upstream strategies that address the social determinants of health — to support the ability to adopt lifestyle changes — are also warranted, given the association between low SES and risk factors of CKD.

Screening and Monitoring Strategies for Adults

Screening for CKD and monitoring progression of the disease can have many health, quality of life and cost-saving benefits. Early cases of CKD (stages 1 and 2), which account for the majority (75%) of cases, typically have no symptoms, and identifying them would prompt the initiation of treatment and lifestyle counselling to slow disease progression and prevent kidney failure (Arora et al., 2013).

A systematic review published by the Agency for Healthcare Research and Quality (AHRQ) found no consistent evidence of the health and cost benefits of systematic screening for early-stage CKD in the general population (Fink et al., 2012). However, the review recognized the potential benefits of targeted screening in high-risk populations with risk factors such as diabetes, hypertension, cardiovascular disease and older age because of the increased risk of requiring treatment for ESKD. Other authors have noted that the complexity of CKD requires screening for a combination of risk factors (e.g., family history of kidney failure, chronic diseases, obesity, advanced age) and indicators of kidney damage (e.g., high proteinuria, low eGFR levels) (Arora et al., 2013; Fink et al., 2012; Kidney Disease Improving Global Outcomes (KDIGO), 2013; Levin et al., 2008; Manns et al., 2010). This approach would be more cost-effective in populations that already have one or more of these risk factors and are thus more likely to develop CKD. Kidney Disease Improving Global Outcomes (KDIGO) recommends screening for CKD in high-risk populations (Levey et al., 2007).

A recent review of studies examining the cost-effectiveness of primary screening for CKD by members of our research team concluded that the most appropriate screening strategy is to target high-risk individuals with diabetes or hypertension (Komenda et al., 2014). Screening populations with a higher incidence of CKD or accelerated progression of CKD may also be cost-effective. Cost-effectiveness in this review was defined as less than $50,000 per quality-adjusted life-year, meaning an intervention costing less than this would yield good value for money from a policy perspective (Komenda et al., 2014).

The AHRQ review found insufficient evidence to conclude whether or not there are potential harms associated with systematic CKD screening and monitoring. As with all screening programs, potential harms may include an increase in patients' anxiety and the delivery of unwarranted health services, with possible adverse effects and elevated healthcare costs (Fink et al., 2012). Fortunately, newer and more accurate methods for CKD screening have decreased the chance of falsely identifying cases of CKD and causing undue medical treatment and anxiety (Tangri et al., 2011).

Progress in screening systems for CKD has also improved their usefulness in several other ways. Earlier screening methods based solely on eGFR, a measure of kidney function, were not successful in capturing the majority of cases. It has now been shown that eGFR alone cannot predict risk for progression over time (Glassock & Winearls, 2008). Measuring urine albumin (protein) excretion can add significantly to the ability to identify individuals most at risk, as higher levels of albuminuria indicate elevated risk of rapid decline in kidney function. In fact, screening patients for albuminuria alone can identify 40% to 50% of undiagnosed cases at increased risk of developing CKD (Van Der Velde et al., 2009). To diagnose risk of progression to ESKD, combining measures of eGFR and albuminuria is optimal (Hallan et al., 2009; Peralta et al., 2011). Reducing levels of albuminuria has been linked to slowing the progression of CKD, making early detection of albuminuria a promising strategy to prevent or delay the need for RRT (Lea et al., 2005; Ruggenenti, Perna, & Remuzzi, 2003).

Treatment of Adults with Chronic Kidney Disease

Primary Care for Chronic Kidney Disease

People in early stages of CKD can be safely managed by primary care providers, and it is essential that patients receive good health information so that they can participate in their care. Implementing routine monitoring through common laboratory testing provides key information for primary care physicians and patients so that treatment goals can be met (Wyatt, Konduri, Eng, & Rohatgi, 2007).

Several randomized controlled trials have reported treatments that are effective at reducing the risk of poor clinical outcomes for people with CKD (Fink et al., 2012). These benefits appear to be limited to certain subgroups of patients. Specifically, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) reduced the risk of ESKD in patients with urinary albumin, diabetes and hypertension. Further, ACE inhibitors also reduced mortality risk in studies examining patients at high risk for cardiovascular complications and urinary albumin. Some studies examined combinations of treatments to determine if one approach is better than another, but they did not find significant differences. These inconclusive studies included high- versus low-doses of ARBs, strict versus standard control of blood pressure and blood sugar, combination versus monotherapy, and usual care versus intensive multidisciplinary interventions where blood pressure, diabetes, cholesterol and reduction of nephrotoxic drug exposure are targeted at the same time (Fink et al., 2012).

This suggests that standard good care (lifestyle counselling, controlling blood sugar and hypertension) should be the goal for people with CKD, along with continued efforts at prevention. Primary care providers should also discontinue medications that may potentially damage the kidneys and instead take advantage of medications known to have a protective effect, including statins, ACE inhibitors and ARBs (Richards et al., 2008). In addition, special care is required for people with diabetes, because this illness is a risk factor for ESKD. The Canadian Diabetic Association recommends annual screening for all patients with diabetes with urinary albumin-creatinine ratios (American Diabetes Association, 2013; Canadian Diabetes Association, 2013). Health care providers should be attentive to and address the mental health needs of people with CKD, given the association that was found between CKD and mental disorders. Untreated mental disorders could interfere with CKD prevention and early intervention efforts.

Primary care chronic disease management models are designed to improve outcomes through the integration of teams of health professionals, electronic medical records, trained staff, and educational components so that patients can learn to monitor their health. Evaluation of these care models is important because not all primary care models yield the desired results. For example, a comparison of care between usual model and new model, among patients with CKD and moderately to severely reduced kidney function, did not detect a difference in outcomes (eGFR decline, control of risk factors). Usual care was family physician-coordinated care, and the new model was nurse-coordinated team care with a nephrologist (Barrett et al., 2011).

Monitoring by Nephrologists

The benefits of early care by a nephrologist for patients with CKD have been studied extensively (Curtis, Barrett, Djurdjev, Singer, & Levin, 2007; Lee et al., 2012). Early nephrology referral, before initiation of dialysis, has been shown to be associated with a reduction in mortality (Winkelmayer, Owen, Jr., Levin, & Avorn, 2003), and to be cost-effective (McLaughlin, Manns, Culleton, Donaldson, & Taub, 2001). In addition, longer duration of nephrology care during the pre-dialysis period is associated with improved long-term survival after dialysis has begun (Jungers et al., 2001). Patients who saw a nephrologist less than five times in the year prior to dialysis had a 15% higher mortality rate in the first year of dialysis compared to those who were seen five times or more (Avorn et al., 2002a). In another study, patients with CKD who were referred late to a nephrologist were less likely to have permanent vascular access prior to starting dialysis, adding to the burden of disease (Avorn et al., 2002b). Given the high prevalence of CKD, it is imperative that nephrology services be used efficiently. Individuals at greatest risk of progression to ESKD benefit most from nephrology care. Current recommendations suggest that coordinated, interprofessional nephrology teams should be consulted when patients' eGFR falls below 30 ml/min per 1.73 m2 (Levey et al., 2003).

Screening, Prevention and Treatments for Children with Chronic Kidney Disease

The epidemiology of pre-dialysis CKD remains largely unknown in children in North America and around the world. The only countries with longitudinal data on population-based estimates of proteinuria in children are Japan, Taiwan and Korea. Japan has had an annual, mandatory school-based screening program for urinary abnormalities since 1973 and has now screened hundreds of thousands of children. The mean prevalence of proteinuria in the 1990s was 0.62% in elementary school children and 0.94% in junior high (Murakami, Yamamoto, Ueda, Murakami, & Yamauchi, 1991), and these rates have remained fairly stable over time (Murakami, Hayakawa, Yanagihara, & Hukunaga, 2005). Rates in Korea are quite similar (Park et al., 2005), whereas they are considerably lower in Taiwan, with a prevalence of proteinuria of only 0.058% on first morning specimens (Lin, Sheng, Chen, Lin, & Chou, 2000). The National Health and Nutrition Examination Survey in the United States (NHANES III) evaluated urine albumin-creatinine ratios in 4,088 children eight to 18 years old in 1999, and 12% had an abnormal result (Mueller & Caudill, 1999). A follow-up NHANES (Add Health Wave III Study) revealed a prevalence of albuminuria of 4.4% and overt proteinuria in 0.8% (Ferris et al., 2007). Data on screening in children in Canada has not been published since the 1970s at which time 1.5% of girls and 0.49% of boys were found to have persistent proteinuria (Silverberg et al., 1973).

No randomized controlled studies have been conducted to establish the efficacy of screening children for CKD or CKD risk factors. However, promising data from the Japan experience suggests that screening and early intervention in populations have decreased ESKD in adolescents (from 174 in 1984 to 108 in 2002) (Urakami et al., 2007). As described earlier in this chapter, screening studies in adults have been shown to be cost-effective only when targeted to high-risk populations (Komenda et al., 2014). There is a clear need for further research in this area to determine if active surveillance in children could decrease the burden of CKD in adolescents and adults (Hogg, 2009).

Once CKD is identified in children, the principles of treatment are quite similar to those in adults. Hypertension and proteinuria are the most important risk factors for progression. Strict blood pressure control is the treatment most supported by both observational and intervention studies (Wong et al., 2012; Wuhl et al., 2009) and ACE inhibitors are the drug of choice (Kidney Disease Improving Global Outcomes (KDIGO), 2012; Wuhl et al., 2009). Treatment of acidosis to slow progression of CKD and optimize growth is also an important treatment target (de Brito-Ashurst, Varagunam, Raftery, & Yaqoob, 2009). In youth with diabetes, optimizing glycemic control is the most important clinical target for disease management (Canadian Diabetes Association, 2013). Healthcare providers should also monitor and treat the mental health of children with CKD, as we found significant increases in rates of mood and anxiety disorders, substance abuse, and suicide in these children (Chapter 5).

Despite the lower rates of CKD in children, there is an increasing population of children affected by CKD risk factors. These include hypertension (Halbach & Flynn, 2013) and type 2 diabetes (Dart A.B. et al., 2015), both largely driven by increasing overweight and obesity rates (Statistics Canada,2013). We were unable to adequately evaluate the prevalence of obesity or hypertension in Manitoba children due to the limitations of administrative data in these areas. However, these health complications in children are highly relevant, as they have the potential to intensify the risk of early onset of CKD in the population over time. A CKD prevention strategy must therefore include a focus on addressing childhood obesity.

Factors Associated with End Stage Kidney Disease Treatment Type in Manitoba

As discussed earlier, the type of RRT used by patients with ESKD has important health and cost implications. Centre-based hemodialysis is associated with lower quality of life for patients, poorer health outcomes and higher costs compared to home-based dialysis options and to kidney transplant. To shed light on some of the factors that can be addressed to shift ESKD patients away from centre-based hemodialysis, we conducted an additional analysis to examine the relationship between a number of factors and the type of treatment that patients used when they began their first RRT.

Using data from the MCHP Repository, we examined sociodemographic and healthcare-related factors for patients who started centre-based hemodialysis versus other types of RRT (home-hemodialysis, peritoneal dialysis and kidney transplant). Our analyses included all Manitoba residents who had started RRT between April 1, 2007, and April 1, 2012. We included patients who had some contact with a nephrologist prior to April 1, 2007, to allow for sufficient time for patients to start some form of dialysis. Patients who died before starting RRT were excluded from the analyses. Logistic regression was conducted to calculate the odds ratios associated with the factors of interest.

We found that a number of factors were associated with the likelihood of starting RRT on centre-based hemodialysis (Table 7.1). Residents living in lower-income areas (odds ratio (OR): 1.847) and those who had not seen a nephrologist before RRT began (OR: 1.389) were significantly more likely to use centre-based hemodialysis than other types of RRT. Patients less likely to start on centre-based hemodialysis as their primary renal replacement therapy were those who were younger than 65 (OR, ages 0–44: 0.416; OR, ages 45–64: 0.467), lived in a region with healthy populations (Southern Health/Santé Sud, OR: 0.573), or received medications that delay CKD progression (ACE inhibitors and ARBs) (OR: 0.622). By healthier populations, we mean regions that have lower premature mortality rates in Fransoo et al. (2013). Gender and diabetes were not significant predictors of the type of RRT that people with ESKD received.

These findings point to several approaches that may help to promote optimal outcomes for patients and optimal use of healthcare resources. Our findings suggest that appropriate referrals to nephrology care teams decreases the use of centre-based hemodialysis in favour of home-based dialysis or kidney transplant. Nephrology care before patients start dialysis has also been shown to increase survival and be cost-effective, as discussed earlier in this chapter (see "Monitoring by Nephrologists").

We note that residents of lower-income areas are about 85% more likely to use centre-based hemodialysis compared to residents of higher-income areas. As described earlier in this chapter, people living in low socioeconomic conditions face barriers in accessing early interventions required to prevent and treat CKD. Addressing the social determinants of health may decrease the number of people who need RRT in the first place. When RRT is required, addressing the socioeconomic barriers to home-based therapies would increase their use and improve both quality of life and cost-effectiveness.

Table 7.1: Factors Associated with Starting Centre-Based Hemodialysis Compared to Other Treatment Types, 2007/08-2011/12

Factors		Adjusted Odds Ratios	95% Confidence Intervals	p-values
Age (Ref: 65 years and older)	0-44	**0.416**	**0.278-0.623**	**<0.001**
	45-64	**0.467**	**0.335-0.651**	**<0.001**
Sex (Ref: Male)	Female	1.026	0.777-1.356	0.8551
Diabetes Diagnosis (Ref: No)	Yes	1.289	0.948-1.751	0.1050
Income Quintile (Ref: Q2-Q5)	Q1 (lowest)	**1.847**	**1.338-2.551**	**0.0002**
Health Region (Ref: Winnipeg)	Southern Health/Santé Sud	**0.573**	**0.372-0.883**	**0.0116**
	Prairie Mountain Health	1.456	0.871-2.432	0.1516
	Interlake Eastern	0.863	0.566-1.315	0.4931
	Northern	1.203	0.763-1.896	0.4267
Nephrologist Visit Before Dialysis (Ref: 1+ years before April 1, 2007)	Not yet Seen	**1.389**	**1.023-1.888**	**0.0355**
	0-90 days	1.028	0.549-1.926	0.9315
	91-365 days	0.971	0.503-1.873	0.9295
ACE Inhibitor & ARB Use (Ref: No)	Yes	**0.622**	**0.427-0.906**	**0.0133**

bolded values indicate that the factor effect is statistically significant

We found a significant association between older age (65 years and older) and centre-based hemodialysis use. As individuals age, they are often faced with physical and cognitive impairment which is exacerbated by the presence of CKD (Walker et al., 2013). Many older patients suffer from multiple comorbidities and may not be strong enough to follow an intensive dialysis schedule. Furthermore, life expectancy of older patients is limited and their quality of life may be significantly reduced on any form of dialysis. A conservative, palliative, non-dialysis approach to care of these patients should be considered on a case-by-case basis.

To further explore factors that may be important in decreasing the use of centre-based hemodialysis in Manitoba, we looked at more recent data (March 2014) on the number and characteristics of people on home hemodialysis (data not shown). It appears that efforts at increasing home hemodialysis starts in Manitoba have been successful. Between 2012 and 2014, the number of patients on home hemodialysis increased considerably, from 31 to 49. Of these 49 cases, 86% were male and 47% were residents of Winnipeg. People most likely to use home hemodialysis were those in the middle-aged group (47%), compared to 16% who were aged 18 to 44, and 37% who were 65 years and older. Home hemodialysis was used as frequently in lower-income areas as in higher-income areas. This description, using recent data, is encouraging given that our findings from the logistic regression (shown above) found that centre-based hemodialysis was used more frequently in lower-income areas.

Current Screening, Prevention and Treatment Initiatives in Manitoba

A number of screening, prevention and treatment efforts have recently been initiated in Manitoba to reduce the burden of CKD. We have listed the main ones and provided a very brief description. Additional information is available on the Kidney Health Website of the Manitoba Renal Program (http://www.kidneyhealth.ca/wp).

The First Nations Community Based Screening to Improve Kidney Health and Prevent Dialysis (FINISHED) Project

This project was launched in 2013 and led by a partnership among the Diabetes Integration Project, the Manitoba Renal Program (MRP), and the Winnipeg Regional Health Authority (Lavallee et al., 2015). The funding is provided by Health Canada's Health Services Integration Fund (Manitoba Renal Program (MRP), 2013). The aim of the project is to provide mobile point-of-care kidney disease screening, risk prediction and treatment through a proven model of delivery in First Nations communities. The goals include immediate prevention and early detection of kidney disease, demonstration of sustainable comprehensive kidney care unique to First Nations people, and ultimately a reduction in the burden of kidney failure requiring dialysis in Manitoba (Manitoba Renal Program (MRP), 2013).

Risk-Based Triage

In 2011, following the launch of automatic eGFR reporting by all labs in Manitoba, the MRP faced a 12- to 18-month wait list for new, non-urgent referrals. A new system was put into place to triage referrals using the Kidney Failure Risk Equation, described in Chapter 8. Patients with a five-year kidney failure risk of less than 3% and having no other high-risk features related to the referral were not seen by a nephrologist. This allowed the nephrology teams to eliminate virtually any wait time to see a nephrologist for patients at high risk of progression to ESKD. This system was made possible at Seven Oaks Hospital and St. Boniface Hospital with the addition of a physician assistant.

Nurse-Led Telehealth Clinics in Thompson

This program began in 2012 with the addition of one-time pilot funding from Manitoba Health, Healthy Living and Seniors. It is run out of the Health Sciences Centre Nephrology Clinic program and uses a fully trained subspecialty CKD nurse in Thompson. The program allows for patients in the Northern Health Region to get full multidisciplinary CKD care in Thompson without having to travel to Winnipeg, providing optimal care closer to home and lower travel costs for patients.

Renal Health Outreach

Renal Health Outreach is an ongoing program run by the MRP offering training for healthcare practitioners in rural and remote communities on prevention, CKD care and types of dialysis.

Electronic Kidney Health Record (eKHR)

The eKHR is a fully functional clinical and administrative data for CKD patients cared for by the MRP (Manitoba Renal Program (MRP), 2013). The system has been ongoing since 2011 and now registers and schedules all dialysis patients (including patients living outside of Winnipeg and peritoneal dialysis patients of local centre dialysis units). The system also houses comprehensive data on vascular access and medications. The system is based on the BC Renal Agency's PROMIS data, and the two provinces have been close collaborators on the project. More modules to enhance CKD surveillance and care of existing patients are planned over the next two years.

CHAPTER 8: KIDNEY FAILURE RISK EQUATION

In this chapter, we describe our evaluation of the Kidney Failure Risk Equation (KFRE), a risk stratification tool for patients with end stage kidney disease (ESKD), to assess its potential benefits for use in Manitoba. The KFRE was developed by Tangri et al. (2011) to identify individuals with chronic kidney disease (CKD) who are at greater risk of developing kidney failure, and thus allow for targeted intervention to prevent progression of the disease. This tool uses routinely collected laboratory data and predicts the progression of CKD to dialysis in patients with moderate to severe loss of kidney function (CKD Stages 3-5). Since 2011, the KFRE has been demonstrated to be accurate in several diverse populations in North America and Western Europe. However, certain minorities with higher rates of kidney failure, such as First Nations people, were underrepresented in the original development population and in the subsequent validation cohorts. Considering Manitoba's ethnic diversity and the high burden of CKD and kidney failure in the province's indigenous communities, a validation study of the KFRE was needed prior to clinical implementation.

Key Findings

- Using routinely collected laboratory data, the KFRE was successful in identifying 97% of Manitobans who required renal replacement therapy (RRT) and correctly identified 62% of those who did not receive RRT within five years.
- This validation study demonstrates the feasibility of using the KFRE as a tool to predict progression to kidney failure in Manitoban's and to guide surveillance of vulnerable populations. The KFRE holds value for clinicians and policy makers in decision-making on appropriate interventions.

Methods of the Validation Study

The KFRE uses four variables (age, sex, estimated glomerular filtration rate (eGFR) and proteinuria) to estimate the risk of progression to ESKD for people with an eGFR less than 60 ml/min/1.73m^2 (see Appendix 1 for more details). Proteinuria values are based on results from dipstick proteinuria, albumin-creatinine ratio (ACR) or protein-creatinine ratio (PCR). Values for eGFR are estimated using the Modification of Diet in Renal Disease (MDRD) method described in Chapter 2.

To validate the model's performance with Manitoba's population, we developed a cohort of 1,512 people with CKD who had Diagnostic Services Manitoba (DSM) laboratory data (eGFR below 60 and either ACR or PCR) from October 1, 2006, to March 31, 2007. The table below shows how we obtained our cohort. It also illustrates that many people were excluded due to unavailable laboratory data. (See Appendix Table 8.1 for characteristics of CKD patients in the cohort.)

Table 8.1: Inclusion and Exclusion Criteria for Patients in the Kidney Failure Risk Equation Validation Cohort by End Stage Kidney Disease (ESKD) Group

Inclusion and Exclusion Criteria (October 1, 2006-March 31, 2007)	Number of Adults by ESKD Group After 5 Years		Total
	ESKD	No ESKD	
Adults in Manitoba (aged 18+)	1,560	907,234	908,794
Exclusions*			
No laboratory tests	872	840,924	841,796
No eGFR tests	60	9,577	9,637
No ACR tests	407	10,956	11,363
eGFR > 60 ml/min/1.73 m^2	70	44,416	44,486
Final cohort**	151	1,361	1,512

* exclusion criteria are based on availability of laboratory data

** adults with available ACR tests and eGFR of 10-60 ml/min/1.73 m^2

We tested the performance of the KFRE based on the model's sensitivity, specificity, positive predictive value, and negative predictive value. Sensitivity tells us the rate of true-positives: the probability that the equation will correctly identify a patient with high risk of progressing to kidney failure. Specificity tells us the rate of true-negatives: the probability that the equation will correctly identify a patient who does not have high risk of disease progression. A small positive predictive value would tell us that the test identifies too many patients as being high risk and may need to be followed up with another assessment. The positive predictive value and negative predictive value are both dependent on the prevalence of an illness. (For equations used for these values, see Chapter 2, "Validation the CKD Definition Using Administrative Data for Children.)

Using data from the MCHP Repository, we examined five different methods for determining which pre-dialysis CKD cases will require RRT after five years:

- KFRE with a less restrictive threshold (3% risk);
- KFRE with a more restrictive threshold (10% risk);
- poor kidney function (eGFR<30 ml/min/1.73m^2);
- less restrictive threshold of poor kidney function (eGFR<45 ml/min/1.73m^2); and
- having a nephrology visit before April 1st, 2007.

Validation and Application in Manitoba

The four-variable KFRE accurately distinguished patients who developed kidney failure within five years from patients who did not develop kidney failure (c-statistic: 0.900; 95% CI: 0.876-0.923) (Table 8.2). In contrast, the current model for detecting CKD in Manitoba (eGFR alone) had much more modest accuracy (c-statistic: 0.784; 95% CI: 0.742-0.826).

Using the threshold of a 3% risk of developing kidney failure over five years, the KFRE had a sensitivity of 97%, meaning that 97% of cases of ESKD were identified correctly. In other words, out of 151 patients who progressed to kidney failure within five years, almost all (146) had a risk greater than 3% at baseline (see Appendix Table 8.2 for patient counts). Specificity at this low-risk threshold was 0.623, meaning that 62% of cases that did not progress to ESKD were identified correctly. When the 10% risk threshold was applied, the KFRE had a lower sensitivity of 0.861 but a higher specificity at 0.802, as expected. In contrast, a conservative eGFR threshold of 45 ml/min/1.73m^2 (moderately to severely decreased eGFR) had lower sensitivity (0.841) and specificity (0.544), as well as lower positive and negative predictive values. An eGFR threshold for severely decreased kidney function (<30 ml/min/1.73m^2) resulted in even lower sensitivity (0.623). Compared to a KFRE threshold of 3% over five years, the nephrology visit threshold resulted in comparable specificity (0.636) but lower sensitivity (0.788). (Appendix Table 8.3 provides results for an additional KFRE validation.)

Table 8.2: Accuracy of Screening Thresholds for Five-Year Progression to End Stage Kidney Disease (ESKD)
2007/08–2011/12

Screening Methods and Risk Thresholds	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Kidney Failure Risk Equation				
> 3% risk of progression to ESKD	0.967	0.619	0.220	0.994
> 10% risk of progression to ESKD	0.861	0.802	0.325	0.981
Estimated Glomerular Filtration Rate				
< 30 ml/min/1.73m^2	0.623	0.837	0.297	0.952
< 45 ml/min/1.73m^2	0.841	0.544	0.170	0.969
Prior Nephrology Visit	0.788	0.636	0.193	0.964

Overall c-statistic for KFRE: 0.900 (95% CI 0.876 - 0.923)

Overall c-statistic for eGFR: 0.784 (95% CI 0.742 - 0.826)

Overall c-statistic for Prior nephrology visit: 0.712 (95% CI 0.677 - 0.747)

These findings demonstrate that the KFRE has improved accuracy, compared to the current method, in predicting the five-year risk of progression to ESKD in a population-based sample of Manitobans with CKD. At a 3% risk threshold over five years, the KFRE is highly sensitive and modestly specific.

This analysis also shows that integration of the KFRE into a passive surveillance system for detecting high-risk CKD is feasible, is likely to result in accurate risk estimates, and may improve clinical decision-making. Currently, estimated GFR is reported routinely in Manitoba, and patients with a low eGFR (<60 ml/min/1.73m^2) are identified as having CKD. Referral to a nephrologist of all patients with an eGFR below 60 or 45 ml/min/1.73m^2 is impractical, infeasible, and unlikely to be of benefit in the majority of people with CKD, who are at low risk of progression. In contrast, our findings indicate that a KFRE-based threshold of 3% should be considered as a criterion for determining nephrology referral.

Implementation of this risk stratification tool would likely result in better resource allocation in CKD care, where treatment intensity is aligned with risk of progressing to ESKD rather than kidney function. Furthermore, as nephrology resources expand or decline, the risk thresholds for referral could be adjusted to 5% or 10%. For example, we observed that fewer people are identified as high risk when we increased the KFRE threshold from 3% to 10%. The KFRE is useful for identifying which patients should receive higher intensity and more costly interdisciplinary nephrology care and those who can be safely managed by the primary care provider alone.

CHAPTER 9: SUMMARY OF RESULTS AND RECOMMENDATIONS

The purpose of this report was to estimate the future burden of end stage kidney disease (ESKD), the most advanced stage of chronic kidney disease (CKD), on Manitoba's healthcare system and to explore measures that might help to decrease the prevalence of these conditions.

Since 2003, Manitoba has had the highest rates of ESKD in Canada, alongside Newfoundland and Labrador (Canadian Institute for Health Information (CIHI), 2014). While the rate of new cases of ESKD appears to have levelled off in Canada, it continues to rise in Manitoba (Canadian Institute for Health Information (CIHI), 2015). As the population ages and the prevalence of diabetes increases — two key risk factors for kidney disease — the number of Manitobans who develop this chronic disease is expected to continue to grow. Among patients receiving dialysis to replace the function of their failing kidneys, ESKD is associated with a poor quality of life, limited survival and high medical costs (costs are detailed in Chapter 3), and Manitoba has higher proportions of people with ESKD who are on centre-based hemodialysis (53.2%) than the Canadian average (45.0%), with the poorer quality of life and higher cost implications of that type of treatment.

Because of these concerns, Manitoba Health, Healthy Living and Seniors asked the Manitoba Centre for Health Policy (MCHP) to explore a series of questions to aid in planning of equipment and resources and to guide policy. In this chapter, we summarize our findings on each question and provide recommendations based on these findings.

Summary of Results

What are the future needs for renal health services (dialysis and kidney transplants) in Manitoba?

To estimate future needs, we examined trends in the use of renal replacement therapy (RRT) in Manitoba from 2004 to 2012. The number of people with ESKD has been increasing over time. In 2012, there were 1,833 Manitoba residents receiving RRT; 32.6% had a functioning kidney transplant and 67.4% were on dialysis. Of those receiving dialysis, 79.0% were on centre-based hemodialysis, 18.5% were on peritoneal dialysis (a home-based procedure) and 2.5% were on home-based hemodialysis. Because of the small number of people on home hemodialysis, our analyses group together the two types of home-based dialysis.

Based on these trends, we estimate that 3,077 Manitoba residents will be receiving RRT by 2024, a 68% increase from 2012. The increases will be more pronounced among people with diabetes and people aged 65 and older.

Given that many factors may change over the course of 12 years, we also examined five "what if" scenarios. By modifying certain variables in our models, we explored hypothetical situations to improve our understanding of how best to decrease the projected number of adults with ESKD and to shift people needing RRT from centre-based hemodialysis (the most expensive and restrictive type of RRT) to home-based dialysis. We explored the following scenarios:

- diabetes prevalence remains at 2012 rates (rather than continuing to increase);
- peritoneal dialysis increases to 30% of new dialysis starts;
- home hemodialysis increases to 8% of new dialysis starts;
- kidney transplants rates increase by 25%;
- mortality rates of people with ESKD decreases by 20%.

The scenario that showed the most significant decrease in the total number of people needing RRT, as well as the largest decrease in the proportion of adults using centre-based hemodialysis, was maintaining diabetes prevalence at its current rate. Not surprisingly, a decrease in mortality rates of adults living with ESKD would increase the number of adults requiring treatment. The number of people on centre-based hemodialysis decreases when more people are started on peritoneal dialysis and home hemodialysis and when more kidney transplants are performed. For example, if measures are taken to increase new starts of peritoneal dialysis to the 30% target, 95 more people would use peritoneal or home hemodialysis dialysis, 15 more would receive kidney transplants and 98 fewer people would require centre-based hemodialysis.

What is the geographic distribution of this population?

We found significant disparity in ESKD prevalence across regions in 2012. Remote communities, where the population is primarily First Nations people, followed by the Northern Health Region have the highest rates of ESKD, after adjusting for age and sex. These areas also have the lowest proportion of kidney transplants relative to other treatment types. Prairie-Mountain Health and the Southern Health/Santé Sud Regions have the lowest ESKD rates in Manitoba. Our results are consistent with previous research showing that ESKD rates are more than twice as high (and rising) for Aboriginal people compared to non-Aboriginal people in Canada (Canadian Institute for Health Information (CIHI), 2013), highlighting the need for targeted prevention and early intervention efforts, particularly among First Nations communities.

Increases in ESKD are expected in all of Manitoba's health regions but varying in magnitude and by type of RRT. The increases in Winnipeg are similar to those in Manitoba overall; Winnipeg will continue to have the highest number of people with ESKD because of its larger population and service capacity. Southern Health/Santé Sud and Northern Health Regions will experience the highest increases in the use of dialysis. In Southern Health/Santé Sud, the number of people on centre-based hemodialysis is projected to increase by 82%, from 68 in 2012 to 124 by 2024. In Northern Health, a 75% increase is projected in the need for centre-based hemodialysis, from 118 people in 2012 to 207 by 2024, and the number of kidney transplants is expected to increase by 130%, from 28 in 2012 to 64 by 2024. The dramatic increase in kidney transplants is likely related to the region's younger population who are better candidates for that procedure.

What are the characteristics of the future population of Manitoba residents who will require renal replacement treatment?

To answer this question, we examined the characteristics not only of people currently requiring RRT, but also of the population with CKD who are at greatest risk for progressing to kidney failure in the future. This provides a clearer picture of the overall CKD spectrum and is crucial in planning early intervention strategies and treatment services for this population.

Characteristics of adults with chronic kidney disease and end stage kidney disease

We estimated the prevalence of CKD in Manitoba adults 18 years and older to be between 7.4% and 13.8%. We observed that Northern and remote communities are disproportionately affected by CKD and ESKD, with rates two to three times higher than the general population. The older population and those living in lower-income areas also have higher rates of CKD and ESKD. Women have slightly higher rates of CKD; however, men have higher rates of ESKD. People with ESKD had the highest rates of co-existing medical conditions, particularly cardiovascular diseases, as well as mental disorders, and high rates of use of prescription drugs and other healthcare services, but the rates are also alarmingly high among those with CKD at high risk of progressing to kidney failure.

Characteristics of children with chronic kidney disease and end stage kidney disease

We identified a prevalence of CKD in Manitoba children of 1.49% to 3.41% and an ESKD prevalence of 58 cases per 1,000,000 children. Although this is lower than the adult rates, affected children had high rates of medical and mental health comorbidities and high use of healthcare services, highlighting the significant health burden of this disease at all stages in children. For children with ESKD, the extent of care is tremendous; we found they had hospitalization rates 73 times higher, ambulatory physician visits nine times higher and specialist visits 33 times higher in children with ESKD, compared with children without CKD. Important regional differences were also seen for children, with Northern and remote communities identified as important priority regions for primary and secondary prevention strategies for all ages. An important finding was the currently low risk for progression for most children in the province with CKD.

What preventive, screening, and education measures and affiliations with existing programs might reduce the number of Manitobans who will require dialysis? (i.e., what are the modifiable risk factors?)

Recent research does not adequately address the question of whether systematic screening for CKD in the general population improves clinical outcomes or increases harms. However, current research supports the potential benefits of screening of high-risk groups, such as First Nations people and populations with high levels of diabetes, hypertension, and cardiovascular disease. In Manitoba, the Northern Health Region and remote communities are disproportionately affected by CKD and ESKD and should be prioritized for screening and intervention strategies. Newer screening methods have decreased the chance of falsely identifying someone with CKD as being at high risk of progressing to ESKD. This improvement in screening methods is important because false-positives may lead to unnecessary medical treatment and anxiety in patients.

Diagnosis of CKD in its early stages is often missed because patients typically have no symptoms. However, early identification of people at greater risk for progressing to ESKD provides the opportunity for lifestyle counselling to address risk factors and treatments to slow the progression of the disease. Therefore, active surveillance strategies in primary care are needed, along with clear guidelines for practitioners to provide these early intervention strategies and referrals to nephrology care for high-risk individuals. Although rates of advanced CKD are lower among children, risk factors are now highly prevalent in Manitoba youth and will contribute to increasing rates of ESKD in adult populations. Prevention and early treatment strategies must therefore include children to decrease the lifetime risk for kidney failure in the population.

We tested the Kidney Failure Risk Equation (KFRE) to determine its validity for use in Manitoba. The KFRE, a highly accurate model for predicting the progression of CKD to kidney failure, was previously developed by members of our research team. Using routinely collected laboratory data, we found that the KFRE successfully identified up to 97% of people who developed ESKD and correctly determined at least 62% of those who did not develop ESKD. This is a considerable improvement over the current system and could easily be incorporated into Manitoba's laboratory system.

We also explored factors that determined which type of RRT patients start on. This helps in the understanding of how to address the important health and cost implications of the different types of dialysis, as centre-based hemodialysis is associated with lower quality of life for patients, poorer health and higher system costs, compared to home-based dialysis or kidney transplant. Patients living in lower-income areas and those who had not seen a nephrologist before starting RRT were significantly more likely to use centre-based hemodialysis than other types of therapy. Patients younger than 65, living in Southern Health/Santé Sud Region, or receiving medications that decrease the progression of CKD (ACE inhibitors and ARBs) were less likely to start on centre-based hemodialysis. Strategies to improve early detection of high-risk in patients with CKD and ensure timely referrals to nephrology will increase the use of home-based dialysis and decrease overall healthcare costs.

Recommendations

Develop a comprehensive public health strategy for chronic diseases (including kidney disease) in Manitoba

The findings of this report and of previous research indicate that ESKD in Manitoba should be addressed within a comprehensive public health strategy that encompasses a range of interrelated chronic diseases. This would be more effective than addressing these conditions separately. The strategy should focus on primary and secondary prevention of CKD in adults and in children by targeting earlier stages of the disease as well as its underlying causes, risk factors, and comorbid conditions, particularly diabetes, hypertension and cardiovascular disease. These conditions have common underlying risk factors related to obesity and health behaviours, and they respond to common treatments and prevention strategies. Partnerships among organizations mandated to improve public awareness of risk factors and health behaviours for chronic diseases would contribute to decreasing rates of CKD and, in turn, ESKD. Including indigenous communities in these partnerships is essential to address their high risk of ESKD. Early intervention in these high risk populations with poorer access to healthcare services (Gao et al., 2007; Martens et al., 2002) should be considered a priority.

A comprehensive public health strategy would also include screening of high-risk populations, with direct referral to appropriate healthcare providers according to patients' risk of progression to kidney failure. An active, laboratory-based surveillance system would ensure that at-risk individuals are not lost to clinical follow-up and care. Timely referrals for high-risk individuals will increase time to plan for RRT and may increase the uptake of home-based therapies. Screening and intervention strategies would be continually evaluated. Strategies to improve the use of more cost-effective types of RRT are also recommended. All of these strategies are described in more detail below.

Address the social determinants of health

Consistent with previous research, we found an association between CKD, ESKD and low socioeconomic status, particularly in the adult population. Despite Canada's universal healthcare system, people living in poverty and in remote communities face barriers to accessing early intervention strategies and treatments required to prevent and manage CKD. We also observed that the highest rates of CKD and ESKD were found in remote communities where living conditions are sometimes challenging due to economic conditions, poor water supply, access to affordable food, as well as limited health, social and recreational services. Improving living conditions and ensuring that economic and social resources are available throughout the province would potentially decrease the development of CKD and other chronic diseases. While there are no simple solutions to reducing poverty, some existing strategies have demonstrated improved outcomes (see Chapter 7).

Implement a targeted chronic kidney disease screening and surveillance system

Targeted screening for CKD in high-risk populations (First Nations people, older people, and people with diabetes, hypertension or cardiovascular disease) would facilitate early intervention efforts. The Kidney Failure Risk Equation could be incorporated into Manitoba's laboratory system, enabling physicians to distinguish between the patients who should receive higher intensity and more costly interdisciplinary nephrology care and those who can be safely managed by a primary care provider.

The Provincial Laboratory Information System (PLIS), being expanded from the Delphic LIS, will capture a larger portion of the provincial laboratory data and could be used for CKD surveillance (Diagnostic Services Manitoba (DSM), 2014). Most laboratories from rural areas will be transferred into PLIS and are listed on the Diagnostic Services Manitoba website (Diagnostic Services Manitoba (DSM), 2015). In time, the Westman data will be transferred to PLIS. There will still be limitations for laboratory tests completed in Winnipeg because privately run laboratories such as Dynacare Medical Laboratories and Unicity Lab Services will not be included in the PLIS. These two labs cover the majority of community clinics within Winnipeg, Brandon, Boundary Trails and Steinbach (Thorlacius L., personal communication, July, 2015).

Build capacity to address chronic kidney disease among primary care physicians and pediatricians

We found that many cases of earlier stages of CKD were not identifiable through the physician claims data, suggesting that many cases of CKD go undetected. Hypertension is also under-diagnosed in Manitoba children and may be contributing to the slow progression of CKD manifesting in adulthood. Given the high prevalence of early stages of CKD in the province, it is imperative that primary care physicians and pediatricians conduct routine health checks for at-risk populations. The KDIGO clinical guidelines for CKD (Kidney Disease Improving Global Outcomes (KDIGO), 2012) and the Canadian Diabetes Association guidelines (Canadian Diabetes Association, 2013) include recommendations for lifestyle counselling, control of blood sugar and hypertension, and avoidance of nephrotoxic substances. Clinical care pathways have been developed to guide primary care practitioners in the treatment of CKD patients (Kidney Health.ca Manitoba Renal Progam, 2015; Ontario Renal Network, 2015; Chronic kidney Disease Clinical Pathway, 2015). Furthermore, there is opportunity for increased knowledge translation to ensure that all care practitioners are aware of these guidelines and have access to them in their practices. We also recommend that alternative models of care be explored to ensure that remote communities have access to primary care and renal healthcare. These could include increasing recruitment and retention of healthcare providers and using technology to link remote areas to specialized services in Winnipeg.

Increase the use of peritoneal dialysis and home hemodialysis to 30% of all dialysis starts

Promotion of home-based dialysis for patients capable of sustaining self-care would be an ideal strategy to make more efficient use of healthcare resources. This will require planning and improving capacity to train and support patients in the use of peritoneal dialysis and home hemodialysis, as a considerable amount of preparation and education for patients is required. Improving early access to nephrologist care for patients at high risk for progressing to ESKD is also critical to this strategy, given that about one-quarter of dialysis patients currently start dialysis unexpectedly without prior consultation with a nephrologist. However, for resource planning, it is important to keep in mind that patients may start on a home-based type of RRT but switch to centre-based hemodialysis because of technique failure (which is the case in as many as 50% of all peritoneal dialysis patients) or, among older patients, because of frailty (Verrelli M, personal communication, August 2, 2015).

Develop and implement strategies to increase availability of kidneys for transplant

Kidney transplants are associated with better health and quality of life than dialysis. However, not everyone with ESKD is a good candidate for the procedure. For those who are, whether they receive a kidney transplant or not depends on the number of kidneys available. Public awareness campaigns to increase donations are needed. In addition, wider use of novel strategies has the potential to increase available transplants and should be considered (Maggiore et al., 2015; Poldervaart et al., 2015; Summers et al., 2015). One example is the paired kidney donation program in which potential transplant opportunities are identified for recipients with a willing living donor who cannot donate to them due to incompatibility issues (Cardinal et al., 2015; Malik & Cole, 2014; Transplant Manitoba, 2015). Another includes creating a national registry for highly sensitized patients (people with previous exposure to foreign tissue and who are therefore more likely to reject a transplanted kidney) to increase their access to a larger number of potential donors and greater chance of finding a good match (Canadian Blood Services, 2015; Nayak et al., 2015).

Evaluate the process and outcomes of new screening and early intervention strategies to inform future policy direction

To increase understanding of the effectiveness of established screening, surveillance and intervention strategies and shed light on how to improve them, it is important to develop a rigorous evaluation framework to monitor changes in the prevalence of ESKD and high-risk CKD in the province over time. Methods developed for this report to assess rates of CKD and ESKD provide a means to measure the efficacy of proposed system changes. Improving access to DSM laboratory data is essential to estimate CKD prevalence and the level of risk of progressing to ESKD in Manitoba's population.

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GLOSSARY

Albuminuria

The most common kind of **proteinuria**, characterized by high levels of albumin (protein) in the urine (KDIGO, 2012; Miller & Keane, 2003).

Kidney Disease Improving Global Outcomes (KDIGO). KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. 2012. http://www.kdigo.org/clinical_ practice_guidelines/pdf/KDIGO_ BP_GL.pdf. Accessed May 4, 2015.

Miller BF, Keane CB. Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, 7th edition. Philadelphia, PA: Saunders; 2003.

Capture-Recapture Method

"A method estimating the size of a target population or a subset of this population that uses overlapping and presumably incomplete but intersecting sets of data about that population. Though the capture-recapture methods have some limitations, they are useful to estimate numbers of cases and numbers at risk in elusive populations". (Last, 2001)

Last JM. A Dictionary of Epidemiology. 4th Edition. In: Spasoff, RA, et. al. (eds). New York, New York: Oxford University Press; 2001.

Diagnostic Services Manitoba (DSM) Laboratory Data

Laboratory data maintained by Diagnostic Services Manitoba (DSM) that provide information about all Cadham Laboratory services in Manitoba in 2006-2012. These data provide summary information about laboratory tests of blood, urine, tissue and other body fluids for more than 70 DSM sites across Manitoba. The data include patient demographic information, collection information (e.g., date, location, laboratory), and test codes, descriptions and results. Data from private laboratories and certain health care facilities are not included and coverage in rural Manitoba may be incomplete.

Estimated Glomerular Filtration Rate (eGFR)

EGFR is a measurement used to assess kidney function. It estimates the flow rate of fluid filtered through the kidneys. Predictive models have been developed for the relationship between serum creatinine and eGFR. Creatinine is filtered from the blood by the kidneys, so decreased kidney function results in elevated serum creatinine levels (KDIGO, 2012).

Kidney Disease Improving Global Outcomes (KDIGO). KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. 2012. http://www.kdigo.org/clinical_ practice_guidelines/pdf/KDIGO_ BP_GL.pdf. Accessed May 4, 2015.

Hemodialysis

A procedure that uses a machine in place of the kidneys to filter the patient's blood. This type of renal replacement therapy requires a strict treatment and dietary schedule, and use of medications. Hemodialysis can be performed in a medical facility (centre-based hemodialysis) or at home (home hemodialysis) with support from trained healthcare professionals (Mayo Clinic; Miller & Keane, 2003).

Mayo Clinic. Tests and procedures. http://www.mayoclinic.org/tests-procedures. Accessed May 11, 2015.

Miller BF, Keane CB. Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, 7th edition. Philadelphia, PA: Saunders; 2003.

Kidney Failure Risk Equation (KFRE)

A group of predictive models developed by Tangri et al., 2011 that evaluate the short-term risk of progression to kidney failure among patients with moderate to severe CKD. The KFRE model used in this report predicts the risk of developing kidney failure based on age, sex, protein levels in the urine and kidney function (eGFR).

Tangri N, Stevens LA, Griffith J, et al. A Predictive Model for Progression of Chronic Kidney Disease to Kidney Failure. JAMA. 2011;305(15):1553-1559.

Manitoba Pediatric Chronic Kidney Disease Registry

Clinical data maintained by the Winnipeg Regional Health Authority (WRHA) that provide information about children with impaired kidney function (**eGFR** under 75 ml/min/1.73 m^2). This information has been collected by the Pediatric Nephrology clinical program at the Children's Hospital (Health Sciences Centre, Winnipeg) since 1995. The data contain clinical and laboratory data, as well as dialysis, transplant, and quality of care indicators.

Manitoba Renal Program (MRP) Data

Administrative data maintained by the Winnipeg Regional Health Authority (WRHA) that provide information about the dialysis services that patients with acute kidney injury or kidney failure have received in 20 renal health centres across Manitoba from 2004 onwards. These centres include four urban and 16 rural and northern locations. These data provide information about the patients' date of entry into the Manitoba Renal Program and type of dialysis services received. In addition to providing dialysis services, MRP provides education and non-dialysis clinical care that promote kidney health, prevention of kidney failure, and disease management.

Markov Model

A modelling approach that predicts how likely an event is to enter a specific state in the future based on the current state of this event and chance (Last, 2001). This approach can use constant likelihood of each event state (stationary model) or changing likelihood of each event state (non-stationary model) (Schaubel et al., 1998). A non-stationary model can account for the influence of factors that might impact the likelihood of future events. The Markov model can evaluate the outcomes of a process, such as whether a patient diagnosed with kidney failure who enters the Manitoba Renal Program will receive **hemodialysis**, **peritoneal dialysis,** home hemodialysis, kidney transplant, or will die.

Last JM. A Dictionary of Epidemiology. 4th Edition. In: Spasoff, RA, et. al. (eds). New York, New York: Oxford University Press; 2001.

Schaubel DE, Morrison HI, Desmeules M, Parsons D, Fenton SS. End-stage renal disease projections for Canada to 2005 using Poisson and Markov models. Int J Epidemiol. 1998;27(2):274-281.

Peritoneal dialysis

A procedure that uses the patient's blood vessels in the abdominal lining in place of the kidneys to filter the patient's blood. This type of renal replacement therapy is less restrictive than hemodialysis because it does not require as strict a diet or medication use and can be performed by the patient in a variety of environments (Mayo Clinic; Miller & Keane, 2003).

Mayo Clinic. Tests and procedures. http://www.mayoclinic.org/tests-procedures. Accessed May 11, 2015.

Miller BF, Keane CB. Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, 7th edition. Philadelphia, PA: Saunders; 2003.

Proteinuria

An excess of protein in the urine due to kidney disease, strenuous exercise, or dehydration. Proteinuria is most commonly caused by damage to the kidney's ability to filter protein, which can make the capillaries in the kidneys more permeable to protein (KDIGO, 2012; Miller & Keane, 2003).

Kidney Disease Improving Global Outcomes (KDIGO). KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. 2012. http://www.kdigo.org/clinical_ practice_guidelines/pdf/KDIGO_ BP_GL.pdf. Accessed May 4, 2015.

Miller BF, Keane CB. Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, 7th edition. Philadelphia, PA: Saunders; 2003.

Remote Communities

Communities in Manitoba that do not have permanent road access (i.e., no all-weather road), are more than a four-hour drive from a major rural hospital (and a dialysis unit), or have rail or fly-in access only.

Renal replacement therapy (RRT)

A therapy for patients with kidney failure that replaces of kidney function (i.e., removal of wastes and excess water from the body) (Miller & Keane, 2003). RRT includes **Hemodialysis** (centre- or home-based), **peritoneal dialysis**, and kidney transplant.

Miller BF, Keane CB. Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, 7th edition. Philadelphia, PA: Saunders; 2003.

APPENDIX 1: TECHNICAL DEFINITIONS OF INDICATORS AND MEASURES USED IN REPORT

Indicators	Technical Definitions and Codes
End-stage kidney disease & renal replacement therapy	
End-stage kidney disease	Age groups: • Children: 0-17 years old as of dialysis start or transplant date • Adults: 18 years and older as of dialysis start or transplant date Data sources: • Renal Pediatrics Demographics File • Manitoba Renal Program • Hospital Abstracts • Physician Claims Defined as Manitoba residents receiving dialysis or kidney transplant April 1, 1999 – March 31, 2012: • dialysis for 90 days or until death with no gaps > 15 days between sessions (physician tariffs: 3792, 3790, 3793, 3794, 3800, 3801, 3803, 3804, 3805, 9610, 9798, 9799, 9801, 9802, 9805, 9806, 9807, 9814, 9819, 9820, 9821), or • at least 1 physician claim for kidney transplant (ICD-9-CM procedure: 556; tariff: 5883), or • at least 1 hospitalization for kidney transplant (ICD-10-CA intervention: 1PC85, 1OK85) Dialysis in children is restricted to children listed in the Renal Pediatrics Demographics File.
Dialysis start	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims • Manitoba Renal Program Defined as the first dialysis session of Manitoba residents in April 1, 1999 – March 31, 2012 where: • dialysis continues for 90 days or until death with no gaps > 15 days between sessions (physician tariffs: 3792, 3790, 3793, 3794, 3800, 3801, 3803, 3804, 3805, 9610, 9798, 9799, 9801, 9802, 9805, 9806, 9807, 9814, 9819, 9820, 9821) Note: Dialysis starts before January 1, 2004 were identified using physician claims. Dialysis starts on January 1, 2004, or later were identified using the Manitoba Renal Program data.

Indicators	Technical Definitions and Codes
Dialysis exit	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims • MCHP Registry Data • Hospital abstracts Defined as Manitoba residents with: • At least 180 days has elapsed since the last physician claim for dialysis (physician claim tariffs: 3792, 3790, 3793, 3794, 3800, 3801, 3803, 3804, 3805, 9610, 9798, 9799, 9801, 9802, 9805, 9806, 9807, 9814, 9819, 9820, 9821), or • at least 1 physician claim for kidney transplant (ICD-9-CM procedure: 556; tariff: 5883), or • at least 1 hospitalization for kidney transplant (ICD-10-CA intervention: 1PC349, 1OK85), or • death or end of health insurance coverage in registry.

Indicators	Technical Definitions and Codes
Chronic kidney disease (CKD)	
Chronic Kidney Disease (administrative data)	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Hospital Abstracts • Physician Claims • Drug Program Information Network (DPIN) Defined as Manitoba residents with the following diagnoses and drug prescriptions from April 1, 2009 – March 31, 2012: • Two or more physician claims with diagnoses for hypertensive chronic kidney disease, hypertensive heart and chronic kidney disease, acute glomerulonephritis, nephrotic syndrome, chronic glomerulonephritis, nephritis and nephropathy not specified as acute or chronic, chronic kidney disease, renal failure (unspecified), renal sclerosis (unspecified), disorders resulting from impaired renal function, hydronephrosis, other disorders of kidney and ureter, congenital anomalies of urinary system (ICD-9-CM: 403, 404, 580, 581, 582, 583, 585, 586, 587, 588, 591, 593, 753), or • One or more hospitalizations with diagnoses for diabetes with renal manifestations, hypertensive chronic kidney disease, hypertensive heart and chronic kidney disease, acute glomerulonephritis, nephrotic syndrome, chronic glomerulonephritis, nephritis and nephropathy not specified as acute or chronic, chronic kidney disease, renal failure (unspecified), renal sclerosis (unspecified), disorders resulting from impaired renal function, hydronephrosis, unspecified disorder of kidney and ureter, congenital anomalies of urinary system (ICD-9-CM: 250.4, 403, 404, 580, 581, 582, 583, 585, 586, 587, 588, 591, 593.9, 753; ICD-10-CA: E10.2, E11.2, I12, I13, N18, N19, N00-16, N25, N26, N28.82, N39.1, Q60-64), or • One or more filled prescriptions for drugs used in CKD management: ○ generic names: Vitamin B Complex/Vitamin C, Calcitriol, Epoetin Alfa, Sodium Polystyrene Sulfonate, Sevelamer HCL, Darbepoetin Alfa, Alfacalcidol, Cinacalcet HCL, Calcium Polystyrene sulphonate, Polystyrene Sod Sulfonate 454, doxercalciferol, paricalcitol, lanthanum, calcium acetate, calcium carbonate, peginesatide, replavite, lanthanum, or ○ Anatomical Therapeutic Chemical (ATC) codes: A11CC04, A11CC03, H05BX03, H05BX02, V03AE02, V03AE03, V03AE04, B03XA01, B03XA02, B03XA04, V03AE03, V03AE01, A02AC01, A12AA04, H05BX01, or ○ Drug Information Number (DINs): 00800970, 02017741, 80007498, 02240409, 02244872, 00646873, 00761281, 00667501, 01981708, 00722308, 00731250, 00644684, 00626341, 00643971, 00622710, 00802077, 00708704, 00530328, 00033197, 01902776

Indicators	Technical Definitions and Codes
Chronic Kidney Disease (laboratory data)	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Diagnostic Services Manitoba Laboratory data (2006/07-2011/12) Defined as Manitoba residents with: • Two abnormal tests for proteinuria (ACR or PCR) at least 90 days apart, or • One abnormal proteinuria test with a diagnosis of CKD based on administrative data, or • Two abnormal eGFR tests at least 90 days apart, or • One abnormal eGFR test with an administrative diagnosis of CKD Abnormal test values were defined as: • ACR >=3 mg/mmol or PCR >=15 mg/mmol • eGFR values <90 for children and <60 for adults
Albumin-Creatinine Ratio (ACR)	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Diagnostic Services Manitoba Laboratory data Defined as the ratio of Urine Albumin (test code 1384; mg/mmol) to Urine Creatinine (test code 0232; mg/mmol). ACR greater than or equal to 3 mg/mmol is considered abnormal. Tests missing date of collection were excluded.

Note: Fiscal year XXXX/YY is defined as April 1, XXXX to March 31, YYYY

Indicators	Technical Definitions and Codes
Protein-Creatinine Ratio (PCR)	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Diagnostic Services Manitoba Laboratory data Defined as the ratio of urine protein to Urine Creatinine. Urine protein was measured using either Urine Protein (test code 0720) or, when Urine Protein test results were not available, Dipstick Protein Urinalysis (test code 0740). PCR greater than or equal to 15 mg/mmol is considered abnormal. <u>Dipstick Protein Urinalysis</u> The dipstick method gives a categorical measurement of urine protein (0 to 4) which is less precise than a Urine Protein test. A dipstick protein level greater than or equal to 0.3 g/L is considered abnormally high. A comparison of same-day Dipstick and Urine Protein test results showed moderate agreement (kappa = 0.48): • Dipstick Protein = 0 comparable to Urine Protein < 15 mg/mmol • Dipstick Protein = 1 comparable to Urine Protein 15-50 mg/mmol • Dipstick Protein = 2-4 comparable to Urine Protein >50 mg/mmol. Tests missing date of collection were excluded.
Estimated Glomerular Filtration Rate (eGFR)	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Diagnostic Services Manitoba (DSM) Laboratory data Calculated based on Serum Creatinine (SCr; test code 0214, mg/dL) and age (years) in adults, or Serum Creatinine and height (cm) in children. <u>Adults</u> Modification of Diet in Renal Disease (MDRD) equation (Kidney Disease Improving Global Outcomes (KDIGO), 2013) *Men:* eGFR = $\left[175 \times \left(\frac{S_{cr}}{88.4}\right)^{-1.154}\right] \times (age)^{-0.203}$ *Women: eGFR = 0.742 x* $\left[175 \times \left(\frac{S_{cr}}{88.4}\right)^{-1.154}\right] \times (age)^{-0.203}$ <u>Children</u> Modified Pediatric Schwartz equation (Schwartz et al., 2009) eGFR = $36.51 \times \left(\frac{height\ (cm)}{S_{cr}(\frac{\mu mol}{L})}\right)$ Measured height from DSM was used where available (n = 100 as of March 2012). When height measurements were not available in DSM, height was estimated using age and gender-specific growth curves. To maximize the sensitivity of the determination, the 3rd percentile of height was used in the Schwartz formula.

Indicators	Technical Definitions and Codes
Chronic Kidney Disease (administrative & laboratory data)	Defined as Manitoba residents with CKD identified through either administrative data or laboratory data (see definitions above).
Risk of CKD progression to ESKD (heat map)	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Diagnostic Services Manitoba (DSM) Laboratory data Prognosis of CKD in Manitoba residents was evaluated based on the latest available laboratory results in the period April 1 2006 – March 31 2012. The following categories for albuminuria and eGFR define increasing levels of kidney failure risk: <u>Persistent albuminuria categories</u> A1 (normal to mildly increased): ACR <3 mg/mmol or PCR <15 mg/mmol A2 (moderately increased): ACR 3-30 mg/mmol or PCR 15-50 mg/mmol A3 (severely increased): ACR >30 mg/mmol or PCR >50 mg/mmol <u>eGFR categories</u> G1 (normal or high): eGFR values >=90 G2 (mildly decreased): eGFR values within 60-89 G3a (mildly to moderately decreased): eGFR values within 45-59 G3b (moderately to severely decreased): eGFR values within 30-44 G4 (severely decreased): eGFR values within 15-29 G5 (kidney failure): eGFR values <15 Note: The G1 and G2 categories in adults were combined to produce a category for normal eGFR of >= 60. The KDIGO heat map classification groups combinations of these categories into colour groups: Green, Yellow, Orange and Red. We created two broad risk categories from these colour groups: Low Risk: Green, Yellow. High Risk: Orange, Red. In the event that only one of albuminuria or eGFR could be categorized, those who also met the administrative definition for CKD were assigned the following risk categories: Low Risk: Albuminuria A1 or A2, *or* eGFR G1, G2 or G3a. High Risk: Albuminuria A3 *or* eGFR G3b, G4 or G5. Those who met the administrative definition of CKD with no laboratory data to provide information about severity of risk were assigned to an Unknown Risk category.

Indicators	Technical Definitions and Codes
Capture-recapture	Data sources: • Hospital Abstracts • Physician Claims • Drug Program Information Network (DPIN) • Diagnostic Services Manitoba (DSM) Laboratory data A method of estimating population size from multiple independent samples. We used the Chapman estimator (Chapman, 1951): $$N = \left\lfloor \frac{(n_1 + 1) \times (n_2 + 1)}{(m_2 + 1)} \right\rfloor - 1$$ Where N = Estimate of population size n_1 = Size of sample 1 n_2 = Size of sample 2 m_2 = Number in Sample 2 that are also in Sample 1 Using the administrative data definition and lab-based definitions we estimated the total CKD population as: $$N_{CKD} = \left\lfloor \frac{(Admin_{CKD} + 1) \times (Lab_{CKD} + 1)}{(Both_{CKD} + 1)} \right\rfloor - 1$$ Where N_{CKD} = Estimate of total CKD population $Admin_{CKD}$ = Number meeting the administrative definition April 1 2009-March 31 2012 Lab_{CKD} = Number meeting the lab-based definition April 1 2006 – March 31 2012 $Both_{CKD}$ = Number meeting both definitions
Geographic location	
Remote community	Communities in Manitoba that do not have permanent road access (i.e., no all-weather road), are more than a 4-hour drive from a major rural hospital (and a dialysis unit), or have rail or fly-in access only. This includes Norway House, Lynn Lake, Leaf Rapids, Gillam, and Cross Lake. If most communities in a health district are designated as "remote", the entire district is designated as "remote". In Manitoba, remote districts include: • Northern health region: NO23, NO13, NO25, NO16, NO22, NO26, NO28, NO31, and • Interlake-Eastern health region: IE61.
Physical Conditions	
Diabetes	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims • Hospital Abstracts • Drug Program Information Network (DPIN) data Defined as Manitoba residents receiving the following diagnoses or prescriptions in the three-year fiscal period 2009/10-2011/12: • One or more inpatient hospitalizations with a diabetes diagnosis (ICD-9-CM: 250, ICD-10-CA: E10-E14), or • Two or more physician claims with diabetes diagnosis (prefix=7, ICD-9-CM: 250), or • One or more prescription drugs for diabetes treatment (ATC code A10)

Indicators	Technical Definitions and Codes
Lower-limb amputation among those with diabetes	Age groups: • Adults: 18 years and older with diabetes Note: number of events among children 0-17 was too low to report. Data sources: • Physician Claims • Hospital Abstracts • Drug Program Information Network (DPIN) data Defined as Manitoba residents receiving the following diagnoses and procedure or intervention codes in the five-year fiscal period 2007/08-2011/12: • One or more hospitalizations with a procedure indicating lower-limb amputation (ICD-9: 84.10-84.17, CCI: 1.VC.93, 1.VG.93, 1.VQ.93, 1.WA.93, 1.WE.93, 1.WJ.93, 1.WL.93, 1.WM.93) and a diagnosis for diabetes (ICD-9-CM: 250, ICD-10-CA: E10-E14). Exclusions: • Defined only among those meeting the definition for diabetes • Diagnosis code for accidental injury in same hospitalization (ICD-9-CM: 895-897, ICD-10-CA: S78, S88, S98, T05.3, T05.4, T05.5, T13.6) • Interventions coded as out-of-hospital
Hypertension	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims • Hospital Abstracts • Drug Program Information Network (DPIN) data Defined as Manitoba residents receiving the following diagnoses or prescriptions in the one-year fiscal period 2011/12: • One or more inpatient hospitalizations for hypertensive disease (ICD-9-CM: 401-405, ICD-10-CA: I10-I13, I15), or • One or more physician claims for hypertensive disease (prefix=7, ICD-9-CM: 401-405), or • One or more prescriptions for antihypertensive drugs, diuretics, beta blocking agents, calcium channel blockers, agents acting on the renin-angiotensin system, atorvastatin, or terazosin with the following ATC codes: C02AB01, C02AB02, C02AC01, C02CA04, C02CA05, C02DB02, C02DC01, C02LA01, C02LB01, C03AA03, C03BA04, C03BA11, C03CA01, C03CA02, C03CC01, C03DA01, C03DB01, C03DB02, C03EA01, C07AA02, C07AA03, C07AA05, C07AA06, C07AA12, C07AB02, C07AB03, C07AB04, C07AB07, C07AG01, C07BA05, C07BA06, C07CA03, C07CB03, C08CA01, C08CA02, C08CA04, C08CA05, C08CA06, C08DA01, C08DB01, C09AA01, C09AA02, C09AA03, C09AA04, C09AA05, C09AA06, C09AA07, C09AA08, C09AA09, C09AA10, C09BA02, C09BA03, C09BA04, C09BA06, C09BA08, C09BB10, C09CA01, C09CA02, C09CA03, C09CA04, C09CA06, C09CA07, C09CA08, C09DA01, C09DA02, C09DA03, C09DA04, C09DA06, C09DA07, C09DA08, C09DB02, C09XA02, C09XA52, C10BX03, G04CA03 Exclusions: • Generic name spironolactone • DINs 00028606, 00180408, 00285455, 00594377, 00613215, 00613223, 00613231, 00657182

Indicators	Technical Definitions and Codes
Ischemic Heart Disease (IHD)	Age groups: • Adults: 18 years and older Data sources: • Physician Claims • Hospital Abstracts • Drug Program Information Network (DPIN) data Defined as Manitoba residents receiving the following diagnoses or prescriptions in the five-year fiscal period 2007/08-2011/12: • One or more inpatient hospitalizations for ischemic heart disease (ICD-9-CM: 410-414, ICD-10-CA: I20-I22, I24, I25), or • Two or more physician claims for ischemic heart disease (prefix=7, ICD-9-CM: 401-405), or • One or more prescriptions for platelet aggregation inhibitors, organic nitrates, ubidecarenone, reserpine and diuretics, beta blocking agents, calcium channel blockers, agents acting on the renin-angiotensin system, HMG CoA reductase inhibitors, fibrates, ezetimibe with the following ATC codes: B01AC04, B01AC22, B01AC24, C01DA02, C01DA05, C01DA08, C01DA14, C01EB09, C02LA01, C07AA02, C07AA03, C07AA05, C07AA06, C07AA12, C07AB02, C07AB03, C07AB04, C07AB07, C07AG01, C07BA05, C07BA06, C07BA12, C07CA03, C07CB03, C08CA01, C08CA02, C08CA04, C08CA05, C08CA06, C08DA01, C08DB01, C09AA01, C09AA02, C09AA03, C09AA04, C09AA05, C09AA06, C09AA07, C09AA08, C09AA09, C09AA10, C09BA02, C09BA03, C09BA04, C09BA06, C09BA08, C09CA01, C09CA02, C09CA03, C09CA04, C09CA06, C09CA07, C09CA08, C09DA01, C09DA02, C09DA03, C09DA04, C09DA06, C09DA07, C09DA08, C09DB02, C10AA01, C10AA02, C10AA03, C10AA04, C10AA05, C10AA06, C10AA07, C10AA08, C10AB04, C10AB05, C10AB02, C10AX09, C10BX03, or • One or more prescriptions for low-dose aspirin (≤ 325 mg; DINs: N02BA01, N02BA51, N02BA71)
Congestive Heart Failure (CHF)	Age groups: • Adults: 40 years and older Data sources: • Physician Claims • Hospital Abstracts Defined as Manitoba residents receiving the following diagnoses or prescriptions in the three-year fiscal period 2009/10-2011/12: • One or more inpatient hospitalizations with congestive heart failure (ICD-9-CM: 428, ICD-10-CA: I50), or • Two or more physician claims with congestive heart failure (prefix=7, ICD-9-CM: 428)
Acute Myocardial Infarction (AMI)	Age groups: • Adults: 40 years and older Data sources: • Hospital Abstracts • Vital Statistics mortality data Defined as Manitoba residents receiving the following diagnoses in the five-year fiscal period 2007/08-2011/12: • One or more hospitalizations with a most responsible diagnosis of AMI and length of stay of three or more days (ICD-9-CM: 410, ICD-10-CA: I21), or • Vital Statistics cause of death coded as AMI (ICD-10: I21)

Indicators	Technical Definitions and Codes
Stroke	Age groups: • Adults: 40 years and older Data sources: • Hospital Abstracts • Vital Statistics mortality data Defined as Manitoba residents receiving the following diagnoses in the five-year fiscal period 2007/08-2011/12: • One or more hospitalizations with a most responsible diagnosis of stroke (ICD-9-CM: 431, 434, 436; ICD-10-CA: I61, I63, I64), or • Vital Statistics cause of death coded as stroke (ICD-10: I61, I63, I64)
Atrial fibrillation	Age groups: • Adults: 18 years and older Data sources: • Physician Claims • Hospital Abstracts Defined as Manitoba residents receiving the following diagnoses or prescriptions in the three-year fiscal period 2009/10- 2011/12: • One or more inpatient hospitalizations with diagnosis of atrial fibrillation (ICD-9-CM: 427, ICD-10-CA: I48), or • Two or more physician claims with diagnoses for atrial fibrillation (prefix=7, ICD-9-CM: 427)
Mental Health Disorders	
Mood and anxiety disorders	Age groups: • Children: 10-17 years old • Adults: 18 years and older Data sources: • Physician Claims • Hospital Abstracts • Drug Program Information Network (DPIN) data Defined as Manitoba residents receiving the following diagnoses or prescriptions in the five-year fiscal period 2007/08-2011/12: • One or more hospitalizations with diagnosis codes for episodic mood disorders, anxiety disorder, adjustment reaction, or depressive disorder not elsewhere classified: ○ ICD-9-CM: 296.1-296.8, 300.0, 300.2, 300.3, 300.4, 300.7, 309, 311; ○ ICD-10-CA: F31-F33, F34.1, F38.0, F38.1, F40, F41.0, F41.1, F41.2, F41.3, F41.8, F41.9, F42, F43.1, F43.2, F43.8, F45.2, F53.0, F93.0, or • One or more hospitalizations with diagnosis codes for an anxiety disorder: ○ ICD-9-CM: 300; ○ ICD-10-CA F32, F34.1, F40, F41, F42, F44, F45.0, F45.1, F45.2, F48, F68.0 F99, and ○ One or more prescriptions for an antidepressant or mood stabilizer: ATC codes N05AN01, N05BA, N06A, or • One or more physician visits with a diagnosis code for episodic mood disorder or depressive disorder not elsewhere classified: ○ ICD-9-CM: 296, 311, or • One or more physician visits with a diagnosis code for an anxiety disorder: ○ ICD-9-CM: 300, and ○ One or more prescriptions for an antidepressant or mood stabilizer: ATC codes N05AN01, N05BA, N06A, or • Three or more physician visits with a diagnosis code for anxiety disorder or adjustment reaction: ○ ICD-9-CM: 300, 309

Indicators	Technical Definitions and Codes
Dementia	Age groups: • Adults: 55 years and older Data sources: • Physician Claims • Hospital Abstracts Defined as Manitoba residents receiving the following diagnoses in the five-year fiscal period 2007/08-2011/12: • One or more hospitalizations with a diagnosis for dementia, including organic psychotic conditions, cerebral degenerations, and senility ○ ICD-9-CA: 290, 291.1, 292.2, 292.82, 294, 331, 797 ○ ICD-10-CM: F00, F01, F02, F03, F04, F05.1, F06.5, F06.6, F06.8, F06.9, F09, F10.7, F11.7, F12.7, F13.7, F14.7, F15.7, F16.7, F17.7, F18.7, F19.7, G30, G31.0, G31.1, G31.9, G32.8, G91, G93.7, G94, R54 • One or more physician visits with a diagnosis for dementia ○ ICD-9-CA: 290, 294, 331, 797
Suicide and suicide attempts	Age groups: • Children: 13-17 years old • Adults: 18 years and older Data sources: • Hospital Abstracts • Physician Claims • Vital Statistics Defined as Manitoba residents receiving the following diagnoses in April 1, 2009-December 31, 2012: • Suicide or accidental poisoning as cause of death in the Vital Statistics mortality data ○ ICD-10: X40-X42, X46, X47, X60-X84, Y10-Y12, Y16, Y17 • One or more hospitalizations for suicide or self-inflicted injury ○ ICD-9-CM: E950-E959 ○ ICD-10-CA: X60-X84 Hospitalizations for accidental poisoning were included when they occurred within 30 days of a physician claim with a psychiatric tariff code: • One or more hospitalizations for accidental poisoning ○ ICD-9-CM: 965, 967, 969, 977.9, 986, E850-E854, E858, E862, E868 ○ ICD-10-CA: T39, T40,T42.3, T42.4, T42.7,T43, T50.9, T58, X40-X42, X44, X46, X47, Y10-Y12, Y16, Y17, along with • One or more physician claims with a diagnosis of poisoning during this hospitalization or within 30 days after discharge from hospital ○ ICD-9-CM: 965, 967, 969, 977, 986 ○ Tariff codes for psychiatric therapy: • 8444, 8446, 8472, 8475, 8476, 8503, 8504, 8553, 8554, 8581, 8584, 8588, 8596, 8580, 8587, 8589

Indicators	Technical Definitions and Codes
Substance abuse	Age groups: • Children: 13-17 years old • Adults: 18 years and older Data sources: • Hospital Abstracts • Physician Claims Defined as Manitoba residents receiving the following diagnoses in the five-year fiscal period 2007/08-2011/12: • One or more inpatient hospitalizations with diagnoses for alcohol or drug-induced mental disorders, alcohol or drug dependence syndrome, non-dependent abuse of drugs (ICD-9-CM: 291, 292, 303, 304, 305, ICD-10-CA: F10-F19, F55), or • One or more physician claims with diagnoses for alcohol or drug-induced mental disorders, alcohol or drug dependence syndrome, non-dependent abuse of drugs (ICD-9-CM: 291, 292, 303, 304, 305)
Developmental disabilities	Age groups: • Children: 0-17 years old Data sources: • Hospital Abstracts • Physician Claims Defined as Manitoba residents receiving the following diagnoses in the five-year fiscal period 2007/08-2011/12: • One or more hospitalizations with diagnoses for intellectual disabilities, pervasive developmental disorders, Down's syndrome, autosomal deletion syndromes, Prader-Willi syndrome, other specified congenital anomalies, or FASD: ○ ICD-9-CM: 317, 318, 319, 299, 758.0, 758.3, 759.81, 759.89, 760.71 ○ ICD-10-CA: F70.0, F70.1, F70.8, F70.9, F71.0, F71.1, F71.8, F71.9, F72.0, F72.1, F72.8, F72.9, F73.0, F73.1, F73.8, F73.9, F78.0, F78.1, F78.8, F78.9, F79.0, F79.1, F79.8, F79.9, F84.0, F84.1, F84.3, F84.4, F84.5, F84.8, F84.9, P04.3, Q86.0, Q86.1, Q86.2, Q86.8, Q87.0, Q87.1, Q87.2, Q87.3, Q87.5, Q87.8, Q89.8, Q90.0, Q90.1, Q90.2, Q90.9, Q91.0, Q91.1, Q91.2, Q91.3, Q91.4, Q91.5, Q91.6, Q91.7, Q93.0, Q93.1, Q93.2, Q93.3, Q93.4, Q93.5, Q93.6, Q93.7, Q93.8, Q93.9, Q99.2 • One or more physician claims with diagnoses for for intellectual disabilities, pervasive developmental disorders: ○ ICD-9-CM: 317, 318, 319, 299

Indicators	Technical Definitions and Codes
Attention-deficit hyperactivity disorder (ADHD)	Age groups: • Children: 6-17 years old Data sources: • Hospital Abstracts • Physician Claims • Drug Program Information Network (DPIN) data Defined as Manitoba residents receiving the following diagnoses in the five-year fiscal period 2007/08-2011/12: • One or more hospitalizations with diagnosis of hyperkinetic syndrome ○ ICD-9-CM: 314, ICD-10-CA: F90, or • One or more physician claims with diagnosis of hyperkinetic syndrome ○ ICD-9-CM: 314, or, ○ Two or more prescriptions for drugs for ADHD treatment in one fiscal year without a diagnosis in the same fiscal year of: • conduct disorder (ICD-9-CM: 312, ICD-10-CA: F63, F91, F92), or • disturbance of emotions (ICD-9-CM: 313, ICD-10-CA: F93, F94), or • cataplexy/narcolepsy (ICD-9-CM: 347, ICD-10-CA: G47.4); or, • One or more prescriptions for ADHD drugs with diagnosis of hyperkinetic syndrome (ICD-9-CM: 314, ICD-10-CA: F90. Note: Due to the small size of some of the CKD subgroups we used a five-year time frame for all mental disorders.
Schizophrenia	Age groups: Children: 13-17 years old Adults: 18 years and older Data sources: Hospital Abstracts Physician Claims Defined as Manitoba residents receiving the following diagnoses in the five-year fiscal period 2007/08-2011/12: One or more hospitalizations with diagnosis of schizophrenia (ICD-9-CM: 295, ICD-10-CA: F20, F21, F23.2, F25), or One or more physician claims with diagnosis of schizophrenia (ICD-9-CM: 295)

Indicators	Technical Definitions and Codes
Personality disorder	Age groups: Adults: 18 years and older Data sources: Hospital Abstracts Physician Claims Defined as Manitoba residents receiving the following diagnoses in the five-year fiscal period 2007/08-2011/12: One or more hospitalizations with diagnosis of personality disorder (ICD-9-CM: 301, ICD-10-CA: F34.0, F60-F62, F68.1, F69), or One or more physician claims with diagnosis of personality disorder (ICD-9-CM: 301)
Any mental disorder	• Age groups: Children: 0-17 years old • Adults: 18 years and older Data sources: • Hospital Abstracts • Physician Claims • Drug Program Information Network (DPIN) data Defined as children in Manitoba diagnosed with any of the following disorders in the five-year fiscal period 2007/08-2011/12: • ADHD • Mood and Anxiety Disorders • Developmental Disabilities • Schizophrenia • Substance Abuse Adults in Manitoba diagnosed with any of the following disorders in the five-year period April 1, 2007-March 31, 2012: • Mood and Anxiety Disorders • Substance Abuse • Schizophrenia • Personality Disorders Definitions for these indicators can be found in this Technical Appendix.

Indicators	Technical Definitions and Codes
Prescription medication use	
Anti-hypertensive drug prescriptions	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Drug Program Information Network (DPIN) data Defined as Manitoba residents receiving the following prescriptions in the one-year fiscal period 2011/12: • One or more prescriptions for antihypertensive drugs, diuretics, beta blocking agents, calcium channel blockers, agents acting on the renin-angiotensin system, atorvastatin, or terazosin with the following ATC codes (ATC codes: C02AB01, C02AB02, C02AC01, C02CA04, C02CA05, C02DB02, C02DC01, C02LA01, C02LB01, C03AA03, C03BA04, C03BA11, C03CA01, C03CA02, C03CC01, C03DA01, C03DB01, C03DB02, C03EA01, C07AA02, C07AA03, C07AA05, C07AA06, C07AA12, C07AB02, C07AB03, C07AB04, C07AB07, C07AG01, C07BA05, C07BA06, C07CA03, C07CB03, C08CA01, C08CA02, C08CA04, C08CA05, C08CA06, C08DA01, C08DB01, C09AA01, C09AA02, C09AA03, C09AA04, C09AA05, C09AA06, C09AA07, C09AA08, C09AA09, C09AA10, C09BA02, C09BA03, C09BA04, C09BA06, C09BA08, C09BB10, C09CA01, C09CA02, C09CA03, C09CA04, C09CA06, C09CA07, C09CA08, C09DA01, C09DA02, C09DA03, C09DA04, C09DA06, C09DA07, C09DA08, C09DB02, C09XA02, C09XA52, C10BX03, G04CA03) Exclusions: • Generic name spironolactone • DINs: 00028606, 00180408, 00285455, 00594377, 00613215, 00613223, 00613231, 00657182

Indicators	Technical Definitions and Codes
Angiotensin converting enzyme (ACE) inhibitors and Angiotensin Receptor Blocker (ARB) prescriptions	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Drug Program Information Network (DPIN) data Defined as Manitoba residents with the following drug prescription dispensations in the one-year fiscal period 2011/12. • One or more prescriptions for ACE Inhibitors (ATC codes C09A, C09B), or • One or more prescriptions for ARB (ATC codes C09C, C09D)
Angiotensin converting enzyme (ACE) inhibitors and Angiotensin Receptor Blocker (ARB) prescriptions among those with diabetes	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims (to determine diabetes status) • Hospital Abstracts (to determine diabetes status) • Drug Program Information Network (DPIN) data Defined as Manitoba residents with the following diagnoses and prescriptions in the one-year fiscal period 2011/12: • One or more inpatient hospitalizations with a diabetes diagnosis (ICD-9-CM: 250, ICD-10-CA: E10-E14), or • Two or more physician claims a diabetes diagnosis (prefix=7, ICD-9-CM: 250), or • One or more prescriptions for a drug used to treat diabetes (ATC code A10); and • One or more prescriptions for ACE Inhibitors (ATC codes C09A, C09B), or • One or more prescriptions for ARB (ATC codes C09C, C09D)
Number of different prescribed drugs	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Drug Program Information Network (DPIN) data Defined as the average number of different types of drugs prescribed to Manitoba residents in the one-year fiscal period 2011/12. Each fourth–level ATC class of prescribed pharmaceutical agents is counted as a new drug for each resident. Multiple prescriptions for a resident for drugs in the same fourth–level ATC class count as one drug type in that year. Nearly all prescriptions dispensed from community–based pharmacies across the province were included. Exclusions: • Manitobans not covered by Manitoba Health's Pharmacare Program, or • Manitobans without filled drug prescriptions in the year, or • Prescription drugs given to hospitalized patients and some nursing home residents in personal care homes (PCHs) with hospital–based pharmacies , or • Prescriptions for over the counter drugs

Indicators	Technical Definitions and Codes
Healthcare use	
Inpatient hospitalizations	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Hospital Abstracts Defined as the admission of Manitoba residents to the hospital for diagnostic, medical or surgical treatment for one or more days in the fiscal period 2011/12. Multiple admissions of the same person were counted as separate events. Out of province hospitalizations for Manitoba residents were also included. Exclusions: • Personal care homes (PCHs), nursing stations, long–term care facilities (Deer Lodge Centre, Manitoba Adolescent Treatment Centre, Rehabilitation Centre for Children and Riverview Health Centre) • Hospitalizations of newborns at birth
Top five causes of inpatient hospitalizations	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Hospital Abstracts Defined as the five most frequent most responsible diagnoses (DIAG01) in inpatient admissions of Manitoba residents to the hospital for diagnostic, medical or surgical treatment for one or more days in the fiscal period 2011/12. Multiple admissions of the same person were counted as separate events. Out of province hospitalizations for Manitoba residents were also included. Exclusions: • Personal care homes (PCHs), nursing stations, long–term care facilities (Deer Lodge Centre, Manitoba Adolescent Treatment Centre, Rehabilitation Centre for Children and Riverview Health Centre) • Hospitalizations of newborns at birth
Days in hospital	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Hospital Abstracts Defined as the total length of stay of Manitoba residents during all inpatient hospitalizations discharged in the fiscal period 2011/12. Inpatient stays which extended after March 31, 2012 were truncated to the number of days spent in hospital within fiscal year 2011/12.

Indicators	Technical Definitions and Codes
Ambulatory physician visits	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims • Hospital Abstracts Defined as contacts with physicians in an outpatient setting (general practitioners, family physicians and specialists) in the fiscal period 2011/12. This includes office visits, walk–in clinic visits, home visits, personal care home (PCH; nursing home) visits and visits to outpatient departments. Exclusions: Physician visits while admitted to hospital or in the emergency department.
Top five causes of physician contacts	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims • Hospital Abstracts Defined as the five most diagnoses recorded on contacts with physicians in an outpatient setting (general practitioners, family physicians and specialists) in the fiscal period 2011/12. This includes office visits, walk–in clinic visits, home visits, personal care home (PCH; nursing home) visits and visits to outpatient departments. Exclusions: Physician visits while admitted to hospital or in the emergency department.
Nephrologist visits	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims • Defined as visits to a nephrologist (MD Bloc 016) by Manitoba residents in fiscal year 2011/12. Pediatric nephrologists were identified using physician billing numbers.
Length of Time Between First Nephrologist Visit and Dialysis Start	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims • Manitoba Renal Program Data Defined as the number of days between the first contact of Manitoba residents with a nephrologist (MD Bloc 016) since April 1, 1984 and dialysis start date as recorded in the Manitoba Renal Program data over the period 2004/05-2011/12.

Indicators	Technical Definitions and Codes
Other specialist visits	Age groups: • Children: 0-17 years old • Adults: 18 years and older Data sources: • Physician Claims Defined as ambulatory visits of Manitoba residents to specialists in internal medicine (MD Bloc 01), psychiatry (MD Bloc 03), general surgery (MD Bloc 041), surgical specialties excluding dental (MD Bloc 042 to 046, 049, 141, 142), ophthalmology (MD Bloc 051), otorhinolaryngology (MD Bloc 052), EENT (MD Bloc 053), dermatology (MD Bloc 06), OB/GYN (MD Bloc 09), physical medicine (MD Bloc 12), and oncology (MD Bloc 15) in fiscal year 2011/12. Exclusions: • Visits to nephrologists (adult and pediatric) as defined above. • Visits to pediatricians
Prevention and screening	
Kidney Failure Risk Equation (KFRE)	A model to predict kidney failure using laboratory data and demographic variables (Tangri et al., 2011). $$p = 1 - S_{ave}(t = 1{,}826)^{a}$$ $$a = -0.55418 \times \left[\left(\frac{eGFR}{5}\right) - 7.22\right] + 0.26940 \times (male - 0.56) + 0.45608 \times [in(ACR) - 5.2774] - 0.21670 \times \left[\left(\frac{age}{10}\right) - 7.04\right]$$ Where p = Five-year risk of kidney failure S_{ave}(t=1826) = Five-year survival rate for an individual with the average value of covariates in the risk equation and was 0.929 in the development dataset eGFR = Estimated GFR (ml/min/1.73m^2) ln(ACR) = Natural logarithm of Albumin Creatinine Ratio (mg/g) male = Indicator for sex (male = 1, female = 0) age = Age (years) at test date Validation cohort was based on test results October 1 2006 – March 31 2007.

APPENDIX 2: MARKOV MODEL TRANSITIONAL PROBABILITY MATRIX

The Markov model for this study is based on risks at each 3 month period for people who are stratified by age group, health region and diagnosis of diabetes. A transitional probability matrix is calculated for 30 groups based on data from January 2004 to March 2012. All the data was used for the transition matrices, although data from 2008-2012 was weighted more heavily to capture current treatment patterns. This provided enough time points for stable estimates and reflected the most current trends. Each member of the cohort can transition to one of four states: Centre-based Hemodialysis (HD), Home-based Dialysis (Peritoneal Dialysis (PD) or Home Hemodialysis (HHD)), Kidney Transplant or Death. Home-based Dialysis consisted of two types of dialysis because there were too few cases of Home Hemodialysis with the available data to calculate them separately. An example of a transitional probability matrix is found in the table below.

Markov allows for changes in probabilities (non-stationary model) which would influence the projections. It is conceivable that as technology, medical practices or the health of patients changes, the probability of going from one state into another might change. Significant changes in these probabilities were determined by testing for an interaction between time and the rates of changes in states (e.g., death). A multinomial logistic model was used to generate predicted probabilities of transitions from states of centre-based hemodialysis, peritoneal hemodialysis and kidney transplant into centre-based hemodialysis, PD and transplant and death and to test for interactions.

Only one transition showed a time-dependence: from centre-based hemodialysis into the other states. The odds ratio for centre-based hemodialysis and peritoneal dialysis show that their probability is increasing relative to death over time. The probability of transplant appears to be dropping slightly relative to death over time, although this individual parameter estimate is not significant (p=0.173). The interaction between time and RHA, age and diabetes was tested, but the interactions were not significant. A non-significant effect for age, for example, means that a separated age effect need not be estimated for each subgroup, but a common age effect can be used. This improves accuracy by pooling data across subgroups. Because so few of the transitions showed any evidence of time dependence, we used a simpler stationary model and generated sets of projections incorporating the observed time trends explicitly. We did this by modelling decreased death rates and increased peritoneal dialysis rates.

Appendix Table 2.1: Transitional Probability Matrix for Patients with End Stage Kidney Disease and Diabetes Winnipeg residents, January 1, 2004-March 31, 2012

		Probability of State Transition				
		Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	No Dialysis Record	Death or No Health Coverage
State Before Transition	Hemodialysis	92.52%	0.43%	0.02%	0.44%	6.60%
	Peritoneal Dialysis and Home Hemodialysis	2.58%	89.74%	0.25%	0.29%	7.14%
	Kidney Transplant	0.33%	0.03%	99.02%	0.00%	0.62%
	No Dialysis Record	2.44%	0.12%	0.00%	96.46%	0.98%
	Death or No Health Coverage	0.00%	0.00%	0.00%	0.00%	100%

Appendix Table 2.2: Odds Ratios of State Transition in Patients with End Stage Kidney Disease

		Odds Ratio of State Transition				Effect of Time (p-value)
		Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	Death or No Health Coverage	
State Before Transition	Hemodialysis	**1.007**	**1.037**	**0.981**	**reference**	**0.0025**
	Peritoneal Dialysis and Home Hemodialysis	ns	ns	ns	reference	0.5939
	Kidney Transplant	ns	ns	ns	reference	0.4571

Bolded values indicate a statistically signigificant odds ratio

ns indicates odds ratios not significant

APPENDIX 3: COMPARISON BETWEEN PATIENTS WITH CHRONIC KIDNEY DISEASE BY RISK OF PROGRESSION TO END STAGE KIDNEY DISEASE

Appendix Table 3.1: Comparison Between Patients with Chronic Kidney Disease by Risk of Progression to End Stage Kidney Disease, March 31, 2012

	Low Risk*	High Risk (excluding A3/G5)	Very High Risk (A3/G5)
Number of Patients	33,097	22,713	838
Age (years)			
18-44	24.91%	5.68%	8.70%
45-64	33.24%	21.38%	33.10%
65+	41.84%	72.93%	58.20%
Average Age and Standard Deviation (years)	58.5 (20.0)	72.4 (15.4)	66.3 (15.4)
Male (%)	38.08%	43.84%	46.18%
Region (%)			
Southern Health/Santé Sud	7.16%	5.87%	6.00%
Winnipeg	69.52%	78.76%	73.40%
Prairie-Mountain Health	5.21%	3.51%	2.00%
Interlake-Eastern	11.05%	8.41%	10.60%
Northern	7.06%	3.45%	8.00%
Remote Community	5.56%	2.51%	5.70%
Lowest Income Quintile (Q1, %)	26.42%	25.18%	27.70%
Nephrologist Visit in Previous 5 years	15.43%	29.49%	68.50%
Dialysis Treatment in Following Year			
Not on dialysis	96.11%	88.63%	66.71%
Started dialysis	0.03%	0.49%	17.78%
Died without dialysis	3.28%	10.45%	15.27%

* risk of progression to ESKD is based on heat map in Chapter 2

APPENDIX 4: RELATIVE RISKS COMPARING RATES OF CHRONIC KIDNEY DISEASE AND END STAGE KIDNEY DISEASE IN ADULTS BY REGION TO THE MANITOBA RATE

Appendix Table 4.1: Relative Risks Comparing Rates of Chronic Kidney Disease in Adults by Region to the Manitoba Rate, by Risk of Progression to End Stage Kidney Disease

Age- and sex-adjusted, residents aged 18+ on March 31, 2012

	Relative Risks (95% Confidence Intervals) by Risk of Progression to ESKD		
	Unknown	**Low**	**High**
Southern Health/Santé Sud	1.21 (0.94-1.55)	**0.62 (0.48-0.79)**	**0.42 (0.32-0.55)**
Winnipeg	**0.41 (0.32-0.52)**	1.13 (0.89-1.45)	**1.33 (1.01-1.75)**
Prairie Mountain Health	**2.51 (1.96-3.22)**	**0.42 (0.33-0.54)**	**0.20 (0.15-0.27)**
Interlake-Eastern	1.10 (0.86-1.42)	1.21 (0.95-1.55)	0.83 (0.63-1.09)
Northern	**2.97 (2.30-3.82)**	**1.67 (1.30-2.14)**	1.27 (0.96-1.67)
Remote Communities	**2.47 (1.81-3.37)**	**3.42 (2.59-4.51)**	**3.15 (2.40-4.13)**

bolded values indicate statistically significant difference from the Manitoba rate

Appendix Table 4.2: Relative Risks Comparing Rates of End Stage Kidney Disease in Adults by Region to the Manitoba Rate, by Treatment Type

Age- and sex-adjusted, residents aged 18+ on March 31, 2012

	Relative Risks (95% Confidence Intervals) by Treatment Type		
	Transplant	**Dialysis**	**All ESKD**
Southern Health/Santé Sud	0.95 (0.75-1.20)	**0.64 (0.51-0.79)**	**0.74 (0.63-0.87)**
Winnipeg	1.07 (0.94-1.21)	1.04 (0.93-1.17)	1.05 (0.96-1.15)
Prairie Mountain Health	0.81 (0.63-1.04)	**0.72 (0.59-0.87)**	**0.75 (0.64-0.87)**
Interlake-Eastern	0.81 (0.61-1.08)	1.01 (0.84-1.23)	0.95 (0.81-1.11)
Northern	1.24 (0.89-1.74)	**2.53 (2.07-3.07)**	**2.05 (1.73-2.43)**
Remote Communities	**1.86 (1.18-2.94)**	**4.39 (3.46-5.57)**	**3.42 (2.77-4.23)**

bolded values indicate statistically significant difference from the Manitoba rate

APPENDIX 5: VALIDATION OF ADMINISTRATIVE DATA DEFINITION OF CHRONIC KIDNEY DISEASE IN CHILDREN

We validated the CKD definition that we used for children aged 0 to 17. The population included in this validation analysis is described in Table 5.1 below. A total of 18,099 children (6.2% of population) in Manitoba had a laboratory test for serum creatinine to calculate eGFR or a urine test to evaluate proteinuria between April 1, 2009 and March 31, 2012. Approximately 14,171 children in Manitoba had two laboratory tests to allow the determination of chronicity. After excluding children already on renal replacement therapy or with acute kidney injury, 918 children with confirmed CKD (using our definition described in Methods) were identified from laboratory data.

Appendix Table 5.1: Characteristics of Children in the Chronic Kidney Disease Validation Cohort
April 1, 2009-March 31, 2012

Characteristics	Administrative Data	Laboratory Data	Administrative and Laboratory Data
Average age and standard deviation (years)	7.5 (5.8)	14.6 (3.4)	10.4 (5.2)
Male (%)	50.9%	48.5%	53.6%
Lowest Income Quintile (Q1, %)	29.0%	23.4%	29.9%
Urban Areas (Winnipeg and Brandon, %)	46.9%	70.9%	55.1%
Diagnosed with Hypertension (%)	14.5%	6.3%	52.8%
Seen by a Nephrologist (%)	34.2%	15.7%	94.2%
At High Risk for Progression to End Stage Kidney Disease (%)	n/a	4.9%	22.9%

n/a indicates not applicable

APPENDIX 6: RELATIVE RISKS COMPARING RATES OF CHRONIC KIDNEY DISEASE IN CHILDREN BY REGION TO THE MANITOBA RATE

Appendix Table 6.1: Relative Risks Comparing Rates of Chronic Kidney Disease in Children by Region to the Manitoba Rate, by Risk of Progression to End Stage Kidney Disease

Age- and sex-adjusted, residents aged 0-17+ on March 31, 2012

	Relative Risks (95% Confidence Intervals) by Risk of Progression to ESKD		
	Unknown	**Low**	**High**
Southern Health/Santé Sud	1.11 (0.95-1.29)	**0.66 (0.51-0.86)**	**0.68 (0.50-0.93)**
Winnipeg	**0.84 (0.74-0.96)**	1.12 (0.90-1.39)	1.14 (0.92-1.42)
Prairie Mountain Health	0.93 (0.79-1.11)	**0.43 (0.32-0.59)**	**0.57 (0.39-0.82)**
Interlake-Eastern	1.06 (0.89-1.27)	1.14 (0.88-1.48)	0.90 (0.64-1.28)
Northern	**1.74 (1.48-2.03)**	**1.55 (1.21-1.99)**	**1.48 (1.10-2.00)**
Remote Communities	**2.11 (1.71-2.61)**	**2.84 (2.37-3.41)**	**2.27 (1.63-3.16)**

bolded values indicate statistically significant difference from the Manitoba rate

APPENDIX 7: SUMMARY OF "WHAT IF" PROJECTION SCENARIOS BY HEALTH REGION

Appendix Table 7.1: Observed and Projected Number of Patients with End Stage Kidney Disease in Winnipeg Health Region, by "What If" Projection Scenario and Treatment Type, 2012 and 2024

	Average Number of Patients (95% Confidence Interval)			Total Number of ESKD Patients
	Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	
Observed (2012)	558	141*	367	1,066
Projected (2024)	944 (881–1,010)	198 (173–226)	626 (585–671)	1,769
"What If Scenarios" (2024)				
Constant diabetes prevalence	830 (770–892)	179 (155–205)	613 (570–655)	1,622
30% peritoneal dialysis rate	883 (815–946)	253 (223–287)	637 (593–680)	1,773
8% of starts are home hemodialysis	904 (838–969)	233 (203–266)**	631 (591–673)	1,791
25% increase in kidney transplant rate	916 (850–988)	189 (162–215)	687 (641–734)	1,972
20% decrease in mortality rate	1,083 (1,009–1,156)	223 (192–253)	666 (624–710)	1,603

* Peritoneal dialysis: 124; home hemodialysis: 17

** Peritoneal dialysis: 174; home hemodialysis: 59

Appendix Table 7.2: Observed and Projected Number of Patients with End Stage Kidney Disease in Southern Health/Santé Sud, by "What If" Projection Scenario and Treatment Type, 2012 and 2024

	Average Number of Patients (95% Confidence Interval)			Total Number of ESKD Patients
	Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	
Observed (2012)	68	35*	77	180
Projected (2024)	124 (99–150)	61 (45–78)	139 (117–160)	323
"What If Scenarios" (2024)				
Constant diabetes prevalence	109 (85–132)	55 (39–70)	136 (115–156)	299
30% peritoneal dialysis rate	123 (100–148)	61 (45–79)	139 (119–161)	324
8% of starts are home hemodialysis	118 (93–143)	67 (50–84)**	140 (118–162)	329
25% increase in kidney transplant rate	119 (96–144)	57 (42–71)	153 (130–176)	358
20% decrease in mortality rate	142 (113–171)	68 (49–87)	148 (127–170)	296

* Peritoneal dialysis: s; home hemodialysis: s

** Peritoneal dialysis: 52; home hemodialysis: 15

s indicates data suppressed due to small numbers

Appendix Table 7.3: Observed and Projected Number of Patients with End Stage Kidney Disease in Prairie Mountain Health Region, by "What If" Projection Scenario and Treatment Type, 2012 and 2024

	Average Number of Patients (95% Confidence Interval)			Total Number of ESKD Patients
	Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	
Observed (2012)	112	14*	74	200
Projected (2024)	181 (153–211)	24 (15–34)	123 (103–145)	328
"What If Scenarios" (2024)				
Constant diabetes prevalence	160 (133–189)	21 (12–31)	121 (103–139)	302
30% peritoneal dialysis rate	169 (142–198)	37 (26–50)	124 (105–144)	330
8% of starts are home hemodialysis	175 (145–208)	30 (19–41)**	124 (106–144)	334
25% increase in kidney transplant rate	175 (145–206)	23 (13–33)	136 (116–157)	369
20% decrease in mortality rate	210 (176–247)	26 (16–38)	132 (114–153)	295

* Peritoneal dialysis: s; home hemodialysis: s

** Peritoneal dialysis: 24; home hemodialysis: 6

s indicates data suppressed due to small numbers

Appendix Table 7.4: Observed and Projected Number of Patients with End Stage Kidney Disease in Northern Health Region, by "What If" Projection Scenario and Treatment Type, 2012 and 2024

	Average Number of Patients (95% Confidence Interval)			Total Number of ESKD Patients
	Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	
Observed (2012)	118	35*	28	181
Projected (2024)	207 (174–242)	54 (40–69)	64 (51–79)	325
"What If Scenarios" (2024)				
Constant diabetes prevalence	173 (144–203)	46 (33–62)	62 (49–76)	281
30% peritoneal dialysis rate	194 (163–228)	71 (54–90)	64 (51–79)	330
8% of starts are home hemodialysis	200 (168–233)	63 (45–80)**	64 (50–79)	327
25% increase in kidney transplant rate	202 (169–238)	52 (37–67)	73 (58–89)	368
20% decrease in mortality rate	238 (203–277)	61 (45–79)	70 (55–85)	289

* Peritoneal dialysis: s; home hemodialysis: s

** Peritoneal dialysis: 49; home hemodialysis: 14

s indicates data suppressed due to small numbers

Appendix Table 7.5: Observed and Projected Number of Patients with End Stage Kidney Disease in Interlake-Eastern Health Region, by "What If" Projection Scenario and Treatment Type, 2012 and 2024

	Average Number of Patients (95% Confidence Interval)			Total Number of ESKD Patients
	Hemodialysis	Peritoneal Dialysis and Home Hemodialysis	Kidney Transplant	
Observed (2012)	120	35*	51	206
Projected (2024)	198 (168–234)	49 (36–63)	86 (71–102)	333
"What If Scenarios" (2024)				
Constant diabetes prevalence	174 (145–205)	44 (31–58)	83 (69–99)	301
30% peritoneal dialysis rate	186 (155–218)	59 (43–75)	87 (71–104)	332
8% of starts are home hemodialysis	190 (158–225)	56 (41–73)**	86 (71–103)	336
25% increase in kidney transplant rate	195 (163–229)	48 (33–63)	94 (76–112)	378
20% decrease in mortality rate	230 (196–268)	57 (41–74)	91 (76–109)	298

* Peritoneal dialysis: 29; home hemodialysis: 6

** Peritoneal dialysis: 41; home hemodialysis: 15

APPENDIX 8: KIDNEY FAILURE RISK EQUATION (KFRE) COHORT

Appendix Table 8.1 shows the characteristics of the KFRE validation cohort five years prior to the validation in 2007/08-2011/12, as well as the health outcomes of the cohort at the time of the validation. As seen in Table 8.1 in Chapter 8, the cohort comprised of 151 people who had ESKD in 2007/08-2011/12 and 1,361 people who did not develop ESKD. In the previous five years, the majority of these 1,512 people had mild to severe CKD (1,196) and a smaller number of people had more advanced CKD. About half of the cohort was male and almost 60% were more than 65 years old. Of those in CKD Stage G4-5 (severe CKD to kidney failure), 76.6% had had a prior nephrologist visit. As expected, the CKD Stage G4-5 group had a higher percentage kidney failure, mortality and of laboratory results indicative of kidney dysfunction compared to the CKD Stage 3 group.

Appendix Table 8.1: Characteristics of Patients with Chronic Kidney Disease (CKD) in the Kidney Failure Risk Equation Validation Cohort by CKD Severity

Residents aged 18+ on March 31, 2007

	Patients with CKD by Severity (Oct 1, 2006-Mar 31, 2007)	
	Mild to Severe (Stage G3)	**Severe or Kidney Failure (Stage G4-G5)**
Number of patients	1,196	316
Demographics on March 31, 2007		
Age Group (Years)		
18-65	40.90%	42.10%
65+	59.00%	57.90%
Average Age & Standard Deviation (Years)	67 (13)	66 (14)
Male	50.30%	49.70%
Kidney Health in Previous 6 Months		
Urine Albumin to Creatinine Ratio (mg/g)		
< 30	42.40%	21.20%
30-300	35.10%	30.10%
≥ 300	22.50%	48.70%
Serum Creatinine (mg/dL)	1.4	2.8
Glomerular Filtration Rate (mL/min/1.73 m^2)	47.9	21.3
Seen by Nephrologist in Previous 5 Years	31.20%	76.60%
Physical Health Within Previous 5 Years		
Diabetes Prevalence**	76.60%	73.10%
Ischemic Heart Disease Prevalence†	37.90%	38.00%
Congestive Heart Failure Prevalence**	17.40%	27.90%
Atrial Fibrillation Prevalence**	5.90%	5.70%
Disease Progression During 5-Year Follow-Up		
End Stage Kidney Disease Prevalence	4.80%	29.80%
Mortality Rate	26.30%	32.90%

* CKD severity based on heat map categories in Chapter 2

** 2004/05-2006/07

† 2002/03-2006/07

Appendix Table 8.2 shows the number of patients in the groups described by Kidney Failure Risk Equation Threshold. It complements the results in Chapter 8 where an explanation of the thresholds are found.

Appendix Table 8.2: Patients with Chronic Kidney Disease Stratified by Progression to End Stage Kidney Disease (ESKD) and Screening Method

2007/08-2011/12

Screening Method and Risk Threshold	Number of Patients by Progression to ESKD		
	Yes	No	Total
Kidney Failure Risk Equation			
0-3% risk of progression to ESKD	5	842	847
> 3% risk of progression to ESKD	146	519	665
Total	151	1,361	1,512
0-10% risk of progression to ESKD	21	1,091	1,112
> 10% risk of progression to ESKD	130	270	400
Total	151	1,361	1,512
Estimated Glomerular Filtration Rate			
> 30 ml/min/1.73m^2	57	1,139	1,196
< 30 ml/min/1.73m^2	94	222	316
Total	151	1,361	1,512
> 45 ml/min/1.73m^2	24	740	764
< 45 ml/min/1.73m^2	127	621	748
Total	151	1,361	1,512
Prior Nephrologist Visit			
Yes	119	496	615
No	32	865	897
Total	151	1,361	1,512

In addition to this forward-looking analysis, which starts with laboratory tests and looks for ESKD in the next five years, we also started with people who have ESKD in the time period from April 1, 2010 to March 31, 2012 and laboratory tests at least one year prior (Appendix Table 8.3). Almost 70% of people were 65 years and older, male (54.8%), had high rates of comorbid conditions and laboratory test results indicative of kidney dysfunction. Using a 10% threshold the KFRE successfully predicts 84.3% of these will progress to ESKD. Using a less restrictive 3% threshold, 94.6% are predicted to progress. Only 5.4% are assigned the lowest 0-<3% risk category.

Appendix Table 8.3: Characteristics and Predicted Risk Thresholds of Patients with End Stage Kidney Failure
Residents aged 18+ on March 31, 2009

	Patients with ESKD (2010/11-2011/12)
Number of patients	166
Demographics on March 31, 2009	
Age Group (Years)	
18-65	69.90%
65+	30.10%
Average Age & Standard Deviation (Years)	58 (14)
Male	54.80%
Kidney Health in Previous 3 Years	
Urine Albumin to Creatinine Ratio (mg/g)	
< 30	4.80%
30-300	15.10%
≥ 300	80.10%
Serum Creatinine (mg/dL)	2.5
Glomerular Filtration Rate (mL/min/1.73 m^2)	28
Physical Health Within Previous 5 Years	
Diabetes Prevalence*	78.30%
Ischemic Heart Disease Prevalence**	32.50%
Congestive Heart Failure Prevalence*	16.30%
Atrial Fibrillation Prevalence*	3.00%
Kidney Failure Risk Equation Prediction	
Risk of Progression to ESKD (%)	
< 3	5.40%
3-10	10.20%
≥ 10	84.30%
Median Risk of Progression to ESKD	0.565

* 2006/07-2008/09

** 2004/05-2008/09

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