

DEVELOPING A PROJECTION MODEL FOR DIABETIC END STAGE RENAL
DISEASE IN SASKATCHEWAN USING AN AGENT BASED MODEL

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By

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ABSTRACT

Our epidemiology research found that the incident and prevalent rates for Diabetes mellitus (DM) and Diabetic End Stage Renal Disease (DM-ESRD) were at rise in Saskatchewan between year 1980 and 2005. Combining concerns regarding the rising trends reported by research studies with the concerns of the significant health and financial burden imposed by DM-ESRD on individuals and societies, we sought to project the number of DM-ESRD patients in Saskatchewan up to year 2025 with the cost required for caring for those patients.

An agent-based model (ABM) is developed to simulate DM to ESRD progression, treatments for DM-ESRD patients, and the assessments and waiting list processes preparing patients for kidney transplants. The model parameters were estimated from a wide variety of data sources. The agent based modeling approach is chosen for projections regarding the DM-ESRD situation in Saskatchewan because of its advantage in capturing heterogeneities of individual patients, ability to retain biographical information on patients, capacity to capture time-varying competing risks, better presentations features and easy integration with existing models built in either agent based or System Dynamic methods. The approach was also attractive due to its flexibility for future expansion to represent social networks.

The model projects the incident and prevalent case count, cost, and person years lived for the DM-ESRD population in Saskatchewan between year 1980 and 2025. The projections captured the great challenges brought by the fast growing number of DM-ESRD patients and substantial cost associated with managing the disease. In addition to producing projection results, the research presented here demonstrates how the model can be used by policy makers to experiment and evaluate different policy/interventions in a safe context. By capturing both the individual level records and population level statistics, the model provide a wealth of data for

detailed analysis, which can help health policy makers gain insights in the current and future diabetic-ESRD situation in the province, aiding in resources planning for managing the fast-growing ESRD population and the growing need for dialysis services.

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LIST OF ABBREVIATIONS

ABM	Agent Based Model
BMI	Body Mass Index
CAPD	Continuous Ambulatory Peritoneal Dialysis
CCPD	Continuous Cycler-assisted Peritoneal Dialysis
CKD	Chronic Kidney Disease
CORR	Canadian Organ Replacement Register
CV	Cardiovascular
DM	Diabetes Mellitus
ESRD	End Stage Renal Disease
FN	First Nation
GDM	Gestational Diabetes Mellitus
HD	Hemodialysis
OSK	Other Saskatchewan Residents
PD	Peritoneal Dialysis
RHA	Regional Health Authority
RI	Registered Indian
RRT	Renal Replacement Therapy
SK	Saskatchewan

CHAPTER 1

BACKGROUND AND INTRODUCTION

The first chapter of the thesis provides background information regarding diabetic end stage renal disease (DM-ESRD), the cause, and treatment options. The local health care system is discussed next as it is responsible for providing care to the DM-ESRD patients in the province. In the last two sections of this chapter, the motivations, the goal and the methodology selected for the thesis research are presented.

1.1 Diabetic-ESRD and Treatment Options

1.1.1 Diabetic Mellitus (DM)

Diabetes is a condition in which the glucose levels in the blood are poorly regulated, leading to periods with abnormally high blood sugar. The human body uses insulin to break down sugar in order to produce energy. When the pancreas is not able to produce enough insulin or the body cannot use the insulin effectively, the glucose level in the blood will rise and exceed the normal range. There are three types of diabetes: Type 1, Type 2, and gestational diabetes. Type 1 diabetes refers to cases in which the pancreas is not producing enough insulin for the body to use. Research has shown that genetics play an important role in developing Type 1 diabetes [1]. Type 1 diabetes is commonly seen in childhood or early adulthood. Less than ten per cent of cases of diabetes fall into this category. Type 2 diabetes refers to cases in which the body either cannot produce enough insulin and/or cannot use the insulin effectively [1]. Several risk factors for Type 2 diabetes have been identified including body weight, ethnicity, age, sex, family history, history of gestational diabetes and life style. Type 2 diabetes is mainly found in patients who are in their 40s and older. Type 2 diabetes forms more than 90% of all diabetes cases in the general population. Unlike Type 1 or Type 2 diabetes, gestational diabetes mellitus

(GDM) is usually a temporary condition during pregnancy. It takes place in 2% to 4% of all pregnancies. For most of the patients the condition will go away after the birth of the child. Having gestational diabetes increases the chance of developing type 2 diabetes later in life for both the mothers and babies [3].

Most people with Type 2 diabetes can be managed by medications, improved diet and healthier life styles. However, improper management of diabetes can result in prolonged exposure to high blood glucose levels, which can lead to serious complications in organs such as the cardiovascular system, kidneys, eyes, and nerves. Moreover, diabetes patients are twice as likely to have premature death as those without diabetes.

Another challenge presented by diabetes is that as many as one third of all diabetes cases remain undiagnosed. Patients with undiagnosed diabetes are at increased risk of developing diabetes-related complications [2]. Therefore, it is important to have screening programs developed for people who are at higher risk for developing diabetes so as to enhance early detection.

Diabetes has become a prevailing epidemic worldwide, including Canada. In fiscal year 2006 - 2007, there were two million people living with diagnosed diabetes in Canada. The prevalence of diagnosed diabetes has increased by 21% from fiscal year 2002 - 2003 to fiscal year 2006 – 2007 [1]. As baby boomers enter older age and with increased survival of people with diabetes, it is likely we will see even bigger increases in diabetes prevalence in the next few years. Among Canadians, it has been reported that people of aboriginal background are experiencing a more severe epidemic of diabetes. Aboriginal people have higher diabetes prevalence and incidence rates, and also have diabetes at an earlier age. Compared to other provinces in Canada, we have a higher proportion of First Nation people in Saskatchewan. Thus,

we are particularly interested in seeing how the epidemic of diabetes presents itself in Saskatchewan and impacts the provincial health care system.

1.1.2 Diabetic End Stage Renal Disease (DM-ESRD)

Diabetes is the leading cause for ESRD in Canada, and serves as the underlying factor for more than 35% of the new ESRD cases [7]. Kidneys are damaged by the exposure to high glucose levels over years. One serious complication of diabetes is ESRD or kidney failure, which occurs when kidneys can no longer remove waste products from the blood. Not all people with diabetes will develop ESRD. Some can live with earlier stages of chronic kidney disease (CKD) without reaching kidney failure. Past studies found that people from certain ethnic subgroups like African American, American Indian, and Hispanics/Latinos are at higher rate for developing ESRD [4]. Other research has shown risk factors for developing ESRD include obesity, medical conditions, older age and male sex [7].

In Canada, there are three main types of treatments for patients with ESRD: Haemodialysis (HD), Peritoneal Dialysis (PD) and Kidney Transplantation. As reported by CORR, in 2008, among all ESRD treatments, HD accounts for 48.5%, PD accounts for 10.9%, and kidney transplantation accounts for 41% [7] of the treatments. More details about these treatments are discussed in the following section.

1.1.3 Haemodialysis (HD)

During HD sessions, a dialysis machine is connected to the patient to remove waste products, excess minerals and fluid from the blood [5]. Blood is pumped from a patient's vein, into a dialysis machine, and then back into the patient. Usually, patients on HD go for three 3 – 5 hour sessions a week. In Canada, HD can be performed in-center (hospital or community based)

or at home. In-Center HD is the predominant form of dialysis when compared with HD performed at home and PD [7].

1.1.4 Peritoneal Dialysis (PD)

PD uses a patient's peritoneal membrane to filter the waste and extra fluid from the blood [6]. A dialysis solution is instilled into the patient's abdominal cavity, where waste products and fluid are filtered from the blood through the peritoneal membrane into the dialysis solution before it is drained from the body. This process is usually repeated four times a day, and each time the dialysis solution stays in the body for four to six hours. There are two forms of PD: continuous ambulatory peritoneal dialysis (CAPD) and continuous cycler-assisted peritoneal dialysis (CCPD). CAPD fills and drains the dialysis solution using gravity. On the other hand, the CCPD automates the filling and draining process by using a machine called a cycler.

Compared to HD, PD is a less resource intensive treatment. It can be carried out at home, and patients do not have to be connected to a dialysis machine inside a clinic for the length of a HD session. Patients on PD can have much greater mobility than patients on HD.

As for switching between dialysis treatments, it was reported that 60% of patients underwent only one type of dialysis treatments, 28% have experienced two different types of treatments; 9% have three different treatments and the rest have four or more different treatments [25].

1.1.5 Kidney Transplantation.

Kidney transplantation is a surgical operation in which a working kidney from a donor is implanted into a person with ESRD. The donor can be a deceased person or a living person (related or unrelated). Most of the ESRD patients receive dialysis treatments prior to getting kidney transplants. However, a small portion of the ESRD patients receive kidney transplant

without ever getting dialysed, which is referred as “Pre-Emptive” kidney transplants. ESRD patients who are eligible to receive kidney transplants will be put on a waiting list because of the limited availability of organs. In more recent decades, the number of living donor kidney transplants has been growing steadily but the number of cadaveric kidney transplants has remained stable [20]. With a growing number of ESRD patients requiring transplants, the available organs from living and deceased donors are not meeting the demand. The current wait time taken from the 2008 CORR report is shown below.

Table 1-1. Transplant Wait Time Spent on Dialysis Prior to First Kidney Transplant by Province of Treatment, Adult Kidney Transplant Recipients, Canada, 2006 – 2008. Image of the table was taken from [9].

	B.C.	Alta.	Sask.	Man.	Ont.	Que.	N.S.	Canada
Duration on Dialysis (Median Days), Deceased Donor	2,266	1,073	1,001	1,599	1,778	824	756	1,283
Duration on Dialysis (Median Days), Deceased Donor, No Pre-Emptive	2,286	1,095	1,007	1,599	1,789	955	794	1,324
Duration on Dialysis (Median Days), Living Donor	212	390	465	532	344	283	208	323
Duration on Dialysis (Median Days), Living Donor, No Pre-Emptive	536	561	735	575	595	431	458	549

Notes

In the calculation of median days on dialysis, pre-emptive kidney transplant recipients were given a value of 0 for their wait time.

There were 3,135 adult first kidney transplants performed in Canada between 2006 and 2008, 459 of which were pre-emptive transplants.

Source

Canadian Organ Replacement Register, 2009, Canadian Institute for Health Information.

Though facing post-transplant challenges like rejections and other complications, kidney transplantation has become a more favourable choice for ESRD patients compared to dialysis. As shown in Figure 1-1 and Figure 1-2 from CORR, the five year survival outcome is much better for transplant patients than for dialysis patients.

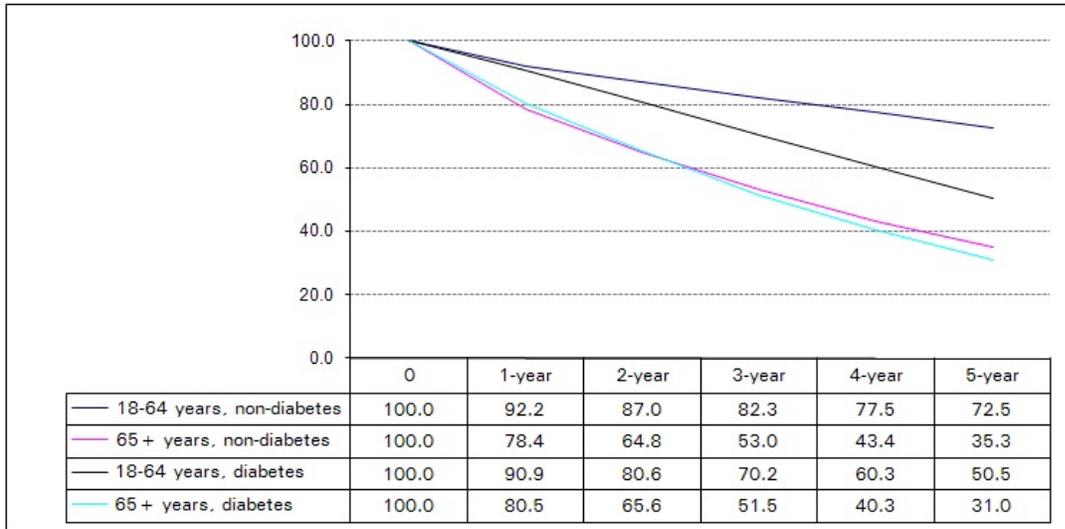


Figure 1-1. Five Year Survival in ESRD Patients on Dialysis, with or without Diabetes, by Age, 2004 - 2008 Period Survival. Figure was taken from [22]

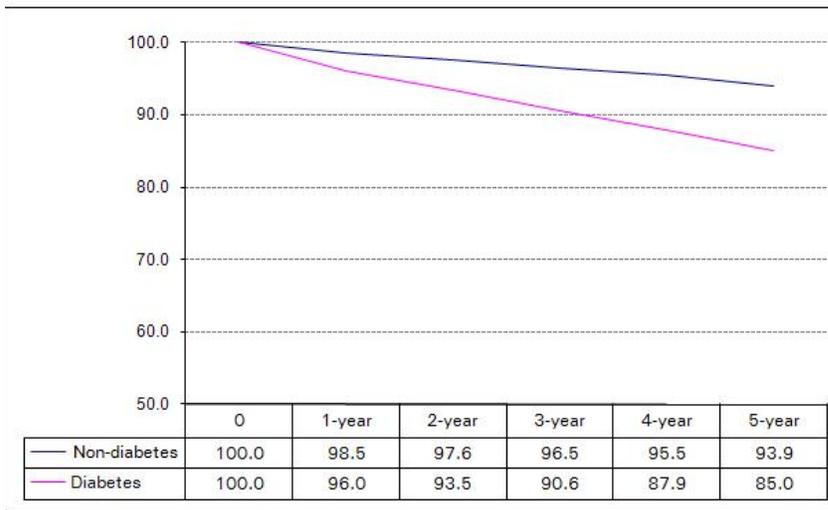


Figure 1-2. Five Year Survival in Patients with Kidney Transplant, with or without Diabetes, by Age, 2004 - 2008 Period Survival [23]

HD, PD and Kidney Transplantations are all costly and resource intensive treatments. Any of the three treatments greatly impacts patients and their families, and also puts a heavy

financial burden on the health care system and society. In the next section, the regional ESRD program and funding structure in Saskatchewan will be discussed.

1.2 Local Health Care System in Saskatchewan

In Saskatchewan, ESRD care is carried out by the regional renal programs. The outpatient HD service is provided in the two hospital renal units at St. Paul's and Regina General Hospital, as well as in several satellite dialysis clinics throughout the province. The renal programs also train patients to perform dialysis at home. Currently in Saskatchewan, living donor transplants are performed in St. Paul's hospital and, temporarily, deceased donor kidney transplants are carried out in Edmonton, Alberta. Shown below is a detailed report provided by CORR on the prevalence of ESRD patients by location of treatment in Saskatchewan.

Table 1-2. Prevalent End-Stage Renal Disease Patients by Location of Treatment in Saskatchewan. Image of table was taken from [24].

Facility Region	Treatment Modality	Sex	Metrics		Number of Prevalent ESRD Patients										
			Calendar Year	Year	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	Total
Regina Qu'Appelle RHA					164	186	255	262	311	325	354	377	400	384	3,018
	Function Transplant				0	0	11	15	21	25	38	43	45	42	240
		Female					4	5	7	7	9	12	15	14	73
		Male					7	10	14	18	29	31	30	28	167
	Hemodialysis				147	170	220	227	256	256	266	276	290	282	2,390
		Female			64	64	84	84	94	96	101	99	97	102	885
		Male			83	106	136	143	162	160	165	177	193	180	1,505
	Peritoneal Dialysis				17	16	24	20	34	44	50	58	65	60	388
		Female			7	8	12	9	15	17	23	27	30	26	174
		Male			10	8	12	11	19	27	27	31	35	34	214
Saskatoon RHA					534	579	604	632	639	652	593	607	645	685	6,170
	Function Transplant				309	325	329	342	349	348	276	288	292	311	3,169
		Female			101	105	108	117	127	132	108	115	117	124	1,154
		Male			208	220	221	225	222	216	168	173	175	187	2,015
	Hemodialysis				167	186	203	208	219	231	242	248	263	277	2,244
		Female			80	85	94	97	99	114	115	115	123	122	1,044
		Male			87	101	109	111	120	117	127	133	140	155	1,200
	Peritoneal Dialysis				58	68	72	82	71	73	75	71	90	97	757
		Female			26	25	30	28	28	31	37	31	36	41	313
		Male			32	43	42	54	43	42	38	40	54	56	444
Total					698	765	859	894	950	977	947	984	1,045	1,069	9,188

In Saskatchewan, the regional renal program funded by the provincial health care budget completely covers the cost of outpatient dialysis, medications and inpatient hospitalizations for ESRD patients who are eligible for the Saskatchewan Health Insurance Plan. Disability benefits are not covered by the Saskatchewan Health Plan but are rather provided by either private insurance, a federal government program such as CPP, or unemployment insurance.

1.3 Research Motivation and Goal

As discussed in previous sections, ESRD is a major complication of diabetes and is both serious and costly. In Saskatchewan, it is the responsibility of the provincial government to provide health care for ESRD patients and to bear the associated cost. For planning purposes, we want to know the future demands resulting from the care of DM-ESRD patients in the years to come. Factors like demographic changes and epidemiological characteristics of diabetes and diabetic – ESRD could all impact the DM- ESRD situation in Saskatchewan.

Demographic studies have shown that Saskatchewan is one of two provinces in Canada which have the highest Aboriginal (a term that includes First Nations, Metis and Inuit people) population concentrations. From the epidemiological studies conducted in this province and elsewhere, we know that the First Nation population exhibits different patterns for diabetes and its complications like ESRD. Here are some findings from various demographics projections for the next 15 years, and some highlights from our previous epidemiological studies on diabetes and diabetic – ESRD conducted in Saskatchewan.

Our previous research found that the prevalence and incidence for diabetes and diabetic – ESRD are higher in certain population subgroups. As we found in our Saskatchewan Diabetic-ESRD study [19], between 1981 and 2005, most of the DM-ESRD cases occurred in the 40 - 59 age group for FN and the 60 plus age group for OSK. In the Saskatchewan Diabetes study [18],

between 1980 to 2005, we found that diabetes incident cases are highest in the 40 - 49 age group for FN and the age 70 plus group for OSK. Moreover, it was found that the prevalence rates of diabetes increased at different rates for different genders and ethnicities. The diabetes prevalence increased from 9.5% to 20.3% in FN females and from 4.9% to 16.0% in FN males. Among OSK, diabetes prevalence increased from 2.0% to 5.5% among females and from 2.0% to 6.2% among males.

In demographic studies for Saskatchewan, it is predicted that there will be rapid population growth for the same age and ethnic groups as noted by the above epidemiological researches. In the Registered Indian (i.e. FN) population projection (medium growth scenario) conducted by Indian and Northern Affairs Canada [33], from 2009 to 2024, the population for Registered Indians in the 40 - 59 age group will increase by a range of 8.5% to 18.5% every 5 years, and a total of 42.4% across the 15 years projection period; for people who are in the 40 - 49 age group, the five year growth rate is from 2.3% to 9.8%, yielding a total growth of 20.6%.

In the Saskatchewan general population projection (medium growth scenario; included both FN and OSK) conducted by Stats Canada [31], from 2011 to 2026, there will be a 9.5% to 13% population growth every 5 years for people over 60 years old, and a total of 39.2% growth across the 15 years projection period; for people 70 years and over, there will be a 4% to 18% growth every 5 years, yielding a total of 39.6%.

With the above findings in diabetes and diabetic - ESRD rates and the trends in population projections, it follows that we will likely face a substantial increase in DM-ESRD prevalence and incidence as well as related health care spending in Saskatchewan. However, due to the complexity of this problem, it will be difficult to obtain a good approximation of the future situation without a suitable methodology. We chose to use dynamic modelling approach for our

research problem because it offers several advantages, which will be discussed in the next section.

1.4 The Choice of a Dynamic Modeling Approach for this Research

In the last 10 years, there has been an increasing application of system science methods to study problems in the public health domain because system science methods have offered many benefits for investigating public health problem [27].

First of all, system science methods can better capture the structured complexity and the dynamic complexity of public health problems. Public health problems could have many components in their scope. For instance, one health economic problem usually involves the disease itself, demographics, risk factor dynamics, local and/or global economy, facilities, equipment, human resources, policy, budgets, transportation, and much more. The traditional scientific approach follows a reductionist strategy, which focuses on one aspect of the health problem. The reductionist strategy is great for gaining insights into the working mechanisms behind a set of components in a particular area of the public health. However, it often misses many interactions between sets of disparate components. In comparison, system science methods take all components and the context into consideration; therefore it can facilitate reasoning regarding the complex and dynamic behaviour found in a public health question. When public health problems are studied as complex systems, emergent behaviours like exponential growth, delays, oscillations, and tipping points can be explained by the collective interactions of all the components within the system. As stated above, the traditional epidemiological methods aren't by themselves equipped to help us understand the dynamic complexity present within the public health problem. System science methods complement such traditional methods in providing insights.

Secondly, system methods can help address many challenges presented in public health research: communications, misperceptions, and prioritization of research and data collection. Nowadays, collective efforts are normally required from a team of researchers with different knowledge backgrounds for solving public health problems. A System Dynamics Model which is based on system science is a great communication tool. It helps with the visualizations of conceptual model for discussion and collective refinements from modellers, health care practitioners and policy makers. It presents all the components in the scope, and the hypothesized causal relationship between components. Moreover, the values for the parameters in the System Dynamics model explicitly lay out the assumptions for particular epidemiological contexts. All of the above facilitates communications among the research team members.

In addition to aiding communication among team members, the simulation of the System Dynamics model can help our hypotheses regarding factors contributing to the problem. The simulation of a System Dynamics model can be used to gain insights on how changes in the system structures and contexts can affect the overall system behaviour over time. The inconsistency found between the simulation results and expected behaviours from the system can help us identify and correct misperceptions of the underlying mechanisms.

Another challenge often faced by public health researchers is prioritizing research and data collections. One important note is that system methods do not depend on the completeness of data. The calibration process can systemically estimate some missing data input. This being said, a sufficient amount of data input is still required to start meaningful calibration. Examining sensitivity of the model results and interpreting trade-offs to various pieces of data can help researchers identify which missing data would contribute the most value to our decision making

and understanding of future system evolution. Based on that, we can decide which missing data are most needed for our research.

In addition to the benefits being mentioned above, system methods are used for understanding future system evolution, either with a default “status quo” or in response to possible interventions.

Finally, simulations of the dynamic model can also help policy makers to select and evaluate policies. Consequences of varying scenarios can be observed through the simulation of the model, and they can be used to answer the what-if questions that cannot normally be tried out in reality due to ethical and resource constraints. Also, finding the drivers for trends observed in the simulations can be used to identify the leverage points in the system and formulate cost effective policies. As shown above, by using dynamic model simulations, the formulation and emulations of the cost effective and robust policies can be done transparently.

As one type of dynamic modeling, agent based modeling (ABM) offers all of the advantages noted above. Nevertheless, ABM also has a different focus, which makes it better to address certain type of public health problem. It can capture the interactions between individuals within the populations at a greater level of detail, so it is a better candidate for doing social network analysis than other types of dynamic models. It can also record all the historical events for individuals in a population, which allows comparisons of statistics on such histories and on real world individual data. In addition, ABM is designed to preserve the heterogeneity among individuals. It can capture transition probabilities that vary with the length of time spent in a state.

Compared with Markov models which are frequently applied for making projections, ABM models have several distinct features. First of all, ABM can easily retain a memory of past

states an agent has transitioned as well as the length of time it spent in those states. Unlike Markov models where the decisions are made only based on the last state, simulated interventions in ABM can be made contingent upon the history information, and this information can be compared with empirical data. Secondly, ABM can easily capture the heterogeneities within the modelled population. Population characteristics like age, sex, and ethnicity can be captured as parameters in ABM, where in a Markov model those would require multiple copies of similar states, with each copy of a given state being specific to a particular subgroup of the population. A heterogeneous characteristic like age can have continuous value in ABM, but not in a Markov model. Another distinct feature is that a traditional Markov model usually follows a cohort without having birth or immigration into the model, whereas ABM can simulate new person flowing into the model by adding members into the agent population. Moreover, probabilities defined for a particular transition can vary with time in an ABM (for instance, the rate for getting infected can vary depending on the counts of infected neighbours for an agent at any given time), where in a traditional Markov model transitions are fixed throughout the simulation. In addition to those features noted above, ABM is a better candidate when a projection is involved with interactions among diverse populations or spatial or geographical planning.

For my thesis project, an ABM will be used to project the DM-ESRD cost in Saskatchewan from the year 2011 to 2025. We chose an ABM because we might extend the model to capture more additional attributes -- especially continuous ones like body mass index (BMI) -- and possibly add connections between individuals (e.g. capturing influences of parents on children via imitative behavior, or via intra-uterine exposure to high blood sugar) in the future.

Since ABM is better for keeping the heterogeneity for individuals, detailed interactions between individuals, history dependent processes, we made it our choice for this thesis project.

CHAPTER 2

LITERATURE REVIEW

In this chapter, a literature search was performed to find other research work on the projections of prevalence, incidence and cost for diabetic-ESRD. I used sets of keywords like “projections diabetes complications prevalence”, “projection end stage renal disease prevalence”, “projections diabetes cost”, and “projections end stage renal disease cost” to search for publications in PubMed online database. Four studies from the returned search results were selected because they were conducted more recently and the methodologies applied were popular in producing similar projections. Those papers are chosen for review because they are either done in Canada or U.S, which share close geographical location and similar health care settings with our research. In addition, the two papers from the U.S are included in our literature review because their model incorporated more risk factors for diabetes, and produced projections for finer population subgroups.

2.1 Research Focusing on the Prevalence and Cost of Diabetes and Diabetes ESRD

Ohinmaa et al. [Error! Reference source not found.]. In 2004 Ohinmaa A et al. projected that the number of diabetes patients in Canada would increase from 1.4 million in 2000 to 2.4 million in 2016, and the direct health care cost for diabetes and its complications would increase from \$4.66 billion Canadian dollars in 2000 to \$8.14 billion Canadian dollars in 2016. The projection of yearly diabetes prevalence was performed by applying the population projection by Statistics Canada to the projections of diabetes prevalence, incidence and mortality rates from a simulation model by Blanchard in Manitoba [20]. The total diabetes related health cost each year was calculated by applying the direct health care cost per capita to the projected number of diabetes patients in that year. The direct health care cost for diabetes and its

complications came from a previous study conducted by the author using the Saskatchewan Administrative databases. The projected prevalence and health care cost for diabetes and its complications covered the period from 2000 to 2016. The projections were for subpopulation groups which are broken down by age groups and gender. One major limitation noted by the authors was that the current projection did not separate Aboriginal people from the general population. This is important since it was shown in other studies that Aboriginal people have higher diabetes prevalence and costs than the general population, as well as higher rates of population growth.

Schaubel et al. [10]. In 1999 the authors projected that the number of End Stage Renal Disease patients will increase from 17,807 at the end of 1996 to 32,952 at the end of 2005 basing on Canadian Organ Replacement Register (CORR) data from 1981 and 1996,. The annual increase in the prevalence of each ESRD treatment were as follows: 6.0% for PD, 5.9% for HD, and 5.7% for functioning kidney transplants. The projection of ESRD prevalence was conducted for each province in Canada. The patients were broken down into three age groups (≤ 44 years, 45-64 years, ≥ 65 years), and by province and diabetes status. The incident rates by province, age groups and diabetes status were projected from 1997 to 2005 using a Poisson regression model. A special Markov model was then used to project the number of patients on different ESRD treatments through the projection periods. The projection showed that the ESRD incident rates were increased more in diabetes patients than those without diabetes. However, the cause of such increase could not be clearly pinpointed to either a sole increase in ESRD incidence rates or to a simultaneous increase in the prevalence of diabetes and incident rates in ESRD.

Gilbertson et al. [11]. In their study published in 2005, Gilbertson and et al used a Markov model to predict ESRD prevalence, ESRD incidence and mortality from 1978 to 2015 in

United States. The model consists of four major states: ESRD incidence with Diabetes Mellitus (DM), ESRD incidence without DM, ESRD prevalent cases with DM, and ESRD prevalence cases without DM. Each of those states has 21 sub-states: 7 age groups (0 to 18, 19 to 40, 41 to 64, 65 to 69, 70 to 74, 75 to 79 and ≥ 80 years old) x 3 racial groups (white, black and other). The counts of ESRD incident cases from 1978 to 2015 by age, race and DM status were obtained using various data sources and explorations. The actual ESRD prevalence in 1978 from USRD 2002 report was fed into the model. The probabilities of transition to death were calculated for each of the 42 groups (age, race, and DM status) within the prevalence and incidence state from 1978 to 2000, and then extrapolated to 2015. The model predicted that from year 2000 to 2015, ESRD incident cases will increase by 44 % (136,166 incident cases in 2015), and ESRD prevalent cases will increase by 85% (712,290 prevalent cases in 2015). Annual deaths with ESRD will reach 107,760 in 2015. One limitation with the model is that it assumes the death probability is the same for all prevalent ESRD patients despite the different number of years for which they have been under treatments.

Huang et al. [12]. In 2009 the authors used a Markov model to project prevalence and incidence of diabetes (both diagnosed and undiagnosed) and associated spending for caring for diabetes and its complications from 2009 to 2034 in U.S. The model accounted for important diabetes risk factor like BMI changes over the projection years in addition to other factors like gender, ethnicities, and age (from 24 to 85 years). The cohort in the model consisted of the prevalence cohort and the incidence cohort. The prevalence cohort were people with diabetes in 2008 in the U.S. The incidence cohort were the newly diagnosed cases for every year after 2008. A Markov model was developed to estimate the incidence of diabetes. For diabetes incidence, the BMI will change with age, which will then affect people's transitions into diabetes. The

model considered both diagnosed and undiagnosed diabetes cases as well as the transitions between them. The model also kept track of the duration of diabetes, which is important for complications development and therefore calculating cost for complications. In the lifetime simulation model of diabetes complications within the study, it accounted for the effect of using medications to manage different complications. The result of running the model showed that the BMI distributions in population without diabetes will remain relatively stable in the next 25 years. Between 2009 and 2034, the prevalent cases of diabetes will increase from 23.7 million to 44.1 million, and the related spending will rise from \$113 billion per year to \$336 billion per year. The model also reported prevalence and spending for people who are eligible for receiving Medicare over the projection period.

2.2 Research Focusing on the Cost of ESRD Treatments in Canada

To obtain cost information regarding ESRD treatments in Canada, I surveyed the Canadian medical literature by searching the PubMed online database using two sets of keywords, “cost, ESRD, Canada” and “cost, diabetes, complications, Canada”. I selected five relevant papers from the search results. The cost of ESRD treatments in Canada will be used in my simulation model to project the cost of treating DM-ESRD patients in Saskatchewan during the projection period.

Zelmer et al. [13]. In their study published in 2007, Zelmer et al. estimated the economic burden of ESRD in Canada would be \$1.9 billion in year 2000. All the costs came from three categories: direct cost (\$1,273 million, 69%), mortality cost (\$434 million, 23%) and morbidity cost (\$149 million, 8%). Based on the information collected from other research studies and Ontario health administrative systems, the direct health care cost per capita per year was summarized for each renal replacement therapy: center HD was \$66,259, self/home HD was

\$50,982, PD was \$45,400, the first transplant year cost was \$96,040, and the functioning transplant care cost was \$31,222. For living kidney transplant procedure, it cost \$5,890 to care for the kidney donor. For cadaveric kidney transplantation, it cost \$5,850 to retrieve a kidney. The number of patients who had undergone different treatments was obtained from CORR, which is listed under column “n” in Table 2-1. Using the number of patients treated with each renal replacement therapy and the cost per capita information, the total of direct health care cost was \$1273 million in 2000.

Table 2-1. Direct health-Care cost of end stage renal disease in Canada in 2000. Image of table was taken from [13]

Category	<i>n</i>	Inflation-adjusted cost per capita in 2000	Baseline estimate
<i>Direct health-care costs</i>			
Living kidney donors ^a	389	\$5890	\$2 million
Cadaveric kidney retrieval (donors)	470	\$5850	\$3 million
Transplant care (year of transplant)	1105	\$96 040	\$106 million
Functioning transplant care (later years)	9249	\$31 222	\$289 million
Center hemodialysis	9752	\$66 259	\$646 million
Self/home hemodialysis	1568	\$50 982	\$80 million
Peritoneal dialysis	3247	\$45 400	\$147 million
Total direct costs			\$1273 million

^aIncludes health-care costs for care of living donors only. Costs of transplantation and aftercare for recipients are included in the relevant entries.

In addition to reporting the direct cost, the indirect cost was also estimated for mortality and morbidity, which accounts for up to 31% of the total economic burden. The mortality cost was based on the loss of productivity due to premature death, which counts both paid work and unpaid work (e.g. housekeeping). A sex and age specific profile was drawn on to obtain data on average income, workforce participation, unpaid work and life expectancy. For a patient who died in 2000, the mortality cost was the sum of the value of lost production from mid year 2000, and all the subsequent years until reaching the end of life expectancy year for the general population without ESRD.

The cost of living with morbidity and loss of productivity due to receiving RRT were also estimated using a human capital approach. The author assigned a different disability weight for patients with functional transplant, transplant recipients who recently received transplant surgery, and dialysis patients. Among them, some of the dialysis patients experienced a more severe and long-term impact of their illness than patients in the other two groups.

Simpson et al. [14]. In 2003 the authors published the results from their study on the cost of diabetes and its complications. Based on data extracted from the Saskatchewan Health administrative database on prescription drugs, hospital records, and physician services, a total of \$134.3 million was spent on caring for 38,124 (3.6% of the provincial population) diabetes patients in the province in 1996. The total expenditures were broken down into different resource categories and co-morbidities in Table 2-2. It also listed per capita cost for general population and Registered Indians separately. It did not include the prescription drug cost for Registered Indians because of the lack of data availability. The average yearly expenditure for caring for a diabetes patient excluding prescription drug costs is \$2,768. As reported in the study, many diabetes patients have one or more comorbidities: 46.6% of the patients had a cardiovascular-related history, 19.8% of them had an ophthalmic-related history and 6.6% had a renal-related history. The cost for caring for these three major comorbidities added up to 36.4% of the total expenditures (26.4% for cardiovascular related; 7.5% for renal related; 2.5% for ophthalmic related). The study found differences in patient characteristics between Registered Indian and the general population. Registered Indian diabetes patients were younger, and there were more females having diabetes. Also, Registered Indians were more likely to develop renal complications (11.7% v. 6.0%), but those in the general population had more cardiovascular and ophthalmic comorbidities (cardiovascular, 35.1% v. 47.9%; ophthalmic, 12.0% v. 20.0%). In

terms of expenditures, before the age of 60, the median expenditures were similar for general population and Registered Indians; however, after the age of 60, the median expenditure increased more rapidly for Registered Indians than the general population. Also, it cost more to care for Registered Indian diabetes patients with cardiovascular and renal complications than their general population counterparts. Using a multivariate regression model, Simpson et al. showed the relationship between major co-morbidities with health care expenditures in Table 2-2 from their paper. The results showed that the expenditures go up as the patient has more comorbidities. The study also found that sex, age and Registered Indian status each had their own important impact on the cost.

Table 2-2. Health care expenditures among Saskatchewan residents with diabetes mellitus in 1996. Image of table was taken from [14]

Resource category* and comorbidity	Expenditure, \$				
	Subtotal (and %)	General population		Registered Indians	
		Group total	Per-person mean (and SD)	Group total	Per-person mean (and SD)
Hospitalizations					
All	73 817 661 (54.9)	65 075 649	1889 (7243)	8 742 012	2376 (9439)
Cardiovascular		19 184 779	557 (3744)	2 174 460	591 (7567)
Renal		2 151 601	62 (1316)	602 832	164 (1454)
Ophthalmic		276 806	8 (172)	72 939	20 (390)
Physician services					
All	22 525 542 (16.8)	20 080 639	583 (847)	2 444 903	664 (1001)
Cardiovascular		3 707 246	108 (355)	255 484	69 (278)
Renal		645 221	19 (268)	229 686	62 (510)
Ophthalmic		1 527 859	44 (160)	111 052	30 (143)
Day surgery					
All	3 546 893 (2.6)	3 299 287	96 (311)	247 606	67 (236)
Cardiovascular		251 435	7 (72)	14 678	4 (50)
Renal		55 520	2 (35)	13 401	4 (55)
Ophthalmic		939 372	27 (151)	61 263	17 (117)
Dialysis	5 653 049 (4.2)	3 949 277	115 (2179)	1 703 772	463 (4149)
Prescription drugs					
All	28 811 212 (21.5)	28 811 212	836 (1078)		
Cardiovascular		9 885 642	287 (458)		
Renal		715 379	21 (376)		
Ophthalmic		349 466	10 (60)		

*Prescription drug expenditures were not available for the registered Indian group.

Lee et al. [15]. Based on the data collected from a Calgary dialysis clinic, Lee et al. reported the annual direct health care cost for patients on different dialysis modalities in year 2000 U.S. dollars. The results were listed in Table 2-3: in-center HD \$51,252, satellite HD

\$42,057, home/self-care HD \$29,961, and PD \$26,959. The study, published in the year 2002, also applied a multiple linear regression model to uncover the predictors of cost. Comorbidities of patients in this study were measured using the Charlson comorbidity score, which predicted the cumulative increased likelihood of death based on the number and severities of the comorbidities [30]. Higher Charlson comorbidity score predicts higher mortality. In the study by Lee et al, among all predictors (age, sex, need for assisted living, work status, education, Charlson comorbidity score, and dialysis modality), the Charlson comorbidity score and dialysis modalities were the two variables independently associated with the total cost. Each increase in Charlson score by 1 will bring an additional \$2,234 in direct health care cost. For ESRD patients with diabetes, their direct health cost per year is \$8,016 more than those ESRD patients without diabetes. Interestingly, other patient characteristics like age, sex, work status and education status are not the predictors of the direct health care cost. The study showed that the cost discrepancy between in center dialysis and home/self care dialysis persisted even after removing the comorbidity variable. The difference in cost between the above two modalities mostly arose from the differences in the level of nursing care required. Based on cost findings in the study, the authors strongly promoted higher ratio of self-care/home HD and PD as treatment options to allow more resources to be released for treating awaiting patients.

Table 2-3. Annual Health Care Related Costs Per Patient by Modality. Image of table was taken from [13]

Cost Category	Hemodialysis			
	In-Center (n = 88)	Satellite (n = 31)	Home/Self-Care (n = 9)	Peritoneal Dialysis (CAPD and CCPD) (n = 38)
Outpatient dialysis costs* (\$)	26,692 (26,627, 26,282-26,982)	24,113 (23,549, 23,326-23,947)	14,282 (14,317, 13,018-15,472)	12,494 (12,082, 11,406-13,210)
Inpatient costs*† (\$)	6,148 (0, 0-6,891)	1,792 (0, 0-2,149)	2,163 (0, 0-0)	3,870 (0, 0-3,381)
Outpatient nondialysis costs (\$)				
Clinic visits*	43 (35, 25-61)	34 (32, 16-64)	41 (48, 16-48)	54 (48, 32-64)
Emergency room*	205 (70, 0-348)	157 (97, 0-252)	216 (0, 0-97)	352 (103, 0-341)
Day surgery*	236 (0, 0-0)	277 (0, 0-0)	197 (0, 0-422)	44 (0, 0-0)
Laboratory costs*	653 (524, 370-852)	332 (257, 190-391)	305 (288, 254-427)	439 (295, 208-616)
Diagnostic imaging*	1,703 (597, 99-2,168)	1,218 (519, 97-2,060)	1,701 (421, 200-2,626)	756 (97, 0-648)
Erythropoietin*‡	5,355 (4,037, 2,450-7,351)	4,310 (2,450, 0-7,351)	5,039 (4,901, 2,450-6,749)	4,054 (3,880, 1,125-7,351)
Venofer*	381 (615, 0-615)	446 (615, 0-615)	404 (556, 308-615)	110 (0, 0-278)
Medications*§	2,932 (2,612, 1,758-3,743)	2,616 (2,452, 1,859-3,386)	2,737 (2,482, 1,750-2,553)	2,941 (2,788, 1,460-3,618)
Total outpatient costs	11,418 (10,025-12,811)	9,391 (7,540-11,242)	10,639 (5,104-16,175)	8,780 (7,278-10,283)
Physician billing*	6,995 (6,283, 6,283-7,412)	6,761 (6,283, 6,283-6,722)	2,877 (2,877, 2,877-2,877)	1,899 (1,550, 1,550-2,568)
Total expenses	51,252 (47,680-54,824)	42,057 (39,523-44,592)	29,961 (21,252-38,670)	26,959¶ (23,500-30,416)

NOTE. Values expressed as mean (median, 25th to 75th percentile) unless noted otherwise.

*Reported as median with 25th to 75th percentile because distribution not normal.

†Including nursing, medications, laboratory tests, diagnostic imaging, support staff, surgery, and supplies.

‡Locally, erythropoietin is administered only through the subcutaneous route.

§Excluding erythropoietin and Venofer.

||Values expressed as mean (95% CI).

¶P < 0.001 comparing the four modalities using one-way ANOVA.

Pohar et al. [16]. In 2007, Pohar et al. compared the per capita health care utilization and expenditures among four subgroups according to diabetes and Registered Indian status using Saskatchewan Health databases. The total health care cost came from four health care services: physician visits, hospitalizations, day surgeries, and dialysis. People with diabetes used more services in all four categories, resulting in more than two times higher cost than people without the disease. With the sole exception of day surgery, Registered Indian people with and without diabetes had much higher utilization in all other three health care services and incurred 40% to 60% higher overall health care expenditures compared to their general population counterparts. The Registered Indian diabetes cohort had two distinct characteristics in terms of age and sex. First, they were about 13 years younger than the general population cohort. Second, there were more diabetes cases among registered Indian females than males (57.7% of the cohort are female); whereas diabetes cases were predominantly males within the general population subgroup (46.8% of the total general population diabetes case were females). Diabetes status increased the chance of using all four health care services, and it was especially prominent in HD.

The odds of receiving HD was 8.6 times higher for diabetics in the general population, and 14.2 times higher for registered Indian diabetics when compared with their controls without the disease. People with diabetes also had 5 to 6 times more physician visits, twice as many hospitalization and 40 - 50% more day surgeries. As a consequence of the heavy usage in all four health care services, diabetes patients had more than two times higher per capita health care expenditures than their controls.

Barnieh et al. [34]. O'Brien et al. compared the direct health care costs for living donor kidney transplants with the cost for deceased donor transplants. From the database for the Southern Alberta Transplant Program, a total of 357 patients who received first time kidney-only transplants (at the age of 18 and older) between April 1st, 1998 and March 31, 2006 were identified. Among them, 130 received living donor transplant, and the remaining 227 patients received deceased donor transplants. The cost included both costs for recipient and donor. The direct health care cost for the recipients included the following items: outpatient care, inpatient care, transplant surgery, physician services, imaging and tests, and medications post-transplant (i.e. immunosuppressant and anti-infective medications). On the donor side, the cost accounted for were surgery cost, physician fees, and inpatient and outpatient costs (only accounted for living donors). As shown in Table 6, the cost for the recipient was categorized and summarized into five time periods based on time of occurrence: pre-transplant work up, transplantation, post-transplant to 90 days, 91 days to 365 days and 366 days to 730 days. In addition to direct costs, the living donor transplant recipients waited a shorter time to be transplanted than the deceased donor transplant: living donor recipient spent 1.2 years on dialysis whereas the deceased donor transplant recipients spent 3.2 years on dialysis prior to being transplanted. Removing the time spent during transplant work up, living donor transplant recipients spent less a year on the

waiting list compared with 2.5 years of waiting on the waiting list for deceased donor transplant recipients.

Table 2-4. Cost for Transplants categorized by donor type and time period. Image of table was taken from [34]

	Recipients of living donor kidney	Recipients of deceased donor kidney
Donors		
Pretransplant workup for all living donors	2261	209
Mean (95% CI)	(2096–2425)	(122–296)
Donor graft removal+	18 129	36989
Mean (95% CI)	(16 845–19 414)	(34 421–39 558)
Donor follow-up to 90 days	598	N/A
Mean (95% CI)	(322–873)	
Recipient		
Pretransplant workup	2370	2917
Mean (95% CI)	(2139–2600)	(2657–3178)
Transplantation	20 108	23 818
Mean (95% CI)	(18 108–22 108)	(20 666–26 971)
Posttransplant to 90 days	31 618	28 200
Mean (95% CI)	(27 078–36 157)	(25 582–30 818)
91–365 days	21 932	25 903
Mean (95% CI)	(19 178–24 686)	(23 387–28 420)
366–730 days	19 974	22 233
Mean (95% CI)	(17 880–22 067)	(20 128–24 338)
Total	118 347	121 121*
Mean (95% CI)	(110 395–126 299)	(114 287–127 956)

*+ Refers to deceased donors, this includes the intensive care unit stay and was subsequently divided in two if the donor gave two kidneys when determining the total cost.

*p = 0.7107.

O'Brien et al. [17]. In 2003, using information drawn primarily from Canadian sources, O'Brien et al estimated the cost for managing each complication of diabetes by applying the unit cost to a typical patient profile of that complication. The cost for a complication was organized into event cost (the cost for the episode and the subsequent care in the year following the event) and state cost (the yearly cost for continually managing the condition). For kidney complications, the event cost and state cost for microalbuminuria were \$62 and \$10; for gross proteinuria, they were \$54 and \$18. The cost for managing microalbuminuria and gross proteinuria included only laboratory tests and physician visits. Drug cost was excluded from the total cost, even though drugs such as ACE inhibitors were considered to bring benefits to certain patients. For ESRD, the state cost was \$63,045, which was derived from the distributions of the patients receiving the different modalities of ESRD treatments (HD, PD and renal transplantation). The related cost

information for all ESRD treatments were collected from literatures and updated to year 2000 values.

CHAPTER 3

MODEL POPULATION

This chapter describes the cohort in the model. There are three sections in this chapter, and each section focuses on one sub group of the cohort. The cohort (model population) includes all diabetes patients in Saskatchewan -- historic and projected -- between year 1980 and 2025. The whole cohort was categorized into three groups: “Saskatchewan DM prevalent patients in 1980”, “Saskatchewan DM-ESRD prevalent patients in 1980”, and “the DM incident patients between year 1980 and 2025”.

As model start on Jan 1st, 1980, previously diagnosed prevalent diabetes patients were added to the model as the starting population. Those people received a diabetes diagnosis prior to Jan 1, 1980 and were alive on that date. Among them, some had already developed ESRD and were receiving ESRD treatments (referred as “DM-ESRD Prevalent cases in 1980”); others had been living with diabetes but without ESRD (referred as “DM Prevalent Cases in 1980”).

In addition to the prevalent diabetes patients on Jan 1st, 1980, each year there were new patients in Saskatchewan who were diagnosed with diabetes and added to our model population. The new diabetes cases between 1980 and 2005 (inclusive) were obtained from the Saskatchewan Health Databases (referred to as “Diabetes Incident Patients between 1980 to 2005”). Yet the new diabetes cases from 2006 to 2025 (inclusive) were estimated based on scaled-up output from the previously constructed Saskatoon Diabetes Model (referred as “Diabetes Incident Patients from year 2006 to 2025”).

Each of these three groups of patients will be discussed in detail in the sections below regarding the information sources used to create them, their life cycle in the model, and the assumptions we made regarding them.

3.1 The Saskatchewan DM-ESRD Prevalent Patients in 1980

To start the model simulation on Jan 1st, 1980, the DM-ESRD prevalent cases at that time are required for initializing the model population. The DM-ESRD prevalent cases at the model start time include those who had diabetes and had developed ESRD prior to Jan 1st, 1980 in Saskatchewan. We gathered the DM-ESRD prevalent cases as of Jan 1st, 1980 from the Saskatchewan DM population between 1970 and 2005 retrieved from the Saskatchewan Ministry of Health databases. Table 3-1 shows the sample data format of the DM-ESRD prevalent cases at Jan 1st, 1980.

Table 3-1. Data Format of DM-ESRD Prevalent Cases as of Jan1st, 1980

Ethnicity (FN=1, OSK=0)	Gender (Male=0, Female=1)	Age of Receiving Diabetes Diagnosis	Year of Receiving Diabetes Diagnosis	Year of Receiving ESRD Diagnosis	Year of Death
0	0	44	1978	1978	1981
0	0	55	1974	1979	1981

There were a total of twelve DM-ESRD prevalent cases as of Jan 1st, 1980 and the database provided the specified year of death, as well as characteristics like ethnicity, gender and age of receiving diabetes diagnosis. Treatment information for those patients were not available to us, but is required for assigning each patient to an ESRD modality at model start time. We decided to estimate the ESRD modality for those patients by using the treatment data from 1985 to 1989 which was the closest empirical treatment data in time available to us. We first

calculated the distribution of DM-ESRD patients on different ESRD treatments (HD, PD, and Transplant) for each year between 1985 and 1989 [38]. Then an average from the distributions in those five years was obtained. Later, the averaged distribution was used in the model for assigning an ESRD treatment to each DM-ESRD prevalent patient at the model start time (as in model event “add1980ESRDPrevalentCase” in the Main Class). In the Person Class, the 1980 DM-ESRD prevalent patient entered their assigned treatment modality states immediately after they were created by following either transition “prevalent1980_Dialysis” or “prevalent1980_Tx”.

Also, according to death information in the historical data, most of the twelve DM-ESRD patients died within one or two years of 1980. Since most of those patients only survived a short period of time after the model start date, their health was unlikely to be sufficiently robust to be considered for treatment, and we decided to simplify their activities in the model by not allowing those on dialysis treatments to go through the transplant assessment process or receive a transplant. As shown in the statechart “assessmentStages” of Figure 3-1, the 1980 DM-ESRD prevalent patients were placed in a special state named “NoAssessment” that side-steps the assessment process. Moreover, while the timing (including year) of death is normally determined dynamically within the model, the timing of deaths for 1980 DM-ESRD prevalent patients are determined by the death year recorded in the historical data rather than via a mortality risk calculated daily in the model. This choice is partly motivated by the fact that the mortality risk calculated in the model for a patient normally requires as an input the duration that the patient has been receiving the treatment. For those prevalent ESRD cases at the time of model start, we would have to derive an estimate of this quantity because of the absence of historical data to directly inform it. Thus we chose to use the death year to determine when the

patient will die. Since the specific date of the death is not given in the historical data, a date within the death year is selected by the model from a uniform distribution spanning the entire year. Because it leverages more accurate information when it is available (rather than imposing questionable assumptions applicable only to this subset of participants), this mechanism reduces the risk to calibration discrepancies that could be caused by less grounded assumptions.

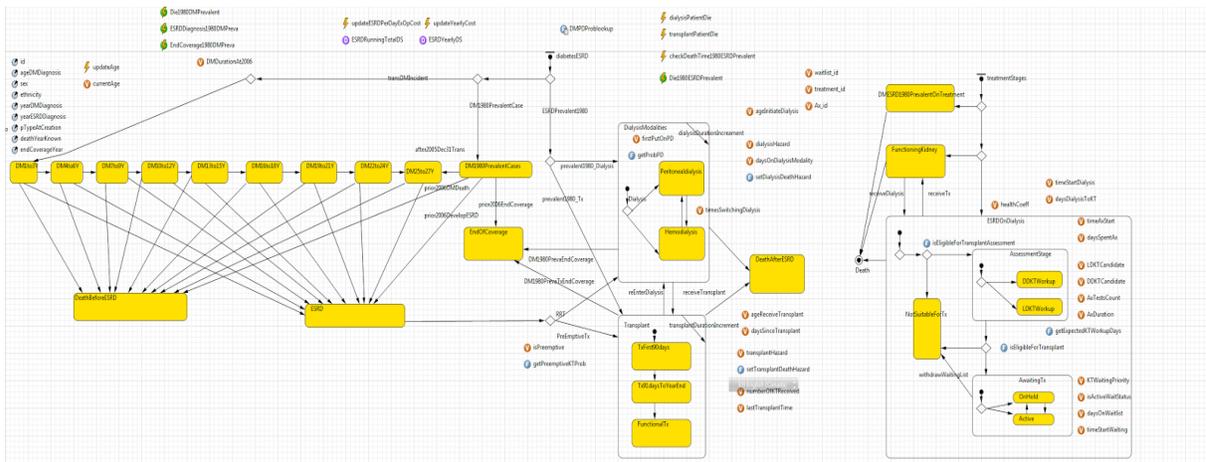


Figure 3-1. Statechart of the Person Object in Saskatchewan DM-ESRD Model

3.2 The Saskatchewan DM Prevalent Patients in 1980

Along with the twelve DM-ESRD prevalent patients discussed in the above section, a total of 14,151 DM prevalent patients form the starting population for the model. The Saskatchewan DM prevalent patients are patients who had received DM diagnosis but not ESRD diagnosis as of Jan 1st, 1980. Those patients were followed until the end of 2005, and information from the Saskatchewan Administrative database was used for an epidemiology study conducted by the thesis author and other researchers. As shown in Table 3-2, information available on the DM prevalent cases included year of birth, ethnicity, gender, year of receiving diabetes diagnosis, year of receiving ESRD diagnosis, age of receiving diabetes diagnosis, year

of exiting the study, reason for exiting the study (death/end of coverage/end of study) and age when exiting the study. This information was used in the model for initialization of the patient’s characteristics, and determination of the occurrence of important events such as receiving ESRD diagnosis and treatment, termination of coverage and death.

Table 3-2. Sample Data for the 1980 Prevalent Patients

Ethnicity	Gender	DM Diagnosis Year	ESRD Diagnosis Year	Exit Reason	Exit Year	Age at Exit	Age at DM Diagnosis
0	1	1975	1986	1	1988	39	26
0	1	1979		1	1994	93	78
0	1	1979		0	2005	58	32
0	1	1979		2	1980	29	28
0	1	1971		1	1980	95	86

3.2.1 The 1980 DM Prevalent Patients in the Diabetes States

At the model start time of Jan 1, 1980, all DM prevalent patients begin their life in the model in the “HavingDM_1980Prevalent” state, which is a special state designed for holding the DM prevalent cases of 1980 between Jan 1st, 1980 and Dec 31st, 2005. While in the “HavingDM_1980Prevalent” state, the diabetes prevalent patient could either die without ESRD (moving to the “DeathBeforeESRD” state), receive ESRD diagnosis (moving to the “ESRD” state), or patients could end their health coverage in Saskatchewan (moving from “HavingDM_1980Prevalent” to “EndOfCoverage” state). For this special class of population (those patients who were recorded as having diabetes as of the model start), these movements are dictated by the patient’s administrative data (See Table 3-2). If a patient hadn’t died or developed ESRD by the end of year 2005, the person will still stay in the

“HavingDM_1980Prevalent” state. As soon as the model clock strikes Jan 1st, 2006, the patient will move from “HavingDM_1980Prevalent” state to “DM25to27YBeyond” state because the patient will have already spent at least 25 years in the model (i.e. 1980 to 2005). Once in the “DM25to27YBeyond” state, the determination of death before ESRD and development of ESRD are no longer based on patients’ historical records; rather those are based on risks associated with the number of years of having diabetes. The “DM25to27YBeyond” is the most advanced DM state in the model. There is no other state defined for diabetes patients who have had diabetes more than 27 years. Even if a patient ended up having diabetes for 40 years, that patient will remain in the “DM25to27YBeyond” state until he either dies or develops ESRD. This also means that the risk for death before ESRD and developing ESRD will remain unchanged for the 1980 DM prevalent patients after Dec 31, 2005 up until the time they leave “DM25to27YBeyond”. As was the case in the last section, the mechanisms used here are motivated by the desire to avoid important calibration findings (which focus on mechanisms applicable for patients looking forward in time) being thrown off by the vagaries of assumptions (far less central to model operation) concerning this initial group of patients.

3.2.2 The Year 1980 DM Prevalent Patients in the ESRD States and Transplant Assessment State

Once patients receive ESRD diagnosis, they begin ESRD treatment right away. In the model, the person will flow from “ESRD” state to “DialysisModalities” State. Based on the year, the chance of starting with either PD or HD is different as found in the historical data (reference to data source), which is used for selecting the initial dialysis treatment for a patient. People can also switch between PD and HD based on the probabilities observed in the ESRD treatment data in Saskatchewan from January 2006 to December 2010 (reference to the “switch modality

calculation”). For example, a patient can start in “Peritonealdialysis” state, later move to the “Hemodialysis” state, and move back to “Peritonealdialysis” state.

When the patient is not yet diagnosed with ESRD, they have functioning kidneys, which is represented by the “FunctionalKidney” state in the “AssessmentStages” state chart. As soon as patients start on dialysis, they move from “FunctionalKidney” state to the “AssessmentAndWaiting” state. If patients successfully pass the transplant assessments, they will be put on the waiting list for a transplant. The corresponding state is the “AwaitingTx” state. When a patient gets transplanted, they will move to the “Transplant” state in the “diabetesESRD” statechart. Simultaneously, the patient will also move to the “Functional Transplant” state in the “AssessmentStages” statechart.

The death for patients who were among the initial diabetic population receiving ESRD treatments was determined differently over time. If the model time is prior to Jan 1st, 2006, the death of the patient occurs at a time point drawn from a uniform distribution spanning the death year recorded in the historical data. If it is Jan 1st, 2006 or after, the death will depend on the mortality risks dependent upon a patient’s characteristics, type of treatment and duration of treatments.

In theory, those patients who developed ESRD can also leave the Saskatchewan Health plan, and transitions should be built for allowing patients to move from ESRD treatments states into the “EndofCoverage” state. However, among the 14,000 DM prevalent patients, there are only three patients who have later developed ESRD and ended their coverage before the end of 2005. This likely reflects the fact that very ill individuals are less likely to undergo the dislocation of a move. Since this is a very small number of patients, we decided not to build the transitions from ESRD treatments to the “EndOfCoverage” state. We instead made the

assumption that those three patients did not leave the plan, and that their death will be determined the same way as others who are also receiving ESRD treatments.

3.3 The DM Incident Patients between Year 1980 and 2025

The DM incident patients enter the model upon receiving DM diagnosis. Between year 1980 and 2005, the DM incident patients are initialized with detailed historical records; whereas between year 2006 and 2025, the DM incident patients were provided by a System Dynamics model. Corresponding to the different sources, DM incident patients are discussed in two subsections: 3.3.1 for DM incident patients from year 1980 to 2005 and 3.3.2 for DM incident patients from year 2006 to 2025. Despite the differences in sources, the state charts and transitions are the same for all DM incident patients as illustrated in section 3.3.3.

3.3.1 DM Incident patients from Year 1980 to 2005

In addition to those who had already received diabetes diagnosis prior to Jan 1st, 1980 in Saskatchewan, each year there were new patients who developed diabetes (received a diabetes diagnosis). Those diabetes incident cases should be added to the model population. From the Saskatchewan Administrative database, the DM incident case count was obtained for each subpopulation group (defined by ethnicity, gender, age at DM diagnosis) in Saskatchewan for each year between 1980 and 2005. As shown in the first row of Table 3-3, in 1980, there were a total of thirty three patients who received a diabetes diagnosis, and they were all in the subpopulation group characterized as “OSK,MALE, and 54 years old at year 1980”. The model uses the dynamic event mechanism to select with uniform probability a specific date and time in year 1980 for each of the thirty three patients to receive their diabetes diagnosis. At that point, the patient will enter the model. The life cycle for the DM incident patients will be explained in the next section (“Life Cycle of Diabetes Incident Patients”).

Table 3-3. Sample data regarding Diabetes Incident Patients from 1980 to 2005.

Ethnicity (OSK=0, FN=1)	Gender (MALE=0, FEMALE=1)	Age at DM Diagnosis	Year Receive DM Diagnosis	Count of People
0	0	54	1980	33
0	0	55	1980	36
0	0	56	1980	33
0	0	57	1980	33
0	0	58	1980	35

3.3.2 DM Incident Patients from Year 2006 to 2025

To use the model for projecting the DM-ESRD situation in Saskatchewan for the years 2006 to 2025, information on the diabetes incident cases for that same projection period are required as an input in the model. Such input data are not readily available. Neither is the historical data from year 2006 to 2013 (the current year) or the future diabetes incident cases from year 2013 and beyond. While searching for those data, the Saskatoon Diabetes Model [36] was found to be a well-fit candidate to provide the input for reasons laid out as follows. First of all, it is a System Dynamics model which can run forward to project the diabetes incident cases covering all the projection years. Secondly, the output from the model includes details regarding ethnicity, gender and age (category) of receiving diabetes diagnosis, which meet our input data requirements. Moreover, the design and implementation of the Saskatoon Diabetes Model was informed by the diabetes epidemiology in the Saskatoon Health Region, which shares significant similarities with the province. Thus, the result from the Saskatoon Diabetes Model can be scaled up to resemble diabetes epidemiology in Saskatchewan. Most importantly, the Saskatoon Diabetes Model allows us to try out upstream policy (e.g. varying assumptions regarding obesity

incidence or diagnosis rates for pre-diabetics) to see how that will impact the ESRD incident rates and associated costs in our model.

The population of the Saskatoon Diabetes Model includes residents of the Saskatoon Health Region. The diabetes incident case counts from the Saskatoon Diabetes Model need to be scaled up to reflect the diabetes situation for the province of Saskatchewan. The Saskatchewan diabetes cases can be estimated by applying a scaling ratio to the diabetes case count for the Saskatoon Health Region. The yearly case count for each sub-population group for Saskatoon is shown below in the last column of Table 3-4.

Table 3-4. Sample Output from the Saskatoon Diabetes Model.

Year	Age Group	Ethnicity(OSK=0, FN=1)	Gender (MALE=0, FEMALE=1)	Case Count
2024	65to69	1	0	2
2024	65to69	1	1	3
2024	65to69	0	0	50
2024	65to69	0	1	52
2024	70to74	1	0	2
2024	70to74	1	1	2
2024	70to74	0	0	39
2024	70to74	0	1	43
2024	75to79	1	0	1
2024	75to79	1	1	1
2024	75to79	0	0	28
2024	75to79	0	1	33
2024	80plus	1	0	1

2024	80plus	1	1	1
2024	80plus	0	0	34
2024	80plus	0	1	55

The scaling ratio is obtained by comparing the diabetes incident case counts from the Saskatoon Diabetes Model with the historical data on diabetic incident cases in Saskatchewan from year 2001 to 2005. To be more specific, for each year between 2001 and 2005, the case count for every sub population group (stratified by gender and ethnicity) were compared, and a scaling ratio was calculated. For instance, for year 2001, the diabetes incident case count for Aboriginal females from the Saskatoon Diabetes Model is 50, and the count from the historical data for Saskatchewan is 298. Thus the scaling ratio for aboriginal female in year 2001 is 5.96 (298 divided by 50). The scaling ratios for each subpopulation group from different years are listed in the below. To consolidate the ratios for those 5 years (2001 to 2005) into one ratio for each sub population group, we used the average of the scaling ratio from year 2001 to 2005. For instance, the scaling ratio for aboriginal female is 6.008 (which is the average of 5.96, 6.22, 6.24, 5.93 and 5.96). The ratio for every sub population group is listed in , in which the ratios are assumed to stay the same for the entire projection period (i.e. 2006 to 2025).

Table 3-5. The Scaling Ratio Calculated by Comparing the Historical Saskatchewan Data with the Output from the Saskatoon Diabetes Model (data were from year 2001 to 2005).

Ethnicity [0=OSK, 1=FN]	Sex [0=Male,1=Female]	Year	SK Vs STooRatio
0	0	2001	5.343529
0	1	2001	5.122857
1	0	2001	5.219512
1	1	2001	5.96

0	0	2002	5.656109
0	1	2002	5.242667
1	0	2002	6.421053
1	1	2002	6.222222
0	0	2003	5.079295
0	1	2003	4.751899
1	0	2003	6.888889
1	1	2003	6.238095
0	0	2004	4.927195
0	1	2004	4.683453
1	0	2004	6.914286
1	1	2004	5.928571
0	0	2005	3.900415
0	1	2005	3.622426
1	0	2005	6.121212
1	1	2005	5.692308

Table 3-6. The Average Scaling Ratio Used in the model for converting Diabetes Incident Case Count for Saskatoon to Saskatchewan.

Sub Population Group	Scaling Ratio
OSK MALE	4.981
OSK FEMALE	4.685
FN MALE	6.313
FN FEMALE	6.008

In addition to scaling up the diabetes case counts for Saskatchewan, the age of receiving a diabetes diagnosis obtained from the Saskatoon Diabetes Model needs further refinement as well.

The Saskatchewan DM-ESRD model requires the case count for a specific age rather than for an age group such as provided by the Saskatoon Diabetes model. Using the total case count for an age group, we can estimate the diabetes case count for a specific age within the group. In order to this, we have made assumptions on how cases would be distributed within its group. For ages younger than 70, we assume the cases are uniformly distributed among the ages within its five year group. For instance, at year 2024, for OSK women whose ages are between 65 and 69, the total number of diabetic incident case count is 52 in Saskatoon. After applying the corresponding scaling ratio 4.685, the count for this sub-population group in Saskatchewan is 244. In the Saskatchewan DM-ESRD model, the total count of 244 diabetes incident cases were uniformly distributed within the age group (i.e. 65, 66, 67, 68 and 69). Each model simulation might have generated different counts for those ages because the model is stochastic. However, over many simulations, the case count for the ages should follow the uniform distribution we have assumed. For the ages older than 70, we also made assumption about how the cases would be distributed among the ages within their age group. Rather than assuming a uniform distribution as with the younger age groups, we assumed that they would follow the distribution existing in the historical data for the projection years. To obtain the distribution from the historical data, we studied the historical diabetes incident cases from 2001 to 2005 for older than 70 years in Saskatchewan. The distribution for those aged 70 and older was then applied to the Saskatchewan DM-ESRD model to generate the case count for each specific age for the four sub-population groups defined by ethnicity and gender. Finally, we obtained the yearly diabetes incident case counts for all subpopulation groups (stratified by diabetes diagnosis age, ethnicity and gender) in Saskatchewan over the projection years. The DM incident patients from 2006 to 2025 would have the same information available to the model as the DM incident patients from

1980 to 2005. Moreover, the life cycle for the DM incident patients are the same in the model regardless which time period and data source they were from. The details about the life cycle of DM incident patients can be found in the earlier section “Life Cycle of Diabetes Patients”.

3.3.3 Life Cycle of Diabetes Incident Patients

Patients will go through both the “DiabetesESRD” statechart (Figure 3-2) and the “AssessmentStages” statechart (Figure 3-3) for their time in the model. Upon entering the model, patients will start their journey in the “DM1to3Y” state of the “DiabetesESRD” statechart, and in the “FunctionalKidney” state of the “AssessmentStages” statechart. In a diabetes state, a patient can either die, receive ESRD diagnosis or live with diabetes beyond three years. If a death occurred before developing ESRD, patients will move from the diabetes state to the “DeathBeforeESRD” state in the “DiabetesESRD” statechart; also, at the same time, they will move from the “FunctionalKidney” state to the “DeathState” in the “AssessmentStages” statechart. If the patient hasn’t died or developed ESRD, they will move to the next Diabetes state after exactly three years of time (e.g. moving from the “DM1to3Y” state to “DM4to6Y” state).

If patients develop ESRD, they will start receiving ESRD treatments. Occasionally, patients can receive a preemptive transplant (transitioning from the “ESRD” state to “Transplant” state). More likely, people will start with either PD (moving from the “ESRD” state to the “Peritonealdialysis” state) or HD (moving from the “ESRD” state to the “Hemodialysis” state). As soon as they start on dialysis, patients will undergo a transplant assessment process, as illustrated in the “AssessmentAndWaiting” state of the “AssessmentStages” statechart. Once approved by assessments, patients will be put on a waiting list for transplant (move from “WorkUpStage” to “AwaitingTx” state of the “AssessmentStages” statechart). When a transplant

has taken place, patient will move from the “DialysisModalities” State (either “Hemodialysis” state or “Peritonealdialysis” state) into the “Transplant” state. Patients will move to the “DeathAfterESRD” state and the “Death” state of the “AssessmentStages” statechart if they die while getting dialysis or after receiving transplant. Upon death, patients complete the last step of their cycle in the model. The life cycle for diabetes incident patients is the same regardless of the time period when they enter the model.

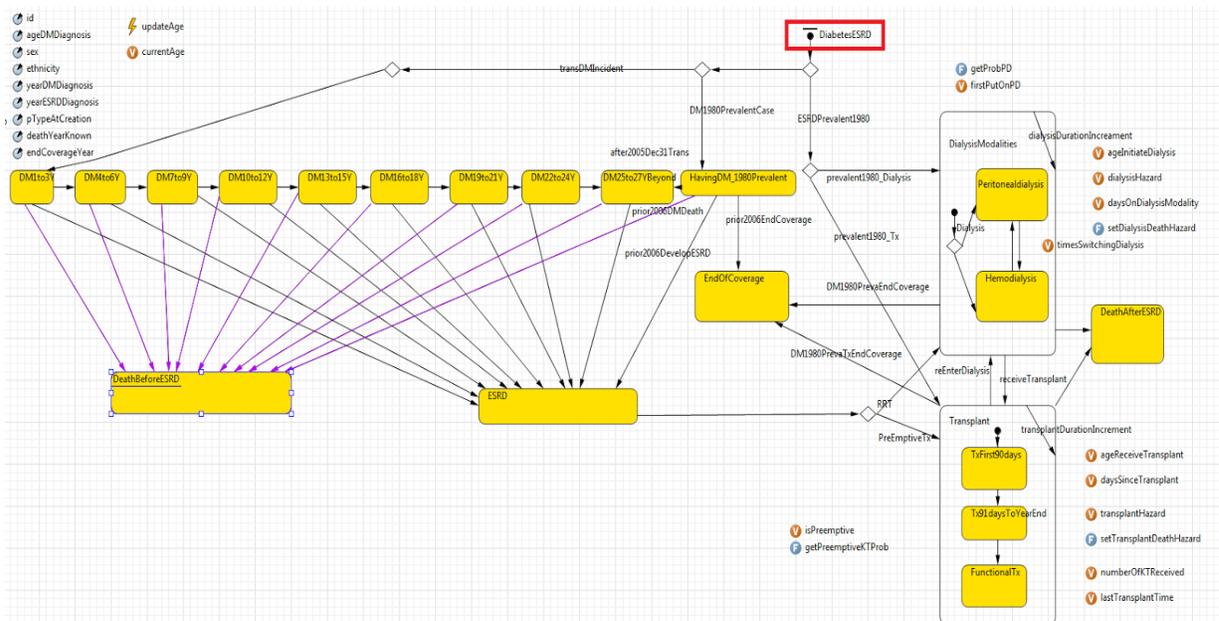


Figure 3-2. The “DiabetesESRD” Statechart of A Person Object

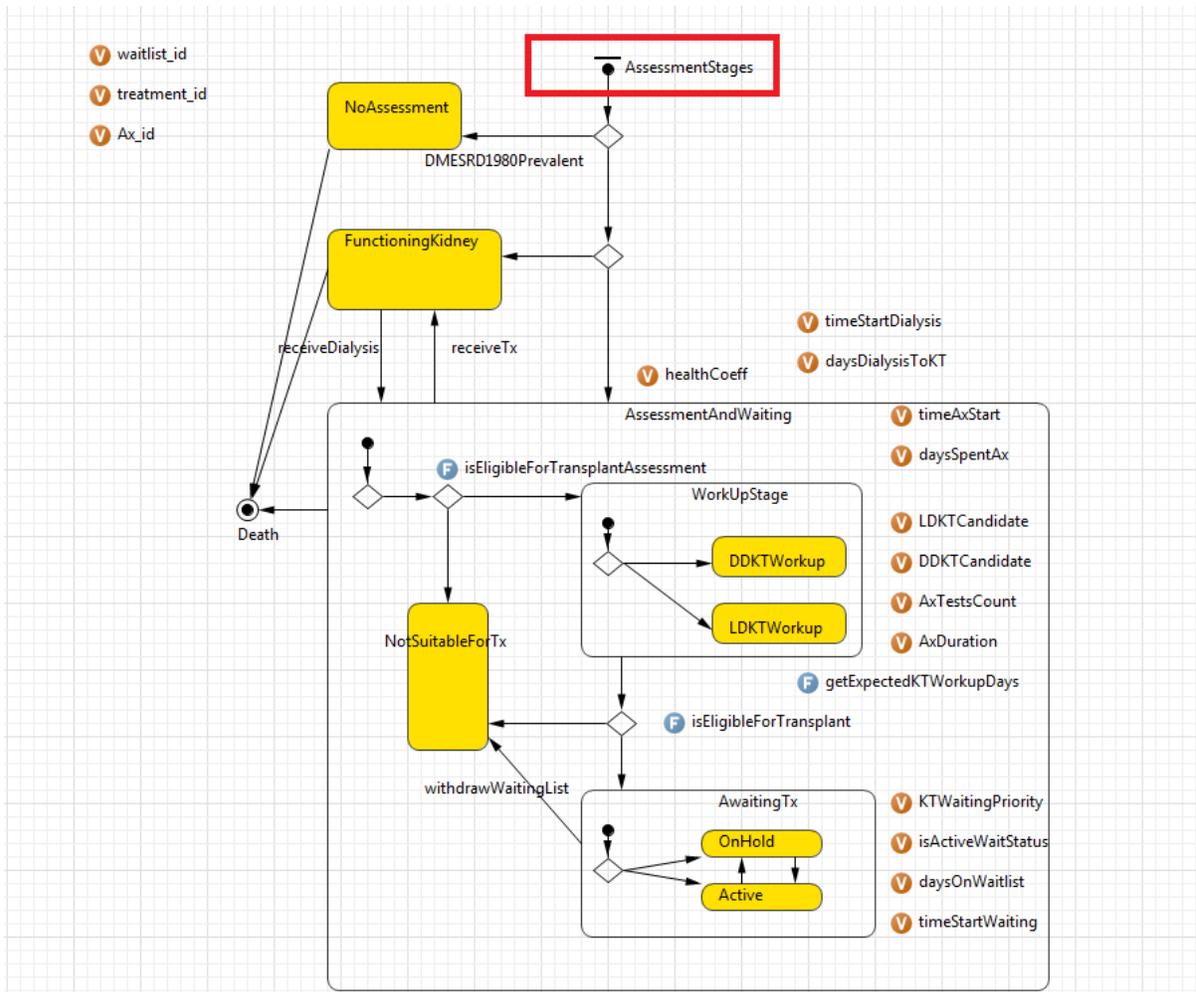


Figure 3-3. The “AssessmentStages” Statechart of A Person Object

DM incident patients from year 2006 to 2025 were projected from the Saskatoon diabetes model [36] and scaled up to reflect the total Saskatchewan population. The life cycle of such patients in the model is the same as for the DM incident patients obtained from the Saskatchewan Administrative database for year 1980 to 2005. The next section will focus on how we estimated the diabetes incident case counts from the Saskatoon Diabetes Model.

CHAPTER 4

MODEL STRUCTURE

This chapter presents the model structures for simulating the important processes in a diabetic patient's life. There are four processes which are of interest in this thesis and are represented in the model: progression of diabetes to develop ESRD, receiving ESRD treatments, assessment for a kidney transplant, and waiting for a transplant on a waiting list after an approved assessment. Figure 4-1 presents the overview of a person statechart in the model, which illustrates the life cycle of a patient in the model. The three blue boxes enclose the state charts and transitions for the four critical processes in a patient's life. The left one corresponds to "DM to ESRD progression". The middle one represents to "ESRD treatment options". The right one is for both "transplant assessment" and "waiting list" process.

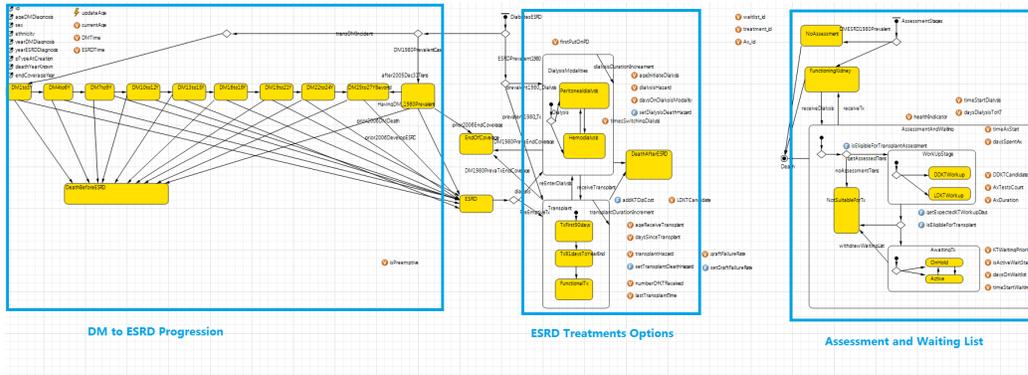


Figure 4-1. Overview of Model Structure

4.1 DM to ESRD progression

The statecharts and transitions used to simulate patient's DM to ESRD progression is discussed in this section. Since the DM incident patients and the DM prevalent patients at 1980

require different model structures, so each group of patients are discussed in a distinct subsection.

4.1.1 DM Incident patients

Diabetes patients start their journey in the model at the time they receive the DM diagnosis. As diabetes progresses, patients either die or develop ESRD as a complication. Only a small portion of DM patients will develop ESRD. The majority will continue living without ESRD or die from causes other than ESRD. In reality, there are DM patients who end their Saskatchewan health coverage because they move out of the province. Correspondingly, at the time of ending their coverage, they have neither died without ESRD nor developed ESRD. There should have been a transition from the DM states to the “End of Coverage” state. However, such transitions are not currently built for DM incident patients, which is one of the limitations of the model. The “End of Coverage” state is only for “the DM prevalent patients at year 1980” as marked in the red box in Figure 4-3. More details regarding the DM prevalent patients at year 1980’s move to the end of coverage state will be discussed in section 4.1.2.

This thesis focused on that subset of DM patients who eventually developed ESRD, and the treatments and services provided to them. Yet the diabetes progression process cannot be left out of this model because it determines a person’s chance of developing ESRD, and represents a key area on which to focus prevention efforts. We adopted the representation of progression of diabetes from another – much smaller – agent based model created as part of student Ying Jiang’s M.Sc. thesis work (conducted under the supervision of Dr. Osgood and Dr. Hyun Lim of the Department of Community Health & Epidemiology). In Ying’s Master’s thesis [37], a competing risks analysis was conducted to quantify the risk of dying (prior to having ESRD) and the risk of developing ESRD at various DM stages. Using the results of the analysis, an agent

based model was built by Ying to simulate the process for diabetics progressing to either ESRD or Death. Figure 4-2 shows the original statechart from Ying’s model. Figure 4-3 shows the adopted form of the statechart in our model.

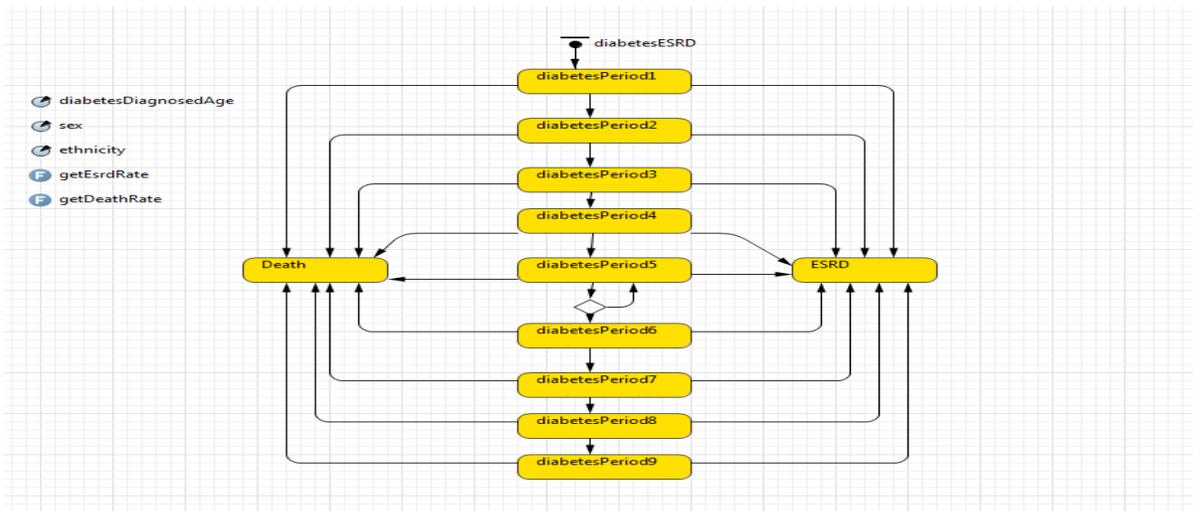


Figure 4-2. Original Statechart in Ying’s Model on Diabetes Progression to ESRD and Death

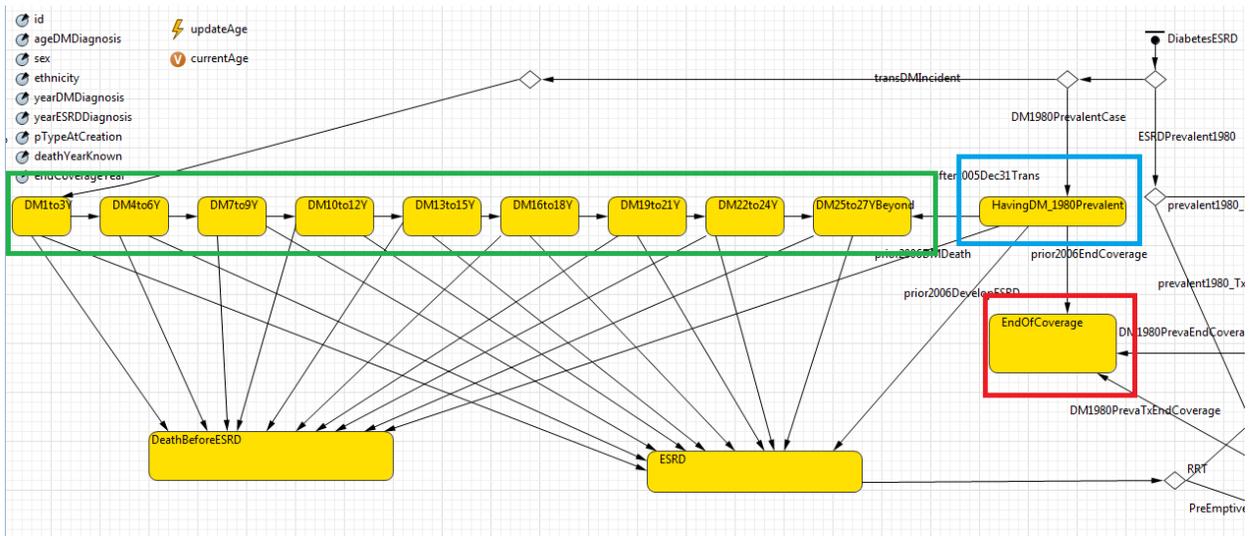


Figure 4-3. Adopted Statechart in Saskatchewan DM-ESRD Model Regarding Progression of Diabetes to ESRD or Death

As marked in the green box in Figure 4-3, there are a total of nine diabetes stages (i.e. “DM1to3Y” state, “DM4to6Y” state, etc.), which were defined based on the duration with which a patient has experienced diabetes. The first eight stages are each associated with a three year interval, whereas the last stage is for patients who have had diabetes for 25 years and beyond. The diabetes stages were divided in this manner due to the way the competing risks analysis was conducted on the Saskatchewan diabetes population between 1980 and 2005. That research determined a patient’s hazard (chance per unit time) of dying prior to getting ESRD and hazard of developing ESRD at each diabetes state. These hazards were then used for triggering a patient’s transition from the diabetes states to either the “DeathBeforeESRD” state or the “ESRD” state. If a patient remained in a 3-year diabetes state for three years without having died or developed ESRD, they would move to the next more advanced diabetes state that is next to it. For patients who were already in the last DM state (“DM25to27Beyond” state), there is no more advanced DM state. Thus patients remain in the last DM state until either death or developing ESRD. As patients move through diabetes states, both mortality and ESRD hazard are increased, and are recalculated every time patients move to the next DM state. The hazards depend on a number of factors: the DM stage, and patient’s age, gender and ethnicity.

The diabetes states and the related transitions were only used for modeling diabetic progression for patients who developed ESRD within the model. As discussed in the next section, for the year 1980 DM prevalent patients, the diabetes progression was handled differently in the model than for subsequent incident patients.

4.1.2 Special Handling for the 1980 DM Prevalent Cases

In contrast to the DM incident patients progressing through the Nine DM States, the year 1980 DM prevalent patients start their lives in the model in a special state named

“HavingDM_1980Prevalent”, as marked in a blue box in Figure 4-3. Upon entering the model, the year 1980 DM prevalent patients branch into the “HavingDM_1980Prevalent” state while the DM incident patients go to the “DM1to3Y” state. The reason for using a designated state for the year 1980 DM patients was due to the concerns regarding the reliability of the inferences instead of “DM diagnosis time” for those patients. We now provide additional details on the associated design considerations. .

In theory, the 1980 diabetes patients can start their life in the standard sequence of diabetes states (e.g. “DM1to3Y”) at model start time. By using patient’s DM diagnosis time, the duration of having diabetes could be calculated and used for assigning patients to DM states. For instance, a patient who received DM diagnosis at year 1972 would have had diabetes for 8 years by Jan 1st 1980, and the patient could start in the “DM7to9Y” state. However, while examining the historical data for the DM prevalent patients, we found that the reported years of receiving DM diagnosis only ranged from 1970 to 1979 among the 14,000 DM prevalent patients at 1980. The fact that not even one DM patient was reported as receiving a DM diagnosis prior to 1970 is highly suspect. After consulting with the experts, we learned that the DM diagnosis prior to 1970 were not properly recorded, and were instead assumed to fall into years following 1970. Because the reported DM diagnosis time for those who began the study period with diabetes are inaccurate, reliance on this data would mean that many of the year 1980 DM prevalent patients would not start in the correct DM states. As discussed in the earlier section, the risk for death prior to ESRD and risk for developing ESRD both depend on the DM state a patient is in. Consequently, the chance of death and receiving ESRD diagnosis wouldn’t be correct for those patients with an inaccurate DM diagnosis time. Incorrect mortality and ESRD

hazards could, in turn, cause problems for the calibration of other model processes. We therefore sought an alternative way for determining those risks.

Rather than relying on risk calculations based on inaccurate DM diagnosis times, we sought to take advantage of the fact that for virtually all 1980 prevalent diabetics, we have highly accurate individual-level information available on recorded year of death, end of coverage and development of ESRD from the individual-level historical data. Between Jan 1st, 1980 and Dec 31, 2005, the year of death, end of coverage and ESRD diagnosis were recorded for the 1980 prevalent cohort. Although the specific dates within a year for a given event were not available in the historical data, the inaccuracies associated with those uncertainties were expected to be comparatively minor compared to what would result from uncertainties concerning the year of diabetes incidence. Operationally, such dates can be randomly generated in the model and used together with the given year for scheduling events in the model. When the prescheduled “Death”, “ESRD” and “End of Coverage” events take place, patients will move to the corresponding states. For example, suppose one patient has a prescheduled “ESRD” event on Feb 3, 1982, and another pre-scheduled “End of Coverage” event on May 15, 1986. The corresponding scenario in the model will be as follows: When the model begins on Jan 1st, 1980, the patient starts in the “HavingDM_1980Prevalent” state. When the model clock reaches Feb 3, 1982, the patient moves from the “HavingDM_1980Prevalent” state to the “ESRD” state; no transition to ESRD is possible for the patient prior to that point. The patient then moves from the “ESRD” state to some treatment states or might proceed through some transplant assessment states. However, when being treated with the RRT, the patient would not be subject to risk of death which is only applicable to DM-ESRD patients receiving ESRD diagnosis after Jan 1st, 1980 (the DM-ESRD incident patients in the model). And no matter which state the patient was in, on May 15, 1986,

the patient would move from his/her state at the moment (e.g. HD) to the “End of Coverage” state. Similarly, when a patient has a death event scheduled, if the historical data reveals that the death occurred before the patient developed ESRD, the patient would move from the “HavingDM_1980Prevalent” to the “DeathBeforeESRD” state. Or if the death event took place after patient’s ESRD diagnosis, the patient would move from one of the ESRD treatment states (e.g. “FunctionalTx”) to the “DeathAfterESRD” state. Prior to Dec 31, 2005, those patients’ chances of receiving certain ESRD treatments and getting through the transplant assessment process were determined by the logic built within the model transitions. However, their death, ending health coverage and developing ESRD were all prescheduled according to historical data.

After Dec 31, 2005, there are no more pre-scheduled events for the year 1980 prevalent patients, because there is no historical data available. As a result and following that point, those patients’ mortality and ESRD hazards are handled in the same way as the incident patients as discussed above in the section “Diabetes to ESRD progression - DM Incident patients”. To be more specific, as soon as the model time strikes Jan 1st, 2006, patients who are still in the “HavingDM_1980Prevalent” state move to the “DM25to27YBeyond” state; this movement reflects the fact that they had already been having diabetes for at least 26 years (from 1980 to 2005). Once patients are in the “DM25to27YBeyond” state, their risks of death or developing ESRD are based on the formula from Ying’s competing risk analysis.

For patients who have received ESRD diagnosis, they move from a DM state into the “ESRD” state. Such patients then initiate Renal Replacement Therapy (RRT), the details of which will be discussed in the following section.

4.2 ESRD treatment Options and Death

Depending on an ESRD patient's medical condition and treatment availability, renal replacement therapy options include HD, PD, or kidney transplantation. Very few ESRD patients receive a pre-emptive transplant – a kidney transplant before being dialysed. Most patients begin with either PD or HD as their initial treatment, followed by kidney transplantation.

4.2.1 Selection between PD and HD

For most patients with ESRD, a dialysis type must be selected. In reality, the choice between PD and HD is made based on several factors including patient attributes and availability of treatment. However, in the model, the selection of treatments was simplified as a draw from a Bernoulli distribution. The probability of receiving PD (as an initial treatment in Saskatchewan) used for that Bernoulli draw was obtained from CIHI through a special data request. The details about probability distribution and data source can be found in the section “Model Data Source”.

As shown in Figure 4-4, if PD is selected as the initial treatment, the patient will move out of the “ESRD” state and branch into the “Peritonealdialysis” state inside of the “DialysisModalities” composite state. By contrast, if PD is not selected, then the patient will move to the “Hemodialysis” state.

4.2.2 Switching between PD and HD

Patients will sometimes switch between PD and HD for medical and personal reasons. As shown in the Figure 4-4, transitions were set up between “Peritonealdialysis” state and “Hemodialysis” state, allowing patients to change from one type of dialysis to another. Rates (hazards) used in those transitions were calculated based on the dialysis treatments received between Jan 1st, 2006 and Dec 31, 2010 by the Saskatchewan DM-ESRD patients. The details

on the rates and the data source used here can be found in the section “Model Data Source” of this thesis.

4.2.3 Pre-emptive Kidney Transplantation

In Saskatchewan, very few ESRD patients receive pre-emptive kidney transplantation. Most of the patients receive dialysis first and then some are transplanted. Occasionally, a patient may receive a pre-emptive transplant, and it is most likely to be a living donor kidney transplant. A kidney from a deceased donor would virtually always be given to a dialysis patient on the waiting list, unless a match cannot be found among patients on the waiting list. Despite being uncommon, the pre-emptive transplant process was included in the model for the purpose of facilitating policy experiments. The transitions marked in blue in Figure 4-4 showed the choices between pre-emptive transplantation and dialysis treatments for patients who just received ESRD diagnosis. The probability of receiving a pre-emptive transplant over dialysis as initial treatment is used to control which treatment the patient would receive. The type of the kidney transplant will be based on the supplied probability distribution of living donor and deceased donor pre-emptive transplantations. Once a pre-emptive transplant operation takes place, the patient will move to the “Transplant” composite state, which is the same designated state as for those transplant recipients who went through dialysis prior to transplant. The “Transplant” composite state will be discussed in the next section.

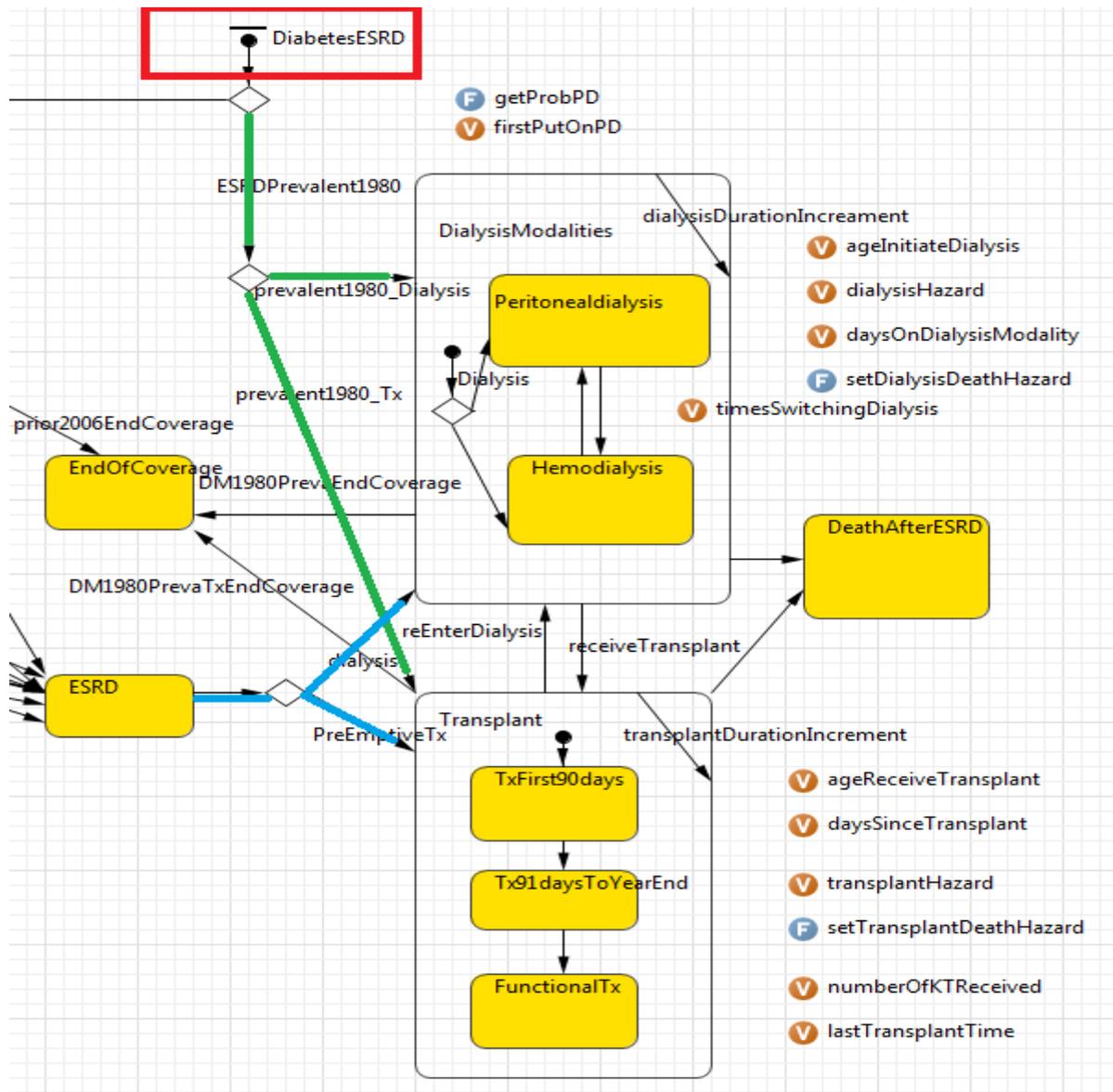


Figure 4-4. Statechart Regarding ESRD Treatments and Death

4.2.4 Post Kidney Transplantation

While patients are receiving dialysis, they might go through the transplant assessment process and wait for a transplant on the waiting list. The transplant assessment and waiting list process was represented in a separate statechart, the details of which are discussed in the sections “Transplant Assessment” and “Waiting list and Transplant”. The inclusion of those processes in

a separate statechart reflects the fact that when patients are waiting for kidney transplantation, they remain on dialysis. In the model, when it is a patient's turn to be transplanted, a message is sent to the patient (agent) to notify them. Upon receiving the "getting transplant" message, the patient will move from the dialysis state to the transplant state via the "receiveTransplant" transition. As shown in Figure 5, the time following kidney transplantation was divided into three states: "TxFirst90days", "Tx91daysToYearEnd", and "FunctionalTx". The reason for breaking the time into those states is due to the cost difference associated with the three periods following the transplant operation [34]. After kidney transplantation, a patient would first start in the "TxFirst90days" state. After 90 days post transplantation, the patient would move from the "TxFirst90days" state to the "Tx91daysToYearEnd" state, and remain in that state for the balance of the year following transplant. Finally, one year after having received the kidney transplant, the patient would move to the "FunctionalTx" state.

4.2.5 Return to Dialysis after Graft failure

When a transplanted kidney fails, the patient needs to restart dialysis treatment. In the "DiabetesESRD" statechart, the patient will move from the transplant state back to the dialysis state via the transition "reEnterDialysis". The hazard of returning from transplant to dialysis was based on graft failure rates, which were calculated from the graft survival rates for ESRD patients (not specific to DM-ESRD patients) given in the 2011 CORR Annual Reports [38]. The graft failure rates were computed for eight sub-population groups stratified by transplant donor type (living and deceased) and four age groups (age 18 to 44, age 45 to 54, age 55- 64 and age 65+). The details about the rate calculation and data sources can be found in section "Model Data Source". For patients whose transplanted kidney fails, upon re-entering the dialysis state,

the type of dialysis would be drawn from the same probability distribution used by patients who undergo dialysis for the first time.

4.2.6 Mortality Risks on ESRD Treatments

Patients are at risk of dying while they receive ESRD treatments. A patient's daily mortality risk on an ESRD treatment was calculated by a hazard function, which required input such as gender, ethnicity, age when initializing the treatment, type of treatment, and the length of time on the treatment. The hazard function in the model was derived from a risk adjusted survival analysis conducted by CIHI upon our request. Because the mortality hazard changes significantly over time since transplant, mortality hazard varying on a day-by-day basis was used in the model. When the patient died while receiving ESRD treatment, he or she will move to the "DeathAfterESRD" state in the "DiabetesESRD" statechart. Correspondingly, the same patient will also move into the "Death" state in the "AssessmentStages" statechart, as marked in the blue box in Figure 4-5.

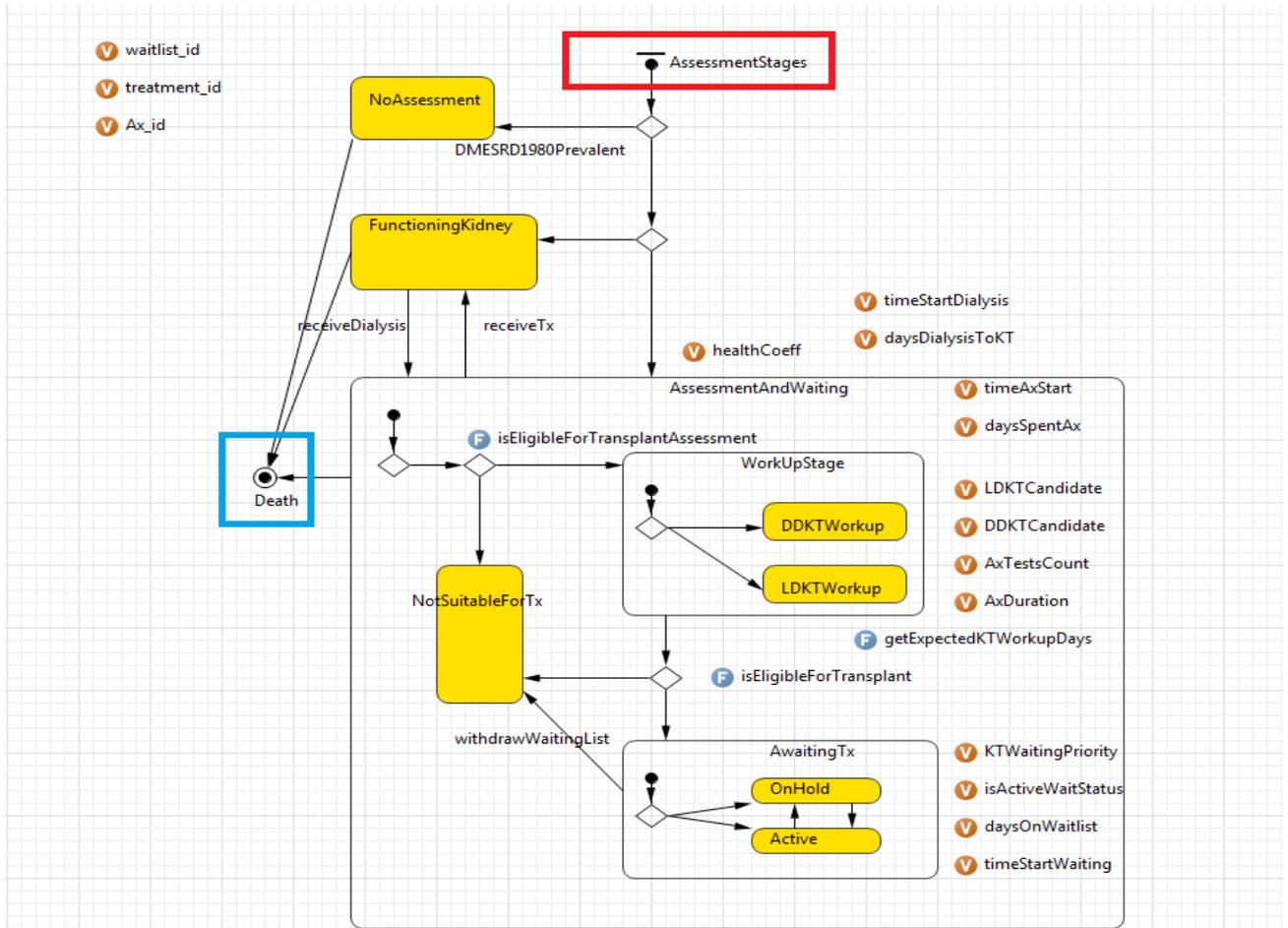


Figure 4-5. Transplant Assessment and Waiting List

4.3 Transplant Assessment

The transplant assessment process evaluates a dialysis patient’s eligibility for kidney transplantation. This process is used for patients who first receive dialysis treatments and then receive a transplant, but not for patients who receive pre-emptive transplantation (although the latter patients also require pre-transplant assessment). The assessment for a dialysis patient consists of three important processes: evaluation of the patient’s suitability for transplant assessment, determination of the type of kidney transplant, and assessment of the patient’s eligibility for transplant.

4.3.1 Evaluation of Patient's Suitability for Transplant Assessment

While receiving dialysis, most patients are sent for a transplant assessment, except those who are very old. After consulting a specialist, we have implemented the following selection criteria for sending patients for transplant assessment in the model. First, since most patients over 75 years old are deemed not suitable for transplant, they won't be assessed in the model. Second, patients between age 66 and age 75 have a 25% chance of receiving transplant assessment. Finally, patients who are 65 years old or younger will always be assessed.

4.3.2 Determination of the Type of Kidney Transplantation

The type of the transplant is important to our study because candidates for living donor transplantation and deceased donor transplantation may be on separate waiting lists. Moreover, in addition to the examinations required for the recipient, donors for living donor transplantation need to be evaluated as well, which means the cost for assessment would be not be the same for living and deceased donor transplants. Reflecting these factors, the selection of transplant type is made at an early stage of the assessment in the model. The choice between living and deceased donor transplants are made based on the proportion of living and deceased donor transplants among all kidney transplants that took place in Saskatchewan from year 1981 to 1999. This data was located in the CORR annual reports [38], and the rates were for all ESRD patients who received transplants rather than being specific to DM-ESRD patients (more information about the data is in the "Model Data Source" section). Once the type of the transplant is chosen, the patient will begin the assessment for that type of transplant. As shown in Figure 4-5, living donor transplant candidates will start their assessment in the "LDKTWorkup" state, whereas the deceased donor transplant candidate will stay in the "DDKTWorkup" state during the transplant

assessment process. Further details on the transplant assessment process are discussed in the next section.

4.3.3 Assessing Patient’s Eligibility for Kidney Transplantation

The assessment process evaluates a patient’s health by conducting a number of examinations, which seek to determine if that patient is a suitable candidate for a kidney transplant. In the model, two considerations come out of the assessment process: the length of time the assessment takes, and whether the patient is deemed eligible for a transplant. The duration of the assessment is used to control how long the patient remains in the “Workup Stage” state in the “AssessmentStages” statechart. In the real world, appointments and examinations with different specialists during assessment might vary in number and length of time. Thus, the total time for completing the assessment can be different for different individuals. In the model, an Erlang distribution function was used to estimate the duration of the assessment for patients who never received transplant before, or their last but failed transplant was more than a year ago. The Erlang distribution considered two input parameters: the total number of appointments and examinations required for the individual to complete the assessment, and the average time to complete a test. For patients who had a kidney transplant within a year, we assume it would take them the minimum time to go through the assessment process again. Since we have limited data on the assessment process, we made our guesses on the number of examinations required, and the minimum time required for those patients who were transplanted within a year. We calibrated those values so that patient’s time spent on assessment together with the time that approved patients spent on the waiting list would match with the historical data (see the “Calibration Section”).

By the time patients complete their assessment, their eligibility for transplant should be determined. In the model, we didn't implement the methodology used in the real world situation for evaluating patient's suitability for kidney transplantation, due to the scope of this thesis. Rather we simply used an abstract "health coefficient" to represent patient's overall health level, and used a calibrated cut off value of the health coefficient to determine a patient's eligibility for a kidney transplant. Those who are deemed suitable for kidney transplant are then put on the waiting list for the appropriate type of transplant. Correspondingly, in the model, patients would move into the "AwaitingTx" state. Those who are not eligible to have a transplant would be moved to the "NotSuitableForTx" state.

4.4 Transplant Waiting List and Kidney Transplant

When patients complete the transplant assessment and meet the eligibility requirements for a transplant, they will be placed onto a waiting list. While awaiting a transplant, patients may leave the waiting list either by receiving a transplant, withdrawal from the waiting list, or due to death prior to receiving a transplant. A number of factors work together to decide when a transplant will take place and who will get a transplant. The following sections discuss each of those determinants.

4.4.1 Priority on Transplant Waiting List

Based on the donor type, there are effectively two waiting lists for kidney transplant: one for living donor transplant candidates and one for deceased donor transplant candidates (although the same person could potentially be on both lists). Living donor transplants typically involve a much shorter wait, because the wait is primarily for surgical resources (e.g. surgeon availability and operation room). On the other hand, for a deceased donor transplant, patients mainly wait for availability of an organ. For both deceased donor and living donor transplant candidates, the

length of wait for a transplant operation is also determined by their priorities on the waiting list. In reality, the priority on the waiting list is calculated based on a number of health related factors for a patient. In Canada, provinces have their own methods for determining the priorities, and maintain their own waiting lists for kidney transplantation. Currently in the model, the priority is randomly generated and is assigned to patients when they are added to the waiting list. An algorithm for determining the priority based on patient's health state is beyond the scope of this thesis; we anticipate the implementation of such an algorithm as future work. The priority sets the order in which patients receive transplants. Moreover, a patient's status on the waiting list has to be "active" in order to receive kidney transplantation; this notion is described further below. The patients selected for kidney transplant must have the highest priority on the waiting list to which they belong and an active status; ties are handled according to the timing with which they were added to the queue.

4.4.2 On hold and Active Status on Waiting List

The "On hold" and "Active" status of the waiting list mark a patient's short-term suitability for transplant. Some patients, who have passed the transplant assessment phase and are deemed suitable for kidney transplant, might be temporarily prevented from receiving a kidney transplant operation due to a new but transient medical condition (e.g. an infection). Under such conditions, their status on the waiting list will be put "on hold". In the model, the patient will move to the "OnHold" state. As soon as the patient recovers from the condition, their status on the waiting list will be restored to "Active". Correspondingly, in the model, the agent representing the patient will move back to the "Active" state in the model. The historical data on waiting list status was studied. Patients on the waiting list were randomly marked as "On Hold" according to the probabilities of being on hold based on the historical data. The priority of the

patients and their status on the waiting list were used for selecting candidate for the next transplant when the resource (e.g. a donor kidney) is ready. The numbers of kidneys available determine how frequently kidney transplants can take place.

4.4.3 Kidney Transplantation

The frequency of kidney transplants is restricted by the availability of resources required for performing the transplant; these resource constraints are different for living donor and deceased donor transplant. The frequency of deceased donor transplantation depends on when a kidney is available. The frequency of performing living donor transplant also depends on the surgical resources (surgeon and operation room). In the model, two rates representing the frequency of living donor and deceased donor transplants were used to schedule the occurrences of the two types of kidney transplants. Patients with the highest priority and an active status on the waiting list will be called to receive a transplant.. In the model, when a transplant operation takes place, the patient would move out of the “AssessmentAndWaiting” state and go to the “FunctioningKidney” state in the “AssessmentStages” statechart, as shown in Figure 4-5. Simultaneously, in the “DiabetesESRD” statechart as shown in Figure 4-4, a patient will move from the dialysis states to the “Transplant” state.

CHAPTER 5

MODEL PARAMETERS

As described in the previous chapter, model transitions move patients from one state to another. The driving forces behind them are the various formulae and parameters. This chapter is devoted to describing those model transitions where the data and formulae came from sound historical sources such as CORR annual reports, CIHI data requests, the Saskatchewan health administrative database, and Saskatchewan renal program reports.

5.1 Mortality Risks for Dialysis and Transplant Patients.

The mortality risk at a given time for individuals receiving dialysis treatment or post kidney transplantation is calculated by using a Cox Proportional Hazards model whose parameter values were provided by CORR. Upon our request, CORR conducted survival analysis on the ESRD patients on dialysis or after kidney transplantation in Canada between 1999 and 2008. For dialysis patients, the hazard ratios were estimated for covariates such as treatment modalities (HD or PD), diabetes status, ethnicities (FN, OSK, and other), gender and age groups (every 5 years are grouped together for the age 20 to 75, and one group for age over 75). The covariates and coefficient estimates are listed in Table 5-1 below. Moreover, the baseline survival and the cumulative hazard for day 0 to day 3581 were provided.

Table 5-1. Regression Coefficients used in Cox Proportional Hazard Model for Mortality Risks, Dialysis Patients, Canada, 1999- 2008. Provided by CORR based through A Data Request

Parameter	Estimate	Standard Error	Coding
PD	-0.2135	0.0188	HD:0, PD: 1
Diabetes	0.2168	0.0138	Non-diabetes:0, diabetes:1
Male	0.0755	0.0137	Female:0, Male:1
Aboriginal	0.1653	0.0327	Caucasian:0, Aboriginal:1, other:2

Other race	-0.2296	0.0170	
25 - 29 years	0.1266	0.2200	20 - 24 years:0
30 - 34 years	0.6794	0.1944	
35 - 39 years	0.8886	0.1856	
40 - 44 years	1.0855	0.1809	
45 - 49 years	1.2224	0.1782	
50 - 54 years	1.3968	0.1769	
55 - 59 years	1.6663	0.1758	
60 - 64 years	1.8005	0.1754	
65 - 69 years	1.9834	0.1751	
70 - 75 years	2.2071	0.1748	
>75 years	2.5042	0.1744	

For each individual, mortality risk on a given day can be calculated using the hazard model (5.1).

$$H_0(t) = h_0(t) \times e^{(\beta_1 \times X_1 + \dots + \beta_P \times X_P)}$$

- $\beta_1 \dots \beta_P$ is the log of the hazard ratio (coefficient estimates)
- $X_1 \dots X_P$ are the covariates.

(5.1)

Since the baseline hazard rate $h_0(t)$ generally varies over time, the estimated mortality risk for a person $H_0(t)$ gets updated at every model time unit (day) by a function named “setDialysisDeathHazard” in the Person object. The updated mortality risk is then used in the rate based event “dialysisPatientDie” to determine person’s hazard (probability density of death) at the moment while the patients is getting dialysed.

For estimating the mortality risks for transplant patients, a Cox Proportional Hazards model was provided by CORR as well. The survival study was conducted on ESRD patients living with a functioning kidney between year 1999 and 2008. The hazard ratio was provided for covariates including diabetes status, ethnicities, gender and age groups as shown in Table 5-2.

The hazard rates for transplant patients were calculated in similar fashion as for the dialysis patients. The base line hazard rate is updated every day in a function called “setTransplantDeathHazard” based on the number of days which transplant patients have survived following their transplant, and the resultant hazard rate is used in event “transplantPatientDie” for determining the mortality hazard for patients living with functioning transplants.

Table 5-2. Regression Coefficients used in Cox Proportional Hazard Model for Mortality Risks, Transplant Patients, Canada, 1999- 2008. Provided by CORR through A Data Request.

Parameter	Estimate	Standard Error	Code
Diabetes	0.6809	0.0762	Non-diabetes:0, diabetes:1
Male	0.1883	0.0791	Female:0, Male:1
Aboriginal	0.2567	0.1914	Caucasian:0, Aboriginal:1, other:2
Other race	-0.3187	0.0949	
25 - 29 years	-0.4852	0.4005	20 - 24 years:0
30 - 34 years	-0.2992	0.3690	
35 - 39 years	0.0040	0.3353	
40 - 44 years	0.2937	0.3186	
45 - 49 years	0.3453	0.3120	
50 - 54 years	0.6417	0.3080	
55 - 59 years	0.9368	0.3030	
60 - 64 years	1.3649	0.3022	
65 - 69 years	1.5031	0.3057	
70 - 75 years	1.9382	0.3143	
>75 years	2.5485	0.3844	

Based on the calculated hazard rates, the function “transplantPatientDie” and “dialysisPatientDie” will send a message to trigger the movement from either the “Peritonealdialysis” state, “Hemodialysis” state or “Transplant” state to the “DeathAfterESRD” state in the “DiabeticESRD” statechart. Simultaneously, in the “AssessmentStages” statechart, patients will move to the “Death” state.

5.2 Selection between PD and HD

In the model, the selection between PD and HD for DM-ESRD incident patients depends on the empirical probability of receiving one type of treatment modality over another found in the historical data on treatment modalities. Through a special data request, CIHI provided the count of DM-ESRD patients who received HD or PD as their initial treatments in Saskatchewan from year 1981 to 2011. The historical counts were used for calculating the probabilities of receiving PD vs. HD treatment as an initial dialysis treatment for DM-ESRD patients. The year and probability rate pairs for year 1981 to 2011 were saved in the table function¹ named “PDInitialProb”. For years between 1981 and 2011, the probability of having PD as initial treatment can be directly retrieved from the table function “PDInitialProb”. For the years outside that range (i.e. 1980 and years after 2011), we made the assumption that the probability of having PD is the same as the values in the nearest year for which data is available. For instance, the probability of having PD for year 2012 or 2013 will be the same as in year 2011. We could also change the assumption so that the probability of having PD in the future years is estimated based on the extrapolation of the historical data. The AnyLogic table function can accommodate such change in assumption by modifying the values supplied to the “Interpolation” and “Out of Range” parameters, as shown in Figure 5-2. The probability of receiving PD is passed as an input parameter to the AnyLogic build-in probability distribution function “randomTrue” to perform a Random draw from a Bernoulli distribution based on this probability. The transition “dialysis” (highlighted in green, on the left in Figure 5-1) makes use of this mechanism to determine whether the first treatment for DM-ESRD patients will be PD or HD. The transition “reEnterDialysis” (highlighted in green, on the right in Figure 5-1) also uses the same

¹ A Table Function in AnyLogic is table form function which can be used for defining non-linear relationship.

mechanism to choose HD or PD treatment for transplant patients returning to dialysis treatment. If the result of the “randomTrue” function is true (corresponding to a value of 1 from the Bernoulli Distribution), then the patient will start PD as initial treatment; otherwise, the patient will begin with HD treatment.

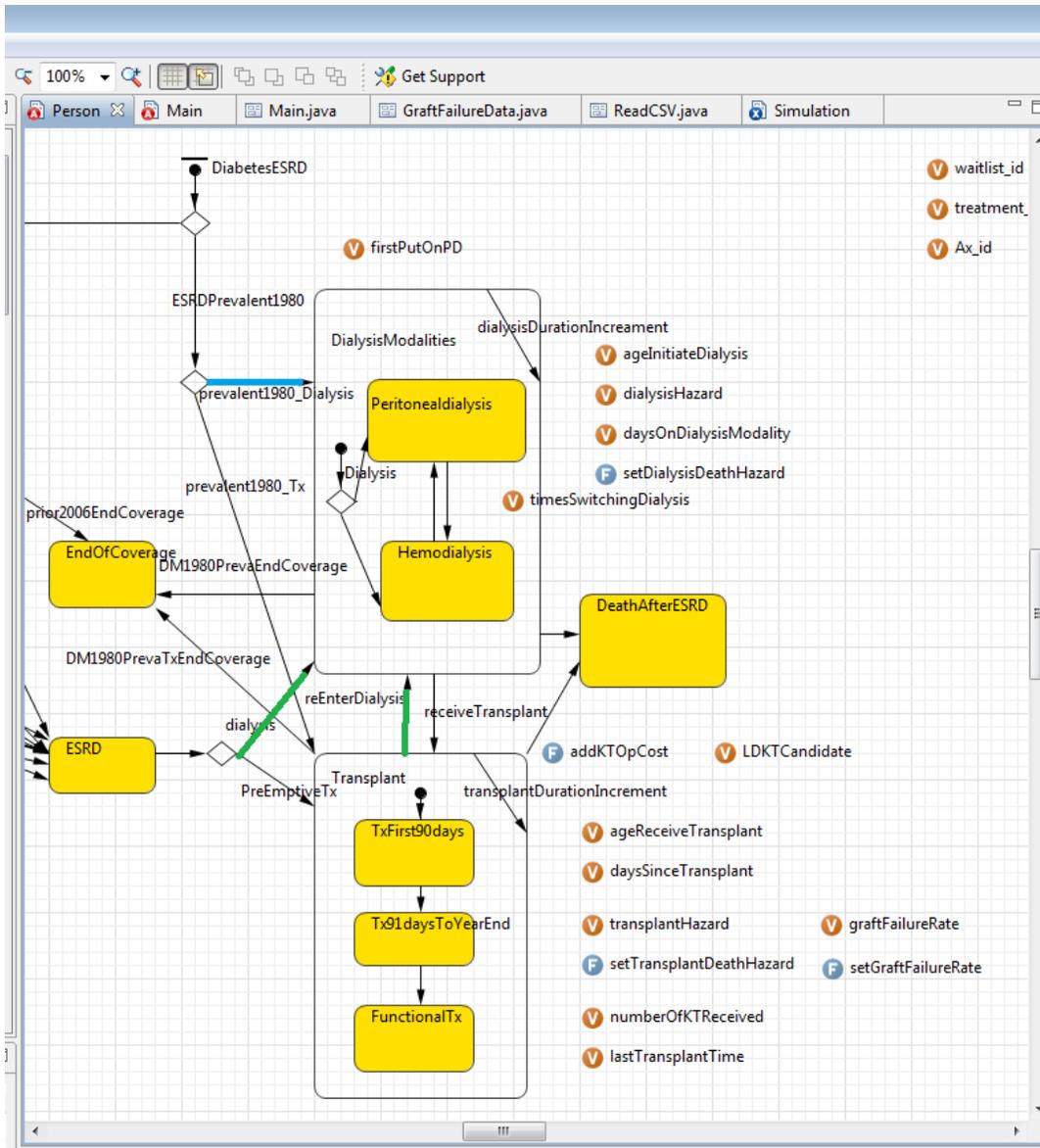


Figure 5-1. Transitions in which the Dialysis Modalities were Determined

The selection of dialysis modalities for DM-ESRD patients was based on the probabilities of receiving PD as an initial treatment found among the Saskatchewan DM-ESRD patients between year 1981 and 2005. However, when initializing the year 1980 DM-Prevalent cases at model start time, assigning patients to HD, PD and Transplant as ongoing treatment was based on the distribution of DM-ESRD prevalent patients among those treatments modalities on Dec 31, 1981. Ideally, the distribution of DM-Prevalent patients on treatment at year end of 1979 should be used, rather than based on the distribution found at the end of year 1981. However, due to the lack of information on prevalent case in 1979, we had to use the corresponding data from year 1981. The distribution of DM-ESRD patients on different modalities was saved in the table function named “modalityDistri1980DMESRDPrevalent”, which was used in a custom distribution function for assigning patients to treatments according to the historical distribution found in the year 1981 DM-ESRD prevalent patients.

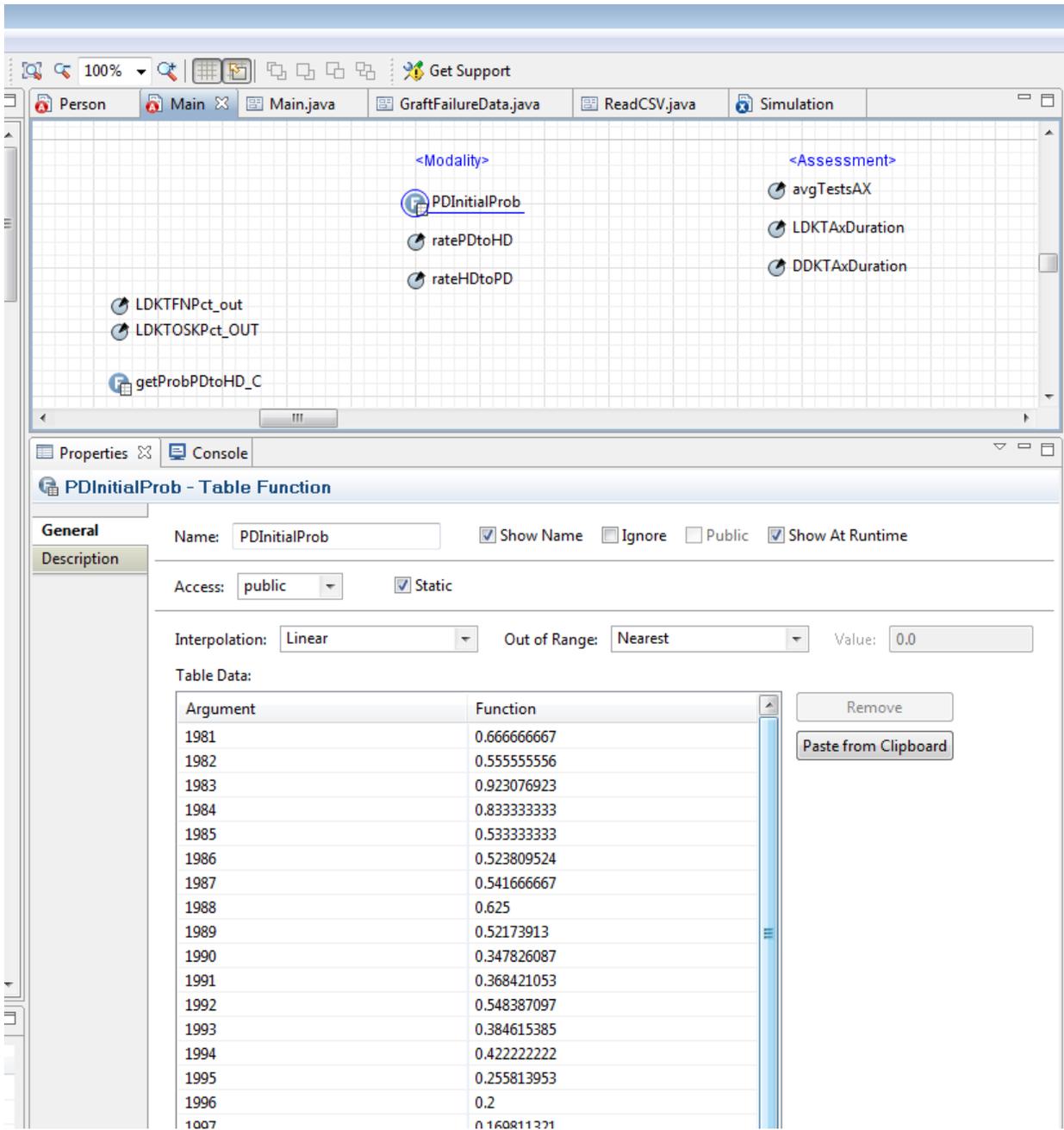


Figure 5-2. Setting up table function “PDInitialProb”

5.3 Hazard of Switching between HD and PD

The hazard (per day probability density) for switching from one type of dialysis to another is estimated using information regarding dialysis treatments received by DM-ESRD

patients in Saskatchewan between January 1st, 2006 and December 31st, 2010. The historical data on dialysis treatments was provided by Dr. J. Kappel. The method for estimating the probability of switching from HD to PD based on historical treatment information is illustrated in detail below, with an aim towards the hazard of switching from HD to PD.

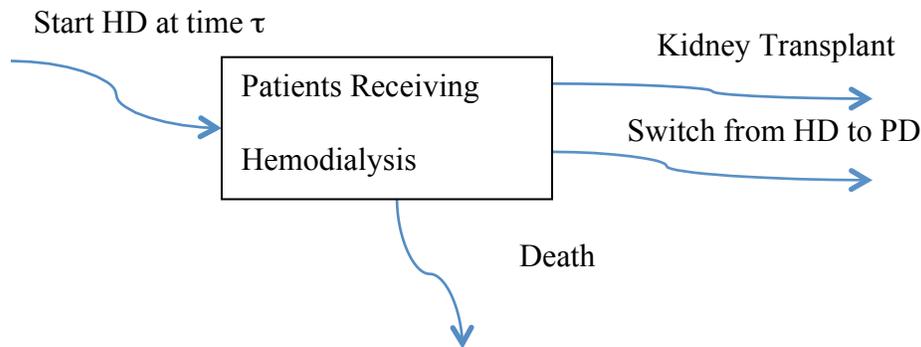


Figure 5-3. Out flow of Patients Receiving HD Treatments

As shown in Figure 5-3 above, for patients receiving HD, there are three ways of leaving the treatment: transplantation, switching from HD to PD and death. The first step is to estimate the hazard of leaving HD regardless of reasons (transplantation, switching treatment or death). Normally, if a person starts in a specific dialysis modality at time 0, and if that person has a hazard rate λ of leaving that modality to any other modality, the probability of that person remaining in that state at time t is given by the formula $e^{-\lambda t}$. In this case, patients started HD at various times between 2006 and 2010. Suppose that we approximate the continuous time at which patients arrive as a series of discrete days τ , and consider the patients starting dialysis i , on each successive day. Then the fraction of people who remain under that dialysis modality is given by:

$$\sum_{\tau=1}^t (i_{\tau} e^{-(h_t+h_d+h_p)(t-\tau)})$$

- t is the last day of the study
- τ is when patients begin on HD
- i_{τ} is the proportion of all patients who start HD at time τ
- h_t is the hazard rate of leaving HD due to transplant.
- h_d is the hazard rate of leaving HD due to death.
- h_p is the hazard rate of leaving HD due to switching to PD.

(5.2)

By analysing the treatment information between 2006 and 2010, the probability of leaving HD ($h_t + h_d + h_p$) can be solved. The counts of patients who began HD at various days τ determine the values for i_{τ} . Also, the proportion of patients who remain without changing from HD at the end of 2010 can be calculated from the historical data. By setting the formula in (5.2) equal to this proportion and using the values of i_{τ} , the sum of h_t , h_d , and h_p can be found.

To further derive the value of h_p , the proportion of patients switching to PD among all patients leaving HD were applied to the sum of the hazard rates for leaving HD due to all causes, as shown in (5.3), the proportion of patients switching to PD among all patients leaving HD were obtained by dividing the count of patients switching to PD by the count of all patients leaving

$$\text{HD} \left(\frac{N_p}{(N_p+N_t+N_d)} \right).$$

$$h_p = (h_p + h_t + h_d) \times \frac{N_p}{(N_p + N_t + N_d)}$$

- N_p is the number of patients who switched from HD to PD.
- N_t is the number of patients who received transplant following HD.
- N_d is the number of patients who died while receiving HD.

(5.3)

The probability of switching from PD to HD is calculated in the same way as for the probability of switching from HD to PD, and both rates were the driving forces for the “switchHDtoPD” and “switchPDtoHD” transitions between HD and PD.

It should be recognized that the derivation done above for the hazard rates of switching dialysis modalities is an important approximation. Specifically, the formula assumes that the sum of hazard rates of leaving HD due to PD, transplant and death ($h_p + h_t + h_d$) is constant, but in fact this rate varies over time.

5.4. Graft Failure Rate

The graft failure rate (hazard) is used in the model for determining when a transplanted graft fails and patients return to dialysis. The graft failure rate was estimated based on the graft survival levels published in the 2012 CORR annual reports - the unadjusted three month, one year, three year, and five year graft survival rates for adult kidney transplant patients (living donor or deceased donor). The estimated graft failure rates were applied to entire projection periods including those earlier years back to year 1980. Since the graft failure rates from later years are lower than from the earlier years, our assumption of using later year’s graft failure rates for the entire projection period will result less graft failed for earlier years. We realized that it is not ideal to have a unified graft failure rates. In the sensitivity analysis chapter, we verified the

impact of setting graft failure rates to zero in section 8.2.6. The details of deriving the graft failure rates from graft survival data are discussed next. Table 5-3 below shows the graft survival levels taken directly from the year 2012 CORR reports. By assuming the graft failure among transplant patients followed a curve locally characterized by an exponential decay (reflecting a memoryless process, where the hazard is a fixed rate), the graft failure rate at different points can be calculated over time.

Table 5-3. Unadjusted one month, three month, one year, three year and five year graft survival rates for transplant patients (living and deceased donor) in Canada between year 2000 and 2010

Donor Type	Age Group	0	3 Months	1 Year	3 Years	5 Years
Living	Age 18–44	99.8	98.0	96.8	94.7	90.3
	Age 45–54	99.9	98.4	97.6	94.4	90.8
	Age 55–64	99.9	98.3	96.6	91.5	87.8
	Age 65+	99.7	98.4	95.9	92.0	83.0
Deceased	Age 18–44	99.4	95.9	94.1	88.8	82.2
	Age 45–54	99.8	97.0	94.8	90.2	85.3
	Age 55–64	99.4	94.7	91.0	84.9	79.6
	Age 65+	99.8	95.0	90.2	81.8	74.3

Consider a situation where the graft survival levels $x(t)$ are known for two successive points, $x(t)$ and $x(t+\Delta t)$. Suppose we wish to treat the mortality according to a fixed rate between these points. This means that for each individual who has survived until time t post-transplant, the probability of remaining alive following time Δt is declines as $e^{-\lambda \Delta t}$. The total number of individuals who remain alive at time $t+\Delta t$ is $x(t+\Delta t) = x(t)e^{-\lambda \Delta t}$. Given the empirical values $x(t+\Delta t)$ and $x(t)$ and the value of Δt , we can estimate the rate λ using the following derivation:

$$x(t + \Delta t) = x(t)e^{-\lambda\Delta t}$$

$$e^{\lambda\Delta t} = \frac{x(t)}{x(t + \Delta t)}$$

$$\lambda\Delta t = \ln \frac{x(t)}{x(t + \Delta t)} = \ln(x(t)) - \ln(x(t + \Delta t))$$

$$\lambda = \frac{\ln(x(t)) - \ln(x(t + \Delta t))}{\Delta t}$$

(5.4)

In Table 5-3, the graft survival rates are known for day 0, day 90 (3 months), day 365 (1 year), day 1065 (3 years) and day 1825 (5 years) for each age group and each type of transplant.

Using equations (5.4), the graft failure rates (hazards) can be calculated for day 0, day 90 (3 months), day 365 (1 year), day 1065 (3 years) and day 1825 (5 years). Further, to get the graft failure rates for each day in 5 years, the graft failure rates were interpolated between each nearest two days where the graft failure rates were calculated. For example, the graft failure rates for every day falling between day 365 and day 1065 should be interpolated using the graft failure rates of day 365 and day 1065. For the days between year five and year ten, we extrapolated the graft failure rates for each day in the last five years based on the graft failures calculated in the first five years. Thus, within the span of a given day interval following transplant, the death process is memoryless (independent of the time within that day), but each successive day leads to a new rate.

Following the steps described in above sections, a total of eight sets of graft failure rates were calculated for each of the eight groups of patients stratified by age and transplant donor

type, and each set of graft failure rates were saved in a comma separated file and loaded into table functions in the model at model start. Table 5-4 lists the name of the file to which graft failure rates were saved and the name of the table function into which the graft failure rates got loaded for each group of transplant patients. And the details regarding the calculation of the graft failure rates can be found in the file “Calculation_GraftFailureTxPatients.xlsx”.

Table 5-4. Graft Failure Rates, Files and Table Functions for Transplant Patient Groups stratified by Age and Donor Type

Transplant Patient Groups	Comma Delimited file	Name of the Table Function
Living Donor, Age 18 -44	LD18_44GraftFailure.csv	GraftFailureTFLD18_44
Living Donor, Age 45 -54	LD45_54GraftFailure.csv	GraftFailureTFLD45_54
Living Donor, Age 55 -64	LD55_64GraftFailure.csv	GraftFailureTFLD55_64
Living Donor, Age 65+	LD65PlusGraftFailure.csv	GraftFailureTFLD65Plus
Deceased Donor, Age 18 -44	DD18_44GraftFailure.csv	GraftFailureTFDDKT18_44
Deceased Donor, Age 45 -54	DD45_54GraftFailure.csv	GraftFailureTFDDKT45_54
Deceased Donor, Age 55 -64	DD55_64GraftFailure.csv	GraftFailureTFDDKT55_64
Deceased Donor, Age 65+	DD65PlusGraftFailure.csv	GraftFailureTFDDKT65Plus

During simulation, the graft failure rate is updated daily for each transplant patient by looking up in the corresponding table function based on the number of days post-transplant. The graft failure rates are then passed to an event named “graftFailed” as the hazard (departure rate, i.e. chance of departure per day) for transplant graft failure. When graft failure occurs, the “graftFailed” event will send a “Graft Failed” message to the person in the “Transplant” state, and the patient will return to the “Dialysis” state in the DiabetesESRD statechart. At the same time, the patient will move from the “FunctioningKidney” state into the “AssessmentAndWaiting” state in the “AssessmentStages” statechart.

5.5. Rate of Living and Deceased Donor Transplant Operations in Saskatchewan

The rates of living and deceased transplants determine how many living and deceased donor transplants for DM-ESRD patients will take place each year in Saskatchewan. Ideally, if we know the number of DM-ESRD patients who received transplants each year, then per day rates can be calculated by dividing the counts by the number of days in a year. However, the counts of living donor and deceased donor transplants for DM-ESRD patients in Saskatchewan are not readily available; we therefore use two pieces of historical data for estimating the counts: the count of diabetic patients receiving kidney transplants (regardless of transplant type) between year 1983 and 2009 in Saskatchewan, and the breakdown of the incident transplant cases between living donor type and deceased donor types for ESRD patients in Saskatchewan for the years between 1992 and 2007.

The total annual number of transplants that have taken place for DM-ESRD patients in Saskatchewan between years 1983 and 2009 were provided to us by CORR through a special data request as shown in the first column of Table 5-6. This data is specific to DM-ESRD patients but it is not broken down by the transplant donor type. To split the total count of the incident transplant cases between living and deceased donor type, we used the proportion of living donor vs. deceased donor transplants for Saskatchewan ESRD patients as a whole (regardless of cause) as an estimate. The diabetic transplant patients might not follow the exact breakdown between living and deceased donor transplants as ESRD patients with all types of primary diagnosis. However, we were unable to locate data regarding the breakdown on the type of transplants specific to DM-ESRD patients.

The proportion of transplants for each donor type is calculated based on separate counts of ESRD patients receiving living donor and deceased donor type of transplant in Saskatchewan

between year 1992 and 2007. The historical data was found in the “2007 – 2008 Highlights” published by the Saskatchewan Renal Program, and is listed under the second and the third columns in Table 5-5. The proportions were calculated and listed in the last two columns in the same table. The historical data only provided data to compute proportions between year 1992 and 2007. For years when historical data was not available (i.e. between year 1983 and 1991; and year 2008 and 2009), the proportions were extrapolated in Excel based on the rates of known years. The breakdown in transplant type for ESRD patients of all primary diagnoses are applied to the total number of the transplant for Diabetic-ESRD patients in Table 5-6,, and the number of DM-ESRD patients receiving living and deceased donor transplants were estimated. The split count of transplant cases for each donor type were further divided by the number of days in a year to obtain per day rates, which were saved into two table functions in the model: “LDKTDailyRateLookup” and “DDKTDailyRateLookup”.

During simulation, the events “PatientsReceiveDDKT” and “PatientsReceiveLDKT” use the transplant hazards from table functions “LDKTDailyRateLookup” and “DDKTDailyRateLookup”, then schedule the occurrence of the transplant according to the rates, and finally send messages to patients on the transplant waiting list to receive a kidney transplant. For the years that fall outside of the years where the rates are known, the table function will use the rates from the nearest year as an estimate.

Table 5-5. Historical Count of ESRD Patients Receiving Living and Deceased Donor Transplants in Saskatchewan between 1992 and 2007.

Calendar Yr	Living Donor	Cadaveric	TOTAL	Proportion of TX is Living Donor Type	Proportion of TX is Deceased Donor Type
'92	3	20	23	0.130435	0.869565
'93	5	19	24	0.208333	0.791667
'94	8	21	29	0.275862	0.724138
'95	3	23	26	0.115385	0.884615
'96	13	9	22	0.590909	0.409091
'97	17	16	33	0.515152	0.484848
'98	27	35	62	0.435484	0.564516
'99	16	35	51	0.313725	0.686275
'00	7	20	27	0.259259	0.740741
'01	8	28	36	0.222222	0.777778
'02	14	22	36	0.388889	0.611111
'03	7	25	32	0.21875	0.78125
'04	14	18	32	0.4375	0.5625
'05	11	20	31	0.354839	0.645161

'06	8	21	29	0.275862	0.724138
'07	7	25	32	0.21875	0.78125

Table 5-6. The Historical Estimated Count of Diabetic Patients Receiving Living Donor and Deceased Donor Transplants in Saskatchewan.

Year	Count of Transplant for DM-ESRD	Proportion of living donor TX	Proportion of Deceased donor TX	Count of DM-ESRD Receiving Living Donor TX	Count of DM-ESRD Receiving Deceased Donor TX
1983	2	0.260592	0.739408	1	1
1984	6	0.263591	0.736409	2	4
1985	5	0.266591	0.733409	1	4
1986	5	0.269591	0.730409	1	4
1987	7	0.27259	0.72741	2	5
1988	8	0.27559	0.72441	2	6
1989	7	0.278589	0.721411	2	5
1990	6	0.281589	0.718411	2	4
1991	5	0.284588	0.715412	1	4
1992	7	0.130435	0.869565	1	6

1993	3	0.208333	0.791667	1	2
1994	4	0.275862	0.724138	1	3
1995	7	0.115385	0.884615	1	6
1996	5	0.590909	0.409091	3	2
1997	6	0.515152	0.484848	3	3
1998	13	0.435484	0.564516	6	7
1999	12	0.313725	0.686275	4	8
2000	7	0.259259	0.740741	2	5
2001	6	0.222222	0.777778	1	5
2002	8	0.388889	0.611111	3	5
2003	13	0.21875	0.78125	3	10
2004	4	0.4375	0.5625	2	2
2005	7	0.354839	0.645161	2	5
2006	5	0.275862	0.724138	1	4
2007	3	0.21875	0.78125	1	2
2008	6	0.335581	0.664419	2	4

2009	4	0.338581	0.661419	1	3
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5.6 Cost of Treatment

The various costs for treating ESRD patients were taken from one single data source, a published research study [34] reporting the direct medical cost for the recipients and donor of both living and deceased donor transplant based on data from the database for the Southern Alberta Transplant Program. Table 5-7 shows the cost item, the amount of cost in year 2008 dollars, and the corresponding model element. The transplant related cost was taken directly from the results of the above mentioned study, whereas the cost of HD and PD were not part of the study results but were used for comparisons with the transplant cost by the authors. In the model, the cost items were given as cost per year and were converted into per day cost because the accumulated costs are updated daily. This function is named “personDaysLivedCostUpdate”. The function counted the number of patients in each treatment modality at the end of the day, and calculated the daily total operation cost using formula (5.5).

$$Cost_t = Count_t \times Cost_i$$

- $Cost_t$ is the total cost for caring patients on a particular treatment modalities in the model at a particular day. $Cost_t$ does not include cost of transplant operations occur in that day.
- $Count_t$ is the number of patients receiving a particular treatment modality in the model at the end of day.
- $Cost_i$ is the average cost per day for caring patients in particular treatment modalities.

(5.5)

Table 5-7. Item, Cost, Sources, Dollar Value in Original Year, and Corresponding Model Element.

Cost Item	Original value (Year 2008 Value)	Model Element
Per-year cost for HD Patients	\$83,398	Variable named “HDperDayCost”
Per-year cost for PD (CAPD or CCPD) Patients	\$48,472	Variable named “PDperDayCost”
Cost for Living Donor Transplant Operation	\$ 20,108	Variable named “LDKTOpCost”
Donor related cost (living donor)	\$20,988	Variable named “LDKTDonorCost”
Cost for caring for patients who received a living donor transplant from day 0 to the day 90 after transplant operation	\$31,618	Variable named “LDKTFirst90PerDayCost”
Cost for caring patients who received a living donor transplant from day 91 to day 365	\$21,932	Variable named “LDKT91to365PerDayCost”
Per-year cost for caring patients who received a living donor transplant after the 1 st year	\$19,974	Variable named “LDKTAfter1stYearPerDayCost”
Cost for deceased donor transplant operation	\$23,818	Variable named “DDKTOpCost”
Donor related cost (deceased donor)	\$37,198	Variable named “DDKTDonorCost”
Cost for caring for patients who received a deceased donor transplant from day 0 to the day 90 after transplant operation	\$28,200	Variable named “DDKTFirst90PerDayCost”
Cost for caring for patients who received a deceased donor transplant from day 91 to day 365	\$25,903	Variable named “DDKT91to365PerDayCost”
Per-year cost for caring for patients who received deceased donor after the 1 st year	\$ 22,233	Variable named “DDKTAfter1stYearPerDayCost”

Year 2008 is chosen to be the year for reporting the cost output from the model. The costs projected by the model are in both the absolute value term and the discounted present value term, which is calculated basing on the standard 3% discount rate [40].

5.7 Risk of Death Prior to Developing ESRD and Risk of Developing ESRD

The risks of developing ESRD or dying prior to developing ESRD for diabetes patients were studied in a competing risk analysis by Ying Jiang in her Master's thesis [37]. Ying studied the diabetes population in Saskatchewan from 1980 and 2005. Hazards of death prior to developing ESRD (5.6), shows the form of the three year interval based Piecewise Exponential Hazard Model resulting from Ying's research:

$$h_i(t) = \lambda_{0j} \exp(\beta_1 x_{1i} + \beta_2 x_{2i} + \dots + \beta_k x_{ki})$$

- $h_i(t)$ represents the hazard function of a particular i^{th} patient at time t for time interval I_j , with $t \in I_j$, and $j=1, \dots, p$ representing indices of time intervals
- λ_{0j} is the baseline hazard for time interval I_j .
- $\beta_1, \beta_2, \dots, \beta_k$ are coefficients of exploratory variables.

(5.6)

Table 5-8 and Table 5-9, list the Coefficients for covariates in the three year interval based Piecewise Exponential Hazard Model. In the model, the risk of dying prior to developing ESRD and the risk of developing ESRD are both calculated using Ying's piecewise exponential hazard model, which were firstly converted into per-day hazards and supplied to the model transitions from the diabetes states (i.e. state named "DM1to3Y", "DM25to27YBeyond", etc.) to the "DeathBeforeESRD" state or the "ESRD" state in the "DiabeticESRD" statechart.

Table 5-8. Coefficients for variables in the Piecewise Exponential Hazard Model for Risks of Developing ESRD

Variable	β estimate
Intercept	-4.55
Male	0.49
FN	1.09
Diabetes age	-0.01
j1	-2.17
j2	-2.21
j3	-1.93
j4	-1.50
j5	-1.07
j6	-0.48
j7	-0.34
j8	-0.45

Table 5-9. Coefficients for variables in the Piecewise Exponential Hazard Model for Risks of Death Prior to Developing ESRD.

Variable	β estimate
Intercept	-6.71
Male	0.82
FN	1.20
Diabetes age	0.08
Male*Diabetes age	-0.01
FN*Diabetes age	-0.015
j1	-1.75

j2	-1.76
j3	-1.47
j4	-1.16
j5	-0.86
j6	-0.59
j7	-0.30
j8	-0.06

5.8 Probability Density Used for Selecting Patients for Kidney Transplant Assessment

Not every patient on dialysis will get sent for transplant assessment because their age and health condition. In general, younger patients tend to be healthier, and thus have a greater chance to be sent for assessment. In the model, based on the suggestion of Drs. Kappel and Dyck, we implemented a simple logic representing the relationship between age and percentage of patients in that age range that will be sent for transplant assessment, as shown in Table 5-10.

Table 5-10. Percentage of Patients getting assessed for Transplant based on Age

Age	Percentage of Patients Sent for Transplant Assessment
65 and younger	100%
66 to 75	25%
76 and older	0%

The estimated percentage of patients who are sent for assessment is then used as the probability that an individual patient (of a particular age) will be assessed. The logic is implemented in the function named “isEligibleForTransplantAssessment”, which yields a true or false value representing whether the patient will be sent for assessment. Each time when a patient enters the assessment stage, their eligibilities for receiving a transplant assessment will be re-determined by the same function “isEligibleForTransplantAssessment”. In other words, patients with failed kidney transplant, prior to send them for transplant assesment, will get re-

evaluated following the same logic as those patients who never had a transplant before. As shown in Figure 5-4, if patients are sent for assessment, they will go to the “WorkUpStage”; otherwise, they will go to the state named “NotSuitableForTx” in the “AssessmentStages” statechart.

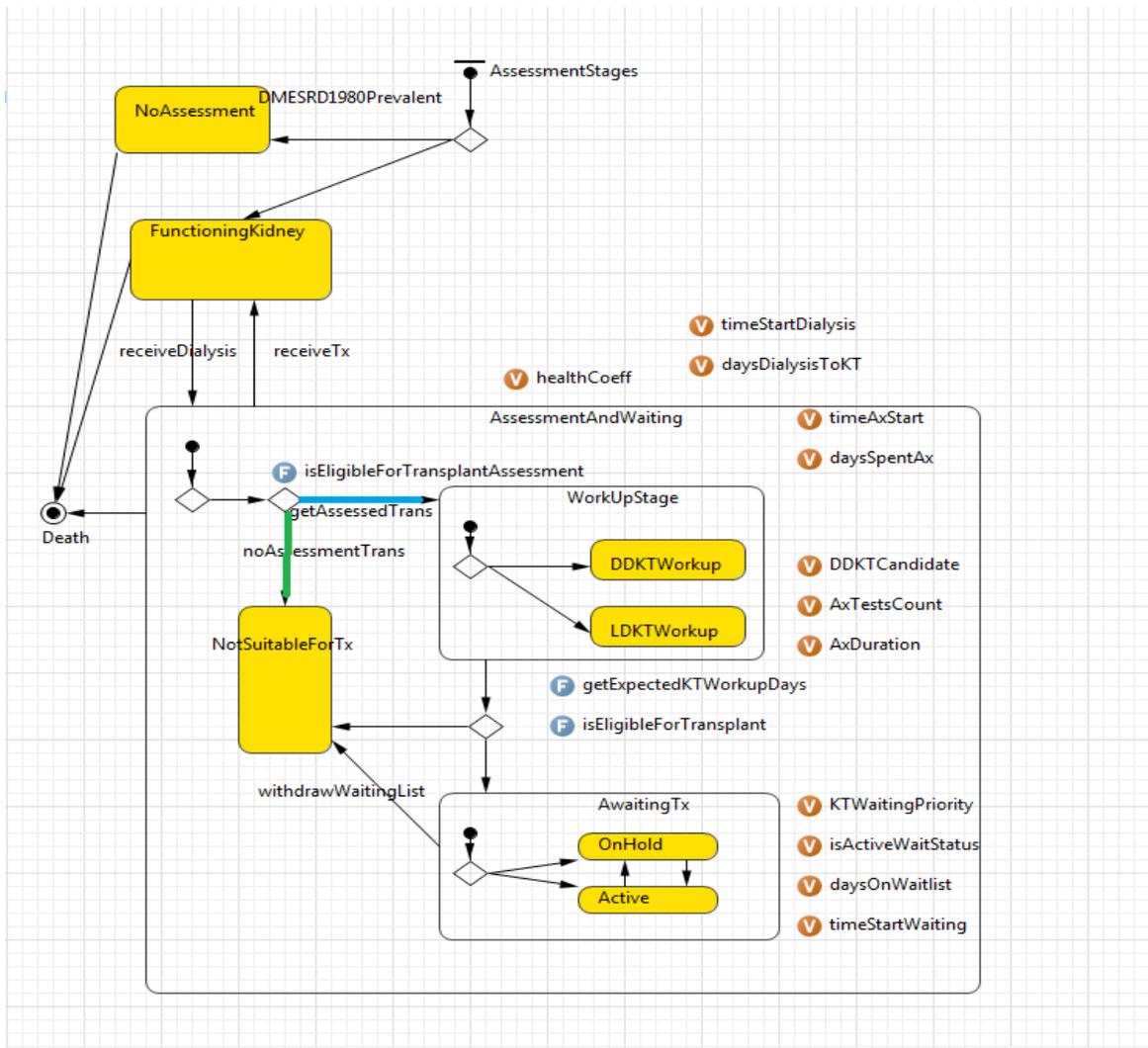


Figure 5-4. Transitions to the “WorkUpStage” state and “NotSuitableForTx” state

CHAPTER 6

CALIBRATED PARAMETERS

This chapter illustrates how parameters lacking reliable historical sources got set by calibration process. The calibration process makes estimates on those parameters by constantly re-adjusting the parameters and comparing the model output with desired value until a match is achieved. In this chapter, all the calibrated parameters in the model will be discussed in details, including which model transitions are parameterized with them, which model output can be affected by a change in those parameters, and the value of those parameters that were estimated by the calibration process.

6.1 Rate of Withdrawing from Transplant Waiting List

Patients can withdraw from the waiting list due to health and personal reasons, which is represented with a separate transition “withdrawWaitingList” in the model to distinguish with the other two causes for leaving the waiting list such as getting kidney transplantation and death while on the waiting list. Following the “withdrawWaitingList” transition, some patients will move from the “AwaitingTx” state to the “NotSuitableForTx” state. The per day rate of withdrawing from the transplant waiting list is represented by a variable named “withdrawWaitListAjd”, and is used in the transition “withdrawWaitingList”. There is no data on the rate of withdrawing from the waiting list. However, Table 6-1 shows that for the provinces where the number of withdrawals and deaths were tracked for patients on the waiting list, in more than half of the cases, there are more withdrawals than death for the same waiting list.

Table 6-1. Death and Withdrawals on Transplant Waiting List in Canadian Provinces Found in CORR Annual Reports

Year	Alberta		Ontario		Quebec	
	Death	With drawals	Death	With drawals	Death	With drawals
2011 (ref-table 2C, 2011 report)	13	21	36	78	20	58
2010 (ref-table 2B, 2010 report)	16	23	34	149	55	14
2009 (ref-table 2B, 2009 report)	11	14	29	11	42	27

Based on the observations regarding the count of deaths and withdrawals on the waiting list, during calibration, we adjusted the rates of withdrawal so that the number of patients withdrawing from the waiting list within a given period is 1.5 to 2 times higher than the number of deaths on the waiting list in that same period. Figure 6-1 is generated based from the simulation output, and comparison is made between the annual number of withdrawals and deaths on waiting list.

Withdraw from Waitlist

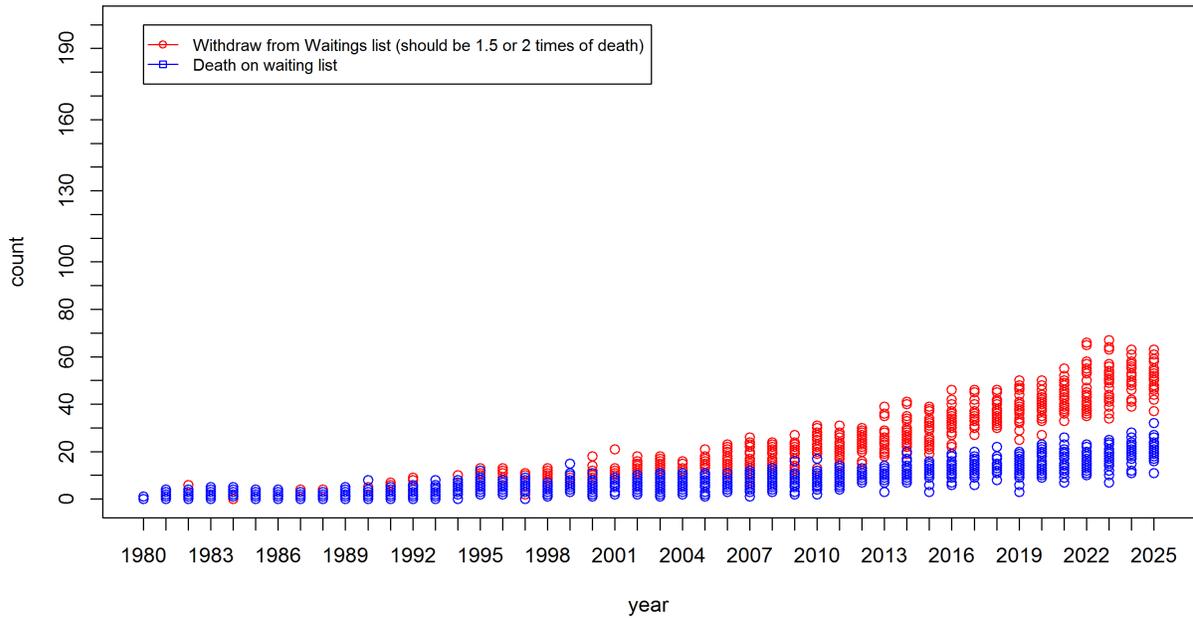


Figure 6-1. Result from Model Simulation Regarding the Withdrawal and Deaths on Waiting List

6.2 Assessing the Eligibility for Kidney Transplant

The process of assessing patients' transplant eligibilities is represented in the model in a very simplified version. In practice, thorough examinations and evaluations are conducted to assess a patient's health conditions. Only suitable patients are sent for transplantation. As observed, healthier patients, more often younger, are more likely to be selected as transplant candidates. In the model, a health indicator is designed to represent a patient's state of health, and it is used in assessing a patient's eligibility for kidney transplant. There is not enough information available regarding a patient's health and a valid algorithm has not been developed for measuring a patient's health conditions. Therefore, in this model, a simple formula was designed for assigning values to the health indicator based on patient's age, with an eye towards future extendibility to incorporate additional factors. The formula used in the model is shown in

equation 6.1. In general, a patient’s health will decline with age. A calibrated parameter “ageHealthCorr” is used to signify the degree of impact of age on overall health. Also, the formula takes into consideration the fact that patients’ health conditions might vary among individuals even at the same age, and the variable “healthRandom” is used to denote other variations in patient’s health not captured by age. The value of “healthRandom” is drawn from a Weibull distribution, however, because the only the ranking -- and not the absolute value -- of the parameter is considered, the result is not dependent on the distribution used.

$$\text{HealthIndicator} = e^{(-1.0 \times \text{ageHealthCorr} \times \text{CurrentAge})} \times 1000 \times \text{healthRandom} \quad (6.1)$$

The value of HealthIndicator is set by the formula when a patient finishes the assessment (leaves “WorkUpStage” state), and it is evaluated against the cut off value for passing transplant assessment in the function named “isEligibleForTransplant”. Patients with a value of health indicator greater than the cut off value will pass the assessment for transplant and be put on the waiting list (go to the “AwaitingTX” state).

Both the cut off value for passing assessment and the parameter ageHealthCorr mediating the relationship between age and health were calibrated through simulation. When a higher value is set for parameter ageHealthCorr, the health indicator of older patients will get lower values. Thus fewer older patients will pass the assessment, and the average age of receiving kidney transplant will be younger. The historical data regarding the average age of receiving a transplant can be used to compare with model results, and aid with making further adjustment of the parameter ageHealthCorr. However, the correlation factor between age and health (parameter ageHealthCorr) is not the only force impacting the average age of receiving transplant. Adjusting the cut off value of the health indicator can also change the average age of

receiving transplant. With a lower cut off value of the health indicator, more patients at older age will pass the assessment, thus increasing the age of patients receiving transplants. Moreover, as the cutoff drops, with more patients eligible for transplant and placed on waiting list, the length of a wait becomes longer, so that a patient's age will be older at the time of the transplant due to the longer wait. Therefore, the average age of receiving transplant should be matched during calibration when adjusting both the parameter ageHealthCorr and the cut off value for transplant.

In Figure 6-2 and Figure 6-3 below, the calibration results were compared with historical data regarding the average age of patients receiving deceased and living donor kidney transplant. The model output was shown in 2D histogram, whereas the historical data were plotted as lines in blue color.

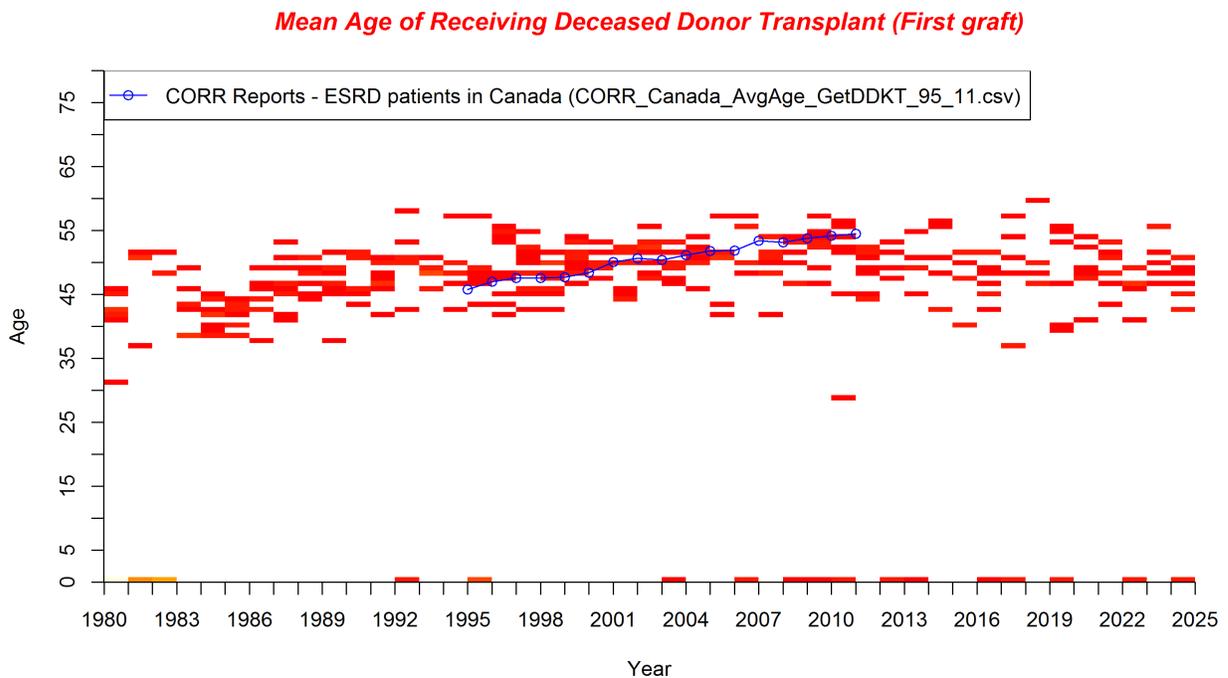


Figure 6-2. Model Result - Mean Age of Receiving DDKT (First Graft)

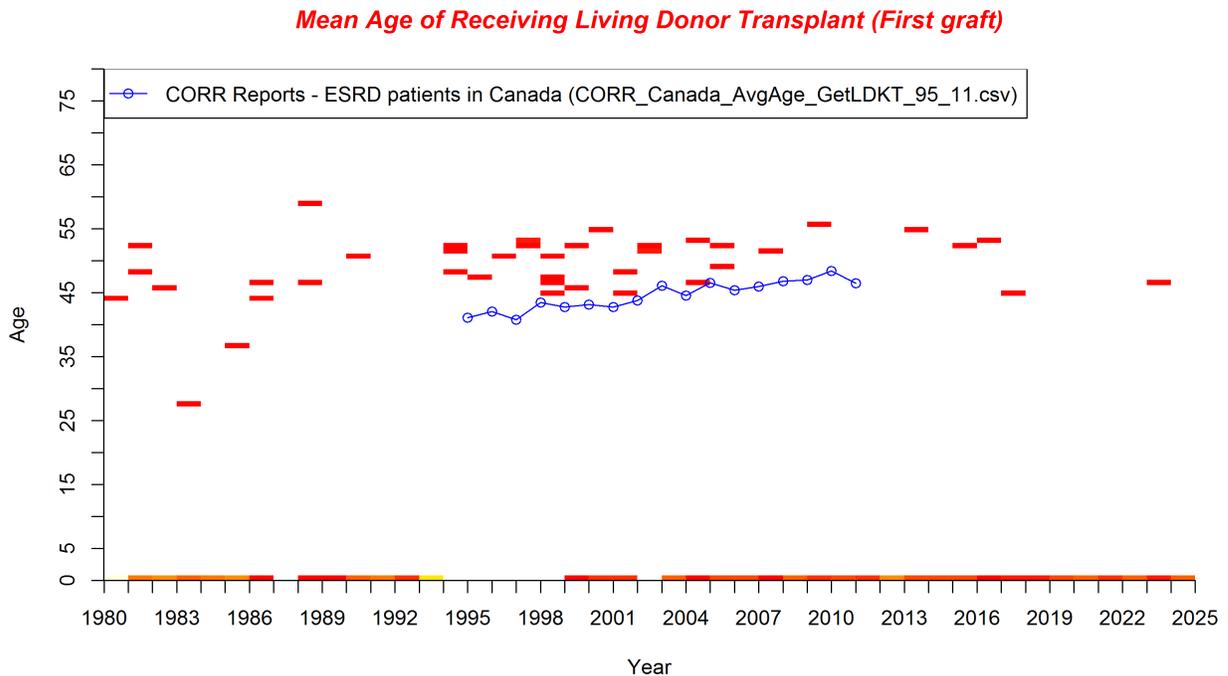


Figure 6-3. Model Result - Mean Age of Receiving LDKT (First Graft)

In addition to the mean age of receiving a transplant, there are another two model outputs which should be examined while calibrating the cut off value for transplant eligibility: the head count on the wait list and the median days spent on dialysis prior to having a kidney transplant. Lowering the cut off value will allow more patients on the waiting list, and lengthening the wait on dialysis. However, the wait list head count is not only controlled by the cut off value, but also depends on the withdraw rate from waiting list, death on the waiting list (mortality risk for HD and PD patients), rate of transplant and the duration of the assessment. All the factors impacting head count on the waiting list also play roles in changing the wait time on dialysis.

6.3 Duration of Assessment for Transplant

The duration of the assessment is also a calibrated parameter due to the limited amount of information available regarding the assessment process. A few assumptions were made regarding the assessment process, and relevant parameters were set through calibration. Firstly, for patients who had a graft failure, return to dialysis and were sent for transplant assessment again, if their last transplant was done within a year, we assume that assessment will take less time since many tests were completed not long ago. Secondly, for patients who never had a transplant before or whose most recent transplant was over a year ago, the duration of assessment were assumed to depend on several factors: the number of the tests taken, the type of transplant for which a patient is preparing, and the average time required to complete a test in the assessment. All the above three impacting factors have been formulated into the distribution function to draw the days spent on assessment for each patient. More details can be found in Appendix C.

The calibrated parameters related to the assessment process are listed in Table 6-2. As discussed earlier, the duration assessment can be calibrated by comparing the model output of time spent on dialysis with the historical data (Figure 6-5 and Figure 6-6). A shorter assessment would bring more people on the waiting list, thus the model result regarding head count on waiting list (Figure 6-4) should be inspected during calibration.

Table 6-2. Calibrated Parameters Related to the Duration of Assessment

Item	Value	Model Element
Minimum days required to complete assessment for patients whose last transplant is within a year from the current time	90	minAxDurationRKT
Average number of	3	Variable named “avgTestsAX”

tests for which patients were sent during assessment		
Average days spent on assessment prepared for living donor transplant based on the year when the assessment begins.	From year 1980 to year 2010, the average days spent on assessment ranged from 120 to 360 days for different time periods. In the earlier years, the assessment time was shorter.	Table Function “workUpDaysEstimatesLKDT”
The Ratio of days spent on assessment for deceased donor transplant to days for living donor transplant	1.3	Variable named “DDvsLDWorkUpDaysRatioAdj”

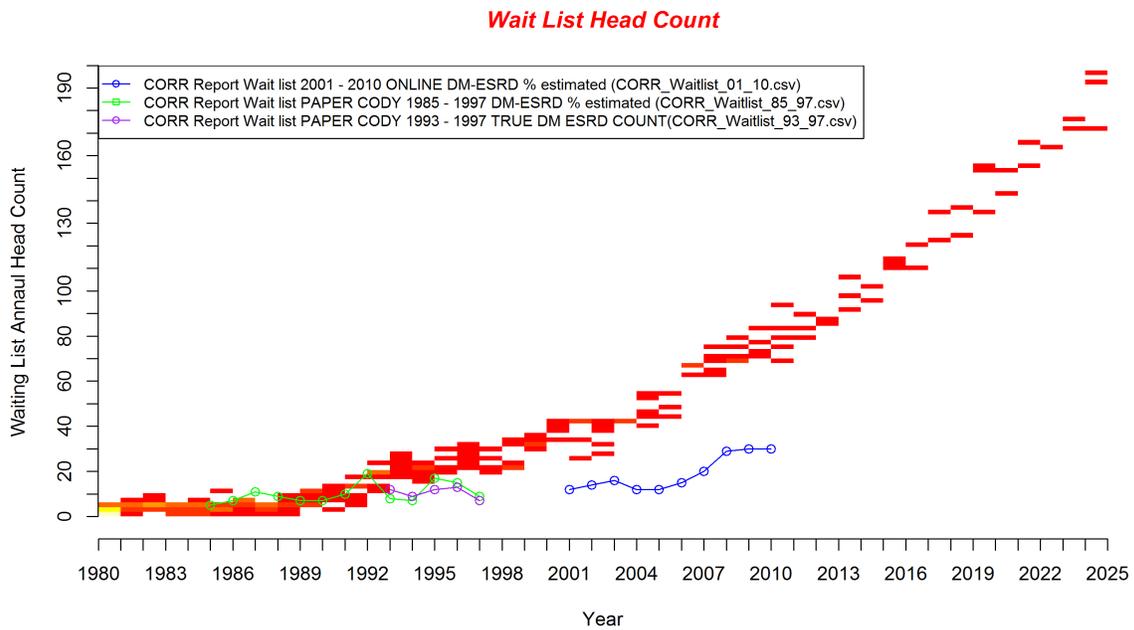


Figure 6-4. Comparing Model Result with Historical Data Regarding Head Count on Waiting List

Median Days On Dialysis Prior to DDKT

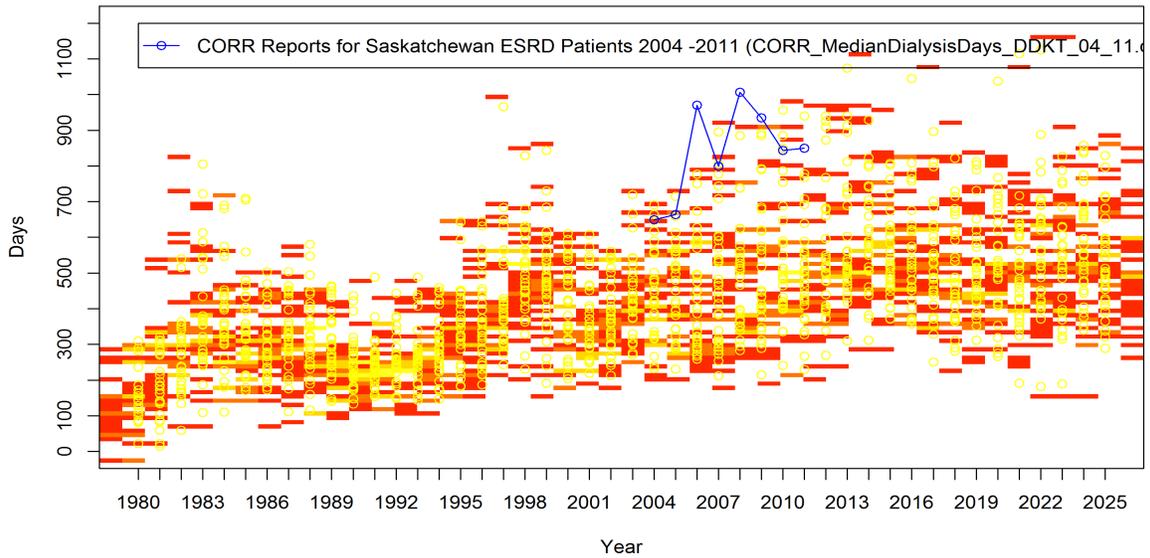


Figure 6-5. Comparing Model Result with Historical Data - Median Days on Dialysis Prior to DDKT

Median Days On Dialysis Prior to LDKT

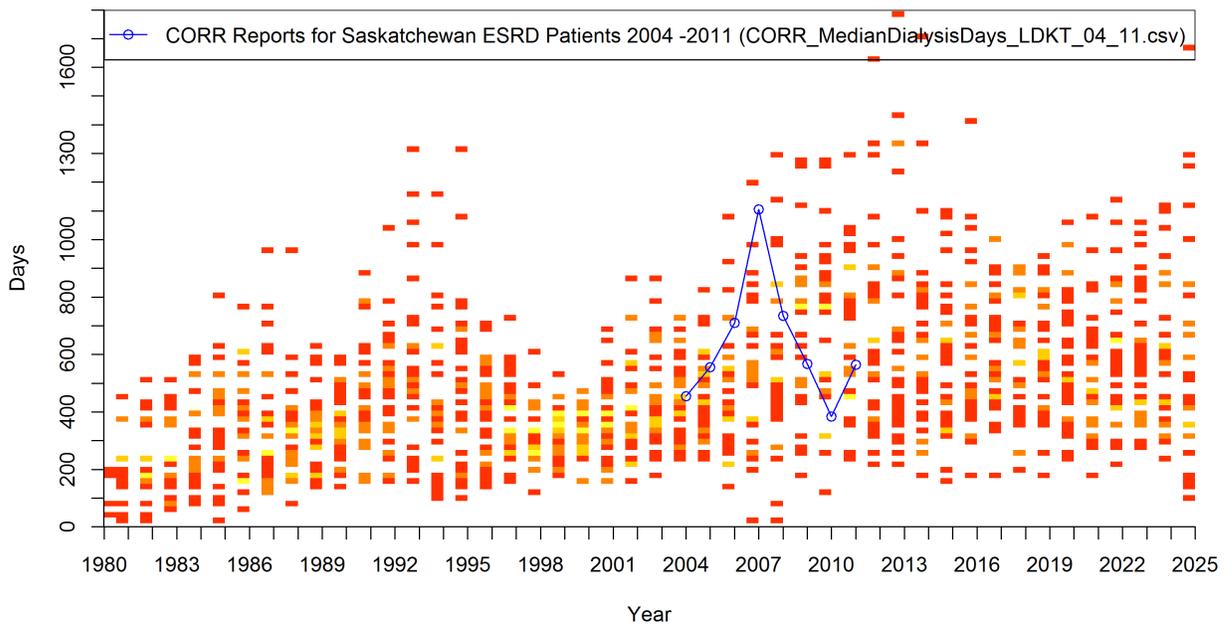


Figure 6-6. Comparing Model Result with Historical Data - Median Days on Dialysis Prior to LDKT

In summary, the health indicator, the cut off for eligibility of transplant, and the duration of assessment should all be examined and adjusted together through calibration. Most of the time, those parameters worked together in changing the model outputs.

6.4 Hazard Ratio of Calendar Period in Death Hazard Model for Dialysis and Transplant Patients

In the CORR reports published before 2000, the Cox regression analysis for the survival of the transplant and dialysis patients both included one important covariate: the calendar period when the treatment began in. As found in the report, patients whose dialysis or transplant took place in later time periods had much lower mortality risk compared to those whose treatments were started earlier [38]. The hazard model (6.2) currently used for estimating the hazard of death in our model was developed basing on patients who began their treatment from 1999 to 2008. Yet the hazard model was done without including the calendar year as a covariate. Recognizing that the calendar year covariate is missing from the Cox proportional hazards model currently used in the simulation model, an approximation was added back into the hazard function using an estimated hazard ratio. The “Calendar Period” is added as another covariate X_p , and the value of coefficient β_P is set through calibration.

$$H_0(t) = h_0(t) \times e^{(\beta_1 \times X_1 + \dots + \beta_P \times X_p)}$$

- $\beta_1 \dots \beta_P$ are the parameter estimates
- $X_1 \dots X_p$ Are the covariates.

(6.2)

The hazard ratio for the covariate “calendar period” is saved into the table function named “dialysisDeathHazardCalendarYearAdj” and “TXDeathHazardCalendarYearAdj” for the hazard models for dialysis patients and transplant patients respectively. As shown in Table 6-3, estimates of the coefficient for the earlier time period has a much higher value, which will increase the mortality hazard for patients who began treatments in earlier years. When calibrating the hazard ratio for covariate “calendar period”, the prevalent case count for transplant and dialysis patients can be compared with the corresponding historical data.

Table 6-3. Estimates for covariate “Calendar Period” in the Cox proportional hazards model for dialysis patients

Year	Estimates of Coefficient B for different value of calendar periods
1985	1.8
1990	1.6
1995	1.4
2000	1.0
2005	0.3
2010	0

Through calibration, we found that by adding the “calendar period” covariate to the hazard model for dialysis patients, the prevalent case count of dialysis patients resulting from the calibrated simulation run matched better with the historical data in comparison with model results of the model realizations without having the “calendar period” covariate. Therefore, the covariate “calendar period” will be added to the hazard function for dialysis patients.

On the other hand, the covariate “calendar period” will not be added to the hazard function in the simulation model for transplant patients. As shown in Figure 6-7, there is already a gap existing between the prevalent case counts of transplant patients with the historical count without adding the “calendar covariate”. With the “calendar period” covariate added, the gap

between model result and historical data will grow even bigger. Before making further adjustment the hazard function with the “calendar covariate”, we prefer to investigate the cause of gap between model result and historical data first, which is one of the future works out of the scope of this thesis. The model variable “TXDeathHazardCalendarYearAdj” having the values of the hazard ratio for covariate “calendar period” for transplant patients will remain in the model as a place holder until investigation of the gap completes.

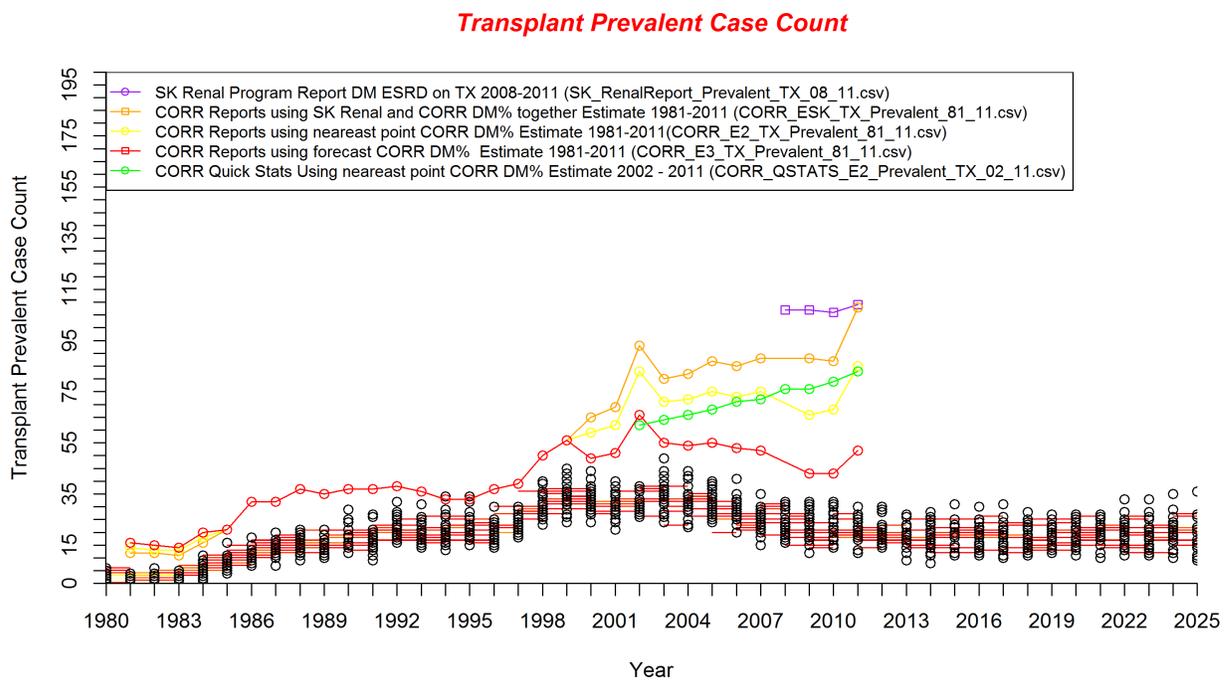


Figure 6-7. Gaps in Transplant Prevalent Case Count between model results and the historical data

6.5 Pre-Emptive Transplant Rate and Type

The pre-emptive transplant rate and type were used to schedule the occurrence of pre-emptive transplants and the type of pre-emptive transplants in the model. Currently in the model, the rate of pre-emptive transplant is set to zero because it is rare to have pre-emptive transplants

in Saskatchewan for all ESRD patients, and it is even rarer for DM-ESRD patients. Until there is data available regarding to the count of the pre-emptive transplant for DM-ESRD patients, the rate of the pre-emptive transplant will remain as zero in the model.

CHAPTER 7

MODEL OUTPUT

This chapter focuses on the output collected from model realizations. It is broken into two sections: section 7.1 is devoted to the high level statistics collected on model population, and section 7.2 describes a database designed and created for saving individual level data for each patient in the model. The high level and individual level output each offer different benefits: high level statistics provide a quick summary of the simulation results and can be used in model validation and sensitivity analysis; whereas individual level data saved in a database offers the potential for conducting research on longitudinal data .

7.1 Statistics Collected on Model Population

Many statistics were collected on the model population when patients went through the important model process such as the diabetes to ESRD progression, receiving RRT treatments, being assessed for kidney transplant and waiting for the transplant operation. Due to space limit, only a few essential statistics are discussed in this section. The complete list of statistics collected during simulation is explained in Appendix A.

The choice of which statistics to be collected in the model is driven by availabilities of historical data, need in policy investigation and goal of the thesis. Since both the incident and prevalent case count were widely reported in the historical data, we collected the incident and prevalent case counts from many processes in the model.

The incident case count is the number of new patients entering a state or starting a process between Jan 1st and Dec 31st in a given year. For instance, the incident case count for HD summarized the number of patients beginning HD treatment in a given year

The prevalent case count is the number of the patients alive in a state or a process at Dec 31st of a given year. In the model, we collected the prevalent case count for patients having DM-ESRD. When the DM-ESRD prevalent case count reported by the simulation is compared with the corresponding historical data, it will help us determine correctness of the model.

In addition to the incident and prevalent case count, the cost is another essential output from the model because it serves as a metric in evaluating different scenarios in Chapter 8. Moreover, it is the goal of this thesis for making projection on cost. The per year cost measures the cost occurred in a given year for caring DM-ESRD patients. The accumulated cost reported the cost for caring DM-ESRD patients accumulated since the beginning of the simulation time (i.e. Jan 1st, 1980) to each year end (Dec 31st of a given year) during simulation period and up to the end of the simulation time (i.e. Dec 31st, 2025).

As mentioned above, there are many more statistics collected by the model but not discussed in this section. Appendix A has the full descriptions of those statistics, what they are and how they are collected.

7.2 Database for the Saskatchewan DM-ESRD Model

A relational database was created using MySQL to save the patients' demographic information and their activities during simulation run. The database offered modellers and policy makers the options to retrieve detailed history of individuals as well as to cross check the with the population statistics saved in the comma delimited files . The MySql database management system became our choice for implementing database because it is the most widely used database system, is open source software (and therefore imposes no cost), and because it can be easily integrated with model built in AnyLogic. A full description of the database created for this model can be found in Appendix D.

CHAPTER 8

VALIDATION AND RESULTS

In this chapter, a few selected model outputs were first compared with the corresponding historical trajectories for proving correctness of the model. Once we had confidence in the model results, a total of nine scenarios were set up to run in the model so that the effects of varying parameters values can be investigated. The observed impact on model output is used for both sensitivity analysis and policy evaluation. Lastly, the projections made by the model were presented together with limitations in the last two sections of this chapter.

8.1. Model Validation and Sensitivity Analysis

Model outputs were validated against various sources of historical data to enhance confidence in the model. Only a subset of the output listed in section 7.1 was selected for model validation. The selection depended on availability of the corresponding empirical data for the Saskatchewan DM-ESRD population.

The historical data used for validating model results were from sources such as the Saskatchewan Administrative database, the Saskatchewan Renal Program, special data requests filled by CIHI, and the data tables published in the CORR Annual Report between year 1981 and year 2012. Some historical data require some degree of processing before it can be used in comparisons with model outputs. As an example, while model output relates to Diabetic – ESRD patients, in many cases the empirical data were collected for all ESRD patients rather than being restricted to DM-ESRD patients. Thus, many historical data for Saskatchewan were processed so that a count for DM-ESRD patients was estimated from the count for all ESRD patients. The definition and the source of the historical data, and the details regarding how the data was processed were captured in the document named as “Technical Report – Historical

Data”. This document is among the supplemental materials of the thesis, and is available upon request to the author.

The comparisons made between model output and corresponding historical data were performed by visually inspecting the alignment of the trajectories created from the output values and the historical data values. A script was written in the statistical package R² to plot each model output and the corresponding historical data on one graph. To work with the stochastic nature of the simulation, we ran the model with 30 realizations, each associated with a different random number sequence (as triggered by distinct random number “seeds”). Each realization generated a set of output values. We decided to plot the values of a given output variable from all 30 realizations into a 2D histogram, so the most frequent values of the variable can be easily spotted. Sometimes there are multiple sources of historical data for comparison with a given output variable. However, in many cases, the historical data was only an approximation of what the output variable measures and might further involve some degree of approximate corrections. We decided to plot the historical data for a given output variable as lines onto the same graph where the output from the realizations was shown as 2D histogram. In this way, the difference between model results and historical data -- and even the differences existing among multiple historical sources -- can be examined in one place.

The prevalent case count of DM-ESRD patients is an essential output to be examined while attempting to raise confidence in the model because it is controlled by two main driving forces in the model: the inflow of patients who receive DM-ESRD diagnosis and the outflow of patients who died while being treated for ESRD. The inflow of patients receiving DM-ESRD is determined by the likelihood with which diabetes patients develop ESRD before death, which

² R is programming language and a software environment, which is used for statistical computing and creating graphics.

builds atop an already validated model from a previous Master's thesis [37]. To prove that the hazard of developing ESRD from diabetics is correctly built in our Saskatchewan DM-ESRD model, Figure 8-1 shows the close alignment between the two lines plotted using the historical data (on the one hand) and the 2D histogram plotted from the incident case count output by the model (on the other). When the inflow rates of DM-ESRD patients is matching well with reality, as long as the mortality rates of DM-ESRD patients and the initial DM-ESRD population is set up right, the number of patients living with DM-ESRD in the model at each year end should align with corresponding historical numbers. As shown in Figure 8-2, the prevalent case count output from the model, which counts number of DM-ESRD patients who are alive on Dec. 31 of a year, is compared with historical data from multiple historical sources. The names of the historical data files were given in the legend, which can be used as an identifier to locate more details regarding the historical data in one of the supplemental document for the thesis – “Technical Report – Historical Data”. For instance, in Figure 8-2, the purple line was created from historical data recorded in the file named “SK_RenalReport_Prevalent_HD_08_11.csv”, and the details regarding that data can be found in section A.3 of the document named “Technical Report – Historical Data”. Figure 8-2 demonstrates that the prevalent case count output from the model is in a close match with the historical data collected on the Saskatchewan DM-ESRD population, which lends confidence to believe the mortality hazards for DM-ESRD patients and the initial DM-ESRD population loading into the model were correct.

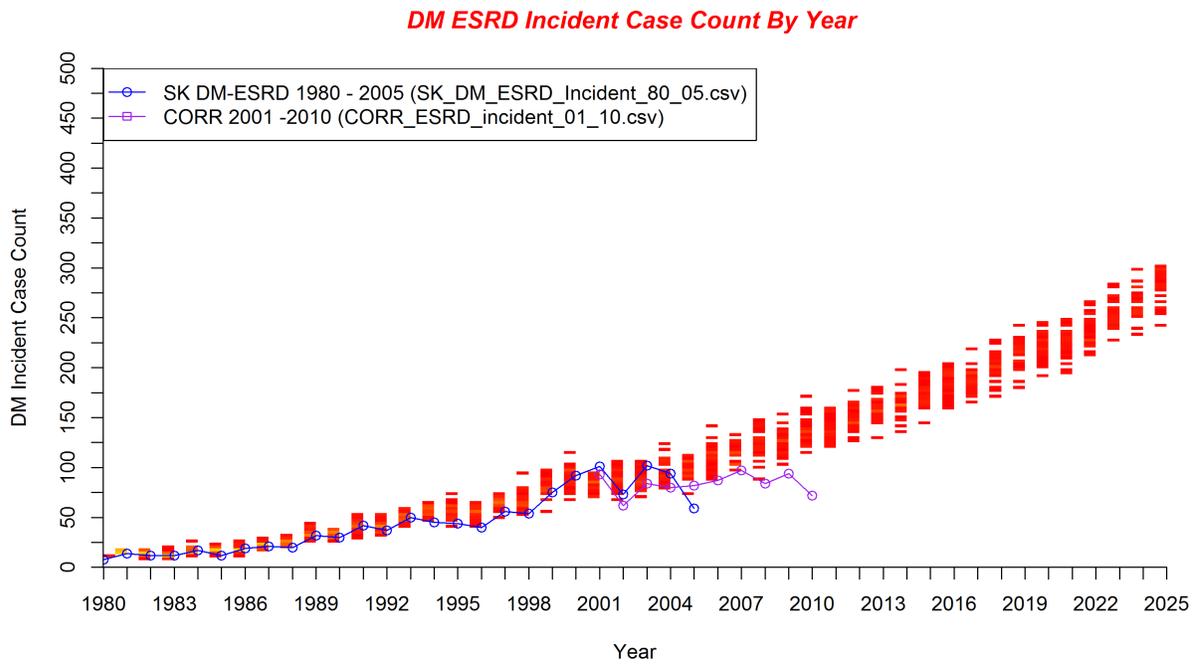


Figure 8-1. DM - ESRD Incident Case Count

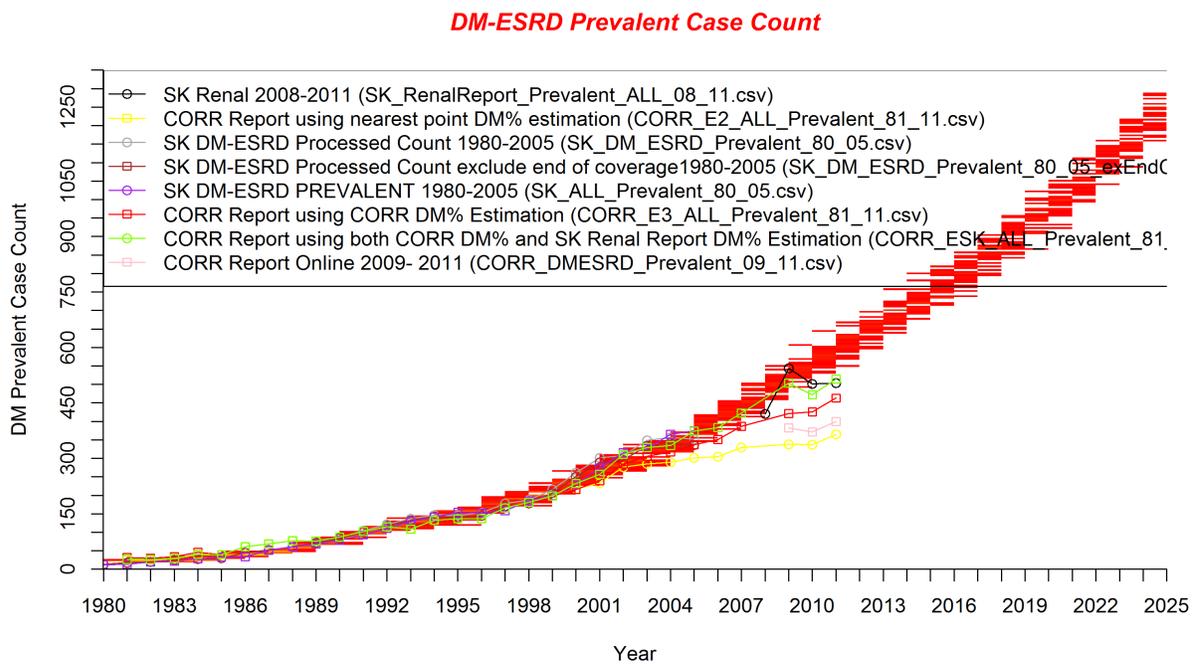


Figure 8-2. DM-ESRD Prevalent Case Count

The overall incident and prevalent case counts for all the DM-ESRD patients were essential for model validation, as are the incident and prevalent case counts broken down for DM-ESRD patients receiving different ESRD treatments. Verification of the incident case count for HD and PD patients can help indicate whether the allocation of the incident DM-ESRD patients to HD and PD is properly done in the model. As shown in Figure 8-3 and Figure 8-5, the model output on incident case counts of patients receiving HD and PD treatments can be compared respectively with the corresponding historical data. The fact that the model output matches well with the respective historic data suggests that the selection of HD vs. PD treatments is well captured in the model for diabetic-ESRD patients who recently receive ESRD diagnosis (DM-ESRD incident patients). Moreover, the prevalent case counts of model population receiving HD and PD aligns well with the respective historical data, as illustrated in Figure 8-4 and Figure 8-6. The successful validation of prevalent case counts on HD and PD treatments further suggests that the mortality risks for patients on those two treatments were accurate and properly implemented in the model. Other than the mortality rates, the transplant incident rates and graft failure rates can both play a role in changing the prevalent case counts of HD and PD patients in the model. As shown in Figure 8-7, the transplant incident case count in the model matched well with the historical data. The graft failure rate was not directly validated because the historical data on the failed transplant grafts were not available to us. So far, for the three ESRD treatment modalities, the incident and prevalent case count for HD and PD, and the incident case count for transplant were all successfully validated with historical counts. The validation on the transplant prevalent case count in the model is going to be discussed in detail below.

HD Incident Case Count Initial Treatment

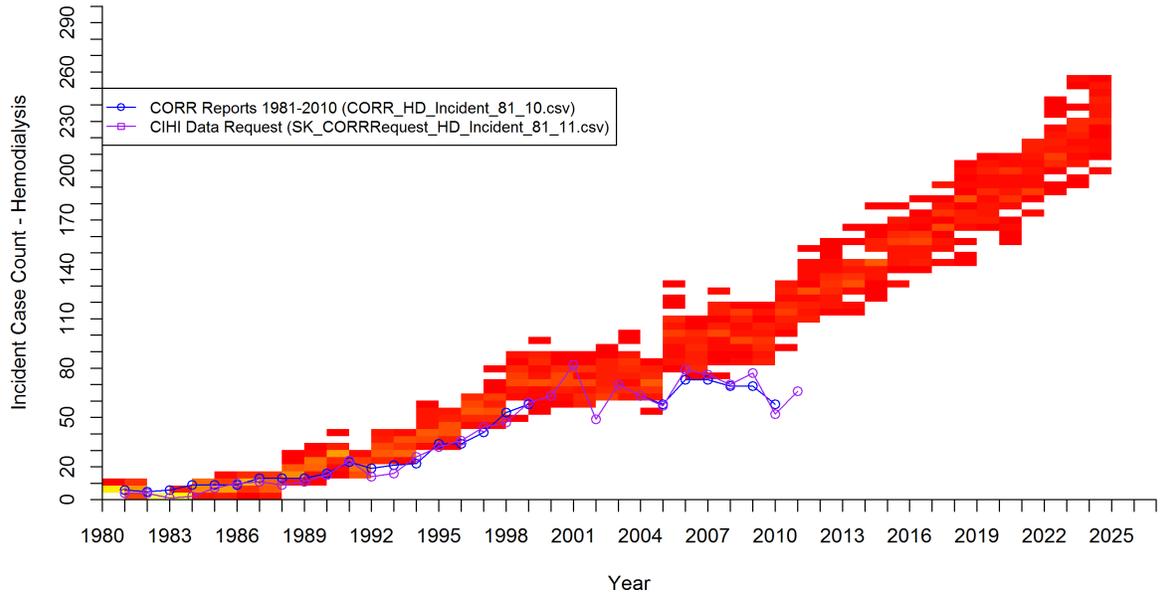


Figure 8-3. HD Incident Case Count

HD Prevalent Case Count

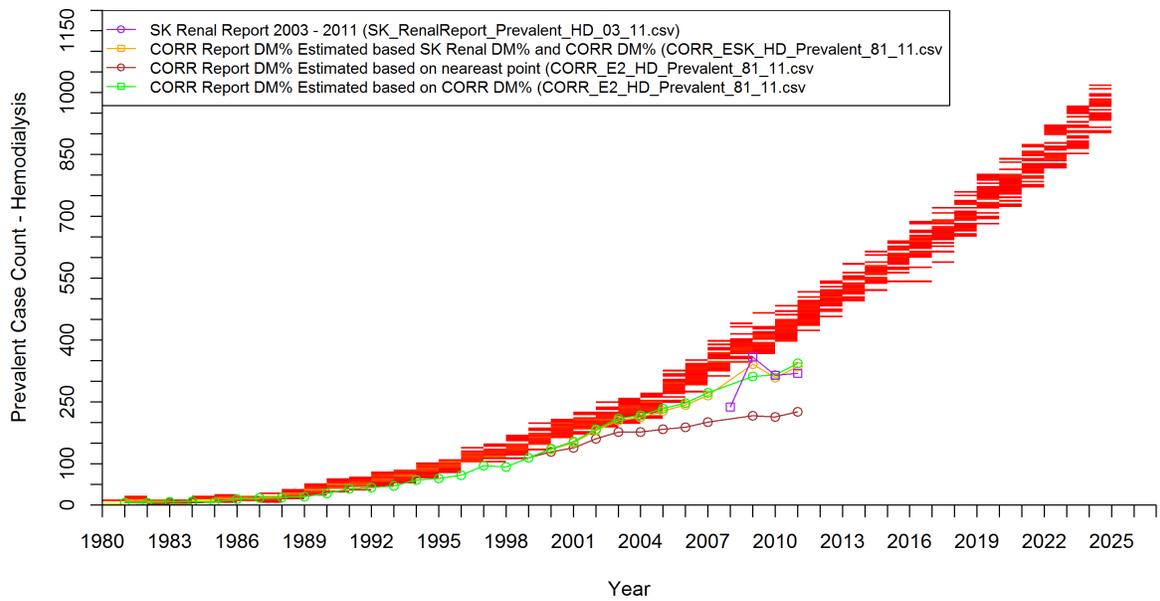


Figure 8-4. HD Prevalent Case Count

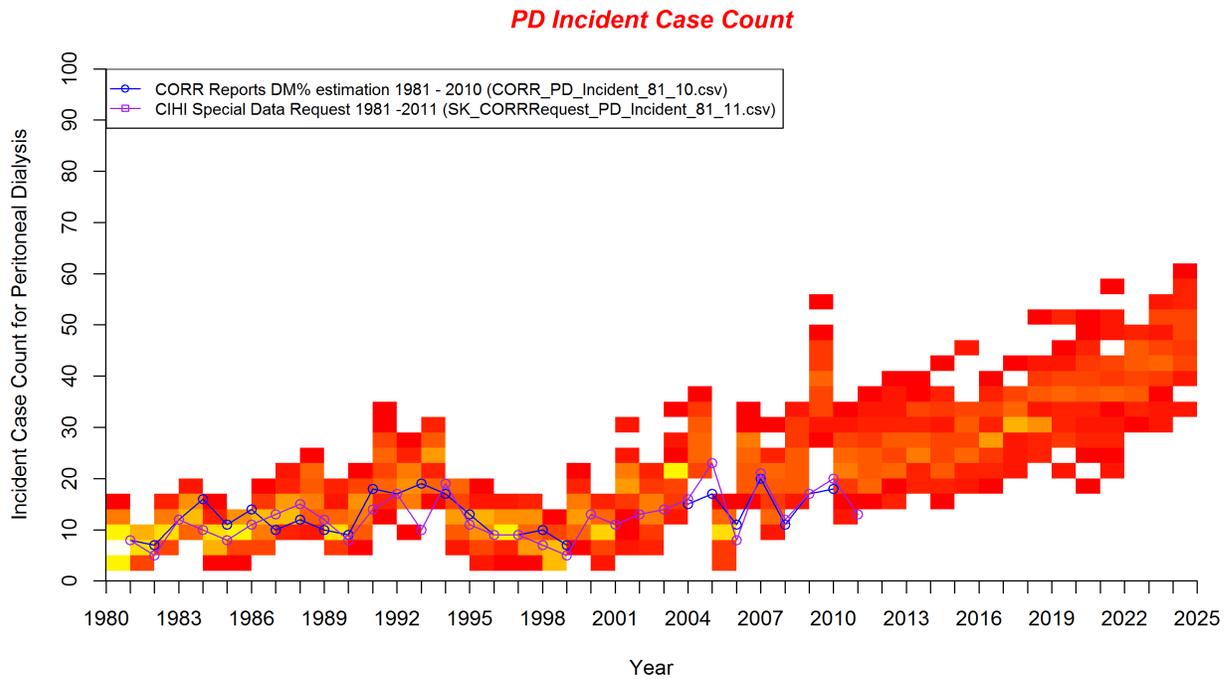


Figure 8-5. PD Incident Case Count

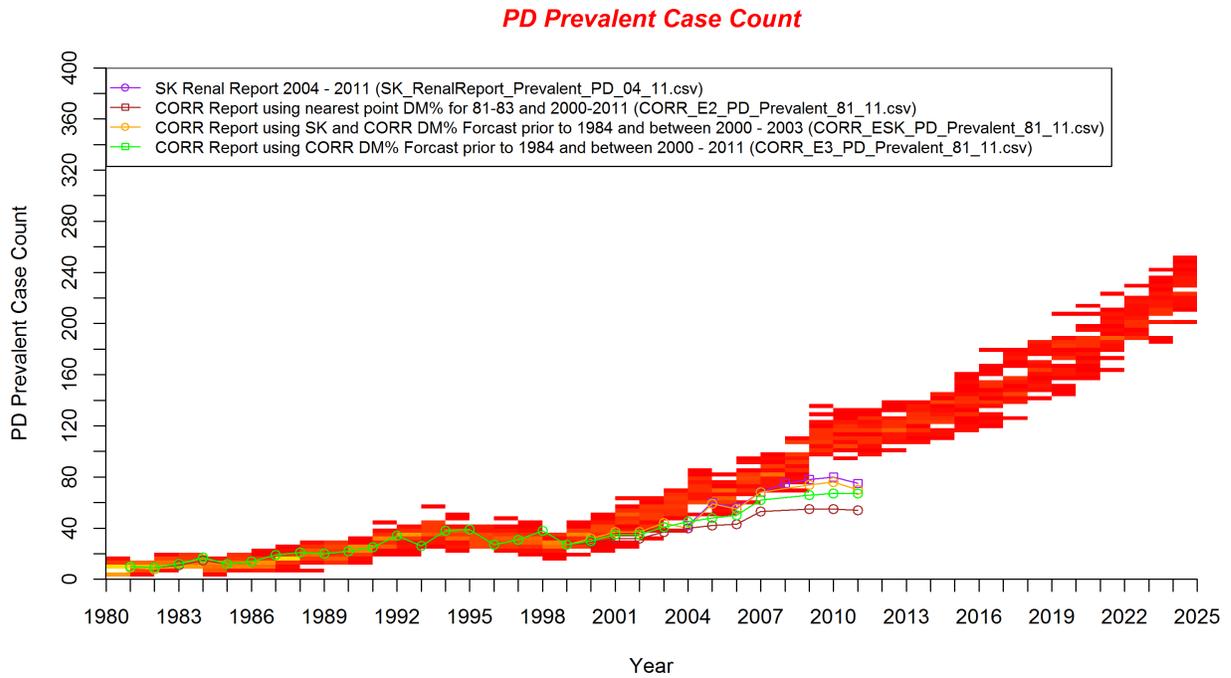


Figure 8-6. PD Prevalent Case Count

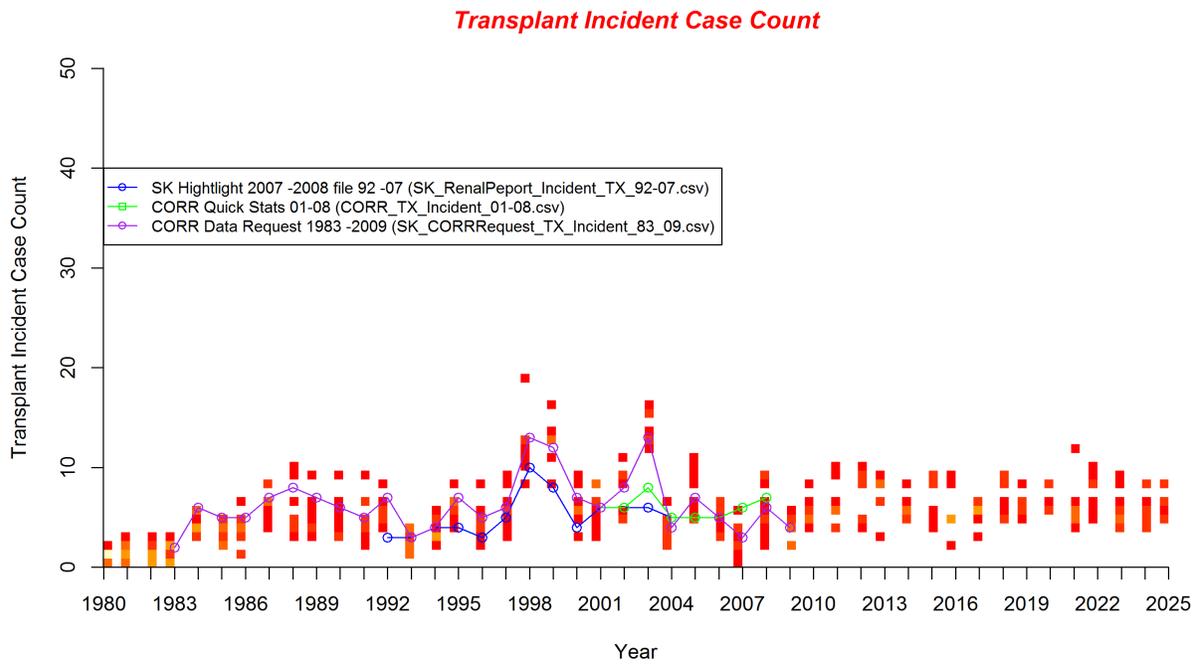


Figure 8-7. Transplant Incident Case Count

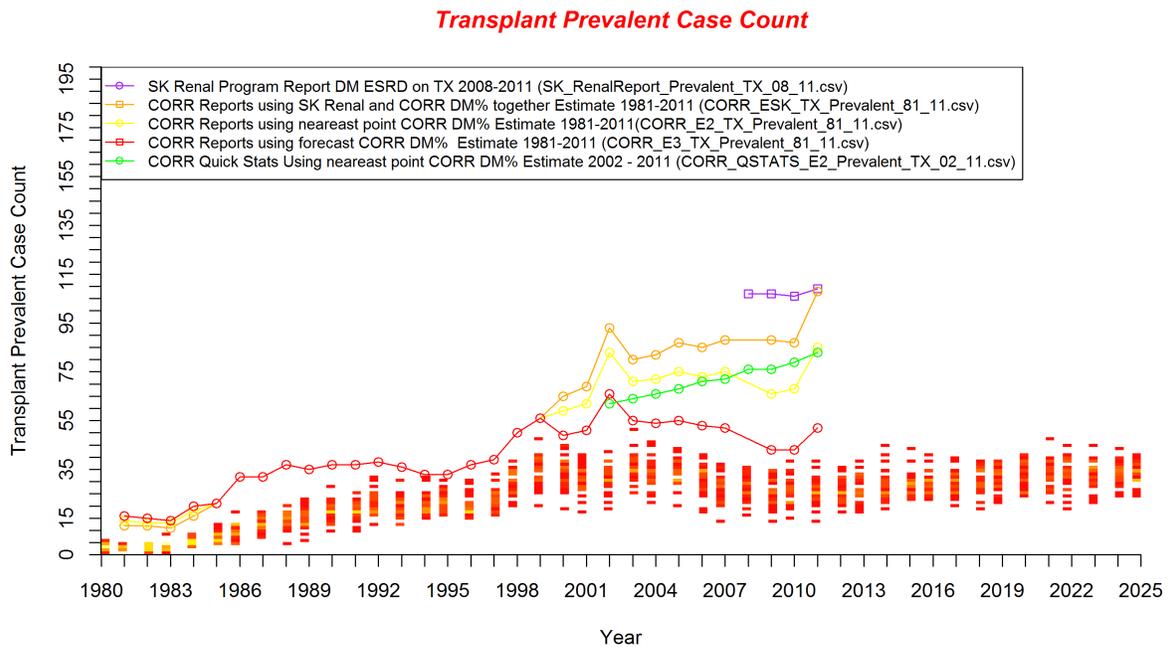


Figure 8-8. Transplant Prevalent Case Count

The transplant prevalent case count is the only model output that exhibits a significant disparity with the historical data. Figure 8-8 shows that the trend of the model output generally follows the trend exhibited in the historical data. However, the actual counts of the transplant prevalent cases in the model were consistently lower than the historical records. We tried to investigate the possible factors contributing to such differences such as the processes within the model and the quality of the historical data.

The list of factors in the model which could affect the transplant prevalent case count were each investigated in turn, such as the mortality hazards for transplant patients, the graft failure rates, the transplant incident case count, the time spent on assessment and waiting list, and selection of transplant candidates for transplants based on health indicators. After considering each of them, it does not appear plausible that reasonable errors in any one of them would be sufficient to increase the prevalent case count in the model to match the historical data.

In addition to investigating model parameters that could contribute to the discrepancy, the historical data was examined to see if they might include patients that are not counted in the model. In the model, the prevalent case counts are restricted to patients who first had diabetes and subsequently developed ESRD (presumably as a complication). All of the historical sources of transplant prevalent cases include in their counts patients who have both diabetes and ESRD, which means those counts include not only patients who develop ESRD after having diabetes, but also patients who first have ESRD and then develop diabetes after receiving a kidney transplant (a condition called post-transplant diabetes mellitus). After consulting with a nephrologist (Dr. Dyck), we learned that there are substantial number of kidney transplant recipients who will develop diabetes after the transplant, with this number elevated as a side effect of some of the treatments involved. As reported in patients from one Canadian transplant

center [35], as many as 9.8% of kidney transplant recipients developed diabetes post-transplant. Since the historical data do not single out patients with post-transplant diabetes mellitus, we do wonder whether the occurrence of post-transplant diabetes mellitus might account for most of the discrepancy between model and historical estimates of transplant prevalent cases.

A few other less important model outputs were also selected for model validation in addition to the prevalent and incident case count from different ESRD modalities. The mean age of initiating HD, PD or receiving living donor transplant or deceased donor transplant were compared with the corresponding historical data, as shown in Figure 8-9, Figure 8-10, Figure 8-11 and Figure 8-12. Moreover, outputs in relation to the kidney transplant assessment and the waiting list such as the median days spent on dialysis prior to kidney transplant and the head count on the waiting list were also being validated against historical data, as shown in Figure 8-13, Figure 8-14 and Figure 8-15. Above comparisons between model output and historical data yield a close match.

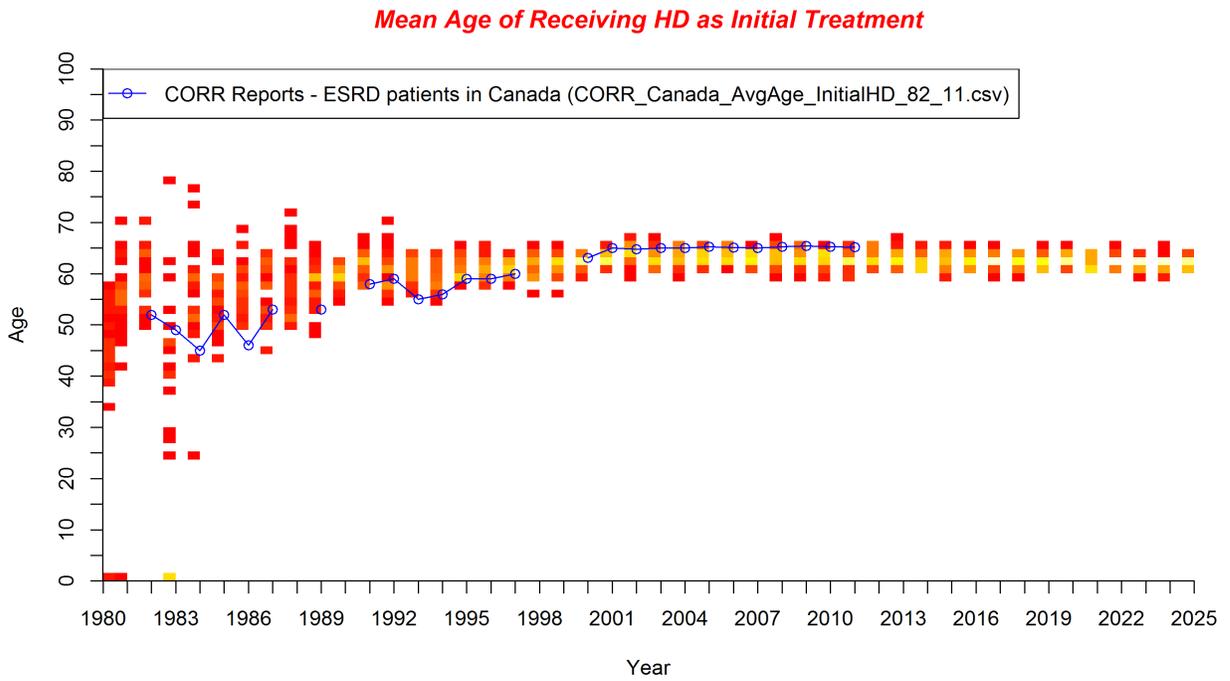


Figure 8-9. Mean Age of Patients Initiating HD

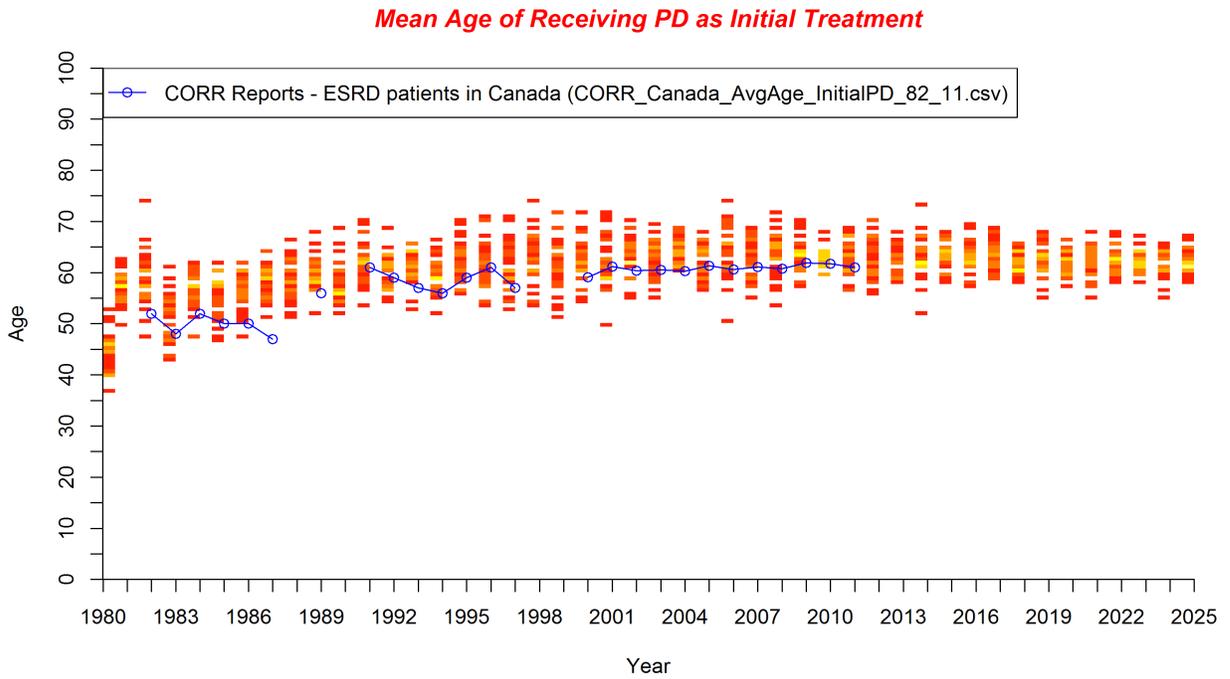


Figure 8-10. Mean Age of Patients Initiating PD

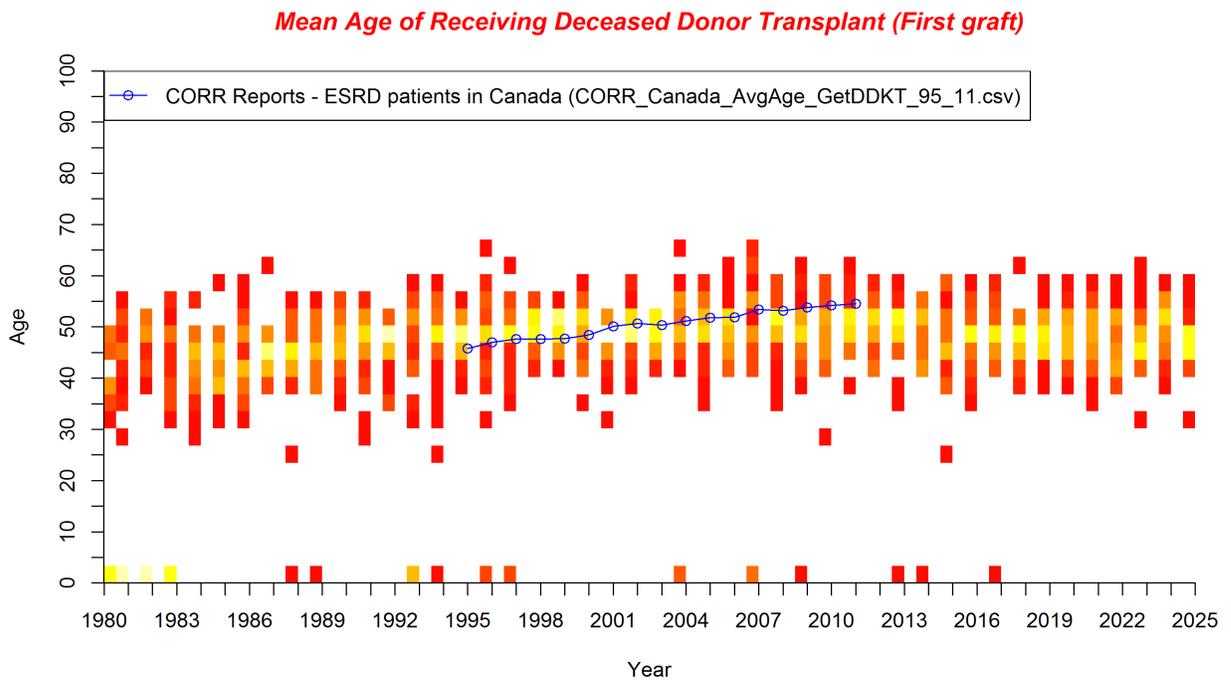


Figure 8-11. Mean Age of Receiving Deceased Donor Kidney Transplant

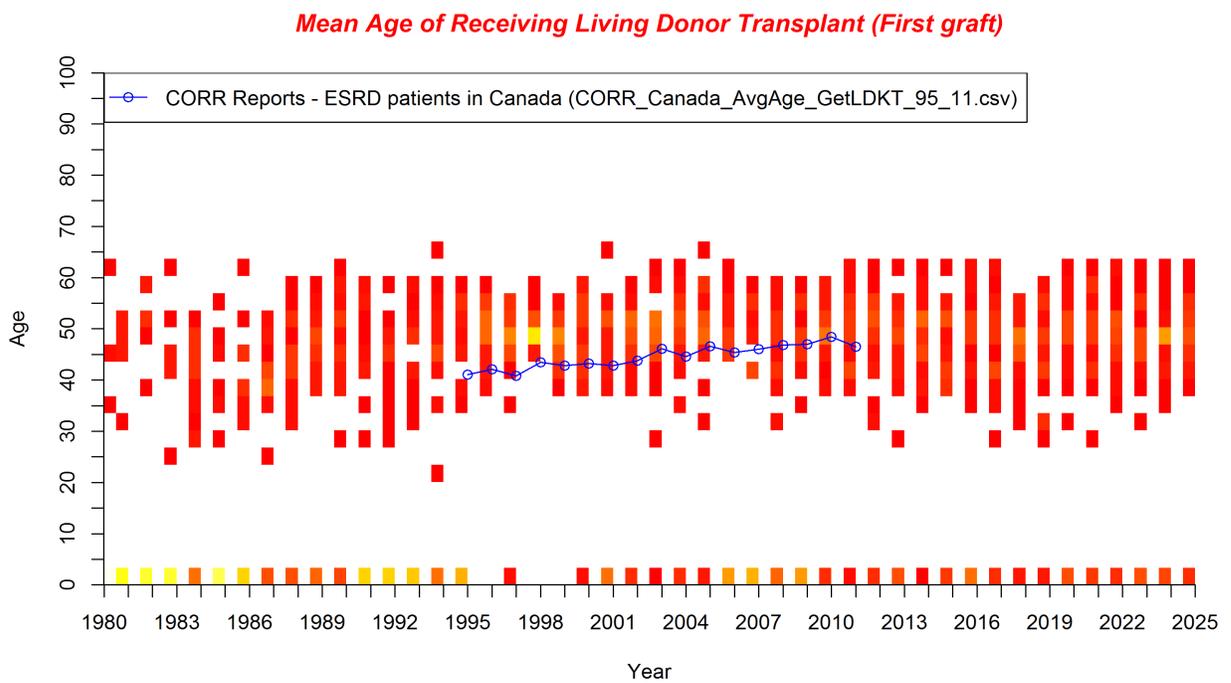


Figure 8-12. Mean Age of Receiving Living Donor Kidney Transplant

Median Days On Dialysis Priort to LDKT

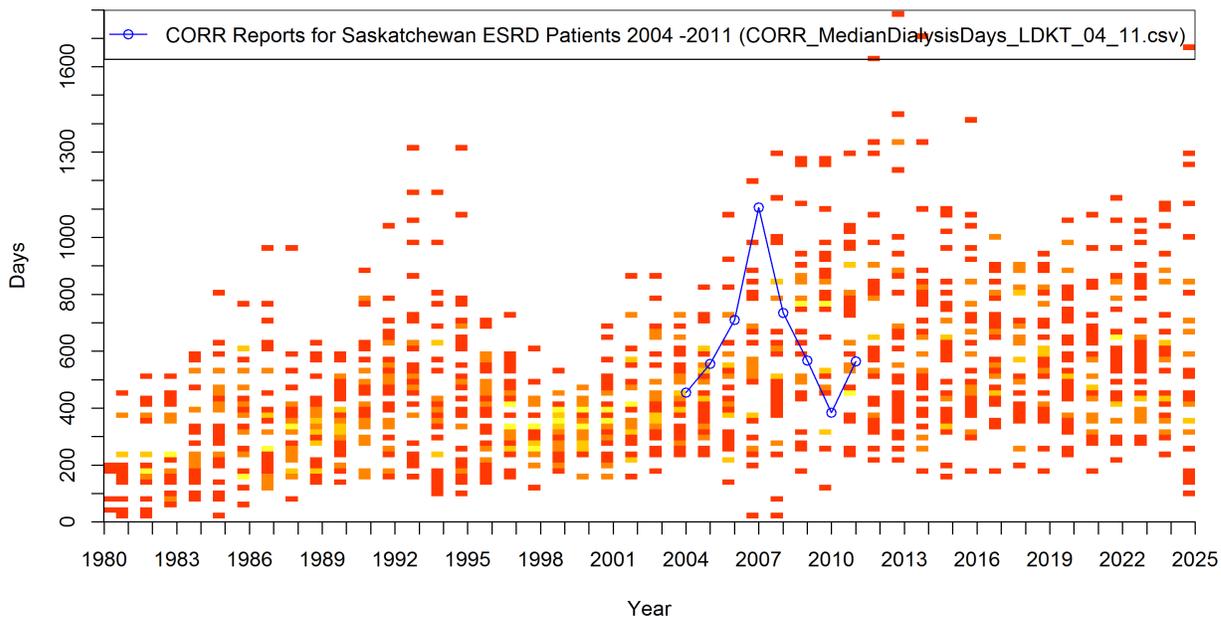


Figure 8-13. Median Days On Dialysis Prior to Living Donor Kidney Transplant

Median Days On Dialysis Priort to DDKT

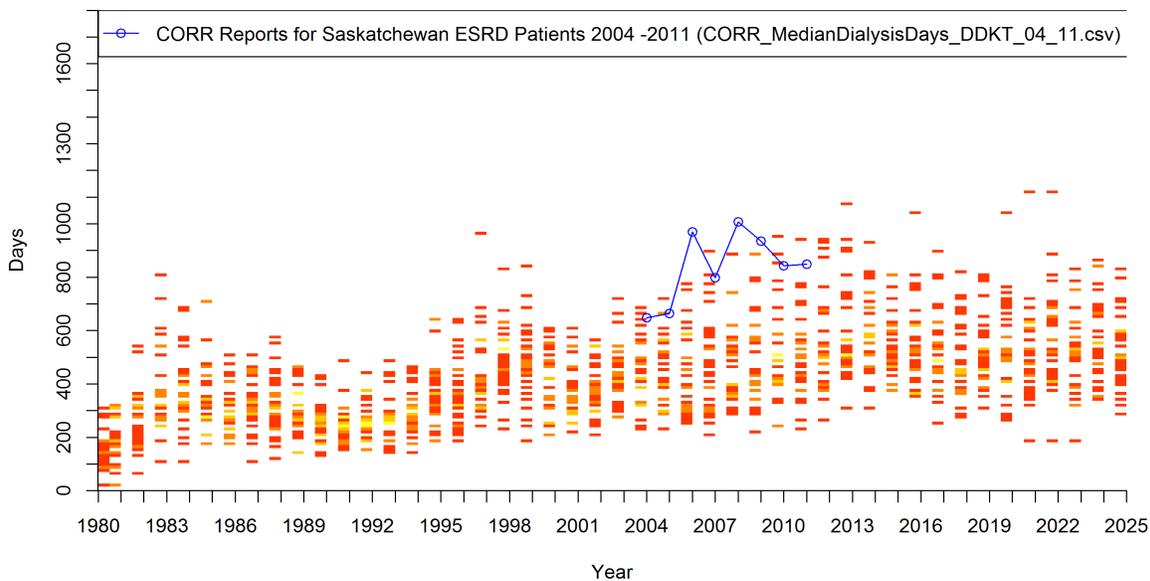


Figure 8-14. Median Days On Dialysis Prior to Deceased Donor Kidney Transplant

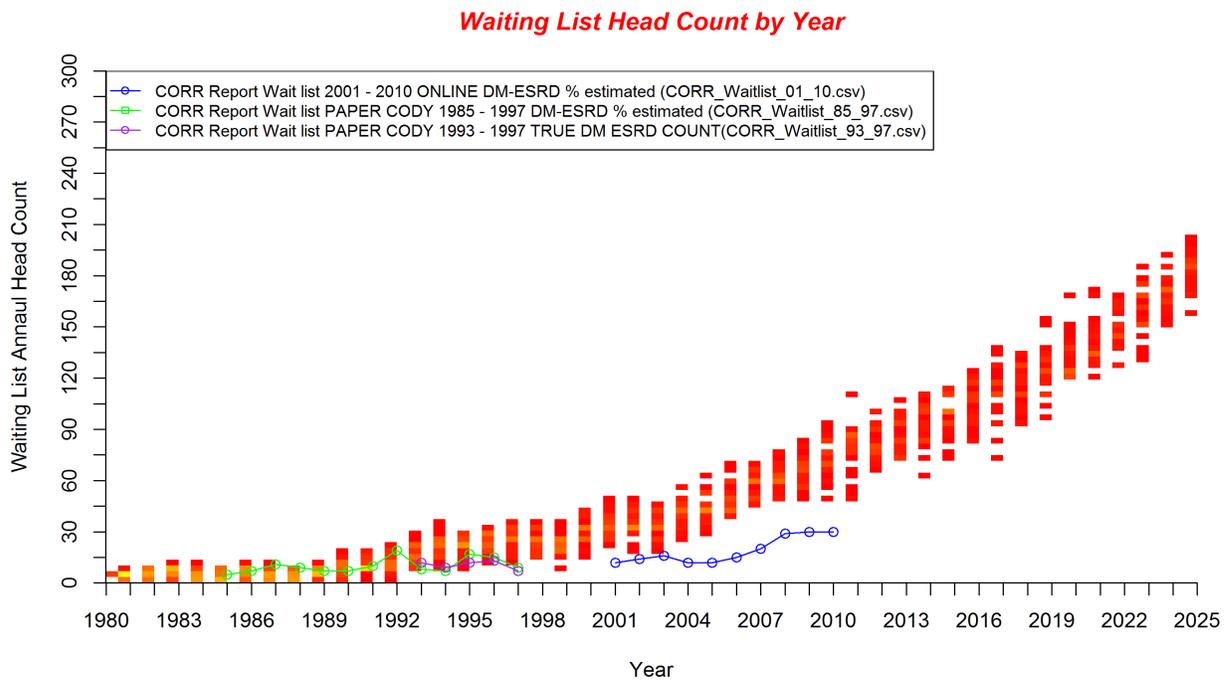


Figure 8-15. Waiting List Head Count

In summary, a number of model outputs were selected for comparison with the corresponding historical data for the purpose of validating the correctness of the model. The model output chosen for model validation include: the prevalent and incident case count for all DM-ESRD patients, the prevalent and incident case count for patients on each ESRD treatment modality (HD, PD, and Transplant), and the mean age of patients initiating HD/PD/Transplant, head count on the waiting list and the median days spent on dialysis prior to transplant. Both the model output and the historical data were plotted in graphs and comparisons were made by visually inspecting the alignment of plots. All the model output except the transplant prevalent case count align well with the historical data. One possible explanation for the discrepancy uncovered for the transplant prevalent case count is that the historical data include patients who developed diabetes post-transplant, which are excluded from the prevalent case count in the

model. Nevertheless, despite the divergence in transplant prevalent case count, all major model output has a strong match with historical data, suggesting that the model captures relevant processes and is likely to be correctly implemented, with the model output matching historical numbers.

8.2 Scenarios and Sensitivity Analysis

The model ran a set of nine scenarios. Each scenario varied some parameters and changed some model assumptions. The models run each scenario with 30 realizations; and each scenario took 2.5 to 3 hours to complete. During the model development phase, we found out that the run time can be significantly and adversely impacted by the usage of the population statistics function offered in Anylogic software package. When calling multiple population statistics during run time, the length of time required to complete simulation can be dramatically longer. For instance, at one point in time, 30 realizations of a scenario took up to 60 hours to complete. The problem with using population statistics function built-in with Anylogic software is that each function call iterates through the entire population and collects only one metric from every agent in the population. When we call several population statistics functions at the end of each day to collect multiple metrics from the agents, the computation cost is very high. To achieve better run time efficiency, we redesigned the model with a customized function to go through the population once at the end of each day to collect all metrics together rather than looping through the population several times. Such a change allowed us to reduce the run time from 60 hours to 3 hours.

By comparing the output of scenarios with corresponding output variables from the base line scenario, we know how sensitive the critical model output (e.g. prevalent case count, cost, personal year lived) are in response to the changes. Also, some of the scenarios could help us

understand the degree of impact by health care policy changes for managing DM-ESRD patients. In the sections below, each scenario will be described in detail; the comparisons made with baseline outputs will be discussed as well.

8.2.1 Scenario #1 - All DM-ESRD Patients Receive Pre-Emptive Transplant as Initial Treatment

In the baseline, the pre-emptive transplant is not available to DM-ESRD patients since it is very rare in Saskatchewan. By contrast, in Scenario #1, when Diabetes patients received ESRD diagnosis, the model treats the only treatment available as pre-emptive transplant instead of HD and PD. Also, the scenario is set up in such a way that when transplant patients experience graft failures, they will spend a minimum amount of time (i.e. 90 days) on dialysis prior to receiving another transplant again. The purpose for having this scenario is to investigate the impact – taken to an extreme – of having a high level of pre-emptive transplants versus dialysis on outcomes such as prevalent case count, costs and person years lived. The comparisons made for each outcome variable between scenario #1 and the baseline scenario are plotted in Figure 8-16, Figure 8-17 and Figure 8-18 respectively. As shown in those figures, with all of the DM-ESRD incident patients receiving pre-emptive transplants, there is a significant increase in the number of patients living with Diabetic-ESRD (DM-ESRD Prevalent Case Count as in Figure 8-16) because of the lower mortality hazards experienced by transplant patients when compared to dialysis patients. Correspondingly, as more DM-ESRD patients are living longer, both the ESRD prevalent case count and the accumulated values (person-years lived) are also much higher in scenario #1 in comparison with the baseline scenario. Despite a larger count of patients living longer, the cost of caring for those patients is actually lower than in the baseline scenario, as shown in Figure 8-17. The reason reflects the fact that the cost for

caring transplant patients is significantly lower than the cost associated with those on dialysis, especially following the first year of transplant. Even though in real life it is unlikely that resources would be sufficient to provide all patients with pre-emptive transplants, scenario #1 as an extreme case does highlight the pronounced benefits of having more pre-emptive transplants over dialysis.

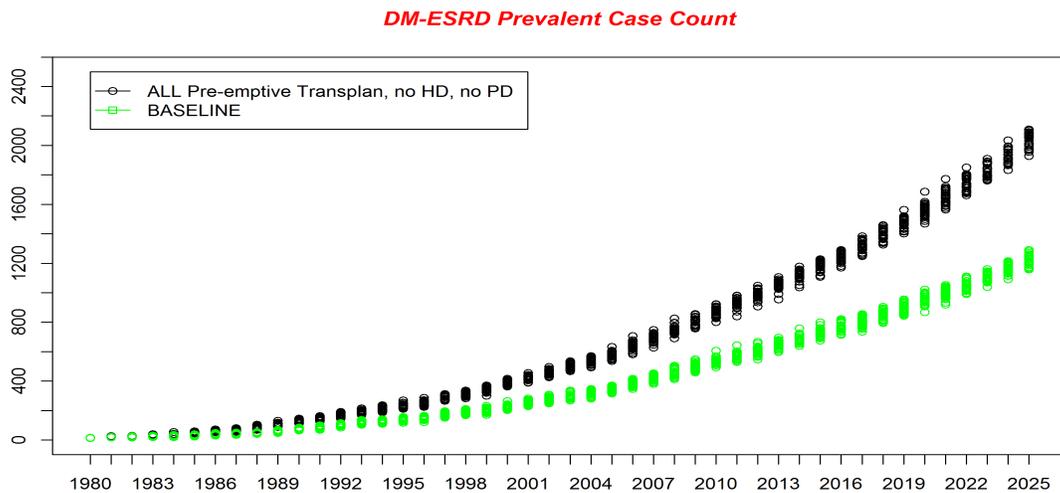


Figure 8-16. DM-ESRD Prevalent Case Count, Scenario #1 Compared to Baseline

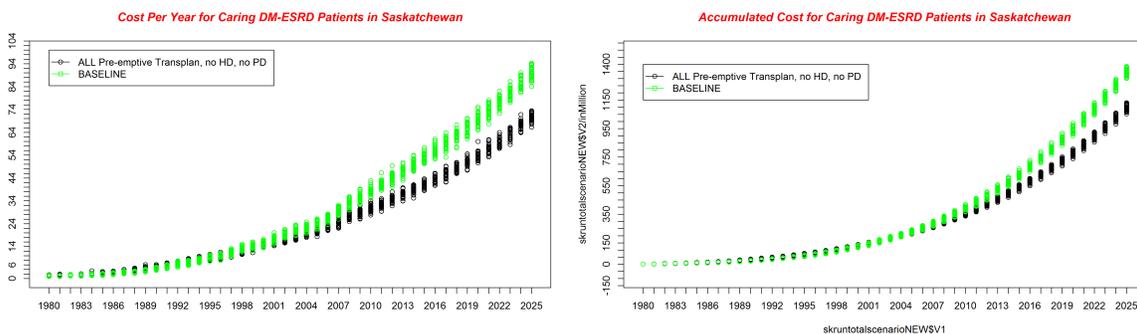


Figure 8-17. Cost, Accumulated and Per Year, Scenario #1 Compared to Baseline

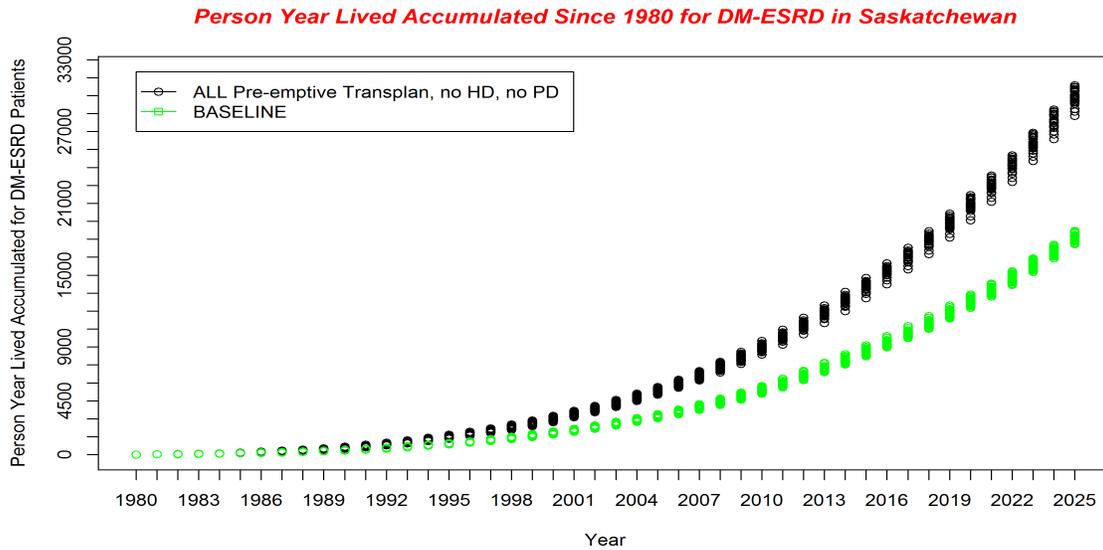


Figure 8-18. Person Years Lived, Accumulated, Scenario #1 Compared to Baseline

8.2.2 Scenario #2 – All DM-ESRD Incident Patients Receiving HD Only As Initial Treatment

In the baseline, DM-ESRD incident patients have certain probability of receiving either HD or PD as their initial treatment with the fact more patients will start on HD. By contrast, in scenario #2, the only treatment option available to DM-ESRD incident patient is HD rather than both HD and PD. Moreover, patients are not allowed to switch from HD to PD. Such a set up will allow us to see the effects of having more patients receiving HD on the outcomes variables. The prevalent case count and person years lived output from scenario #2 did not show any significant differences when compared with the baseline scenario as shown in Figure 8-19 and Figure 8-21, respectively. The subtle differences between scenario #2 and baseline could be due to the fact that between 80% and 90% of the DM-ESRD patients were already started with HD in the baseline scenario; having all of the DM-ESRD patients starting HD in scenario #2 wouldn't produce noticeable differences in results. On the other hand, the per-year and accumulated cost

in scenario #2 are higher than what are in the baseline scenario, which could be caused by more people receiving the most expensive form of ESRD treatment, HD.

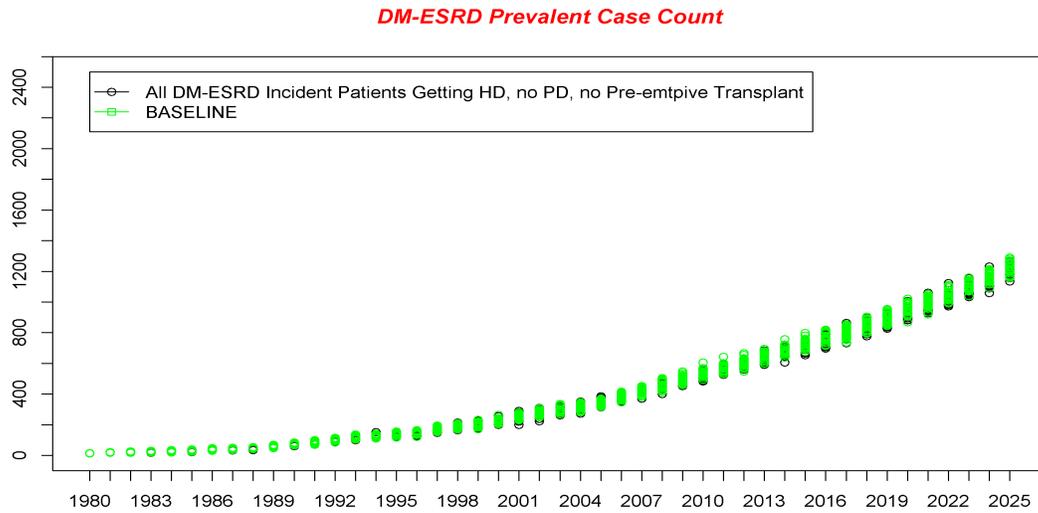


Figure 8-19. DM-ESRD Prevalent Case Count, Scenario #2 Compared to Baseline

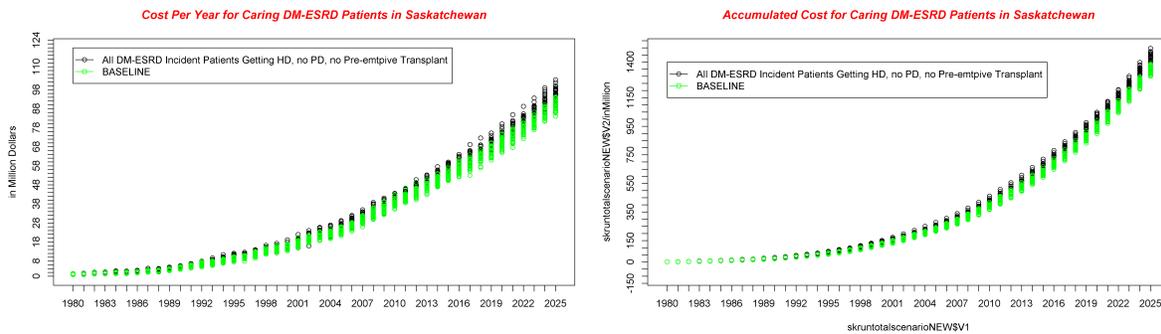


Figure 8-20. Cost, Accumulated and Per Year, Scenario #2 Compared to Baseline

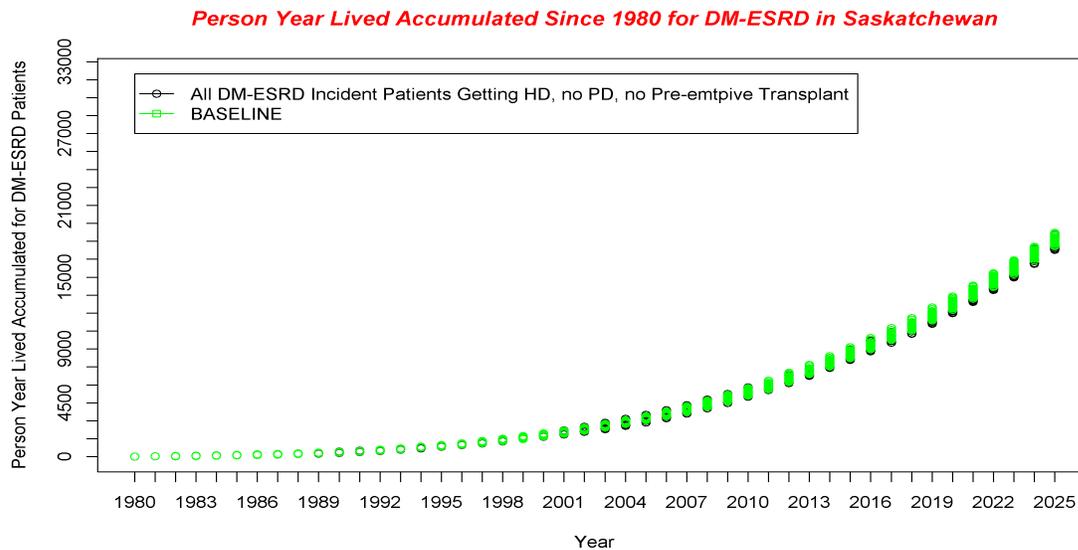


Figure 8-21. Person Years Lived, Accumulated, Scenario #2 Compared to Baseline

8.2.3 Scenario #3 – All DM-ESRD Incident Patients Receiving PD Only As Initial

Treatment

Whereas in the baseline scenario, majority of the DM-ESRD patients start on HD as their initial treatment, in scenario #3, all the DM-ESRD incident patients start with PD. Figure 8-22 shows the prevalent case count becomes increasingly larger than in the baseline when all DM-ESRD patients receive PD as initial treatments. Also, the person year lived outcome from scenario #3 demonstrate visible improvement as illustrated in Figure 8-24. The higher prevalent case count and person year lived are a reflection of the lower mortality rates for patients receiving PD over HD. Also, given that PD is a less expensive treatment than HD, the per-year and accumulated cost for treating DM-ESRD patients in scenario #3 are much less than in the baseline scenario. Health policy makers should consider the marked benefits brought by more patients receiving PD when develop relevant health policies.

DM-ESRD Prevalent Case Count

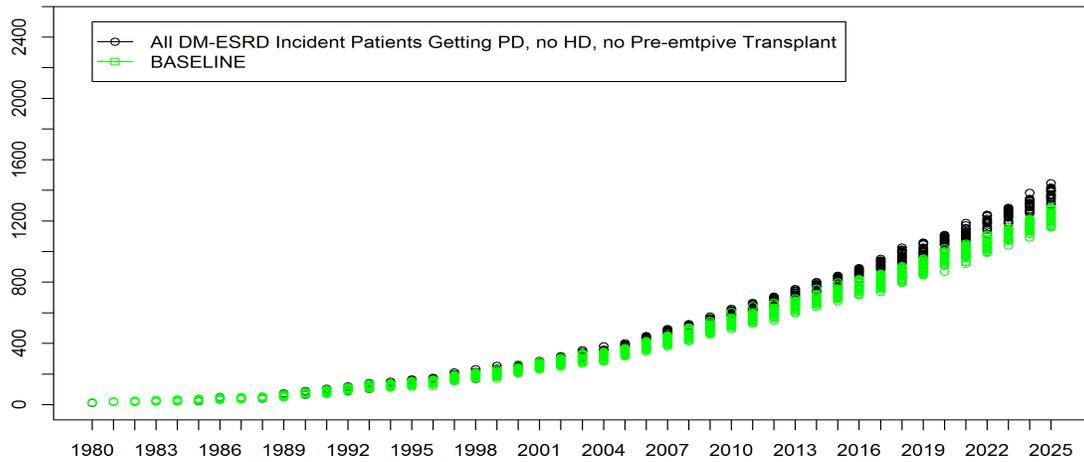


Figure 8-22. DM-ESRD Prevalent Case Count, Scenario #3 Compared to Baseline

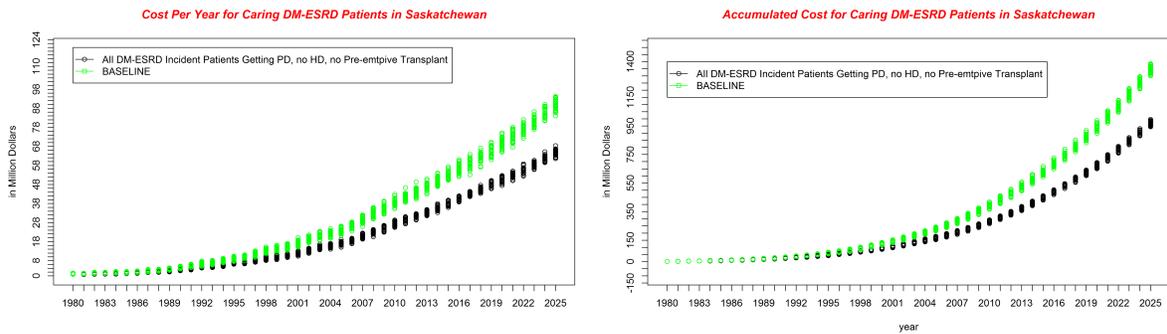


Figure 8-23. Cost, Accumulated and Per Year, Scenario #3 Compared to Baseline

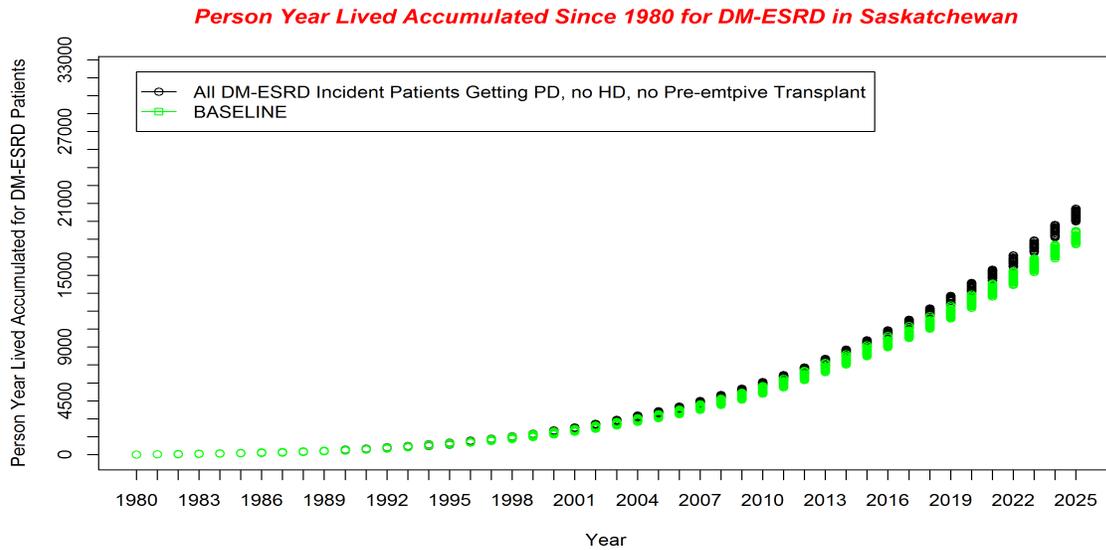


Figure 8-24. Person Year Lived, Accumulated, Scenario #3 Compared to Baseline

8.2.4 Scenario #4 – No DM Incident Patients from Year 2006 to 2025

In the baseline scenario, the DM-ESRD incident case count is driven by the number of patients living with diabetes which is affected by the diabetes incident cases fed into the model as input. In scenario #4, we set up the experiment in a way so that there are no new diabetes cases coming into the model between Jan 1st, 2006 and Dec 31st, 2025. This can also be seen as an extreme case in which diabetes mellitus has been entirely prevented since Jan 1st, 2006. This should cut down a large portion of new DM-ESRD patients because there are no new DM patients who would develop ESRD as complication from Jan 1st, 2006 onwards. Of course, the patients who developed DM prior to that date could still develop ESRD as complications. While being extreme in its design, Scenario #4 aids understanding the impact of reducing DM incident cases on the outcomes in future years. As shown in Figure 8-25, the ESRD prevalent case count in scenario #4 does not begin to decline until year 2019, which is 13 years after diabetes incidence has ceased. Similar trends were also observed in the plots for cost and person years

lived in Figure 8-26 and Figure 8-27. Even in the extreme case depicted in scenario #4, where the DM incident case are cut down to zero at the beginning of year 2006 – and where tremendous inertia remains in the system – for many years after that, the resource demands associated with caring for the existing patients remain at an elevated level and continue at rise.

DM-ESRD Prevalent Case Count

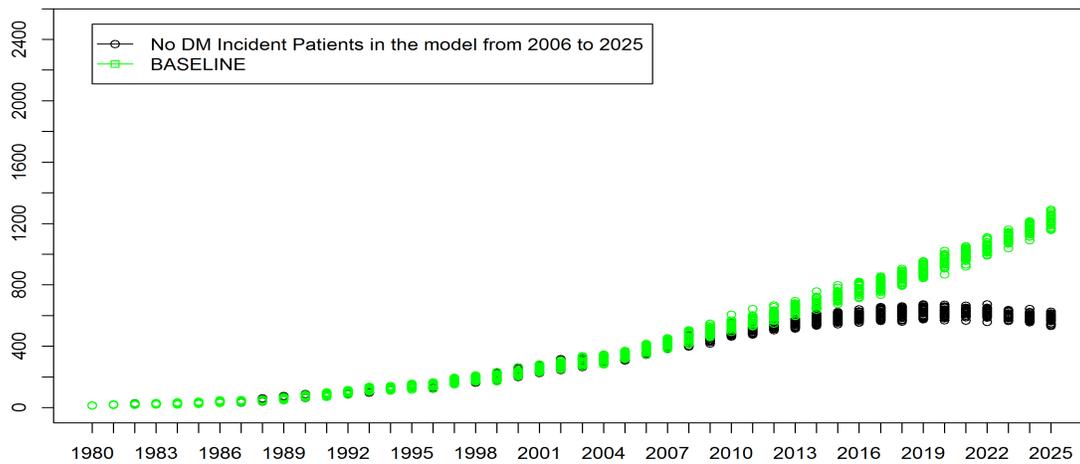


Figure 8-25. DM-ESRD Prevalent Case Count, Scenario #4 Compared with Baseline

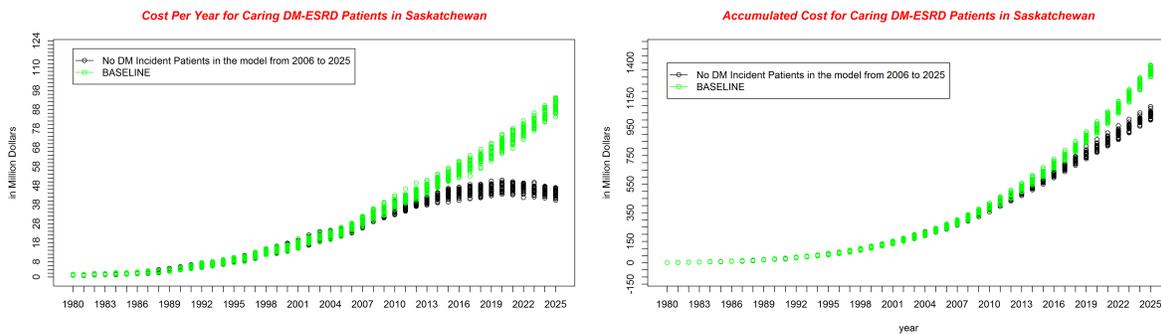


Figure 8-26. Cost, Accumulated and Per Year, Scenario #4 Compared to Baseline

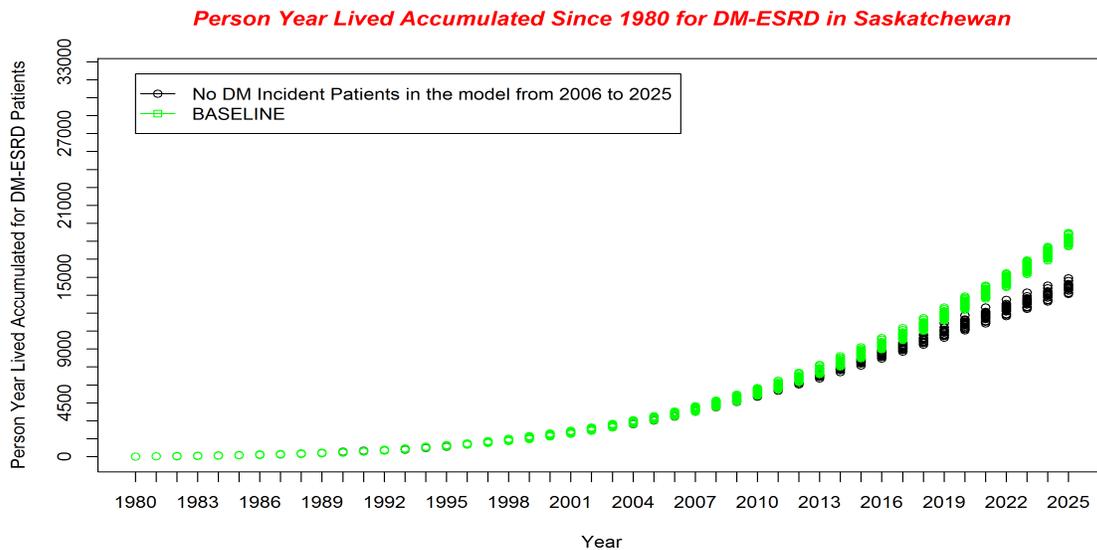


Figure 8-27. Person Year Lived, Accumulated, Scenario #4 Compared to Baseline

8.2.5 Scenario #5 – Reduce Mortality Hazards by Half for Dialysis and Transplant Patients

In scenario #5, the mortality hazards for HD, PD and transplant patients are all reduced to half of their original values. As expected, both the prevalent case count (Figure 8-28) and person years lived (Figure 8-30) in scenario #5 were much higher than in the baseline scenario due to lower mortality rates. As patients live and receive ESRD treatments over a longer period, both the cost per year and the accumulated cost rise significantly higher, as shown in Figure 8-27.

This is the situation when the mortality risk was lower but the treatment plan remains the same (i.e. similar distribution are chosen among HD, PD and Transplant). On the other hand, in scenario #1, the prevalent case count and the person years lived was as high as in scenario #5, due to the lower mortality for transplant patients in the former scenario. However, astonishing differences between scenario #1 and scenario #5 are found in cost. The cost in scenario #1 is less than in baseline; whereas the cost is more in scenario #5 than in the baseline. At the end of year 2025, the per year cost in scenario #1 is only about half of the cost in scenario #5, given the fact

that the prevalence case count in scenarios#1 is even higher than in scenario #5 as shown in Figure 8-31 . When both person years lived and cost are under consideration, the benefits of choosing a more cost-effective treatment are very clear.

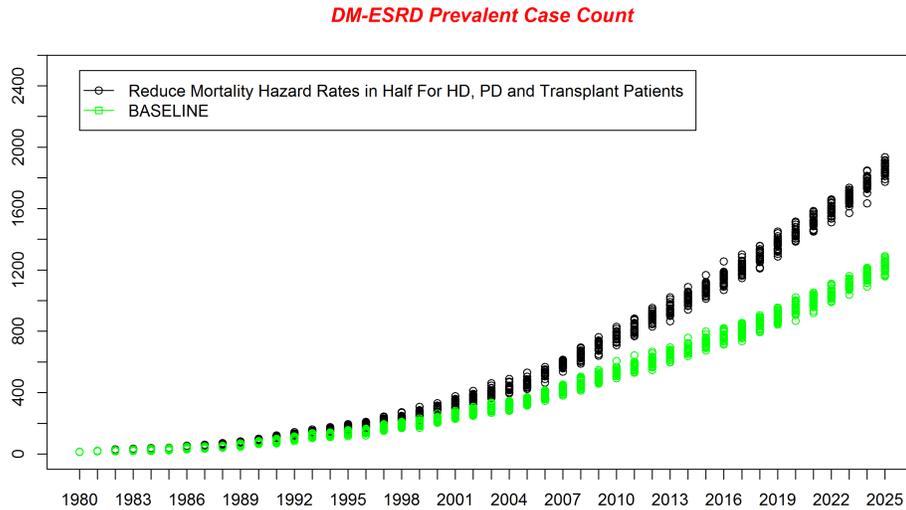


Figure 8-28. DM-ESRD Prevalent Case Count, Scenario #5 Compared to Baseline

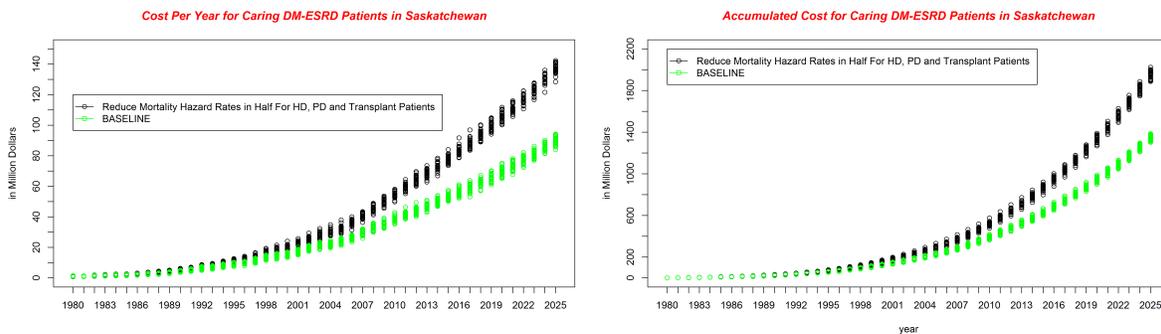


Figure 8-29. Cost, Accumulated and Per Year, Scenario #5 Compared to Baseline

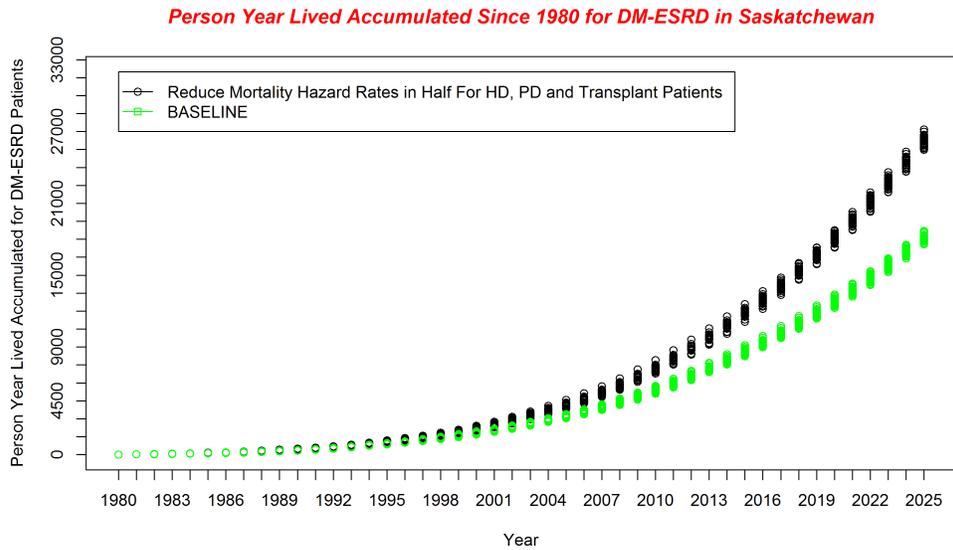


Figure 8-30. Person Year Lived, Accumulated, Scenario #5 Comparing with Baseline

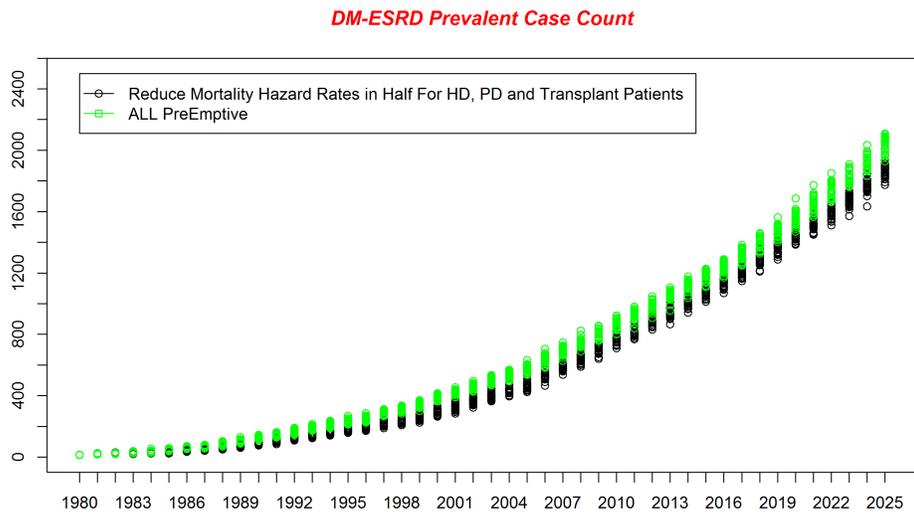


Figure 8-31. DM-ESRD Prevalent Case count, Scenario #5 compared to Scenario #1

8.2.6 Scenario #6 – Zero Graft Failure Rate

In Scenario #6, the graft failure rate in the model is set to zero, which means that transplant patients in the model will not experience failure of their transplanted kidney. The

graft failure rates used in the baseline are calculated by us based on some assumptions, the details of which can be found in Section 5.4. Eliminating the graft failure process in the model will help us understand how much impact the graft failure rate imposes on outcomes of the model. In Figure 8-32, the count of transplant patients living with a functional transplanted kidney graft exhibits elevated levels compared to the baseline after graft failure is set to zero. This is as expected because patients won't experience a graft failure and the number of patients living with a functional graft will therefore be higher. However, the impact of having zero graft failure on the central model outcomes is minimal, as shown in Figure 8-33, Figure 8-34 and Figure 8-35. This could be due to fact the transplant patients only comprise a small portion of all DM-ESRD patients. Thus, a small increase in the number of transplant prevalent patients does not affect the central outcome of the model very much.

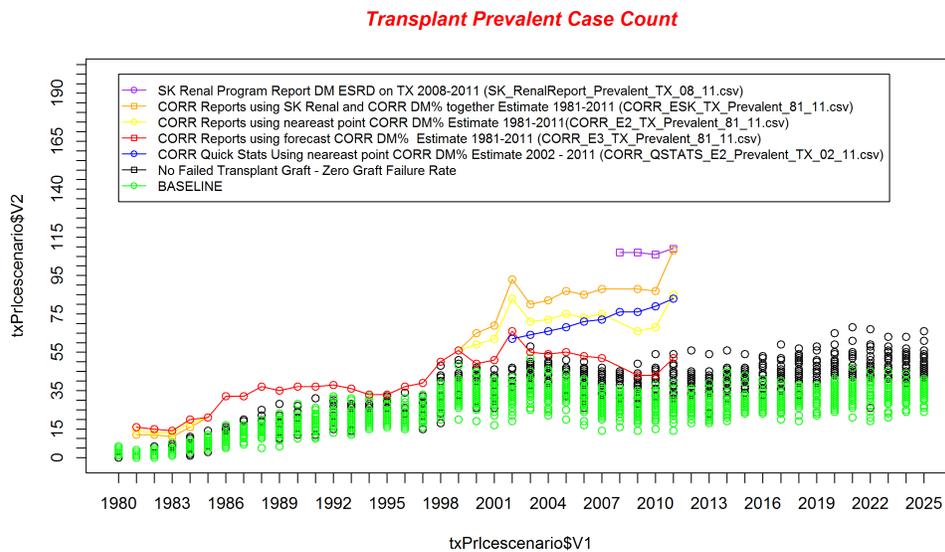


Figure 8-32. Transplant Prevalent Case Count in Scenario #6

DM-ESRD Prevalent Case Count

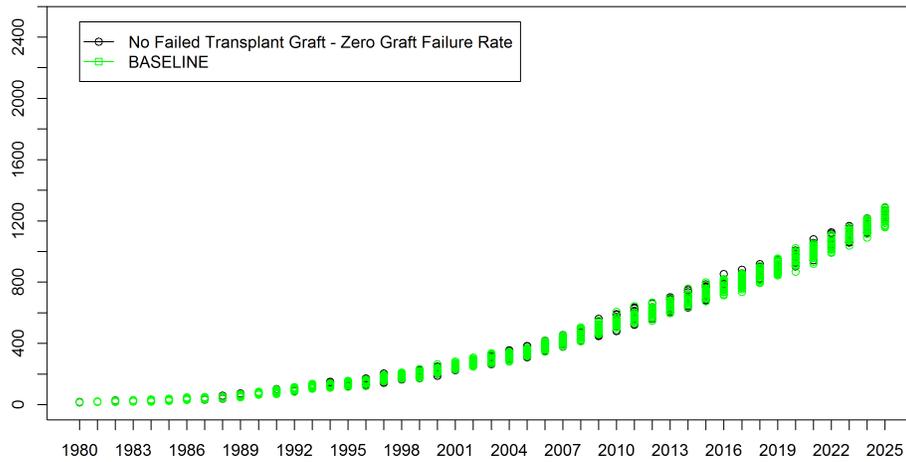


Figure 8-33. DM-ESRD Prevalent Case Count, Scenario #6 Compared to Baseline

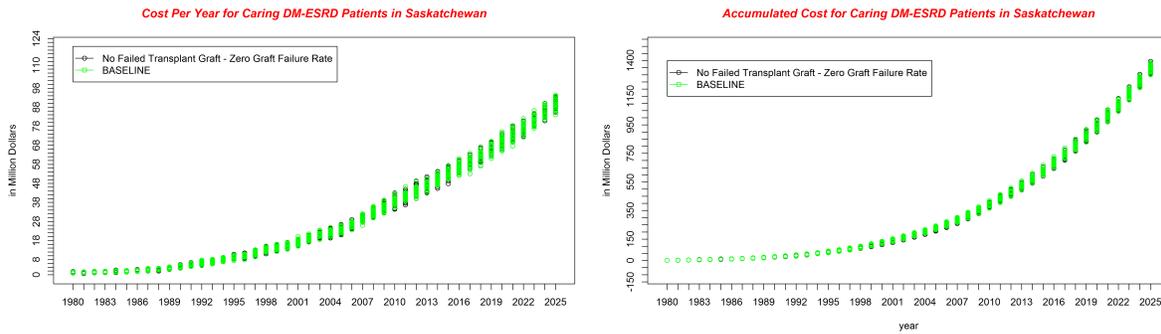


Figure 8-34. Cost, Accumulated and Per Year, Scenario #6 Compared to Baseline

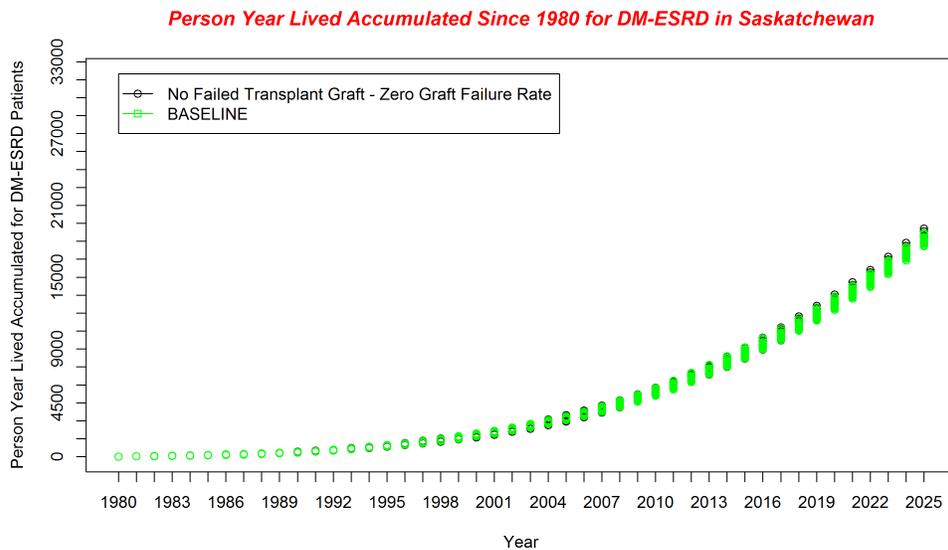


Figure 8-35. Person Year Lived, Accumulated and Per Year, Scenario #6 Compared to Baseline

8.2.7 Scenario #7 – Shorter Transplant Assessment Time as 90 days, Transplant Rate Remain the Same as Baseline Scenario

The purpose of scenario #7 is to investigate the impact of assessment time on the overall outcome of the model. In this scenario, it takes 90 days for a patient to complete eligibility assessment no matter in which year the assessment was conducted. By contrast, in the baseline scenario, the assessment time is a calibrated parameter which varies for each individual, and with its value dependent in the year the assessment was conducted. The details on the calibrated parameter assessment time can be found in Chapter 6.3. As shown in Figure 8-36, Figure 8-37 and Figure 8-38, the differences in prevalent case count, cost and person years lived between scenario #7 and baseline is not evident. The reason for not having noteworthy impact by varying assessment time is due to the small portion taken by transplant patients among all the DM-ESRD patients. Also, with a shorter assessment time, a larger fraction of patients who was

originally in the assessment process will be put on waiting list quicker. With a longer waiting list, it will take longer for patients to receive transplants than before. Moreover, with the unchanged transplant rates and shorter assessment time, patients will die on the transplant waiting list rather than during assessment phase. Thus, the impact of having a shorter assessment is proved to be limited on the overall wait time and the receipt of the transplant. In other words, the number of organs available for transplantation rather than assessment time is the most important determining factor in the model outcome.

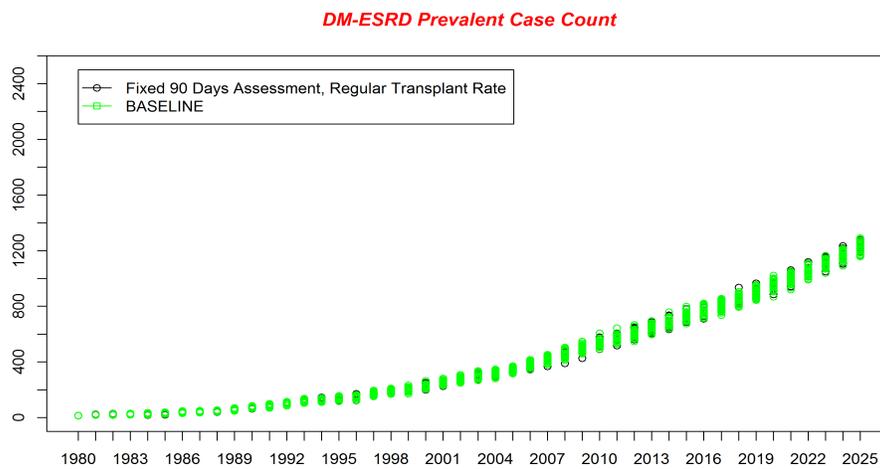


Figure 8-36. DM-ESRD Prevalent Case Count, Scenario #7 Compared to Baseline

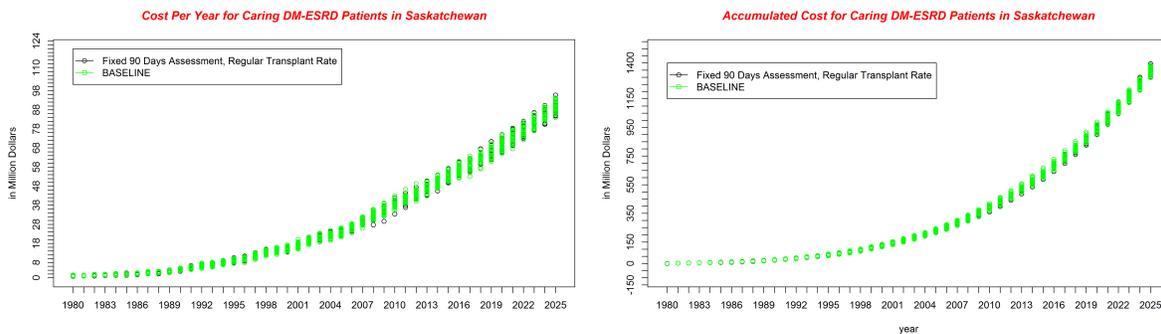


Figure 8-37. Cost, Accumulated and Per Year, Scenario #7 Compared to Baseline

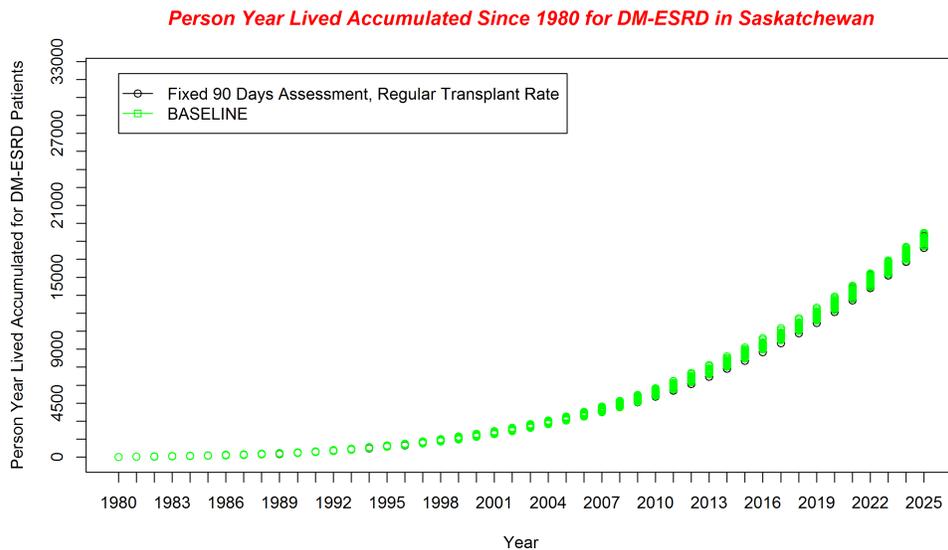


Figure 8-38. Person Year Lived, Accumulated, Scenario #7 Compared to Baseline

8.2.8 Scenario #8 – Regular Assessment Time, Eliminating Transplant Waiting list by Increased Transplant Rates

In scenario #8, the rates of living donor transplant have been increased dramatically comparing to what is in the baseline. In the baseline scenario, there are fewer than five cases of living donor transplants per year, and less than 10 case of deceased donor transplant a year, as listed in Table 5-6. By contrast, in scenario #8, there the resources are assumed to be in place to allow for up to 365 cases of living donor transplant and 365 deceased donor transplants in a year if patients complete the assessment and are placed on the waiting list. Since the transplant rates are set to be so high in scenario #8, in fact there are essentially no patients on the waiting list. Despite these dramatic differences in the resources available for transplantation, differences are hardly noticeable when comparing the prevalent case count and the person years lived outcome in scenario #8 with baseline. One possible explanation for not seeing a significant increase in the

prevalent case count and person years lived despite the increased rates of transplant is due to a lengthy assessment process. When the assessment process took over two years and even longer, many patients died while still receiving dialysis. And even though the transplant rate in Scenario #8 is set high enough to essentially eliminate the waiting list, there is simply not that many patients ready to be transplanted because the demand (the flow of patients completing the assessment process) is far lower than the supply (the in flow of available kidneys). Since patients remain dialyzed while being assessed, the prevalent case count and the person years lived was not elevated strongly. By contrast, the total cost dropped some because per treatment cost difference between dialysis and transplant is significant. Thus with even a small portion of patients getting transplant instead of dialysis, the difference in cost is still considerable.

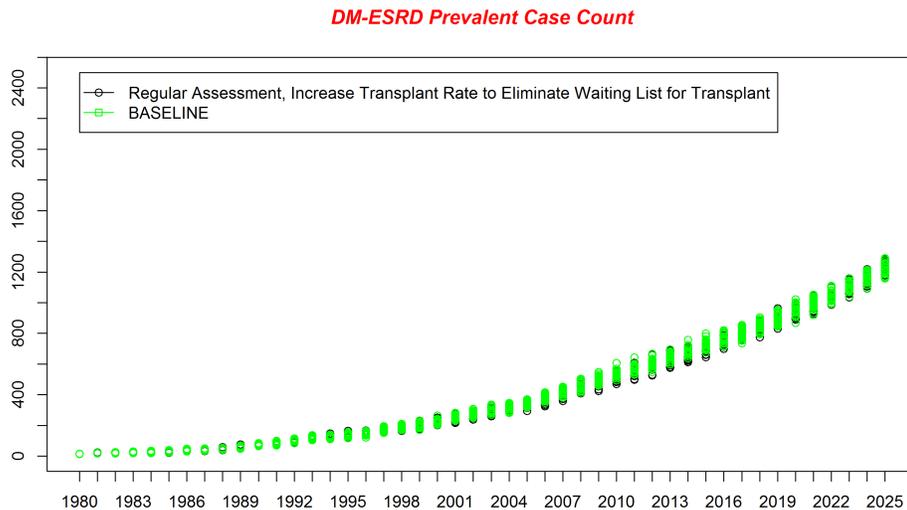


Figure 8-39. DM-ESRD Prevalent Case Count, Scenario #8 Compared to Baseline

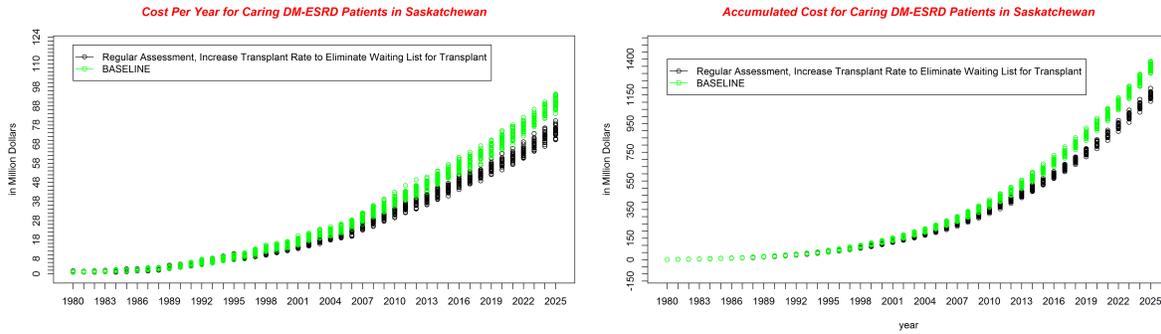


Figure 8-40. Cost, Accumulated and Per Year, Scenario #8 Compared to Baseline

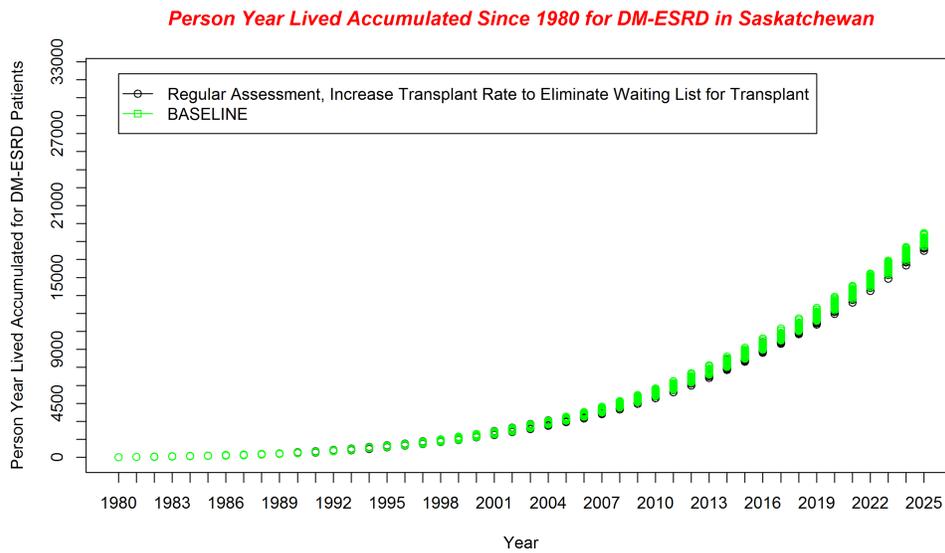


Figure 8-41. Person Year Lived, Accumulated, Scenario #8 Compared to Baseline

8.2.9 Scenario #9 –Shorter Transplant Assessment Time as 90 days, and Eliminate Waiting List by Increased Transplant Rates

Scenario #9 can be seen as the combination of scenario #7 and #8. In this experiment, it only takes 90 days for patients to complete the assessment process for transplant. Also, the transplant rates are set to have 365 cases of living donor transplant and 365 case of deceased

donor in a year, which basically eliminates the waiting list for transplants. As shown in Figure 8-42 and Figure 8-44, the differences in prevalent case count and person years lived between baseline and scenario #9 is not evident. Yet the cost has declined further, which could be due to patients remaining on dialysis for shorter time and getting transplanted quicker. Since the transplant cost much less than HD, the difference in cost is clear.

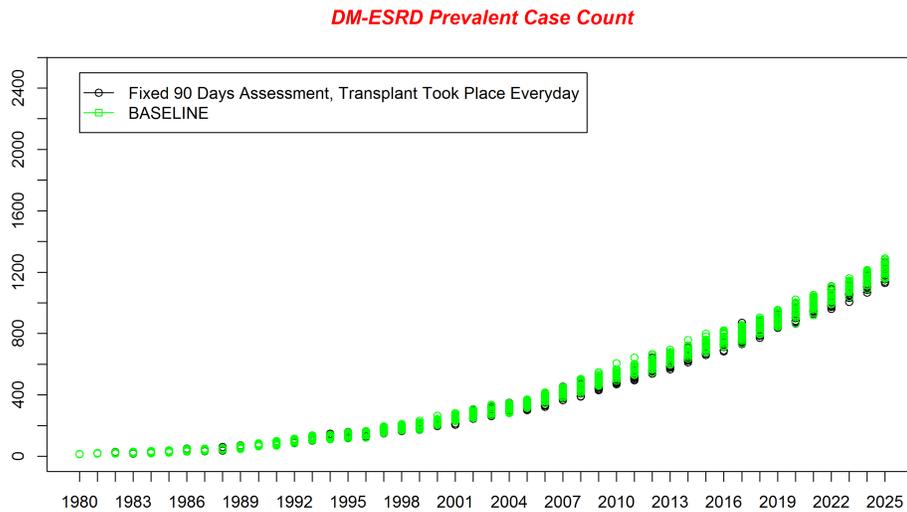


Figure 8-42. DM-ESRD Prevalent Case Count, Scenario #9 Compared to Baseline

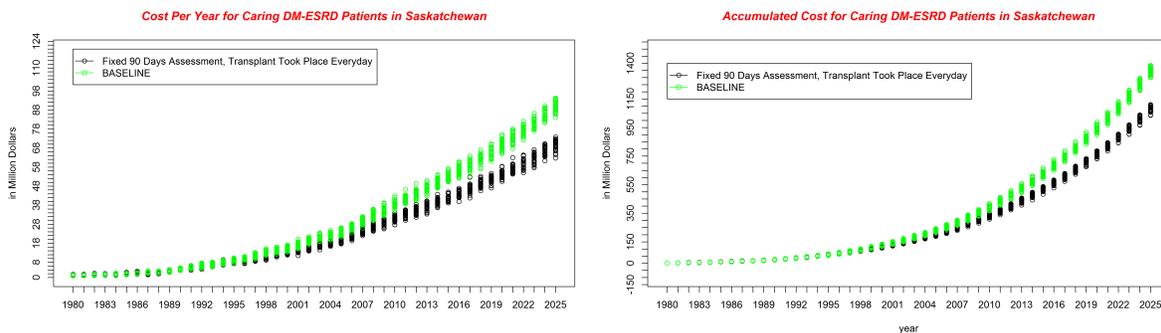


Figure 8-43. Cost, Accumulated and Per Year, Scenario #9 Compared to Baseline

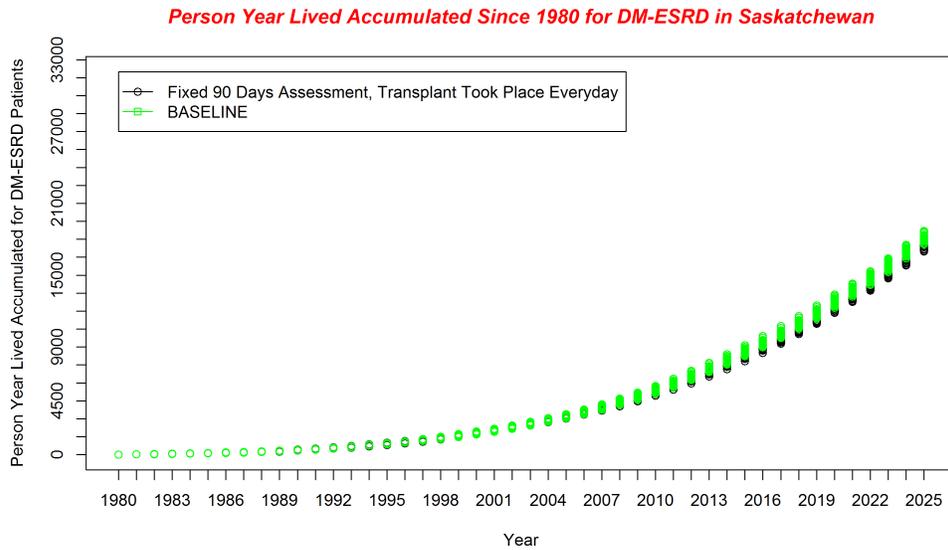


Figure 8-44. Person Year Lived, Accumulated, Scenario #9 Compared to Baseline

8.3 Results and Limitation

One goal of this thesis is to project the incident and prevalent case count of DM-ESRD patients in Saskatchewan and estimate cost for caring those patients through 2025. In addition, because of the high and rapidly rising burden of both DM and DM-ESRD among First Nations peoples [18,0], we want to know the prevalent case count, cost and person year lived broken down by First Nations status.

In section 8.1, while validating the model result with historical data, we presented a series of model output for all DM-ESRD patients rather than groups stratified by ethnicity. Those outputs include the incident case count and prevalent case counts for all DM-ERSD patients in Saskatchewan, and respective incident and prevalent case counts for patients receiving different ESRD modalities. To be more specific, the output shown in section 8.1 includes the following: incident case count (Figure 8 -1), the prevalent case count (Figure 8-2), the incident case count of DM-ESRD patient receiving HD (Figure 8-3), the prevalent case count of DM-ESRD patients

receiving HD(Figure 8-4), the incident case count of DM-ESRD patients receiving PD (Figure 8-5), the prevalent case count of DM-ESRD receiving PD (Figure 8-6), the incident of DM-ESRD patient receiving kidney transplant (Figure 8-7), and the prevalent case count of transplanted DM-ESRD patients (Figure 8-8). The output for individual ethnic group is presented and discussed next.

Due to space limits, only a few of the important ethnicity-specific outputs – such as prevalent case count, cost and person years lived –are presented in this thesis. Figure 8-45 shows the prevalent case count for First Nation (FN), Other Saskatchewan people (OSK), and all Saskatchewan patients (both FN and OSK). The median of prevalent case count were taken among all 30 realizations of the baseline. For both FN and OSK, the prevalent case counts are 75 in year 1990, 231 in year 2000, 611.5 in year 2012 and 1228.5 in year 2025. At the same points of time, the prevalent case count for FN are 14.5 in year 1990, 62 in year 2000, 176 in year 2012 and 342 in year 2025. As observed in Figure 8-45 and confirmed by the prevalent case count listed above, the prevalent case count for all Saskatchewan DM-ESRD patients and those in the FN subgroup has doubled or even tripled every ten years over the projection period. Also, by comparing the prevalent case count for FN with the count for all DM-ESRD patients, it is found that FN patients constituted 19% of all patients in year 1990 among all Saskatchewan DM-ESRD patients, and increased to 27% in year 2025. This finding is to be considered in light of the fact that less than 12% of Saskatchewan population are registered as First Nations in year 2006³. . The model output confirms the finding that the DM-ESRD as a disease affected FN disproportionately comparing to their OSK counterpart as stated in the DM-ESRD paper [19].

³In the year 2006 census, only 12% of people in Saskatchewan are North American Indians [28]. Since the definition of North American Indian includes more people than the definition of First Nations people, it follows that less than 12% of Saskatchewan population hold First Nations status

DM-ESRD Prevalent Case Count

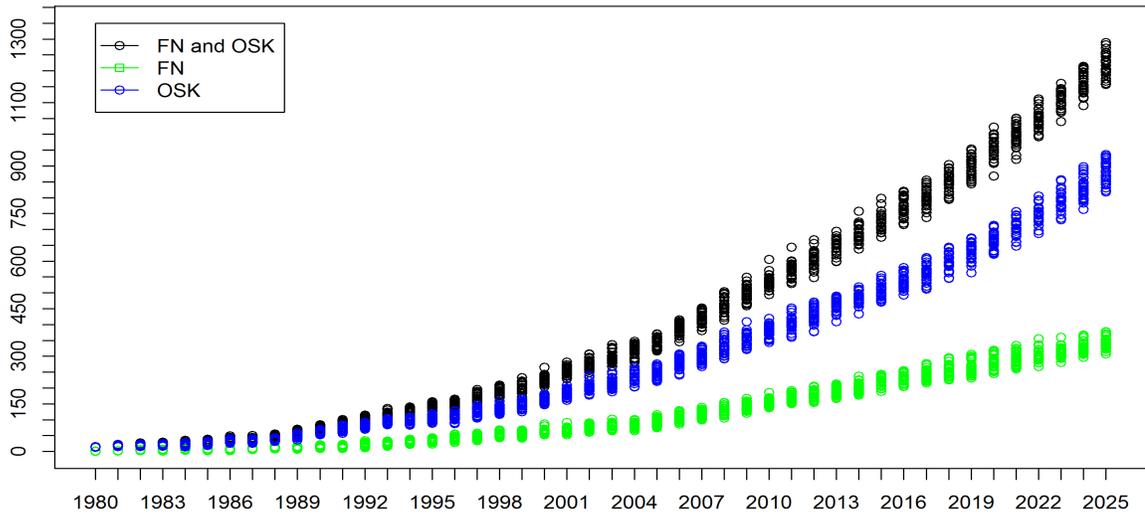


Figure 8-45 DM-ESRD Prevalent Case Count by Ethnicity

The cost per year for caring for all DM-ESRD patients in Saskatchewan (both FN and OSK), and the ethnicity-specific cost of FN and OSK are shown in Figure 8-46. The median of the cost from 30 realizations of the baseline scenarios are taken at four time points. The absolute cost (i.e. cost not yet converted into discounted present value) for delivering services (delineated in Chapter 5.6 to all DM-ESRD patients in Saskatchewan is \$4,311,953 in year 1990, \$15,613,408 in year 2000, \$44,576,879 in year 2012, and \$89,789,222. When the absolute cost values get converted into the year 2008 Canadian dollar values, the costs associated with delivering services to all DM-ESRD patients in Saskatchewan are \$7,399,341 in year 1990, \$19,848,532 in year 2000, \$39,536,145 in year 2012, and \$53,918,031 in year 2025. The trend in cost per year is similar to the trend found in the prevalent case count because the cost is driven by the number of DM-ESRD patients alive, which is the prevalent case count. For First Nations

patients, the cost is \$896,629.6 in year 1990, \$4,237,449 in year 2000, \$12,932,595 in year 2012 and \$25,318,310 in year 2025.

The accumulated cost since Jan 1st, 1980 up to each successive year for caring for DM-ESRD patients and patients in the FN and OSK sub-groups are shown in Figure 8-47. The accumulated cost in absolute term for all DM-ESRD patients in Saskatchewan is \$24,183,503 by year 1990, \$125,742,414 by year 2000, \$476,280,951 by year 2012 and \$1,352,471,113 by year 2025. The above costs are presented in 2008 Canadian dollars as \$46,646,935 in year 1990, \$190,852,390 in year 2000, \$549,213,219 in year 2012 and \$1,163,473,213 in year 2025. When the cost is broken down for First Nations patients, the cost in absolute form is \$4,490,945 in year 1990, \$30,166,558 in year 2000, \$128,020,907 in year 2012 and \$382,802,510 in year 2025.

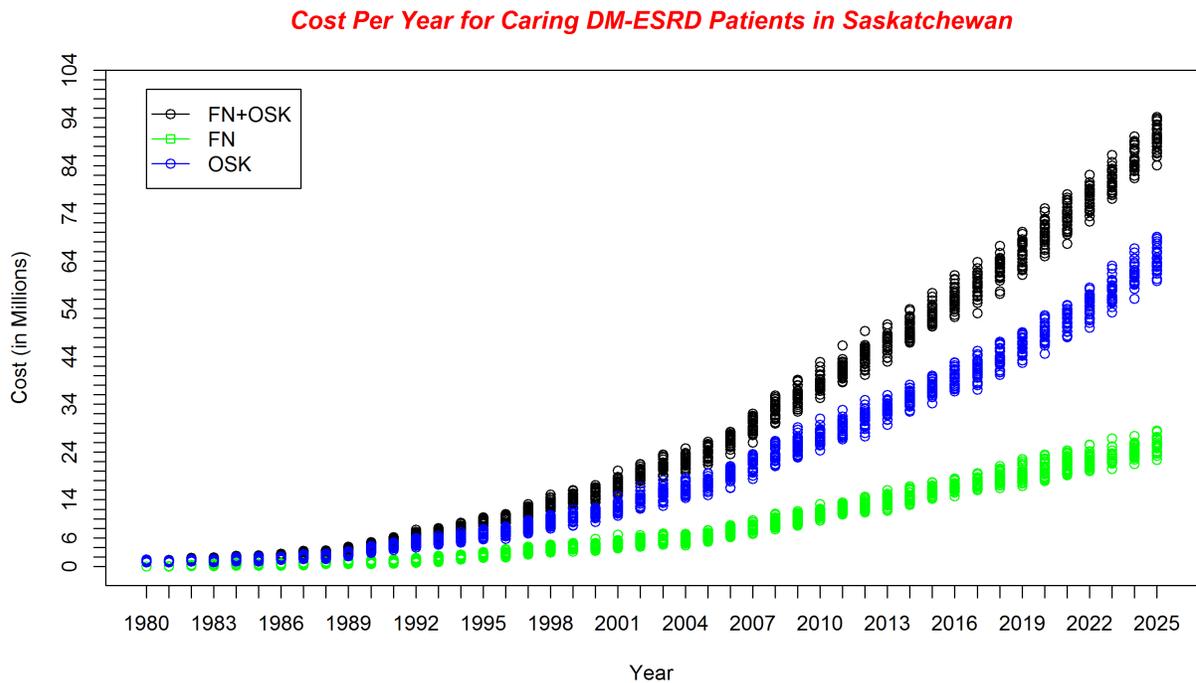


Figure 8-46 Cost Per Year by Ethnicity

Accumulated Cost for Caring DM-ESRD Patients in Saskatchewan since 1980

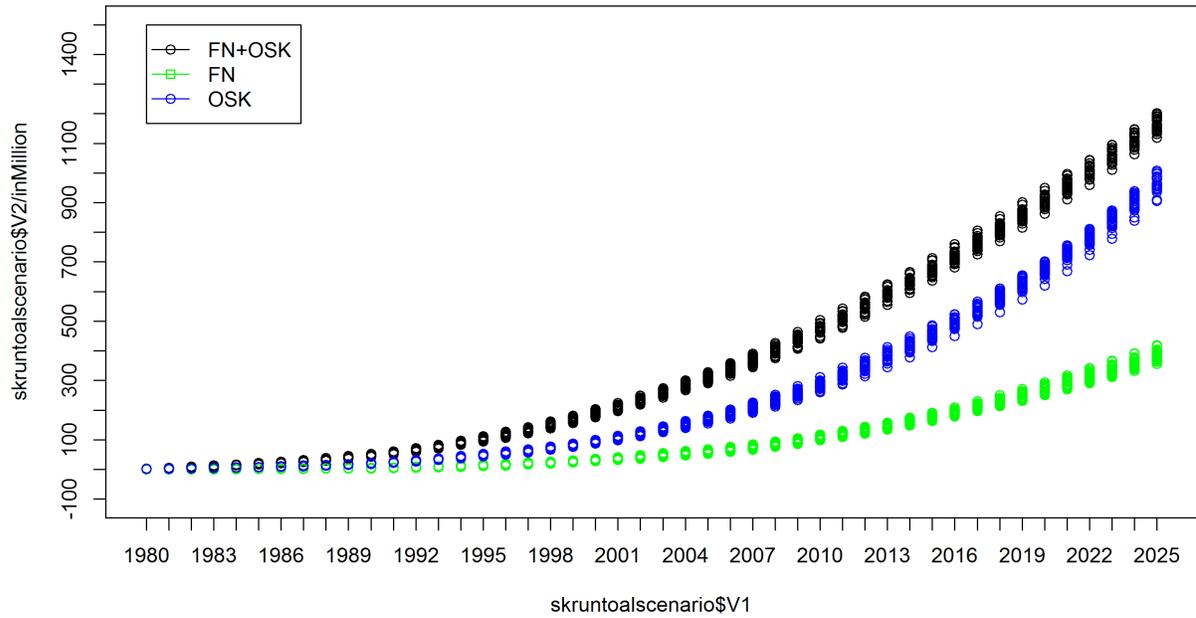


Figure 8-47 Accumulated Cost by Ethnicity

The accumulated person year lived is shown in Figure 8-48 and for all DM-ESRD patients (both FN and OSK), FN patients and OSK patients. Since the model start, the accumulated number of person years lived for all DM-ESRD patients in Saskatchewan are 364 by year 1990, 1818 by year 2000, 6622 by year 2012 and 18179 by year 2025. For First Nations DM-ESRD patients, the person years lived at corresponding time points are as follows: 66 by year 1990, 410 by year 2000, 1759 by year 2012, and 5161 by year 2025.

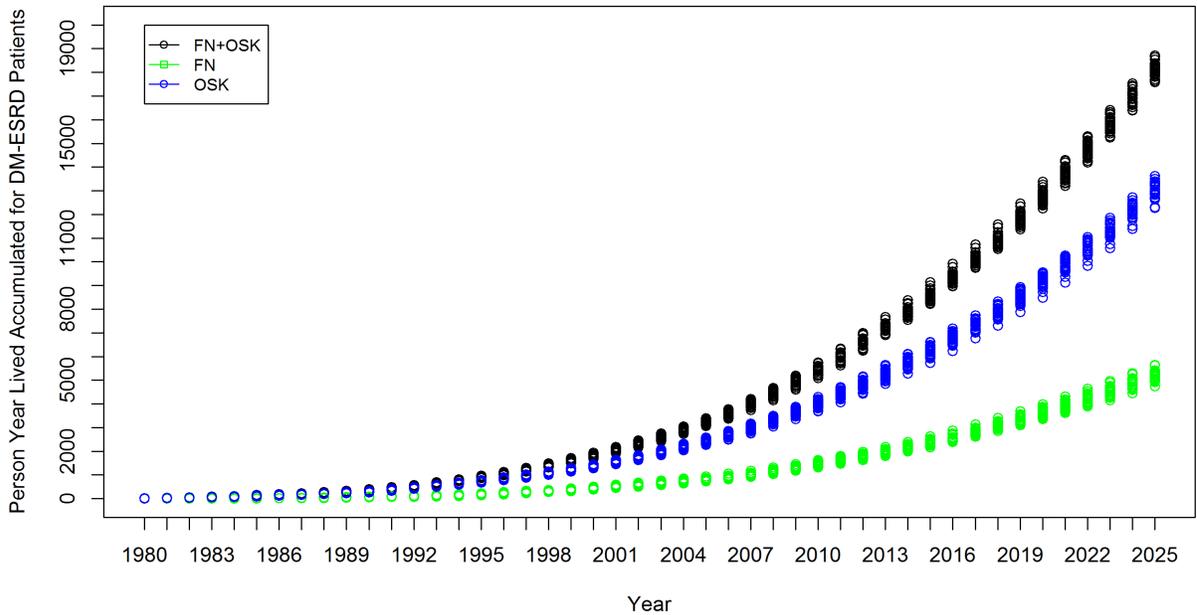


Figure 8-48. Person Years Lived Accumulated by Ethnicity

In summary, the prevalent case count, cost and person years lived for the DM-ESRD patients in Saskatchewan have continued to rise through the projection years. Bigger increases were seen in the first 20 years prior to year 2000, yet for the later years, the numbers keep increasing at slower rates. Also, the model reported the shocking amount of money required for caring for a small group of patients through the projection periods. For instance, for the set of cost items considered in this thesis, it will cost about \$54 million dollars (in 2008 dollar values) to care for 1229 DM-ESRD patients in Saskatchewan in year 2025. Also, the model findings confirmed that First Nations patients will continue to be affected by the DM-ESRD diseases disproportionately compared with other Saskatchewan residents.

8.4 Limitations

The results presented in Section 8.3 should be viewed in light of the limitations associated with the model structures and the input parameters. First of all, currently in the model,

DM incident patients can either die before developing ESRD or developing ESRD. In reality, another possible destination yet missing from the model structure is “end of coverage”. Thus, those patients who might end their coverage in reality in the model would be treated as either dying without ESRD or developing ESRD, which might result in a slightly more DM-ESRD incident patients in the model than would obtain in reality. Secondly, the model selects transplant candidates only based on their age (and a randomly selected age-related factor), whereas in reality the patients were selected based on their health condition and suitability for transplant. Without such algorithms in the model, the patients getting transplanted in the model might die quicker or slower than the well selected candidates. The current design for determining suitability of transplant based on age is unlikely to have a noticeable impact on the outcome from the baseline scenario, as the number of transplant is low and there are many patients waiting to be transplanted. However, in alternative scenario where more patients could receive transplant, the selection criteria could make a bigger difference in terms of patient’s survival time and other considerations. In addition to the limitations with model structures, misestimates of the input parameters used in the model might affect the model results.

When viewing the cost output from the model, it is important to keep in mind that cost data input were taken from a research study based on services and costs obtaining in Calgary rather than in Saskatchewan, and there might be considerable differences for managing DM-ESRD patients between those two provinces. Also, as discussed earlier, the Cox Proportional Hazards model used in the model for dialysis patients was conducted on patients from 1999 to 2008, and we adjusted the values for different time periods by an added calendar covariate. Especially for later years in the projection period, the approximation we made with the calendar adjustment covariate might diverge from reality, which is likely to impose unrealistically higher

or lower mortality rates used in the model for dialysis patients. Moreover, we used a scaling factor for scaling the Saskatoon Diabetes Population to the Saskatchewan Diabetes Population starting in year 2006, which is one simple number refined for sub-population groups. This is likely to be significantly off; for example, the proportion of First Nations people in the Saskatoon Health Region might be different than the proportion of First Nations people in the province. Also, the same scaling ratio used for 2006 were used for all the years between 2006 and 2025. This is another oversimplified approximation because it is likely the scaling ratio will change over a 20 year's period, especially given the slowly rising urbanization of the population. Also, many rates (e.g. the selection between HD and PD as initial treatment, the transplant rates) used for projection are based on the last several years in which the values are known, and those rates remain invariant throughout the projection period. It is highly likely that those rates in the future would be different than in the last several years where we do have data.

The model output is generated with the limitations in the model structure and data input as discussed above. Although in Section 8.1 the model output was validated against history data successfully, it is important to know that the limitations exists and that model output especially in the later years of the projection period should to be viewed with those limitations in mind. To improve model results in the future, refined model structure should be worked on, and more data from recent years should be entered into the model.

CHAPTER 9

CONCLUSION

This chapter first provides a summary of the development of the Saskatchewan DM-ESRD model, the results of sensitivity analysis, and the projection made by the model. We then turn to discuss the contribution made by this thesis research. Finally, areas of future work are identified.

9.1 Summary of Thesis Research

Our diabetes study [18] reported that from 1980 to 2005, diabetes prevalence in Saskatchewan is rising at an alarming rate, which would inevitably affect the DM-ESRD situation in the provinces for many years down the road. This research helped motivate us to develop an agent based model for studying the DM-ESRD situation in Saskatchewan and to use the model for projecting the prevalent case count of DM-ESRD patients and associated cost for caring for those patients for up to year 2025.

Diabetes patients enter the model when they are diagnosed with diabetes and leave the model upon their death. During a simulated diabetic's life in the model, there are three important process represented, including progression of Diabetes to ESRD, ESRD treatment options, and the process involving transplant assessment and occupying the waiting list. The part of the model which handles Diabetes to ESRD progress is adopted from a previously built agent based model on the basis of competing risk analysis research on the Saskatchewan Diabetic population between year 1980 and 2005 [37]. Based on hazards derived from the competing risk analysis, Diabetes patients will either die prior to ESRD or develop ESRD. The ESRD treatment options are available to patients developing ESRD as a complication. After developing ESRD, patients start with either HD or PD. Also, for those patients who undergo kidney transplants, the model

used three stages to classify the time post kidney transplant because of the significant cost differences among those time periods. The transplant assessment and waiting list process in the model determines a patient's suitability for transplant, and places eligible patients on the transplant waiting list. Patients then receive transplants based on their priorities on the waiting list.

The model simulates lives of the diabetic population in Saskatchewan between Jan 1st, 1980 and Dec 31st, 2025. Prior to the start of model simulation, diabetic patients who are alive and who have not yet developed ESRD (referred as “the year 1980 DM Prevalent patients”) and those who are alive and who have developed DM-ESRD (referred as “the year 1980 DM-ESRD prevalent patients”) are both loaded into the model as the initial model population. After the simulation begins on Jan 1st, 1980, patients enter the model at the time they receive diabetes diagnosis. The diabetes incident patients between 1980 and 2005 were obtained from the Saskatchewan Administrative database. Between 2006 and 2025, the diabetes incident patients were projected by the Saskatoon Diabetes Model [36] and adjusted by a scaling ratio for the province as a whole.

The essential model transitions are parameterized with rates based on historical data from reliable data sources. The deaths of patients receiving HD, PD and Transplant were based on a Cox Proportional Hazards model provided by a data request fulfilled by CIHI. The itemized cost data is from a published study carried out in Calgary [34]. The graft failure rates were from the year 2012 CORR annual report. The hazard of switching between HD and PD treatment were calculated based on the dialysis treatment data between 2006 and 2010 provided by Dr. Kappel of the Saskatchewan Renal Program. The rates of living and deceased donor transplant for DM-

ESRD patients in Saskatchewan were calculated based on data from a data request fulfilled by CIHI and the data on “2007 – 2008 Highlights” published by the Saskatchewan Renal Program.

For some transitions where there is limited historical data available, parameters were set through calibrations. Most of the calibrated rates were for the transplant assessment and waiting list process, including rates of withdrawing from the waiting list, the rates associated with assessing the eligibility for transplant, and the duration of the assessment. Moreover, in recognition of the shortcomings of the Cox Proportional Hazards model used for calculating the mortality risks for dialysis patients, we added a missing and yet important covariate – the calendar year period. We calibrated the value of added covariate for the Cox Proportional Hazards model.

The model output includes both high level statistics collected on model population, and the detailed longitudinal records of an individual patient’s activities in the model. The high level statistics were saved into flat data files and can be visualized in graphs created by an R script. The high level statistics were used for model validation and sensitivity analysis. The detailed records of individuals were saved to a MySQL database specially created for the thesis research, which allows investigators to trace the activities of an individual throughout their lifetime in the model.

To validate the correctness of the model, a number of model outputs were selected for comparison with the corresponding historical data. The model output chosen for model validation include the prevalent and incident case count for all DM-ESRD patients, the prevalent and incident case count for patients on each ESRD treatment modalities (HD, PD, and Transplant), and the mean age of patients initiating HD/PD/Transplant, head count on the waiting list and the median days spent on dialysis prior to transplant. All the model output

except the transplant prevalent case count aligns well with the historical data, which suggesting that the model captures well relevant processes and is likely to be correctly implemented.

To understand the sensitivity of model outputs in response to changes in certain parameters and assumptions, a few scenarios were set up. Critical model outputs were selected for making comparisons between the base line scenario and the alternative scenario used for sensitivity; such outputs included prevalent case count, cost, and person years lived. We make a few remarks here on some results. The results suggest that the prevalent case count is not sensitive to changes made to graft failure rates (scenario #6), assessment time (scenario #7) and even the rates of transplant (scenario #8). The reason is likely to be the small portion of all DM-ESRD patients occupied by transplant patients. However, the model prevalent case count is sensitive to changes in mortality rates (scenario #5) and selection of treatment modalities (scenario #1, #2 and #3), which could be explained with the changes affected by HD in the model. Since HD patients form the majority of DM-ESRD patients, any changes affecting this group will be reflected clearly in the overall prevalent case count and cost. Other than being used for sensitivity analysis, results from those scenarios can further be used for lending insights regarding the potential impact of broad policy changes. For instance, scenario #1 allows all patients receiving pre-emptive transplant (shedding light on the impact of changing the availability of pre-emptive transplants) where scenario #5 reduced the mortality risks in half for all patients (giving a sense of many changes likely to result from advances in treatment technologies and clinical practice). Both scenarios increased prevalent case counts and person years lived by approximately the same amount. However, astonishing differences between scenario #1 and scenario #5 are found in cost. The cost in scenario #1 is less than in the baseline scenario; whereas the cost is more in scenario #5 than in the baseline. At the end of year 2025,

the per year cost in scenario #1 is only about half of the cost in scenario #5. The results can suggest to policy maker which policy could bring more cost effective results. Also, as in the extreme case depicted in scenario #4, where the DM incident cases are reduced to zero at the beginning of year 2006 for many years after that, the resource demands associated with caring for the existing patients remain at an elevated level and continue at rise. This result suggests the tremendous inertia present in the system, which places limits on the short-term gains that can be anticipated even through even the most extreme advances in the prevention of diabetes.

Finally, as seen in the baseline projections were made by the model, the prevalent case count, cost and person years lived by DM-ESRD patients in Saskatchewan have continued at rise throughout the entire projection period. Bigger increases were seen in the first 20 years prior to year 2000, yet for later years, the numbers remain increasing at slower rates. Also, the model reported the shocking amount of money required for caring a small group of patients through the projection periods. For instance, for the set of cost items considered in this thesis, it will cost about \$54 million dollars (in 2008 dollar values) to care for 1229 DM-ESRD patients in Saskatchewan in year 2025. Also, the model findings confirmed that First Nations patients can be anticipated to continue to be affected by the DM-ESRD diseases disproportionately compared to other Saskatchewan residents.

9.2 Contributions

The thesis research made contributions in two primary areas. Firstly, the calculation of the DM and DM-ESRD prevalent and incident rates contributed (via joint work) to DM and DM-ESRD research in Saskatchewan featured in three publications [18, 0, 40]. Secondly – and most importantly – the development Saskatchewan DM-ESRD model made its own contributions in the fields, which will be discussed in great detail in section 9.2.2.

9.2.1 Contributions in DM and DM-ESRD Research

Using diabetes and ESRD data supplied to our research team by the Saskatchewan Ministry of Health and the covered population data collected from the Saskatchewan Ministry of Health web site [26], I calculated the standardized prevalence and incidence rates for diabetes and diabetic-ESRD in the province of Saskatchewan between 1980 and 2005. The details of the calculation of diabetes and diabetic-ESRD rates are found in Appendix B. The calculation of those rates contributed to the diabetes and DM-ESRD research led by Drs. Dyck and Osgood. The DM-ESRD research [20] identified disparities among all the sub-population groups stratified by ethnicity, gender and age when experiencing Diabetes and DM-ESRD. Those findings in diabetes [18] and diabetic-ESRD research [19] provided not only the motivations for us to develop the Agent Based model presented here to further study the DM-ESRD situations in Saskatchewan, but also a concrete base of empirical data for grounding the SK diabetic – ESRD model.

9.2.2 Contributions through the Development of the SK DM-ESRD Model

Our model was developed specifically to study DM-ESRD. Other Canadian projections focus on prevalence and cost for diabetes and all its major complications. Among all diabetes related complications, Cardiovascular disease (CVD) complications takes the largest proportion in cost, which therefore has been studied the most. Diabetic CKD and ESRD, which is less common compared to CVD, has been addressed in many studies but not in as great detail as CVD complications. Our study recognized that while even fewer diabetics have developed ESRD, the cost per capita is the highest of all diabetes complications due to the costly nature of renal replacement therapy. Moreover, supporting ESRD patients requires capital infrastructure – in the form of dialysis clinics – whose construction requires planning years before that

infrastructure is commissioned. Therefore, our model was developed to project the prevalence and cost for all DM-ESRD patients in Saskatchewan and the prevalent and incident count for patients receiving each renal replacement treatment, which can provide valuable information for resource planning.

In addition to having a more specific focus, our model can offer more refined projections of incident and prevalent cases of DM-ESRD than have past projections. Other Canadian research only projects diabetes prevalence on refined age groups but not on other diabetes risk factors, and assumes a flat incidence rate of diabetes complications in its projection years [8]. A Manitoba study [20] projected diabetes prevalence by age group, by status Indian and gender, and by age group and Indian status, but not by all three together; it also projected new persons with diabetes on Dialysis by registered Indian status. Our projected diabetic-ESRD prevalence is broken down by age, gender and ethnicity/Indian Status. Those three factors have been demonstrated in previous research [20] as important risk factors for diabetes. Our most critical model inputs are broken down by age, gender and ethnicity: the DM and DM-ESRD prevalent cases at 1980 loaded into the model as the initial population, the yearly diabetes incident cases, the competing risk analysis for diabetes patients to develop ESRD or die, the Cox Proportional Hazards for DM-ESRD patients receiving the three renal replacement modalities (HD, PD and kidney transplant).

Another advantage with our model is the quality of the data used. The critical data input for our model came from published research studies conducted in Saskatchewan as well as data requests filled by CIHI, which administrates the national database for organ transplants and end stage renal disease in Canada. Information such as age, sex, ethnicity, age of getting diabetes diagnosis for each individual in the model population came from the Saskatchewan Health

Administrative database. The competing risks analysis of developing ESRD or death without ESRD for diabetes patients in Saskatchewan conducted in a previous study [37] were based on data from the Saskatchewan Health Administrative database as well. The mortality hazard function used for patients receiving renal replacement treatment modalities were provided by CIHI using 1999 -2008 data. The itemised cost information was taken from published research conducted using cost information from Calgary. Both the transplant rates and the possibility of receiving one type of dialysis were provided by CIHI data request.

Through insightful design, careful implementation of the model, making use data from the reliable data authorities and incorporation of relevant research studies, we were aiming to build a model correctly representing the DM-ESRD situation in Saskatchewan. The model output which measures different underlying processing within the model haven been extensively validated against historical data from multiple sources including over 25 years longitudinal data.

Most importantly, the current model has demonstrated the capacity for straightforward integration with other Anylogic models such as the model of competing risk analysis for diabetes patients [37]. Our model also used the diabetes incident cases projected by the Saskatoon Diabetes Model, which is a System Dynamics model. Though the current interaction between the Saskatoon Diabetes Model (System Dynamics model) and our Saskatchewan DM-ESRD model (Agent Based Model) is currently merely undertaken by data feed files, Anylogic does have the capacity to adopt a System Dynamics Model into its environment and allow the incorporation between the two types of models. While adoption of the Saskatoon Diabetes Model using Anylogic is out of scope of this thesis, it is among one of the avenues for future work discussed below.

Moreover, given the availability of the model presented here in AnyLogic, the Saskatchewan Gestational Diabetes Mellitus (GDM) model – another agent based Anylogic model developed based on the findings in the GDM research [31] – can be readily integrated with the Saskatchewan DM-ESRD model. The GDM model captures fact that babies of diabetic mothers have a higher risk of developing diabetes during their lifetime, and is used to study the impact of GDM on diabetes situation in Saskatchewan. In conclusion, the Saskatchewan DM-ESRD Model, the Saskatoon DM Model, and the Saskatchewan GDM model, each focusing different aspects of the diabetes research, can all be incorporated together to form a larger and richer models for studying diabetes and ESRD as its complications.

Most of the previous modelling work following a mathematical modeling approach offered a less intuitive interface for policy makers to view and work with the model. Our model is built with Anylogic software, which offers an animated presentation layer for people to understand structures of the system, and provides tools to help policy makers to try out different policies in more effortless way.

Other than the benefits offered by using the Anylogic software, our Saskatchewan DM-ESRD model is equipped with a database which can record demographics information, treatment histories, waitlist, assessment and cost data for every patient in the model population. The database allows tracing activities and events relevant to DM and DM-ESRD for each individual, so that more analysis can be carried out during simulation time and after simulation ends. A more detailed calibration and validation can be achieved using longitudinal data collected in the model (e.g. waiting list time). Moreover, the capacity to collect such information permits treatment choice or design in the model to be based the individual's medical histories retrieved from the database.

In addition to a database for saving data at individual level, the Saskatchewan DM-ESRD model also saves aggregated data regarding the model population into flat data files. An R script is developed to automatically retrieve the data from those flat files and present data into graphic format for interpretations and comparison.

In summary, when compared to similar research work, our research is distinguished in choosing agent based modeling to study the research question, the sound data used for making the projection, and a more detailed projection resulted from the careful design of the model. To the best of our knowledge, our model is the first agent based model being applied to project the prevalence and cost of diabetic – ESRD in Saskatchewan, and likely in Canada as well. The ability to project the detailed treatments of Aboriginal population also sets our research apart from other research work. In addition, the data used in our model is from sound research conducted in Saskatchewan [18,0] and using Saskatchewan statistics as well as the national database for organ replacements CORR. Our model produces a refined projection of the prevalence and cost for sub-population groups which are broken down by critical population characteristics such as age, sex and ethnicity. Based on the benefits mentioned above, we believe our model offers a substantial contribution to the field.

9.3 Future Work

A few improvements have been identified in model structures and model input data sources through the development of the Saskatchewan DM-ESRD model, yet fall outside the scope of this thesis due to time or other consideration. The areas that merit additional work in the future are laid out in detail below.

More work is required in the transplant assessment and waiting list process as the current representation in the model is an over-simplified version of reality. First of all, an algorithm for

evaluating patient's suitability for kidney transplant based on their health conditions should be developed. The type of medical examinations required as part of the transplant assessment and the length of time for completing those examinations require additional investigation. The result of the medical examinations will likely to be used as input parameters in the algorithm for determining patient's suitability for transplant. The length of time required to complete those examinations will affect the time spent on dialysis prior to transplant, which is the combined time of time spent on assessment and time spent on waiting list. Secondly, an algorithm for determining a patient's priority on the transplant waiting list should be developed. Currently, the priority is randomly generated without basing it on a patient's characteristics. In reality, there is a complex algorithm for determining patient's priority, which should be replicated in the model (although likely with some stochastic components). Moreover, additional investigation is required regarding the process of placing patients on the waiting list on hold due to temporary health condition which made them unsuitable for transplant. Currently in the model, the structure for the "On Hold" and "Active" status on waiting list is implemented but disabled; moving forward, the rates for switching patients' "On Hold" and "Active" status should be found and supplied to the model. Lastly, further research should be conducted with regards to withdrawing patients from the waiting list. Currently, the rate of withdrawing patients from waiting list is calibrated through simulations instead of coming from historical data.

In addition, the "end of coverage" rates among Diabetes incident patients should be researched. Currently, only patients who have developed Diabetes prior to Jan 1st, 1980 (also referred as the 1980 DM Prevalent Cases) could end their health coverage in the model, but not the diabetes incident patients. The diabetes incident patients in the model currently have two options, including death before developing ESRD or develop ESRD as complication, without the

possibility to end their health care coverage, which is the missing third option. Although the number of patients who should have ended their coverage in reality and received ESRD diagnosis in the model is likely to be very small, improvements are advised in future versions of the model.

Lastly, improvement should be made on regarding integration with the Saskatoon Diabetes Model. There are two areas that should be improved, including the scaling ratio used and the mechanism of receiving input from the Saskatoon Diabetes Model. The Saskatoon Diabetes Model projects the diabetes case count from 2006 to 2025 for the Saskatoon Health Region. To scale up the projection for Saskatoon to Saskatchewan, a simple ratio is used in our model. More research should be carried to either modify the Saskatoon Diabetes Model to project for the Saskatchewan Diabetes situation or further refine the ratio used in the DM-ESRD model so that the projection is more accurate for the sub-population groups and for later years of the projection period.

In addition to future improvements made to the model structures and data, more thought should be given to the application of the model in policy evaluation. One possible direction could be using the model to evaluate combinations of policies which could impact several processes in the model at once – potentially identifying policy synergies where “the whole is greater than the sum of the parts”. An example might be combination of policies focusing on upstream issues paired with downstream issues. The metrics or measurement of the effectiveness of the policy could include – but is not limited to – the ratio of saving on resources over the investment required for implementation and execution of those policy combinations. To make the model a practical application in the real world, we would expect more thorough research and lots of collaborations with practitioners in the field.

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APPENDIX A

STATISTICS COLLECTED ON MODEL POPULATION DURING SIMULATIONS

Statistics were collected on the model population during simulations for the purpose of model validation, sensitivity analysis and projections. In the tables below, those statistics were categorized by the process to which they are related. In each table within this section, each statistic was described, both in terms of what they are and what model elements were involved for collecting and processing them. The statistics were saved in a comma delimited file for future analysis. In most of the cases, the output statistics were saved with metadata given the year it was collected for and identified by the simulation run from which statistics were collected.

Table A-1. Statistics Related to DM

Statistics and Output File Name	Model Elements
<p>Per-year count of DM Patients who died before developing ESRD per year DeathB4ESRD.csv</p>	<p>In the Main class, the number of DM patients who died prior to developing ESRD is kept in the variable named “deathB4ESRDYearlyCount”. The entry action handler of the state named “DeathBeforeESRD” is established so that each time a patient enters the state, the variable “deathB4ESRDYearlyCount” will get incremented by 1. At the end of each year, the value of variable “deathB4ESRDYearlyCount” and the value of the current year will be saved to the data set named “deathB4ESRDIncidenceDS”. The values in the data set “deathB4ESRDIncidenceDS” will be saved to the file named “DeathB4ESRD.csv” at the end of the simulation.</p>
<p>The person years lived for overall model population per year since model start time PersonYearLived_DM_Yearly.csv</p> <p>The cumulative person years lived for the entire model population collected</p>	<p>The person years lived for the model population in a year are accumulated by counting the person days lived for the model population for each day within the year. At the end of every day, the person days lived for the model population is collected by counting the number of people alive in the model at that moment. We assume each of those patients who is alive at the end of the day has already lived a full day. This is an approximation, as with this assumption, patients who enter the model for only half a day will be counted as living in the model for a</p>

<p>between the model start time and the end of each year. PersonYearLived_DM_RunTotal.csv</p>	<p>full day. Patients who die in the middle of the day will not be counted. In the model, the number of DM patients alive was counted by a population statistics “DMPatientsAlive”. In the event “personDaysLivedUpdate”, at end of end of every day, the count from “DMPatientsAlive” was converted from days into years, and was added to a variable “runTotalDMPersonYearLived” which keeps track of the running total of years lived by all DM patients in the model since the model start time. At each year end, in the function named “updateResultSetYearEnd”, the “person year lived” recorded in the variable “runTotalDMPersonDayLived” will be saved into two data sets “yearlyDMPersonYearDS” and “runTotalDMPersonYearDS”. When the simulation ends, the year and value pair in data set “yearlyDMPersonYearDS” will be written to file named “PersonYearLived_DM_Yealy.csv” and the data set “runTotalDMPersonYearDS” will be written to file named “PersonYearLived_DM_RunTotal.csv”.</p>
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Table A-2. Statistics related to DM to ESRD progression

Statistics and Output File Name	Model Elements
<p>The number of new patients diagnosed with ESRD in a year. ESRDIncident.csv</p>	<p>The variable named “ESRDIncidentCount” in the Main class is used to keep track of the new patients receiving ESRD diagnosis in a year. The value of the variable “ESRDIncidenceCount” should be equal to the sum of the count of patients who have initiated HD, PD and Pre-Emptive Transplant. The variable “ESRDIncidenceCount” gets incremented in the “ESRD” state each time a patient enters the state. The value of variable “ESRDIncidentCount” and the value of the current year get saved to the dataset named “ESRDIncidenceDS”. At the end of a simulation, values in data set “ESRDIncidenceDS” will be written to a file named “ESRDIncident.csv”.</p>
<p>The number of patients living with ESRD (Prevalent Cases) at each year’s end.</p>	<p>The total number of patients receiving ESRD treatments at the end of Dec 31 of every year was</p>

<p>DMESRDPrevalent.csv</p>	<p>collected by adding up the count of patients receiving HD, PD and Transplant, kept track by the population statistics “CountHD”, “CountPD”, and “CountTransplant”, respectively. The count of patients receiving ESRD treatments at each year’s end together with the value of the year are saved in to the data set named “ESRDPrevalentDS”. At the end of a simulation, the values in the data set “ESRDPrevalentDS” will be written to the file named “DMESRDPrevalent.csv”.</p>
<p>The number of DM-ESRD patients who died in a year. DeathDMESRDPerYear.csv</p>	<p>The variable named “deathDMESRDPerYearCount” in the Main class is used to keep track of the number of deaths per year for DM-ESRD patients. In the state named “DeathAfterESRD”, the variable “deathDMESRDPerYearCount” gets incremented each time when a DM-ESRD patient dies. At the end of each year, the value of variable “deathDMESRDPerYearCount” and the value of the current year will get saved to the data set named “deathDMESRDPerYearDS”. At the end of the simulation, the values from data set “deathDMESRDPerYearDS” will be written to the file named “DeathDMESRDPerYear.csv”.</p>
<p>The person years lived for DM-ESRD patients per year since the model start time PersonYearLived_DMERSD_Yealy.csv The accumulated person years lived for DM-ESRD patients at year end since the model start time PersonYearLived_DMESRD_RunTotal.csv</p>	<p>The person years lived was collected for DM-ESRD patients in a similar fashion to the person years lived for all DM patients. In the model, the number of DM-ESRD patients alive at the end of every day was counted by population statistic “DMESRDPatientsAlive”. At of the end of every day, the event “personDaysLivedUpdate” is triggered. This event first converts the count by the statistic “DMESRDPatientsAlive” from “person days lived” to “person years lived”, and adds the result to the variable named “runTotalESRDPersonYearLived”, which keeps track of the running total of years lived by the DM-ESRD patients in the model since the model start time. At the end of each year, in the function named “updateResultSetYearEnd”, the “personday lived” recorded in the variable “runTotalESRDPersonYearLived” gets saved into two data sets “yearlyESRDPersonYearDS” and</p>

	<p>“runTotalESRDPersonYearDS”. When a simulation ends, the year and value pair in the data set “yearLESRDPersonYearDS” is written to the file named “PersonYearLived_DMERSD_Yealy.csv”, and the data set “runTotalESRDPersonYearDS” is written to the file named “PersonYearLived_DMESRD_RunTotal.csv”.</p>
<p>The cost for caring for DM-ESRD patients in Saskatchewan for a year SKYearlyTotalCost.csv The accumulated cost for caring DM-ESRD patients in Saskatchewan at year’s end. SKRunningTotalCost.csv</p>	<p>The cost varied for patients receiving different ESRD treatments. The cost for caring all DM-ESRD patients per day was calculated by adding up the cost for caring HD, PD and transplant patients each day. The per day cost of caring for patients on a given ESRD treatment is computed by multiplying the number of patients receiving that treatment by the average daily, per-patient cost of running the treatment . In the model, the number of patients on each treatment was collected at the end of each day by querying the population statistics ”CountHD”, “CountPD”, “CountLDKTTXFirst90Days”, “CountLDKTTX91DaysToOneYear”, “CountLDKTFunctionalTX”, “CountDDKTTXFirst90Days”, “CountDDKTTX91DaysToOneYear”, and “CountDDKTFunctionalTX”. The cost for a kidney transplant operation is considered as one time cost rather than the everyday cost so it is excluded from the per day cost for caring for transplant patients; the operation cost is added to total cost at the time an operation takes place. The total cost exerted for a given day for caring DM-ESRD patients are accumulated on a daily basis into per year cost, which gets saved into the data set “yearlyCostDS” at the time of a year end. The running total cost for caring all DM-ESRD patients throughout the model simulation period is saved into the “runTotalDMESRDCostDS” data set.. At the end of the simulation, the year and cost value pair in the “yearlyCostDS” data set will be written to file named “SKYearlyTotalCost.csv”; the values in the “runTotalDMESRDCostDS” data set will get written to file named “SKRunningTotalCost.csv”.</p>

Table A-3. Statistics for Patients Receiving HD

Statistics and Output File Name	Model Elements
<p>Count of new HD patients in a year who have never received any ESRD treatment before. HD_Initial.csv</p>	<p>The “HDIncidenceCountInitial” variable in the main object is used to keep track of the number of new patients who start HD as initial ESRD treatment. In the entry action of the “Hemodialysis” state, this variable gets incremented only when the patients have HD as their initial ESRD treatment and they are not among those year 1980 DM-ESRD Patients who started on HD at model start time. The value of variable “HDIncidenceCountInitial” and the current year value will be saved together into the data set named “HDIncidenceInitialDS” at each year end. The data set “HDIncidenceInitialDS” will be written to “HD_Initial.csv” at the end of the simulation.</p>
<p>Count of patients who begin HD treatment in a year. Patients starting HD treatments could be returned from failed transplant, or be switching from PD treatments. HD_Activity.csv</p>	<p>The “HDIncidenceCountActivity” variable in the Main object is used to keep track of the number of patients who began HD treatment. In the entry action handler of the “Hemodialysis” state, this variable gets incremented as soon as patients begin HD. The value of variable “HDIncidenceCountActivity” and the current year value will be saved together into the data set named “HDIncidenceActivityDS” at each year end. The data set “HDIncidenceActivityDS” will be written to “HD_Activity.csv” at the end of the simulation.</p>
<p>Count of Patients who are receiving HD treatment at the end of each year (prevalent case count) HDPrevalent.csv</p>	<p>The population statistics “CountHD” is used to keep track of the number of patients who are receiving HD treatment in the model. At the end of each year, the value of “CountHD” and the value of the year were saved together into the “HDPrevalentDS” data set. At the end of the simulation, the values in “HDPrevalentDS” will be written to a file named “HDPrevalent.csv”.</p>
<p>The yearly number of patients who died while receiving HD treatments in a year. DeathHDPerYear.csv</p>	<p>The variable named “deathHDPerYearCount” is used for keeping track of the death of HD patients in a year. In the transition named “dialysisToDeathTrans”, the variable “deathHDPerYearCount” gets incremented when patients receiving HD treatment die. At the end of each year, the value of variable “deathHDPerYearCount” and the value of the current year will be saved as a pair into the data set named</p>

	<p>“deathHDPerYearDS”; the value of deathHDPerYearCount is then reset to 0. At the end of the simulation, the values in the data set “deathHDPerYearDS” will be written to the file named “DeathHDPerYear.csv”.</p>
<p>Average age of Patients who start dialysis HD as initial treatment in the year</p> <ul style="list-style-type: none"> - AvgAgeInitialHD.csv 	<p>In the transition “receivePD” of the DiabeticESRD statechart, the age of patients entering the transition would be added to a statistics object named “ageInitialPDStats” in the Main Class. At each year end, the mean is collected from all the ages in the “ageInitialHDStats” object, which gets the average age of the patients who initiated HD treatment in that year. And the resulting average age will be added to the “ageAvgInitialHDDS” data set with the value of the year. At the end of the simulation, the year and mean age value pair will be written from the “ageAvgInitialHDDS” data set to a file named “AvgAgeInitialHD.csv”.</p>
<p>The median of days lived from the start of HD treatment to death among people who have died in the current year and within the last four years.</p> <p>DaysLivedToDeathHD.csv</p>	<p>The vector named “HDdayslivedPriorToDeathVector” in main class is used to collect the number of days lived during HD treatment for each HD patients died in a year. At the end of the year, the vector “HDdayslivedPriorToDeathVector” and the value of the current year are added to the hash table named “HDdayslivedPriorToDeathHT”, and the median number of days lived among those HD patients who died within last five years are calculated by a function “getMedianDayslastNYear” (Note, the median can be calculated from data from many more years. The parameter “nYearBack” of function “getMedianDayslastNYear” is for setting the number of years to which the median calculation should go back.). The median of days lived by HD patients was then added to a data set named “HDdayslivedPriorToDeathDS”. At the end of the simulation, the values in the “HDdayslivedPriorToDeathDS” data set will be written to the file named “DaysLivedToDeathHD.csv”.</p>

Table A-4. Statistics for Patients Receiving PD

Statistics and Output File Name	Model Elements
<p>Count of new PD patients in a year who have never received any ESRD treatment before. PD_Initial.csv</p>	<p>The “PDIncidenceCountInitial” variable in the main object is used to keep track of the number of new patients who start PD as initial ESRD treatment. In the entry action handler of the “Peritonealdialysis” state, this variable gets incremented only when the patients have PD as their initial ESRD treatments and when they are not among those year 1980 DM-ESRD patients who started on PD at the model start time. The value of variable “PDIncidenceCountInitial” with the current year will be saved together into the data set named “PDIncidenceInitialDS” at each year end. The data set “PDIncidenceInitialDS” will be written to “PD_Initial.csv” at the end of the simulation.</p>
<p>Count of patients who begin PD treatment in a year. Patients starting PD treatments could be returned from failed transplant, or switching from HD treatment. PD_Activity.csv</p>	<p>The “PDIncidenceCountActivity” variable in the main object is used to keep track of the number of patients who began PD treatment. In the entry action of the “Peritonealdialysis” state, this variable gets incremented only as soon as patients began HD. The value of variable “PDIncidenceCountActivity” and the current year will be saved together into the data set named “PDIncidenceActivityDS” at each year end. The data set “PDIncidenceActivityDS” will be written to “PD_Activity.csv” at the end of the simulation.</p>
<p>Count of patients who are receiving PD treatment on Dec 31 of each year (prevalent case count) PDPrevalent.csv</p>	<p>The population statistics “CountPD” is used to keep track of the number of patients who are receiving PD treatment in the model. At the end of each year, the value of “CountPD” and the year were saved together into the “PDPrevalentDS” data set. At the end of the simulation, the values in “PDPrevalentDS” will be written to a file named “PDPrevalent.csv”.</p>
<p>Average age of patients who start PD as initial treatment in a year. AvgAgeInitialPD.csv</p>	<p>In the handler for the transition “receiveHD” of the DiabeticESRD statechart, the age of patients entering the transition is added to a statistics object named “ageInitialPDStats” of the Main Class. At each year end, the mean is collected from all ages that have been added to the “ageInitialHDStats” object, thereby computing the average age of the patients initialized PD treatment in that year. And the resulted averagewill be added to the</p>

	<p>“ageAvgInitialPDDS” data set with the value of the year. At the end of the simulation, the year and mean age value pair will be written from the “ageAvgInitialPDDS” data set to file named “AvgAgeInitialPD.csv”.</p>
<p>The number of patients who died while receiving PD treatments in a year. DeathPDPerYear.csv</p>	<p>The variable named “deathPDPerYearCount” is used for keeping track of the death of PD patients in a year. In the transition named “dialysisToDeathTrans”, the variable “deathPDPerYearCount” gets updated when patients receiving PD treatment died. At the end of each year, the value of variable “deathPDPerYearCount” and the value of the current year will be saved as a pair into the data set named “deathPDPerYearDS”. At the end of the simulation, the values in the data set “deathPDPerYearDS” will be written to the file named “DeathPDPerYear.csv”.</p>
<p>The median of days lived from the starting of PD treatment to death among people who have died in the current year and within the last four years. DaysLivedToDeathPD.csv</p>	<p>The vector named “PDdayslivedPriorToDeathVector” in main class is used to collect the number of days lived during PD treatment for each PD patient who has died within the current year. At the end of the year, the vector “PDdayslivedPriorToDeathVector” and the value of the current year are added to the hash table named “PDdayslivedPriorToDeathHT”, and the median number of days lived among those PD patients died within last five years are calculated by a function “getMedianDayslastNYear” (Note, the median can be calculated from data from many more years. The parameter “nYearBack” of function “getMedianDayslastNYear” is for setting the time window over which the median calculation should be performed). The median of days lived for PD patients was then added to a data set named “PDdayslivedPriorToDeathDS”. At the end of the simulation, the values in the “PDdayslivedPriorToDeathDS” data set will be written to the file named “DaysLivedToDeathPD.csv”.</p>

Table A-5. Statistics related to Patients Receiving HD or PD

Statistics and Output File Name	Model Elements
Count of deaths on Dialysis (HD or PD) in a	The dataset named “deathDialysisPerYearDS” are used to keep track of the number of patients died while receiving dialysis

year. DeathDialysisPerYear.csv	treatment (either HD or PD) in a year. At the end of a simulation, the values in data set “deathDialysisPerYearDS” will be saved to the file named “DeathDialysisPerYear.csv”.
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Table A-6. Output related to Patients Receiving Kidney Transplants

Statistics and Output File Name	Model Element
The number of pre-emptive kidney transplants per year PreEmptKT.csv	The variable named “PreEmptiveKTIncidentCount” in Main object is used for holding the count of the pre-emptive kidney transplant that have taken place in a year. In the “PreEmptiveTx” transition, the variable “PreEmptiveKTIncidentCount” gets incremented each time a pre-emptive transplant gets performed. At the end of a year, the value of variable “PreEmptiveKTIncidentCount” and the value of the current year will get saved to a data set named “PreEmptiveKTIncidentDS”; the variable “PreEmptiveKTIncidentCount” is reset to 0. At the end of the simulations, values in data set “PreEmptiveKTIncidentDS” will be written to a file named “PreEmptKT.csv”.
The yearly number of living donor kidney transplants that have taken place (incident case count). The count only includes those living donor transplants for patients who were on dialysis prior to the transplant, and excludes pre-emptive transplant. LDKT.csv	The variable named “LDKTIncidentCount” in Main Class is used to keep track of the cumulative number of living donor kidney transplant that have taken place in the current year. In the handler for the transition “receiveTx” transition of the “AssessmentStages” statechart, the variable “LDKTIncidentCount” gets incremented each time there is a living donor kidney transplant performed. The value of variable “LDKTIncidentCount” and the value of the current year will be saved to the data set named “LDKTIncidentDS”, and the variable LDKTIncidentCount is reset to 0. At the end of the simulation, the values in data set “LDKTIncidentDS” will be written to a file named “LDKT.csv”.
The yearly number of deceased donor kidney transplants that have taken place (incident case count). The count only includes those deceased donor transplants for patients who were on dialysis prior to the transplant, and excludes pre-emptive transplant.	The variable named “DDKTIncidentCount” in Main Class is used to keep track of the cumulative number of living donor kidney transplants that have taken place in the current year. In the transition “receiveTx” transition of the “AssessmentStages” statechart, the variable “DDKTIncidentCount” gets incremented each time there is a living donor kidney transplant performed. The value of variable “DDKTIncidentCount” and the value of the current year will be saved to the data set named “DDKTIncidentDS”,

DDKT.csv	and the variable DDKTIncidentCount is reset to 0. At the end of the simulation, the values in data set “DDKTIncidentDS” will be written to a file named “DDKT.csv”.
Yearly count of transplants following dialysis (incident case count) KT.csv	The sum of the living donor and deceased donor kidney transplants taking place in each year will be saved to a data set named “KTIncidentDS”. The values in “KTIncidentDS” will be written to a file named “KT.csv”.
Count of people living with functional transplant (prevalent case count) TransplantPrevalent.csv	The population statistic “CountTransplant” is used to keep track of the number of patients in the model who are living with functioningtransplanted kidney. At the end of each year, the value of “CountTransplant” and the value of the year were saved together into the “TransplantPrevalentDS” data set. At the end of the simulation, the values in “TransplantPrevalentDS” will be written to a file named “TransplantPrevalent.csv”.
Count of Graft Failures per year GraftFailure.csv	The cumulative number of grafts that have failed in a year is recorded in a variable named “graftFailureCount” in the Main Class. In the transition named “reEnterDialysis”, this variable is incremented each time a graft has failed. At the end of every year, the value of the variable “graftFailureCount” and the value of the current year will be saved to the data set named “GraftFailureIncidentDS”, and the variable graftFailureCount is reset to 0. At the end of a simulation, the values in the data set “GraftFailureIncidentDS” will be written to a file named “GraftFailure.csv”.
The number of patients who have died while receiving HD treatments in a year. DeathTXPerYear.csv	The variable named “deathTXPerYearCount” in the Main class is for keeping track of the cumulative count of patients who have died with a functioning kidney transplant in the current year. In the transition named “transplantToDeathTrans” in the “DiabetesESRD” statechart, the variable “deathTXPerYearCount” get incremented each time when patients with functional kidney transplants died. At the end of a year, the value of variable “deathTXPerYearCount” and the value of the current year will be saved to a data set named “deathTXPerYearDS”, and the variable deathTXPerYearCount is reset to 0. At the end of a simulation, the values in the data set “deathTXPerYearDS” will be written to the file named “DeathTXPerYear.csv”

<p>The average age of patients when patients receive kidney transplant (first graft) AvgAgeInitialTX.csv</p>	<p>In the “Transplant” state of the DiabetesESRD statechart, the age of patients who first received kidney transplant would be added to the statistic object named “ageInitialTXStats” in the Main Class. At each year end, the mean is collected from all the ages that have been added to the “ageInitialTXStats” object, which will then be added to the “ageAvgInitialTXDS” data set with the corresponding year value. The “ageAvgInitialTXDS” statistic object will be reset after the mean was added to the “ageAvgInitialTXDS” data set. At the end of the simulation, the values in the “ageAvgInitialTXDS” data set will be written to file “AvgAgeInitialTX.csv”.</p>
<p>The median of days lived counted from the day of the kidney transplant operation to the day of death among patients who have died in the current year and within the last four years. DaysLivedToDeathTX.csv</p>	<p>The vector named “TXdayslivedPriorToDeathVector” in the Main class is used to collect the number of days lived following kidney transplant until death for each kidney transplant patients who has died in the current year. At the end of the year, the vector “TXdayslivedPriorToDeathVector” and the valued of the current year are added to the hash table named “TXdayslivedPriorToDeathHT”, and the median number of days lived among those transplant patients died within last five years are calculated by a function “getMedianDayslastNYear” (Note, the median can be calculated from data from many more years. The parameter “nYearBack” of function “getMedianDayslastNYear” is for setting the size of the time window over which the median calculation should be performed). The median of days lived by transplant patients was then added to a data set named “TXdayslivedPriorToDeathDS”. At the end of the simulation, the values in the “TXdayslivedPriorToDeathDS” data set will be written to the file named “DaysLivedToDeathTX.csv”.</p>

Table A-7. Output Collected on Assessment Process

Statistics and Output File Name	Model Element
<p>Count of patients who weren’t sent for kidney assessment in a year. NotEligibleAssessment.csv</p>	<p>The variable named “countNotEligibleForAx” in Main class is used to record the number of patients who are deemed not suitable for transplant assessment in a year. In the transition named “notEligibleAssessmentTrans”, the variable “countNotEligibleForAx” gets incremented each</p>

	<p>time a patient was not sent for transplant assessment. At end of a year, the value in variable “countNotEligibleForAx” and the value of the year will be saved to the data set named “countNotEligibleAxDS”, the value of which will be written the file named “NotEligibleAssessment.csv” at the end of the simulation. The value of the variable countNotEligibleForAx is then reset to 0.</p>
<p>Count of patients who got sent for transplant assessment in a year. EligibleAssessment.csv</p>	<p>The variable named “countEligibleForAx” in Main class is used to record the cumulative number of patients who deemed suitable and were sent for transplant assessment in the current year. In the handler for the transition named “eligibleForAssessmentTrans”, the variable “countEligibleForAx” gets incremented each time a patient was sent for transplant assessment. At end of a year, the value in variable “countEligibleForAx” and the value of the year will be saved to the data set named “countEligibleAxDS”, the value of which will be written the file named “EligibleAssessment.csv” at the end of the simulation. The variable “countEligibleForAx” is then reset to 0.</p>
<p>End of year count of patients who remain in the assessment process as potential candidates for a living donor or deceased donor transplant. HeadCountAssessment.csv</p>	<p>The total number of patients who remain in the assessment process at the end of the year are obtained by adding up the count collected by population statistics objects “HeadCountDDKTWorkup” and “HeadCountLDKTWorkup”. The count and the value of the year are saved into the data set named “AssessmentHeadCountDS” at the end of the year. The values in the data set “AssessmentHeadCountDS” will be written to the file named “HeadCountAssessment.csv” at the end of the simulation.</p>
<p>The fraction of patients who passed the assessment and are deemed eligible for transplant. AssessmentPassRatio.csv</p>	<p>The fraction is calculated by dividing the number of patients passed the assessment by the total number of patients who pass or failed the assessment in a year. The variable named “countPassAX” is used for recording the number of patients who pass the assessment in a year. This variable gets updated in the handler for the transition named “putOnTransplantWaitingListTrans. The variable named “countFailAX” is for keeping track of the</p>

	<p>number of patients who fail the assessment in a year and it gets updated in transition “failAssessmentTrans”. The ratio for each year is saved to a data set named “AxPassRatioDS”, which will be written to the file named “AssessmentPassRatio.csv”. Both of the variables “countPassAX” and “countFailAX” are then reset to 0.</p>
<p>The number of patients who have died during the transplant assessment process in a year. DeathDuringAX.csv</p>	<p>The variable named “deathDuringAX” in Main class is used for keeping track of the number of patients died during assessment in a year. In the handler for the transition named “AxOrWaitingToDeathTrans”, the variable “deathDuringAX” gets incremented when the patient was last in the “WorkUpStage” state prior to death. At the end of year, the value of the variable “deathDuringAX” and the value of the year get saved to the data set named “deathDuringAXDS”. At the end of the simulation, the values in data set “deathDuringAXDS” will be written to a file named “DeathDuringAX.csv”. “deathDuringAX” is then reset to 0 at the end of the year.</p>
<p>Median Days spent on assessment for those patients who received transplant in this year and within the last two years. (Either living donor or deceased donor type). MedianDaysDDKTAXLast3Y.csv MedianDaysLDKTAXLast3Y.csv</p>	<p>The vector named “LDKTDaysAXVector” is used to collect the number of days spent on assessment for each patient who has received a living donor transplant within the current. At the end of a year, the contents of the vector “LDKTDaysAXVector” are added to the hash table “LDKTDaysAXHT”, and the function named “getMedianDayslastNYear” is called to calculate the median of the days spent on assessment among patients who got transplanted in the current year and in the last two years. The median based on three year’s data are then added to the data set named “LDKTDaysAXDS”, the values of which got written to the file named “MedianDaysLDKTAXLast3Y.csv”. The median of days spent on assessment for patients who received a deceased donor transplant was calculated in a similar fashion to that for patients received living donor transplant. The median was written to the file named “MedianDaysDDKTAXLast3Y.csv”.</p>

Table A-8. Output Related to Waiting List for Kidney Transplant

Statistics	Model Element
<p>End of year head count for patients on the waiting list for a living donor kidney transplant. HeadCountOnLDKTWaitList.csv</p>	<p>The population statistic named “HeadCountWaitingListLDKT” is used to calculate the number of patients who are waiting for a living donor transplant on the waiting list at the end of the year. The count and value of the year are saved as a pair into the data set named “WaitListLDKTHeadCountDS” at the end of the year. The values in “WaitListLDKTHeadCountDS” are written to the file named “HeadCountOnLDKTWaitList.csv” at the end of a simulation.</p>
<p>End of year head count for patients on the waiting list for a deceased donor kidney transplant HeadCountOnDDKTWaitList.csv</p>	<p>The population statistic named “HeadCountWaitingListDDKT” is used to calculate the number of patients who are waiting for deceased donor transplant on the waiting list at the end of the year. The count and value of the year are saved as a pair into the data set named “WaitListDDKTHeadCountDS” at the end of the year. The values in “WaitListDDKTHeadCountDS” are written to the file named “HeadCountOnDDKTWaitList.csv” at the end of a simulation.</p>
<p>End of year head count for patients on the waiting list for either the living donor or deceased donor transplant. HeadCountOnWaitList.csv</p>	<p>The total number of patients waiting for either a living donor transplant or a deceased donor transplant is saved into the data set named “WaitListHeadCountDS”. At end of the simulation, the values in the data set “WaitListHeadCountDS” are written to the file named “HeadCountOnWaitList.csv”.</p>
<p>The yearly number of patients who died while on the waiting list. DeathOnWaitList.csv</p>	<p>A variable named “deathOnWaitList” in the Main class is used to keep track of the cumulative number of patients who have died on the waiting list in the current year. In the handler for the transition “AxOrWaitingToDeathTrans” of the “AssessmentStages” statechart, the variable “deathOnWaitList” is incremented if the patient was on the waiting list prior to death (i.e. if the patient was in state “AwaitingTx”). The value of the variable “deathOnWaitList” and the value of the year will be saved to a data set named</p>

	<p>“deathOnWaitListDS” at the end of each year. The variable “deathOnWaitList” is then set to 0. The values in the data set “deathOnWaitListDS” will be written to the file named “DeathOnWaitList.csv” at the end of a simulation.</p>
<p>The yearly number of patients who withdrew from the transplant waiting list.</p> <p>WithdrewWaitList.csv</p>	<p>A variable named “countWithdrawWaitList” in the Main class is used to keep track of the number of patients who have withdrawn from the waitlist during a year. At the end of a year, the value of “countWithdrawWaitList” and the value of the year will be saved into the data set named “withdrawWaitListDS”. The value of “countWithdrawWaitList” is then set to 0. At the end of the simulation, the values in data set “withdrawWaitListDS” will be written to the file named “WithdrewWaitList.csv”.</p>
<p>Median Days spent on the transplant waiting list for those patients who received a transplant (with either living donor or deceased donor type) in this year and in the last two years.</p> <p>MedianDaysLDKTWaitListLast3Y.csv MedianDaysDDKTWaitListLast3Y.csv</p>	<p>The median for days spent on transplant on the waiting list is calculated in a similar way as for median days spent on assessment. The model elements involved are the vector named “LDKTDaysWaitListVector”, the hash table named “LDKTDaysWaitListHT” and the data set named “LDKTDaysWaitListDS”. At the end of the simulation, the median days spent on waiting list are written to the file named “MedianDaysLDKTWaitListLast3Y.csv”.</p> <p>The median for days spent on transplant waiting list is calculated in a similar way as for median days spent on assessment. The model elements involved are the vector named “DDKTDaysWaitListVector”, the hash table named “DDKTDaysWaitListHT” and the data set named “DDKTDaysWaitListDS”. At the end of the simulation, the median days spent on waiting list are written to the file named “MedianDaysDDKTWaitListLast3Y.csv”.</p>

Table A-9. Output Related to Waiting List and Assessment Process

Statistics	Model Element
Median number of days spent in	The median for days spent on dialysis

<p>assessment and on the wait list prior to getting transplant for those patients who received a transplant (either living donor or deceased donor type) in this year and the last two years. MedianDaysLDKTDialysisToTXLast3Y.csv MedianDaysLDKTDialysisToTXLast3Y.csv</p>	<p>(assessment time + waiting list time) prior to getting living donor transplant is calculated in a similar way as is used for median days spent on assessment. The model elements involved for living donor type of transplant are the vector named “LDKTDaysDialysisToTXVector”, the hash table named “LDKTDaysDialysisToTXHT” and the data set named “LDKTDaysDialysisToTXDS”. At the end of the simulation, the median days spent on waiting list are written to the file named “MedianDaysLDKTDialysisToTXLast3Y.csv”.</p> <p>The median for days spent on dialysis (assessment time + waiting list time) prior to receiving a deceased donor transplant is calculated in the same way as for median days spent on assessment. The model elements involved for living donor type of transplant are the vector named “DDKTDaysDialysisToTXVector”, the hash table named “DDKTDaysDialysisToTXHT” and the data set named “DDKTDaysDialysisToTXDS”. At the end of the simulation, the median days spent on waiting list are written to the file named “MedianDaysDDKTDialysisToTXLast3Y.csv”.</p>
<p>The average days spent on assessment, waiting list and dialysis (assessment and waiting list) among all patients receiving transplant in the model (over entire simulation period). WaitAxAvgDays.csv</p>	<p>The days spent on assessment/waitlist/dialysis by patients who are potential candidates for or who receive living donor transplant between 1980 and 2025 are collected in the statistic objects named “LDKTAxTime”, “LDKTWaitTime”, and “LDKTDialysisTime”. For patients who are potential candidates for or who receive a deceased donor transplant, the relevant statistics objects are “DDKTAxTime”, “DDKTWaitTime”, and “DDKTDialysisTime”. The means were taken from those statistics object and got written to the file named “WaitAxAvgDays.csv” by the function named “writeMeanWaitToFile”.</p>

APPENDIX B

CALCULATION OF AGE SPECIFIC AND AGE STANDARDIZED PREVALENCE AND INCIDENCE RATES FOR DIABETES AND DIABETIC- ESRD RESEARCH

In the following sections, all information related to the calculation of diabetes incidence rates are included: the data sources, preparation of the data, and formula used for calculating the incidence and prevalence rates for diabetes and diabetic-ESRD.

B.1 Data Preparation - Covered Population Data

Covered Population data was used as the denominators in the calculation of prevalence and incidence rates for diabetes and DM-ESRD. The covered population data, published yearly by Saskatchewan Health, is a count of all persons who held Saskatchewan Government Health Coverage on June 30th of that year. This count excludes members of Canadian Armed Force, RCMP, and inmates of federal prisons. It does not include people who do not meet the residency requirement (Health coverage begins on the first day of the third calendar month since the date they move to Saskatchewan). (For more information on methodology and the content of the covered population data, please visit the following link: <http://www.health.gov.sk.ca/covered-population2007/NoticetoReaders2007.htm>)

For our research purposes, we want to calculate separated rates for Registered Indian (RI) and other Saskatchewan Residents (OSK). The covered population data files were obtained from the Saskatchewan Ministry of Health and reformatted to meet our need. RI is defined as “a person who registered under Section 6 of The Indian Act and has been assigned a ten digit number in the Indian Registry” [26]. In the covered population data files, RI can be identified by a five digit

residence code starting with '7'. OSK are people who are covered under Saskatchewan Health Insurance but do not fall into the definition of RI. The majority of OSK are Caucasian. A very small proportion of OSK are visible minorities, who are Chinese, South Asian, Black and Filipino [28]. Most importantly, OSK include people of Aboriginal heritage who cannot be classified as RI, such as Métis people.

For year 1990 to 2007, 1987, 1986, and 1981, the covered population data are available for both RI and OSK. For RI, the head count is broken down by regional health authority (RHA), 5 years age group (except for younger than 5 or older than 94) and sex. For OSK, the head count is broken down by residence code, 5 years age group (except for younger than 5 or older than 94) and sex. We are not interested in the head count subdivided by RHA or residence code as provided in the original data file. We want to get the total head count by 5 years group, sex, and ethnicity (RI/OSK) in a particular year. To meet our research needs, I aggregated the head count from all the residence codes for OSK by each 5 year age group and sex, and I aggregated the head count from all RHA in the case of RI for each 5 year age group and sex. In the original data, there wasn't an age group for age 0-4, but there were two age groups age < 1 and age 1-4. I combined the head count of those two age groups into one total head count for age group 0-4, which is the youngest age group in our study.

For year 1988-1989, 1982 – 1985 and 1980, the covered population data files for each year are not available on the Saskatchewan Health Ministry of Health website. We obtained the data for those years from Health Information Solution Center, Saskatchewan Ministry of Health in Regina. The head counts are broken down by residence code, 5 year age group (except for younger than 5 or older than 94) and sex, but not broken down by RI and OSK. To place those year's data into the same format as above years (e.g. 1990 and after), the first step is to get the

total head counts and the RI head counts. For a particular year, the total head count for each 5 year age group and sex is obtained by summing up the head counts from every residence code in the file. The RI head counts for each 5 year age group is then obtained by summing up the head counts for any residence code starting with '7' and followed by another 4 digits. To get the head counts for OSK, the head counts for RI is subtracted from the corresponding total head counts. Similar work is done as for the youngest age group in 1990 and after. To get the head counts for age group 0-4 for a particular year, I sum the head counts from the under 1 year age group to that for the 1-4 age group.

After the above work is completed for each set of years in turn, we have got the head counts for RI Male, RI Female, OSK Male and OSK Female broken down by 5 year age group and each year between 1980 and 2007. The result is in a file named as "cleaned_covered_population.xls". Thus, the covered population data has been reformatted for our research need and is ready to be used in the calculating the rates of diabetes incidence and prevalence.

B.2 Other Data Sources

Annual Frequency of Incident Diabetes and Prevalent Diabetes. To calculate the diabetes rates, we will use the above reformatted covered population data in the denominators. We also need annual frequency of incident diabetes and prevalence information, which is obtained from the Saskatchewan Ministry of Health. The annual frequency of incident diabetes and prevalent diabetes are stratified by 5 year age group for age 0-79 (and one group for age 80+), sex, RI status and each year from 1980 to 2005.

Annual Frequency of Incident Diabetic-ESRD and Prevalent Diabetic-ESRD. To calculate the diabetic-ESRD rates, we will need the Annual Frequency of Prevalent Diabetes. In

addition, we also need the Annual Frequency of Incident Diabetic-ESRD and Prevalent Diabetic-ESRD. The format of the incident and prevalent diabetic-ESRD are the same as same information for diabetes. The data are stratified by 5 year age group for age 0-79 (and one group for age 80+), sex, RI status and each year from 1980 to 2005.

B.3 Age Specific Diabetic Incidence and Prevalence Rates

Formula for Age Specific Diabetes Incidence Rate

The formula used for calculating age (*a*), sex (*s*) and ethnicity (*e*) specific diabetes incidence for a given year (*y*) is as follows:

$$Diabetes\ Incidence_{asey} = \frac{Cases\ of\ Incident\ Diabetes_{asey}}{Covered\ Population_{asey} - Cases\ of\ Prevalent\ Diabetes_{asey}}$$

Note: the cases of prevalent diabetes don't include the diabetes incident cases of that year. Therefore, the denominator above will yield the number of people who are at risk of developing diabetes for a particular year

Formula for Age Specific Diabetes Prevalence Rates

The formula used for calculating diabetes prevalence is as follows:

$$Diabetes\ Prevalence_{asey} = \frac{Cases\ of\ Prevalent\ Diabetes_{asey}}{Annual\ Covered\ Population_{asey}}$$

The following specifications define the time frame and specific populations for which the diabetic incidence and prevalence rates are calculated.

- **Annual Diabetes Incidence and Prevalence Rate from year 1980 to 2005.**

The rates are stratified by four factors: Each year from 1980 to 2005, RI status (RI or OSK), sex (Male or Female) and age groups. The population are

broken down by the method as follow: From age 20 to 64, it was broken down into 5 years groups (i.e. 0-4 or 40-44); from age 65 to 74, there is one 10 year age group; and for year 75 and plus, there is one group.

B.4 Age Specific Diabetic-ESRD Incidence and Prevalence Rates

Note, in the following sections, sometimes we use ESRD to refer to Diabetic-ESRD.

Formula for Age Specific Diabetic-ESRD Incidence

$$ESRD\ Incidence_{asey} = \frac{Cases\ of\ Incident\ ESRD_{asey}}{Cases\ of\ Prevalent\ Diabetes_{asey} - Cases\ of\ Prevalent\ ESRD_{asey}}$$

Note: Someone who is an incident case of diabetes and ESRD in the same year won't be included in the denominator here. Therefore, the ESRD incidence calculated could be overestimated (bigger than its real number).

Formula for Age Specific Diabetic-ESRD Prevalence

$$ESRD\ Prevalence_{asey} = \frac{Annual\ Frequency\ of\ Prevalent\ ESRD_{asey}}{Annual\ Frequency\ of\ Prevalent\ Diabetes_{asey}}$$

The following specifications specify the time frame and specific populations for which the diabetic-ESRD rates are calculated for.

- **Annual Diabetic-ESRD Incidence and Prevalence Rate from year 1980 to 2005.** The time frame is each year from 1980 to 2005. The rates are also stratified by RI status (RI/OSK), sex (Male/Female) and different age groups. The age of subjects is from age 0 to 80+ and it has been broken down into

three groups: children and youth (Age 0-19), adults (20-80+) and all age groups combined (0 – 80+; also known as the crude rate).

- **Three or Five Year Average Diabetic-ESRD Incidence and Prevalence Rates.** There are three versions of diabetic-ESRD prevalence rates calculated, and each one is prepared for the studied population stratified by a different group of factors. The three group factors are explained as follows:

- **Stratifying factor group #1: Five-year-length time period, age group, RI status and sex.** For the time period, we excluded the first year in our study and broke down the remainder of the 25 years from 1981 to 2005 into 5 five- year-length periods: 1981 - 1985, 1986 - 1990, 1991 - 1995, 1996 - 2000, and 2001 to 2005. In addition to the time period, the studied population is broken down into six age groups as follows: Children and Youth (Age 0-19), Young Adults (Age 20-39), Middle Age Adults (Age 40-59), Elders (Age 60+), all Adults (Age 20+), and Older Adults (Age 40+). The studied population is also broken down by RI status, which has two values: RI or non-RI (also known as OSK). Last, the studied population is broken down by sex.

- **Stratifying factor group #2: Five-year-length time period, age group and RI status.** There are three same stratifying factors in group #2 as in group #1: five-year-length time period, age group and RI status. The definitions are exactly the same for those three factors. The difference is that sex is not included in the second group of

stratifying factors. Therefore, the rates defined by factor group #1 are sex specific, whereas the rates specified by factor group #2 are sex-combined rates.

- **Stratifying factor group #3: Five or three-year-length time period, age group, RI status and sex.** The rates defined by factor group #3 are later to be age-standardized, and the definitions for time period and age group are different than what was used for factor group #1 and #2. The five - year - length time periods were used in group #1 and #2, because we have concern on the limited number of ESRD cases in a shorter time frame. However, we believed that after 1990s, the number of ESRD cases in three year time windows would still give us a sufficient number of cases to perform calculations. Therefore, for the time period, we divided the total 25 years into 7 groups as follows: 1981 – 1985, 1986 – 1990, 1991 – 1993, 1994 – 1996, 1997 - 1999, 2000 - 2002 and 2003 - 2005. For age groups, we decided not to calculate rates for the younger than 20 age group because there are hardly any ESRD cases in that age range. The older than 20 study populations are broken down into five age groups as follows: 20-39, 40-49, 50-59, 60-74, and 75+. In addition to time period and age groups specified above, the populations are further broken down by RI status (RI or OSK) and sex.
- **Stratifying factor group #4: Five or three-year-length time period, age group and RI status.** The definitions of the sharing factors are

the same for group # 3 and #4. The difference is that sex is absent from the factors breaking down the study population. Therefore, the rates defined using group #4 are sex-combined rates.

B5. Age Standardized Diabetes Incidence and Prevalence Rates

B5-1 Introduction to Age standardization

Age can be a very important risk factor which confounds comparisons made on the findings of a health condition among population groups with different age distributions. Age standardization is a way of controlling the confounding effects of age, and allows fairer comparisons to be made among different population groups. In short, age standardization takes away the distortion of different age structures among groups from the research results, thereby allowing us to compare rates across different points in time or different populations. Our research involves the comparison of the prevalence and incidence rates for diabetes and diabetic-ESRD among four sex and ethnicity divided subgroups (RI Female, RI Male, OSK Female and OSK Male). Since age is a confounding factor in both diabetes and diabetic-ESRD, we want to age-standardize the prevalence and incidence rates for those two diseases for each of these subgroups in turns. Generally, there are two steps taken to age-standardize rates [29]. The first step is to choose a standard population which should be widely used in related studies so that comparisons can be draw. The second step is to apply the age specific rates (the ones to be age standardized) to the proportion of the people in that age group within the standard population. Given a population with p_a people in each age category, and with age-specific rates (W_a) to be age-standardized, the equation below is used for age standardization. In essence, this is a weighted sum of the prevalence within each age group in turn, with the weighting given by the proportion of the standardized population that lies within this age group.

$$\text{Age standardized prevalence} = \sum_{a \in \text{Ages}} \left(W_a \frac{p_a}{\sum_{a \in \text{Ages}} p_a} \right)$$

B5-2. Age standardization of Diabetes Prevalence and Incidence Rates

We age standardized the diabetes prevalence and incidence rates by following the two steps introduced in the section above. First of all, we choose a standard population. We decided to use the 1991 Canadian census tables for standardizing prevalence and incidence rates of diabetes and diabetic-ESRD, because it was widely used for age standardization of rates in the health studies led by most of the Canadian agencies like Statistics Canada, the Public Health Agency of Canada and Canadian Diabetes Associations. The 1991 Canadian census table was derived from an e-stat Statistics Canada Table called "1991, 2A Profile, Provinces and Territories in Canada". The population count was broken down by sex, provinces/territories, and age groups. We are only interested in the head counts for Canada but not at the provinces/territories level, so the population counts from provinces and territories have been aggregated into a total for Canada for each sex and age group. The 1991 census age group was broken down as follows: from age 0 to 64, it was broken down into 5 years groups (i.e. 0-4 or 40-44); from age 65 to 74, there is one 10 year age group; and for year 75 and plus, there is one group.

The second step is to standardize the age specific prevalence and incidence rates against the 1991 census. We decide to ignore the 0 to 19 age group because the diabetes cases for those under 20 years old is very small. Also, there is nearly zero ESRD case in less than 20 year old age group. The standardization is being conducted by following the procedures as listed below:

1. For a given RI status and sex, multiply the age specific diabetes prevalence or incidence rates of each age group (RI status and sex stratified) by the fraction of

people of that RI status and sex who are in the corresponding age group in the 1991 census. Add up the products obtained by procedure 1 into a total.

2. This is the age standardized diabetes prevalence or incidence rates.

Using the procedures illustrated above, the following rates have been the result of the age standardization:

- Age standardized diabetes incidence rates by sex and RI status, age group, and each year from 1980 to 2005.
- Age standardized diabetes incidence rates by RI status (sex combined), age group and each year from 1980 to 2005.
- Age standardized diabetes prevalence rates by sex and RI status, age group, and each year from 1980 to 2005.
- Age standardized diabetes prevalence rates by RI status (sex combined), age group, and each year from 1980 to 2005.

B5-3 Age standardization of ESRD Prevalence and Incidence Rates

Similar steps are taken to standardize the diabetic-ESRD prevalence and incidence rates. As noted above, the 1991 Canadian census is chosen as standard population because it was widely used as standard population in other literatures. The following diabetic-ESRD rates have been the result of age standardization:

- Age standardized diabetic-ESRD incidence rates by sex and RI status, age groups, and five/three year length time period.
- Age standardized diabetic-ESRD incidence rates by RI status (sex combined), age groups, and five/three year length time periods.

- Age standardized diabetic-ESRD prevalence rates by sex and RI status, age groups, and five/three year length time periods.
- Age standardized diabetic-ESRD prevalence rates by RI status (sex combined), age groups, and five/three year length time periods.

Note #1: The way in which the age group were broken down was used method #2 as illustrated in earlier sections.

Note #2: The definition of “The five/three year time period” can be found in the earlier section under the title Stratifying factor group #3.

APPENDIX C

PROGRAM CODE FOR GENERATING DAYS REQUIRED FOR
ASSESSMENT

Figure C-1 shows that the pseudo code used in the model for drawing the days required for the assessment. Each step in Figure C regarding the prediction of the assessment time will be discussed next.

```
/* Variable testCount is the number of tests required for the patient
   Variable x is average number of tests normally required in the assessment.
*/
testCount = geometric(probability of having x number of tests);

/*Query the duration of assessment based on the type of transplant, the year when
the assessment starts
*/
if (the patient is Candidate for living donor transplant){
    durationAssessment = historicalAssessmentLDKTDuration(currentYear);
}
else //patient is candidate for deceased donor transplant{
    durationAssessment = DDvsLDWorkUpDaysRatioAdjustFactor*
    historicalAssessmentLDKTDuration(currentYear);
}

/*calculate the average of duration per test in an assessment by dividing the
durationOfAssessment and the average number of tests normally required
*/

avgDurationPerTest = durationAssessment/x;

/*The duration of assessment for the patient is a draw from an erlang distribution
which takes in the average duration per test and the number of test the patient is
expected to go through in the assessment process*/

DurationAssessment= erlang(avgDurationPerTest , testCount);
```

Figure C-1. Pseudo Code for Predicting the Duration of the Assessment in Days

Firstly, a geometric distribution is used to draw the number of tests needed during assessment, where the input probability is calculated from the average number of tests required in the assessment process. Then, based on the donor type of the transplant for which the assessment is being performed, the average days spent on assessment for the particular type of transplant was looked up from a table function based on the year when the assessment begins.

The use of a table function to capture the days spent on assessment from different time periods reflects the fact that the assessment time was not the same over the years. Even without any historical source regarding the assessment time, historical data has shown the total wait time prior to transplant, which is the sum of the time spent on assessment and on transplant waiting list, has increased over years. For instance, the wait time was within half a year before year 1990 [38], but is close to three or four years currently. As part of the total wait time prior to transplant, the assessment time may be following the same trend: the duration of assessment has become longer and longer. We estimated assessment time required in a table function “historicalAssessmentLDKTDuration”, which is used for looking up the average assessment time required for living donor transplant candidates. For candidates for deceased donor transplants, the historical data has shown that the assessment took longer compared to the assessment of candidates for living donor transplant. A variable named “DDvsLDWorkUpDaysRatioAdjustFactor” was created to save the ratio obtained by comparing the assessment time required for candidates of deceased donor transplant over the time spent by candidates of living donor transplant. This ratio is used for calculating the average days required to assess deceased donor candidates by applying the ratio to the assessment time required for living donor transplant candidates. With the duration of assessment and the average number of tests needed in assessment process, the average time per test was calculated which, together with the average number of tests, was supplied as inputs to an Erlang distribution to get the number of days required to finish the assessment.

APPENDIX D

DATABASE CREATED FOR SASKATCHEWAN DM-ESRD MODEL

Figure D-1 shows an Enhanced Entity Relationship (EER) diagram illustrating the design of the “sk_dm_esrd_model” database. A total of nine database tables were designed and created for saving data regarding to realizations, patients, and processes. Each table will be described in greater details in the next section.

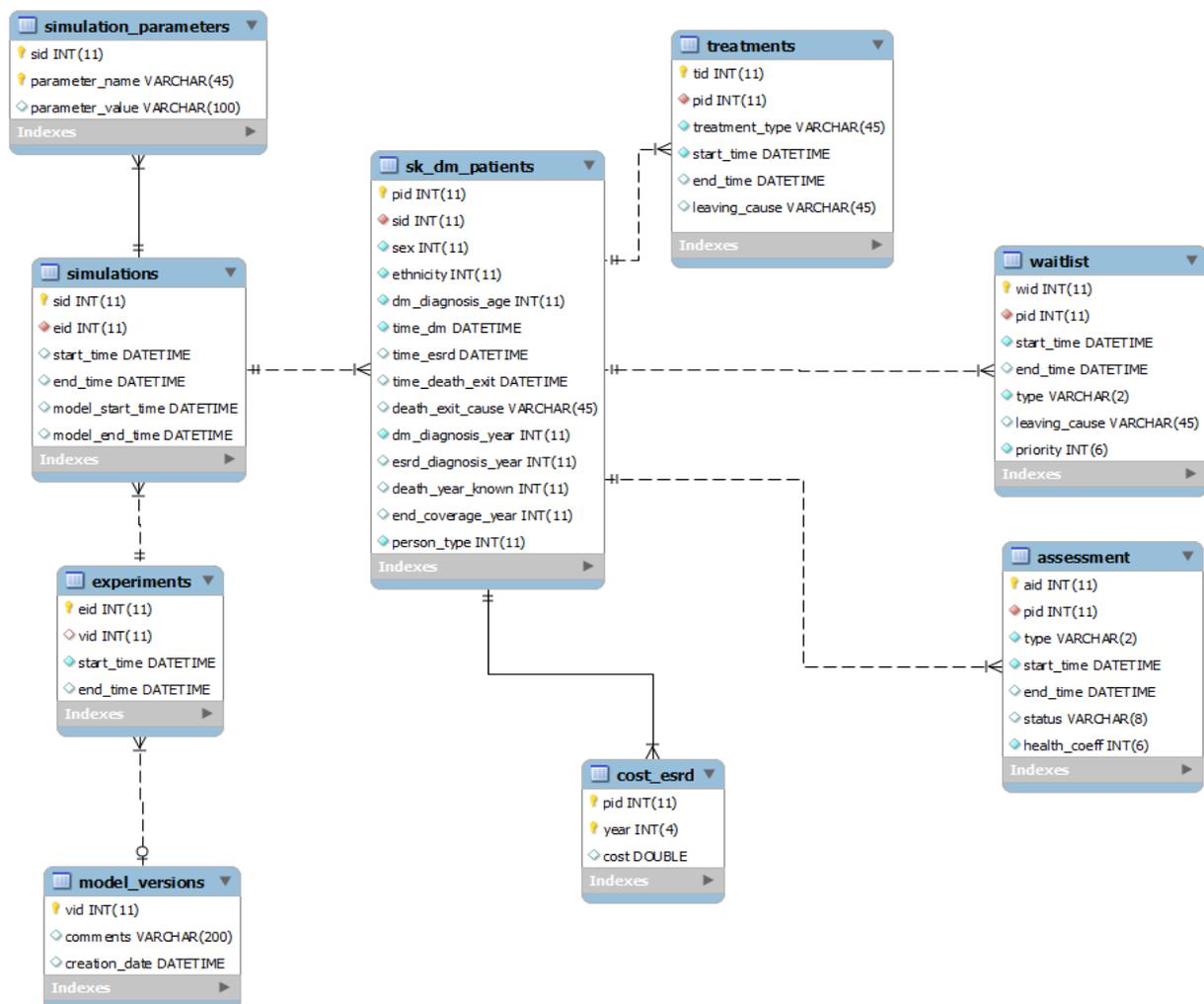


Figure D-1. EER Diagram for the “sk_dm_esrd_model” Database

Model versions. The model can evolve in successive versions, each associated with distinct structure. The “model_versions” table saves information on versions of the model. The “vid” field is a unique identifier for each model version. The “comments” field saves a description of the version. The creation date saves the time when the version of the model was last modified. Experiments can be run from different versions of the model. That is why the vid serves as a foreign key in the experiment table.

Experiments. An Experiment in the database can be viewed as a container, and it can be associated with one single realization or a group of realizations. Each experiment is uniquely assigned and identified by an experiment ID “eid”. The start time of the experiment and finish time for the experiment are recorded in fields “start_time” and “end_time”, respectively. The version of the model on which the experiment was run is recorded in the field “vid”.

Simulations. A Simulation in the database represents one single realization of the model. Simulation is uniquely identified by primary key “sid”. One experiment might consist of one or multiple simulations. Each simulation can only belong to one experiment, the identification of which is recorded as “eid” in the Simulations table. For a simulation, the start time and end time is recorded in fields “start_time” and “end_time”, respectively.

Simulation Parameters. The parameters used to run the simulations are saved into the “simulation_parameters” table. A “sid” identifies to which simulation a parameter name and value pair is attached. The name and values of the parameters are saved in fields “parameter_name” and “parameter_value”.

SK DM Patients. Information on the simulated Saskatchewan Diabetes Patients (the model population) are saved into “sk_dm_patients” table. The “pid” is used for uniquely identifying patients. The “sid” identifies the simulation in which the patient was created/to which

the patient belongs. The “person_type” field indicates the type of the patient in the model, the value of which ranged from 0 to 4. Type 0 indicates patient is a member of the incident DM patients; Type 1, 2, 3 indicates that patients belong to the 1980 DM-ESRD prevalent patients group, and were receiving HD, PD and Transplant treatment on Jan 1st, 1980. Type 4 indicates patients are a member of the 1980 DM patient group. More details regarding the patient type can be found in the Model Population Chapter of this thesis.

The demographic information of the patients is saved in “sex”, “ethnicity”, and “dm_diganosis_age”. The data in the “dm_diagnosis_age” field is the age when the patient first entered the model (the diabetic population).

Several of the sk_dm_patients fields are used to store available historical data for the 1980 DM and DM-ESRD prevalent patients. Specifically, the fields store any information available in the year of receiving diabetes diagnosis, year of receiving ESRD diagnosis, the year of death and year of coverage termination. The corresponding fields are “dm_diagnosis_year”, “esrd_diagnosis_year”, “death_year_known” and “end_coverage_year”, respectively.

In contrast to the historical data – which only provides information on the year – the events of diagnosis, death and exiting occur at a specific date and time within the model. The actual time of those events are saved into “sk_dm_patients” in fields “time_dm” and “time_esrd”, and “time_death_exit”. The “time_death_exit” field is used to record the time when patients either die or exit their health coverage, since only one of those two events can take place, but not both.

Treatments. Information regarding ESRD treatments received by patients are saved in the “treatments” table. Treatment is uniquely identified by the field “tid”. The “pid” is the id of the patient who received the treatment. The type of the treatment is recorded in field

“treatment_type”. The begin and end time of the treatment are saved into the “start_time” and “end_time” fields, respectively. When patient leaves the treatment due to a change in treatment type, death or end of coverage, the reason will be recorded in field “leaving_cause”.

Waitlist. Following the addition of a patient to the kidney transplant waiting list, the information regarding the wait will be recorded in the table named “waitlist”. The “wid” field uniquely identifies each record in the waiting list table. The pid indicates which patient is on the waiting list. The “type” field records the type of transplant for which the patient is waiting. The “priority” saves the assigned priority of the patients. The “start_time” and “end_time” fields are used to save the time when the patients were put on and taken off the waiting list. Patients can leave the waiting list because of death, some unclear reasons (withdrawing from waiting list), or undergoing a kidney transplant. The reason for leaving the waitlist is then recorded in the “leaving_cause” field.

Assessment. The “assessment” table is for recording information regarding patients going through the assessment process. The “aid” field has the unique identifier for each assessment record. Each assessment record has a “pid” which identifies the patient who has undergone assessment. The “type” field is used to store the type of kidney transplant (Living Donor or Deceased Donor) for which the patient is being assessed. The “start_time” and “end_time” fields are used for saving the time when patients start and finish the assessment, respectively. A patient’s overall health condition represented by a health coefficient number is being evaluated during the assessment. The health coefficient is saved to “health_coeff” field. When the assessment is completed, a decision will be made regarding to whether the patient is suitable for kidney transplant. The decision will be recorded in the “status” field.

Cost ESRD. The “cost_esrd” table records the per year cost (accumulated across the year) for treating ESRD for a patient. The “pid” identifies the patient to whom the cost is associated in a given year.