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A TRIPARTITE HYBRID MODEL ARCHITECTURE FOR INVESTIGATING HEALTH AND COST IMPACTS AND INTERVENTION TRADEOFFS FOR DIABETIC END-STAGE RENAL DISEASE

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ABSTRACT

Like most countries, Canada faces rising rates of diabetes and diabetic ESRD, which adversely affect cost, morbidity/mortality and quality of life. These trends raise great challenges for financial, human resource and facility planning and place a premium on understanding tradeoffs between different intervention strategies. We describe here our hybrid simulation model built to inform such efforts. To secure computational economies while supporting upstream intervention investigation, we use System Dynamics to characterize evolution of the health, body weight and (pre-diabetes) diagnosis status of non-diabetics. Upon developing diabetes, population members are individuated into agents, thereby supporting key functionality, including accumulation of longitudinal statistics, and investigation of differential treatment regimens based on patient history. Finally, discrete event modeling is used to characterize patient progression through health care processes, so as to capture impact of resource availability, enforce queuing discipline, etc. The paper discusses model findings and tradeoffs associated with the architecture.

1 INTRODUCTION

Our research in Saskatchewan found that the incidence and prevalence of diabetes mellitus (DM) and diabetic end stage renal disease (DM-ESRD) rose significantly between 1980 and 2005. Concerns about these rising trends and the associated health and financial burden on individuals and societies, led us to project the number and associated costs of DM-ESRD patients in Saskatchewan up to 2025.

We describe here the development, current status, and example results of our hybrid simulation model that simulates the development of DM, DM to ESRD progression, treatments for DM-ESRD patients, and the assessments and waiting list processes preparing patients for kidney transplants. To support this task, the model interweaves three popular simulation modeling approaches: System Dynamics (SD), Agent-Based (ABM), and Discrete event (DES) modeling. Exploiting the computationally frugal character of aggregate models, and the coarser-grained depiction acceptable for the non-diabetic population, we adapted the normo- and pre-diabetes sections of our model from our previously developed System Dynamics model. ABM was used to represent diabetic individuals, to allow scalable characterization of this population, to capture time-varying competing risks, to permit collecting and calibrating to longitudinal information, and to permit expansion to capture social network effects and geographical information. Finally, we used discrete event modeling to capture the pathways of health care progression of those with DM-ESRD. Model parameters were estimated from a wide variety of data sources.

The model projects the incident and prevalent case count, cost, and person years lived for the DM-ESRD population in Saskatchewan 1980 to 2025. The projections captured the challenges brought on by the growing numbers of DM-ESRD patients and associated costs in disease management. In addition to projection results, this research also demonstrates how the model can be used to experiment and evaluate different policy/interventions in a safe context. By capturing both individual level records and population level statistics, the model provides extensive data for detailed analysis, which can help policy makers gain insights into the current and future DM-ESRD situation in the province, aiding in resources planning for the fast-growing DM-ESRD population and the growing need for dialysis services.

The paper is organized as follows: Section 2 provides background on DM-ESRD. Section 3 describes the model design, rationale for using a hybrid model, and stages of model development. We also briefly note some of the data sources used to parameterize and calibrate the model. Section 4 sketches findings from this progression.

2 BACKGROUND

2.1 Diabetes

Diabetes mellitus (DM) is a condition in which blood glucose levels are poorly regulated, leading to abnormally high blood sugar. There are three types of diabetes: Type 1, Type 2, and gestational DM (GDM). While other simulation models by the authors have explored the impact of GDM (Osgood, Dyck, and Grassmann 2011) – a condition occurring during pregnancy – our focus here is on Types 1 and 2 DM. People with Type 2 DM can usually be managed by medications and healthier life styles. However, suboptimal management of DM can result in prolonged hyperglycemia, which can lead to chronic complications (heart attacks, strokes, kidney failure, blindness) and to premature death.

Diabetes has reached epidemic proportions in Canada and worldwide. Our research found that rates of DM and DM-ESRD are higher in certain sub-populations and by gender. In our Saskatchewan study (Dyck et al. 2010), the prevalence of diabetes increased from 9.5% to 20.3% in First Nations (FN) females and from 4.9% to 16.0% in FN males. Among non-FN adults, it increased from 2.0% to 5.5% among females and from 2.0% to 6.2% among males.

2.2 Diabetic End Stage Renal Disease (DM-ESRD)

DM is the leading cause for ESRD in Canada, accounting for more than 35% of new ESRD cases. Kidneys are damaged from chronic exposure to high glucose levels, and ESRD (kidney failure) occurs when kidneys can no longer remove waste products from the blood. Most people with DM can live with earlier stages of chronic kidney disease (CKD) without reaching ESRD. Our previous research demonstrated that FN individuals not only suffer a higher risk of DM, but also of DM-ESRD (Jiang et al. 2014; Dyck, Jiang, and Osgood 2014).

There are three types of treatments for people with ESRD: Haemodialysis (HD), Peritoneal Dialysis (PD) and Kidney Transplantation. Among all ESRD treatments in Canada in 2008, HD accounted for 48.5%, PD for 10.9%, and kidney transplantation for 41% of the treatments. During HD, a dialysis machine is connected to the patient to remove waste products, excess minerals and fluid from the blood. PD uses a patient's peritoneal membrane to filter the waste and extra fluid from the blood into a dialysis solution instilled into the patient's abdominal cavity and periodically drained from the body.

Kidney transplantation is a surgical operation in which a 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 ESRD patients receive dialysis treatments prior to receiving kidney transplants. Numbers of living donor kidney transplants have been growing steadily in recent years while the number of cadaveric kidney transplants has remained stable. With more ESRD patients requiring transplants, available organs are not meeting the demand. The transplant operation and immediate follow-up care is expensive, but is less expensive than either PD and HD after the first year of treatment. All three treatments greatly impacts patients and their families, and place a heavy financial burden on the health care system and society.

Given the increasing rates of DM and DM-ESRD, we will likely face a substantial increase in related health care spending in Saskatchewan. However, because these trends and intervention effects are mediated by delays, non-linearities, feedbacks, path dependence and heterogeneity – classic hallmarks of complex systems – it is difficult to obtain a good approximation of the future situation without a suitable methodology. We therefore chose to adopt a simulation modelling approach for our research problem.

3 MODEL DESIGN

3.1 Purpose

The goal of the model is to: A) Project the incident and prevalent case count, cost, and person years lived for the DM-ESRD population in Saskatchewan from 1980 to 2025; B) Examine health and cost impacts of upstream and downstream interventions related to DM and ESRD.

3.2 Model Evolution

While this paper focuses on the current stage of model development, this model has meshed components originating in several distinct models, and has been transformed by a variety of stages of development and cleanup. Because this evolution sheds light on the promise and potential of the hybrid approach, we briefly comment on it here. The non-diabetic section of the model (including both normo- and pre-glycemic stages, and diagnosis rates) were originally created as part of our stand-alone SD model of diabetic progression for the Saskatoon Health Region (Grassmann et al. 2012). The progression from diabetes to ESRD in the context of mortality risk was also the subject of stand-alone SD and (subsequently) ABM models parameterized by a formal competing risks analysis (Jiang 2012).

Finally, the hybrid integrative DM-ESRD model described here began with a tenuous, manual linkage in which data output by manual runs of scenarios within the afore-mentioned SD model of diabetic progression (Grassmann et al. 2012) were used as input into a purely ABM of DM-ESRD progression. This (manually) downstream ABM characterized each of pre-ESRD diabetic progression (using the agent-based competing-risks model of Jiang 2012), evolution of individual health states, as well as processes of health care delivery. While this manually linked model served as a hybrid ABM-SD model (e.g., to support examine impacts of anti-obesity programs on ESRD outcomes), it lacked flexibility. Of particular concern was the fact that examination of interventions and other scenarios that included upstream prevention and screening components would require re-running the System Dynamics model, and manually feeding the results into the ABM. Moreover, the depiction of health care processes within the ABM required custom mechanisms (e.g., Java priority queues, AnyLogic events, health-care oriented statecharts) to capture resource dependencies and patient flow effects that were capable of crisper and more transparent articulation in a discrete event context. Moreover, the use of ABM to characterize such process-centric phenomena failed to reify certain resource dependencies associated with the assessment, waiting list and transplant phases. This complicated prospects for examination of effects of interventions involving changes in resource availability (e.g., changing the availability of doctors during the assessment phase, of transplant surgeons, transplant nephrologists, etc.).

The final stage of work associated with the model described here involved reworking the model – in a way that improved design without changing behavior that is just being completed at time of submission – to characterize the health care processes using DES (rather than ABM). The original model was built in AnyLogic 6.8.1, and was adapted to AnyLogic 7 (AnyLogic Corporation 2014) in this final phase.

3.3 Current Hybrid Architecture

Within our hybrid model, SD is used to characterize the upstream population – non-diabetic individuals – by stratifying by 17 age categories, 2 sexes, 2 ethnicities, 3 weight classes and two diagnosis states with respect to pre-diabetes. ABM is used to capture the population of greatest interest – diagnosed diabetics – with respect to the same characteristics, as well as continuous attributes and aspects of individual history. DEM is used to characterize an individual's flow through and status with respect to health care processes.

The hybrid architecture of the model leverages two different types of hybrid relationships. There is a producer-consumer (upstream-downstream) relationship between SD and ABM components, with population members initially being represented as a simple member of a (subscripted) stock within the SD model, and then flowing out of that stock and becoming reified as individual within the ABM at the point diagnosis with diabetes. By contrast, the ABM and DES components of the model operate concurrently for a given individual, with the use of both approaches speaking to the principle of separation of concerns: While an individual incident diabetic starts off in the ABM component, following development of ESRD, they are simultaneously present in both the ABM and DES portions of the model. For flexibility, the ABM tracks health, history, and other individual-level information, while DES captures the status and evolution of that person via health care delivery processes and resource availability.

3.4 Empirical Data

Data for model parameters came from Canadian Organ Replacement Registry (www.cantransplant.ca) annual reports, Canadian Institute for Health Information (CIHI; http://www.cihi.ca) data requests, Saskatchewan health administrative data, Saskatchewan renal program reports and from experts familiar with the system.

3.5 Model Components

3.5.1 Non-Diabetic Population Model

A stock-and-flow model component represents individuals from birth through death or diagnosis with diabetes. The logic of this portion of the model was previously published (Grassmann et al. 2012). The stocks of the model distinguish normo-glycemic individuals according to weight status, and pre-diabetic individuals according to whether their pre-diabetic condition is diagnosed. To capture the disparities associated with diabetes incidence across age, gender and ethnicity (Dyck et al. 2010), the model is further stratified into 17 age categories, two genders and two ethnicities (FN and non-FN individuals). An individual is born into in the "normal weight" stock, and flows into other stocks as their weight and dysglycemic status evolve.

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 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.

3.6 Agent-Based Model

The Agent-Based model depicts progression of diabetes to develop ESRD and receipt of ESRD treatments. Figure 1 presents the overview of a person's statechart in the model, which illustrates the life cycle of a patient in the model. The two blue boxes enclose the state charts and transitions for the two critical processes in a patient's life. The left one corresponds to "DM to ESRD progression". The right one represents to "ESRD treatment options."

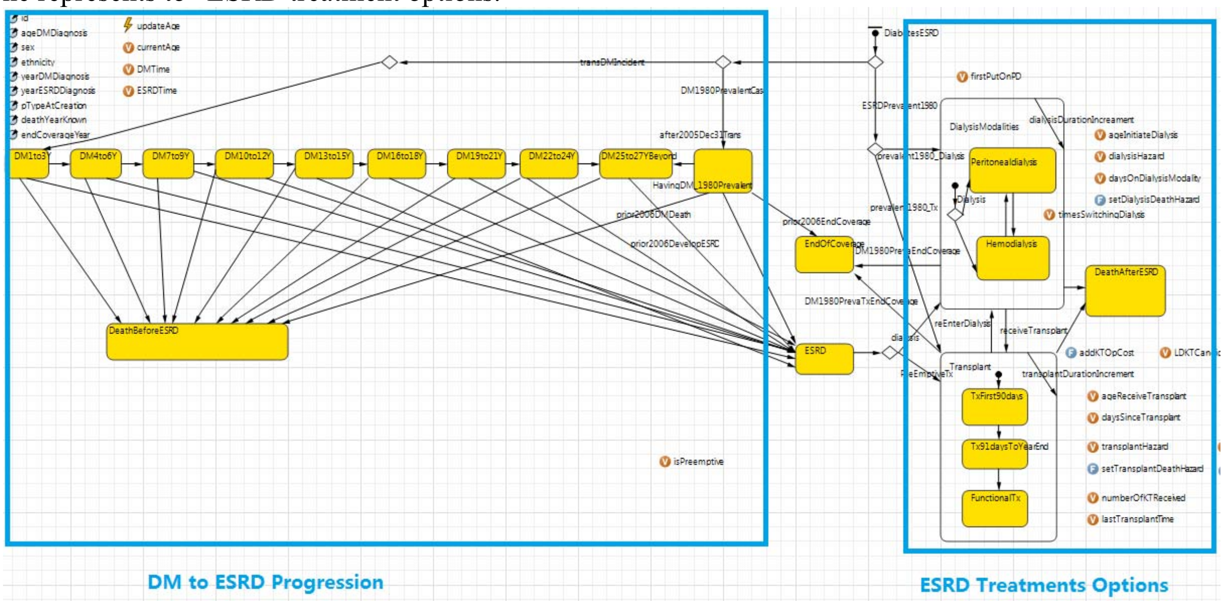

Figure 1: Overview of agent-based model structure.

3.6.1 DM to ESRD Progression

This study focused on the subset of DM patients who eventually developed ESRD, and the treatments provided to them. The diabetes progression process is also represented in this model because it determines much of a person's ESRD risk, and is a key area on which to focus prevention efforts. We adopted the representation of progression of diabetes from our competing risks analysis of the diabetic to ESRD transition (Jiang et al. 2014; Jiang 2012). The statecharts and transitions used to simulate a patient's DM to ESRD progression is discussed in this section. The DM incident patients and the DM prevalent patients at 1980 require different model structures. DM incident patients start their journey in the model at the time they receive DM diagnosis. As diabetes progresses, simulated 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. While the model includes an "End of Coverage" state, transitions to that state are not supported by for DM incident patients. To exploit available individual-level information when possible and to secure maximal resolution when calibrating parameters for the population of greatest interest (DM incident patients), patients who were DM prevalent cases at the time of model start and whose fates were known were required to transition in a way dictated by the historically recorded data. At the point when no previous data are available, such cases transition according to the rates applying to the DM Incident cases. Upon receiving an ESRD diagnosis, patients 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.

3.7 ESRD Treatment Options and Death

Depending on an ESRD patient's medical condition and treatment availability, therapy options include HD, PD, or kidney transplantation. Very few ESRD patients receive a pre-emptive transplant – a kidney transplant before being dialyzed. Most patients begin with either PD or HD as their initial treatment, followed by kidney transplantation. Such health progression is depicted in the right blue box in Figure 1.

3.7.1 Selection Between PD and HD

For patients with ESRD, the choice between PD and HD is 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 2, 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.

3.7.2 Switching Between PD and HD

Patients will sometimes switch between PD and HD for medical and personal reasons. As shown in Figure 2, transitions were set up between the PD and HD states, allowing patients to change from one type of dialysis to another. Rates (hazards) calculations used in those transitions were based on dialysis treatments received between Jan 1st, 2006 and Dec 31, 2010 by Saskatchewan DM-ESRD patients. Details on the rates and the data source used here can be found in Gao (2013).

3.7.3 Pre-Emptive Kidney Transplantation

In Saskatchewan, very few ESRD patients receive pre-emptive kidney transplants. Most patients receive dialysis first and then some are transplanted. Occasionally, a patient may receive a pre-emptive transplant, most likely from a living donor. With few exceptions, a deceased donor kidney would almost always be given to a dialysis patient on the transplant waiting list. Despite being uncommon, the pre-emptive transplant process was included in the model for the purpose of facilitating policy experiments.

3.7.4 Post Kidney Transplantation

Some patients on dialysis will be assessed as suitable for a transplant and be placed on a transplant waiting list. The transplant assessment and waiting list process is represented using the discrete event modeling discussed in Section 3.9. The inclusion of those processes in a separate statechart reflects the fact that patients waiting for a kidney transplant remain on dialysis. In the model, a message is sent to patients (agents) when they are to be transplanted. Upon receiving the "getting transplant" message, a patient moves from the dialysis state to the transplant state via the "receiveTransplant" transition. As shown in Figure 1, the time after kidney transplantation is divided into three temporally delineated states: "TxFirst90days", "Tx91daysToYearEnd", and "FunctionalTx". While a time-specific hazard rate is used to capture mortality risk (see below), the use of three post-transplant states reflects the cost differential associated with them.

3.8 Return to Dialysis After Graft Failure

If a kidney transplant fails, the patient needs to restart dialysis. In the "DiabetesESRD" statechart, the patient moves from the transplant state back to the dialysis state via the transition "reEnterDialysis", and uses the same modality distribution. The hazard of returning from transplant to dialysis was calculated from graft survival rates for all ESRD patients published by the Canadian Organ Replacement Registry. The graft failure rates were computed for eight sub-population groups stratified by transplant donor type (living and deceased) and four age groups (age 18-44, age 45-54, age 55-64 and age 65+).

3.8.1 Mortality Risks on ESRD Treatments

ESRD patients may die despite being treated. An ESRD patient's daily mortality risk was calculated by a hazard function, which was based on gender, ethnicity, age when initiating treatment, type of treatment, and length of time on treatment. The model's hazard function was derived from a risk adjusted survival analysis conducted by CIHI. Since the mortality hazard changes significantly over time since transplant, The model used a mortality hazard varying on a day-by-day basis. When patients die while receiving ESRD treatment, they transition to the "DeathAfterESRD" state in the "DiabetesESRD" statechart.

3.9 Discrete Event Modeling

The discrete event model operates in parallel with the ABM and includes representation of two primary resource-constrained processes: Assessment for a kidney transplant, and queuing for a transplant on a waiting list after an approved assessment. We describe the components of this area of the model below.

3.9.1 Transplant Assessment

Transplant assessment for dialysis patients consists of three processes: deciding who will undergo transplant assessment, determining the type of kidney transplant, and assessing the patient's eligibility for a transplant. The first of these is primarily an age-related decision. The transplant type (living donor or deceased donor transplantation) determines on what waiting list the person is placed and impacts cost – both recipients and donors for living donor transplantation need extensive evaluations, which means the cost for assessment is higher than for deceased donor transplants. In the model, therefore, the selection of transplant type is made at an early stage of assessment, and the choice between living and deceased donor transplants is based on the historical proportion of each among provincial kidney transplants.

The final transplant assessment evaluates a patient's health and other factors to determine if a patient is a suitable candidate for a kidney transplant. In the model, there are two considerations: assessment duration, and patient eligibility for a transplant. The assessment duration determines how long the patient is in the "Workup Stage" state in the "AssessmentStages" statechart. In reality, appointments/examinations vary in number and length of time, and assessment duration varies for different individuals. In the model, we used an Erlang distribution function to estimate assessment duration for patients who had never received a transplant, or whose last transplant had failed more than a year ago. The Erlang distribution considered the number of appointments/examinations required to complete the assessment (itself drawn from a geometric distribution), and the mean time to complete each appointment. For patients whose transplant had failed within one year, we assumed the time of the re-assessment would be minimal. We based the number of examinations and time required for examinations on discussions with a transplant nephrologist. We calibrated those values so that the time patients spent on assessment plus the time spent on the waiting list would match the historical data.

In reality, transplant eligibility is determined at the end of the assessment. In the model, however, we used an abstract "health coefficient" to represent a 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. In reality, suitable kidney transplant candidates are placed on a health-prioritized waiting list for the appropriate type of transplant. Correspondingly, in the model, patients move into the "AwaitingTx" state. Those who are not eligible to have a transplant would be moved to the "NotSuitableForTx" state.

3.9.1.1 Transplant Waiting List

Following transplant assessment, eligible transplant candidates are placed on a waiting list from which they are withdrawn by receiving a transplant, becoming transplant ineligible, or by dying. A number of factors determine who will receive a transplant, and when. The following sections discuss each of these.

3.9.1.2 Priority on Transplant Waiting List

There are effectively two transplant waiting lists: one for living donor and one for deceased donor transplants (a candidate could be eligible for both). Living donor transplants may involve a shorter wait (e.g., for surgeon and operating room availability) than for a deceased donor transplant (e.g., patients wait for organ availability). The wait time is also determined by a candidate's priority on the waiting list which is based on a number of health and other factors. In Canada, each province has its own waiting lists and methods for prioritizing kidney transplants. In the model, priority is randomly generated for each patient on the waiting list; this priority determines the transplant order for patients deemed to be "active" (see below). A patient selected for a kidney transplant must have the highest priority and an "active" status.

3.9.1.3 On hold and Active Status on Waiting List

The "On hold" and "Active" status designate a patient's immediate suitability for transplantation. Some suitable transplant candidates are temporarily withdrawn from the transplant waiting list due to a new medical condition (e.g., an infection). In the model, the patient will move to the "OnHold" state; when the patient recovers, their status is restored to "Active". Patients on the waiting list were randomly marked as "On Hold" according to the probabilities of being on hold based on historic data.

3.9.1.4 Kidney Transplantation

Kidney transplant numbers are restricted by essential resources which are somewhat different for living and deceased donor transplants. Deceased donor transplants depend on available kidneys while living donor transplants also depend on surgical scheduling. In the model, living and deceased donor kidneys arrive periodically. The agent representing the waiting list patient with the highest priority and an active status will move from one of the dialysis states to the "Transplant" state in the appropriate statechart.

4 RESULTS

Within this discussion, we present example model results. These results were generated from the model, although prior to refactoring. Space constraints rule out showing anything more than a few outcomes; readers seeking additional results are referred to (Gao 2013).

4.1 Baseline

Figure 2 depicts HD and PD incident case counts, and shows Transplant case counts, and Figure 3 illustrates how the individual-based nature of the model supports statistics based on individual history.

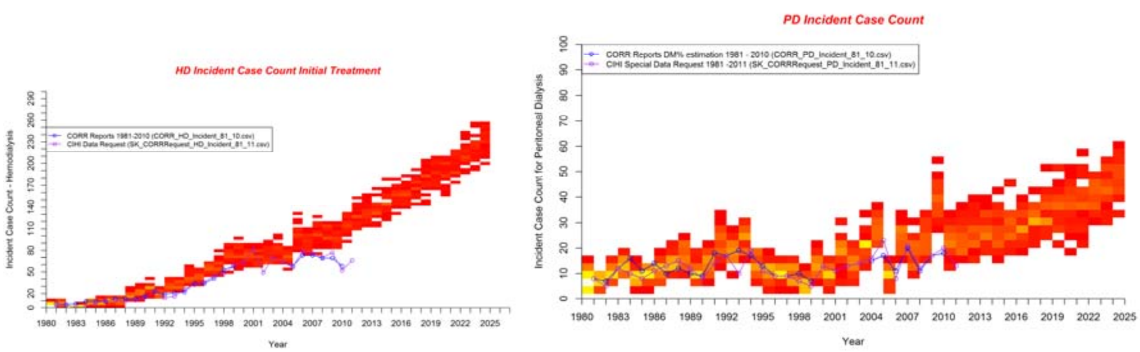

Figure 2: HD (Left) and PD (Right) incident case counts.

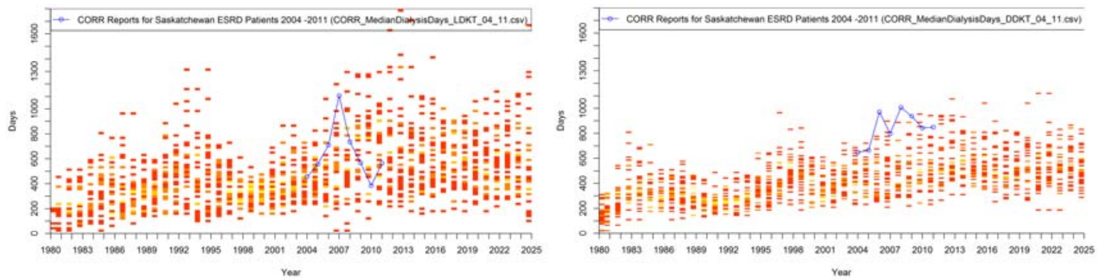

Figure 3: Examples of longitudinal statistics results: mean days on dialysis prior to living donor (left) and deceased donor (right) transplant.

4.2 Alternative Scenarios and Sensitivity Analysis

We present output from 3 scenarios with different parameters and model assumptions. The models run each scenario with 30 realizations as a parameter variation experiment in AnyLogic 6.8.1; each scenario took 2.5 to 3 hours to complete under Windows 7 on an Intel Quad Core with 8GB of RAM.

4.2.1 All DM-ESRD Patients Receive Pre-Emptive Transplant as Initial Treatment

Our first scenario examined the impact of providing all patients with pre-emptive transplants and having transplant patients with graft failure spend minimal time (90 days) on dialysis prior to re-transplantation. This scenario investigates how an unrealistic level of pre-emptive transplantations (versus dialysis) effects outcomes such as prevalent case count, costs and person years lived. With all DM-ESRD incident patients receiving pre-emptive transplants, there is a significant increase in the number of prevalent ESRD patients (Figure 4) because of lower mortality experienced by transplant patients. As more DM-ESRD patients live longer, both the ESRD prevalent case count and the accumulated values (person-years lived) are also much higher in the current scenario, when compared with baseline. 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 5. This reflects the significantly lower cost of caring for transplant patients compared with those on dialysis, especially following the first year post-transplant. Although unrealistic, this extreme scenario does highlight the pronounced benefits of having more pre-emptive transplants.

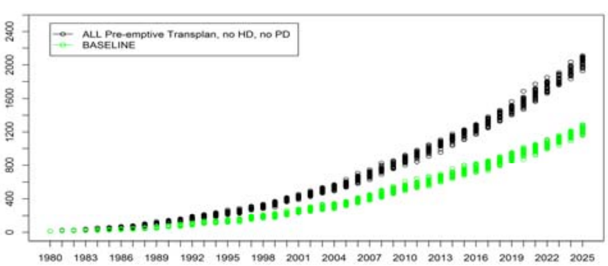

Figure 4: DM-ESRD prevalent case count, baseline vs. preemptive transplants.

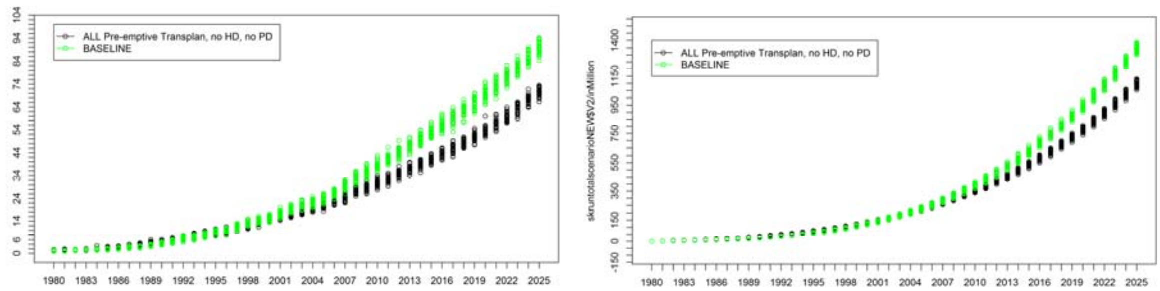

Figure 5: Cost, accumulated and per year, baseline vs. preemptive transplants.

4.2.2 No DM Incident Patients from Year 2006 to 2025

At baseline, the DM-ESRD incident case count is driven by the diabetes incident cases fed into the model as input. In this scenario, no new diabetes cases entered the model between Jan 1st, 2006 and Dec 31st, 2025. We expect the prevention of diabetes mellitus after Jan 1st, 2006 to significantly reduce numbers of new DM-ESRD patients because only DM patients from before 2006 would be at risk of developing ESRD. While extreme in its design, this shows the impact of reducing DM incident cases on future outcomes. Thus, the ESRD prevalent case count does not begin to decline until year 2019 or 13 years after diabetes incidence has ceased. (Figure 6). Similar trends were also observed in the plots for cost and person years lived in Figure 7. Even in the extreme case depicted here, where the DM incident case are cut down to zero at the beginning of year 2006, tremendous inertia remains in the system. For many years after 2006, the resource demands associated with caring for the existing patients remain at an elevated level and continue at rise.

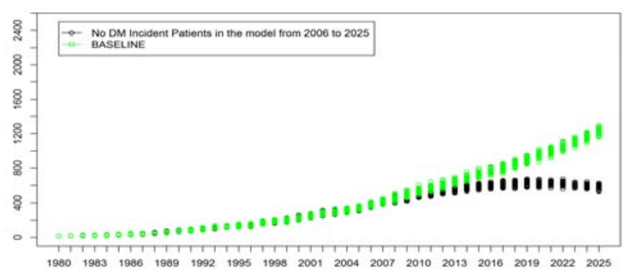

Figure 6: DM-ESRD prevalent case count, comparing baseline with situation with incident cases of diabetes from 2006 onwards.

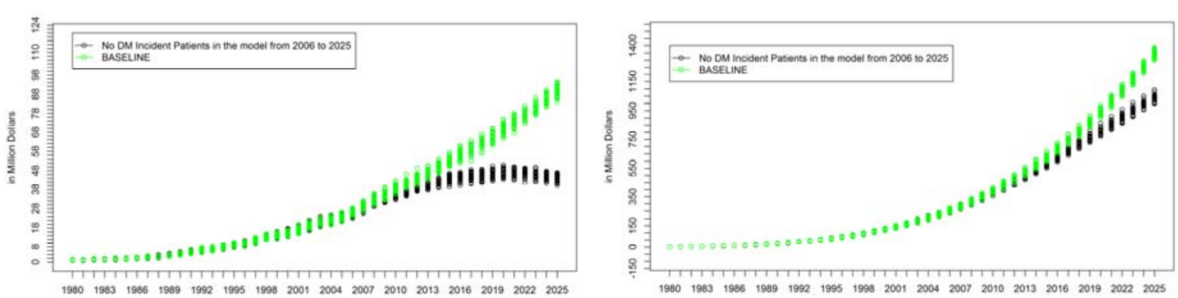

Figure 7: Cost, accumulated and per year, comparing baseline with situation with incident cases of diabetes from 2006 onwards.

4.3 Shorter Transplant Assessment Time as 90 Days, and Eliminate Waiting List by Increased Transplant Rates

In this scenario, patients take only 90 days to transplant assessment, and transplant rates are set at 365 cases of living donor transplant and 365 case of deceased donor in a year. This basically eliminates the waiting list for transplants. Figure 8 shows that the differences in prevalent case count and person years lived between baseline and the current scenario is minimal. However, Figure 9 shows that cost has declined, likely due to patients remaining on dialysis for a shorter time and being transplanted more quickly. Since renal transplantation costs much less than HD, the difference in cost is clear.

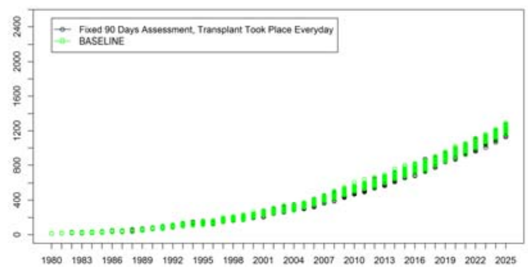

Figure 8: DM-ESRD prevalent case count, baseline vs. faster assessment and increased transplant rates.

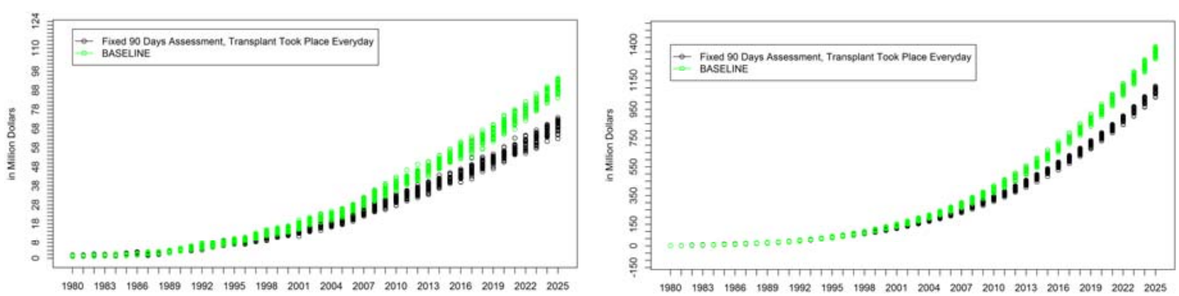

Figure 9: Cost, accumulated and per year, baseline vs. faster assessment and increased transplant rate**.**

5 CONCLUSIONS

We introduce here a tripartite model to project the cost and health impacts of DM-ESRD in Saskatchewan. In addition to providing the first locally grounded, simulation-based projections for DM-ESRD in Saskatchewan, the model presented here advances a generalizable, insightful but economical architecture. This scheme involves securing the capacity to examine upstream interventions while capturing computational economies by simulating the health status of a broader population (e.g., to investigate upstream interventions) in an aggregate fashion using SD, using ABM to represent key populations of focus on which detailed information (e.g., individual history, social network structure or spatial location) is required, and using DES in parallel with the ABM for that population of focus to capture additional patterns of involvement with the health care system. Beyond the simulation model results reported here, we believe that this architecture offers potential across diverse health applications.

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