Increasing the Use of Marginal Kidneys in Manitoba's Older-Adult End-Stage Renal Disease Population: Survival and Cost-Utility Implications

By

Ryan J. Bamforth

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University of Manitoba

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Abstract

Kidney transplantation is the optimal treatment for patients with end-stage kidney disease, offering increased survival and reduced costs in comparison to dialysis. Transplant programs worldwide have increasingly relied upon organs from deceased donors to increase the supply of viable transplantable kidneys as current supply is unable to meet demand. The implications of transplantation with marginal kidneys, defined by a Kidney Donor Profile Index (KDPI) ≥86 from both an economic and patient survival perspective has not been assessed in the Canadian context. The purpose of this project is to describe the survival implications and cost-utility of increasing the use of marginal kidneys in Manitoba's older-adult end-stage renal-disease patient population.

We constructed a cost-utility model with microsimulation from the perspective of the Canadian single payer health system for incident transplant waitlisted patients aged 60 and over. Patients were followed for 10 years from date of waitlisting. We included Manitoba specific data pertaining to potential KDPI ≥86 kidney supply, transplant ineligibility, receiving a transplant, and death on the waitlist. Remaining model inputs were sourced from the literature. Our analysis compared the intervention (Marginal Kidney scenario) to usual care (Status Quo scenario). All costs are presented in 2019 Canadian dollars.

The ten-year mean cost and quality-adjusted life years (QALYs) per patient in the Marginal Kidney scenario were estimated at $362,116.54 (SD: $149,037.69) and 4.52 (SD: 1.84). In the Status Quo scenario, the mean cost and QALYs per patient were estimated at $365,624.71 (SD: $152,647.93) and 4.35 (SD: 1.81). The incremental cost-utility ratio between the two scenarios was estimated at -$20,573.03. At ten years., 60.1% of the cohort in the Marginal Kidney scenario remained alive, compared to 56.7% in the Status Quo scenario. Mean survival for marginal kidney recipients and transplant-naïve patients were 115.59 and 80.37 months respectively.

Increasing the use of marginal kidneys in Manitoba's end-stage renal-disease population aged 60 and over may offer cost savings, increased quality-of-life, and increased survival in comparison to usual care. Further research is needed regarding the effects of human leukocyte antigen mismatches, differences by blood-type, the allowance for multiple transplants, and preemptive transplantation on costs, QALYs, and survival.

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Chapter I: Introduction

The incidence and prevalence of end-stage kidney disease (ESKD) are increasing worldwide (1-3). Contributing factors include longer life expectancy (4), rising rates of hypertension (5), and diabetes mellitus (6). Although kidney transplantation is the ideal treatment for ESKD with respect to long-run costs, patient survival, and quality of life (7-9), the current supply of donor organs is unable to meet the demand, thus the majority of patients depend upon life-saving dialysis therapies (1).

Manitoba has the highest rate of ESKD in Canada, estimated at 1,703 per million population (1, 10). Northern rural regions of Manitoba are exceedingly burdened by ESKD, with rates being an estimated 3-fold higher than other regions in the Province (11) With respect to treatment mix, Manitoba has among the lowest proportion of patients receiving kidney transplants in Canada, resulting in the highest utilization of dialysis country wide (1). Providing in-centre dialysis therapy for patients with kidney failure imposes a high cost-burden on the health care system, exceeding $200,000 per patient per year in certain rural and remote regions of Manitoba (12) with the comparable treatment in an urban setting costing approximately $64,000 (13). In addition, dialysis imposes a burden on patient quality-of-life, which is more pronounced in rural and remote communities where patients may be required to travel long distances or relocate to receive care (7, 14).

Patients requiring a kidney transplant may receive an organ from a living or deceased donor. Living donor organs have been shown to offer benefits to recipients such as improved long-term graft survival, acute rejection rates, patient survival, and decreased costs in comparison to deceased donor organs (15-17). Barriers to living donor kidney transplantation for end-stage kidney disease patients include lack of knowledge, motivation, recipient eligibility, and lifestyle changes, which have been shown to compound due to factors such as disparities in income, education, and health care access (18, 19). Moreover, patients who have access to a living donor organ may not accept. One qualitative study has shown that most deceased donor organ recipients had prior access to a living donor organ but refused for reasons such as concern for the donor's health and anticipated negative relationship changes (20). In a systematic review evaluating 5139 donors, it was found that that the majority of donors experienced no change, or an improved relationship with their recipient after an average follow-up time of 4 years post-transplant (21).

Transplant programs in Canada as well as worldwide have increasingly relied upon kidneys from deceased donors to expand the supply of viable kidneys (1, 22). Deceased donors have historically been classified as either standard criteria donors (SCD) or extended criteria donors (ECD), where ECD donors were defined as deceased donors aged 60 or older, or deceased donors aged 50-59 with two or more of the following criteria: history of hypertension, serum creatinine level over 1.5 mg/dL, or death due to a cerebrovascular incident (23). More recently, the kidney donor profile index (KDPI) has replaced the SCD/ECD classification system in certain jurisdictions as a more granular metric to define the quality and risks associated with each deceased donor kidney, improving the organ matching process and aiding in the acceptance/rejection decision making process (24, 25). Based upon Organ Procurement and Transplantation Network (OPTN) deceased-donor cohorts, the KDPI consists of 10 donor factors (age, height, weight, cause of death, last serum creatinine, history of diabetes, hypertension, HCV-infection, ethnicity, and the discrimination between donation after brain death versus donation after cardiac death) and has proven to be an adequate predictor of donor organ influence on transplant outcomes such as delayed graft function and graft failure (25, 26). The OPTN estimates that kidneys with a KDPI between 0-20%, 21-85% and >85% survive for on average 11.5, 9 and 5.5 years respectively (27). Comparatively, they estimate that a living donor organ survives for 12 years on average (27). Moreover, the KDPI score has been shown to interact with the recipient characteristics such as those quantified within the Estimated Post Transplant Survival (EPTS) score (diagnosis of diabetes, candidate time on dialysis, number of prior organ transplants and candidate age) to affect clinical outcomes such as patient survival (28).

Data considering the KDPI score of transplanted or discarded deceased donor organs in Canada is limited. With respect to overall deceased donor organs, recent estimates place Manitoba with the third lowest usage rate in the Country at 14.9 per million population (1). British Columbia demonstrated the highest rate at 24.9 per million population (1). The percentage of deceased donors aged 60 and over was the lowest Country wide as well at 9%, contrasted to Quebec at 34% (29). To provide an international comparison, countries such as Spain experiences deceased donor rates of 33-35 per million population, with up to 45% of those donors being 60 years or older as of 2009 (22). Increasing the usage of kidneys from marginal deceased donors defined by their suboptimal KDPI rating (≥86) may be considered a strategy to reduce the quantity of declined donors, subsequently elevating the number of transplants and reducing the proportion of patients on dialysis. To date, no analysis has been conducted to determine the associated costs and benefits of such an intervention in the Manitoban context.

The purpose of this project is to use data from Transplant Manitoba's pre and post-transplant dataset (30), deceased donor organ decline dataset (31) as well as available costing, clinical and quality-of-life information to describe the survival implications and cost-utility of increasing the rate of marginal kidney (KDPI ≥85) usage in Manitoba's older adult end-stage renal disease patient population. By using a cost-utility approach, program specific costs will be estimated, allowing for differences in patient quality-of-life by treatment to evaluate the aforementioned approach as an alternative to usual care.

Chapter II: Literature Review

Patient Survival

Patients ultimately have the choice to either accept a high-KDPI kidney or remain on the waitlist in hopes of receiving a higher quality kidney in the future. Evidence suggests that patients may receive survival benefit from accepting a marginal kidney earlier rather than remaining on the waitlist (24, 28, 32-34). One study considering recipients of high KDPI kidneys (grouped 71-80, 81-90 and 91-100) aged 50 and over in centers with median wait-times over 33 months have shown to experience higher short-term mortality risk in comparison to those who received a low-KDPI kidney (grouped 0-70), yet lower long-term mortality risk compared to waiting on dialysis for a low-KDPI kidney for all three KDPI groups (32). The break-even point of cumulative survival between high and low-KDPI kidneys increased as the KDPI groupings increased (7.7, 19.0 and 19.8 months respectively) with survival benefit being more pronounced in older recipients (over 50 years of age) and patients at centers with median transplant wait times of at least 33 months, (32). Other studies have found similar results with respect to survival benefits of transplantation with a high-KDPI kidney in comparison to those who opted to remain on the wait-list, receiving a lower-KDPI kidney (28, 33-35), highlighting the potential benefit of undergoing transplant with an ECD kidney rather than declining and waiting for a higher quality organ (33, 34). Moreover, evidence studying a European cohort comparing survival rates between KDPI groupings (<35, 35-85,>85) found that recipients of kidneys with a KDPI <35 experienced statistically similar survival rates in comparison to those in the 35-85 KDPI grouping, while both groups had improved survival rates in comparison to the >85 KDPI patient grouping (24). A limitation of this study is that it only considered evidence from a single-centre in Germany (24), whereas the previous studies considered much larger sample sizes drawn from all across the United States (28, 33, 34).

Graft Survival

Conclusions in the literature with respect to the association of KDPI rating and graft survival are mixed. One study using a European cohort found a significant negative relationship between KDPI and death-censored allograft survival and was determined to be a marginally superior predictor (KDPI and age p-values <0.001 and 0.004 respectively) of death-censored graft survival in comparison to age alone (24). Similar results were found by other researchers evaluating cumulative five-year graft loss by KDPI category (20≦, 21-85,>85) (36). Moreover, a recent study concluded similar results, associating each 10-unit increase in the KDPI score with a 0.006 and 0.001 reduction in the probability of graft survival at both 1 and 5 year post-transplant respectively (37). Weaknesses of the first study are that the sample size was small (n=580) and limited to one centre in Germany (38). The second and third studies accounted for these weaknesses by considering much larger sample sizes from across numerous sites (n= 84,451 and n=48,945) (36). Contrarily, evidence from a study which retrospectively calculated the KDPI rating for 442 donor kidneys transplanted (340 single and 102 dual renal transplants) in three Italian kidney transplant centers found that those who received marginal kidneys experienced similar graft survival rates after a median follow-up time of 3.3 years (39). Note that the graft survival rate in the comparator SCD group was 61.7% throughout this time period, which is drastically lower than those reported in CORR over a similar time period (1).

In cases where individuals decline a marginal kidney and return to the wait-list, evidence suggests that patients aged 30-40 who accepted the marginal kidney (KDPI ≥85) after being on the wait-list for 5 years experienced a higher probability of having a functioning graft throughout the 5 years post offering in comparison to their counterparts who declined (40). A study using data from the Scientific Registry of Transplant Recipients (SRTR) in the United States concluded similar results at 3 years post kidney-transplant and demonstrated that restricting donor pools by KDPI rating (above both 70 and 90 KDPI) had a negative effect on graft-survival (35). The model was calibrated in the given population with an error between expected and observed graft and patient survival 3 years after a declined offer of less than 3% and a C-statistic of .69, demonstrating adequate predictive abilities, contributing to the reliability of the results (35).

Effects of failed/multiple transplants

Although research has established that kidney transplantation offers superior survival in comparison to maintenance dialysis (8), once a graft is lost these benefits may dissipate. Research has shown an over three-fold increase in risk of death in patients who experience graft failure in comparison to those who maintain graft-function (41, 42). Studies also estimate that less than 50% of patients who suffer graft loss will survive 5 years post loss, decreasing to less than 40% at 10 years. While these survival probabilities are significantly lower than patients with a functioning renal graft (42, 43) and lower than for dialysis patients on the waitlist for transplant, they are still better than those of the general dialysis population. (8, 43). Patient time on dialysis was associated with poor survival outcomes, highlighting the benefits of earlier transplant (42). One Canadian study using data from the Canadian Organ Replacement Registry (CORR) found no difference in survival rates between dialysis patients after graft failure and transplant-naïve dialysis patients (44). Patients who experience graft loss have been shown to have decreased quality-of-life (45) [as measured by the kidney disease quality-of-life instrument (KDQOL-SF)] and increased complications such as hospitalizations during the first year of re-initiating dialysis (46) in comparison to transplant-naïve patients on the wait-list (45, 46). Decreased quality of life was primarily driven by high infection rates (45).

Furthermore, type I diabetic and non-diabetic patients who receive secondary renal transplants after returning to dialysis post initial graft failure have been shown to experience statistically significant lower long-term mortality rates in comparison to their counterparts remaining on dialysis with prior renal-transplant failures [relative risk (RR)=0.55 and 0.77 respectively] (47). Note that only a small proportion of patients in this study ultimately received a second transplant during the follow-up period (15%), and of those, 17.6% were from living donors (47). Although such evidence highlights the potential detrimental effects of graft loss on patient survival and quality-of-life as well as the benefits of re-transplantation, patients who experience graft failure may become highly sensitized, thus decreasing their likelihood of being re-transplanted. In addition, human leukocyte antigen (HLA) mismatching has been associated with increased allo-sensitization in graft loss cases, negatively affecting re-transplantation outcomes (48).

HLA Mismatching

The immune system considers cells of non-self-human leukocyte antigen (HLA) types as threats, producing antibodies which attack grafted organs and reduce graft function and survival (37). Although advances in immunosuppressive medications have minimized the effects of human leukocyte antigen (HLA) incompatibility on post renal transplant outcomes, the magnitude of the effects remain in question. In the United-States, the importance given to patient and donor HLA matching in organ allocation has been reduced to mitigate the negative impact of cold-ischemic time on the graft as HLA matched recipients may reside a great distance from the procurement site (49). In Manitoba, HLA matching remains an important criterion. The Provincial Priority Ranking Allocation Criteria Guideline takes number of matches into consideration when calculating patient priority scores for the purpose of allocating deceased donor kidneys (50). Zero HLA mismatches between patient and donor provides the wait-list patient a score of 3 points, which is equivalent to 3 years on maintenance dialysis (1 point allocated per year) (50). 2 points are given when 1 HLA-DR+Q mismatch between the patient and donor are present and finally 1 point when 2 HLA-DR+Q mismatches are present (50).

A meta-analysis considering 23 cohort studies involving 486,608 total deceased donor kidney recipients found a significant relationship between the number of HLA mismatches between patient and donor and increased risks of overall graft failure [hazard ratio (HR) 1.06; 95% confidence interval (CI), 1.05-1.07], and death-censored graft failure (HR - 1.09; 95% CI - 1.06–1.12) (51). Sub-analyses by type of HLA mismatch (DR, A, and B) showed varying associations as HLA-DR mismatches had a large impact on graft survival, whereas HLA-A and -B mismatches had no significant associations at $\alpha=0.05$ (51). A more recently published study found similar results, associating each HLA mismatch (regardless of typing) with a 0.001 absolute reduction in the probability of 1 year survival, and a 0.009 reduction in 5 year survival (37). For recipients of living donor kidneys, research has demonstrated no association between 3 year graft survival rates and number of HLA mismatches (52). Note, the small sample size in this study (n=487) may contribute to the conflicting results in comparison to the previous studies as each HLA mismatch can vary significantly at the molecular level.

For recipients of deceased donor kidneys, an increased incidence of death with a functioning graft from 1-5 years post-transplant has been associated with HLA-mismatching (53).This was determined to be primarily due to the higher risk of infection and cardiovascular disease related to increased usage of immunosuppression doses and anti-rejection therapy when HLA-mismatches are present in transplants (53). With respect to all-cause mortality, research has demonstrated a significant negative relationship between HLA per mismatch and all-cause mortality in deceased donor kidney transplant recipients (HR: 1.04; 95% CI: 1.02–1.07) (51). For recipients of living donor kidneys, research has found no association between patient survival rates and number of HLA matching (52).

ABO-Incompatibility

Although severe donor organ shortages have forced jurisdictions worldwide to consider ABO-incompatible (ABOi) donors, the costs associated with preconditioning and post-transplant care as well as the risks of irreversible antibody-mediated rejection (AMR) may be factors contributing to their limited use (54, 55). With that in mind, the results stemming from the literature with respect to graft and patient survival are mixed. Evidence from a single-centre in the United-States which performed 60 consecutive living donor ABOi transplants found this cohort experienced similar graft survival rates at 1,3 and 5 years post-transplant in comparison to compatible live donors and no grafts were lost to AMR (54). Additional research evaluating Medicare data between 2000 and 2011 demonstrated lower three-year patient survival as well as death-censored graft survival for those receiving ABOi donor kidneys in comparison to ABO compatible transplants (55).

Contrarily, research has shown that ABOi transplant recipients experienced significantly lower graft survival rates from 1-8 years follow-up, yet similar survival rates throughout identical follow-up time in comparison to ABO-compatible recipients (56). These contradicting results may be due to the different populations studied as the first two stem from the United-States whereas the third study looked at ABOi recipients from Japan (54-56). In addition, the data used in the third study considered ABOi recipients between January 1989 and December 1995 whereas the first two are more recent, which may impact the conclusions drawn (54-56).

Economic Analysis

There is a dearth of research considering the economic implications of kidney transplants with varying KDPI ratings. This section will consider the existing body of evidence pertaining to economic assessments of high-KDPI kidney transplants as well as ECD kidney transplants as it was the previous indicator of a marginal kidney prior to the implementation of the KDPI rating.

Economic evaluations have demonstrated higher long-term total expenditures associated with ECD kidney transplants in comparison to SCD kidney transplants as well as maintenance hemodialysis (57, 58). An economic assessment published in 2018 using de-identified registry data from the United States Renal Data System (USRDS) and patient-level data from the Scientific Registry for Transplant Recipients (SRTR) found that transplants from living as well as low-KDPI donors was cost-saving in comparison to dialysis over a ten-year period (59).

Moreover, kidney transplantation with high-KDPI donors was concluded to be more costly than maintenance dialysis over a ten-year time-horizon (mean $330,576 USD in comparison to $292,117). This elevated cost was attributed to the survival benefit of high KDPI kidney recipients, as they incur ongoing costs for an extended period in-comparison to those on maintenance dialysis (59). Considering QALYS, high KDPI kidney recipients experienced quality-adjusted survival benefits in comparison to dialysis patients over the same period (mean 5.20 QALYS versus 4.03 QALYS) (59). With that, transplants utilizing high-KDPI kidneys were deemed cost-effective at <$100,000 per QALY (59). Living donor kidney transplants where there were 0-3 HLA mismatches was found to have the lowest mean cost/QALY over a ten-year period at $39,939/QALY (59). This study considered the standard costs related to living and deceased donor transplants as well as costs of immunosuppressive therapies related to HLA mismatches (0-3 and 4-6) and ABOi living donors, which have not been considered in previous economic analyses (57-59). Living donor transplants with 0-3 and 4-6 HLA mismatches between donor and recipient added mean costs to the overall procedure of $1334 and $1345 per month respectively to the overall mean cost of transplantation, which was ultimately minimal relative to the overall cost (59, 60). ABOi living donor transplants had a total mean cost of $130,000 in comparison to $94,000 for compatible living donors, translating to a marginal increase of $36,000 (55, 59).

There still exist gaps in the current knowledge related to the putative cost-utility of kidney transplantation, KDPI rating/EPTS combination, particularly in the local context as much of the prevailing research stems from the United-States (57-59). Moreover, much of the evidence is dated (57, 58), which may impact conclusions drawn. Deceased donor renal transplant outcomes have been improving in recent years and generic medications have become available, reducing transplant related costs (61).

Chapter III: Materials and Methods

Research Questions and Hypotheses

Study Aim 1

Determine whether end-stage renal-disease patients 60 years of age and over receive survival benefit over a ten-year time horizon in a scenario where additional kidneys with a KDPI ≥86 are introduced and accepted for transplant.

Hypothesis 1

End-stage renal-disease patients ≥60 years of age will receive survival benefit from earlier transplantation over a ten-year time horizon in a scenario where the supply of high KDPI (≥86) kidneys is increased in comparison to the usual care, status quo scenario.

Study Aim 2

Determine the cost-utility of increasing the usage of marginal kidneys in Manitoba's older adult (age ≥60) end-stage renal-disease patient population where marginal kidney is defined as a kidney with a KDPI ≥86.

Hypothesis 2

Increasing the use of marginal kidneys in Manitoba's older adult (age ≥60) end-stage renal-disease patient population will be cost-effective (≤$100,000/quality-adjusted life-year incremental cost-effectiveness ratio) in comparison to the current rate of use (usual care, status quo scenario).

Study Aim 1

The first aim of this study was to determine whether patients 60 years of age or over would derive any survival benefit in a scenario where additional kidneys with a KDPI ≥86 are introduced and accepted for transplant in comparison to the status quo scenario where these additional organs are unavailable.

Study Population

The study population considered under this aim included all transplant eligible end-stage renal-disease patients in Manitoba aged 60 or over who have been placed on the pre-transplant waitlist between January 2011 and January 2021. Only those aged 60 and over on the date of dialysis initiation (the time in which wait time began accruing) were considered. Data from those who underwent preemptive transplant were not included. Data from the deceased donor decline dataset (31) coupled with actual transplant numbers from the pre and post-transplant dataset (30) was used to inform actual and hypothetical kidney supplies in the province.

Study Design

To address Aim 1, the patient survival rate in a new Marginal Kidney scenario where additional kidneys with a KDPI ≥86 are accepted and transplanted was compared to the patient survival rate in the usual care, Status Quo scenario at the end of ten years. Main outcomes are presented as the absolute difference in patient survival between the two scenarios and mean survival for patients who received a marginal kidney (KDPI ≥86) in comparison to transplant-naïve incident waitlist patients in the Marginal Kidney Scenario.

Model Overview

A decision analytic Markov model using micro simulation with TreeAge Pro 2019 (Williamstown, MA) was developed, following published economic evaluations in healthcare guidelines (62, 63). Patients transitioned through the various states of the model, being wait-listed, death on the waitlist, transplant-ineligible, transplant (KDPI groupings: ≥86, 60-85, 36-59, and 20-35), surviving post-transplant with functioning graft, graft failure, permanent dialysis, and death. This model took into consideration wait-times, transplant ineligibility, mortality rates and graft failure rates associated with patients ≥60 years of age in the new Marginal Kidney scenario compared to the Status Quo scenario to evaluate patient survival over the ten-year time horizon. Each stage within the model will be one month, totaling 120 stages for ten-years. Wait-times were incorporated with a modifiable variable (or probability factor) for ease of interchangeability, reflecting changes in organ supply and organ acceptance rate. Transplant ineligibility within the data was determined if the patient was coded as “ineligible”, “moved”, “no interest”, or “unknown” as their most recent status within the data. Transplant-naïve patients will consist of those who never received a kidney transplant within the duration of the model (patients who remain on the waitlist throughout the full model duration, patients who transition to death prior to receiving a transplant, and who become ineligible prior to receiving a transplant). This model used a half-cycle correction to account for the overestimation of state membership as patients ultimately transition from state-to-state at different times within cycles. An overview of the model which has been separated into three sections for ease of evaluation is located in Figure 1, Figure 2 and Figure 3. Figure 1 depicts patient transitions through the waitlist, Figure 2 depicts patient pathways immediately post-transplant, and Figure 3 depicts patient pathways both post-graft failure or after being deemed transplant ineligible (permanent dialysis).

Figure 1. Model Overview: Waitlist

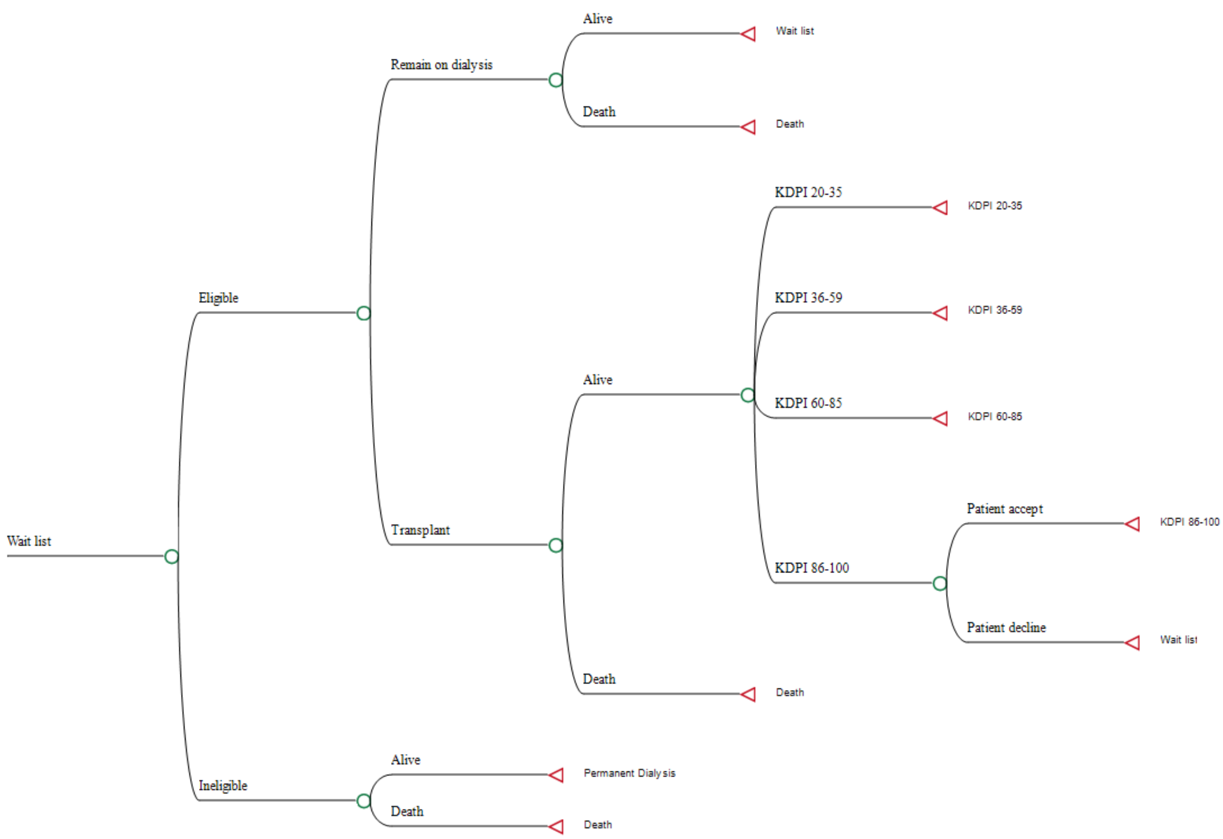


Figure 2. Model Overview: Post-transplant

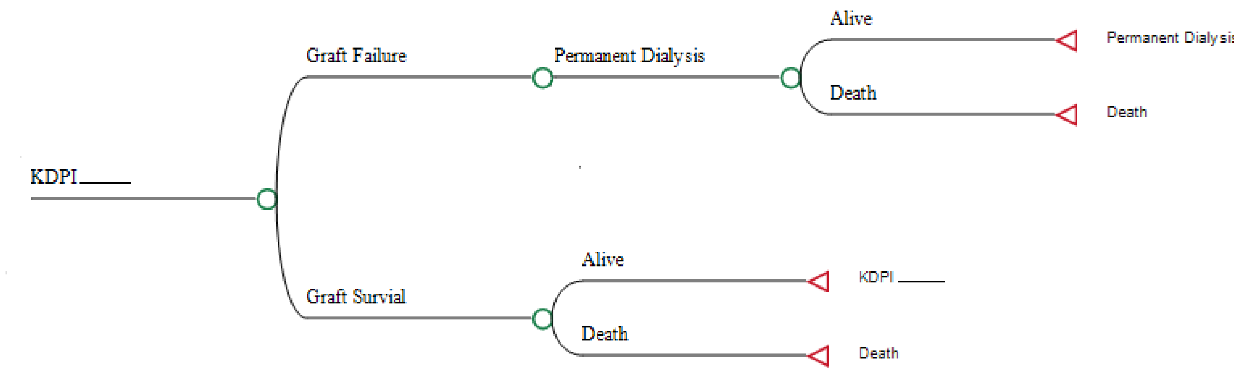
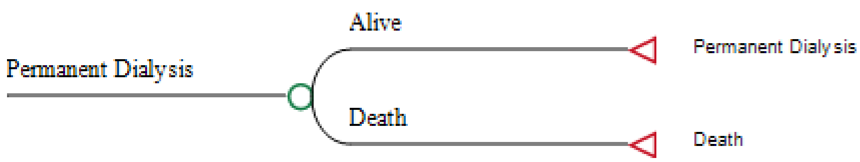


Figure 3. Model Overview: Permanent dialysis



In accordance with Priority Ranking Allocation Criteria Guidelines in Manitoba, patients over or equal to 60 years of age are ineligible to receive kidneys with a KDPI <20. As such, only organs with a KDPI between 20-100 were considered in this analysis (50). In Manitoba, a patient's probability of being offered a donor kidney is driven from their calculated patient priority score, which according to the Provincial Priority Ranking Allocation Criteria Guidelines, considers HLA matching, time spent on the wait-list and sensitization in the calculation (50). Due to lack of data, HLA matching and sensitization was not considered in this analysis, leaving patient time spent on the waitlist as the sole contributing factor contributing to a patient's probability of being offered a donor organ in this analysis. Over-riding priority patients [highly sensitized patients

(PRA ≥95%) and medically urgent] and high priority patients (pediatric recipients and previous living donors) was omitted from this analysis.

In Manitoba, patients who experience graft failure within the first 90 days post-transplant return to the waitlist and maintain their pre-transplant priority score which drives their probability of receiving a transplant. Furthermore, patients who experience graft failure at any point may be deemed fit to return to the waitlist in hopes of receiving another donor organ in the real-world scenario. As per the data sourced from Transplant Manitoba, no waitlisted-patient aged 60 and over placed on the pre-transplant waitlist between January 2011 and January 2021 has appeared twice on the waitlist (30). Altogether, for simplicity and practicality, living patients who experience graft failure at any point were deemed ineligible to receive a second transplant, thus directly transitioning to permanent dialysis in this analysis. Finally, current practice in Manitoba is such that no patient is to be considered for a kidney in which the donor is of an incompatible blood-type. Due to lack of data, blood-type specific transplant probabilities were not considered in this model.

Model Inputs

Five year post-transplant survival benefits by EPTS/KDPI combination (KDPI grouped: ≥86, 85-60, 59-36, and 35-20) as compared to remaining on the waitlist were determined by using an online tool developed by the Epidemiology Research Group for Organ Transplantation at the John Hopkins School of Medicine and are based upon U.S data (64). As survival benefits in comparison to remaining on the waitlist after 60 months post-transplant by EPTS/KDPI score are publicly unavailable, a life-table approach was taken to determine patient survival after that point. Published death probabilities by age (based upon the United-States population as to maintain consistency with the KDPI/EPTS survival benefits) will be multiplied by the ten-year relative survival estimates of patients post-first deceased donor kidney transplant compared to those who have never received a kidney transplant by age group (65, 66). Both the monthly five-year death probability estimates by KDPI/EPTS combination as well as monthly life-table relative death probability estimates can be found in the Appendix, Item 1, and Item 2.

Five-year graft failure rates by KDPI groupings (21-35, 36-85 and 86-100) sourced from the literature were used to derive the probability of graft failure (38). Patients receiving a deceased donor organ with a KDPI = 20 will be given a graft failure rate from the KDPI 21-35 group. The probability of graft failure at 5 years post-transplant was be assumed for every cycle after that point in time as data evaluating graft-survival by KDPI score post five years is unavailable to our knowledge. Monthly graft failure probabilities by KDPI grouping are in the Appendix, Item 4, Item 5, and Item 6. Transplant Manitoba data was used to derive the probability of death on the waitlist pre-transplant, the probability of becoming ineligible for a transplant as well as the probability of receiving a transplant. The probability of death once patients transition to permanent dialysis due to ineligibility was assumed to be that of the regular Canadian dialysis population, sourced from the Canadian Organ Replacement Registry (CORR) (Appendix, Item 7) (67). The probability of death post-graft failure was determined by multiplying the probability of death on the waitlist by the hazard ratio for death in patients post-graft failure in comparison to those on the waitlist (30, 44). Monthly estimates by year are in the Appendix, Item 8, Item 9, and Item 10. The probability of receiving a transplant in the Marginal Kidney scenario was derived simply by multiplying the probability of receiving a transplant in the Status Quo scenario by the factor in which the supply of kidneys with a KDPI 86-100 increased by. The total number of kidneys declined for transplant due to their quality with a KDPI 86-100 in the years 2018/2019 as a percentage of the number of deceased donor transplants within the time period was used to create the new potential kidney supply (31). This model assumed a 100% acceptance rate of possible marginal kidneys. The number of transplanted organs with a KDPI <86 was be stabilized between scenarios, leaving the increased transplants to be of kidneys with a KDPI between 86-100. Furthermore, ten-year waitlist survival rates were assumed for patients who transition to permanent dialysis after becoming transplant ineligible.

The KDPI score consists of 10 donor characteristics: age, height, weight, ethnicity, history of hypertension, history of diabetes, cause of death, serum creatinine level, hepatitis C virus (HCV) status, and whether the donor meets the donation after circulatory death (DCD) criteria. Although there exists some historical data regarding the KDPI of transplanted donor organs in Manitoba, we opted to use a distribution sourced from the literature which was sourced from OPTN in the United States (28). This distribution is based upon kidneys transplanted in the United States between January 1, 2005, and December 31, 2016, and provides more granular data in comparison to the Manitoba specific data (28, 68). At a high level, the distribution by KDPI groupings 20-35, 36-59, 60-85 and 86-100 were deemed to be similar between the two data sources (28, 68). The new kidney supply distribution was derived by adding the additional marginal kidneys available for transplant to the original kidney supply sourced from the literature (28, 31). The graphical kidney distribution of the original kidney supply by KDPI as well as the new kidney supply can be found in the Appendix, Item 11, and Item 12.

Four inputs are needed to determine recipient EPTS score: diagnosis of diabetes, candidate time on dialysis, number of prior organ transplants, and candidate age. A Canadian study was used to create the distribution of diabetes diagnoses (Yes or No) in the wait-list population (69). Candidate time on dialysis prior to entering the model was 0 months as data used to derive waitlist transitions was based upon dialysis start date. After waitlist initiation, the model tracked unique patient time on dialysis by month. Candidate age entering the model were assumed to be 60 as marginal kidneys are only offered to this patient population as per the Provincial Priority Ranking Allocation Criteria Guidelines (50). Candidate age was tracked by month within the model. All rates were first converted to instantaneous rates, then into monthly probabilities taking into consideration their respective time-frame differences. The source of each model input used to address aim 1 can be found in Table 1.

Table 1. Model Inputs: Aim 1

Variable	Point Estimate	Distribution	Source
Recipient EPTS Score	**-**	-	-
Diagnosis of Diabetes	0.937	-	Arora et al.(69)
Candidate time on dialysis	Enter model at 0	-	Model Dependent
Prior organ transplants	0	-	Assumption
Candidate Age	60	-	Assumption/Model determined

Variable	Point Estimate	Distri bution	Source
Estimated original and new kidney supply by KDPI	See Appendix, Item 11, and Item 12	-	Bae et al.(28) + Transplant Manitoba (31)
Probability of death on the waitlist	See Appendix, Item 8	-	Transplant Manitoba (30)
Probability of becoming ineligible	See Appendix, Item 9	-	Transplant Manitoba (30)
Probability of receiving a transplant	See Appendix, Item 10	-	Transplant Manitoba (30)
Probability of graft failure	See Appendix, Item 4, Item 5, and Item 6	-	Gupta et al. (38)
Probability of death post transplant	See Appendix, Item 2, and Item 3	-	Bae et al. (28) + Gondos et al. (65) + Arias et al. (66)
Probability of death, permanent dialysis due to ineligibility	See Appendix, Item 7	-	CORR (67)
Probability of death, permanent dialysis post graft-failure (hazard ratio)	1.78	-	Transplant Manitoba (30) + Rao et al. (44)

Scenario Analysis

Deterministic sensitivity analysis was performed by simulating the waitlist cohort of 584 patients using first-order Monte Carlo trials to estimate variation among individual expected survival. In main analyses, a 100% acceptance rate of the additional kidneys was assumed. We performed scenario analysis considering 75%, 50%, and 25% acceptance to rate to evaluate differences in absolute patient survival in each scenario.

Study Aim 2

The second aim of this project was to determine the cost-utility of increasing the usage of marginal kidneys (KDPI ≥86) in Manitoba's waitlist eligible patient population aged 60 and over. This analysis followed the Provincial Priority Ranking Allocation Criteria Guideline, dictating that only patients on the waitlist who are ≥ 60 years of age are eligible to receive kidneys with a KDPI ≥86 (50).

Study Population

The study population considered all transplant eligible patients in Manitoba aged 60 and over who have been placed on the pre-transplant waitlist between January 2011 and January 2021, which translates to a total sample of 584 individuals (30). Data from those who underwent preemptive transplant will not be included. Data from the deceased donor decline dataset (31) coupled with actual transplant numbers from the pre and post-transplant dataset (30) were used to inform hypothetical kidney supplies in the province.

Study Design

An incremental cost-utility analysis comparing the scenario in which all kidneys with a KDPI≥85 will be accepted for transplant in comparison to usual care in which sub-optimal kidneys are able to be discarded was used to address study aim 2. This analysis took the perspective of the Canadian public health payer. Main outcomes of this analysis include the mean cost of care and QALYs per patient and mean cost/QALY. All costs are presented in 2019 Canadian dollars, with past estimates inflated using the Canadian consumer price index (CPI) (Appendix, Item 1) (70). All benefits are presented in quality-adjusted life-years (QALYs). All costs and benefits were discounted at a rate of 5%, following the Canadian Agency for Drugs and Technologies in Health (CADTH) guidelines for economic evaluations (62).

Model Overview

Like aim 1, this analysis was conducted by developing a decision analytic Markov model using microsimulation with TreeAge Pro 2019 (Williamstown, MA), following published guidelines for economic evaluations in healthcare (62, 63). Unique organ demand, and associated kidney supplies/wait-times was developed using numbers from the pre and post-transplant dataset (30) as well as the deceased donor organ decline dataset sourced from Transplant Manitoba (30, 31).

Organ supply was created to be modifiable by using a transplant probability factor to incorporate changes in anticipated wait-times and acceptance rates. Patients transitioned through the various states of the model, being wait-listed, death on the waitlist, transplant-ineligible, transplant (KDPI groupings: ≥86, 60-85, 36-59, and 20-35), surviving post-transplant with functioning graft, graft failure, permanent dialysis and death accumulating costs and effectiveness (QALYs) based upon time in each state. Total costs were divided by total QALYs at the end of the time-horizon to determine the cost-utility ratios associated with each scenario. As a baseline assumption, patients were unable to refuse marginal kidney offers, thus choosing to undergo transplantation immediately. Post graft-failure, patients transitioned to the permanent dialysis state until death or the ending of the model time-horizon. This model used a half-cycle correction to account for the overestimation of state membership as patients ultimately transition from state-to-state at different times within cycles in TreeAge Pro. Similar to aim 1, an overview of the model which has been separated into three sections for ease of evaluation, is located in Figure 1, Figure 2, and Figure 3.

Model Inputs

In addition to the model inputs listed under aim 1, utility estimates (as measured in quality-adjusted life year weights) for dialysis and transplant patients were sourced from a systematic review quality of life in chronic kidney disease treatments, reporting an annual utility score of 0.7 for dialysis patients and 0.82 for transplant patients (71). An assumption was made that kidney transplants yield the same baseline utility scores regardless of KDPI rating.

Costs

Annual dialysis costs were sourced from a recently published Manitoba specific study conducted from the perspective of the public payer (13). This study considered costs related to dialysis care such as: labor, supplies, equipment, dialysis specific pharmaceuticals, overhead, initial patient training and capital costs which were split out by modality (in-centre hemodialysis, home hemodialysis and peritoneal dialysis) (13). A blended approach taking into consideration the dialysis modality mix in Manitoba as of January 2019 (72) was used to determine the average cost of dialysis per patient. Donor and recipient transplant costs related to pretransplant workup, graft removal, outpatient care, diagnostic imaging, inpatient care, physician claims and laboratory tests were drawn from a Canada specific study which estimated donor and recipient-related costs for living and deceased donor transplantation (16). Although transplant related medication costs were included in this published study, they were replaced with current costs in Manitoba as generic medications have become available since the date of publication (list price as of 2009), drastically reducing the per unit price (73). The distributional properties from the published inpatient costs were standardized and applied to the new inpatient mean costs reflective of the updated medication prices. All identified model and cost inputs used to address study aim 2 alongside their sources are in Table 2.

Table 2. Model Inputs: Aim 2

Variable	Point Estimate	Distribution	Source
Discount rate, costs	0.5	-	CADTH (62)
Discount rate, utilities	0.5	-	CADTH (62)
CPI	Appendix, Item 1	-	Statistics Canada (70)
Utility, hemodialysis facility-based	0.71 (SD: 0.04)	Normal (Mean, SD)	Wyld et al. (71)
Utility, peritoneal dialysis	0.71 (SD: 0.04)	Normal (Mean, SD)	Wyld et al. (71)

Variable	Point Estimate	Distribution	Source
Utility, home hemodialysis	0.71 (SD: 0.04)	Normal (Mean, SD)	Wyld et al. (71)
Utility, transplant	0.82 (SD: 0.04)	Normal (Mean, SD)	Wyld et al. (71)
Recipient EPTS Score	**-**	-	-
Diagnosis of Diabetes	0.937	-	Arora et al. (69)
Candidate time on dialysis	Enter model at 0	-	Model Dependent
Prior organ transplants	0	-	Assumption
Candidate Age	60	-	Assumption/Model determined
Monthly dialysis costs (2016 CAD)	-	-	-
Peritoneal Dialysis, month 1	\$10,378.50 (Alpha: ((10378.50)^2)/((10378.50*.25)^2), Lambda: (10378.50)/((10378.50*.25)^2))	Gamma (Alpha, Lambda)	Beaudry et al.(13)

Variable	Point Estimate	Distribution	Source
Peritoneal Dialysis, month 2+	$3,221.50 (Alpha: ((3221.50)^2)/((3221.50*.25)^2), Lambda: (3221.50)/((3221.50*.25)^2))	Gamma (Alpha, Lambda)	Beaudry et al. (13)
Home Hemodialysis, month 1	$15,459.17 (Alpha: ((15459.17)^2)/((15459.17*.25)^2), Lambda: (15459.17)/((15459.17*.25)^2))	Gamma (Alpha, Lambda)	Beaudry et al. (13)
Home Hemodialysis, month 2+	$3,269.67 (Alpha: ((3269.67)^2)/((3269.67*.25)^2), Lambda: (3269.67)/((3269.67*.25)^2))	Gamma (Alpha, Lambda)	Beaudry et al. (13)
In-centre Hemodialysis, month 1+	$5,351.17 (Alpha: ((5351.17)^2)/((5351.17*.25)^2), Lambda: (5351.17)/((5351.17*.25)^2))	Gamma (Alpha, Lambda)	Beaudry et al. (13)
Dialysis modality proportions	-	-	-
Peritoneal Dialysis	14.7%	-	Manitoba Renal Program (72)

Variable	Point Estimate	Distribution	Source
Home Hemodialysis	7.0%	-	Manitoba Renal Program (72)
In-centre Hemodialysis	78.3%	-	Manitoba Renal Program (72)
Recipient related transplant costs	-	-	-
Labs, year 1 (2008 CAD)	5292 (Alpha: ((5292)^2)/((5292*.106)^2), Lambda: (5292)/((5292*.106)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Labs, year 2+ (2008 CAD)	1759 (Alpha: ((1759^2)/(((1759*.095)^2), Lambda: (1759)/((1759*.095)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Diagnostic Imaging, year 1 (2008 CAD)	2385 (Alpha: ((2385)^2)/((2385*.106)^2), Lambda: (2385)/((2385*.106)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)

Variable	Point Estimate	Distribution	Source
Diagnostic Imaging, year 2+ (2008 CAD)	712 (Alpha: ((712)^2)/((712*.095)^2), Lambda: (712)/((712*.095)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Physician Services, year 1 (2008 CAD)	6330 (Alpha: ((6330)^2)/((6330*.106)^2), Lambda: (6330)/((6330*.106)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Physician Services, year 2+ (2008 CAD)	2049 (Alpha: ((2049)^2)/((2049*.095)^2), Lambda: (2049)/((2049*.095)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Inpatient Services, year 1 (2008 CAD)	32005.00 (Alpha: ((32005)^2)/((32005*.106)^2), Lambda: (32005)/((32005*.106)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Inpatient Services, year 2+ (2008 CAD)	3344.00 (Alpha: ((3344)^2)/((3344*.095)^2), Lambda: (3344)/((3344*.095)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)

Variable	Point Estimate	Distribution	Source
Outpatient Services, year 1 (2008 CAD)	8647.00 (Alpha: ((8647)^2)/((8647*.106)^2), Lambda: (8647)/((8647*.106)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Outpatient Services, year 2+ (2008 CAD)	4248.00 (Alpha: ((4248)^2)/((4248*.095)^2), Lambda: (4248)/((4248*.095)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Medication, year 1 (2019 CAD)	10059.47 (Alpha: ((10059.47)^2)/(((10059.47 *.106))^2), Lambda: (10059.47)/((10059.47 *.106)^2))	Gamma (Alpha, Lambda)	Transplant Manitoba (73)
Medication, year 2+ (2019 CAD)	33338.83 (Alpha: ((3338.83)^2)/(((3338.83 *.095))^2), Lambda: (3338.83)/((3338.83 *.095)^2))	Gamma (Alpha, Lambda)	Transplant Manitoba (73)
Donor related transplant costs	-	-	-

Variable	Point Estimate	Distribution	Source
Graft Removal	36989.00 (Alpha: ((36989)^2)/(1311)^2), Lambda: (36989)/(1311)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Workup	209.00 (Alpha: ((209)^2)/(44)^2), Lambda: (209)/((44)^2))	Gamma (Alpha, Lambda)	Barnieh et al. (16)
Estimated original and new kidney supply by KDPI	See Appendix, Item 10, and Item 11	-	Bae et al. (28) + Transplant Manitoba (31)
Probability of death on the waitlist	See Appendix, Item 8	-	Transplant Manitoba (30)
Probability of becoming ineligible for a transplant	See Appendix, Item 9	-	Transplant Manitoba (30)

Variable	Point Estimate	Distribution	Source
Probability of receiving a transplant	See Appendix, Item 10	-	Transplant Manitoba (30)
Probability of graft failure	See Appendix, Item 4, Item 5, Item 6	-	Gupta et al. (38)
Probability of death post transplant	See Appendix, Item 2, and Item 3	-	Bae et al. (28) + Gondos et al. (65) + Arias et al. (66)
Probability of death, permanent dialysis due to ineligibility	See Appendix, Item 7	-	CORR (67)
Probability of death, permanent dialysis post graft-failure (hazard ratio)	1.78	-	Transplant Manitoba (30) + Rao et al. (44)

Sensitivity and Scenario Analysis

Univariate sensitivity analysis was performed on main cost parameters by varying their estimates by +/-25% from baseline to determine their individual impact on the cost, and ultimately the cost-effectiveness of each treatment. Wait-times were varied by altering the percentage of marginal kidneys accepted for transplant (100%, 75%, 50% and 25%) to evaluate new cost-effectiveness ratios per treatment. Deterministic sensitivity analysis was performed by simulating 584 random first-order Monte Carlo trials to estimate variation among individual expected lifetime costs and effectiveness. Probabilistic sensitivity analysis (second-order Monte Carlo simulation) was performed on 100 samples for baseline costs and effectiveness estimates to evaluate parameter uncertainty by varying model inputs over plausible distributions.

Validation

Data from Transplant Manitoba was used to derive monthly transition probabilities for incident waitlisted patients aged 60 and over to the following health states: becoming ineligible for a transplant, receiving a transplant as well as death prior to transplant. Competing risk analysis was performed using SAS software, Version [9.4], (Cary, NC, USA), with outputted state survival probabilities from the waitlist to the aforementioned health states calibrated using the calibration function within TreeAge Pro 2019 (Williamstown, MA) to better approximate historical data. Model outputted values pertaining to the number of patients becoming ineligible for a transplant, receiving a transplant as well as death prior to transplant will be compared against those from the data as waitlist validation. Additionally, the number of transplants by KDPI grouping will be compared between scenarios to ensure no additional kidneys with a KDPI <86 are being transplanted in the Marginal Kidney scenario, Finally, the number of additional kidneys with a KDPI ≥86 being transplanted in the Marginal Kidney scenario will be validated against the maximum number of additional supply available in Manitoba to ensure no additional organs are being allocated in the new scenario.

Ethics

Ethical approval for this proposed project was obtained from the University of Manitoba Research Ethics Board [Ethics #: HS23415 (H2019:344)]. All members involved in this thesis project have completed training and are certified in the Tri-Council Policy Statement (TCPS) 2 Course on Research Ethics and the Personal Health Information Act (PHIA). The databases used in this analysis contained indirect identifiers such as patient date of birth, which was required to determine model inputs such as patient age at transplant and length of time on the transplant wait-list. Line level data access was given solely to the principal investigator (R.B.) post-transfer and all information disseminated is in aggregate form. In addition, all data analyzed will be destroyed upon the completion of the proposed thesis project.

Chapter IV: Results

Validation

Model predicted values with respect to the number of patients on the waitlist becoming ineligible for a transplant, the number of transplants, and waitlist deaths in comparison to Transplant Manitoba data by year can be found in Table 3. Over 10 years, the model predicted number of patients on the waitlist becoming ineligible for a transplant was 169, which equals the observed values found in the Transplant Manitoba data. At the end of years 1 through 9, the model predicted values also matched the observed data values. The number of waitlist deaths over 10 years predicted by the model was 79, which matches the value observed in the Transplant Manitoba data. At the end of years 1 through 9, the model predicted values also matched the observed data values.

Table 3. Waitlist Validation, Transplant Manitoba Data Versus Model Output

	Ineligible			Waitlist Deaths			Transplants		
Year	**Transplant Manitoba Data**	**Model Output**	**Validation**	**Transplant Manitoba Data**	**Model Output**	**Validation**	**Transplant Manitoba Data**	**Model Output**	**Validation**
1	27	27	100.0%	8	8	100.0%	13	13	100.0%
2	28	28	100.0%	15	15	100.0%	14	14	100.0%
3	28	28	100.0%	10	10	100.0%	11	11	100.0%
4	29	29	100.0%	13	13	100.0%	6	6	100.0%
5	15	15	100.0%	10	10	100.0%	9	9	100.0%
6	9	9	100.0%	9	9	100.0%	13	13	100.0%
7	10	10	100.0%	6	6	100.0%	4	4	100.0%
8	9	9	100.0%	6	6	100.0%	2	2	100.0%
9	7	7	100.0%	0	0	100.0%	2	2	100.0%
10	7	7	100.0%	2	2	100.0%	5	5	100.0%

Table 4 contains model predicted number of transplants by year, by KDPI grouping in the Status Quo scenario in comparison to the Marginal Kidney scenario. The model predicted percent of kidneys transplanted in KDPI groupings 20-35, 36-59, 60-85 and 86-100 were 26.6%, 35.4%, 26.6%, and 11.4% respectively. In comparison, the percentages sourced from the literature by KDPI groupings 20-35, 36-59, 60-85, and 86-100 were 19.2%, 34.8%, 32.1% and 13.9%, representing a difference of 6, 1, 4, and 2 kidneys transplanted in each group, respectively.

Regarding the comparison of kidneys transplanted by KDPI grouping in the Status Quo and Marginal Kidney scenarios, the numbers transplanted in groupings 20-35, 36-59 and 60-85 match between scenarios (Table 4). As per data sourced from Transplant Manitoba, the percent of kidneys deemed ineligible for transplant due to high KDPI amounted to 87.3% of all kidneys transplanted in 2018 and 2019. The additional 78 kidneys in the 86-100 KDPI grouping transplanted in the Marginal Kidney scenario translates to 98.7% of total kidneys transplanted in the Status Quo scenario, which was 11.4% (or approximately 9 kidneys) above the 87.3% total potential increase in transplants.

Table 4. 10 Year Total Transplants by KDPI Grouping, by Scenario

KDPI Group	Status Quo Scenario	Marginal Kidney Scenario
20-35	21	21
36-59	28	28
60-85	21	21
86-100	9	87
Total Transplants	79	157

State Transition

State transition and membership over time by scenario are located in Figure 4 and

Figure ***5*** with results after 10 years found in Table 5. Patients with a functioning graft (KDPI 20-35, 36-59 and 60-85) at 10 years were similar between both scenarios. In the Marginal Kidney scenario, 8.9% of the cohort had a functioning graft with a KDPI between 86-100 inclusive at the end of 10 years. In the Status Quo scenario, 0.5% of the cohort had a functioning graft with a KDPI between 86-100 inclusive at the end of 10 years. As per our model, 46.2% of the cohort in the Status Quo scenario remained on the waitlist at the end of time horizon. In comparison, 38.0% remained on the waitlist in the Marginal Kidney scenario, representing a 8.2% difference between scenarios. In the Status Quo and Marginal Kidney scenarios, 3.1% and 6.7% of the cohort respectively were on dialysis permanently due to graft failure or transplant ineligibility at the end of 10 years. Finally, 43.3% of the total cohort in the Status Quo scenario were in the death state at the end of the ten-year time horizon, compared to 39.9% in the Marginal Kidney scenario.

Figure 4. State Membership Over Time, Status Quo Scenario

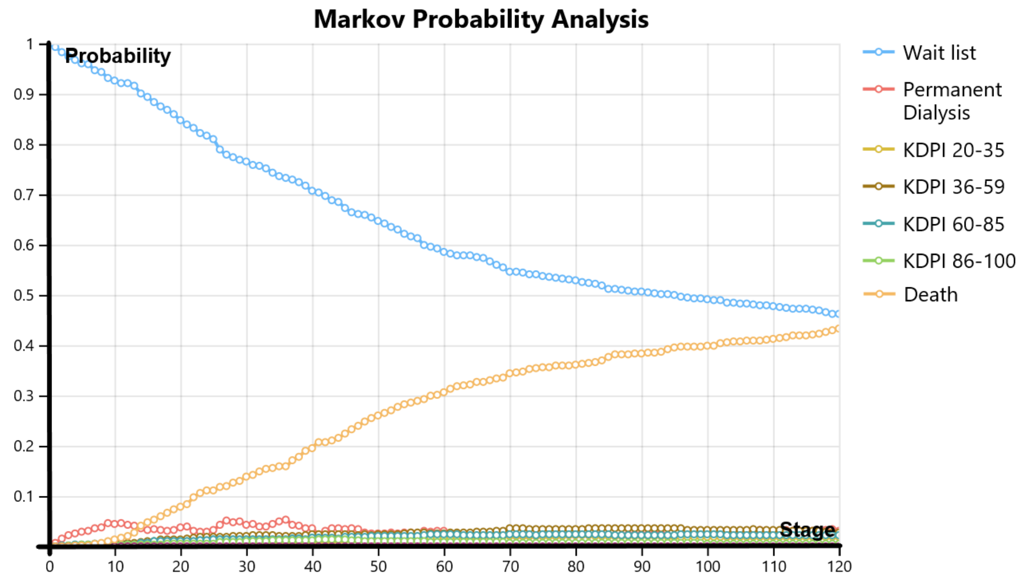


Figure 5. State Membership Over Time, Marginal Kidney Scenario

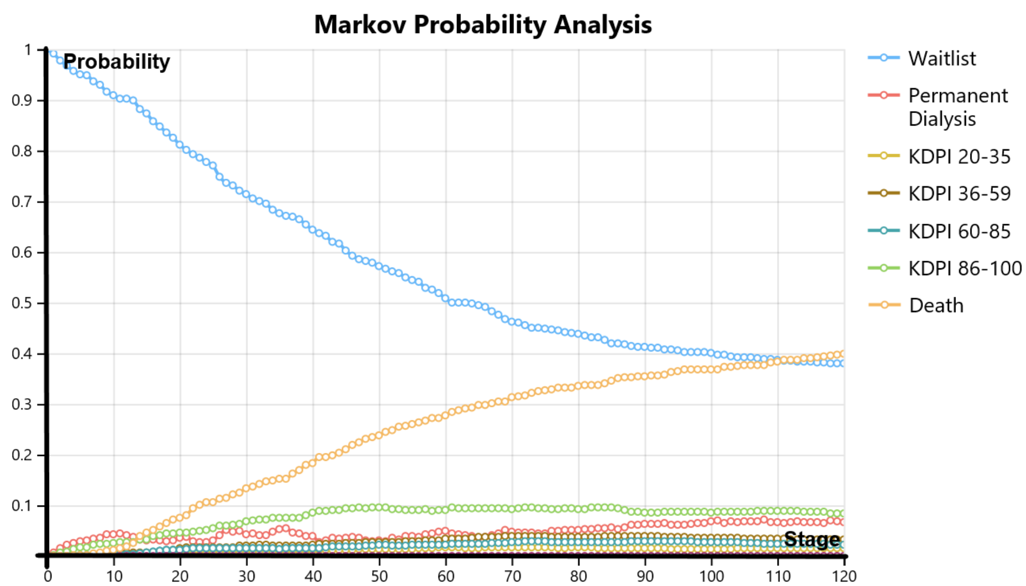


Table 5. State Membership Over 10 Years, by Scenario

	Scenario	
State membership	**Status Quo**	**Marginal Kidney**
Waitlist	46.2%	38.0%
Permanent Dialysis	3.1%	6.7%
Functioning Graft (KDPI 20-35)	1.9%	1.5%
Functioning Graft (KDPI 36-59)	2.7%	3.3%
Functioning Graft (KDPI 60-85)	2.2%	2.2%
Functioning Graft (KDPI 86-100)	0.5%	8.4%
Death	43.3%	39.9%

Aim 1

Survival

Cohort patient survival rates by scenario are presented in Figure 6 and

Figure 7. Overall, 56.7% of the incident waitlisted patients survived over 10 years in the Status Quo scenario. In the Marginal Kidney scenario, 60.1% of the incident waitlisted patients survived over 10 years, representing a difference of 5.6%. As per

Table **6**, patients who received a marginal kidney in the Marginal Kidney scenario survived 115.59 months on average. In comparison, mean survival in months for transplant-naïve patients (including patients who remain on the waitlist throughout the full model duration, patients who transition to death prior to receiving a transplant, and who become ineligible prior to receiving a transplant) was 80.37 months on, representing a difference of 35.22 months.

Figure 6. Ten-year patient survival, Status Quo Scenario

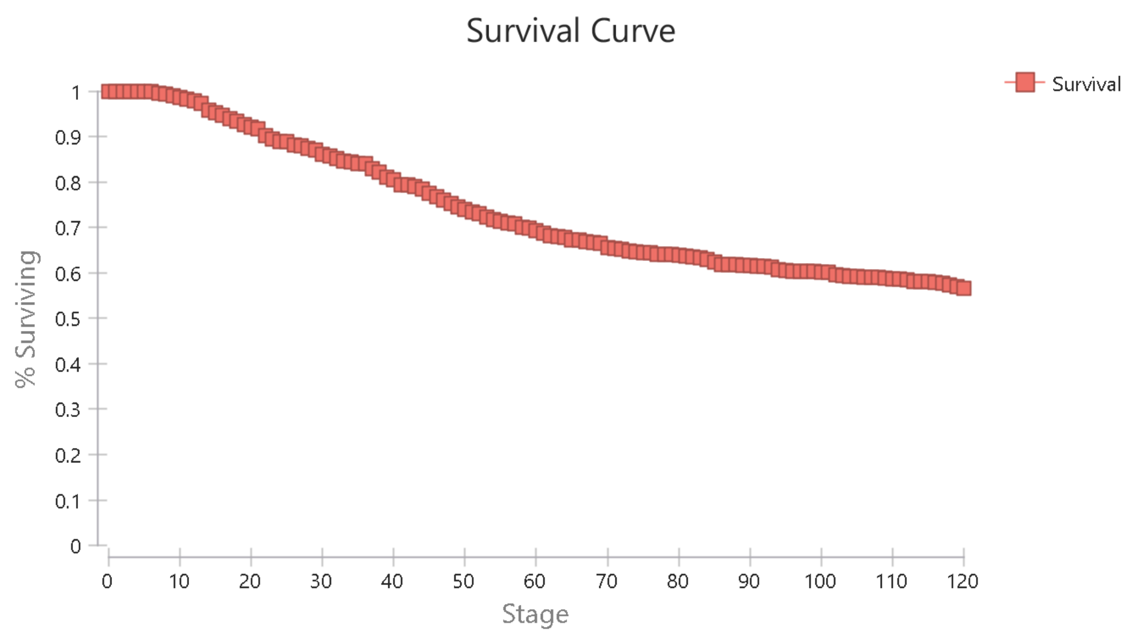


Figure 7. Ten-year patient survival, Marginal Kidney Scenario

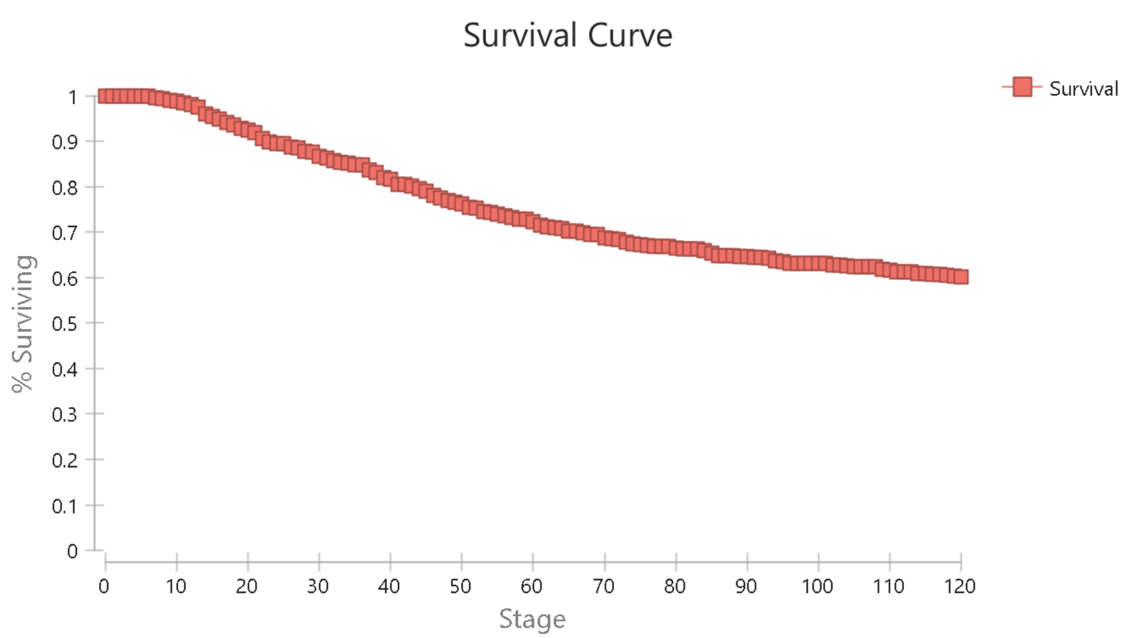


Table 6. 10 Year Mean Survival in Months, Transplant-Naïve Versus Marginal Kidney Recipients, Marginal Kidney Scenario

Group	Mean Survival (Months)
Transplant-Naïve	80.37
Marginal Kidney Recipient	115.59

Scenario Analysis

Scenario analysis results are in Table 7. As per main analysis results, 62.3% of the Marginal Kidney cohort survived at 10 years post waitlist initiation in our simulation. When the acceptance rate was reduced to 75%, 50% and 25%, the survival rate changed to 59.4%, 58.0% and 57.9% respectively.

Table 7. 10 Year Patient Survival by Kidney Acceptance Rate, Marginal Kidney Scenario

Percent of Marginal Kidneys Accepted	Marginal Kidney Scenario	Transplant Probability Factor
100%	60.1%	2.09
75%	59.4%	1.82
50%	58.0%	1.55
25%	57.9%	1.27

Aim 2

Costs

Total mean (SD) and associated 25%, 50%, and 75% percentile costs at 1, 2, 3, 5 and 10 years for 60-year-old incident kidney transplant waitlist patients are summarized in

Table ***8***. The mean cost of care in the Status Quo scenario at 1, 2, 3 and 5 years were $63,260.15 (SD: $7,056.78) , $118,487.01 (SD: $17,061.77) , $165,777.19 (SD: $31,510.62), and $241,393.70 (SD: $66,696.44) per patient. Similarly, the mean cost of care per patient at 1, 2, 3, and 5 years in the Marginal Kidney scenario were $64,332.65 (SD: $10,077.15), $120,392.16 (SD: $19,111.71), $167,917.81 (SD: $32,819.54), and $242,489.58 (SD: $67,085.07) respectively. Over 10 years, the total mean cost per patient in the Status Quo scenario was estimated at $365,624.71 (SD: $152,647.93). In the Marginal Kidney scenario, the total mean cost per patient over 10 years was $362,116.54 (SD: $149,037.69), representing a $3,508.17 reduction in cost per patient in comparison to the Status Quo scenario.

Table 8. Treatment Specific Costs per Patient (First-Order Monte Carlo Simulation)

Scenario	Cost	1 Year	2 Year	3 Year	5 Year	10 Year
Status Quo	**Mean**	$63,260.15	$118,487.01	$165,777.19	$241,393.70	$365,624.71
	(SD)	($7,056.78)	($17,061.77)	($31,510.62)	($66,696.44)	($152,647.93)
	25%	$62,608.01	$120,421.68	$175,482.32	$223,392.89	$232,574.73
	50%	$62,608.01	$120,421.68	$175,482.32	$277,862.65	$465,853.49
	75%	$62,608.01	$120,421.68	$175,482.32	$277,862.65	$494,083.73
Marginal Kidney	**Mean**	$64,332.65	$120,392.16	$167,917.81	$242,489.58	$362,116.54
	(SD)	($10,077.15)	($19,111.71)	($32,819.54)	($67,085.07)	($149,037.69)
	25%	$62,608.01	$120,421.68	$175,482.32	$219,727.54	$242,457.51
	50%	$62,608.01	$120,421.68	$175,482.32	$277,862.65	$415,661.26
	75%	$62,608.01	$120,421.68	$175,482.32	$277,862.65	$494,083.73

Quality of life

1, 2, 3, 5 and 10 year mean and associated 25%, 50%, and 75% percentile QALY estimates per patient, by scenario are outlined in Table 9. At 1, 2, 3, and 5 years, the mean QALYs in the Status Quo scenario were 0.69 (SD: 0.04), 1.32 (SD: 0.16), 1.87 (0.34) and 2.77 (0.76) per patient. In the Marginal Kidney scenario, the mean QALYs per patient at 1, 2, 3, and 5 years were 0.69 (SD: 0.04), 1.32 (SD: 0.16), 1.88 (SD: 0.34) and 2.82 (SD: 0.76) respectively. Over 10 years, the mean QALYs per patient in the Status Quo and Marginal Kidney scenarios were 4.35

(SD: 1.81) and 4.52 (SD: 1.84), representing a difference of 0.17 QALYs per patient in favor of the Marginal Kidney scenario.

Table 9. Quality Adjusted Life Years per Patient (First-Order Monte Carlo Simulation)

Scenario	QALYs	1 Year	2 Year	3 Year	5 Year	10 Year
Status Quo	**Mean (SD)**	0.69 (0.04)	1.32 (0.16)	1.87 (0.34)	2.77 (0.76)	4.35 (1.81)
	25%	0.69	1.35	1.98	2.66	2.66
	50%	0.69	1.35	1.98	3.15	5.62
	75%	0.69	1.35	1.98	3.15	5.62
Marginal Kidney	**Mean (SD)**	0.69 (0.04)	1.32 (0.16)	1.88 (0.34)	2.82 (0.76)	4.52 (1.84)
	25%	0.69	1.35	1.98	2.85	2.85
	50%	0.69	1.35	1.98	3.15	5.62
	75%	0.69	1.35	1.98	3.15	5.62

Cost-Utility

Table 10 contains mean and associated 25%, 50%, and 75% percentile cost-utility ratios at 1, 2, 3, 5, and 10 years by scenario. The mean cost-utility ratio per waitlist patient aged 60 at 1, 2, 3, and 5 years were $91,260.13, $90,035.99, $88,741.38, and $87,088.98 per QALY in the Status Quo scenario. In the Marginal Kidney scenario, the associated cost-utility ratios per patient were $92,640.40, $91,049.84, $89,160.41, and $85,873.60 per QALY, respectively. Over the complete time horizon of the study (10 years), the mean cost-utility ratio in the Status Quo and Marginal Kidney scenarios were $84,029.73 and $80,084.90 per waitlisted patient. The difference in cost-utility ratios between the Status Quo and Marginal Kidney scenarios was $3,944.83 per QALY in favor of the Marginal Kidney scenario. The incremental cost-utility ratio (ICUR) between the two scenarios was estimated at -$20,573.03, indicating that the new intervention is less costly and more effectiveness in comparison to usual care.

Table 10. Cost per Quality Adjusted Life Years per Patient (First-Order Monte Carlo Simulation)

Scenario	QALYs	1 Year	2 Year	3 Year	5 Year	10 Year
Status Quo	Mean	$91,260.13	$90,035.99	$88,741.38	$87,088.98	$84,029.73
	25%	$101,902.77	$89,008.76	$88,562.43	$84,029.43	$87,483.19
	50%	$101,902.77	$89,008.76	$88,562.43	$88,205.99	$82,915.89
	75%	$101,902.77	$89,008.76	$88,562.43	$88,205.99	$87,940.51
Marginal Kidney	Mean	$92,640.40	$91,049.84	$89,160.41	$85,873.60	$80,084.90
	25%	$101,902.77	$89,008.76	$88,562.43	$77,138.20	$85,117.84
	50%	$101,902.77	$89,008.76	$88,562.43	$88,205.99	$73,982.33
	75%	$101,902.77	$89,008.76	$88,562.43	$88,205.99	$87,940.51

Sensitivity and Scenario Analyses

Univariate sensitivity analysis results by scenario can be found in Table 11, with graphical results represented in Figure 8 and

Figure **9**. In both scenarios, the most influential cost parameter was identified as the monthly cost of dialysis. Altering the monthly cost of dialysis by +/-25% varied the 10 year mean cost of care by +/- $86,785.70 (spread =$173,571.40) in the Status Quo scenario and by +/- $80,728.80 (spread = $161,457.60) in the Marginal Kidney scenario. The 10 year mean cost of care per patient in the Marginal Kidney scenario remained below that in the Status Quo scenario when costs were increased by 25% ($442,845.34 versus $452,410.42 When dialysis costs were reduced by 25%, the mean cost per patient was higher in the Marginal Kidney scenario in comparison to the Status Quo scenario ($281,387.74 versus $278,839.01). Moreover, altering yearly recipient transplant costs (year 1 and year 2+ inclusive) by +/-25% varied the 10 year mean cost of care per patient by $3,474.39 (spread = $6,948.79) and $7,386.99 (spread = $14,773.98) in the Status Quo and Marginal Kidney scenarios, respectively. Additionally, a +/-25% change in the upfront donor related transplant cost varied the 10 year mean cost of care by $1,146.08 (spread = $2,292.16) per patient in the Status Quo scenario, and $2,413.35 (spread = $4,826.70) in the Marginal Kidney scenario. When varying transplant costs (both recipient and donor related) by +/-25%, the cost per patient in the Marginal Kidney scenario remained below that in the Status Quo scenario.

Table 11. Univariate Sensitivity Analysis – 10 Year Cost Variation by Scenario

Scenario	Cost Input	Mean Cost per Scenario	-25%	+25%	Spread
Status Quo	Dialysis	$365,624.71	$278,839.01	$452,410.42	$173,571.40
	Transplant, recipient all years	$365,624.71	$362,150.32	$369,099.11	$6,948.79
	Transplant, recipient year 1	$365,624.71	$363,859.31	$367,390.11	$3,530.80
	Transplant, recipient year 2+	$365,624.71	$363,915.72	$367,333.71	$3,417.99
	Transplant, donor	$365,624.71	$364,478.63	$366,770.79	$2,292.16
Marginal Kidney	Dialysis	$362,116.54	$281,387.74	$442,845.34	$161,457.60
	Transplant, recipient all years	$362,116.54	$354,729.55	$369,503.53	$14,773.98
	Transplant, recipient year 1	$362,116.54	$358,316.63	$365,916.45	$7,599.81
	Transplant, recipient year 2+	$362,116.54	$358,529.46	$365,703.62	$7,174.16
	Transplant, donor	$362,116.54	$359,703.19	$364,529.89	$4,826.70

Figure 8. Univariate Sensitivity Analysis – 10 Year Cost Variation, Status Quo Scenario

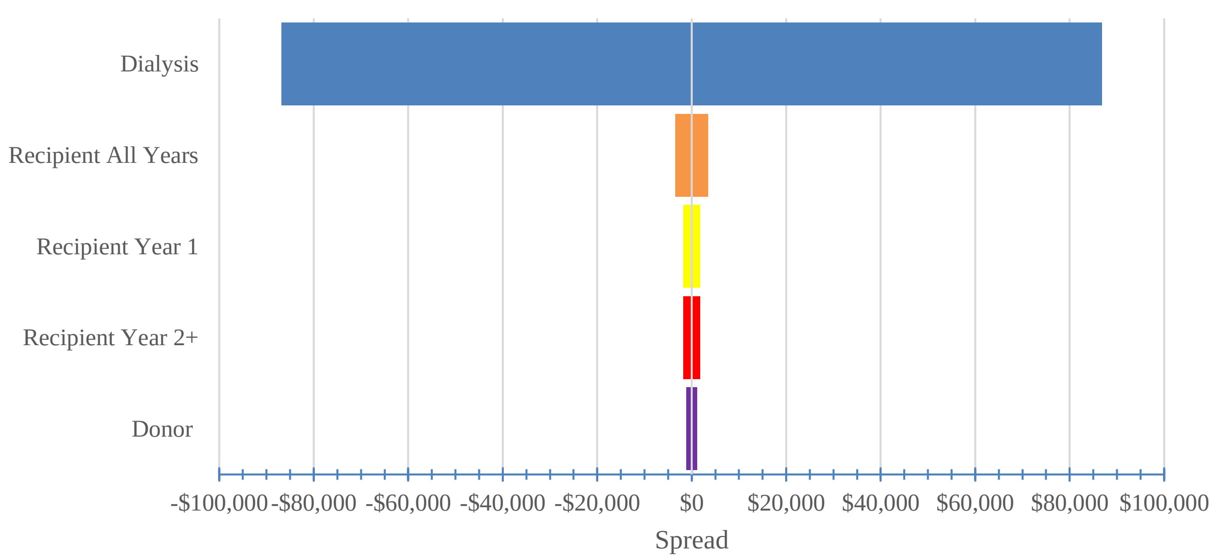
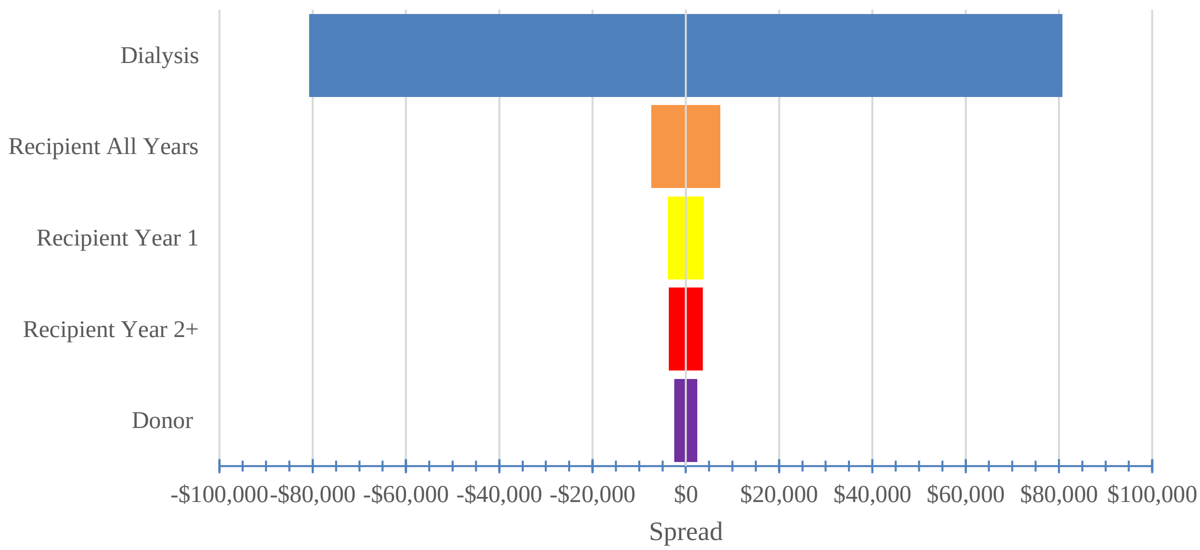


Figure 9. Univariate Sensitivity Analysis – 10 Year Cost Variation, Marginal Kidney Scenario



Probabilistic sensitivity analysis drawing on 100 random samples yielded a mean ten-year cost per patient in the Status Quo scenario of $438,989.28 (SD: $89,018.49), with quality adjusted life years over the same time period of 5.21 (SD: 0.21). In the Marginal Kidney scenario, the mean ten-year cost and quality adjusted life years were $431,171.71 (SD: $83,616.73) and 5.27 (0.20) per patient, respectively. Mean and 25%, 50%, and 75% percentile results by scenario can be found in Table 12, with the mean results by sample represented graphically in

Figure **10** and Figure 11.

Table 12. Probabilistic Sensitivity Analysis – Costs and Quality Adjusted Life Years Results

Scenario	QALYs	Cost	QALYs
Status Quo	**Mean (SD)**	$438,989.28 ($89,018.49)	5.21 (0.21)
	25%	$371,746.47	5.09
	50%	$442,052.14	5.19
	75%	$506,924.34	5.34
Marginal Kidney	**Mean**	$431,171.71 ($83,616.73)	5.27 (0.20)
	25%	$367,888.68	5.14
	50%	$433,503.12	5.25
	75%	$495,392.46	5.40

Figure 10. Probabilistic Sensitivity Analysis – Costs and QALYs, Status Quo Scenario

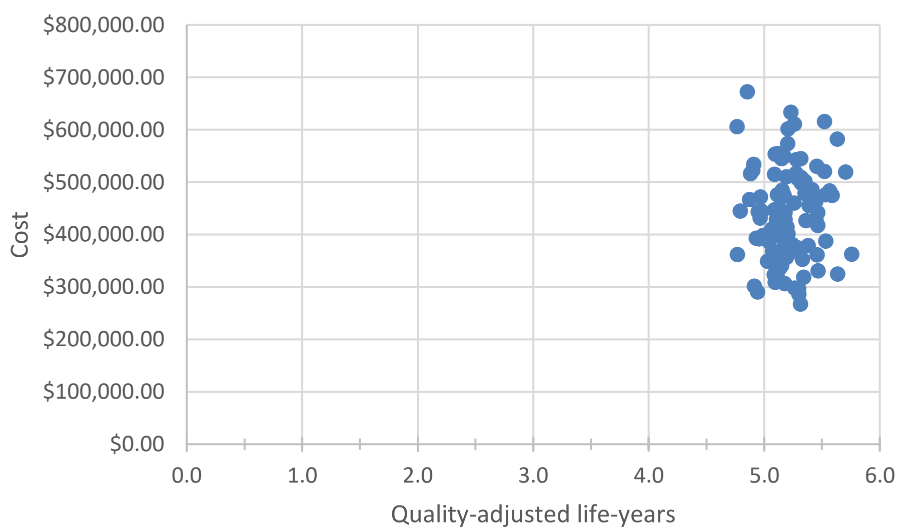
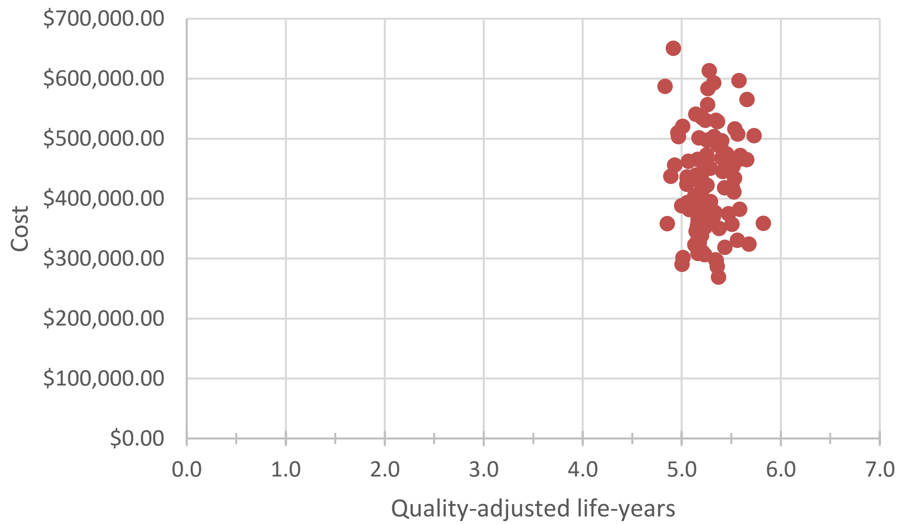
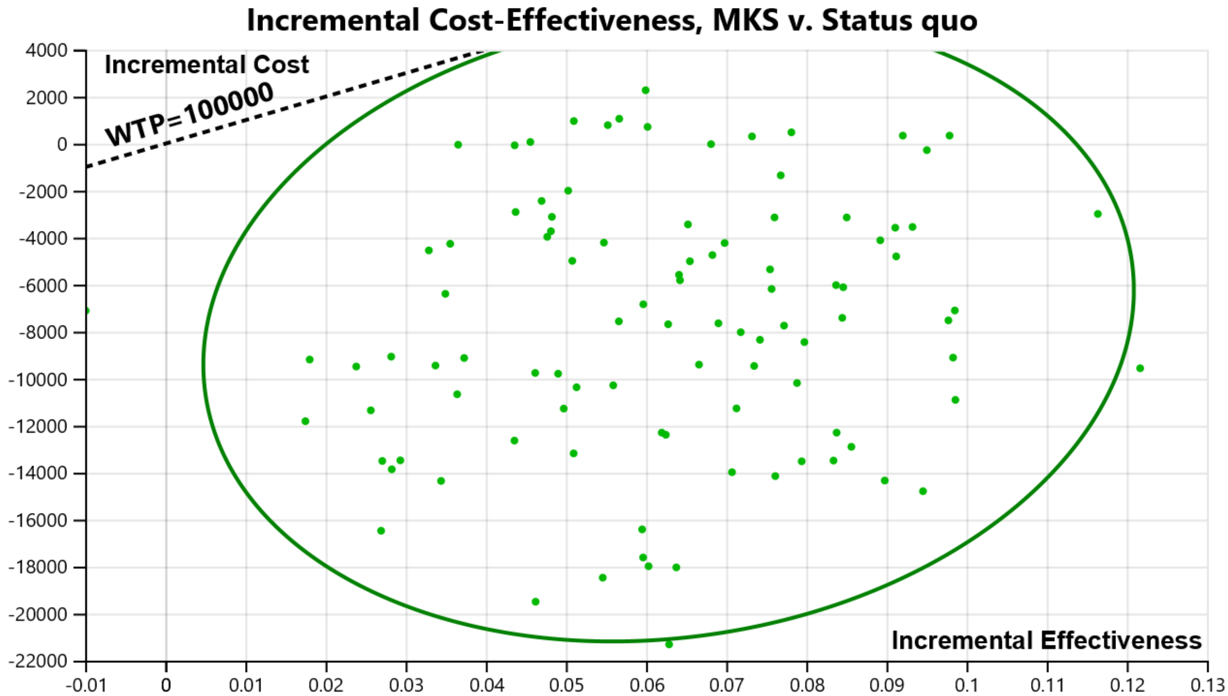


Figure 11. Probabilistic Sensitivity Analysis – Costs and QALYs, Marginal Kidney Scenario



Furthermore, the incremental cost-utility comparing the Marginal Kidney scenario versus the Status Quo scenario was analyzed using the probabilistic sensitivity analysis results (Figure 12). When drawing upon 100 random samples, the 89% of the incremental cost-utility results were considered dominant, representing lower mean costs and increased quality adjusted life years in the Marginal Kidney scenario compared to the Status Quo scenario. 10% of the samples yielded results which indicated higher costs and higher effectiveness in the Marginal Kidney scenario in comparison to the Status Quo scenario. The remaining 1% of samples yielded results which showed lower costs and lower effectiveness in the Marginal Kidney scenario compared to the Status Quo scenario. All samples were within a willingness-to-pay threshold of $100,000 CAD.

Figure 12. Incremental Cost-Utility, Marginal Kidney scenario versus the Status Quo scenario



Scenario analysis considering varying levels of marginal kidneys accepted for transplant are in Table 13. At a 100% acceptance rate, there was an 87.3% increase in the proportion of total kidneys (KDPI 0-100) transplanted as per Transplant Manitoba data. Adding these additional marginal kidneys (KDPI 86-100) increased the proportion of kidneys available to those aged 60 and over (KDPI 20-100) by a factor of 2.09. When considering 75%, 50% and 25% acceptance rates, the kidney supply for those aged 60 and over increased by 1.82, 1.55, and 1.27 times, respectively.

When accepting only 75% of potential kidneys in the KDPI 86-100 range, the mean cost and QALYs per patient over the ten-year time horizon were $362,812.84 and 4.50. At a 50% acceptance rate, the mean cost and QALY per patient throughout the same time period was $364,412.70 and 4.43. Finally, at a 25% acceptance rate, the 10 year mean cost and QALY per patient were $366,232.14 and 4.41.

Table 13. Scenario Analysis – Mean Cost and QALYs by Marginal Kidney Acceptance Rate, Marginal Kidney Scenario

Percent of Marginal Kidneys Accepted	Mean cost	Mean QALYs	Transplant Probability Factor
100%	$ 362,116.54	4.52	2.09
75%	$ 362,812.84	4.50	1.82
50%	$ 364,412.70	4.43	1.55
25%	$ 366,232.14	4.41	1.27

Cost and QALY scenario analysis results considering 15 and 20 year time horizons are in Table 14 and

Table **15**. Over 15 years, the mean cost per patient in the Status Quo and Marginal Kidney scenarios were $446,101.05 (SD: $220,635.16) and $439,950.45 (SD: $214,397.59). Over 20 years, the mean cost per patient increased to $495,491.22 (SD: $267,992.94) in the Status Quo scenario, and $489,432.36 (SD: $260,379.44) in the Marginal Kidney scenario. Considering QALYs, over 15 years, the mean QALYs per patient in the Status Quo and Marginal Kidney scenarios were 5.39 (SD: 2.6) and 5.65 (SD: 2.71) respectively. Over 20 years, the mean QALYs per patient rose to 6.02 (SD: 3.2) in the Status Quo scenario, and 6.34(SD: 3.33) in the Marginal Kidney scenario.

Table 14. 15 and 20 Year Treatment Specific Costs per Patient (First-Order Monte Carlo Simulation)

Scenario	QALYs	15 Year	20 Year
Status Quo	**Mean (SD)**	$446.101.05 ($220,635.16)	$495,491.22 ($267,992.94)
	25%	$232,574.73	$232,574.73
	50%	$495,002.83	$517,909.83
	75%	$663,498.61	$796,239.60
Marginal Kidney	**Mean (SD)**	$439,950.45 ($214,397.59)	$489,432.36 ($260,379.44)
	25%	$242,457.51	$242,457.51
	50%	$459,244.70	$493,746.02
	75%	$663,498.61	$786,156.08

Table 15. 15 and 20 Year Quality Adjusted Life Years per Patient (First-Order Monte Carlo Simulation)

Scenario	Cost	15 Year	20 Year
Status Quo	**Mean (SD)**	5.39 (2.66)	6.02 (3.26)
	25%	2.66	2.66
	50%	7.12	7.12
	75%	7.55	9.07
Marginal Kidney	**Mean (SD)**	5.65 (2.71)	6.34 (3.33)
	25%	2.85	2.84
	50%	7.55	7.56
	75%	7.55	9.07

Chapter V: Discussion

Over the ten-year time horizon considered in this model's simulation, patients aged 60 and over on the kidney transplant waitlist in Manitoba were treated at a cost-utility ratio of $84,029.73 in the Status Quo scenario and $80,084.90 in the Marginal Kidney scenario. Additionally, our model estimated that 56.7% and 60.1% of the Status Quo scenario and Marginal Kidney scenarios cohorts respectively would remain living at the end of 10 years. In comparison to transplant-naïve patients, our model estimated that those who received marginal kidneys on average survived for 35.22 more months (transplant-naïve = 80.37 months versus marginal kidney recipient = 115.59 months).

This model represents a comprehensive tool which can be used to describe the associated costs, utility, and survival in older adults (aged ≥60) on the kidney transplant waitlist in Manitoba over varying kidney supplies, and kidney quality. Furthermore, this model can be easily adapted to fit unique healthcare settings and population by adjusting parameters and assumptions accordingly.

There exists gaps on the current knowledge related to the cost-utility of kidney transplantation, which is more pronounced in the Canadian context. Our model improves upon the existing literature by considering both patient (EPTS) as well as donor related (KDPI) characteristics to simulate patient survival post-transplant. Moreover, much of the prevailing evidence is dated (57, 58). As such, this model provides a more accurate representation of the current cost-utility associated with deceased donor kidney transplants in older adults (aged ≥60). To our knowledge, this is the first study to incorporate both KDPI and EPTS scores to derive the cost-utility of marginal kidney use in a Canadian healthcare setting.

The relative cost-utility of the two scenario remains an important question for decision makers in the Manitoban health care system, as well as in jurisdictions worldwide. Both scenarios approach the upper end of the World Health Organization's recommended willingness-to-pay threshold of between 1x to 3x GDP per capita given that they each present cost-utility ratios between $80 000-$100 000/QALY. Notwithstanding, the cost-utility ratio associated with the Marginal Kidney scenario is lower than that associated with the Status Quo scenario, contributing to its comparative attractiveness as a strategy to pursue from a healthcare policy perspective aimed at reducing costs and improving quality-of-life for older waitlisted patients. The results of this model coincide with prevailing research, showing a cost-effectiveness associated with high-KDPI deceased donor transplants at <$100,000 per QALY (59).

As per our model, the estimated costs of care in the Marginal Kidney scenario were higher than those experienced in the Status Quo scenario at years 1, 2, 3, and 5. The cost-neutrality point, or the time in which the cumulative costs of care are even between the two scenarios occurs between years 5 and 6 post waitlist initiation, after which the Marginal Kidney scenario offers reduced costs per patient. This is primarily being driven by both recipient and donor related transplant costs and their relative size over time in comparison to initial training and maintenance dialysis costs. In this first year post deceased donor transplant, the undiscounted mean cost of care per patient inclusive of both upfront donor related transplant costs, and monthly recipient related transplant costs was $114,296.27 in 2019 CAD. After the first year, the yearly cost decreased to $17,077.21 per patient. In comparison, the undiscounted blended annual cost of dialysis in the first inclusive of maintenance and training per patient was $65,111.02 in 2019 CAD and reduced slightly to $63,667.74 in each subsequent year. As such, with an increased proportion of patients receiving transplants in the Marginal Kidney scenario coupled with higher per annum costs in the first-year post-transplant, it would be expected that short-term costs be elevated with cost-savings being realized over-time as patient survival with a functioning graft accrues. Moreover, as the time horizon chosen for this analysis was 10 years, the longer-term benefits associated with receiving a transplant (reduced costs over time, increased QALYs) may not be fully realized. As such, the main results of this model may be considered conservative. When extending the time-horizon of this model to 15 and 20 years, scenario analyses results indicated more pronounced cost benefits and similar QALYs per patient in the Marginal Kidney scenario compared to the Status Quo. The Marginal Kidney scenario offered cost savings of $6,150.60 per patient at 15 years, and $6,058.86 at 20 years. When considering QALYs, the outputted means per patient in the Status Quo and Marginal Kidney scenarios at 15 years were 5.39 and 5.65 QALYs per patient and 6.02 and 6.34 at 20 years respectively. It is important to note that the ten-year model inputs used in the main analyses were extended an additional 5 and 10 years in the scenario analyses. As such, this analysis may not be indicative of real-world circumstances in the 5 and 10 years proceeding the main analysis time horizon. These results are meant to provide an idea as to what the longer-term implications of both scenarios might be and should be taken with caution. Further research consisting of extending the time-horizon of this model using inputs proper to the time period considered is needed to understand the long-term (<10 years) cost-utility implications.

This model used 10 year Manitoba specific waitlist data (up to November, 2020) to derive the probability of dying on the waitlist pre-transplant as well as the probability of receiving a transplant (30). Within the local context, wait-times to receive a deceased donor kidney transplant have been increasing over the same time-period (30). One would expect the cost and QALY benefits associated with increased marginal kidney use to become more pronounced as wait times increase due to mitigating the overall time spent on dialysis. Furthermore, it is important to consider non-quality adjusted patient survival as marginal kidneys are associated with increased graft failure rates compared to higher quality kidneys (38), and patients who return to maintenance dialysis post graft failure experience higher death rates in comparison to those on the waitlist (74). Further research is required to understand the cost, QALYs and survival implications associated with increased wait times.

Regarding survival, our model estimated that 5.6% more patients would transition to the death state in the Status Quo scenario in comparison to the Marginal Kidney scenario. In addition, those who received a marginal kidney survived on average an additional 35.22 months in comparison to waitlisted patients who never received a kidney transplant. In an ideal scenario, matching patients with similar life expectancies to the survival expectancy of the graft would provide the maximum benefit per donor organ.

The total number of additional kidneys transplanted (KDPI 86-100) in the Marginal Kidney scenario was 78, which is approximately 98.7% of total kidneys transplanted in the Status Quo scenario. As per data sourced from Transplant Manitoba, the total number of deceased donor kidneys not accepted for transplant due to their quality as a percent of overall transplants was 87.3%. This model allowed for approximately an additional 9 of kidneys to be transplanted over the ten-year time horizon when assuming a 100% acceptance rate. Notwithstanding, in sensitivity analysis adjusting for lower acceptance rates (75%, 50%, and 25% acceptance), calculated costs and QALYs per patient were found to be of similar relative direction between scenarios, showing consistency with the main analysis. Moreover, assuming a 100% acceptance rate of marginal kidneys both at the clinical as well as patient level may not be indicative of potential real-world practices. Although a deceased donor organ may be available for transplant, there are many donor, program and clinical related reasonings as to why it may be refused (e.g. donor age or quality, abnormal biopsy etc.) (75). Patients may also decide to reject an offered donor organ, opting to remain on the waitlist in hopes of receiving a higher quality kidney. Together, these suggest that assuming a lower acceptance rate may be more realistic. Sensitivity analyses showed that the Marginal Kidney scenario was a dominant strategy over a ten-year time horizon even when considering an acceptance rate as low as 25%.

The proportion of kidneys transplanted by KDPI grouping in our model was estimated based upon actual transplant data in the United States (Organ Procurement and Transplantation Network) between January 1, 2005, and December 31, 2016, which was sourced from the literature (28). This estimated proportion of transplants in this data for KDPI groupings 20-35, 36-59, 60-85 and 86-100 were 19.2%, 34.8%, 32.1% and 13.9% respectively. Our model outputted 18.6%, 38.6%, 30.0% and 12.8% for the related KDPI groupings 20-35, 36-59, 60-85 and 86-100 in the Status Quo scenario. This indicates that our model was in relative agreeance with the distribution of kidneys used to inform the analysis. Note that this data was sourced from the literature as local data was unavailable. As such, this does not represent actual transplant in Manitoba, but more so creates a hypothetical situation. Moreover, the number of kidneys transplanted with a KDPI under 86 between scenarios were identical. Altogether, this difference in allocation may be of little impact to conclusions drawn and represents a minor deviation from the model inputs used. One would expect that as the number of transplants increased, the proportions of kidneys transplanted by KDPI grouping would approach their mean values. Further research regarding varying KDPI distributions is needed to understand its impact.

Univariate sensitivity analysis results indicated that dialysis was the most influential cost parameter for waitlisted patients. It impacted the per patient cost variation in the Status Quo scenario more substantially compared to the Marginal Kidney scenario, which could be explained by the higher proportion of waitlisted patients relying upon dialysis care in the former. When varied by both - 25%, the mean cost of care per patient was lower in the Status Quo scenario in comparison to the Marginal Kidney scenario. Alternatively, the mean cost per patient was lower in the Marginal Kidney Scenario when dialysis costs were increased by 25%. While the mean cost per patient was lower over 10 years in the Status Quo scenario when dialysis costs were reduced by 25%, dialysis costs are unlikely to fall in the foreseeable future (76), contributing to the potential upside risk associated with the Marginal Kidney scenario from a strictly costing perspective.

Transplant related costs (both recipient and donor) impacted the 10 year mean cost of care marginally in comparison to the cost of dialysis, highlighting the importance of reducing dialysis use if costs are to be reduced. Current dialysis costs are high and are expected to continue rising due to factors such as increased life expectancy and improved therapies for factors which lead to kidney failure (diabetes mellitus, cardiovascular disease) (76). Although increasing the number of viable organs may be a beneficial strategy to reduce dialysis use, it is nonetheless reactionary in nature. As of 2013, Manitoba had an end-stage kidney disease population with the highest rate of diabetes mellitus, second lowest socio-economic status (as measured by residential mean income), and the highest proportion being Indigenous in comparison to other provinces (77). Research has shown that Indigenous peoples with chronic kidney disease (CKD) are more likely to receive dialysis, to be obese, and to have a diagnosis of diabetes in comparison to other Canadian CKD patients (78). Indigenous peoples are less likely to initiate home peritoneal dialysis, which has been shown to be the least expensive modality in Manitoba, in comparison to white patients (13, 79). Furthermore, low socio-economic status has been shown to be associated with CKD, and as well as ESKD progression (80). Public health strategies aimed at lowering the incidence of top contributors of end stage kidney disease such as diabetes mellitus, obesity, and hypertension (81, 82) in higher risk populations may be effective at lowering the number of incident dialysis patients, thus reducing costs. Additionally, a lower demand for donor organs would contribute to a reduction in dialysis use as wait times would lessen, all else equal. Such public health strategies may require a longer time period to have a quantifiable impact, highlighting the importance of coupled shorter term solutions to reduce stress to the health system.

The model determined 10 year mean cost per patient are comparable to those reported in the literature. A recently published Canadian study evaluating the mean cost of care over 10 years for adults initiating dialysis in Canada reported a mean cost of $350,774.39 (SD: $204,703.55) per patient in 2016 CAD (83). Using the Canadian Consumer Price Index, this is equivalent to $371,536.74 (SD: $216,819.96) in 2019 Canadian dollars. Although mean costs between studies are similar and well within 1 standard deviation of one another, an explanation for the slight variation in the mean costs may be attributable to the difference in costing inputs considered. The aforementioned study included costs related to: PD catheter placements, hemodialysis access (imaging, surgery, outpatient infections, tissue plasminogen activator, and access monitoring), infection related and all-cause hospitalizations as well as erythropoietin. These additional costs might contribute to the differences between results. Additionally, the costing model in which the Ontario Renal Network relies upon to pay for dialysis care is one based upon "quality-based procedures" (bundled payments), with Nephrologists being paid fee-for-service (84, 85). Manitoba funds their dialysis care through a mixed fee for service model for Nephrologists, and a block funding model provided to the Service Delivery Organization. This may contribute to differences in costs per patient depending upon the individual characteristics of the reimbursement schemes.

The mean QALYs per patient reported in the aforementioned Canadian study was 3.38 (SD: 2.05) over 10 years for all dialysis starters (83). Our study found mean QALYs per patient over the same time period of 4.35 (SD: 1.81) in the Status Quo scenario and 4.52 (SD: 1.84) in the Marginal Kidney scenario. Although our study reported a higher mean value, the results between studies are both are within 1 SD of one another. The differences between results may be again partly due to the patient population considered. Our study considered older adults who were at one time eligible to receive a kidney transplant within our data, whereas the comparative Canadian study considered all adult incident dialysis starters (83). Among all incident dialysis patients, there is a proportion who are never eligible to receive a transplant due to their health condition (75, 86). Thus, a patient population consisting of only those eligible for a transplant may be of improved health status in comparison to the average dialysis patient, contributing to increased mean QALYs per patient.

Moreover, a recently published economic assessment using United States specific data found that patients transplanted with high-KDPI organs experienced higher mean ten-year costs in comparison to those on maintenance dialysis ($330,576 in comparison to $292,117 in 2016 US dollars) (59). Additionally, they found that high KDPI kidney recipients experienced quality-adjusted survival benefits in comparison to dialysis patients over the same period (mean 5.20 QALYS versus 4.52 QALYS), translating to a cost-utility ratio of $63,572.31 per QALY in 2016 US dollars (59). Using unadjusted annual average historical CPI rates experienced in cities across the United States sourced from the U.S. Bureau of Labor Statistics and the 2019 annual average exchange rate between CAD and USD sourced from the Bank of Canada, the cost per patient increases to approximately $466,035.55 in 2019 CAD (87, 88). At 5.20 mean QALYs per patient, the ten-year cost-utility ratio is thus approximately $89,622.22 per QALY, which is similar the results of this model ($80,084.90 per QALY in the Marginal Kidney scenario).

Our model assumed no difference in utility between patients on permanent dialysis post graft loss and waitlisted patients waiting for a transplant. Research has shown that patients who experienced graft loss suffered decreased quality-of-life (45) [as measured by the kidney disease quality-of-life instrument (KDQOL-SF)] and increased complications such as hospitalizations during the first year of re-initiating dialysis (46) in comparison to transplant-naïve patients on the wait-list (45, 46). Thus, our model may over-estimate QALYs for patients who suffered a graft loss. This may impact the mean QALY results of the Marginal Kidney scenario more so than in the Status quo scenario as there were more transplants performed, specifically using kidneys KDPI 86-100. Research also suggests that the probability of graft failure is higher in patients receiving marginal kidneys (38). Further research is required to determine the effects on mean QALYs per scenario as it pertains to this model.

The actual number of transplants in Manitoba by patient time on the waitlist for those aged 60 and over were used to derive the transition probabilities used in the model (30). Although these accurately represent the scenario in the local context, their generalizability to other transplants programs remains unknown. As of 2018, the proportion of prevalent end-stage kidney disease patients with a functioning transplant in Manitoba was 30.0%, which was the lowest amongst all provinces/territories, and 12.2% below the national average (67). This may be indicative of longer wait times for a deceased donor kidney in Manitoba in comparison to other jurisdictions. When considering shorter wait times in this model, the comparative attractiveness of the Marginal Kidney scenario to the Status Quo may be diminished. Nonetheless, our model shows marked mean survival benefit in months among those receiving a marginal kidney transplant in comparison to transplant-naïve waitlist patients. Moreover, this analysis considered kidneys transplanted from all blood types to derive transition probabilities. In Manitoba, historical data on 506 deceased donor transplants in Manitoba show that the average wait time for those with blood type O was 6.16 years (SD: 3.70), followed by 4.46 years (SD: 3.52) for those with blood type A, 3.79 years (SD: 2.36) for those with blood type B and 3.00 years (SD: 2.36) for those with blood type AB (30). Taken together, older patients may choose to remain on the waitlist in hopes of receiving a higher quality kidney knowing they possess a relatively shorter wait time. The benefits associated with the Marginal Kidney scenario from a cost-utility perspective may differ by transplant program and further research is required to understand its application in differing jurisdictions and by blood type.

It is important to note that the KDPI score of a kidney is based upon its relative quality in comparison to kidneys recovered within the previous year (27). Due to this, the KDPI score is a moving target which can change year over year. The conclusions drawn from this model may change if unusual or large fluctuations occur with respect to the quality of kidneys recovered within the previous year. As such, this model may be an ineffective tool to forecast future healthcare resource use and patient survival in similar scenarios if inputs remained unchanged. Taking into consideration changes in the KDPI score relative to previous years is needed when applying this model in future scenarios.

Preemptive kidney transplantation has been shown to offer both improved patient and graft survival in comparison to those who received their donor organ after being on dialysis (89). These benefits may also translate to older patients receiving marginal kidneys (KDPI ≥85) preemptively, with research suggesting similar risk of graft failure and patient death in comparison to those receiving higher quality-organs (KDPI 35-84) who have been on maintenance dialysis between 1-4 years, and lower risk of death in comparison to those receiving a donor organ (KDPI 35-84) with 4-8 years of maintenance dialysis prior to transplant (33). Although our model considers prior dialysis time in the EPTS score calculation, the effects of preemptive transplantation on patient survival and mean costs and QALYs per patient were not specifically evaluated. Further research is needed to understand the implications of offering marginal kidneys preemptively.

Limitations

There are limitations to this model. As local data was unavailable, probability inputs regarding patient survival post-transplant were derived from existing literature and based upon data from the United-States (28). Evidence suggests that patient survival in the first year post-transplant are similar between Canada and the United-States, yet elevated in the United-States beyond that point (90). As such, the results of this model may be considered conservative. Further research which considers the implication of patient and donor characteristics (EPTS and KDPI) on patient survival post-transplant in the local context in needed. Furthermore, five-year patient survival rates post-transplant were used in the model as rates considering a longer time-frame were not publicly available (28). A life-table approach was taken using published survival probabilities by age based upon the United-States population as to maintain consistency, and ten-year relative survival estimates post-first deceased donor kidney transplant compared to those who have never received a kidney transplant by age group (65, 66). These survival probabilities were applied >60 months post-transplant, therefore patient and donor characteristics encompassed in the EPTS and KDPI score were not taken into consideration for those surviving with a functioning graft for more than 5 years.

As ten-year estimates were unavailable for graft survival by KDPI grouping, 5 year estimates specific to the United States were sourced from the literature were used in the model (38). After 60 months post-transplant, the five-year rate was assumed for each subsequent period until the end of the simulation. As such, graft survival rates <60 months may be underestimated in that regard. It is important to note that five-year unadjusted graft survival rates for deceased donor kidneys in the United States are marginally lower in comparison to those observed in Canada [76.6 percent versus 81.3 percent as of 2018 (transplant year 2013)]. This may offset a portion of the effect as US specific rates were used.

A main limitation of this model is encompassed in the perspective taken. By taking the perspective of the public health-payer, indirect costs of care such as patient transportation costs, caregiver costs, patient opportunity costs etc, were not considered. Additionally, the blended cost approach (peritoneal dialysis, home hemodialysis and in-centre hemodialysis) used to derive the monthly cost of dialysis care per patient did not account for costs related to adverse events such as infections, hospitalizations or those associated with patient modality transitions. As a lower proportion of waitlist patients in the Marginal Kidney scenario rely upon dialysis care, these costs may more directly affect those in the Status Quo scenario and may contribute to increased cost and QALY benefits in the former scenario in comparison to the latter. Moreover, the cost of dialysis treatment in rural and/or remote settings can be higher compared to more urban and densely populated settings (12, 91). This model assumed costs sourced from one urban dialysis program, which may understate the mean cost of care for those receiving care outside of this setting.

In this model, patients were assumed to accept any kidney offered to them. This assumption may not be indicative of real-world circumstances as patients are ultimately provided the opportunity to decline an offer, opting to remain on the waitlist. A recent study from the Unites States showed that 84% of kidneys transplanted country wide (cohort included adult waitlisted patient who received a minimum of 1 transplant) between January 1, 2008 and December 31, 2015 were declined by at least 1 patient before being transplanted in another patient (92). Further research is needed to understand organ decline rates in the local context and their associated effects on the cost-utility of care.

This analysis did not differentiate by blood type when deriving transplant probabilities. Within the local context, average wait times have historically differed by blood type. Existing data on 506 deceased donor transplants in Manitoba show that the average wait time for those with blood type O was 6.16 years (SD: 3.70), followed by 4.46 years (SD: 3.52) for those with blood type A, 3.79 years (SD: 2.36) for those with blood type B, and finally 3.00 years (SD: 2.36) for those with blood type AB (30). As such, the results of this analysis may differ when taking into consideration different blood types as individuals may, on average, have differing times on dialysis. For those with blood type O, this analysis may be considered conservative, whereas for those on the lower end of the wait time spectrum (blood type AB). Further research in this area is to be required to understand the effects by blood type.

When assuming a 100% acceptance rate, our model allocated approximately 78 additional kidneys with a KDPI 86-100 in the Marginal Kidney scenario, representing approximately an extra 9 marginal kidneys above the maximum potential supply of 69. This may contribute to an overestimation of the cost-utility benefits experienced in the Marginal Kidney scenario in comparison to the Status quo scenario. This was addressed in sensitivity/scenario analyses which considered lower marginal kidney acceptance rates.

Our model did not take into consideration the effects of HLA mismatching on cost and QALY outcomes. Research has found significant negative relationships between HLA-mismatching and patient outcomes such as increased incidence of death with a functioning graft from 1-5 years post-transplant, all-cause mortality as well as over-all and death-censored graft failure in deceased donor kidney recipients (37, 51, 53). Moreover, HLA mismatches have been associated with higher costs per transplant patient (59). There may be patient-donor HLA mismatches within the additional marginal kidneys transplanted. Our model is unable to account for the potential clinical and cost implications associated with HLA mismatching. Altogether, this indicates that our model may overestimate cost-utility benefits associated with the Marginal Kidney scenario. Further research is needed to account for these factors in the local context. Finally, highly sensitized waitlist patients were excluded from this model, therefore the results do not apply to this population.

Chapter VI: Conclusion

In conclusion, we have developed a model which simulates the cost and utility of care as well as patient survival for kidney transplant waitlisted adults aged 60 and over in Manitoba over a ten-year time horizon. We have shown that the mean cost of care is lower per patient in a scenario where additional marginal kidneys are transplanted in comparison to usual care. Additionally, the mean QALYs per patient in the scenario are higher in comparison to usually care. The ICUR between the two scenarios was estimated at -$20,573.03, indicating that the new intervention is less costly and more effectiveness in comparison to usual care. Finally, our model has shown that overall patient survival is higher when transplanting additional marginal kidneys, and those receiving marginal kidneys survived on average longer in comparison to transplant-naïve patients.

Although this model found that increasing the use of marginal kidneys is favorable to continuing with usual care from cost-utility and survival perspectives in this patient population, waitlisted patients ultimately have the decision to accept or deny an offered donor organ. This research adds to the growing body of evidence regarding transplant practice that health care professionals may rely upon to aid patients in making evidence-informed decisions regarding their personal care.

This model also presents a health policy tool which can aid local decision-makers regarding the decision to transplant additional marginal kidneys in their respective jurisdictions. Moreover, this may act as feasibility evidence for decision makers worldwide to analyze the use of marginal kidneys in their unique transplant programs by adapting the model to utilize local inputs.

The cost of care for patients with renal failure is substantial. As health care programs possess finite resources, it is important to allocate them efficiently in a manner which maximizes utility. Although downstream investments in health are required to address the immediate needs of patients with renal failure, upstream investments in the form of targeted public health strategies are vital to addressing prevention in at risk populations. Coupling the two strategies will ensure that current patients are receiving appropriate care, with future resource use diminishing as demand declines.

This research is important to understand the implications of transplanting additional marginal kidneys from both a health care costing, patient quality-of-life and survival perspectives. Further research is required to determine the effects of human leukocyte antigen (HLA) mismatches, differences by blood type, the allowance for multiple transplants and the effects of preemptive transplants on costs, QALYs, and survival in this patient population.

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Supervisory Committee Members

Dr. Evelyn Forget

Dr. Julie Ho

Dr. Claudio Rigatto

Dr. Navdeep Tangri

Dr. Chris Wiebe

Appendix:

Item 1. Annual Consumer Price Index, annual average - Canada

Consumer Price Index

Year	Value
2000	95.4
2001	97.8
2002	100
2003	102.8
2004	104.7
2005	107
2006	109.1
2007	111.5
2008	114.1
2009	114.4
2010	116.5
2011	119.9
2012	121.7
2013	122.8
2014	125.2
2015	126.6
2016	128.4
2017	130.4
2018	133.4
2019	136.0

Item 2. Proportions Applied to 5 Year Death Probabilities by EPTS and KDPI Combination, Marginal Kidneys

	KDPI														
EPTS	**86**	**87**	**88**	**89**	**90**	**91**	**92**	**93**	**94**	**95**	**96**	**97**	**98**	**99**	**100**
1	56.6%	58.1%	59.7%	61.2%	63.6%	65.1%	67.4%	69.8%	71.3%	73.6%	76.0%	79.1%	80.6%	83.7%	83.7%
2	56.7%	58.2%	59.7%	61.2%	63.4%	64.9%	67.2%	69.4%	70.9%	73.1%	75.4%	77.6%	79.9%	82.8%	82.8%
3	56.1%	58.3%	59.7%	61.2%	63.3%	64.7%	66.9%	69.1%	70.5%	72.7%	74.8%	77.0%	79.9%	82.0%	82.0%
4	55.9%	57.9%	59.3%	60.7%	62.8%	64.1%	66.2%	68.3%	70.3%	71.7%	73.8%	75.9%	78.6%	80.7%	80.7%
5	55.6%	57.0%	58.9%	60.3%	62.3%	63.6%	65.6%	67.5%	69.5%	71.5%	72.8%	75.5%	77.5%	79.5%	79.5%
6	55.4%	56.7%	58.6%	59.9%	61.8%	63.1%	65.0%	66.9%	68.8%	70.1%	72.6%	74.5%	76.4%	78.3%	78.3%
7	55.2%	56.4%	57.7%	59.5%	60.7%	62.6%	64.4%	66.3%	68.1%	69.9%	71.8%	73.6%	75.5%	77.3%	77.3%
8	54.4%	56.2%	57.4%	59.2%	60.4%	62.1%	63.9%	65.7%	67.5%	69.2%	71.0%	72.8%	74.6%	76.9%	76.9%
9	54.0%	55.7%	56.8%	58.5%	59.7%	61.4%	63.1%	64.8%	66.5%	68.2%	69.9%	71.6%	73.3%	75.6%	75.6%
10	53.6%	54.6%	56.3%	57.4%	59.0%	60.7%	62.3%	63.9%	65.6%	67.2%	68.9%	70.5%	72.1%	74.3%	74.3%
11	53.4%	54.5%	56.1%	57.1%	58.7%	60.3%	61.9%	63.0%	64.6%	66.7%	68.3%	69.8%	72.0%	73.5%	73.5%
12	52.6%	54.1%	55.1%	56.6%	58.2%	59.7%	60.7%	62.2%	63.8%	65.8%	67.3%	68.9%	70.9%	72.4%	72.4%
13	52.2%	53.7%	54.7%	56.2%	57.6%	58.6%	60.1%	61.6%	63.1%	65.0%	66.5%	68.0%	70.0%	71.4%	71.4%
14	51.7%	52.6%	54.0%	55.5%	56.4%	57.8%	59.2%	60.7%	62.1%	64.0%	65.4%	66.8%	68.7%	70.6%	70.6%
15	51.4%	52.3%	53.7%	54.6%	56.0%	57.3%	58.7%	60.1%	61.5%	63.3%	64.7%	66.1%	67.9%	69.7%	69.7%
16	50.4%	51.8%	53.1%	54.0%	55.3%	56.6%	58.0%	59.3%	60.6%	62.4%	63.7%	65.0%	66.8%	68.6%	68.6%
17	50.2%	51.5%	52.4%	53.6%	54.9%	56.2%	57.5%	58.8%	60.1%	61.8%	63.1%	64.8%	66.1%	67.8%	67.8%
18	49.8%	50.6%	51.9%	53.1%	54.4%	55.6%	56.8%	58.1%	59.3%	61.0%	62.2%	63.9%	65.1%	66.8%	66.8%
19	49.6%	50.4%	51.6%	52.8%	54.0%	55.2%	56.5%	57.7%	58.9%	60.1%	61.7%	63.3%	64.5%	66.1%	66.1%
20	48.8%	50.0%	51.2%	52.0%	53.1%	54.3%	55.5%	57.0%	58.2%	59.4%	60.9%	62.5%	63.7%	65.2%	65.2%
21	48.5%	49.6%	50.4%	51.5%	52.7%	53.8%	54.9%	56.4%	57.6%	58.7%	60.2%	61.7%	62.9%	64.4%	64.4%
22	48.3%	49.1%	50.2%	51.3%	52.4%	53.5%	54.6%	55.7%	57.2%	58.3%	59.8%	60.9%	62.4%	63.8%	63.8%
23	47.7%	48.7%	49.8%	50.9%	52.0%	53.0%	54.1%	55.2%	56.6%	57.7%	59.1%	60.2%	61.6%	63.1%	63.1%
24	47.6%	48.6%	49.7%	50.7%	51.7%	52.8%	53.8%	54.9%	56.3%	57.3%	58.7%	59.8%	61.2%	62.6%	62.6%
25	47.3%	48.3%	49.3%	50.0%	51.0%	52.4%	53.4%	54.4%	55.4%	56.8%	58.2%	59.2%	60.5%	61.9%	61.9%
26	47.2%	47.8%	48.8%	49.8%	50.8%	51.8%	53.2%	54.2%	55.1%	56.5%	57.5%	58.8%	60.1%	61.5%	61.5%
27	46.8%	47.7%	48.7%	49.7%	50.6%	51.6%	52.6%	53.9%	54.9%	56.2%	57.1%	58.4%	59.7%	61.0%	61.0%
28	46.7%	47.6%	48.6%	49.5%	50.5%	51.4%	52.4%	53.3%	54.6%	55.6%	56.8%	58.1%	59.4%	60.3%	60.3%
29	46.6%	47.2%	48.1%	49.1%	50.0%	50.9%	52.2%	53.1%	54.0%	55.3%	56.5%	57.5%	58.7%	59.9%	59.9%
30	46.3%	47.3%	48.2%	49.1%	50.0%	50.9%	51.8%	53.0%	54.0%	55.2%	56.1%	57.3%	58.5%	59.8%	59.8%
31	46.3%	47.2%	47.8%	48.7%	49.6%	50.7%	51.6%	52.5%	53.7%	54.6%	55.8%	57.0%	58.2%	59.4%	59.4%
32	46.0%	46.9%	47.8%	48.7%	49.6%	50.4%	51.3%	52.5%	53.4%	54.5%	55.7%	56.6%	57.8%	58.9%	58.9%
33	46.1%	47.0%	47.6%	48.4%	49.6%	50.4%	51.3%	52.2%	53.3%	54.2%	55.3%	56.5%	57.6%	58.8%	58.8%
34	46.0%	46.9%	47.7%	48.6%	49.4%	50.3%	51.1%	52.3%	53.1%	54.3%	55.4%	56.3%	57.4%	58.5%	58.5%
35	46.1%	46.6%	47.5%	48.3%	49.4%	50.3%	51.1%	52.0%	53.1%	54.2%	55.0%	56.1%	57.3%	58.4%	58.4%
36	46.0%	46.8%	47.7%	48.5%	49.3%	50.1%	51.2%	52.1%	52.9%	54.0%	55.1%	56.2%	57.3%	58.4%	58.4%
37	46.2%	46.7%	47.6%	48.4%	49.5%	50.3%	51.1%	51.9%	53.0%	54.1%	54.9%	56.0%	57.1%	58.2%	58.2%
38	46.1%	46.9%	47.7%	48.5%	49.3%	50.1%	51.2%	52.0%	53.1%	53.9%	55.0%	56.0%	57.1%	58.2%	58.2%
39	46.3%	46.8%	47.6%	48.4%	49.5%	50.3%	51.1%	52.1%	53.2%	54.0%	55.0%	55.8%	56.9%	57.9%	57.9%
40	46.3%	47.1%	47.9%	48.7%	49.5%	50.3%	51.3%	52.1%	53.1%	53.9%	55.0%	56.0%	57.1%	58.1%	58.1%
41	46.6%	47.2%	47.9%	48.7%	49.7%	50.5%	51.3%	52.3%	53.1%	54.1%	55.2%	56.2%	57.3%	58.3%	58.3%

42	46.7%	47.4%	48.2%	49.0%	49.7%	50.5%	51.5%	52.3%	53.3%	54.4%	55.1%	56.2%	57.2%	58.5%	58.5%
43	47.0%	47.7%	48.5%	49.2%	50.0%	50.8%	51.8%	52.5%	53.6%	54.3%	55.3%	56.3%	57.4%	58.4%	58.4%
44	47.0%	47.7%	48.5%	49.2%	50.3%	51.0%	51.8%	52.8%	53.5%	54.5%	55.5%	56.5%	57.5%	58.5%	58.5%
45	47.3%	48.0%	48.8%	49.5%	50.2%	51.2%	52.0%	52.7%	53.7%	54.7%	55.7%	56.7%	57.7%	58.7%	58.7%
46	47.7%	48.4%	49.1%	49.9%	50.6%	51.4%	52.3%	53.1%	54.1%	55.1%	56.0%	56.8%	58.0%	59.0%	59.0%
47	47.9%	48.7%	49.4%	50.1%	50.9%	51.6%	52.6%	53.3%	54.3%	55.3%	56.0%	57.0%	58.2%	59.2%	59.2%
48	48.3%	49.0%	49.8%	50.5%	51.2%	51.9%	52.9%	53.6%	54.6%	55.6%	56.3%	57.3%	58.5%	59.5%	59.5%
49	48.7%	49.2%	50.1%	50.8%	51.6%	52.3%	53.3%	54.0%	54.9%	55.9%	56.6%	57.6%	58.8%	59.8%	59.8%
50	49.0%	49.8%	50.5%	51.2%	51.9%	52.6%	53.6%	54.3%	55.3%	56.2%	57.2%	58.1%	59.1%	60.0%	60.0%
51	49.4%	50.1%	50.8%	51.5%	52.3%	53.0%	53.9%	54.6%	55.6%	56.5%	57.5%	58.4%	59.4%	60.3%	60.3%
52	49.8%	50.5%	51.2%	51.9%	52.6%	53.5%	54.2%	55.2%	55.9%	56.8%	57.8%	58.7%	59.7%	60.6%	60.6%
53	50.1%	50.8%	51.5%	52.2%	52.9%	53.9%	54.6%	55.5%	56.2%	57.1%	58.1%	59.0%	60.0%	60.9%	60.9%
54	50.5%	51.2%	51.9%	52.6%	53.3%	54.2%	54.9%	55.8%	56.5%	57.4%	58.4%	59.3%	60.2%	61.2%	61.2%
55	50.8%	51.5%	52.2%	52.9%	53.6%	54.5%	55.2%	56.1%	57.0%	57.7%	58.7%	59.6%	60.5%	61.4%	61.4%
56	51.1%	51.8%	52.5%	53.2%	54.1%	54.8%	55.5%	56.4%	57.3%	58.0%	58.9%	59.9%	60.8%	61.7%	61.7%
57	51.6%	52.3%	53.0%	53.7%	54.6%	55.3%	55.9%	56.8%	57.8%	58.4%	59.4%	60.3%	61.2%	62.3%	62.3%
58	51.9%	52.6%	53.3%	54.0%	54.9%	55.6%	56.5%	57.1%	58.0%	59.0%	59.6%	60.5%	61.5%	62.6%	62.6%
59	52.3%	52.9%	53.6%	54.5%	55.2%	55.9%	56.8%	57.4%	58.3%	59.2%	59.9%	60.8%	61.7%	62.8%	62.8%
60	52.6%	53.2%	54.1%	54.8%	55.5%	56.2%	57.0%	57.7%	58.6%	59.5%	60.4%	61.3%	62.2%	63.1%	63.1%
61	53.1%	53.8%	54.4%	55.1%	55.8%	56.7%	57.3%	58.2%	58.9%	59.8%	60.7%	61.6%	62.4%	63.3%	63.3%
62	53.4%	54.1%	54.7%	55.4%	56.1%	57.0%	57.6%	58.5%	59.2%	60.0%	60.9%	61.8%	62.7%	63.6%	63.6%
63	53.7%	54.4%	55.0%	55.7%	56.6%	57.2%	57.9%	58.8%	59.6%	60.3%	61.2%	62.1%	62.9%	63.8%	63.8%
64	54.0%	54.7%	55.3%	56.2%	56.9%	57.5%	58.4%	59.0%	59.9%	60.8%	61.4%	62.3%	63.2%	64.1%	64.1%
65	54.5%	55.2%	55.8%	56.5%	57.1%	58.0%	58.7%	59.5%	60.2%	61.0%	61.9%	62.8%	63.6%	64.5%	64.5%
66	54.8%	55.5%	56.1%	56.8%	57.6%	58.3%	59.1%	59.8%	60.6%	61.3%	62.2%	63.0%	63.9%	64.7%	64.7%
67	55.2%	55.9%	56.5%	57.1%	57.8%	58.6%	59.3%	60.1%	60.8%	61.6%	62.5%	63.1%	64.0%	64.8%	64.8%
68	55.5%	56.1%	56.8%	57.6%	58.3%	58.9%	59.7%	60.4%	61.2%	61.9%	62.7%	63.6%	64.4%	65.3%	65.3%
69	55.9%	56.5%	57.1%	57.8%	58.6%	59.2%	59.9%	60.7%	61.3%	62.2%	63.0%	63.9%	64.7%	65.5%	65.5%
70	56.3%	56.9%	57.5%	58.1%	58.8%	59.6%	60.2%	61.0%	61.7%	62.5%	63.3%	64.0%	64.8%	65.6%	65.6%
71	56.6%	57.2%	57.9%	58.5%	59.1%	59.7%	60.5%	61.2%	62.0%	62.8%	63.4%	64.3%	65.1%	65.9%	65.9%
72	56.8%	57.6%	58.2%	58.8%	59.4%	60.0%	60.9%	61.5%	62.3%	63.1%	63.7%	64.5%	65.4%	66.2%	66.2%
73	57.3%	57.9%	58.5%	59.1%	59.8%	60.4%	61.2%	61.8%	62.6%	63.4%	64.0%	64.8%	65.7%	66.5%	66.5%
74	57.7%	58.3%	58.9%	59.5%	60.1%	60.9%	61.5%	62.3%	62.9%	63.7%	64.5%	65.1%	65.9%	66.7%	66.7%
75	58.0%	58.6%	59.2%	59.8%	60.6%	61.2%	61.8%	62.6%	63.2%	64.0%	64.8%	65.6%	66.4%	67.2%	67.2%
76	58.2%	58.8%	59.4%	60.2%	60.8%	61.4%	62.2%	62.8%	63.6%	64.2%	65.0%	65.7%	66.5%	67.3%	67.3%
77	58.7%	59.3%	59.9%	60.5%	61.1%	61.9%	62.5%	63.3%	63.9%	64.6%	65.4%	66.2%	66.8%	67.6%	67.6%
78	58.9%	59.5%	60.1%	60.9%	61.5%	62.1%	62.8%	63.4%	64.2%	64.8%	65.6%	66.3%	67.1%	67.9%	67.9%
79	59.3%	59.9%	60.5%	61.1%	61.8%	62.4%	63.0%	63.8%	64.4%	65.1%	65.9%	66.7%	67.2%	68.0%	68.0%
80	59.7%	60.3%	60.9%	61.5%	62.0%	62.8%	63.4%	63.9%	64.7%	65.5%	66.0%	66.8%	67.6%	68.3%	68.3%
81	60.0%	60.6%	61.2%	61.9%	62.5%	63.1%	63.8%	64.4%	65.2%	65.7%	66.5%	67.2%	68.0%	68.8%	68.8%
82	60.4%	61.0%	61.5%	62.3%	62.9%	63.4%	64.2%	64.7%	65.5%	66.0%	66.8%	67.5%	68.3%	69.0%	69.0%
83	60.8%	61.3%	61.9%	62.5%	63.2%	63.8%	64.3%	65.1%	65.6%	66.4%	67.1%	67.8%	68.4%	69.1%	69.1%
84	61.1%	61.7%	62.2%	62.8%	63.5%	64.1%	64.6%	65.4%	65.9%	66.7%	67.4%	68.0%	68.7%	69.4%	69.4%

85	61.4%	61.9%	62.5%	63.2%	63.8%	64.3%	65.0%	65.6%	66.1%	66.8%	67.6%	68.3%	68.9%	69.6%	69.6%
86	61.9%	62.5%	63.0%	63.5%	64.1%	64.6%	65.3%	65.9%	66.6%	67.1%	67.9%	68.6%	69.1%	69.9%	69.9%
87	62.3%	62.8%	63.3%	63.9%	64.4%	65.1%	65.7%	66.2%	66.9%	67.4%	68.2%	68.9%	69.6%	70.1%	70.1%
88	62.5%	63.0%	63.5%	64.1%	64.8%	65.3%	65.8%	66.5%	67.1%	67.8%	68.3%	69.0%	69.7%	70.4%	70.4%
89	63.0%	63.5%	64.0%	64.6%	65.1%	65.6%	66.3%	66.8%	67.5%	68.1%	68.8%	69.3%	70.0%	70.7%	70.7%
90	63.3%	63.8%	64.3%	65.0%	65.6%	66.1%	66.6%	67.3%	67.8%	68.5%	69.0%	69.7%	70.4%	71.1%	71.1%
91	63.7%	64.2%	64.7%	65.2%	65.7%	66.4%	67.0%	67.5%	68.2%	68.7%	69.4%	70.1%	70.6%	71.3%	71.3%
92	64.2%	64.7%	65.2%	65.7%	66.2%	66.7%	67.4%	67.9%	68.6%	69.1%	69.8%	70.3%	71.0%	71.7%	71.7%
93	64.5%	65.0%	65.5%	66.0%	66.6%	67.1%	67.7%	68.2%	68.8%	69.4%	69.9%	70.6%	71.3%	72.0%	72.0%
94	64.9%	65.4%	65.9%	66.4%	66.9%	67.4%	68.1%	68.6%	69.1%	69.7%	70.2%	70.9%	71.6%	72.2%	72.2%
95	65.3%	65.8%	66.3%	66.8%	67.3%	67.8%	68.5%	69.0%	69.5%	70.1%	70.6%	71.3%	72.0%	72.6%	72.6%
96	65.8%	66.2%	66.7%	67.2%	67.8%	68.3%	68.8%	69.3%	70.0%	70.4%	71.1%	71.6%	72.2%	72.9%	72.9%
97	66.2%	66.7%	67.2%	67.6%	68.1%	68.6%	69.1%	69.8%	70.2%	70.7%	71.4%	72.0%	72.5%	73.2%	73.2%
98	66.8%	67.1%	67.6%	68.1%	68.5%	69.2%	69.7%	70.2%	70.6%	71.3%	71.8%	72.4%	73.1%	73.5%	73.5%
99	67.1%	67.6%	68.1%	68.5%	69.0%	69.5%	70.0%	70.6%	71.1%	71.6%	72.2%	72.8%	73.3%	74.0%	74.0%
100	67.6%	68.0%	68.5%	69.0%	69.5%	69.9%	70.4%	70.9%	71.5%	72.0%	72.6%	73.1%	73.7%	74.4%	74.4%

Item 3. Monthly Probability of Death Post-Transplant by Age Group, >60 months

Age	Value
0	0.00051441
1	0.00003401
2	0.00002212
3	0.00001717
4	0.00001325
5	0.00001255
6	0.00001122
7	0.00001017
8	0.00000924
9	0.00000849
10	0.00000828
11	0.00000917
12	0.00001180
13	0.00001656
14	0.00002301
15	0.00003013
16	0.00003747

17	0.00004540
18	0.00005761
19	0.00006666
20	0.00007595
21	0.00008495
22	0.00009267
23	0.00009861
24	0.00010318
25	0.00010722
26	0.00011128
27	0.00011530
28	0.00011956
29	0.00012416
30	0.00012900
31	0.00013391
32	0.00013889
33	0.00014380
34	0.00014866
35	0.00015423
36	0.00016033
37	0.00016618
38	0.00017170
39	0.00017760
40	0.00019857
41	0.00020882
42	0.00022151
43	0.00023647
44	0.00025332
45	0.00027151
46	0.00029186
47	0.00031573
48	0.00034430
49	0.00037760
50	0.00047180

51	0.00051526
52	0.00056432
53	0.00061873
54	0.00067647
55	0.00073561
56	0.00079536
57	0.00085673
58	0.00092111
59	0.00098983
60	0.00131435
61	0.00141184
62	0.00151286
63	0.00161594
64	0.00172298
65	0.00183684
66	0.00196833
67	0.00211255
68	0.00227853
69	0.00247041
70	0.00266207
71	0.00293447
72	0.00319187
73	0.00349343
74	0.00380305
75	0.00419200
76	0.00461813
77	0.00511363
78	0.00566234
79	0.00625694
80	0.00694240
81	0.00766804
82	0.00853224
83	0.00958205
84	0.01065326

85	0.01178434
86	0.01305939
87	0.01463677
88	0.01636517
89	0.01824949
90	0.02029252
91	0.02249448
92	0.02485249
93	0.02736031
94	0.03000801
95	0.03278185
96	0.03566445
97	0.03863496
98	0.04166965
99	0.04474260

Item 4. Monthly Transition Probabilities, Graft failure KDPI 20-35

Month	Value
1	0.00582
12	0.00582
13	0.00186
60	0.00186

Item 5. Monthly Transition Probabilities, Graft failure KDPI 36-85

Month	Value
1	0.00722
12	0.00722
13	0.00419
60	0.00419

Item 6. Monthly Transition Probabilities, Graft failure KDPI 86-100

Month	Value
1	0.01538
12	0.01538
13	0.00495
60	0.00495

Item 6. Monthly Transition Probabilities, Death on permanent dialysis

Age Group	3 months	1 year	3 years	5 years	10 years
Age 55–64	0.017142	0.04319	0.107356	0.173878	0.29948
Age 65–74	0.027013	0.062742	0.144608	0.21735	0.321824
Age 75+	0.040421	0.091151	0.19218	0.267637	0.347505

Item 8. Calibrated Monthly Transition Probabilities by Year, Waitlist to Death

Year	Value
1	0.000897
2	0.002909
3	0.001426
4	0.003025
5	0.00283
6	0.0029

7	0.001784
8	0.001646
9	0
10	0.00129

Item 9. Calibrated Monthly Transition Probabilities by Year, Waitlist to Ineligible

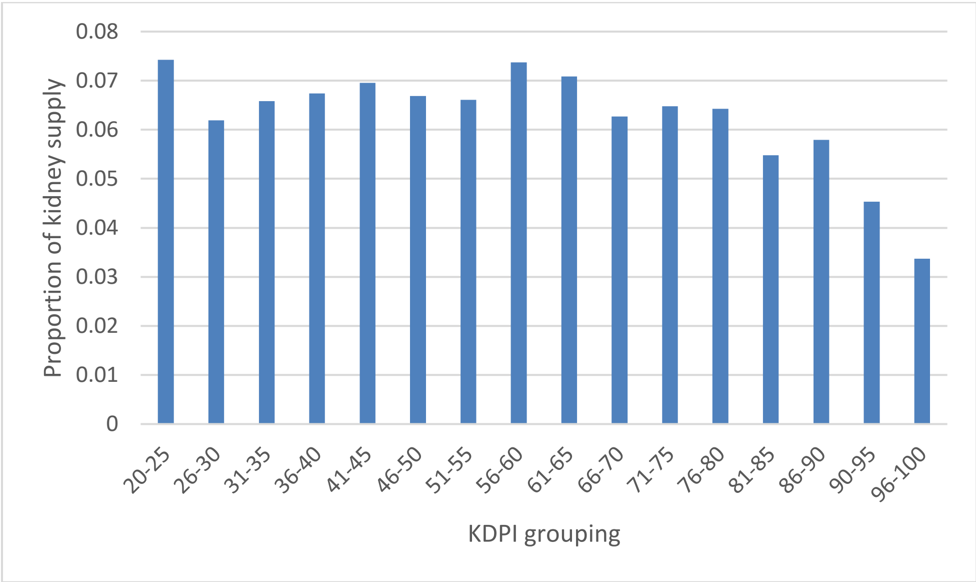
Year	Value
1	0.003946
2	0.005918
3	0.006255
4	0.004508
5	0.003851
6	0.001601
7	0.002419
8	0.00248
9	0.002474
10	0.00244

Item 10. Calibrated Monthly Transition Probabilities by Year, Waitlist to Transplant

Year	Value
1	0.000995
2	0.002753
3	0.002259
4	0.002028
5	0.002121
6	0.002655
7	0.001415
8	0.000796
9	0.000517

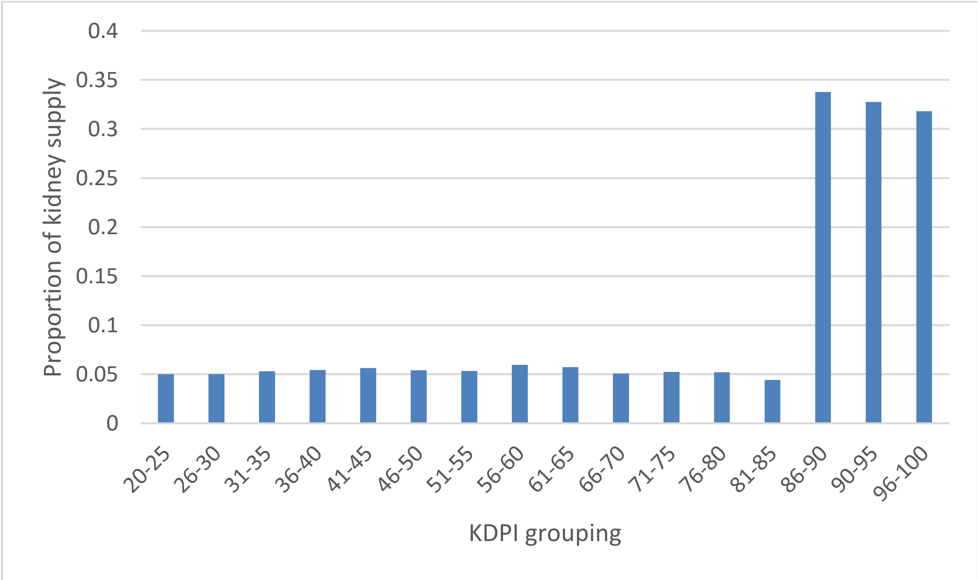
10	0.000689

Item 11. Estimated original kidney supply KDPI 20-100, Status Quo scenario



Note: Sourced from Bae et al (28). As specific numbers were unavailable, estimates were taken.

Item 12. Estimated new kidney supply KDPI 20-100, Marginal Kidney scenario



Note: Based upon original supply sourced from Bae et al (28). As specific numbers were unavailable, estimates were taken.