

UNIVERSITY OF CALGARY

Living kidney donation: Increasing utilization and assessing costs

by

Lianne Josephine Barnieh

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## **Abstract**

The incidence of end-stage renal disease, a condition requiring renal replacement therapy to sustain life, is increasing. Transplantation is considered the optimal treatment, and living donor kidney transplantation in particular has superior clinical outcomes.

However, the number of recipients waiting for a transplant far exceeds the availability of deceased donor kidneys. We undertook a randomized controlled trial (RCT) to determine if an educational intervention would increase the pursuit of living kidney donation in eligible candidates. We initially developed, validated and administered a questionnaire to assess why eligible kidney transplant candidates do not pursue living donation as a treatment option. We found that most candidates do have family or friends who can donate a kidney (66%), but the majority do not know how to ask (71%). Questionnaire results were used to develop the intervention for the RCT, an education session. We randomized 50 patients to the education intervention and 50 to standard care, and found that the education intervention did not increase the likelihood of a potential donor contacting the living donor program. However, patients who received the education session were more likely to change their treatment preference to living donation at study completion.

We also undertook a detailed cost analysis of kidney transplantation to determine if there are differences in the cost and resource utilization between recipients who receive a deceased or a living donor kidney. Using administrative data from local and provincial health care databases, transplant-related costs (both recipient and donor) were assessed before transplant and all costs (out- and in-patient care, diagnostic imaging, laboratory

tests and transplant medications) were assessed for two years after transplant. We found that there was no significant difference in the mean cost of transplantation (which included donor costs), for recipients of living and deceased donors. Predictors of total two-year recipient costs were presence of diabetes, time spent on the waiting list and non-zero panel reactive antibody.

In summary, given its superior clinical outcomes for recipients and similar costs to deceased kidney donation, effective strategies to increase the pursuit of living donation remain to be determined.

## Preface

The following manuscripts were published from this thesis. For both papers LB obtained the data, undertook the analysis, interpreted the results, and wrote the paper, with guidance from her thesis committee (BRH, BJM, KM, SWK). All authors provided critical review of the papers. Written permission for the reproduction of the articles in their entirety has been obtained from the respective publishers.

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## Table of Contents

Abstract.....	ii
Preface .....	iv
Acknowledgements .....	v
Table of Contents .....	vi
List of Tables.....	ix
List of Figures .....	x
List of Abbreviations .....	xi
Epigraph.....	xii
<b>CHAPTER ONE: INTRODUCTION .....</b>	<b>1</b>
1.1 The Burden of End-Stage Renal Disease in Canada.....	2
1.2 Treatment Options for Patients with ESRD .....	2
1.3 The Critical Demand for Kidney Transplantation.....	3
1.4 Living Kidney Donation as a Treatment Option .....	4
1.5 Outcomes for the donor in living kidney donation.....	5
1.6 Barriers in Recipients to Living Donation .....	7
1.7 Education in Transplantation.....	9
1.8 Cost issues in renal transplantation.....	12
1.9 Cost Drivers in Transplantation.....	13
1.10 Outline of Thesis Content .....	14
<b>CHAPTER TWO: DEVELOPMENT OF A SURVEY TO IDENTIFY BARRIERS TO LIVING DONATION IN KIDNEY TRANSPLANT CANDIDATES .....</b>	<b>16</b>
2.1 ABSTRACT .....	17
2.2 INTRODUCTION .....	18
2.3 METHODS.....	20
2.3.1 Phase 1: Item identification and preliminary development of the survey .....	20
2.3.2 Phase 2: Instrument Refinement.....	21
2.3.3 Phase 3: Testing the reliability of the survey .....	22
2.4 RESULTS.....	23
2.4.1 Phase 1: Item identification for the instrument .....	23
2.4.2 Phase 2: Survey Refinement.....	24
2.4.3 Phase 3: Testing the reliability of the survey .....	25
2.5 DISCUSSION.....	25
2.6 Final questionnaire.....	29
<b>CHAPTER THREE: BARRIERS TO LIVING KIDNEY DONATION IDENTIFIED BY ELIGIBLE CANDIDATES WITH END-STAGE RENAL DISEASE .....</b>	<b>37</b>
3.1 ABSTRACT .....	38
3.2 INTRODUCTION .....	39
3.3 METHODS.....	40
3.3.1 Eligible subjects.....	40
3.3.2 Administration of Questionnaire .....	41
3.3.3 Analysis of Qualitative Responses .....	42
3.3.4 Statistical Analysis.....	42

3.4 RESULTS.....	44
3.4.1 Qualitative survey results .....	44
3.4.2 Quantitative survey results .....	44
3.4.3 Barriers to living kidney donor transplantation.....	45
3.4.4 Factor Analysis .....	45
3.4.5 Unadjusted analysis .....	46
3.4.6 Adjusted analysis .....	46
3.5 DISCUSSION.....	47
CHAPTER FOUR: EVALUATION OF AN EDUCATION INTERVENTION TO INCREASE THE PURSUIT LIVING KIDNEY DONATION: A RANDOMIZED CONTROLLED TRIAL [ISRCTN APP: 16490].....	58
4.1 ABSTRACT .....	59
4.2 INTRODUCTION .....	60
4.3 SUBJECTS AND METHODS .....	61
4.3.1 Setting and Participants.....	61
4.3.2 Education Intervention.....	62
4.3.3 Randomization.....	63
4.3.4 Measures .....	63
4.3.5 Primary outcome.....	64
4.3.6 Secondary outcome.....	64
4.3.7 Statistical analysis.....	65
4.4 RESULTS.....	66
4.4.1 Recruitment and Follow-up.....	66
4.4.2 Patient characteristics.....	66
4.4.3 Patient’s intention to pursue living donation.....	67
4.4.4 Patient’s treatment preference .....	67
4.5 DISCUSSION.....	68
4.6 Format for the educational intervention.....	72
CHAPTER FIVE: COST ANALYSIS OF RECIPIENTS OF A FIRST RENAL TRANSPLANT: A COMPARISON OF LIVING AND DECEASED DONOR KIDNEYS .....	78
5.1 ABSTRACT .....	79
5.2 INTRODUCTION .....	81
5.3 METHODS.....	82
5.3.1 Settings and Patients .....	82
5.3.2 Data Collection & Sources.....	83
5.3.3 Measuring Costs .....	84
5.3.4 Censoring Costs.....	85
5.3.5 Statistical Analysis.....	85
5.4 RESULTS.....	86
5.4.1 Patients .....	86
5.4.2 Baseline Characteristics .....	86
5.4.3 Recipient Outcomes.....	87
5.4.4 Costs.....	88
5.4.4.1 Donor Costs.....	88



5.4.4.2 Recipient Costs.....	89
5.4.5 Predictors of Costs.....	89
5.5 DISCUSSION.....	90
5.6 Recipient costing information .....	94
5.7 Donor costing information .....	96
5.8 Living donor workup costs.....	97
CHAPTER SIX: SUMMARY .....	105
6.1 Increasing the Pursuit of Living Donation.....	106
6.2 Analyzing Costs in Living and Deceased Donor Transplantation .....	109
6.3 Implications for Practice and Future Directions.....	110
6.4 Conclusions .....	112
6.5 REFERENCES .....	113

## List of Tables

TABLE 2.1 Survey blueprint to determine content validity.....	33
TABLE 2.2 Kappa coefficient and percent agreement of individual items.....	34
TABLE 3.1 Demographics of subjects overall and by whether they had discussed living kidney donation .....	51
TABLE 3.2 Barriers, as identified through quantitative items, to choosing living kidney donation as a treatment option, and % who agreed/strongly agreed.....	52
TABLE 3.3 Barriers, as identified through qualitative items, to choosing living kidney donation as a treatment option, and % who expressed sentiment.....	53
TABLE 3.4 Principal component analysis matrix for knowledge questionnaire items ....	54
TABLE 3.5 Unadjusted analysis of demographic characteristics, principal components and qualitative items with the outcome of having discussed living donation with a family member or friend, n = 142.....	55
TABLE 3.6 Multivariable adjusted analysis of variables associated with having discussed living donation with a family member or friend, n= 142 .....	56
TABLE 4.1 Characteristics of patients who were eligible for a transplant, who received either standard of care or education intervention .....	74
TABLE 4.2 Proportion of patients in each group who ranked living donation as their treatment of preference, among patients who chose another treatment of preference at baseline.....	75
TABLE 4.3 Patients who ranked living donation as the treatment of preference at baseline and at study completion for concordant and discordant cases for control (A) and intervention (B) groups .....	76
TABLE 5.1 Baseline characteristics of recipients.....	98
TABLE 5.2 Recipient outcomes .....	99
TABLE 5.3 Overview of costs by category, kidney donor type and time period.....	100
TABLE 5.4 Multiple linear regression and log-transformed multiple linear regression of total two year recipient costs.....	101

## List of Figures

FIGURE 2.1 Overview of phases for the development and validation of a survey to assess barriers to living donation in kidney transplant candidates .....	35
FIGURE 2.2 Semantic relationship between codes, categories and outcome .....	36
FIGURE 3.1 Relationship between codes, categories and outcome for both quantitative and qualitative portion of questionnaire.....	57
FIGURE 4.1 Flow of patients .....	77
FIGURE 5.1 Mean costs for resource utilization by time period and transplant type (2008 \$CDN) .....	102
FIGURE 5.2 Mean cost of resource utilization year 1 (A) and year 2 (B) for different recipient subgroups (2008 \$CDN).....	103

## List of Abbreviations

<b>Symbol</b>	<b>Definition</b>
ESRD	End-stage renal disease
KT <sub>x</sub>	Kidney transplantation
DD	Deceased donor
LD	Living donor
HLA	Human leukocyte antigen
CB	Clinic based
HB	Home based
ARE	Acute rejection episode
CMV	Cytomegalovirus
LDKT	Living donor kidney transplant
OR	Odds ratio
CI	Confidence interval
LKD	Living kidney donation
ALTRA	Southern Alberta Transplant program database
AHW	Alberta Health and Wellness
CHR	Calgary Health Region
PRA	Panel reactive antibody

## **Epigraph**

I will respect the hard-won scientific gains of those physicians in whose steps I walk, and gladly share such knowledge as is mine with those who are to follow.

*Hippocratic Oath, modern version*

**CHAPTER ONE: INTRODUCTION**

## **1.1 The Burden of End-Stage Renal Disease in Canada**

End-stage renal disease (ESRD) occurs when the kidneys permanently fail and renal replacement therapy is required to sustain life. The number of incident patients with ESRD in Canada has increased by approximately 28% between 1998 and 2007 and diabetic nephropathy was the leading cause of renal failure.<sup>1</sup> Cardiovascular disease is the leading cause of death in patients with ESRD, followed by social causes, which includes treatment withdrawal, treatment refusals and suicides.<sup>2</sup>

## **1.2 Treatment Options for Patients with ESRD**

Patients who develop ESRD can be treated with dialysis or kidney transplantation (KTx). As of December 31, 2007 (the last year for which national data is available), the prevalent ESRD population in Canada being treated for ESRD numbered 35,265. Of these, almost half (49%, n=17,231) were receiving hemodialysis, followed by 40% living with a functioning transplant (n=14,146) and 11% (n=3,888) being treated with peritoneal dialysis.<sup>3</sup> KTx is considered the optimal treatment since transplant recipients live longer,<sup>4</sup> have higher quality of life<sup>6,7</sup> and consume fewer health care resources<sup>6,8-10</sup> compared to patients treated with dialysis.<sup>11</sup> Though not all ESRD patients are medically eligible for transplantation, the best outcomes occur when kidney transplantation is performed as early as possible after the onset of ESRD. Risk of death and graft failure increase as the length of time on dialysis increases.<sup>12</sup>

Kidneys for transplantation can come from either living or deceased donors. The number of deceased donor (DD) transplants in Canada has increased by 20% and the number of living donor (LD) transplants by nearly 40%, over the last decade. Despite this increase in donors, the demand still exceeds the supply, and the waiting list remains constant.<sup>2</sup>

### **1.3 The Critical Demand for Kidney Transplantation**

There is a critical shortage of DD organs available for transplantation. Due to a variety of factors including the aging population, and public health safety measures to decrease traumatic deaths, there are not enough kidneys available from deceased donors.<sup>13</sup> As a result there is a widening gap between the supply and demand for DD organs. The latest available data (2002 to 2004) indicates there are just under 3,000 patients waiting KTx in Canada.<sup>2</sup> The five year survival of patients treated with dialysis is < 50%, and in 2009 4% of patients died while waiting for an organ to become available.<sup>14</sup> The net result is that more patients are waiting longer with less chance of actually receiving a transplant than ever before.

Between 2005 and 2007, patients in Alberta who received a DD kidney spent a median of 1,126 days on dialysis, less than the national median of 1,285 days and about half that of British Columbia. This has increased by approximately 6 months from the reporting period of 2002 to 2004.<sup>2</sup> In comparison, patients in Alberta who received a LD kidney spent 497 days on dialysis.<sup>1</sup> Despite spending almost two years less on dialysis, this figure has also increased since the 2002 to 2004 reporting period, by almost one full year.



## **1.4 Living Kidney Donation as a Treatment Option**

Living kidney donation is when a living person, either related or unrelated to the recipient, donates one of their two kidneys for transplantation. Living kidney donation as a treatment option offers several advantages over deceased donation: among them are the opportunity to receive a transplant more quickly (no waiting list), and superior clinical outcomes, compared with deceased kidney donation.<sup>15, 16</sup> Survival rates are also better in recipients who receive a kidney from a living donor: 5 year allograft survival rate have been found to be over 20% greater for LD grafts than for deceased donor grafts during the same time period<sup>17, 18</sup> and the half-life of a renal allograft from a living donor is 21.6 years compared with 13.8 years for a deceased donor.<sup>15</sup> Other potential advantages of kidneys from LDs include pre-emptive transplantation (receiving a transplant before commencing dialysis), booking of the surgery at an optimal time for both donor and recipient, and increased function of the transplanted kidney due to the immediate transplant. In 2008, nearly 40% of kidney transplants performed in Canada were from LD.<sup>19</sup>

There have been two key changes that have helped drive the growth of using LD as a source of kidneys for transplantation: the availability of minimally invasive donor nephrectomy and the broadening of the definitions for acceptable donors. The first change is the introduction of the minimally invasive donor nephrectomy, which has resulted in with decreased pain, less need for narcotic analgesics, faster post-operative

recovery, and a more rapid return to work.<sup>20, 21</sup> This approach has, in some instances, encouraged donors to proceed with donation.<sup>22, 23</sup> Therefore, the laparoscopic technique may be more of an influence on the decision to proceed with LD with recipients than donors.

The second change in living donation has been the elimination of the presumption that all LD must be genetically related to their recipient. Currently, with the availability of effective immunosuppression regimens, this is no longer true and human leukocyte antigen (HLA) similarity is no longer a prerequisite for donation. Grafts from living unrelated donors have similar 3 and 5 year survival rates as those from living related organs.<sup>17, 24</sup> This, however, does not preclude the fact that many centers require a donor to have an emotional relationship with the recipient in order to proceed with donation.<sup>25,</sup>

26

### **1.5 Outcomes for the donor in living kidney donation**

With the increase in use of LD, there are questions as to the long-term health consequences to the living donor. There are no indications that living kidney donors are at an increased risk of death, when compared with a healthy matched cohort.<sup>27</sup> However, there is a risk for the surgery itself: the peri-operative mortality rate for LD is between 0.02 - 0.03%.<sup>27-29</sup> Research is limited when examining long-term risks to the living donor for developing kidney disease or hypertension. Studies examining the incidence of ESRD among donors did not find any increased risk for living donors compared with

matched control populations.<sup>30,31</sup> A separate study found that African Americans, males and young donors were potentially at higher risk for kidney failure after donation, however, the data was limited by small numbers and a lack of follow-up.<sup>32</sup> In a large survey of 2102 previous living donors, pregnancy outcomes after kidney donation were found to be similar to the general population, however, were inferior to pre-donation pregnancy outcomes, among those who had children pre- and post-donation.<sup>33</sup> Since hypertension is a disease of aging, it is difficult to ascertain whether the incidence of hypertension among donors is due to the strain of having only one remaining kidney or whether it is a natural progression in donors. A meta-analysis assessing the risk for hypertension in living donors found that only one of six studies included reported an increased risk for hypertension.<sup>34</sup> A more recent study examining the health of 3,698 donors found that those who donated a kidney had no significant increase in risk for ESRD or hypertension, even 20 years post-donation.<sup>31</sup> This highlights one of the challenges of ascertaining risks to living donors: as living donors need to be in optimal peak health in order to be considered eligible to donate, who are appropriate controls? A large, national prospective study would be able to provide more detailed information on long-term risks to the donor, and address the limitations of previous research in this area.

Psychological outcomes for the donors post-donation appear to be positive. A systematic review that included over 5,139 donors across all studies found that quality of life scores among living donors were either unchanged, or higher than population norms, post-donation.<sup>31,35</sup> Other studies that included focus groups and qualitative methods with

small samples found that donors reported minimal change in their health status after transplantation, had very high overall satisfaction with the donation process, and would most likely make the same decision again.<sup>22, 36, 37</sup> However, as with long-term health risk assessment in donors, this area of research is hindered by limited studies conducted prospectively, and having already gone through the experience of donation, donors may find it difficult to express negative feelings. The few studies that did assess donors prospectively, were more likely to report post-donation depression, poorer quality of life scores, and psychological functioning.<sup>35</sup>

Long-term health risks to the living donor appear to be no more than that of the general population, however, it is still difficult to conclude that there are no risks due to a lack of large, prospectively conducted studies, with appropriate controls. Though this should not limit living donation in the interim, recipients should be made aware of the potential harm to the donor, in order to make an informed treatment decision.

### **1.6 Barriers in Recipients to Living Donation**

The benefits to the recipients and the low risks to donors in living donation are supported in the literature, however a large proportion of eligible candidates for kidney transplantation do not pursue living kidney donation as a treatment option. Research in this area however is limited.

A few studies have explored attitudes and barriers to LD in potential kidney transplant candidates. Specifically, recipients who support living kidney transplantation are more likely to understand the risks and benefits to recipients and donors<sup>38,39</sup> though many recipients are not aware of the potential benefits to the donor and the reasons that donors donate.<sup>37,39</sup> Recipients feelings of guilt for needing a transplant or if the graft failed, feeling indebted to the donor, worrying about financial repercussions for the donor after donation and the donor suffering have been identified as potential barriers.<sup>36-38, 40-44</sup> These barriers can be significant enough for a patient to not pursue living donation and can lead to years of waiting for a deceased donor kidney, despite an expressed interest in donating a kidney from family members or friends.<sup>45</sup>

Some evidence indicates that patients are unlikely to ask family members about becoming potential donors,<sup>37, 40, 46, 47</sup> and only consider living donation at the insistence of the donor.<sup>48</sup> Compared with DD participants, LD participants were more likely to believe that asking for a kidney is appropriate.<sup>38</sup> Other studies have noted that patients are less willing to pursue living donation when they have concerns about the transplant team's experience.<sup>49</sup>

Three of the above studies used a questionnaire format to assess the barriers in recipients.<sup>38,39,44</sup> Zimmerman et al.<sup>38</sup> using an un-validated questionnaire assessed patients who were undergoing an evaluation for a LDKT, compared with a random sample on the cadaveric transplant wait list. Gourlay et al.<sup>39</sup> compared wait-listed

recipients and recipients of a living donor with a validated questionnaire, though it is not known whether recipients of a living donor may have better knowledge of the process due to having undergone it, or whether those with better knowledge pursue this treatment option. Finally, Pradel et al.<sup>44</sup> assessed attitudes and readiness to pursue LDKT of hemodialysis patients using a non-validated questionnaire, however, their questionnaire did not allow space to capture qualitative comments. Other studies used a qualitative approach to assess barriers, with smaller samples, in focus group settings.<sup>37, 48</sup>

A validated questionnaire, developed in a Canadian setting to assess barriers to LDKT prospectively in renal transplant candidates will contribute to helping develop educational strategies to improve the pursuit of living donation in ESRD patients.

### **1.7 Education in Transplantation**

Providing information about donation and transplantation has been identified as a key and important topic area, endorsed and supported by National agencies, including the Kidney Foundation of Canada. Information on living donation is provided by a patient's nephrologist, when discussing the different treatment options for ESRD. Once referred to the transplant center, a patient can also receive information from the nurse, the transplant nephrologist as well as the social worker. The patient also receives written information on living donation once they have attended the transplant clinic. This method of communicating information may be limited by a number of factors. The first is that this delivery of information is informal and includes only the patient and the individuals who

accompany the patient to any clinic visits. Second, the general information provided may not address patients' primary concerns regarding living donation, such as how to approach someone about living donation. Third, the information given relies on the patient to have a high level of health literacy for themselves and feel comfortable enough with the information to disseminate the information to others, in this case potential living donors.<sup>50</sup> The previous are examples of unstructured, or informal education, however, can formal education motivate a patient to choose a recommended treatment option?<sup>51</sup>

A previous study demonstrated that formal education in chronic kidney disease patients increased the intent to start self-care dialysis.<sup>52</sup> This study found that those in the intervention group who received information at two separate points in time, resulted in a higher proportion of patients who intended to start self-care dialysis at study completion, compared to standard care.

Previous studies have examined formal education programs in the context of living kidney donation. One study assessed the effectiveness of a clinic based educational program (CB) or a CB plus a home based educational program (HB) on the pursuit of living donation through a randomized controlled trial.<sup>50</sup> The study however has several limitations including a *per protocol* approach for analysis,<sup>51</sup> a disproportionately larger dropout in the HB group (over 30% never hosted their home-based intervention), and lack of validation for the questionnaire used, making it difficult to determine whether increases in knowledge for the HB group identified in the study were due to the

intervention. Further this method would require a large amount of resources to implement.

A second study initiated a formal education program using trained nurse coordinators and an educational video, followed by a discussion led by the coordinator.<sup>53</sup> Researchers compared the LD volunteer rates in the 3 years prior and the 18 months after one year of the formal education program. The study found that a formal education program enhanced the rate at which family members and friends contacted the LD program to be considered as potential donors (33.4% before and 39.4% after the education program,  $P=0.03$ ). However, due to the observational design of the study, it is not known whether the results are due to the education program itself or whether the LD program had become more efficient with time and that there was an increase in donor awareness in the general public during the same time period.

Other studies have examined sources of information and timing of delivery to increase the pursuit of living donation. Living kidney donor recipients learned about LD from nephrologists (26%) and from the media (24%). Living kidney donors learned about LD from family members (27%), recipients (20%) and the media (18%).<sup>54</sup> These results highlight the need for clear information to be given to the potential recipients and family members of LD since they are the largest source of information to donors. Gourlay et al. identified that wait-listed patients reported that the preferred source of information about



living donor kidney transplantation would be to speak personally with someone who had previously received a living donor kidney transplant.<sup>39</sup>

The above studies highlight the need for formal education in transplantation, as none so far have addressed the barriers in candidates for living donation in a manner that can be easily implemented in a regional health authority that are tailored to the needs of the candidate.

### **1.8 Cost issues in renal transplantation**

Elevated costs and the increasing prevalence of ESRD highlight the need for programs to search for more cost-efficient care. Currently 1.2% of total health care expenditures are spent on caring for patients with ESRD, including both dialysis and transplant.<sup>8</sup> Living kidney donation has been proposed as one solution to this growing economic problem, as it is cheaper than dialysis and the duration of dialysis therapy is minimized or eliminated.<sup>55</sup> While transplantation has been established as costing less than dialysis, few studies have systematically analyzed cost differences between living and deceased donor kidney transplantation.<sup>6, 56, 57</sup> The cost of caring for a patient who receives a kidney from a living donor may be different compared to a deceased donor. Further, the cost of procurement of a kidney from a living or deceased donor, in addition to any pre-transplant care may differ widely between the two types of transplant.

Previous studies have compared the costs between living and deceased donor transplantation, however they did not examine costs accrued pre-transplant, did not include costs of medications or laboratory tests and did not include the costs of recovering the kidney from the donor.<sup>6, 56, 57</sup> Further, no adjustments were made for important covariates such as age or diabetes, which may affect any observed cost differences. A Canadian study which is often quoted and is the most methodologically rigorous to date, found that recipients of living-related donors had slightly higher costs compared to deceased donors (no p value provided), however, it is now almost 20 years old.<sup>6</sup> Since then, changes in treatment strategies, graft survival and management of donors and recipients has occurred, and the results may no longer be valid.<sup>58</sup> Further, the primary hypothesis of this paper was to determine the cost differences between transplantation and dialysis, and costing information and covariates that may contribute to differences in cost in care in the two groups of recipients were not assessed. Two other studies were done in the United States, examining Medicare payments, and found that living donation was significantly cheaper than deceased donation.<sup>56, 57</sup> Differences in the health care system and costing methodology may limit the generalizability of these results.

### **1.9 Cost Drivers in Transplantation**

Beyond the type of transplantation, there are a few possible predictors of cost in kidney transplantation, including the presence of comorbid conditions. One study reported that patients with diabetes had an increased likelihood of admission due to infections post-

transplant, mean hospital charges and hospital mortality compared to non-diabetic patients.<sup>59</sup> As noted above, there is a difference in graft survival between living and deceased donor kidneys, with those returning to dialysis incurring yearly dialysis costs. There may also be a difference in short term outcomes, such as acute rejection episodes (AREs) or cytomegalovirus (CMV) infection. Though both of these are reversible with therapy, the implications are increased health care costs and potentially poor long-term outcomes.<sup>60, 61</sup>

Given the limited information available to date, there is a need for a detailed, comprehensive study analyzing the costs in recipients of living and deceased donor transplantation, and determining the predictors of cost for transplantation. The results of this study can inform health care programs on transplant treatment options for patients with end-stage renal disease.

### **1.10 Outline of Thesis Content**

This thesis will explore two key areas in living kidney donation: 1) an educational intervention to increase the pursuit of living donation among eligible candidates for transplantation and, 2) an analysis of cost differences in living and deceased donor transplantation. Chapter 2 of this thesis discusses the development and validation of a questionnaire to assess barriers to living kidney donation in eligible transplant candidates while Chapter 3 provides information on the administration of this questionnaire and details both the qualitative and quantitative results. Chapter 4, using the results of the

previous two chapters, describes the randomized controlled trial of an educational intervention to increase living kidney donation. Finally, Chapter 5 examines the cost differences in living and deceased donor kidney transplantation.

Though each of the above four chapters can be read independently, they should be taken into context of the thesis in its entirety with the overall objective of increasing the pursuit of living donation among candidates to renal transplantation, and analyzing any potential differences in costs between living and deceased donor transplantation.

**CHAPTER TWO: DEVELOPMENT OF A SURVEY TO IDENTIFY BARRIERS  
TO LIVING DONATION IN KIDNEY TRANSPLANT CANDIDATES**

## 2.1 ABSTRACT

**Background:** Kidney transplantation from living donors, compared with deceased donors, has improved healthcare outcomes for patients with end-stage renal disease (ESRD), however less than 40% of transplants come from living donors. Numerous barriers may impede the identification of, and transplantation from, a living donor.

**Objective:** The purpose of this study was to develop and validate a survey to identify barriers in candidates to seeking a living donor for kidney transplantation.

**Methods:** The survey was developed in three phases: item identification using stakeholders to identify key components; survey refinement including assessment of content and face validity, and; assessment of test-retest reliability using the kappa coefficient and percent agreement for each of the scaled response items.

**Results:** The final survey contained ten items with a Likert scale response as well as five open-ended questions. Face and content validity of the survey was confirmed by expert nephrologists in the field. The overall kappa coefficient for the scale was 0.76, reflecting excellent agreement, with an overall percent agreement of 88.7%.

**Conclusion:** We developed a survey to identify barriers that kidney transplant candidates may experience when seeking a living donor which demonstrated content and face validity as well as reproducibility. This survey can be used by ESRD programs to identify barriers in candidates seeking a transplant. The results of the survey can be used to develop interventions to overcome such barriers with an ultimate goal of increasing living kidney donation.

## 2.2 INTRODUCTION

Living donor kidney transplantation improves healthcare outcomes for patients with end-stage renal disease (ESRD), and reduces healthcare costs.<sup>6</sup> However, only 35% of kidney transplants in Canada and over 40% in the United States are from a living donor.

Although the rates of living kidney donation have grown in the last decade, waiting lists for kidney transplantation have also grown as the incidence of ESRD has increased. In Canada, approximately 3000 patients are waiting for a kidney in Canada and over 30,000 patients are living with ESRD;<sup>3</sup> in the United States there are almost 80,000 patients waiting for a kidney and over half a million live with ESRD.<sup>62</sup> Thus there remains a huge potential to improve the rates of kidney transplantation by increasing the rates of living donor kidney transplantation.

The advantages of living donor kidney transplantation are numerous and include superior clinical outcomes for recipients including a lower risk of acute rejection, a greater likelihood of long term survival, and optimal timing of the transplant.<sup>16, 20</sup> Despite these advantages, the low rate of living kidney donation suggests that potential recipients may be experiencing “barriers” to seeking a transplant from a live donor. A limited number of studies have been conducted in this area, and available evidence indicates that recipients’ knowledge about transplantation and living donation in particular, is important.

Specifically, recipients who support living kidney transplantation are more likely to understand the risks and benefits to recipients and donors<sup>38</sup> though many recipients are not aware of the potential benefits to the donor and the reasons that donors donate.<sup>37</sup> The

donors in studies in the US and Korea reported the main reason they donated was to improve the health of the recipient<sup>37, 63</sup>; donors also felt proud of their donation and were glad they were able to help.<sup>37, 64</sup> Another benefit to the donors included an increased appreciation of life.<sup>37</sup> Recipients feelings of guilt for needing a transplant or if the graft failed, feeling indebted to the donor, worrying about financial repercussions for the donor after donation and the donor suffering have been identified as potential barriers.<sup>36-38, 40-43</sup> Other studies have noted that patients are less willing to pursue living donation when they have concerns about the transplant team's experience.<sup>49</sup> These barriers can be significant enough for a patient to not pursue living donation and can lead to years of waiting for a deceased donor kidney, despite an expressed interest in donating a kidney from family members or friends.<sup>45</sup> Potential donors, in fact, were found to be more likely than patients to initiate conversations about living donation,<sup>65</sup> and some evidence indicates that patients are unlikely to ask family members about becoming potential donors.<sup>37, 40, 46,</sup>

47

Although studies have been conducted in the past, none have comprehensively and concisely evaluated potential barriers to living donation among transplant candidates. The purpose of this study was to develop and validate a survey that would be able to identify potentially modifiable barriers for candidates seeking kidney transplantation. Improved understanding of kidney transplant candidate barriers to living donation could lead to increased opportunities for living kidney donation, thereby improving recipient outcomes and decreasing the waiting list for kidney transplantation.



## 2.3 METHODS

The Conjoint Medical and Research Ethics Board at the University of Calgary (Alberta, Canada) approved the study protocol. Survey development and validation occurred in three distinct phases: item identification & construction; refinement of the first draft of the survey, and; testing the reliability of the survey (Figure 2.1).

### *2.3.1 Phase 1: Item identification and preliminary development of the survey*

Survey development initially included use of stakeholders to identify key components to determine why kidney transplant recipients may not seek living donation. Stakeholders included five people from each of the following areas: medical professionals, nursing staff, and hemodialysis patients that were not currently eligible for a kidney transplant. Despite not being currently eligible for transplant, nephrologists discuss all treatment options for ESRD with their patients at the initiation of renal replacement therapy. They would therefore be able to still identify items that determine why some patients do not seek living donation as a treatment option. All stakeholders were presented with a form containing 20 sample items, gathered from the literature,<sup>22, 38, 45, 48</sup> that were possible reasons kidney transplant candidates may not choose living donation as a treatment option for ESRD. The stakeholders were asked to select items that they felt were barriers to living donation, as well as to indicate other relevant items. Medical professionals and nursing staff were e-mailed the form and a convenience sample of hemodialysis patients were approached (no a priori identification) during their hemodialysis treatment session. Consent of all stakeholders was implied with completion of the form.

Throughout development of the survey we employed strategies to reduce bias and errors in responding. Specifically, as rating scales are subject to the halo effect (respondents rate all items based on an a priori global impression of the instrument), successive questions were randomly reversed in the positive and negative direction to minimize this possibility. Randomly reversing questions also avoids acquiescence bias,<sup>66</sup> which occurs when the respondent answers all questions in a positive manner. In addition the final item for the Likert scale was an item to assess “social desirability”, also known as a “lie-detector”. This item was used to help identify those who answer the survey only with the intent of pleasing the researcher. The item that was used was: I never eat anything I am not supposed to eat.

### ***2.3.2 Phase 2: Instrument Refinement***

Face validity, or the extent to which a survey appears to be assessing the desired qualities, and content validity, whether there were enough items to adequately cover each domain,<sup>67</sup> were determined by having three nephrologists, familiar with transplantation and donation, independently review the survey to confirm the items chosen.

The next step in refining the instrument consisted of identifying missing or ambiguous items. A convenience sample of 10 adult, English speaking patients on hemodialysis who were interested in, but deemed not eligible for, a kidney transplant were identified. These patients were chosen as we intended to administer the instrument in the next phase of the

study to patients who were eligible for a kidney transplant, thus we didn't want to reduce the sample of eligible participants by using them for testing of the survey.

Each consenting participant was read the questions, which allowed the researcher (LB) to identify verbal cues indicating whether a question was not clear or improperly worded. Participants were also asked to answer the qualitative, open-ended questions. Finally, the participant was asked for feedback on the clarity, brevity, congruency and relevance of the survey to the topic.

### ***2.3.3 Phase 3: Testing the reliability of the survey***

The intra-observer reliability of the survey, using the test-retest technique with scores generated on two separate occasions, was undertaken in Phase 3. The survey was administered to the same ten people identified above, one week after completing the first review of the survey. The same individuals were used as only minor changes were made to the survey and the number of potential individuals to complete this step was limited.

The test-retest reliability was calculated using the kappa coefficient, which represents agreement obtained between two tests (intra or inter-rater) beyond that which would be expected by chance alone.<sup>68</sup> A kappa coefficient of 1.0 represents perfect agreement and a value of 0.0 represents no agreement at all. For the purpose of this study, and consistent with related studies, a kappa of greater than 0.75 was considered to be excellent reproducibility.

To calculate the kappa coefficient, the five Likert scale response categories were collapsed: strongly disagree, disagree and neutral were combined into one category, while agree and strongly agree formed the second category. The rationale for collapsing the response categories was that the responses were viewed as qualitative information, and by collapsing the scale and having fewer categories, inferences about decision making in terms of distinct levels of agreement-disagreement are facilitated.<sup>69</sup> A two-by-two contingency table was then constructed for each item.

## **2.4 RESULTS**

### ***2.4.1 Phase 1: Item identification for the instrument***

The response rate from the stakeholders was 80% (12 of 15 subjects approached completed the form). A list of items identified by stakeholders as potential barriers to living donation was compiled. We achieved 'saturation'; at the end of the compilation no new items were identified. Duplicate items were removed and items were coded using inductive codes, as opposed to defining codes *a priori*. Using Spradley's methodology of transcribing and summarizing free-text data we divided the statements into meaningful codes.<sup>70,71</sup> We identified 12 codes and these codes were then categorized into four categories: lack of knowledge, lack of opportunity, fear for the donor, and feelings of guilt. The semantic relationship between the codes, categories and outcome (failure to identify a living donor) is shown in Figure 2.2.

A minimum of two items from each category were selected to ensure adequate representation in the final survey. The items were ranked according to frequency and this order was used to determine the importance of each item; the top rated items were selected to form the survey blueprint (Table 2.1). The blueprint was constructed to provide content validity and was used as the basis for developing the survey and aided in assessing whether or not each category was adequately represented in the survey.<sup>72</sup> Given the frequency of items addressing knowledge of living donation, this category ended up with five items on the final survey (section 2.6).

Each item was then assessed for its suitability as a statement with a Likert scale response by two researchers (LB, KM) experienced in survey development. Using a Likert scale for certain items, despite collapsing the categories after, provides participants with a range of responses to reflect their intensity in their answer. Items that were highly ranked but not suitable to be answered with a Likert scale were included as open ended questions. Ten items were selected for the Likert scale responses and five open ended questions were included for the domains of opportunity, guilt and fear. Basic demographics, in the form of five questions at the end of the survey, were also included.

#### ***2.4.2 Phase 2: Survey Refinement***

Face and content validity was assessed by 10 nephrologists, familiar with donation and transplantation, who independently reviewed the survey and confirmed that the items chosen were relevant to the outcome with sufficient items representing each domain. Also in this phase the open-ended responses from the participants were reviewed to

ensure that no new ideas emerged that were necessary to include in the final survey. Minor changes were made based on patient feedback, including a restructuring of the order of the items to improve flow, as well as re-phrasing of two items. The revised survey was then reviewed by three medical experts in the area of transplantation, to ensure that the changes did not alter the face or content validity.

### ***2.4.3 Phase 3: Testing the reliability of the survey***

With respect to test-retest, the overall kappa coefficient for the scale was 0.76, reflecting excellent or substantial agreement,<sup>68</sup> with an overall percent agreement of 88.7% (Table 2.2). The percent agreement was calculated in addition to the kappa given limitations to the validity of the kappa if results are predominantly in one cell, or if there are zero cells. As this was the case for some of the items in our survey, we chose to report and consider both when evaluating whether an item was reliable.

## **2.5 DISCUSSION**

Using a three phase approach we developed a survey to identify barriers to seeking living kidney donation in kidney transplant candidates, which demonstrated face and content validity with excellent overall intra-observer reliability. Importantly we were able to capture a comprehensive group of items which included 10 scaled-response items and five open ended questions. The qualitative aspects of this survey will be valuable in identifying barriers in kidney transplant candidates when seeking living kidney donation that may vary between transplant sites.

A limited number of instruments have been previously developed to address barriers to living donation in kidney transplant candidates.<sup>38,39</sup> Gourlay et al.<sup>39</sup> developed and validated an instrument addressing recipient personal characteristics as well as knowledge and beliefs about living donation.<sup>39</sup> Their instrument included similar barriers as those identified in our survey, thus supporting the robustness of the items within our survey.

In addition to the scaled response items within our survey, we also elected to include five open ended questions, a unique component of our instrument compared to that of Gourlay et al.<sup>39</sup> This was undertaken to ensure the responses obtained from the survey would be of sufficient detail to guide the design of an education intervention for barriers to living donation. Incorporating qualitative research into survey design, as represented by open-ended questions, helps the researcher “understand the social world from the viewpoint of the respondent, through their detailed descriptions”.<sup>73</sup> The results by Gourlay et al reported that potential recipients feel guilty about needing a transplant and that donors experience long term health consequences; both of these domains were explored further in our survey using open-ended questions around the domains of fear (for the recipient and donor) and guilt (about needing and asking for a transplant).

Zimmerman et al.<sup>38</sup> developed a mail survey that assessed participants’ socio-demographic characteristics, perception of dialysis, and perception of deceased and living

kidney transplantation among patients being assessed for living donor kidney transplantation as well as those on the waiting list for a deceased donor transplant. The authors reported lack of knowledge and inability to identify a donor as potentially modifiable barriers, similar to the barriers identified within our study. Although their survey was comprehensive in content, it was not validated and the majority of their questions were scaled responses with no opportunity for respondents to expand on specific domains.

Our study has limitations. First, although the study size may be considered small, there is no formal consensus in the literature as to how many patients are needed to validate the content and to test the reliability of an instrument. However, it has been shown that ten subjects, with two separate measurements, will yield a correlation of over 0.8, with 80% power.<sup>74</sup> Further, the purpose of this study was to develop a survey that qualitatively assesses barriers in kidney transplant candidates with no intent of measuring change over time or differences between two groups. We also did not want to draw from the same population we were intending to administer this survey to in the next phase of our research. Since the patients who were used were determined to be medically ineligible for transplant, as opposed to not interested in pursuing transplant, we felt that they were still an appropriate sample in which to test our instrument. A second limitation of our survey was that it was not possible to evaluate for criterion validity due to the lack of gold standard for comparison. However we were able to confirm both face and content validity, confirming that the survey is able to measure what it intends to measure; that is,



the opinions of kidney transplant candidates on why patients do not choose living donation. Third, we used the kappa coefficient as a measure of the test-retest reliability of the survey, despite the acknowledged limitations with this measure.<sup>68, 75, 76</sup> In instances when response distribution is favored by one category, this can greatly reduce the kappa coefficient. For example, if almost all respondents agreed between the two items, this would produce a smaller kappa than if half the respondents disagreed and the other half agreed (on both occasions). We avoided some of these limitations of the kappa coefficient by examining it in conjunction with the percent agreement, which does not take into account the agreement occurring due to chance alone. Ninety percent agreement represents excellent reproducibility, and when interpreted with the kappa coefficient, there is substantial agreement with all of the items.<sup>76</sup>

In summary we developed a survey that has content and face validity as well as excellent overall test-retest reliability to assess barriers to living donation in kidney transplant candidates. This survey can be applied to eligible kidney transplant candidates to identify barriers which may affect their ability and willingness to seek and identify a living donor. Future educational interventions aimed at overcoming these barriers, similar to those conducted in related settings<sup>52, 77</sup> may increase the rate of living kidney donation.

## 2.6 Final questionnaire

### Survey about living kidney donation

- **What is living kidney donation?** Living kidney donation is a surgical procedure in which a healthy kidney is transplanted from a living person into a person with advanced kidney disease. Living kidney donation is an alternative treatment to dialysis for patients with end-stage kidney disease. Living donor kidneys for transplantation can be donated by family members or friends of the person with kidney disease.
- **What is the purpose of this survey?** This survey is being given to patients to find out ways to increase the organ donation rates. Your responses in this questionnaire will not influence your treatment. Responses will be used for two purposes:
  1. **Quality assurance.** This tells us if we are doing the best we can for our patients.
  2. **Research.** This will help us understand how to do better for our patients.
- **Can I discuss these questions with someone?** Yes. However, it is important that you give us your opinion, not that of another person. It is also important that you tell us how you really feel about these statements and not what you think we would like to read.

### Instructions for completing the questionnaire:

To answer some of the questions in this survey you should indicate your degree of agreement or disagreement with each statement by **circling the number corresponding to your choice**. The choice of “Neutral” (number 3) should be made if you do not know the answer to the question, or you do not have an opinion. For example:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
<b>The Calgary Flames are the BEST hockey team in Alberta</b>	1	2	3	4	5

Calgarians would probably circle 4 or 5 whereas Edmonton fans would probably circle 1 or 2. Toronto fans might circle 3.

For questions that require a written answer, respond with as much detail and clarity as you feel comfortable sharing. Your opinion is **valid and important**.

**It is important to realize that there is no “right” or “wrong” answer as we are asking for YOUR OWN PERSONAL OPINION. Your responses will be looked anonymously and only once all questionnaires have been completed.**

If you do not wish to participate in this research study, please check the following box

**For each of the following statements, please indicate your degree of agreement or disagreement:**

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
<b>A family member can donate a kidney to a patient with kidney disease in Calgary</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>A friend can donate a kidney to a patient with kidney disease in Calgary</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Kidneys from living donors do NOT last longer than kidneys from deceased donors</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>The sooner I get a kidney transplant, the better off I will be</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Patients who have a living donor wait less time for a kidney than those without</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>I understand that living donation means that a kidney is donated by a living person</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Individuals who donate a kidney are more likely to end up with kidney failure themselves</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Individuals who donate a kidney are more likely to end up with high blood pressure</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>I could tell someone who is interested in donating a kidney how to contact the living donor program</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>I never eat anything that I am not supposed to</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>I know how I would ask someone to donate their kidney</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

**Please answer the following questions in the space provided:**

**Do you have any family or friends who could donate a kidney to you? In no, please explain why not.**

**Do you feel guilty about needing a kidney transplant? If yes, please explain why.**

**Do you feel guilty about asking someone to donate their kidney to you? If yes, please explain why.**

**What do you fear most for YOURSELF (the recipient) about kidney transplantation, both at the time of the transplant and in the future following transplant?**

**What do you fear most for the DONOR about kidney transplantation, both at the time of the transplant and in the future following transplant?**

Please circle either yes or no for each of the following questions. You may write in comments below.

I have <b>DISCUSSED</b> living kidney donation with my family and/or friends	Yes	No
If yes, I have <b>IDENTIFIED</b> a living kidney donor	Yes	No

Additional comments or feedback (please write in space below):

And finally...

Please indicate which of the following best describes you (please circle the appropriate term or interval):

<b>I am</b>	Male	Female		
<b>I am aged</b>	<20	20 – 40	41 – 60	>60
<b>I am</b>	Married / Significant other	Single	Widowed	Separated / or divorced
<b>I am</b>	Presently employed	Presently unemployed	Retired	Student
<b>I am currently on dialysis</b>	Yes	No		
<b>If yes, for how long</b>	Less than 6 months	More than 6 months – less than 1 year	Between 1 – 4 years	Greater than 4 years

**THANK YOU FOR YOUR TIME AND YOUR VALUABLE CONTRIBUTION**

**TABLE 2.1 Survey blueprint to determine content validity**

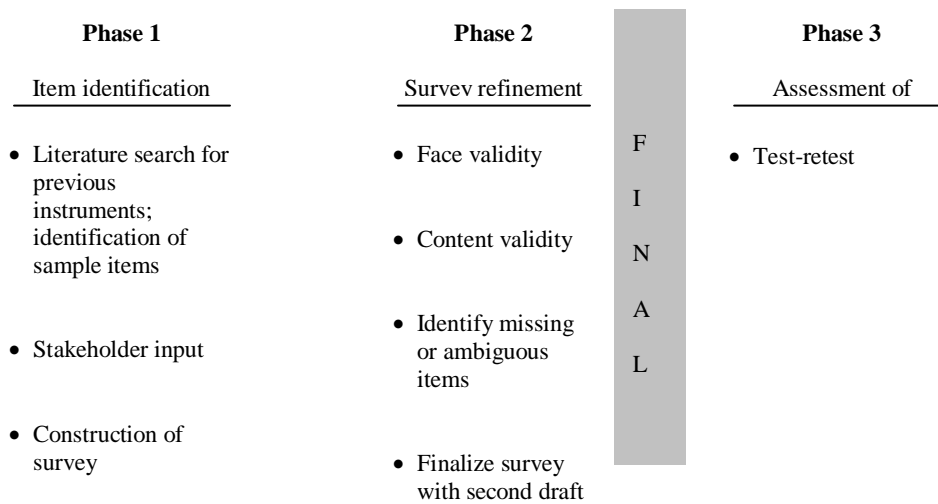
<b>Domain</b>	<b>Barrier</b>
Knowledge	Not knowing enough about living donation
	Not knowing availability of living donation
	Not knowing how to ask for a kidney
	Not knowing that living donor kidneys have better outcomes
	Not knowing how to contact living donation program
Opportunity	No suitable family members
	No suitable friends
Fear	Fear for health implications for donor
	Fear of inconveniencing donor
	Fear of rejecting kidney
Guilt	Guilt about needing a transplant
	Guilt about asking for a transplant

**TABLE 2.2 Kappa coefficient and percent agreement of individual items**

<b>Item</b>	<b>Kappa Coefficient</b>	<b>% agreement</b>
A family member can donate a kidney to a patient with kidney disease	---*	100
A friend can donate a kidney to a patient with kidney disease	---*	90
Kidneys from living donors do NOT last longer than kidneys from deceased donors	0.53	78†
The sooner I get a kidney transplant, the better off I will be	1.0	100†
Patients who have a living donor wait less time for a kidney than those without	0.55	80
I understand that living donation means that a kidney is donated by a living person	0.44	70
Individuals who donate a kidney are more likely to end up with kidney failure themselves	---*	100
Individuals who donate a kidney are more likely to end up with high blood pressure	---*	100
I could tell someone who is interested in donating a kidney how to contact the living donor program	0.44	70
I know how I would ask someone to donate their kidney	1	100

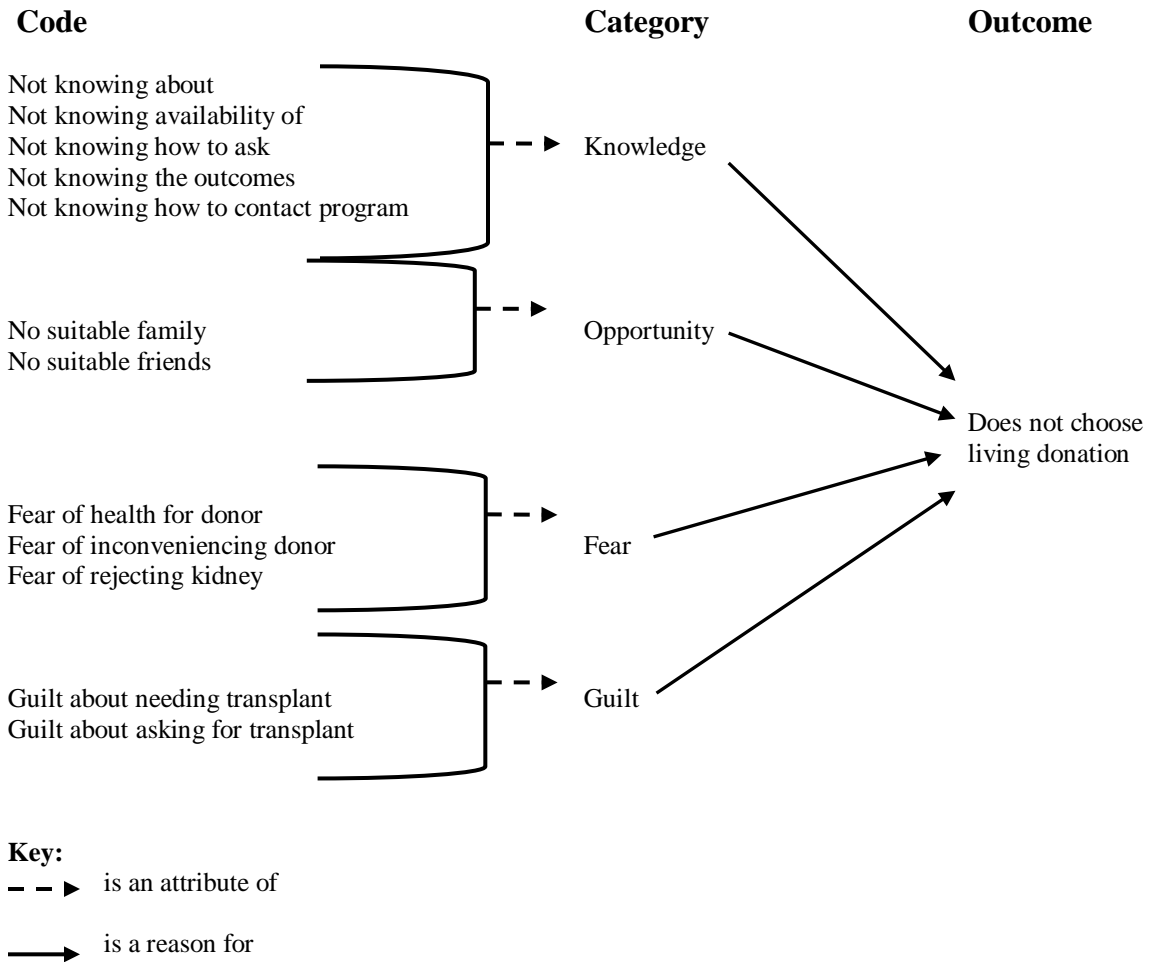
\* unable to calculate as there were zero cells present

† one answer missing



**FIGURE 2.1 Overview of phases for the development and validation of a survey to assess barriers to living donation in kidney transplant candidates**





**FIGURE 2.2 Semantic relationship between codes, categories and outcome**

**CHAPTER THREE: BARRIERS TO LIVING KIDNEY DONATION IDENTIFIED  
BY ELIGIBLE CANDIDATES WITH END-STAGE RENAL DISEASE**

### 3.1 ABSTRACT

**Background:** Among eligible transplant candidates with end-stage renal disease, only a minority receive a living donor kidney transplant (LDKT), suggesting there are barriers to receipt of this optimal therapy.

**Methods:** A validated questionnaire was administered to adults active on the deceased donor transplant wait list, identified from the Southern Alberta Renal Program database. The questionnaire included both quantitative and qualitative items addressing issues related to LDKT in the categories of knowledge, opportunity, fear, and guilt.

**Results:** Of the 196 subjects invited to complete the questionnaire, 145 (74%) responded. Not knowing how to ask someone for their kidney was the most frequently reported barrier, identified by 71% of respondents. Those that stated that living donation did not pose significant long term health risks to the donor (OR = 3.40; 95% CI 1.17 – 9.46;  $p = 0.01$ ), and those who understood how and why to begin the living donation process (OR = 4.21, 95% CI 1.41 – 12.04;  $p = 0.002$ ) were more likely to have discussed living donation with potential donors.

**Conclusions:** Knowledge about living donation was associated with having discussed living donation with a family member or friend. Studies examining the impact of educational programs which address these barriers to living donor kidney transplantation are required.

### 3.2 INTRODUCTION

Transplantation, and in particular living donor kidney transplantation (LDKT), is considered the optimal therapy for end-stage renal disease (ESRD).<sup>11</sup> The advantages of LDKT for the recipient include an increased quality of life<sup>6</sup> and superior clinical outcomes compared with dialysis.<sup>16, 20</sup> Despite this, only 39% of kidney transplants in Canada and 23% in the United States are from a living donor. Although the rates of living kidney donation have grown in the last decade, waiting lists for kidney transplantation have also grown as the incidence of ESRD has increased.<sup>62, 78</sup> The number of deceased organ donors will never meet the demand, no matter how efficient the retrieval process,<sup>79</sup> therefore there is a need to increase the rates of kidney transplantation by increasing the number of living organ donors.

The low rate of LDKT, despite the advantages, suggests that potential recipients may experience barriers to seeking a transplant from a live donor. A limited number of studies in select patient populations have suggested potential barriers are related to the broad categories of knowledge, the ability to ask, guilt, and fear.<sup>37, 38, 41, 42, 45, 53, 80</sup>

Recipients who understand the risks and benefits of LDKT to both the recipient and donor are more likely to support LDKT.<sup>38</sup> “Asking” for a kidney has been identified as a potential barrier in that recipients express reluctance and discomfort at having to ask someone to donate.<sup>37, 80</sup> Also commonly noted are fears for the donors health<sup>41</sup>, or fear of a negative response<sup>41, 42, 45, 53</sup>, as well as feelings of guilt and responsibility towards the donor.<sup>41, 42</sup> Despite these previous studies, a validated questionnaire in a Canadian setting has not been administered to eligible kidney transplant candidates to address barriers to

LDKT. Patients who are predominantly Caucasian in a publicly funded health care system, may have different barriers to selecting living donation as a treatment option.

We previously developed and validated a questionnaire to assess and explore in greater detail barriers to living kidney donation in eligible transplant candidates.<sup>81</sup> By administering this questionnaire to patients with ESRD eligible for a kidney transplant we aimed to further elaborate on the previously identified barriers to living kidney donation. Since health education for the *donor* has been shown to increase LDKT rates,<sup>53</sup> a better understanding of why candidates do not seek living donation could lead to targeted strategies to increase discussion of living donation with potential donors, and ultimately increased living donation rates.

### **3.3 METHODS**

Questionnaire development has been previously described in detail.<sup>81</sup> Briefly we developed a questionnaire to identify barriers that kidney transplant candidates may experience when seeking a living donor which demonstrated content and face validity as well as reproducibility. We conducted a single center, cross-sectional survey of kidney transplant candidates using this questionnaire to identify barriers to LDKT.

#### ***3.3.1 Eligible subjects***

We used the Southern Alberta Renal Program database<sup>82</sup> to identify all patients eligible for a kidney transplant and active on the transplant waiting list. This database captures all patients in Southern Alberta (catchment population 1.5 million) managed by a

nephrologist for their chronic kidney disease. Patients eligible for kidney transplant receive information about living donation both from their nephrologist (either prior to or after commencing dialysis) and from their transplant nephrologist once they have been referred to the transplant program. Eligible patients included those already on dialysis, as well as potential pre-emptive transplant patients not yet requiring renal replacement therapy. We excluded patients if they were less than 18 years of age, had significant cognitive dysfunction, or if they could not read and understand English.

### ***3.3.2 Administration of Questionnaire***

Patients attending in-center hemodialysis were contacted in person and invited to participate; all other patients, including those who were not on dialysis, who lived out of town, or who were on a self-care dialysis modality, were mailed a questionnaire with a stamped, self-addressed envelope. Non-respondents were sent a follow-up reminder letter after two weeks, followed by another questionnaire and self-addressed stamped envelope two weeks later. Subjects who still did not respond were considered to have declined participation.

Our questionnaire comprised 10 individual items assessing potential recipients' knowledge related to living donation, specifically the availability of living donation as a treatment option within the renal program, understanding living donation and knowing the benefits and risks to recipient and donor.<sup>81</sup> Participants rated their degree of agreement with each statement using a five-point Likert scale (from strongly agree to strongly disagree). An additional 5 open-ended questions were included addressing the

categories of opportunity, guilt, and fear as potential barriers to LDKT. The questionnaire also collected basic demographic information including gender, age (20 year age groupings), marital status, employment status, dialysis status and length of time on dialysis (less than 1 year, 1 – 4 years, more than 4 years). We also asked potential recipients if they had discussed living kidney donation with family and/or friends (yes or no). Patient consent was implied with the completion of the questionnaire.

### ***3.3.3 Analysis of Qualitative Responses***

Qualitative questionnaire items were analyzed using inductive coding, rather than *a priori* codes. Inductive coding initially involves transcribing and summarizing free-text data, after which the data is divided into meaningful analytical units, or codes.<sup>70</sup> A single rater (LB) transcribed the data, and two raters (LB and BH) then encoded the data independently. Inter-rater agreement was assessed using the kappa statistic.<sup>71</sup>

### ***3.3.4 Statistical Analysis***

We performed exploratory principal component factor analysis on the individual questionnaire items to assess discriminant validity. Factor analysis is a method for reducing a set of items to a smaller number of underlying principal components, and to uncover the latent structure of the items.<sup>83</sup> These underlying principal components then imply ways to combine variables, simplifying subsequent analysis.<sup>67</sup> Factor analysis can evaluate discrimination by testing statistically whether two or more items differ. Items are considered to be measuring different constructs if they load most heavily on different principal components.<sup>84</sup> Items that load most heavily, or *converge*, on the same principal

component are considered to be measuring the same construct. We used factor analysis with all quantitative items (knowledge domain). We did not include the items for fear, guilt and opportunity as we believed these constituted separate domains. Components with eigenvalues greater than or equal to 1 were retained (Kaiser rule); factors with low eigenvalues contribute little to the explanation of variance in the variables. We then performed factor loading (analogous to a correlation coefficient) on extracted factors, followed by factor rotation and used a cut-off threshold of 0.5 for factor loading. Factor loadings below 0.4 are considered to be “low”, and above 0.6 are considered too “high” for exploratory factor analysis.<sup>85,86</sup>

Logistic regression analysis was then undertaken for the outcome of having discussed living donation with family and/or friends. Independent variables considered were the components identified through the factor analysis, demographics and the coded qualitative data that were associated with the outcome of interest in a univariate analysis ( $p < 0.15$ ). All analyses were two sided and  $p$ -values  $< 0.05$  were considered statistically significant. Statistical analyses were performed using STATA SE version 11.0 software (Stata Corporation, Texas, USA).

The Conjoint Health and Research Ethics Board at the University of Calgary approved the study protocol.



### **3.4 RESULTS**

Of the 196 eligible subjects invited to complete the questionnaire, 145 questionnaires were completed for a response rate of 74%. Among subjects completing the questionnaire the majority were male, over the age of 40 and married. Approximately two thirds of the patients were on dialysis (either self-care or in centre hemodialysis), with the majority (74.7%) on dialysis for less than four years (Table 3.1).

#### ***3.4.1 Qualitative survey results***

144 questionnaires contained completed qualitative responses. Data was missing in one questionnaire for the qualitative portion; this person was excluded from analysis. Inter-rater agreement for the coding of questionnaire data was excellent (kappa statistic 0.91)<sup>68</sup> and resulted in the identification of 8 separate codes, for the three qualitative categories of opportunity, fear and guilt (Figure 3.1).

#### ***3.4.2 Quantitative survey results***

From the 10 questionnaire items assessing knowledge, we collapsed the five Likert categories into two: strongly disagree, disagree and neutral were combined and agree and strongly agreed were combined.<sup>69</sup>

The 8 codes identified from the qualitative questions were combined with the 10 quantitative questionnaire items, and divided into four categories: knowledge (about living kidney donation), opportunity (has family or friends that can donate), fear, and

guilt (Figure 3.1). All categories were used in subsequent analyses as potential barriers to discussing and identifying LDKT.

### ***3.4.3 Barriers to living kidney donor transplantation***

The proportion of respondents who agreed or strongly agreed with each item in the questionnaire, and those who expressed the sentiment in the qualitative proportion, is shown in Table 3.2 and Table 3.3 respectively. The most frequently reported barrier (71%) was not knowing how to ask someone for a kidney. Nearly 65% of respondents reported that they had family and/or friends that could potentially donate a kidney. Over 90% of respondents reported at least one fear (either for themselves or for the donor) and just under 60% reported feelings of guilt (either for asking or for needing the transplant).

### ***3.4.4 Factor Analysis***

The factor analysis identified four principal components (eigenvalues = 2.83, 1.49, 1.25, 1.09), from the ten variables representing knowledge in the questionnaire. These four components accounted for 76.7% of the total variance. Based upon the pattern of factor loading observed, these four components were considered to represent *knowledge of transplant options, risks to the living donor, short-term benefits of living donation and knowing how/why to begin the living donation process*. Each variable contributed equally to the component and was dichotomized for the analysis. Table 3.4 presents the variables from the questionnaire, the four principal components, and their loadings after rotation; only variables with factor loadings greater than 0.5 are presented for clarity.

### ***3.4.5 Unadjusted analysis***

Overall 116 study subjects reported discussing living donation with a family member or friend. Baseline characteristics of these subjects were similar to the overall sample (Table 3.1). Results for the univariate analysis of demographic characteristics, principal components (as identified above) and the qualitative categories of guilt, fear and opportunity with the primary outcome of having discussed living donation are shown in Table 3.5. None of the socio-demographic variables were associated with discussing living donation with a family member or friend in this univariate analysis.

Those who responded that living donation is not associated with significant increased long term health risks to the donor were more likely to have discussed living donation (odds ratio [OR] = 3.40; 95% CI 1.17 – 9.46;  $p = 0.01$ ). As well, those who understood how and why to begin the living donation process were more likely to have discussed living donation (OR = 4.21, 95% CI 1.41 – 12.04;  $p = 0.002$ ). Although not statistically significant, those who expressed either guilt for needing a transplant or guilt for asking for a transplant were less likely to have discussed living donation with a family member of friend.

### ***3.4.6 Adjusted analysis***

Multivariable logistic regression was then undertaken using those variables with a  $p < 0.15$  in the univariate analysis. The results for the multivariate analysis for the outcome '*I have discussed living donation with a family member or friend*' are shown in Table 3.6. Patients who agreed or strongly agreed that donating does not increase the risk of ESRD

or hypertension in the donor were almost 4 times more likely to have discussed it compared with those who didn't know (OR = 3.77, 95% CI 1.40-10.12;  $p = 0.01$ ).

Similarly, patients who knew how to contact the living donor program and that living donors have better allograft survival were almost 5 times more likely to have discussed living donation compared with those who didn't know (OR = 4.62, 95% CI 1.70-12.59;  $p = 0.003$ ).

### **3.5 DISCUSSION**

In this survey of patients with end-stage renal disease eligible for a kidney transplant we identified two attributes that were associated with having discussed living donation with a family member or friend: knowing the risks to the living donor and knowing how and why to begin the living donation process. These results suggest that providing appropriate information about living donation, which can be delivered within a structured educational intervention, could influence the decision to discuss and seek a living donor. Our study is the first to use factor analysis to identify which components of knowledge of living kidney transplantation are associated with discussing living donation with a family member or friend.

In our study, over 80% of respondents stated that they had discussed living donation with a family member or friend, but less than half had identified a living donor, which is consistent with local rates of living donation. Knowing how to ask was the most prevalent barrier identified by study subjects, a finding consistent with previous studies. There are several reasons that may influence a recipients' ability to ask. Recipients have

indicated that the decision to donate should be made by the donor, and that the recipient should not ask for a kidney.<sup>39</sup> Zimmerman et al. noted that patients who had identified a living donor, compared with those waitlisted for a deceased donor, found it more appropriate to ask for kidney.<sup>38</sup> Knowing how to ask for a kidney clearly is an important topic, in fact deceased donor organ requestors are trained to ask families sensitively and appropriately.<sup>87,88</sup> This principal could be applied to candidates of renal transplantation to teach them how to ask for a kidney.

Our measures of knowledge, both knowing the risks to the donor and knowing how and why to begin the living donation process, were strongly associated with having discussed living donation with a family member or friend. Our results corroborate those of Gourlay et al.<sup>39</sup> who found that wait list patients with higher knowledge and belief scores were more likely to have a family member who expressed interest in donation. This raises the issue of the content to provide in education sessions as other studies have found that increasing a patient's knowledge about LDKT will not, by itself, lead to more living donor kidney transplants<sup>50</sup>, nor will a candidate's knowledge about the benefits of LDKT increase identification of donors<sup>89,90</sup> or discussion of LDKT with their nephrologists.<sup>91</sup>

Although risks to the donor are not zero, they are low. In a review of 871 donors, only 8.2% suffered a complication and of these, only 0.2% were considered major.<sup>92</sup> Not surprisingly, transplant candidates willing to consider living donation are more likely to understand the risks and benefits of LDKT.<sup>38</sup> Patients who refuse offers of living donor

kidneys often cite concern for peri-operative complications for the donor.<sup>38</sup> Further, recipients may overestimate donors' surgical pain and recovery time.<sup>36</sup> The fact that recipients overlook their own advantages to living donation due to concerns for the donor highlights the need to focus on the health risks to the recipient should they stay on dialysis to wait for a deceased donor kidney.<sup>37,38</sup> Education should therefore encompass more than just increasing the general knowledge and understanding of living donation, but address directly the risks to the donor, particularly given the availability of laparoscopic nephrectomy<sup>22</sup>, and the short-term benefits of living donation, the specific items identified in our survey.

Our study is not the first to note the guilt present in patients with ESRD. In a study of recipients of deceased and living donor kidney transplants, feelings of guilt around donor morbidity and financial hardship were prominent for recipients of LDKT<sup>93</sup>, as was the unwillingness to burden a loved one.<sup>42</sup>

Our study has limitations. First, we did not translate our questionnaire into other languages, which may limit generalizability to the non-English speaking population. In addition, those who did not respond may have been less knowledgeable or less interested in transplant. However, we feel our sample adequately represents this population as the response rate was high, and the baseline characteristics are representative of other kidney transplant programs.<sup>94</sup> Finally, our study had a cross-sectional design, measuring the different categories and the outcome at one time, indifferent to a candidates' course in the

transplant evaluation and wait time process and irrespective of their source of knowledge (though we did examine results by time on dialysis). A patients' decision to pursue living donation may change over time and should be explored for optimal education opportunities. Further, it is not clear from this study design whether those who pursue LKDT obtain knowledge prior to the transplant to realize their objective, or whether it is a consequence of their decision to seek this treatment. Future studies examining this prospectively will be useful to informing programs.

There is a large pool of potential living donors not being utilized, as two-thirds of respondents stated that they had family or friends who could potentially donate. Knowing the risks to the living donor as well as why and how to begin the living donation process were associated with having discussed living donation with a family member or friend. Educational interventions aimed at not only increasing knowledge about living donation and the benefits, but teaching patients how to ask for kidney, alleviating guilt both pre and post-transplant, and addressing fears for both the recipient and the donor may increase the likelihood of a recipient discussing and identifying a LDKT, and should be assessed in prospective studies.

**TABLE 3.1 Demographics of subjects overall and by whether they had discussed living kidney donation**

	All (n=145)	Discussed living kidney donation (n=116)
<b>Sex, n (%)</b>		
Male	83 (57.2)	66 (56.9)
<b>Age, n (%)</b>		
≤ 40	32 (22.1)	29 (25.0)
> 40	113 (77.9)	87 (75.0)
<b>Marital status, n (%)</b>		
Married	102 (70.3)	80 (69.0)
Single	20 (13.8)	17 (14.7)
Widowed	9 (6.2)	7 (6.0)
Divorced	14 (9.7)	12 (10.3)
<b>Employed, n (%)</b>		
Yes	62 (42.8)	50 (43.1)
<b>Modality type, n (%)</b>		
No dialysis	50 (34.5)	39 (33.6)
Self-care dialysis	55 (37.9)	47 (40.5)
In-centre hemodialysis	40 (27.6)	30 (25.9)
<b>Time on Dialysis, n (%)</b>		
< 4 years	71 (74.7)	58 (75.3)
> 4 years	24 (25.3)	19 (24.7)



**TABLE 3.2 Barriers, as identified through quantitative items, to choosing living kidney donation as a treatment option, and % who agreed/strongly agreed**

Category	Barrier	All (n = 145)
	<i>Quantitative items<sup>1</sup></i>	
<b>Knowledge</b>	A family member can <i>not</i> donate a kidney to a patient with kidney disease in Calgary	5.5
	A friend can <i>not</i> donate a kidney to a patient with kidney disease in Calgary	6.9
	Kidneys from living donors <i>do not</i> last longer than kidneys from deceased donors	11.0
	Getting a kidney transplant sooner will <i>not</i> make me better off	23.5
	Patients who have a living donor <i>do not</i> wait less time for a transplant than those without	15.9
	I do not understand what living donation means	2.1
	Individuals who donate a kidney are <i>more</i> likely to end up with kidney failure themselves	4.8
	Individuals who donate a kidney are <i>more</i> likely to end up with high blood pressure themselves	8.3
	I could <i>not</i> tell someone how to contact the living donor program	17.2
I <i>do not</i> know how I would ask someone to donate their kidney	71.0	

<sup>1</sup> Statements have all been worded in the negative for ease of presentation. In the original questionnaire, statements were randomly reversed between positive and negative.

**TABLE 3.3 Barriers, as identified through qualitative items, to choosing living kidney donation as a treatment option, and % who expressed sentiment**

Category	Barrier	All (n = 144)
<i>Qualitative items</i>		
<b>Opportunity</b>	I have <i>no</i> family or friends that could donate a kidney to me	35.9
<b>Fear</b>	I fear the transplant would <i>not</i> work or that I would reject the kidney	59.3
	I fear for the future health and lifestyle of the donor	50.3
	I am fearful of the operation/surgery	42.1
	I am fearful to ask for a kidney	36.6
<b>Guilt</b>	I feel guilty about <i>asking</i> for a transplant	54.5
	I feel guilty about <i>needing</i> a transplant	22.1

**TABLE 3.4 Principal component analysis matrix for knowledge questionnaire items**

Variable	Factor			
	Knowledge of transplant options	Knowing the risks to the living donor	Short-term benefits of living donation	Knowing how and why to begin the living donation process
Living related donation is possible locally	0.95 <sup>2</sup>			
Living unrelated donation is possible locally	0.96			
LD kidneys have better allograft survival				0.77
Survival benefits of early transplantation			0.70	
Shorter waiting time for LD kidneys			0.83	
LD involves donation by a living person				
Risk of ESRD in donor		0.86		
Risk of hypertension in donor		0.85		
Knowledge of how to contact LD program				0.74
Knowledge of how to ask a donor				
<b>Eigenvalues<sup>3</sup></b>	2.83	1.49	1.25	1.09
<b>Percent of Variance<sup>4</sup></b>	20.0	17.3	15.1	14.3

\* LD = living donation; ESRD = end-stage renal disease

<sup>2</sup> Factor loadings, corresponding to the weights and correlations between each variable and the factor.

<sup>3</sup> Eigenvalues correspond to the total variance accounted for by each factor. The sum of all eigenvalues is equal to the total number of variables (note: not all eigenvalues are presented in this table).

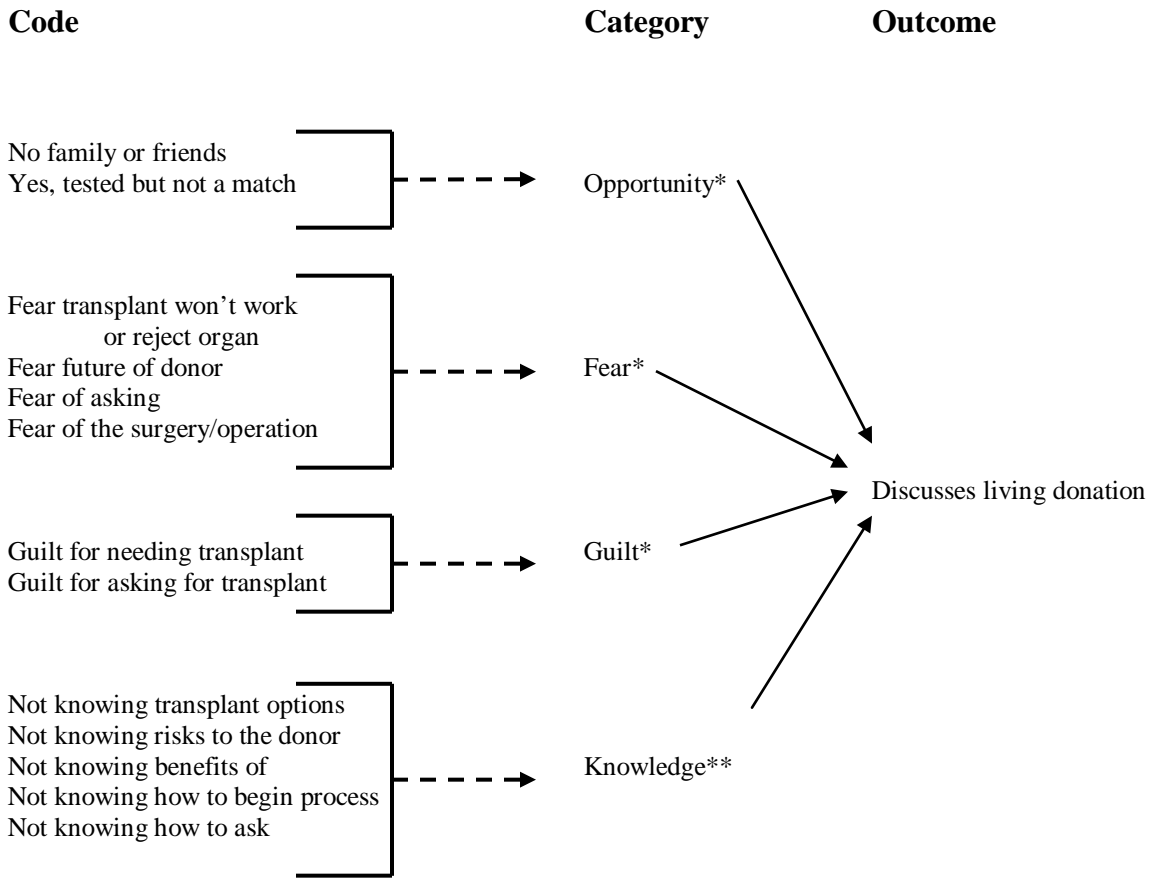
<sup>4</sup> Indicates the relative weight of each factor in the total variance.

**TABLE 3.5 Unadjusted analysis of demographic characteristics, principal components and qualitative items with the outcome of having discussed living donation with a family member or friend, n = 142**

<b>Characteristic/barrier</b>	<b>OR</b>	<b>95% CI</b>	<b>p-value</b>
Age (40 or under)	4.00	0.89-36.7	0.05
Male	0.83	0.31-2.13	0.67
Married	0.67	0.20-1.92	0.42
Employed	0.90	0.34-2.41	0.81
Dialysis	0.88	0.30-2.36	0.78
Knowledge of transplant options	2.90	0.42-15.97	0.15
Knowing the risks to the living donor	3.40	1.17-9.46	0.01
Short term benefits of living donation	0.23	0.01-1.63	0.13
Knowing how and why to begin the living donation process	4.21	1.41-12.04	0.002
Guilt	0.38	0.11-1.08	0.05
Fear	2.12	0.33-10.18	0.29
No opportunity	0.59	0.21-1.72	0.27

**TABLE 3.6 Multivariable adjusted analysis of variables associated with having discussed living donation with a family member or friend, n= 142**

<b>Characteristic/barrier</b>	<b>OR</b>	<b>95% CI</b>	<b>p-value</b>
Risk to the living donor	3.77	1.40-10.12	0.01
Knowing how and why to being the living donation process	4.62	1.70-12.59	0.003



**Key:**  
 - - ► is an attribute of  
 —► is a reason for not doing

\* assessed with qualitative portion of questionnaire  
 \*\* assessed with quantitative portion of questionnaire

**FIGURE 3.1 Relationship between codes, categories and outcome for both quantitative and qualitative portion of questionnaire**

**CHAPTER FOUR: EVALUATION OF AN EDUCATION INTERVENTION TO  
INCREASE THE PURSUIT LIVING KIDNEY DONATION: A RANDOMIZED  
CONTROLLED TRIAL [ISRCTN APP: 16490]**

#### 4.1 ABSTRACT

**Introduction:** Many transplant candidates have concerns about living donation (LD).

This randomized controlled trial investigated whether a structured education session increased eligible kidney transplant candidates' pursuit of LD.

**Methods:** Eligible transplant candidates were randomized to standard of care (n=50) or to the education intervention (n=50), which included both written materials and a two hour education session. The primary outcome was having a living donor contact the transplant program to express interest in donation for a patient, with a secondary outcome being the candidates' treatment preference for end-stage renal disease, both determined at three months after enrollment.

**Results:** Of the 100 patients randomized, 4 in the intervention group and 2 in the standard of care group had a living donor contact the program ( $p = 0.45$ ). Within the education intervention arm, 12 patients changed their treatment preference to living donation from baseline ( $p=0.02$ ), whereas only 4 patients in the standard of care group changed their treatment preference ( $p=0.37$ ).

**Conclusions:** This education intervention did not increase the likelihood of a potential donor contacting the transplant program, compared to standard care. However, patients who received the education session were more likely to change their treatment preference to LD at study completion. Research investigating other methods of increasing living transplant rates, are urgently required.



## 4.2 INTRODUCTION

Living kidney donation (LKD) is considered an optimal therapy for end-stage renal disease (ESRD) as it is associated with superior graft function and patient survival<sup>11</sup>, and is also more cost-effective than long term dialysis or deceased donor transplantation.<sup>6, 56</sup> The waiting list for kidneys for deceased donor transplantation continues to grow, and the number of deceased organ donors is unlikely to ever meet the demand, no matter how efficient the process becomes.<sup>79</sup> Increasing the number of living organ donors is one potential strategy to increase rates of kidney transplantation.

However, many transplant candidates express concerns that may preclude them from pursuing living organ donation. Previous studies suggest that transplant candidates are reluctant to ask someone to donate a kidney<sup>37, 80</sup> both because of fear for the donor's health<sup>41</sup> and fear for a negative response<sup>42, 45</sup>. There are also psychological barriers for living kidney donation, including feelings of guilt and responsibility towards the donor.<sup>41, 42</sup> Potential barriers to seeking a living kidney donor may be amenable to modification with education and information.

Transplant candidates typically receive information about LKD through an informal process including consultations with their nephrologist or the transplant team. While studies have suggested that formal education may increase the rates of living kidney donation,<sup>37, 50, 53, 54</sup> the only randomized controlled trial examining this found no increase in rates of living kidney donation<sup>50</sup>, although their study had limitations including use of

a home based education session (which may not be feasible or sustainable). Further, their results may not be generalizable to Canada, due to demographic racial differences.<sup>50</sup>

Given the limited data in the area examining the efficacy of education interventions on increasing the pursuit of living donation, we sought to determine whether a structured education session that included both health professionals and peer support could increase eligible candidates' pursuit of living donation, compared to standard care. Our secondary objective was to determine whether these education sessions changed patient's preference of treatment modality for ESRD.

## **4.3 SUBJECTS AND METHODS**

### ***4.3.1 Setting and Participants***

Patients were enrolled from the Southern Alberta Transplant Program transplant assessment clinic. The Southern Alberta Transplant Program provides transplant services for all patients in Southern Alberta (catchment population 1,500,000). Approximately twenty new patients are assessed each month in this clinic by a nurse clinician and a transplant nephrologist. At the first clinic visit their potential eligibility for kidney transplantation is determined. We enrolled patients who were considered, after this initial visit, to be medically able to continue with the transplant workup process. We excluded patients with cognitive dysfunction (i.e., significant dementia), who were non-English speaking, less than 18 years of age, who had already identified a living donor. The Conjoint Health and Research Ethics Board at the University of Calgary approved the study protocol.

### ***4.3.2 Education Intervention***

The educational intervention strategy was comprised of both written educational materials and a structured education session, neither of which were provided to the standard of care group. Written materials were provided by mail within two weeks of enrolling in the study. This written material, developed locally following the administration of a validated questionnaire<sup>81</sup>, provided information on the advantages of transplantation and living donation as well as information regarding living donors. The second component of the educational component, which occurred approximately two weeks after receipt of the written materials, included a two-hour small group interactive session involving 3 to 5 patients, their respective family members, a transplant nephrologist, a nurse clinician and both a recipient and a donor from a living kidney transplant (section 4.6).

The main teaching format was problem-based learning in small groups focused around cases that were representative of the local population, which has been shown to be an effective learning format.<sup>95</sup> The session began with brainstorming in which participants described the advantages and disadvantages of dialysis, transplantation in general, and living and deceased kidney donation based on their current knowledge. Following this, participants were divided into smaller groups and given scenarios to problem solve, which involved finding solutions to overcome some of the barriers to living donation. Role playing on how to ask for a kidney was demonstrated by the nurse and nephrologist facilitators. The session concluded with the participants being able to ask questions and discuss with the recipient and donor of a living kidney transplant.

This educational intervention was specifically designed to incorporate a predisposing intervention (written materials) and an enabling intervention (small group session). This design was adopted from previous studies that suggest that combinations of interventions are better than single interventions.<sup>77,96</sup>

#### ***4.3.3 Randomization***

Randomization was performed using a computer-generated sequence in blocks of 6. Patients were randomly assigned to the education intervention or standard of care in a one-to-one ratio using a central phone-in system to achieve allocation concealment. Given the nature of the intervention, neither the investigators, nurse educators or patients were blinded to the treatment.

#### ***4.3.4 Measures***

Participants completed a baseline questionnaire upon randomization, which included information on socio-demographic data (age, gender, race, marital status, education, and employment status), as well as medical information (history of diabetes, hypertension, cardiovascular disease as well as details regarding dialysis for patients on dialysis). The baseline questionnaire also included 10 statements regarding knowledge about living donation, using a five-point Likert scale (1-strongly disagree to 5-strongly agree) for response. Patients were also asked to rank their preference of ESRD treatment (no treatment, dialysis, deceased donor transplantation, living donor transplantation), number of family members and whether they have close friends they would accept a kidney from.

Participants completed a follow-up questionnaire that included the same items assessing the participant's knowledge of living donation and patients were also asked to rank their preferred treatment for ESRD. The follow-up questionnaire was administered 2 weeks after patients in the intervention group attended their small group education session, and a similar point in time for the control group.

#### ***4.3.5 Primary outcome***

Our primary outcome was whether a potential living donor contacted the living donor program on behalf of a patient. This outcome was assessed at three months after enrollment for the control group, and three months after the education session for the intervention group. This was a proxy measure used to define the intention to pursue donation, as it was not influenced by factors beyond the control of the patient (such as the donor not being a match and the length of time it could potentially require to complete the donation process). The primary outcome was assessed using the Southern Alberta Transplant Program database by a data collector who was blinded to patient allocation.

#### ***4.3.6 Secondary outcome***

Our secondary outcome was the ranking of treatment preference for ESRD. Patients ranked the following treatments at baseline and follow-up: living donation, deceased donation, dialysis or no treatment. Those who did not complete the follow-up questionnaire were contacted by phone by a data collector who was blinded to patient

allocation to complete the surveys. For participants who could not be reached, the last observation was carried forward to perform the intent to treat analysis.

#### ***4.3.7 Statistical analysis***

The study was designed to have 80% power to detect a 20% absolute increase in the pursuit of living donation, for those randomized to the education session compared with usual care by enrolling 100 patients per arm over a two-year enrollment period. This estimate was based on assuming an annual primary outcome rate of 30% in the standard of care group (based on data from the program in 2006), a non-adherence rate of 10%, and an  $\alpha$  level of 0.05.

Though there is no consensus for statistical testing for differences in randomized trials<sup>97-99</sup>, due to the small study size and lack of power to detect such differences, along with no a priori evidence that one or more of the covariates collected was strongly associated with the outcome of having identified a living donor, statistical testing for differences in baseline characteristics between groups was not undertaken. A Fisher's exact test was used to compare the proportion of patients who had a potential donor contact the living donor program at study completion between the treatment and control groups. Two analyses were undertaken. The primary analysis was done according to the intention-to-treat principle, where all randomized patients are included in the analysis. Secondly, a per-protocol analysis was done, where only those who adhered to the protocol were included. For the secondary outcome, a Fishers exact test was used to compare the proportion of patients who chose living donation as their treatment of preference.

McNemar's discordant pair test was used to determine within group changes from baseline. STATA SE version 11.0 software (Stata Corporation, Texas, USA) was used for all analyses.

## **4.4 RESULTS**

### ***4.4.1 Recruitment and Follow-up***

Study enrollment commenced on July 1, 2007 and terminated September 24, 2009, with follow-up ending February 10, 2010 (Figure 4.1). Although we aimed to enroll 100 patients per arm, due to difficulties and delays in patient recruitment, enrollment ceased with a total of 429 patients screened and 100 patients randomized. One patient received a deceased donor kidney transplant after randomization but prior to the intervention, and was therefore excluded from the analysis. Of the 49 patients randomized to the education sessions, 37 attended the session. One patient in the standard of care group and three patients in the education intervention did not complete either the baseline or the follow-up questionnaire and were therefore excluded from analysis of the secondary outcome.

### ***4.4.2 Patient characteristics***

Baseline characteristics of the patients, by treatment group, are provided in Table 4.1. The majority of patients were between the ages of 41 and 60, were Caucasian and of male gender. Of the total sample, 55% were receiving dialysis at time of enrollment, and of these 55% had been on dialysis for between 1 and 4 years. 54% of patients stated that they had close friends or family that could donate, but they would not accept a kidney from them. Results appeared similar across groups.

#### ***4.4.3 Patient's intention to pursue living donation***

At study completion 4 patients in the education intervention group and 2 patients in the standard of care group had a living donor contact the program on their behalf ( $p = 0.45$ ). The analysis was repeated including only those who followed the protocol (that is, attended the education session), with similar results; 4 patients in the intervention group and 2 patients in the standard of care group had a living donor contact the program on their behalf ( $p = 0.39$ ). In a post-hoc analysis, we also evaluated the outcome extending the follow-up to six months. In this analysis completed by all patients, 5 patients in the intervention group and 3 patients in the control group had a living donor contact the program on their behalf ( $p = 0.49$ ).

#### ***4.4.4 Patient's treatment preference***

Twenty-six patients in the control group and 20 patients in the education intervention ranked living donation as their treatment of preference at baseline ( $p = 0.3$ ). At study completion, 23 patients in the control group and 29 patients in the education intervention ranked living donation as their treatment of preference ( $p = 0.2$ ).

Among patients who had not initially selected living donation as their treatment of preference at baseline, 4/22 (18.2%) in the standard care group compared with 12/27 (44.4%) in the education intervention chose living donation as their treatment preference at study completion ( $p=0.07$ ) (Table 4.2).



Within group changes were also explored. There was no statistically significant increase in the proportion of patients ranking living donation as their treatment of choice within the control group (Table 4.3-A). However, within the intervention group, there was a significant increase in the number of patients who ranked living donation as their treatment of preference at study completion (Table 4.3-B).

#### 4.5 DISCUSSION

In this randomized controlled trial of an educational intervention to increase living kidney donation we found that, compared to standard care, the intervention did not increase the number of potential donors contacting the living donor program, at either three or six months of follow-up. There was, however, a significant increase of the number of patients who ranked living donation as their treatment of preference at study completion within the education intervention group. As such, our results are consistent with the result of a previous randomized trial which examined the impact of combining both clinic and home based education on living donor inquiries which also showed no difference when analyzed as intent to treat.<sup>50</sup>

Previous studies have identified barriers to living donation<sup>37, 38, 41, 42, 45, 53, 80, 81</sup> and education preferences of candidates.<sup>39, 100</sup> Our education session reflected these issues: speaking personally with someone who has received a LDKT<sup>39, 100</sup>, and including information on what to expect after transplantation and donor risks.<sup>41</sup> Recipients may also not be aware of the potential benefits to the donor and the reasons that donors

donate,<sup>37, 63</sup> including feeling proud of their donation, glad they were able to help,<sup>37, 64</sup> and lack of regret for their decision to donate,<sup>36</sup> even post-transplantation.<sup>22</sup> Our sessions allowed candidates to interact with living donors, hearing first hand their positive experiences. However, despite the relevant content for the education sessions, our intervention did not show a difference in the proportion of patients who had a donor contact the transplant program. There are many possible reasons for this. First of all, our study was under-powered to detect a significant difference if in fact one was present, given the lower than anticipated event rate (we had estimated 30% in the control group, and achieved 4%) and our low enrollment rates. Another possible reason could be the timing of our intervention: by the time a candidate is seen in the transplant clinic, they may have already decided which treatment option is best for them. It is not known at what point during their disease process a patient with ESRD makes a decision on their preferred treatment choice, or at what point in time they are most susceptible to receiving education. Further, a patient's decision to pursue living donation may change over time, depending on the course of their treatment. Finally, our follow-up period of three months may have been too short for a candidate to move from the stage of deciding on living donation and preparing for living donation (by talking to family members who would then contact the living donor program)<sup>101</sup>, though extending follow-up to six months did not change the results.

Our study did, however, demonstrate that patients attending the education sessions were more likely to choose living donation as their treatment preference, a change not

observed in the standard of care group. These results suggest that several interventions, targeted at different times during a patient's stages of change, may be necessary to increase the pursuit of living donation.<sup>96, 101, 102</sup> A first intervention could be directed towards educating patients on the best treatment options for their ESRD, and a second intervention on how to initiate that change, for example, how to ask for a kidney, as one possible sequence.

Our study has limitations. As noted, our study was underpowered since we ended enrollment early due a slower recruitment than anticipated and baseline events rates were lower than expected. Second, our primary outcome was a proxy for living donation. Living donation was not directly measured but was assessed by the *intent* to proceed with living donation by having a donor contact the program. This surrogate end point was chosen as it was meaningful, since it demonstrated that the candidate has initiated a discussion with a potential donor, and was timely and cost effective. Third, we had a higher drop out rate than the 10% we had estimated and this drop out rate can be used to inform future studies. Finally, the feasibility of the intervention itself should be re-addressed in future work, as 30% of patients assigned to the intervention didn't attend the education session. Finally there may be multiple potential barriers to living donation. This study addressed barriers in only the recipient, however, other barriers may exist in potential donors and could limit the living donation process.

Educating patients on their treatment options is a priority given the rates of ESRD, and living kidney donation is an optimal treatment compared with deceased donor transplantation and dialysis. An effective strategy to communicate these benefits to candidates for renal transplantation has not been identified. Future studies should continue to examine education activities to enhance the pursuit of living donation in renal transplant candidates. Given long wait times for kidney transplantation, research investigating other methods of increasing living transplant rates, are urgently required.

#### **4.6 Format for the educational intervention**

- 1) Patients, nurse, and physician introduce themselves. Nurse/physician gives an overview of the session and outlines the “Goals of the course” using a brief PowerPoint presentation.
- 2) Physician gives a brief overview of the different treatment options for ESRD, including dialysis, transplant options and no treatment. Physician highlights the different types of transplantation. Main focus is on living donation.
- 3) From previous knowledge, including their recollection of the reading material, patients are asked to list the advantages and disadvantages of transplantation versus dialysis, then to repeat with the advantages of living donation versus deceased donation. Reassure that there are no right and wrong answers. When writing up the advantages and disadvantages, be specific as to the type of transplantation they apply to. If there are wrong answers then correct them at the end of the brainstorming session. If there are missing points (see list below) then add them.
- 4) Break
- 5) Patients break up into smaller groups and are asked to consider what type of treatment might be best suited to a hypothetical patient described in a short scenario that is provided to them. Patients are asked to determine not only which treatment might be best for the hypothetical patient but also the advantages /disadvantages of the different treatments for that patient. One scenario is given to every 2 patients (plus family members).

- 6) Small groups rejoin. Spokesperson for the group presents the scenario, with their suggestions, to the other groups. Other groups can ask questions.
- 7) Nephrologist and nurse do role playing on how one might ask for a kidney.
- 8) Question and answer period with the peer presenters who represent a recipient of a living donor kidney and a living donor.
- 9) Feedback for the course, along with final questions and wrap-up.

**TABLE 4.1 Characteristics of patients who were eligible for a transplant, who received either standard of care or education intervention**

Characteristic	Education Intervention		Standard of Care	
	n/N	%	n/N	%
<b>Age, years</b>				
19 – 40	1/49	2	10/50	20
41 – 60	24/49	49	24/50	48
> 60	24/49	49	16/50	32
<b>Male</b>	35/49	71	33/50	66
<b>Caucasian</b>	35/49	71	36/50	72
<b>Married or significant other</b>	38/49	78	33/50	66
<b>High school education or less</b>	25/47	53	19/48	40
<b>Employed</b>	18/47	38	14/50	28
<b>Diabetes mellitus</b>	24/49	49	28/50	56
<b>Hypertension</b>	23/49	47	32/50	64
<b>Cardiovascular disease</b>	9/49	18	7/50	14
<b>Dialysis</b>	25/49	51	29/50	58
<b>Dialysis type</b>				
In-center hemodialysis	11/25	44	12/29	41
Peritoneal dialysis	11/25	44	12/29	41
Home hemodialysis	3/25	12	2/29	7
Nocturnal	0/25	0	2/29	7
Self-care dialysis	0/25	0	1/29	3
<b>Time on dialysis</b>				
< 6 months	6/25	24	4/29	14
6 months – 1 year	7/25	28	6/29	21
1 – 4 years	11/25	44	16/29	55
> 4 years	1/25	4	3/29	10
<b>Do you have close friends you would accept a kidney from?</b>				
Yes, have close friends	16/47	30	24/47	51
Yes, but would not accept a kidney	14/47	30	15/47	32
No, have no close friends	17/47	36	8/47	17
	20/46	44	26/48	54

**TABLE 4.2 Proportion of patients in each group who ranked living donation as their treatment of preference, among patients who chose another treatment of preference at baseline**

	Standard care	Education intervention
Proportion ranking living donation as first choice (%): baseline	0/22	0/27
Proportion ranking living donation as first choice (%): follow-up	4/22 (18.2%)	12/27 (44.4%) <sup>a</sup>

<sup>a</sup>  $p = 0.07$  comparing follow-up standard care and educational intervention groups.



**TABLE 4.3 Patients who ranked living donation as the treatment of preference at baseline and at study completion for concordant and discordant cases for control (A) and intervention (B) groups**

**A. Control group**

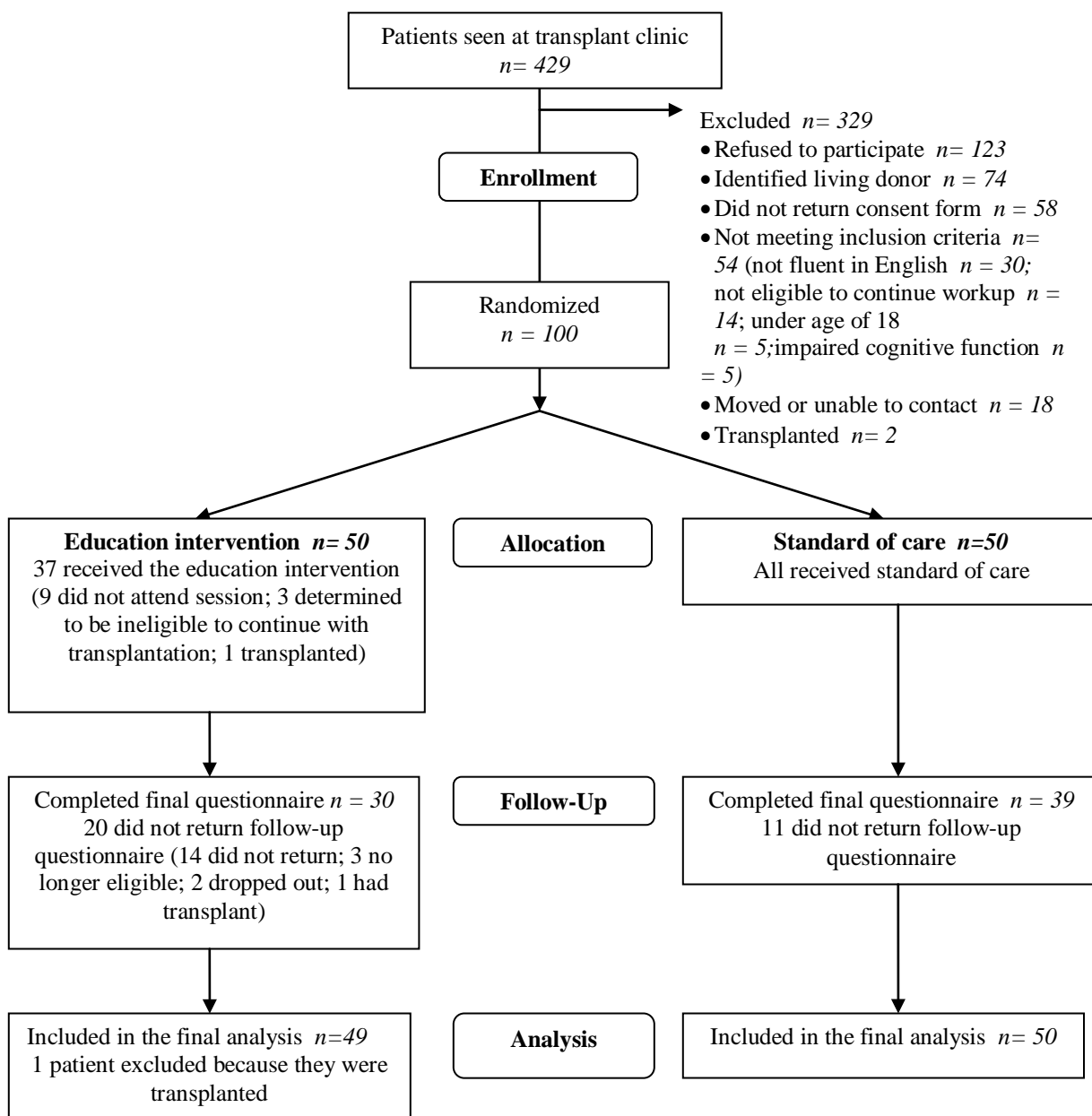
	Living donation <i>not</i> primary treatment of choice at study completion	Living donation primary treatment of choice at study completion
Living donation <i>not</i> primary treatment of choice at baseline	18	4
Living donation primary treatment of choice at baseline	7	19

McNemar's discordant pair test  $p = 0.37$

**B. Intervention group**

	Living donation <i>not</i> primary treatment of choice at study completion	Living donation primary treatment of choice at study completion
Living donation <i>not</i> primary treatment of choice at baseline	15	12
Living donation primary treatment of choice at baseline	3	17

McNemar's discordant pair test  $p = 0.02$



**FIGURE 4.1** Flow of patients

**CHAPTER FIVE: COST ANALYSIS OF RECIPIENTS OF A FIRST RENAL  
TRANSPLANT: A COMPARISON OF LIVING AND DECEASED DONOR  
KIDNEYS**

## 5.1 ABSTRACT

**Background:** Kidney transplantation improves quality of life and survival, and is associated with lower health care costs compared with dialysis for patients with end-stage renal disease. An up-to-date detailed cost analysis of kidney transplantation, including whether there are differences in cost and resource utilization between recipients who receive a deceased or a living donor kidney is not available. The purpose of this study was to provide an updated comparison of the costs of living and deceased donor kidney transplantation.

**Methods:** We used the Southern Alberta Transplant program database (ALTRA) to identify all adult recipients of a first kidney-only transplant in Southern Alberta between April 1, 1998 and March 31, 2006, as well as the donor information. Demographic and clinical information was collected from ALTRA, while costs and resource use were determined for recipients and donors using administrative data. Transplant related costs were assessed before transplant and all costs (outpatient care, diagnostic imaging, inpatient care, physician claims, laboratory tests, and transplant medications) were assessed for two years after transplant.

**Results:** Complete cost information was available for 357 recipients. The mean cost of transplantation, including donor costs, for recipients of living and deceased donors was \$118,347 (95% confidence interval [CI], 110,395 to 126,299) and \$121,121 (95% CI 114,287 to 127,956), respectively ( $P = 0.7$ ). The mean cost of care for a living donor was \$18,129 and for a deceased donor \$36,989. Predictors of total two-year recipient costs were presence of diabetes, time spent on the waiting list and non-zero panel reactive antibody.

**Conclusion:** Living donor kidney transplantation is associated with similar costs compared to deceased donor transplantation. This updated cost of transplantation can be used by health care decision makers to promote expansion of living donor kidney transplantation programs.

## 5.2 INTRODUCTION

Kidney transplantation improves quality of life and survival and is associated with lower health care costs compared with dialysis for patients with end-stage renal disease (ESRD).<sup>6, 9, 103, 104</sup> In Canada and worldwide, there is a widening gap between the need and availability of kidneys for transplantation, resulting in increased wait times and an increasing number of deaths among patients awaiting a kidney transplant.<sup>78</sup> In an attempt to alleviate the scarcity of deceased donor kidneys, programs are further promoting the use of organs from living related and unrelated donors.<sup>105</sup> Promoting and increased funding for identification of deceased donors has also been advocated in Canada.<sup>106</sup> While clinical outcomes of living versus deceased donor transplantation demonstrates that living donor kidney transplantation is a superior treatment option,<sup>104, 107</sup> whether significant cost differences exist for the two treatments is uncertain.

Few studies have systematically analyzed the costs of kidney transplantation,<sup>6, 9, 10, 20, 56, 57, 108-110</sup> despite the fact that transplantation is a very resource-intensive intervention. Of these studies, two based in the United States examined cost differences between living and deceased donor transplants, and found that living donors were less costly than deceased donor transplants.<sup>56, 57</sup> However, these studies did not examine costs accrued pre-transplant, and did not include costs of medications or laboratory tests, focusing on hospitalizations post-transplant. Adjustment for important comorbidities which may affect the observed cost differences between living and deceased donor transplantation were also not accounted for. The most widely quoted and methodologically rigorous (given the prospective nature) costing study of kidney transplantation is a Canadian study

of living and deceased donor transplantation,<sup>6</sup> which is now almost 20 years old. Given the changes in treatment strategies, graft survival and management of donors and recipients over time these results may be less valid.<sup>58</sup> In this study, we sought to provide an updated comparison of the costs of living and deceased donor kidney transplantation, as well as to identify predictors of total two year costs.

## **5.3 METHODS**

### ***5.3.1 Settings and Patients***

The Research Ethics Board at the University of Calgary approved the study.

The Southern Alberta Transplant program provides care to all patients seeking a transplant or wishing to donate in the southern part of the province of Alberta through a single location in Calgary, Alberta (catchment population 1.5 million). The transplant program offers living related, living unrelated, and deceased donor kidney transplant, and also offers kidney-pancreas transplantation for eligible type 1 diabetes patients. The electronic clinical database for the Southern Alberta Transplant Program (ALTRA) was used to identify patients for this study, including all patients  $\geq 18$  years old who were recipients of a first kidney only transplant between April 1, 1998, and March 31, 2006 in the Southern Alberta Transplant program, as well as their corresponding donors. Recipients of kidney/pancreas transplant were excluded.

### ***5.3.2 Data Collection & Sources***

Data for recipients and donors was obtained from three separate data sources: ALTRA, which collects data for the Southern Alberta Transplant Program, Alberta Health and Wellness (AHW), the provincial provider of health care, and the Calgary Health Region (CHR) corporate database which includes detailed costing data for all encounters within the local health region. Direct costs for the recipient were collected for five distinct periods: pre-transplant, transplant, post-transplant to 90 days, remainder of year 1, and year 2 after transplantation. Follow-up for living donors ceased at 90 days as most living donors return to work within 6 weeks of donation.<sup>111</sup>

Demographic information and clinical transplant data, as well as medication use, laboratory tests and pre-transplant diagnostic imaging were obtained from ALTRA (section 5.6). Other health resource utilization data, including outpatient services (day surgery, ambulatory care and emergency department visits), diagnostic imaging, hospitalizations and physician services, were obtained from AHW, using methodology described in section 5.6. AHW captures patient specific health care resource utilization for all Albertans. All permanent residents of Alberta are eligible for insurance by AHW, and greater than 99.9% participate in this coverage. Information and costs on the transplantation procedure for both recipients and donors was collected from the CHR (sections 5.6 & 5.7). For potential and actual living donors, the cost of the workup was determined as per protocol from the Southern Alberta Transplant program (section 5.8). The cost of home care and capital costs were not included in this study.



All costs were inflated to and reported in 2008 Canadian dollars (1CAN\$ = 0.91US\$), using the Consumer Price Index (Statistics Canada).

### *5.3.3 Measuring Costs*

This study took the perspective of the health care payer, and included only direct health care-related costs. Societal costs, time costs and other patient transport costs were excluded as information on patients' activities prior to or after hospital discharge were not available.

In the Canadian healthcare system, provincial governments are the sole payers for hospitalizations and physician services for hospitalized patients. Money is provided to health regions to pay for costs of hospitalization, whereas physician services are billed directly to the government and paid to individual physicians. The health care costs reported in this study reflect the true costs of care, rather than prices, as closely as can be approximated.

The total cost of transplantation for recipients was determined by including the relevant recipient and donor and costs. If a deceased donor had two kidneys recovered and transplanted, costs were halved to determine the total cost per recipient. If a recipient's donor was not included in the cohort (not all recipient-donor pairs were available), then the mean cost for the type of kidney transplanted was imputed. This was the case for 41 recipients of living donors and 77 recipients of deceased donors.

#### *5.3.4 Censoring Costs*

As the primary objective of this study was to determine whether there was a difference in total two year costs between recipients of living and deceased donors, patients with a failed graft during the study remained in the analysis. Recipients who moved out of province were assigned the mean cost for that time period.

#### *5.3.5 Statistical Analysis*

The primary study hypothesis was that there would be no difference in the total cost of care, after 24 months, for patients receiving either a living or a deceased donor kidney. We used descriptive statistics including the mean and 95% confidence intervals (CIs) for normally distributed data and median with interquartile ranges for skewed variables. The Kruskal-Wallis test was used to compare differences between highly skewed variables.

Multiple linear regression was performed for the total two year cost of care for recipients (excluding the cost of the donor), considering the following potential predictor variables: age, sex, waiting time for a transplant, diabetes, last panel reactive antibody (PRA) dichotomized as 0 or 1 if non-zero, number of HLA matches, and type of transplant, since these predictors may be related to graft survival, re-hospitalizations, or infections and hence costs.<sup>59, 112</sup> Manual backward stepwise elimination of the least significant variable was performed. Interaction and confounding were assessed for by considering age and waiting time for a transplant, as well as age and diabetes as potential effect modifiers. Normal plots of residuals of the regression models were examined to test for constant variance.

We initially used multiple linear regression to examine the association between the total two year cost of the recipient and the predictor variables previously noted. Given that total costs were not normally distributed, and the residuals were positively skewed, inferences about the statistical significance of the regression coefficients became questionable.<sup>113</sup> As such, we also assessed predictors of two year costs using linear regression of log-transformed total costs.

## **5.4 RESULTS**

### ***5.4.1 Patients***

Four hundred and seventy-five patients received a first kidney only transplant between April 1, 1998 and March 31, 2006. Of these, 47 were simultaneous kidney/pancreas transplants, 44 were re-transplants, 13 had no costs available from the Calgary Health Region, and 14 did not have a valid personal health number for linkage with the provincial database. Of the 357 patients, 130 received a living donor kidney and 227 received a deceased donor kidney. Over the study period, 13 patients died, and 5 patients moved out of the province, as such, no further costing information was available.

### ***5.4.2 Baseline Characteristics***

Baseline demographic and clinical characteristics are presented in Table 5.1. The mean age at transplant was 47.6 years in all patients, and 58.0% were male. The most frequent cause of end-stage renal disease among all patients was glomerulonephritis, which is consistent with national data.<sup>94</sup> The mean wait time on the transplant list during this

period for a deceased donor was 2.5 years and less than 1 year for recipients of a living donor. Recipients of a deceased donor spent a mean of 3.2 years on dialysis, compared with recipients of living donors who spent 1.2 years on dialysis prior to transplantation. The mean age of donors at time of donation was 42.1 and 39.6 years, for living and deceased donors respectively. Less than half (40.5%) of living donors were male and 71.9% of the donors were related to the recipient. Among deceased donors, 56.6% were male, and the primary cause of death among deceased donors was trauma outside of a motor vehicle collision (41.4%).

#### ***5.4.3 Recipient Outcomes***

Recipient outcomes during the 2-year period are presented in Table 5.2. Delayed graft function was reported for 31 of the 357 patients (8.7%), and was higher in recipients of deceased donors (11.0%). Twenty-four patients experienced an acute rejection episode (ARE) during the primary hospitalization, and 60 patients experienced an ARE during the remainder of year 1. During year 2, 23 patients experienced an ARE. The incidence of ARE was similar for recipients of living and deceased donors. During the first year, 53 patients had at least one CMV infection, and 8 patients had more than one infection during the study period.

Graft failure occurred in 13 patients in year 1 (9 patients during the primary hospitalization and 4 patients in the remainder of year 1), while only 5 graft failures occurred in year 2, for a 2-year graft survival rate of 95.0%. A total of 13 patients (3.6%)

died with a functioning graft, with the majority of these patients being recipients of a deceased donor kidney.

#### **5.4.4 Costs**

##### 5.4.4.1 Donor Costs

Excluding the cost of transplant surgery, the mean work up cost for living donors (including both potential and actual living donors) was \$2,261 and \$209 for recipients who ultimately received a kidney from a living or deceased donor, respectively (Table 5.3). Not all recipients of a deceased donor had a living donor evaluated (mean of 0.35), whereas recipients of a living donor had a mean of 1.8 donors evaluated.

For living donors proceeding to surgery, the mean cost of care for the donor, including physician and surgery costs, was \$18,129. Living donors had an average length of stay of 6 days for the transplantation and 52 patients (58.4%) had an open nephrectomy. The mean cost of the inpatient stay for patients of open nephrectomy was \$13,022, whereas for those who had surgery with the hand assisted technique had a mean cost of surgery of \$19,008 ( $p=0.001$ ). The mean cost of care from discharge of transplant to 90 days follow-up for living donors (including any inpatient hospitalizations, outpatient care, diagnostic imaging and physician visits) was \$598. Only 2 patients were re-hospitalized during the follow-up, with a mean hospital length of stay of 4.5 days. The mean cost of care for deceased donors was \$36,989, and 95 (96.0%) had two kidneys subsequently transplanted.

#### 5.4.4.2 Recipient Costs

There was no difference in the mean cost for all recipients, including donor costs, for recipients of living and deceased donors (\$118,347 and \$121,121, respectively,  $p=0.7$ ) (Table 5.3). Excluding donor costs, there was still no difference in the mean cost for recipients of living and deceased donors ( $p=0.5$ )

Figure 5.1 displays the resource utilization by time period and transplant type. For recipients of deceased donors, the largest proportion of costs in year 1 was attributable to inpatient stays (including the transplantation); in year 2, medications consume the largest proportion of resources. For recipients of living donors, in both year 1 and 2 the largest proportion of resource utilization is for outpatient medications.

Overall mean costs for different recipient subgroups for year 1 and year 2 are presented in Figures 5.2-A and 5.2-B respectively. Recipients with the highest costs in year 1 were those that returned to dialysis (mean overall cost \$127,496) and recipients with diabetes who received a deceased donor kidney (mean overall cost (\$96,541). Similarly, for year 2, those who returned to dialysis had higher costs (mean overall cost \$49,278).

#### ***5.4.5 Predictors of Costs***

The results of each modeling approach are summarized in Table 5.4. The regression diagnostics of the model using log-transformed costs were more favorable than the linear regression model using untransformed cost data, with the distribution of the residuals approximately normal and little evidence of heteroscedasticity. Therefore, we focus on

discussion of the linear regression model with log-transformed costs, which demonstrated that waiting time, diabetes and last PRA were associated with total two year costs.

Interpretation of this model found that every additional year on the wait list is associated with an approximate 5% increase in costs. Further, having diabetes and having a non-zero PRA was associated with an increase in total two year costs of 14% and 21%, respectively.

Of note, in a separate regression model we also considered CMV mismatch and donor age as predictors to total transplant costs, in addition to the other predictors included above, for the 207 recipients for which this data was available. Using backward elimination, these two predictors were eliminated and the model reduced to the predictors identified in the primary analysis, with waiting time, diabetes and last PRA associated with total two year costs.

## **5.5 DISCUSSION**

We provide a high quality, comprehensive and contemporary estimate of the direct costs of kidney transplantation in Canada, including a detailed description of the cost of living and deceased donor transplantation. Our study demonstrated that recipients who receive a living donor kidney transplant experience similar costs compared to those who receive a deceased donor kidney transplant. Since our analysis includes the cost of procurement and workup of all potential living donors, this finding, in and of itself, is important.

The lack of a costing difference between recipients of living and deceased donor kidneys at two years is not surprising, as procurement of a kidney from a live donor is a resource intensive medical intervention, and deceased donors provide two kidneys in most instances (therefore this cost can be spread over two recipients). Given superior long term graft survival for LD transplants, it is possible that the mean costs associated with living kidney donor transplantation might become lower than deceased donor transplant over time. It is notable that the cost of transplantation in the first year (including pre-transplant costs for recipients and donors) is higher than the annual cost of in-centre hemodialysis, \$89,713.03,<sup>114</sup> though the cost of transplantation in the second year is less than a quarter of the annual cost of hemodialysis, and does not differ for living and deceased donors. This difference in costs highlights the need to continue to encourage transplantation as a treatment option for ESRD.

It is difficult to put this study in the context of the few other studies available as costing methodologies, resources costed and the manner in which costs were determined vary greatly. A Canadian study that previously compared the cost of living and deceased donor transplantation noted that recipients of living donor kidneys had higher costs, though it is not known whether the difference was significant.<sup>6</sup> Two separate studies in the US that examined Medicare charges found that recipients of living donors had less total costs than recipients of deceased donors.<sup>56,57</sup> They focused, however, only on the post-transplant period, excluding both pre-transplant and organ acquisition costs.



We found that costs over the total two year period post-transplant for the recipient were not affected by age at transplant, gender, total HLA matches or type of transplant (living versus deceased). Predictors of total two years costs in recipients included the time spent on the waiting list, diabetes, and a non-zero last PRA value. Other studies have found that recipients with diabetes had greater mean hospital charges and mortality post-transplant than non-diabetics.<sup>59</sup> We found that patients with diabetes receiving a solitary kidney transplant (and not combined kidney-pancreas transplantation) were associated with an increase in total two year costs of 14%. The significance of HLA matching predicting graft survival and costs in the literature have differed for recipients of living and deceased donors<sup>112, 115</sup>, and it is possible our study was underpowered or did not have enough follow-up time to detect cost differences based on HLA matching.

Our study has a number of strengths including the use of a comprehensive administrative dataset including costing data for all patients, follow-up of failed grafts as well as successful transplant recipients, prospective measurement of resource use and the costing of donors in addition to recipients.

Our study also has limitations. First, we only had information on direct medical costs, and did not have a measure of non-medical costs, such as time, travel costs, or time off work for recipients or donors, though it is unlikely that this would differ for recipients of living or deceased donor kidneys. Second, for deceased donors other organs and tissues could have been recovered and donated, thereby distributing the cost of transplantation

over several other recipients. In Canada, at least four organs are used from more than half of deceased donors.<sup>116</sup> For the purpose of this analysis, we examined kidneys in an isolated context to be able to make direct comparisons with living donation. Finally, while the generalizability of health care costs from one country to another is important to consider<sup>117</sup>, relative differences between types of kidney transplants are likely valid and these estimates can be used by decision makers in all countries to advocate for living kidney donation.

In conclusion, our study provides up-to-date estimates of the cost of kidney transplantation in North America using contemporary treatments. Over a two year period, the cost of kidney transplantation did not differ for recipients of living and deceased donor transplant. The results of this study will inform policymakers and allow health programs to better allocate resources. Further, the cost estimates provided herein can be used to inform future cost-effectiveness studies in ESRD.

## 5.6 Recipient costing information

Resource utilization category	Time period	Data source	Comments
Medications	Pre-transplant		Not considered
	Post-transplant	ALTRA	All outpatient immunosuppressants and anti-infective medications with frequency, dosage and the duration of medication abstracted from ALTRA. The total daily dose was then multiplied by the unit cost to determine a cost per patient. All medication costs were determined from the Alberta Pharmaceutical Price List 2009, summed to give a total cost per patient. For each medication, a dispensing fee of \$20.94 was added for every three month period the medication was prescribed, as per Alberta Health and Wellness policy.
Laboratory tests	Pre-transplant & post-transplant	ALTRA	All serum and urine laboratory tests that were ordered by the transplant program for each patient, both pre and post transplant, were included. The frequency of each test was multiplied by a unit cost based on a defined workload measurement unit. <sup>118</sup>
Diagnostic imaging	Pre-transplant	ALTRA	Each test recorded in the transplant database (included based on its relevance to transplant eligibility) and was multiplied by the unit costs assigned based on a defined workload measurement unit using similar methods to previous studies. <sup>119</sup>
	Post-transplant	AHW	Post-transplant, the cost of diagnostic imaging services was determined for all outpatient diagnostic imaging tests including allocated radiologist fees for applicable services. <sup>118</sup>
Transplant surgery	Transplant surgery only	CHR	Acquired from the Calgary Health Region corporate database. Resource use was broken down into seven categories: nursing, laboratory, diagnostic, surgical, surgical supplies, medications, and support staff. In-patient costing was calculated using a provincially approved method in accordance with the Provincial and National Management Information Systems guidelines. <sup>120, 121</sup> Resource use (ie, number of medications, laboratory tests, or consumables used; nursing care hours allocated per patient based on a recorded workload measurement unit (WLM)) was measured for all patients. <sup>82</sup> The number of units used by each patient was then multiplied by the cost per unit, which is estimated annually in the CHR, to give an estimate of direct costs. Direct costs were then combined with the estimate of indirect costs (defined as costs not directly associated with patient care, ie, cost of nursing managers, administration) for every in-patient encounter. The quality of data reporting of costs in Alberta has been highly ranked by the Canadian Institutes for Health Information. <sup>122</sup>

Inpatient stays (excluding transplant surgery)	Post-transplant	AHW	Since subsequent hospitalizations could occur inside or outside of the Calgary Health Region, information on all subsequent hospital admissions post transplant for recipients (whether the admission was for reasons related or unrelated to the transplant), including cost, was obtained from Alberta Health and Wellness, using case-mix grouper (CMG) methodology. When possible, Alberta-specific CMGs were used <sup>123</sup> . The quality of data reporting of costs in Alberta has been highly ranked by the Canadian Institutes for Health Information. <sup>122</sup>
Outpatient services	Pre-transplant		Not captured
	Post-transplant	AHW	The number and costs of outpatient visits to the emergency room and day surgery unit was determined using procedure and most responsible diagnostic codes. Dialysis costs, for those patients who returned to dialysis, are tracked using this database.
Physician claims	Pre-transplant	Estimate	Estimated as per the ALTRA standard of care: one nephrology consult per year while on the waiting list, one surgery consult per patient and for patients who had a thallium test or a coronary angiogram as part of their transplant workup, a cardiology consult was included. The costs of these visits were based on standard fees paid by AHW.
	Transplant surgery & post-transplant	AHW	Determined from AHW. All claims were included.

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## 5.7 Donor costing information

Resource utilization category	Time period	Data source	Comments
Medications			Not captured
Laboratory tests			Not captured
Diagnostic imaging	Post-transplant (living donors only)	AHW	Post-transplant, the cost of outpatient diagnostic imaging services was determined by examining actual patient resource consumption based on functional centre codes and allocated radiologist fees for applicable services.
Care for donor	Pre-transplant	CHR	Cost of care for the deceased donor included their entire intensive care unit stay and was determined by microcosting methodology. <sup>118</sup>
Transplant surgery	Transplant surgery (living and deceased donors)	CHR	As per transplant surgery for recipients (Appendix 1)
Inpatient stays (excluding transplant surgery)	Post-transplant (living donors only)	AHW	As per hospitalization for recipients (Appendix 1)
Outpatient services	Post-transplant (living donors only)	AHW	The number and costs of outpatient visits to the emergency room and day surgery unit was determined using procedure and most responsible diagnostic codes. <sup>118</sup>
Physician fees	Transplant surgery & post-transplant (living donors)	AHW	Determined from AHW. All claims were included until follow-up period ended.
	Transplant surgery (deceased donors)	Estimate	Estimated as a surgical fee and an anesthesiologist fee, based on standard fees paid by AHW.

### 5.8 Living donor workup costs

Living donor workup costs were protocol-costed, as per the standard of care by the Southern Alberta transplant program, by determining the number of potential and actual donors attained for each stage per recipient.

<b>Stage</b>	<b>Tests</b>
<b>Stage A</b>	ABO typing
<b>Stage B</b>	Laboratory tests, as determined per protocol
<b>Stage C</b>	Clinic visit
<b>Stage D</b>	Clinic visit + nuclear medicine scan
<b>Stage E</b>	Magnetic resonance imaging + angiogram and/or computed tomography
<b>Stage F</b>	Decision by transplant committee (no cost)
<b>Stage G</b>	Donation

**TABLE 5.1 Baseline characteristics of recipients**

Characteristic	All recipients	Recipients of	Recipients of DD
	<i>n = 357</i>	LD kidney <i>n = 130</i>	kidney <i>n = 227</i>
Age at transplant in years, mean (SD)	47.6 (13.3)	44.7 (13.7)	49.3 (12.8)
Male sex (%)	207 (58.0)	79 (60.1)	128 (56.4)
Caucasian (%)*	236 (70.2)	96 (82.8)	140 (63.6)
Dialysis (%)*	313 (87.7)	100 (76.9)	213 (93.8)
Modality (%)			
Hemodialysis	217 (69.6)	62 (62.6)	155 (72.8)
Peritoneal dialysis	95 (30.5)	37 (37.4)	58 (27.2)
Duration of dialysis,			
Pre-emptive	44 (12.3)	30 (23.1)	14 (6.2)
0 – 12 months	71 (19.9)	45 (34.6)	26 (11.5)
> 12 months	242 (67.8)	55 (42.3)	187 (82.4)
Comorbid conditions (%)			
Hypertension	325 (91.0)	119 (91.5)	206 (90.7)
Diabetes	73 (20.4)	33 (25.4)	40 (17.6)
Cigarette smoking	94 (26.3)	32 (24.6)	62 (27.3)
Hyperlipidemia	91 (25.5)	37 (28.5)	54 (23.8)
Cardiac disease	51 (14.3)	17 (13.1)	34 (15.0)
Cause of end-stage renal disease (%)			
Glomerulonephritis	140 (39.2)	48 (36.9)	92 (40.5)
Diabetes mellitus	59 (16.5)	29 (22.3)	30 (13.2)
Polycystic kidney disease	41 (11.5)	10 (7.7)	31 (13.7)
Hypertensive	20 (5.6)	3 (2.3)	17 (7.5)
Reflux	23 (6.4)	9 (6.9)	14 (6.2)
Other	74 (20.7)	31 (23.9)	43 (18.9)
Wait time on transplant list, years (mean, SD)	2.0 (1.7)	0.96 (0.97)	2.5 (1.9)
Cold ischemic time, hours (mean, SD)*	8.9 (7.4)	0.9 (0.2)	13.6 (5.4)
Last PRA, non-zero (%)	29 (8.1)	4 (3.1)	25 (11.0)
Total HLA matches (median, IQR)	1 (1 - 3)	3 (1 - 3)	1 (0 - 2)

\* data not available for all patients

**TABLE 5.2 Recipient outcomes**

<b>Outcome</b>	<b>All recipients n=357</b>	<b>Recipients of LD kidney n=130</b>	<b>Recipients of DD kidney n=227</b>
Length of stay transplant, median (IQR)	8 (7-12)	7 (6-10)	8 (7-12)
Delayed graft function	31 (8.7)	6 (4.6)	25 (11.0)
Any acute rejection event			
Transplantation	24 (6.7) <sup>e</sup>	8 (6.2) <sup>f</sup>	16 (7.0) <sup>g</sup>
Remainder of year 1	60 (16.9)	21 (16.2)	39 (17.3)
Year 2	23 (6.6)	8 (6.2)	15 (6.9)
Any CMV infection			
Transplantation	0	0	0
Remainder of year 1	53 (14.8)	20 (15.4)	33 (14.6)
Year 2	2 (0.6)	0	2 (0.9)
Graft failure*			
Transplantation	9 (2.5)	5 (3.8)	4 (1.8)
Remainder of year 1	4 (1.1)	1 (0.8)	3 (1.3)
Year 2	5 (1.4)	1 (0.8)	4 (1.8)
Death			
Transplantation	1 (0.3)	0	1 (0.4)
Remainder of year 1	7 (2.0)	1 (0.8)	6 (2.7)
Year 2	5 (1.4)	0	5 (2.3)

Results are presented as N (%). Percent values are percentage of population alive and in province at the start of the related follow-up period.

\*Graft failure does not include recipients who died with a functioning graft

<sup>e</sup> primary hospitalization, n=357; remainder of year 1, n=356; remainder of year 2, n=347

<sup>f</sup> primary hospitalization, n=130; remainder of year 1, n=130; remainder of year 2, n=129

<sup>g</sup> primary hospitalization, n=227, remainder of year 1, n=226; remainder of year 2, n=218



**TABLE 5.3 Overview of costs by category, kidney donor type and time period**

	<b>Recipients of living donor kidney</b>	<b>Recipients of deceased donor kidney</b>
<b>Donors</b>		
<b>Pre-transplant workup for all living donors</b>	2,261	209
Mean (95% CI)	(2,096-2,425)	(122-296)
<b>Donor graft removal+</b>	18,129	36,989
Mean (95% CI)	(16,845-19,414)	(34,421-39,558)
<b>Donor follow-up to 90 days</b>	598	N/A
Mean (95% CI)	(322-873)	
<b>Recipient</b>		
<b>Pre-transplant workup</b>	2,370	2,917
Mean (95% CI)	(2,139-2,600)	(2,657-3,178)
<b>Transplantation</b>	20,108	23,818
Mean (95% CI)	(18,108-22,108)	(20,666-26,971)
<b>Post-transplant to 3 months</b>	31,618	28,200
Mean (95% CI)	(27,078-36,157)	(25,582-30,818)
<b>3 – 12 months</b>	21,932	25,903
Mean (95% CI)	(19,178-24,686)	(23,387-28,420)
<b>12 – 24 months</b>	19,974	22,233
Mean (95% CI)	(17,880-22,067)	(20,128-24,338)
<b>TOTAL</b>	<b>118,347</b>	<b>121,121*</b>
Mean (95% CI)	<b>(110,395-126,299)</b>	<b>(114,287-127,956)</b>

+ for deceased donors, this includes the ICU stay and was subsequently divided in two if the donor gave two kidneys when determining the total cost

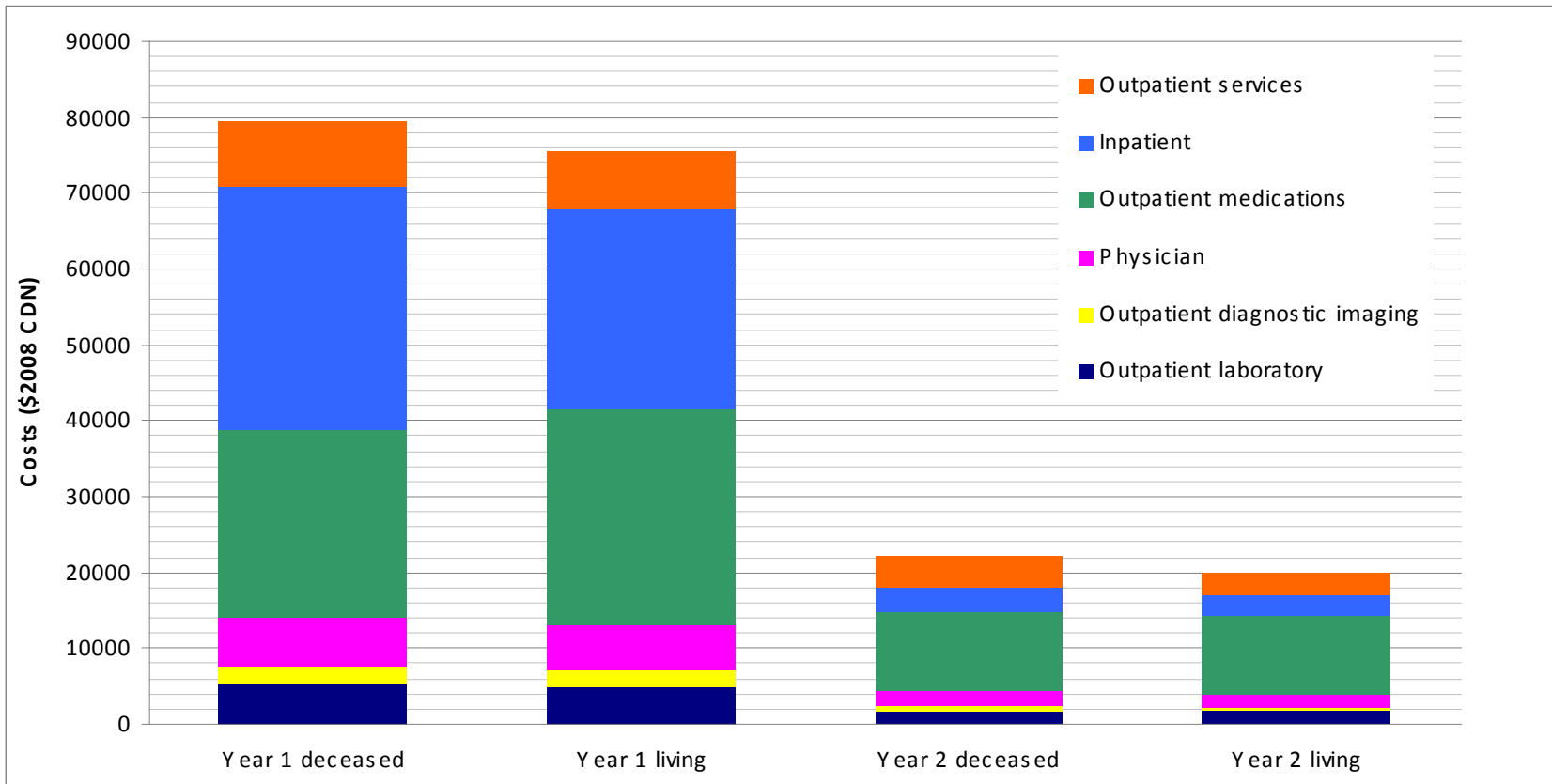
\* p = 0.7107

**TABLE 5.4 Multiple linear regression and log-transformed multiple linear regression of total two year recipient costs<sup>8</sup>**

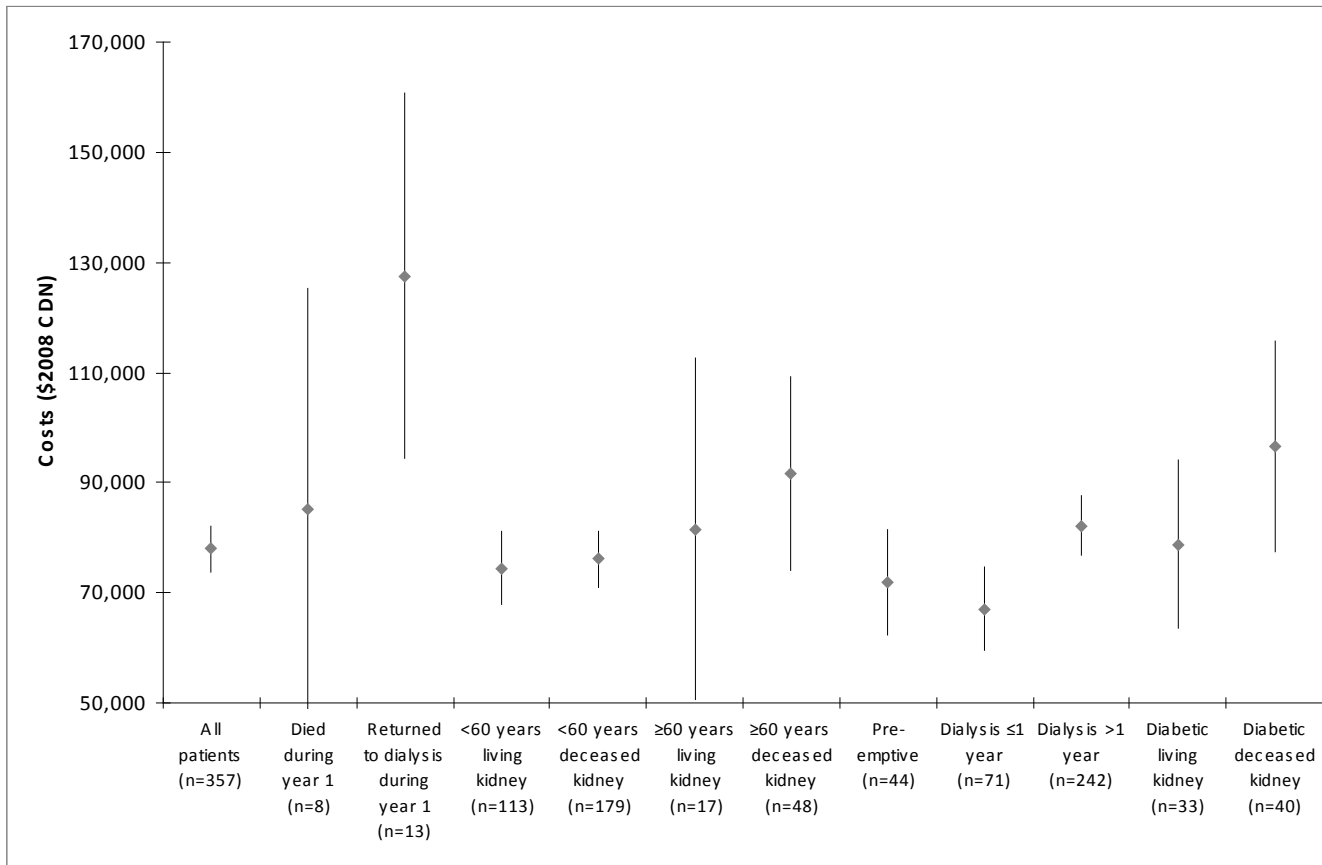
<b>Dependent Variable</b>	<b>Constant (<i>p</i> value)</b>	<b>Wait time (in years) <math>\beta</math> Coefficient (<i>p</i> value)</b>	<b>Diabetes <math>\beta</math> Coefficient (<i>p</i> value)</b>	<b>Last PRA <math>\beta</math> Coefficient (<i>p</i> value)</b>
Linear regression, total cost, in \$	87,683.4 <sup>9</sup>	5,358.03	15,196.31	32,320.45
Log-transformed regression, log total cost, log\$	11.290 (0.000)	0.0538 (0.000)	0.142 (0.012)	0.212 (0.017)

<sup>8</sup> Variables eligible for inclusion in the stepwise regression included age at transplant, gender, wait time on transplant list, diabetes, last PRA (dichotomized as 0 or 1 if non-zero), total HLA matches, and type of transplant

<sup>9</sup> Given the non-normal distribution of the residuals , *p* values are not provided

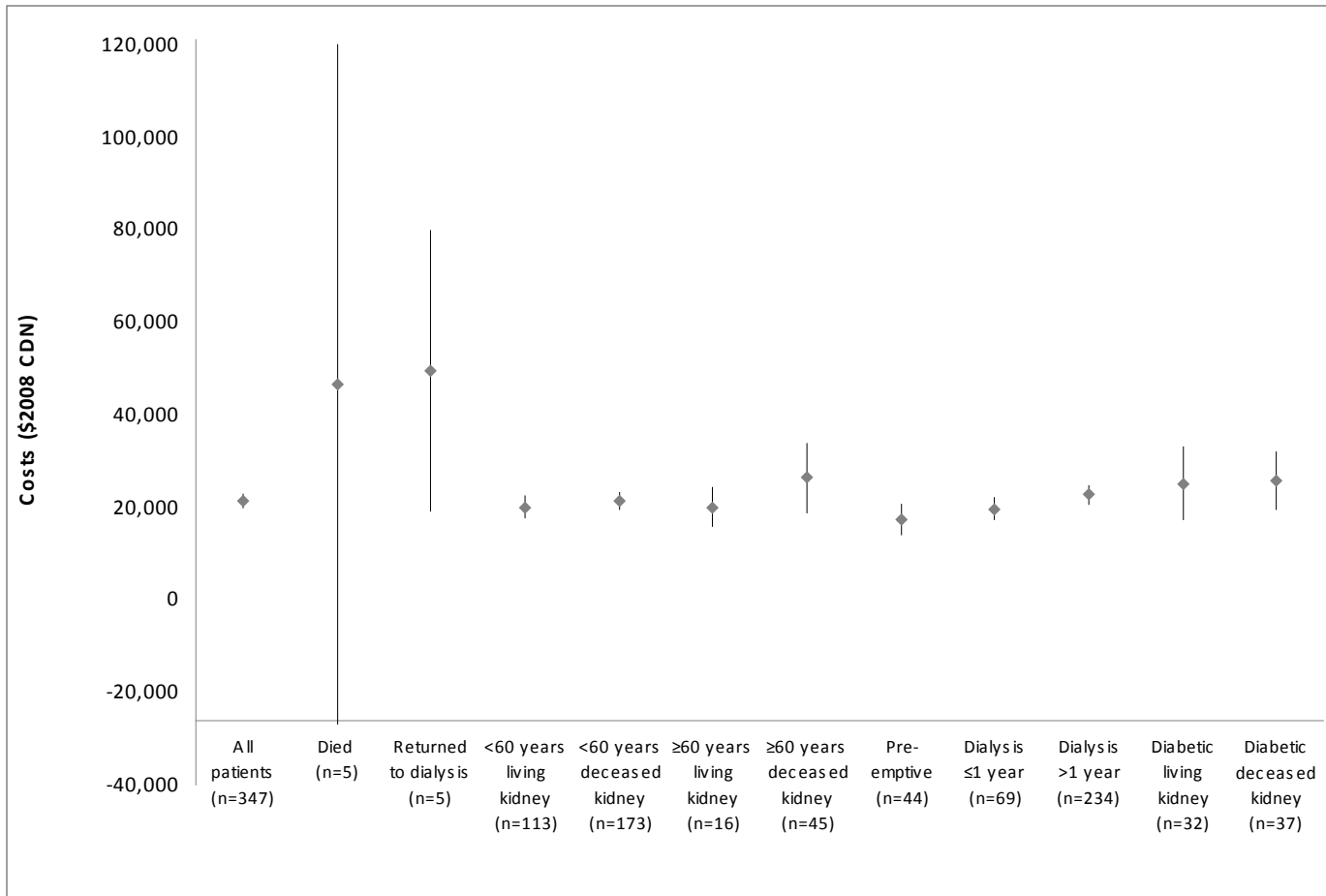


**FIGURE 5.1 Mean costs for resource utilization by time period and transplant type (2008 \$CDN)**



**FIGURE 5.2 Mean cost of resource utilization year 1 (A) and year 2 (B) for different recipient subgroups (2008 \$CDN)**

**A. Mean costs (2008 \$CDN) from the index transplantation to 365 days (year 1), with 95% confidence intervals, for different recipient subgroups**



**B. Mean costs (2008 \$CDN) for 366 – 730 days (year 2), with 95% confidence intervals, for different recipient subgroups**

**CHAPTER SIX: SUMMARY**

## 6.1 Increasing the Pursuit of Living Donation

Nearly 60% of kidneys for transplantation come from a deceased donor. This suggests that a recipient who has end-stage renal disease is more likely to wait for a deceased donor kidney for up to five years, than pursue living donation. Though some potential recipients may not have family or friends to donate a kidney, or the family and friends they have are not a match, this lack of pursuit of a superior treatment option that provides many clinical benefits, is still surprising. The purpose of this thesis was to further explore outstanding issues in living kidney transplantation, specifically whether education in eligible candidates can increase the pursuit of living donation and to determine, if any, differences in costs for recipients of living and deceased donor kidneys.

Prior research has been done exploring barriers in donors for living donation,<sup>36, 48, 63-65, 124, 125</sup> though much of the findings have shown that donors support living donation and that they do not regret their decision to donate.<sup>22, 36</sup> Research as to why potential KTx candidates do or do not pursue living donation has also been undertaken and suggests that candidates who support living donation were more likely to understand risks and benefits to recipients and donors.<sup>38, 39</sup> Reported barriers in candidates can include feelings of guilt, feeling indebted to the donor, financial concerns for the donor, and suffering of the donor.<sup>36-38, 40-43</sup>

Our survey to identify barriers to living kidney donation among eligible recipients found that the most prevalent barrier in knowledge about living donation was how to ask a family member or friend for their kidney. Further, knowing the risks to the living donor

and knowing how and why to begin the living donation process was associated with having discussed living donation with a family member or friend. Though other barriers were identified, such as feelings of guilt or fear for both the donor and the operation itself, these were not significantly related to having discussed living donation with a family member or friend in our study.

The barriers identified from our study informed the structure of the education intervention for our randomized controlled trial, providing information on short and long term risks to the living donor, why living donation is a superior treatment option to deceased donation and how to contact the living donor program and initiate the process. During the education session, a transplant nephrologists and a nurse also modeled one example of how to ask a loved one for a kidney. Despite our well-formed intervention, and due to lack of study power to detect a difference, we found that the education sessions in combination with written material did not increase the number of potential donors contacting the program on behalf of a transplant candidate. However, there was a significant increase in the number of patients who ranked living donation as their treatment preference at study completion within the education intervention group. We interpreted this as a positive sign that despite the lack of significance between the two groups for having a living donor contact the program, a recipient's choice for their own preferred treatment increased from before to after the intervention.



To assess increasing the pursuit of living donation among kidney transplant candidates we developed and validated a survey to assess barrier, administered this survey to evaluate these barriers, and used the results of the questionnaire to develop an education intervention. Our studies had limitations. The questionnaire administered to assess barriers was not translated into other languages. As well, the questionnaire was cross-sectional in design, assessing the different barriers in candidates at a single point in time and irrespective of the individual's course in the transplant evaluation and wait time process. Further, we included patients who were not on dialysis, though they were eligible for a transplant candidate. Patients who haven't started a form of renal replacement therapy may view transplantation and living donation differently from those already on hemodialysis. As a patient's decision to pursue living donation may change over time, barriers in their treatment course may change over time, and the effectiveness of the education intervention (which was based on the questionnaire results) may also change over time in reflection of this. Regarding the randomized controlled trial, our study was underpowered since enrollment ended early due to slower recruitment than we had anticipated, and lower baseline event rates than expected. We also had higher drop out rate than the 10% estimated, though this in itself is informative as an education intervention in this format may not be feasible if 30% of the patients choose not to attend.

In summary we were able to successfully identify potential barriers to living donor transplantation and design an educational intervention to address these barriers. Future

studies adequately powered to evaluate whether educational interventions of this nature are effective in increasing living donor transplantation are required.

## **6.2 Analyzing Costs in Living and Deceased Donor Transplantation**

Few studies have systematically analyzed costs of kidney transplantation.<sup>6, 9, 10, 20, 56, 57, 108-</sup>

<sup>110</sup> The most widely quoted and methodologically rigorous costing study examining living and deceased donor kidney transplantation is a Canadian study, which is now almost 20 years old.<sup>6</sup> We did a high quality, comprehensive and contemporary analysis of direct costs of living and deceased donor transplantation. We found that recipients who receive a living donor kidney transplant experience similar costs compared with recipients of a deceased donor kidney transplant. Given the superior clinical outcomes of living donation, this lack of difference in costs highlights the need to continue to encourage living donation as a treatment option for ESRD.

Our study had limitations. We only assessed direct medical costs, as measures for non-medical costs were not available. Deceased donors often have other organs and tissues recovered for donation, which would distribute the cost of transplantation over several other recipients. We did not adjust for this and examined the cost of kidney transplantation in an isolated context. Further, we included all ICU costs for the deceased donor, not just those costs relevant to donor management. This may have overestimated the cost of care of the deceased donor. We also did not include pre-transplant dialysis costs. The inclusion of these costs would have differed for recipients of living and deceased donors, given their differential wait times for transplantation, however, our

purpose was to examine costs differences in the transplantation itself. Finally, the generalizability of these results to other countries may be limited, however, given that relative differences between the types of kidney transplants are likely valid, the costing estimates above are likely to hold across a variety of health care systems.

In summary we provided a comprehensive, current estimate on the cost of kidney transplantation in a North American setting, using contemporary treatments. When examined over two years, the cost of kidney transplantation did not differ for recipients of living and deceased kidney donors. These cost estimates can be used to inform future cost-effectiveness studies in the area of ESRD.

### **6.3 Implications for Practice and Future Directions**

Lack of knowledge has been identified as a potential barrier to increasing living kidney donation. Opportunities for providing this information and passive learning should be not be overlooked by physicians in charge of care of patients' with end-stage renal disease. For example communicating treatment options as early as possible may help plant the seed about living donation and may spur recipient's to discuss this option with their family or friends. Informing and acknowledging to a candidate that discussing kidney transplantation with a potential donor can be difficult may be enough for them to seek help on this subject area.

Further work examining barriers to living donation in kidney transplant candidates is required. Knowing whether the decision to pursue living donation precedes seeking

information regarding the treatment or whether patients first obtain information about all their treatment options, then make a treatment decision, would be useful to inform programs on how to educate candidates for transplantation. Future studies assessing the effect of education on pursuing living donation should incorporate a longer follow-up than the 3 month interval utilized in our study. In addition, consideration should be given to providing education about living donation as a treatment option earlier in the course of a patient's kidney disease treatment process. Identifying when a patient makes their decision about their preferred treatment may be critical to timing the intervention. The manner in which information is delivered should also be examined. Some patients may prefer to learn with others, whereas others may not be as mobile and may prefer something in the comfort of their own home.

The assessment of indirect medical costs, for both living donors and recipients of living and deceased donors, is required to further inform transplantation programs. These indirect costs, such as time, travel costs or time off work, could potentially affect the pursuit of transplantation, and living donation in particular. Reimbursement of costs for living donors has recently been instituted in the province of Alberta. The impact of such reimbursement on rates of donation should be also be examined, as health programs are continually seeking to better allocate resources. Given that treatment strategies and management of donors has changed over time, an examination of costs over time may be useful to determine where the greatest utilization of resources is currently occurring, and how best to maximize the effectiveness of those treatments.

#### **6.4 Conclusions**

There is a large pool of potential living donors, as two-thirds of candidates in our study stated that they had family or friends who could potentially donate. Strategies to increase the pursuit of living donation should continue to be examined as living donation has not only been established as a treatment with superior clinical outcomes, it has costs which are similar to deceased donor transplantation.

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